HYSEQ INC
Form S-4
November 27, 2002

Table of Contents

As filed with the Securities and Exchange Commission on November 26, 2002

Registration No. 333-

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form S-4

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

Hyseq, Inc.

(Exact name of registrant as specified in its charter)

Nevada	**2835**	**363855489**
(State or other jurisdiction of incorporation or organization)	*(Primary Standard Industrial Classification Code Number)*	*(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.	**Joseph S. Mohr**	**Lewis J. Geffen, Esq.**
Latham & Watkins	**President and Chief Business Officer**	**Andrew J. Merken, Esq.**
135 Commonwealth Drive	**Variagenics, Inc.**	**Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.**
Menlo Park, California 94025	**60 Hampshire Street**	**One Financial Center**
(650) 328-4600	**Cambridge, Massachusetts 02139**	**Boston, Massachusetts 02111**
	(617) 588-5300	**(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. o

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. o

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. o

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price Per Share	Proposed Maximum Aggregate Offering Price(2)	Amount of Registration Fee
Common Stock, par value $0.001 per share, and associated preferred share purchase rights(3)	46,602,586	N/A	$37,109,833.27	$3,414.15

(1) This registration statement covers the maximum number of shares of Hyseq common stock to be issued in connection with the merger described within this registration statement, calculated as the product obtained by multiplying (a) the exchange ratio of 1.6451 shares of Hyseq common stock for each share of Variagenics common stock by (b) the sum of (i) the aggregate number of shares of Variagenics common stock outstanding on November 20, 2002 (other than shares owned by the registrant or any of its subsidiaries) and (ii) the aggregate number of shares of Variagenics common stock issuable pursuant to outstanding options and warrants that are exercisable and under Variagenics Employee Stock Purchase Plan prior to the date the merger is expected to be completed.

(2) Estimated solely for purposes of calculating the registration fee pursuant to Rules 457(f) and 457(c) under the Securities Act of 1933, based on (i) $1.31, the average of the high and low prices of Variagenics common stock, as reported on the Nasdaq National Market on November 22, 2002, and (ii) the maximum number of shares of Variagenics common stock computed as described in footnote (1) above.

(3) The preferred share purchase rights, which are attached to the shares of Hyseq common stock being registered hereunder, will be issued for no additional consideration. Accordingly, no additional registration fee is payable.

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.

Table of Contents

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 November 26, 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 million shares of Hyseq common stock in the merger and that immediately after the merger Variagenics stockholders will hold approximately 64% of the then-outstanding shares of Hyseq common stock, based on the number of shares of Hyseq and Variagenics common stock outstanding on , 2002. Hyseq common stock is traded on the Nasdaq National Market under the trading symbol HYSQ. On , 2002, Hyseq common stock closed at $ 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:

For Variagenics stockholders:

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
President and Chief Executive Officer
Hyseq, Inc.

Sincerely,

JOSEPH S. MOHR
President and Chief Business Officer
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 , 2002, and is first being mailed to Hyseq and Variagenics stockholders on or about , 2002.

Table of Contents

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

To the Stockholders of Hyseq, Inc.:

NOTICE IS HEREBY GIVEN that a Special Meeting of Stockholders of Hyseq, Inc. will be held on at , local time, at 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 , 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

, 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.

Table of Contents

VARIAGENICS, INC.

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

To the Stockholders of Variagenics, Inc.:

NOTICE IS HEREBY GIVEN that a Special Meeting of Stockholders of Variagenics, Inc. will be held on at , local time, at 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 , 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

, 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.

Table of Contents

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 169.

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 , 2002.

TABLE OF CONTENTS

Table of Contents

TABLE OF CONTENTS

Table of Contents

Table of Contents

Table of Contents

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 64% 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 , 2002, Hyseq and Variagenics estimate that Hyseq will issue approximately 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 , California, on , 2003, at .m., local time.

The Variagenics special meeting will take place at , Massachusetts, on , 2003 at .m., local time.

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

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 , 2002, the record date for the special meeting of Hyseq stockholders, directors and executive officers of Hyseq beneficially owning shares of Hyseq common stock, representing approximately % of the outstanding shares of Hyseq common stock, have

Table of Contents

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 , 2002, the record date for the special meeting of Variagenics stockholders, directors and executive officers of Variagenics beneficially owning shares of Variagenics common stock, representing approximately % 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 149.

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 152.

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.

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?

A:

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

Table of Contents

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:

U.S. Stock Transfer Corporation
1745 Gardena Avenue
Glendale, California 91204
(818) 502-1404

if you are a Variagenics stockholder:

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

Table of Contents

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 alfimeprase, 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 and Hyseq anticipates changing its name to . 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 149 and 152)

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

Table of Contents

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 149 and 152)

Hyseq Stockholders

You can vote at the Hyseq special meeting if you owned Hyseq common stock at the close of business on , 2002, the record date for the Hyseq special meeting. On that date, there were 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 , 2002, the record date for the Variagenics special meeting. On that date, there were 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 73)

Hyseq

Hyseq has entered into a stockholder voting agreement with certain directors and 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 shares of Variagenics common stock, representing approximately % 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 shares of Hyseq common stock, representing approximately % 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 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.

Variagenics

On November 8, 2002, SG Cowen Securities Corporation, financial advisor to Variagenics, delivered to the Variagenics board of directors its oral

Table of Contents

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

Hyseq expects to issue approximately million shares of Hyseq common stock in the merger. Based on the number of shares of Hyseq and Variagenics common stock outstanding on , 2002, after completion of the merger, former Variagenics stockholders will own approximately 64% 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 shares of Hyseq common stock, collectively representing approximately % of the 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 executive officers of Variagenics and their affiliates beneficially owned and were entitled to vote approximately shares of Variagenics common stock, collectively representing approximately % percent of the shares of Variagenics common stock outstanding on that date.

Interests of Certain Persons 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.

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 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.

Appraisal Rights (see page 62)

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

3

Table of Contents

Conditions to Completion of the Merger (see page 68)

In order to complete the merger Hyseq and Variagenics must satisfy the conditions described on pages , 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 Nasdaq.

No Solicitation by Variagenics or Hyseq
(see page 65)

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 69)

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 .

Termination Fees and Expenses (see page 70)

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 page 70).

Variagenics Stock Options and Warrants;
Variagenics Employee Stock Purchase Plan
(see pages 60 and 61)

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 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 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

Table of Contents

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.

Table of Contents

(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.

(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.

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 November 22, 2002)	1.90	0.88	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 , 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 $, the closing price of Variagenics common stock on the Nasdaq National Market was $ 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 $ 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.

Table of Contents

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 Varigenics 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 39,655,461 shares of Hyseq common stock will be issued to Variagenics stockholders, and former Variagenics stockholders will own approximately 64% of the combined company. The issuance of approximately 39,655,461 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.

Table of Contents

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;

Table of Contents

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 Certain Persons 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

Table of Contents

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 November 22, 2002, the high and low closing sales price of Hyseq common stock as reported by the Nasdaq National Market was $9.00 and $0.88, respectively, and as of November 12, 2002, Hyseq common stock began closing below $1.00. As of September 30, 2002, Hyseq had stockholders equity of $11.7 million. If the price of Hyseq common stock remains below $1.00 per share, 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.

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 SBH 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, 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;

Table of Contents

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;

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;

Table of Contents

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.

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 polymorpohisms 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.

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

Table of Contents

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 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

Table of Contents

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.

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

Table of Contents

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;

fines;

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.

Table of Contents

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.

Table of Contents

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

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.

Table of Contents

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.

Hyseq has implemented anti-takeover provisions that may reduce the market price of the Hyseq 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 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 Hyseq s shares. As a consequence, they also may inhibit fluctuations in the market price of Hyseq s shares that could result from actual or rumored takeover attempts. Such provisions also may have the effect of preventing changes in Hyseq 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 Hyseq common stock are 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 Hyseq s current 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 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 Hyseq 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

Table of Contents

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 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 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 Hyseq common stock at a premium over market price; and

generally deter efforts to obtain control of Hyseq.

Table of Contents

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-l 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.

Table of Contents

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 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.

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.

Table of Contents

Shortly thereafter, in March 2002, Mr. Vogelbaum contacted Dr. Love to place discussions on hold. In May 2002, Mr. Vogelbaum contacted Dr. Love to reinitiate 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 the potential sale of 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 reinitiated 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

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.

Table of Contents

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

Table of Contents

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.

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 alfimeprase, 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;

the combined company is anticipated to have sufficient financial resources to fund operations though 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;

Table of Contents

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;

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 64% 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;

Table of Contents

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 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 alfimeprase, 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;

Table of Contents

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 alfimeprase, 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 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;

Table of Contents

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 alfimeprase 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 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.

Table of Contents

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 alfimeprase 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 alfimeprase 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 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.

Table of Contents

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 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;

Table of Contents

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.

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

Table of Contents

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 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.

Table of Contents

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		
	Hyseq	Variagenics	Implied Exchange Ratio
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.

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.

Table of Contents

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 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.

Table of Contents

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;

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;

Table of Contents

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 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

Table of Contents

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 64% 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

Table of Contents

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.
- Genaissance 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.

Table of Contents

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:

	High	Median	Mean	Low	Value Implied by Exchange Ratio
			($ 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

Table of Contents

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:

	High	Median	Mean	Low	Value Implied by Exchange Ratio
			($ 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 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	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 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	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

Table of Contents

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.

Table of Contents

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

Table of Contents

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.

51

Table of Contents

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.

Table of Contents

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 will 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

Table of Contents

final purchase price allocation. The purchase 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.

Table of Contents

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 on page .

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.

Table of Contents

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 executive officers of Variagenics beneficially own shares of Variagenics common stock, and accordingly are eligible to receive a maximum aggregate of $ or shares of Hyseq common stock in the merger. In addition, as of the record date, these board members and executive officers hold options to acquire shares of Variagenics common stock, with exercise prices ranging from $ to $ per share, which will be assumed by Hyseq and be converted into options to acquire shares of Hyseq

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;
- 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
- approved by the Board of Directors to amend 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.

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;

Table of Contents

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 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.

Table of Contents

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 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.

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.

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.

Table of Contents

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. Promptly thereafter, Variagenics will be merged upstream into Hyseq and Hyseq will change its legal name to .

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 Hyseq common stock, in a number determined by multiplying the number of Variagenics shares that were

60

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 of the Variagenics certificate is entitled, together with any cash which may be payable instead of fractional

Table of Contents

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.

Table of Contents

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

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.

Table of Contents

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;

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

Table of Contents

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;

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.

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.

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

Table of Contents

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;
- 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

Table of Contents

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 merger 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 merger 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.

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;

Table of Contents

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, 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

Table of Contents

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

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.

Table of Contents

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.

Table of Contents

STOCKHOLDER VOTING AGREEMENTS

The following summary describes certain material provisions of the stockholder voting agreements, the form of which is attached to this joint proxy statement/ prospectus as Annex B and is incorporated by reference into this joint proxy statement/prospectus. This summary may not contain all of the information about the stockholder voting agreement that is important to you. Hyseq and Variagenics encourage you to read the stockholder voting agreement carefully in its 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 officers who hold an aggregate of shares of Variagenics common stock or approximately % of the outstanding Variagenics common stock as of the record date and (ii) all of Hyseq s directors and officers holding an aggregate of shares of Hyseq common stock or approximately % 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 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.

Table of Contents

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 currently estimated, the fair value of the net assets acquired exceeds the estimated purchase price. As a result, the estimated fair values of certain long term-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 will be recorded as an extraordinary gain in Hyseq s statement of operations upon consummation of the merger. The extraordinary gain has been excluded from the pro forma condensed combining statements of operations due to its non-recurring nature. 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 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.

Table of Contents

Pro Forma Condensed Combining Statement of Operations For the Nine Months Ended 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)
Loss before minority interest	(28,580)	(26,200)	1,512	(53,268)
Loss attributable to minority interest	112			112
Net loss	$(28,468)	$(26,200)	$ 1,512	$(53,156)
Basic and diluted net loss per share	$ (1.34)	$ (1.11)		$ (0.88)
Weighted average shares used in computing basic and diluted net loss per share	21,197	23,688		60,166

See accompanying notes to unaudited pro forma condensed combining financial statements.

Table of Contents

Pro Forma Condensed Combining Statement of Operations For the Year Ended December 31, 2001

(In thousands, except per share data)

(unaudited)

	Historical		Pro Forma	
	Hyseq	Variagenics	Adjustments	Combined
Revenues:				
Product sales	$	$ 210	$	$ 210
Contract revenues and other	24,590	2,773		27,363
Total revenues	24,590	2,983		27,573
Operating expenses:				
Cost of product sales		186		186
Research and development	46,506	19,868	(1,397)(E)	64,977
General and administrative	13,452	12,449	(439)(E)	25,462
Restructuring and related charges	825			825
Total operating expenses	60,783	32,503	(1,836)	91,450
Loss from operations	(36,193)	(29,520)	1,836	(63,877)
Interest income	319	4,465		4,784
Interest expense	(891)	(248)		(1,139)
Loss before minority interest	(36,765)	(25,303)	1,836	(60,232)
Loss attributable to minority interest	293			293
Net loss	$(36,472)	$(25,303)	$ 1,836	$(59,939)
Basic and diluted net loss per share	$ (2.26)	$ (1.09)		$ (1.10)
Weighted average shares used in computing basic and diluted net loss per share	16,158	23,295		54,480

See accompanying notes to unaudited pro forma condensed combining financial statements.

Table of Contents

Pro Forma Condensed Combining Balance Sheet as of September 30, 2002

(In thousands)

(unaudited)

	As of September 30, 2002			
	Historical		Pro Forma	
	Hyseq	Variagenics	Adjustments	Combined
ASSETS				
Current assets:				
Cash and cash equivalents	$ 4,272	$ 32,594	$	$ 36,866
Short-term marketable securities		23,104		23,104
Accrued contract revenue	4,743			4,743
Other current assets	2,998	2,457		5,455
Total current assets	12,013	58,155		70,168
Equipment, leasehold improvements and capitalized software, net	16,357	5,531	(5,531)(A)	16,357
Long-term marketable securities		5,085		5,085
Restricted cash	1,106	750		1,856
Other noncurrent assets	2,667	109	(109)(A)	2,667
Total assets	$ 32,143	$ 69,630	$ (5,640)	$ 96,133
LIABILITIES AND STOCKHOLDERS EQUITY				
Current liabilities:				
Accounts payable	$ 2,425	$ 1,213	$ 3,900(B)	$ 7,538
Line of credit	4,000			4,000
Current portion of capital lease and loan obligations	1,510	2,136		3,646
Other current liabilities	7,229	2,350		9,579
Total current liabilities	15,164	5,699	3,900	24,763
Noncurrent portion of capital lease and loan obligations	1,289	1,348		2,637
Note Payable	4,000			4,000
Total liabilities	20,453	7,047	3,900	31,400
Minority interest				
Commitments and contingencies				
Stockholders equity:				
Preferred stock, par value				
Common stock, par value	23	241	(241)(C) 40(D)	63
Additional paid-in capital	148,547	169,847	(169,847)(C) 49,450(D)	197,997
Deferred stock compensation	(18)	(3,183)	3,183(C) (686)(D)	(704)
Accumulated deficit	(136,862)	(104,198)	104,198(C) 4,239(D)	(132,623)
Promissory note from scientific advisor		(118)	118(C)	

Less treasury stock		(6)	6(C)	
Total stockholders equity	11,690	62,583	(9,540)	64,733
Total liabilities and stockholders equity	$ 32,143	$ 69,630	$ (5,640)	$ 96,133

See accompanying notes to unaudited pro forma condensed combining financial statements.

Table of Contents

Notes to Unaudited Pro forma Condensed Combining Financial Statements

1. Basis of Presentation

On November 9, 2002, Hyseq and Variagenics entered into a merger agreement whereby each outstanding share of Variagenics common stock will be exchanged for 1.6451 shares of Hyseq common stock. The merger is expected to qualify as a reorganization within the meaning of Section 368(a) of the Internal Revenue Code.

As of September 30, 2002, there were approximately 24,105,198 shares of Variagenics common stock outstanding and approximately 3,371,288 Variagenics shares issuable upon exercise of outstanding options. Based upon these amounts and the terms outlined above, if the merger had been consummated on September 30, 2002, Variagenics shareholders would have received a total of approximately 39,655,461 shares of Hyseq common stock, and holders of Variagenics options would have received options to purchase approximately 5,546,106 shares of Hyseq common stock, under which the right to purchase approximately 3,161,913 shares of Hyseq common stock would have been fully vested and immediately exercisable. The exact number of shares to be issued and options assumed will depend upon the number of related Variagenics shares and options, respectively, outstanding at the closing of the merger.

2. Preliminary Purchase Price-Variagenics

In determining the Variagenics purchase price, Hyseq used the estimated value of Hyseq common stock of approximately $1.16 per share based upon the average closing price of Hyseq common stock the two trading days before the merger announcement and the two trading days after the merger announcement.

The preliminary fair value of Hyseq s stock options to be issued was determined using the Black-Scholes option pricing model. The following assumptions were used to determine the fair value of the options: expected life of 2.35 years, risk-free interest rate of 3.85%, expected volatility of 0.9247 and no expected dividend yield.

The final purchase price is dependent on the actual number of shares of common stock exchanged, the actual number of options issued, and actual transaction costs. The final purchase price will be determined upon completion of the merger.

The total estimated purchase price of the proposed Variagenics merger is as follows (in thousands):

Value of Hyseq common stock to be issued	$46,001
Value of Hyseq options to be issued(1)	2,803
Estimated transaction costs	1,400
Total estimated purchase price	$50,204

The preliminary allocation of the aggregate purchase price to the tangible assets acquired and liabilities assumed in connection with this acquisition was based upon estimated fair values as determined by management. The preliminary purchase price allocation is summarized below (in thousands):

Tangible assets acquired	$63,990
Unallocated negative goodwill Extraordinary gain	(4,239)
Liabilities assumed	(9,547)
Total estimated purchase price	$50,204

As the estimated fair value of the net assets acquired exceeds the estimated purchase price, the estimated fair values of certain long lived assets were reduced to zero for purchase accounting purposes. After such a

(1) Net of $686 representing the portion of the intrinsic value of Variagenics unvested options applicable to the remaining vesting period.

Table of Contents

reduction in values and in accordance with SFAS No. 141, Business Combinations, estimated remaining negative goodwill of approximately $4.2 million will be recorded as an extraordinary gain in Hyseq s statement of operations upon consummation of the merger. The extraordinary gain has been excluded from the pro forma statements of operations due to its non-recurring nature.

The allocation of the purchase price is preliminary. The purchase 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 combining financial statements.

3. Pro Forma Adjustments

The accompanying unaudited pro forma combined financial statements have been prepared as if the merger was completed on September 30, 2002 for balance sheet purposes and as of January 1, 2001 and January 1, 2002, respectively, for statement of operations purposes and reflect the following pro forma adjustments:

(A) To reduce the carrying value of Variagenics long-lived assets to zero due to the estimated fair value of the acquired net assets exceeding the estimated purchase price. The estimated extraordinary gain of $4.2 million, as a result of remaining negative goodwill, has been excluded from the proforma statements of operations due to its non-recurring nature.

(B) Accrual of transaction related costs, $1.4 million for Hyseq and $2.5 million for Variagenics.

(C) Elimination of Variagenics stockholder equity accounts.

(D) Issuance of Hyseq common stock, $0.001 par value, as discussed above, and to record deferred compensation of $686 related to unvested options.

(E) Elimination of Variagenics historical depreciation expense associated with the carrying value of the long-term assets that were reduced to zero due to estimated fair value of the acquired net assets exceeding the estimated purchase price.

4. Items Not Adjusted

The pro forma adjustments do not reflect any integration adjustments such as restructuring costs to be incurred in connection with the merger or operating efficiencies and cost savings that may be achieved with respect to the combined entity.

5. Common Shares Outstanding

The number of pro forma common shares outstanding after giving effect to the merger for purposes of the pro forma September 30, 2002 balance sheet are (in thousands):

Hyseq s common shares outstanding at September 30, 2002	23,035,854
Increase in common shares attributable to conversion of Variagenics stock (24,105,198 x 1.6451)	39,655,461
Total pro forma common shares outstanding	62,691,315

Table of Contents

6. Pro Forma Combined Net Loss Per Share

The pro forma combined net loss per share attributable to common stockholders, basic and diluted, is computed as follows:

	Nine Months Ended September 30, 2002	Year Ended December 31, 2001
	(In thousands, except per share information)	
Pro forma net loss attributable to common stockholders	$(53,156)	$(59,939)
Weighted average shares used in computing net loss per share attributable to Hyseq common stockholders, basic and diluted	21,197	16,158
Pro forma adjustments:		
Effect of assumed conversion of Variagenics common stock	38,969	38,322
Weighted average shares used in computing pro forma net loss per share attributable to common stockholders of the combined company, basic and diluted	60,166	54,480
Pro forma net loss per share attributable to common stockholders, basic and diluted	$ (0.88)	$ (1.10)

Table of Contents

INFORMATION ABOUT HYSEQ

Business of Hyseq

Company Overview

Hyseq was incorporated in Illinois in August 1992 and reincorporated as a Nevada corporation on November 12, 1993. Hyseq has been doing business as Hyseq Pharmaceuticals, Inc. since October 2001. Hyseq is 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. These product candidates target several markets, including cardiovascular disease and oncology. Hyseq intends to develop and commercialize these types of product candidates on its own or in collaboration with other biotechnology or pharmaceutical companies.

Hyseq believes its signature-by-hybridization platform, which is related to its proprietary sequencing-by-hybridization (or SBH) technology, gives it a significant advantage in discovering novel, rarely-expressed genes. Hyseq believes it possesses one of the most important proprietary databases of full-length human gene sequences and has the potential to develop a significant pipeline of product candidates for research and development. Previously, Hyseq s activities have focused primarily on full-length gene sequencing, patenting, bioinformatics, cloning, and early stage research activities to prioritize potential therapeutic protein candidates. As of November 15, 2002, Hyseq had filed patent applications on approximately 10,000 predicted full-length human gene sequences, and had issued 17 gene-related patents. Hyseq is accelerating its research activities to elucidate the role of novel genes in its proprietary database, their encoded proteins and corresponding antibodies. Hyseq s database includes chemokines, growth factors, stem cell factors, interferons, integrins, hormones, receptors and other potential protein therapeutics or drug targets. Hyseq s focused bioinformatics and screening capabilities have significantly enhanced its understanding of the biological activity of these genes and their corresponding proteins, enabling it to file strategic patent applications that encompass both composition of matter and method of use claims.

Hyseq is primarily focused on discovering and developing therapeutic protein-based products, as it believes that naturally occurring therapeutic proteins have several commercial advantages over small molecule drugs.

In the near term, Hyseq is balancing the risks in developing therapeutics from its full-length gene database by also focusing on an early stage clinical product candidate acquired through collaboration with Amgen, Inc. Hyseq entered into this collaboration in January 2002, with the goal of developing and commercializing alfimeprase, a thrombolytic enzyme, for the treatment of peripheral arterial occlusion (or PAO) and other cardiovascular indications. Pre-clinical studies suggest that alfimeprase is a promising agent for dissolving blood clots (clot lysis) and may be well suited for the PAO indication. In June 2002, Hyseq initiated Phase I clinical trials in a multi-center, open-label, dose-escalation study to evaluate alfimeprase s safety and pharmacokinetics, to be conducted in 20 patients across approximately eight centers in the United States.

Scientific and Industry Background

Genes are the hereditary units that control the structure, health and function of all organisms. The study of genes and their functions has led to the development of products and services for diverse markets, ranging from health care to agriculture. Genomics, the study of all the genetic information of an organism, is a growing field that is expected to lead to the development of additional gene-based therapeutics. The large market potential for gene-based products has led to a worldwide effort to sequence the human genome in the search for new proteins and drug targets for the treatment of disease and unmet medical needs.

The complete set of genetic information of each organism, known as its genome, is encoded in its deoxyribonucleic acid (or DNA). DNA, which is found in the nucleus of cells, is a molecule comprising two complementary strands entwined in the form of a double helix. Various combinations of four chemical

building blocks or bases of DNA, adenine (A), thymine (T), cytosine (C) and guanine (G), are linked together in series to form each DNA strand. The bases of one DNA strand bind to the bases of the other strand in a specific fashion to form base pairs: A pairs with T and G pairs with C. In humans, there are approximately six billion base pairs organized into 23 pairs of DNA structures called chromosomes.

With the development of automated, high throughput DNA sequencing techniques in the early 1990s, researchers accelerated the discovery of novel genes and the proteins they express. Companies in the private sector, as well as publicly-funded research efforts, initiated large-scale activities to create databases of DNA sequence information that could be used to search for important new proteins or drug targets. Early commercial efforts focused on identification of expressed sequence tags, or ESTs, which are short DNA sequences that represent a portion of an expressed gene. At the same time, the U.S. government-funded Human Genome Project, in competition with other national governments and privately funded efforts, set about sequencing the entire human genome. The science of bioinformatics has arisen out of the need to analyze and derive value from this vast quantity of DNA sequence data. Bioinformatics involves the use of high-powered computers, software and analytical tools to interpret, compare and analyze DNA sequence data and can be used to assist in identifying those genes and proteins that are likely to play a meaningful role in human health. In addition to using bioinformatics to screen DNA sequence databases for medically relevant genes, researchers can use bioinformatics to infer important information about a newly discovered gene from its DNA sequence. Drawing on information about previously known genes, researchers can perform comparative analyses with newly discovered genes to obtain insight into their potential functions. Although bioinformatics represents a fundamental advance in the analysis of DNA sequence data, significant challenges remain in discovering how genes and proteins affect human biology and disease.

Prior to the development of robust large DNA sequence databases and the requisite analytical software needed to facilitate bioinformatics analyses, the discovery and development of therapeutic proteins typically involved an intense focus on biological processes of the human body or the pathology of disease. Researchers would study a particular biological process or disease and try to understand the underlying molecular mechanisms that could lead to the identification of potential therapeutic products. This time- and labor-intensive process yielded relatively few newly identified therapeutic protein product candidates. The introduction of methods for rapid DNA sequencing and bioinformatics in the early 1990s enabled an alternative approach to therapeutic protein discovery. Rather than study the biology of an organism or disease to discover a new therapeutic protein, a number of companies directed their efforts to discovering new proteins through bioinformatics and then studying the biology of these newly discovered proteins to determine whether they have therapeutic applications. Hyseq believes that over time this approach has the potential to yield a substantial number of therapeutic candidates, and ultimately approved products, faster and at lower cost than the traditional biology-only driven approach.

Genes that encode proteins are composed of two principal types of information: the primary coding sequence that dictates the composition of the protein as well as additional regulatory sequences that control the actual expression of a gene. The process by which the coding sequence of a gene directs the production of a protein begins with a process in which the gene is copied into a related molecule called messenger ribonucleic acid (or mRNA). The mRNA is used as a template to combine amino acids together in a particular order to form a protein. The regulatory region of a gene is responsible for determining the rate of production of mRNA copies, which can therefore directly affect the amount of the protein product that is produced by the cell. Additional factors besides mRNA abundance can affect the levels of proteins in a cell, and proteins themselves can be modified to affect their biochemical activities. The addition, deletion or substitution of one or more bases in a gene, known as a mutation, can alter the resultant protein s structure and/or level of expression and result in a disease. Most diseases are believed to be polygenic, meaning that the activities of multiple genes interact to cause the disease. In developing a drug for treatment of a polygenic disease, the most effective strategy may be best selected when all genes that interact to cause or affect the disease are known.

Therapeutic proteins include naturally occurring proteins that are administered to patients as drugs. Some naturally occurring proteins replace or supplement a protein that is deficient in the body or defective. Others signal the body to initiate or cease a biological function. Examples of therapeutic proteins include ligands

Table of Contents

such as insulin, which regulates glucose metabolism for the treatment of diabetes, and enzymes such as tissue plasminogen activator, which converts plasminogen to plasmin, a protein that can break down blood clots. Other therapeutic protein-based drugs, although not naturally occurring, have been engineered to provide medical benefit. Examples include monoclonal antibodies such as Herceptin, which targets and destroys breast cancer cells, and soluble receptors such as Enbrel, which binds to and thereby blocks the effect of a ligand implicated in rheumatoid arthritis. Therapeutic proteins and other protein-based products represent a promising class of drugs in the biotechnology industry.

The use of recombinant DNA technology to manufacture therapeutic proteins has been a major breakthrough for the pharmaceutical industry. Recombinant DNA technology is used to insert a gene into non-human production cells. These cells, which are grown in culture, are engineered to produce the desired protein in large quantities. The protein is then isolated from the culture and purified. Recombinant proteins have several advantages over proteins derived from natural sources, such as human or animal pooled blood. First, recombinant DNA technology enables the large-scale production of certain therapeutic proteins that are scarce and thus too difficult or costly to derive from human or animal sources in therapeutically useful quantities. Second, recombinant DNA technology significantly reduces the contamination risks from blood-borne pathogens that cause diseases. Finally, recombinant DNA technology allows the production of therapeutic proteins using reproducible methodologies. This reproducibility in manufacturing provides for consistency between batches of the final protein product, a necessity for creating a safe drug capable of receiving regulatory approval.

Strategy

Hyseq s execution strategy will involve a combination of carefully-staged internal infrastructure growth, strategic relationships to share research and development efforts and marketing opportunities with other biotechnology and pharmaceutical companies, inlicensing product candidates and outsourcing, on a fee-for-service basis, to accelerate and expand its drug discovery and development efforts. Hyseq s goal is to build a fully integrated biopharmaceutical company that commercializes novel therapeutic proteins and other protein-based products derived from its proprietary portfolio of protein candidates. The first part of Hyseq s strategy involves internal infrastructure growth to expand its staff and bring additional expertise into the company. Hyseq s early efforts have been focused on gene discovery, which requires a research staff of molecular biologists and bioinformatics personnel. As Hyseq continues to characterize the genes in its database, it has expanded its research and development staff to include additional expertise in basic biology, physiology, cell biology and protein sciences. Further progress into development will require additional expertise in project management and product development including pharmacology, toxicology, assay development, formulation and process development, medical and regulatory affairs, quality control and quality assurance and an expanded capability in facilities and engineering. Expertise in these areas will be required to ensure that Hyseq meets FDA and foreign regulatory requirements for conducting clinical trials.

The second part of Hyseq s strategy is to focus on the discovery of therapeutic proteins. Hyseq is pursuing a focused strategy to identify the subset of genes that it believes have the highest probability of coding for proteins with therapeutic potential. Specifically, Hyseq is focusing on key protein categories that have members with demonstrated therapeutic potential or medically relevant biological activity. Hyseq is currently utilizing a number of methods to help define the utility of these genes. Once Hyseq has identified a protein candidate with relevant biological activity, it will seek to develop a therapeutic protein directly, or, where appropriate, develop a monoclonal antibody or soluble receptor that targets the protein.

The third part of Hyseq s strategy involves strategic relationships to share research and development efforts and marketing opportunities with other biotechnology and pharmaceutical companies. Hyseq believes this approach will greatly enhance its chances to move a number of drug candidates into clinical trials over the next several years. Hyseq is now focusing on new corporate relationships with other biotechnology and pharmaceutical companies to share costs and expertise of identifying and developing product candidates. This focus also includes plans to collaborate with strategic partners with expertise to develop antibodies and small molecules from Hyseq s proprietary targets.

Table of Contents

The fourth part of Hyseq s strategy involves outsourcing, on a fee-for-service basis, to accelerate and expand its drug discovery and development efforts. Initially, Hyseq intends to use outsourcing while it expands its in-house capabilities, although it expects to continue to use outsourcing when there are opportunities to accelerate and expand its drug discovery and development efforts. Hyseq currently uses contract research organizations and collaborators to supplement its ability to conduct in vitro and in vivo testing of its therapeutic protein candidates. Hyseq also intends to use contract organizations to conduct good laboratory practices (GLP) toxicology and other studies required for filing an Investigational New Drug (IND) application, for the production of any current good manufacturing practices, or cGMP, drug and for conducting clinical trials on its lead therapeutic protein candidates.

Hyseq s strategy also encompasses pursuing comprehensive intellectual property protection. Hyseq seeks to establish patent priority for its gene and protein discoveries at the earliest possible time. Hyseq uses data generated from bioinformatics and exploratory biology to enhance its patent applications.

Because Hyseq expects to generate more product candidates than it has the capacity to develop on its own in the near term, it is pursuing a commercialization strategy with multiple options. Hyseq intends to internally develop and commercialize some product candidates where it believes the clinical trials and sales force requirements are manageable. Hyseq intends to partner with other companies to co-develop and co-promote product candidates in cases where it does not have access to the infrastructure required for development and commercialization. Finally, Hyseq intends to out-license other product candidates and intellectual property that do not fit within its future commercial focus.

Hyseq intends to develop its own manufacturing capabilities in the future, but in the near term it expects to use third-party manufacturers. Hyseq has initiated the design phase for a pilot manufacturing plant, which it intends to use as a source of clinical product supply. Hyseq plans to subsequently develop larger-scale commercial manufacturing facilities as its products progress through clinical development.

Research and Development

Hyseq has discovered a large collection of novel genes with its signature-by-hybridization platform. Since 1997 Hyseq has used its signature-by-hybridization platform to discover genes expressed in a large number of complementary DNA (or cDNA) libraries derived from specific human cells and tissues. These cDNA libraries are spotted onto replica filters which are then hybridized independently with short, distinct DNA probes. After repeated probing, each cDNA develops a characteristic hybridization signature that can be used to group similar clones into clusters. By sequencing only representative cDNAs from each cluster, Hyseq has allowed for an efficient and thorough analysis of all genes expressed in any library. Using bioinformatics and biological screening methods, gene sequences are analyzed to select molecules for pre-clinical testing. In addition, the use of EST data together with genomic sequence data affords Hyseq the opportunity to identify those rare genes that otherwise might go undetected using only EST databases. Genes that are expressed only at low levels are typically underrepresented in or absent from public EST databases. These rarely expressed genes may have potent biological activities with clinical utility.

Hyseq conducts high-throughput gene sequence analysis using advanced informatics tools and protein structure modeling techniques to identify candidate genes for biological screening. In general, most candidates are grouped into the broad categories of potential protein therapeutics and small molecule or antibody targets. Hyseq believes genes with sequence characteristics and motifs similar to those found in known secreted proteins are more likely to be useful as protein therapeutics and those with characteristics of membrane or intracellular proteins are more likely to serve as targets for antibodies and small molecules. Hyseq s focus has been on development of molecules that it believes will result in protein therapeutics. Hyseq plans to pursue targets for antibodies and small molecules through strategic relationships.

Hyseq uses a diverse set of tools to evaluate the biological functions of the genes and proteins it discovers. In Hyseq s collaboration with Kirin Brewery Company, Ltd., it conducts screens in which the gene of interest has been introduced into genetically modified mice (transgenic mice) such that the encoded human protein is expressed in the adult animal. Through Hyseq s collaboration with Deltagen Inc., it can identify the function of its genes by developing knockout mice, in which the corresponding mouse gene has been

Table of Contents

inactivated by genetic manipulation. Hyseq uses dozens of independent assays to investigate the biological and biochemical activities of its novel proteins. To obtain additional information, Hyseq s scientists have adapted or created in vivo laboratory models that mimic human diseases to determine the cause of disease and response to treatment. For certain ligands, Hyseq clones the receptors for the ligand present in a tissue or cell. In addition to providing a marker for tissues that should respond to the protein, the receptors themselves can have therapeutic potential. Hyseq also relies on an external network of collaborators to investigate biology and conduct additional tests that it does not perform in-house.

Within Hyseq s exploratory biology operation, it applies a variety of methods by which it can identify a protein s function, determine whether the protein plays a role in disease, assess its commercial potential, and obtain information about dosing and systemic effects of the product candidate. Assuming positive results, both in terms of efficacy and toxicology, Hyseq may develop a commercial hypothesis for the product candidate. A commercial hypothesis requires the identification of a market opportunity and a preliminary determination that it will be economically feasible to manufacture the product candidate and administer it to patients.

The process of selecting and evaluating drug candidates involves a broad range of skills and a highly trained scientific staff. Following the initial gene assessment by Hyseq s bioinformatics group, full-length genes are obtained, expressed, and screened for biological activity by its cloning and cell screening groups. Once activities have been identified, additional experiments are performed to support the development of a biological hypothesis that describes the protein s function. The protein candidate next moves to the validation stage, in which more directed and focused experiments are performed to confirm the biological activity and to establish a medical hypothesis. Molecules showing biological activity and molecules with sequence or structural homology to known proteins are further evaluated by Hyseq s functional genomics group. Hyseq s protein production and purification group is responsible for providing larger quantities of selected proteins for further in vitro and in vivo testing. These tests are conducted by Hyseq s functional genomics group, working in conjunction with contract research organizations and university collaborators. Throughout this process, information is provided to Hyseq s legal group to pursue patent protection for its candidates. In cases where a protein demonstrates beneficial biological effects, it becomes a product candidate. If a protein has been found to have detrimental effects, Hyseq will focus on generating a monoclonal antibody or soluble receptor to inhibit the activity of the protein. In those cases, a resulting monoclonal antibody or soluble receptor will be the product candidate. Once a product candidate is identified, it moves to the pre-clinical stage, at which time it is tested in specific animal models of diseases for safety and pharmacokinetic analysis. Following initial safety and pharmacokinetic analysis, the pre-clinical safety and efficacy group will be responsible for working with contract research organizations to conduct GLP toxicology and other studies required for filing an IND. Until adequate staff and facilities are established in-house, Hyseq plans to use contract organizations for the production of cGMP drug and for conducting clinical trials on its lead therapeutic protein candidates.

Alfimeprase: Product Candidate for Clot Lysis

Alfimeprase is a thrombolytic agent, that is, it dissolves blood clots. Developed by Amgen, Inc., it is a novel recombinant form of fibrolase, a naturally occurring enzyme. Unlike plasminogen activators, alfimeprase can directly and rapidly degrade the network of fibrin protein that captures red blood cells to form blood clots. The first target medical indication is Peripheral Arterial Occlusion (or PAO). In PAO, a clot blocks blood flow to a distant body part, usually in the leg. It is estimated that more than 100,000 cases of PAO are reported in the United States per year. An IND has been filed in the PAO indication. Hyseq began Phase 1 human studies in June 2002, which are being conducted in 20 patients across eight centers in the United States.

To date none of Hyseq s other therapeutic protein product candidates has progressed beyond pre-clinical testing, aside from alfimeprase. Hyseq has refocused its efforts from previously identified pre-clinical stage product candidates, IL1Hy1 and CD39L4, to other more promising pre-clinical candidates. The results of testing to date may not be indicative of results that will be obtained in further pre-clinical studies or in clinical trials. In addition, human clinical results could be different from Hyseq s expectations following its pre-clinical studies. Consequently, there is no assurance that the results in Hyseq s pre-clinical testing are

Table of Contents

predictive of the results that it will see in its clinical trials with humans. As further results of tests are received, Hyseq may abandon or reduce its efforts regarding particular projects. Additionally, there can be no assurance that clinical trials as to any particular product candidate, if commenced, will be successful, that the proposed disease indication will prove true, or that any product can be successfully commercialized. See Risk Factors Risks Related to the Combined Company.

Intellectual Property

Hyseq seeks patent protection on isolated partial and full-length gene sequences, as well as their encoded protein products, antibodies that bind to these proteins, and methods of using these genes, proteins or antibodies. As of November 15, 2002, Hyseq had filed patent applications on approximately 10,000 predicted full-length gene sequences and their corresponding proteins and antibodies. Hyseq has also filed patent applications on more than 830,000 partial gene sequences. Hyseq holds 17 United States patents relating to its proprietary gene sequences with claims covering the genes, their encoded protein products, corresponding antibodies, or methods of use.

Hyseq s subsidiary Callida Genomics, Inc. holds 23 United States patents with claims covering the methods, compositions, apparatus and applications relating to sequencing-by-hybridization technology. Callida has filed several additional patent applications covering improvements to and new applications of the SBH technology.

Hyseq s success will depend in large part on its ability to:

obtain patent and other proprietary protection for genes and proteins it discovers;

defend patents once obtained;

operate without infringing the patents and proprietary rights of third parties; and

preserve its trade secrets.

Research and Development Collaborations

Hyseq and its subsidiary Callida are focusing on strategic relationships to share research and development efforts and marketing opportunities with other biotechnology and pharmaceutical companies. Hyseq recognizes external collaborations as an important aspect of its success in analyzing and characterizing protein function. Hyseq s current collaborations include research and development collaborations with Aurora Biosciences Corporation, Deltagen, Inc., and Kirin Brewery Co., Ltd., gene discovery collaborations with BASF Plant Sciences GmbH (or BASF), and Chiron Corporation and a collaboration with the University of California, San Francisco (or UCSF). Hyseq had a previous collaboration with Kirin that was completed in March 2001. Hyseq s subsidiary Callida also has a collaboration with Affymetrix, Inc. and has been assigned its previous collaboration with the Applied Biosystems Group of Applera Corporation to commercialize one application of its SBH technology.

Aurora

In July 2001, Hyseq entered into a two-year collaboration and license agreement with Aurora Biosciences Corporation, under which Aurora will screen over 200 secreted proteins from its proprietary collection, using Aurora s proprietary CellSensor Panel, and under which Hyseq received a non-exclusive license to certain fluorescent protein technologies. Aurora will use its technology on Hyseq s behalf to identify proteins of interest as potential therapeutics and will receive upfront payments, licensing fees and technology access fees. The agreement calls for Hyseq to make payments to Aurora of up to $3.5 million over approximately two years, which includes $1.5 million in technology access fees, license fees and milestone payments, and $2.0 million for work performed under that agreement. In addition, Aurora may receive up to $1,150,000 in clinical milestone payments on the first Hyseq product developed under the agreement (contingent upon achievement of such milestones). As part of the agreement, Hyseq will provide Aurora access to selected novel targets from Hyseq s database of proprietary full-length cDNAs. The

agreement calls for Aurora to make payments to Hyseq of up to $1,825,000 over approximately two years, which includes technology and target access fees, license fees, and milestone payments. In addition, Hyseq may receive up to $1,150,000 in clinical milestone payments on the first Aurora product developed under the agreement (contingent upon achievement of such milestones). If none of the clinical milestones are achieved, then none of the milestone payments will be made or received by either party.

Deltagen

In October 2001, Hyseq entered into a collaboration with Deltagen to undertake research and development activities on approximately 200 novel secreted proteins. Hyseq will provide gene sequences encoding for the secreted proteins, and Deltagen will utilize its in vivo mammalian gene knockout technology to identify and validate potential commercially relevant biopharmaceutical drug targets. Both companies will have certain joint development and commercialization rights around potential biopharmaceutical drug targets discovered through the collaboration. The cost of the collaboration will be shared with Deltagen; Hyseq will provide Deltagen with approximately $10 million in research and development payments over two years.

Kirin

In October 1998, Hyseq entered into a collaboration with Kirin in which Hyseq uses its signature-by-hybridization platform to target potential pharmaceutical candidates involved in cell growth regulation from specific cell lines provided by Kirin. During the fourth quarter of 2000, Hyseq extended the term of Hyseq s collaboration with Kirin through March 2001 in order to complete additional research. Hyseq retains rights in North America to develop pharmaceutical products resulting from the collaboration, subject to milestone and royalty payments to Kirin. Kirin has equivalent rights in Asia and Oceania, and Hyseq and Kirin share rights equally in Europe and in the rest of the world. Hyseq s gene sequencing obligations under the original term of the agreement are substantially complete.

In August 2001, Hyseq entered into a new collaboration with Kirin, in which Kirin will fund three years of Hyseq s collaborative research work and both companies will conduct research directed toward discovering proteins and antibodies for a variety of diseases, including hematopoietic and inflammatory diseases. Hyseq will jointly own discoveries made during the collaboration, and it will jointly develop and market the resulting products while sharing costs, efforts, and revenues. Hyseq will have marketing rights in North America on all products discovered and developed under the collaboration. Kirin will have marketing rights in Asia and Ocenia. Hyseq will share marketing rights equally in Europe and the rest of the world.

Revenues from Hyseq s collaborations with Kirin represented 19% of total revenue for fiscal year ended December 31, 1999, and less than 10% of total revenue for fiscal years ended December 31, 2000 and 2001.

BASF

In December 1999, Hyseq entered into a collaboration with American Cyanamid Company in which Hyseq uses its signature-by-hybridization platform to target potential agricultural products. During 2000, BASF Aktiengesellschaft acquired the crop protection business of American Cyanamid Company and subsequently assigned Hyseq s collaboration with American Cyanamid to BASF Plant Sciences GmbH. The collaboration provides for funding of $60 million over its initial term of three and one half years. The collaboration can be extended by mutual agreement, for up to four additional one-year terms. BASF has the exclusive right to commercialize any agricultural products resulting from the collaboration. On May 14, 2002, the Company and BASF agreed to amend the collaboration agreement between the two parties. Under this amendment, both Hyseq s agricultural gene discovery activities and BASF Plant Science s payment schedule will accelerate with early completion scheduled for January 2003, resulting in a cost savings to both parties. The royalties due to the Company from BASF will also be reduced. The collaboration retains its original termination date of June 2003 but will not be renewable for any additional terms. Hyseq must generate data in accordance with a specified work plan which, if not met, could result in Hyseq s breach of the agreement. Revenues from Hyseq s collaboration with BASF represented less than 10% of total revenue for fiscal year

ended December 31, 1999, 75% of total revenue for fiscal year ended December 31, 2000, and 91% of total revenue for fiscal year ended December 31, 2001.

Chiron

In May 1997, Hyseq entered into a collaboration with Chiron in which Hyseq used its signature-by-hybridization platform to target solid tumor cancer therapeutics, diagnostic molecules and vaccines. The collaboration had an initial term of three years ending in May 2000, and has been extended by Chiron for an additional two-year period ending in May 2002. Chiron did not extend the collaboration past May 2002. Hyseq s gene sequencing obligations under the original term of the agreement are substantially completed. Chiron has the exclusive right to commercialize any solid tumor products resulting from the collaboration. Hyseq will receive royalties on any such products. In addition to research funding payments, in 1997 Chiron made an equity investment in Hyseq of $7.5 million in conjunction with the collaboration. Revenues from Hyseq s collaboration with Chiron represented 76% of total revenue for fiscal year ended December 31, 1999, 21% of total revenue for fiscal year ended December 31, 2000, and less than 10% of total revenue for fiscal year ended December 31, 2001.

University of California, San Francisco

In February 1998, Hyseq entered into an agreement with UCSF to conduct research on genes that may have important roles in the development of cardiovascular and related diseases. Under the agreement, researchers at UCSF are collecting DNA samples from up to 20,000 genetically diverse individuals. Hyseq can use these DNA samples to identify genetic traits including traits related to heart disease and hypertension.

Applied Biosystems

In May 1997, Hyseq entered into an agreement with Applied Biosystems to commercialize HyChip products. Pursuant to this agreement, Hyseq was required to commit $5.0 million to further development of the chip component of the HyChip system, which Hyseq satisfied in 1998. Applied Biosystems was also required to commit certain funds for development of the overall system. The collaboration had an initial term of five years and is extended automatically thereafter unless the parties mutually agree to termination. The agreement required Hyseq to design, develop and manufacture the HyChip chip component, while Applied Biosystems was responsible for the design, development and manufacture of the system that processes and analyzes data from the HyChip chip, as well as marketing and customer support. In 1997, Applied Biosystems made an equity investment in Hyseq of $10.0 million in conjunction with the collaboration.

In October 2001, Hyseq amended its agreement with Applied Biosystems to facilitate the settlement with Affymetrix. Significant components of this amendment included the conversion of the prior exclusive marketing arrangement with Applied Biosystems into a non-exclusive arrangement and the conclusion of all further collaboration obligations for each company. This collaboration agreement and amendment were assigned to Hyseq s subsidiary Callida Genomics, Inc. in October 2001.

Affymetrix

In October 2001, incident to Hyseq s settlement of all outstanding litigation with Affymetrix, Hyseq entered into a collaboration with Affymetrix to accelerate development and commercialization of a high speed universal DNA sequencing chip. This collaboration with Affymetrix is through a newly created venture, N-Mer, Inc., that is a wholly owned subsidiary of Callida, which in turn is a newly formed majority-owned subsidiary of Hyseq. Universal chips, or arrays, are DNA arrays designed without reference to specific gene sequences that can be used to sequence any gene sequence. N-Mer will have access to both Hyseq s sequencing-by-hybridization (SBH) technology, through Callida, and to Affymetrix GeneChip technology, a standard platform for array-based experiments. Affymetrix will be the exclusive array and system supplier and is initially authorized to be the exclusive agent for the distribution of N-Mer products.

Table of Contents

Hyseq s Subsidiary Callida Genomics, Inc.

In October 2001, Hyseq formed a new majority-owned subsidiary, Callida Genomics, Inc., to carry out Hyseq s business relating to its proprietary SBH technology. At the same time, Callida formed a wholly owned subsidiary, N-Mer, Inc. to collaborate with Affymetrix, Inc. on developing and commercializing a high speed DNA sequencing chip. Affymetrix has an initial 10% equity interest in Callida which may increase or decrease upon further third party financing of Callida. Hyseq and Affymetrix have agreed to each make additional investments in Callida, which will be conditioned on N-Mer s attainment of a specified technical milestone and the procurement of third-party financing. Callida granted Affymetrix an option to purchase a majority interest in N-Mer, which will be exercisable at any time through October 2006.

Hyseq contributed all of its SBH patents and patent applications to Callida. A team of approximately 30 Hyseq scientists, including one of its founders, Dr. Radoje Drmanac, who pioneered its DNA chip and SBH technology, became full-time employees of Callida. Callida currently has 25 employees. Hyseq s Chairman Dr. Rathmann is also Chairman, Interim President and Chief Executive Officer of Callida. As of November 15, 2002, Hyseq owns 90% of the outstanding equity of Callida.

On October 1, 2002 Hyseq announced the collaboration of its Callida Genomics subsidiary with SurroMed, Inc. of Mountain View, California for the development of a high throughput universal genotyping system. The collaboration will be funded in part by a National Institute of Standards and Technology Advanced Technology Program grant, providing approximately $3.2 million funding for Callida over three years.

SBH technology generally involves using DNA probes of known sequence that are hybridized with DNA samples. Different probe sets can be used for different applications. Callida uses a complete set of probes of a given length, or a subset of probes that are selected based on statistical properties, to assemble an unknown sequence of a DNA sample. DNA analysis applications using complete sets or subsets of probes include de novo sequencing, resequencing, genotyping, mutation discovery, and polymorphism detection. Callida has a license to use Hyseq s proprietary signature-by-hybridization technology in which it uses a small set of probes to screen for and discover genes in a large number of DNA samples.

Licensed Technology

In 1994, Hyseq acquired an exclusive license from Arch Development Corporation, a not-for-profit corporation affiliated with the University of Chicago that manages Argonne National Laboratories, to develop further and use certain SBH improvements developed by one of Hyseq s chief scientists while he was at Argonne. In July 1997, Hyseq began paying minimum royalties as required under the exclusive license. This license agreement was assigned to Hyseq s subsidiary Callida in October 2001.

Patents and Trade Secrets

The U.S. Patent and Trademark Office and patent authorities outside the United States issue patents for inventions based on genes that have been isolated from their natural state (through a purifying step that separates the gene from other molecules naturally associated with it), but only if the invention meets all the criteria for a patent. Each country has its own standards for granting a patent. In the United States, to be eligible for patent protection, an invention must at least be novel and useful and the patent application must contain sufficient detail to allow one skilled in the art or technology to reproduce the invention. Hyseq applies for patent applications on both partial and full-length gene sequences. As of November 15, 2002, Hyseq had filed patent applications on approximately 10,000 predicted full-length gene sequences and their corresponding proteins. Fewer than 10,000 applications are pending because some of Hyseq s patent applications include many gene sequences in one application. These applications may or may not result in the issuance of patents. In January 2001, the U.S. Patent and Trademark Office issued final revised guidelines on the standard of utility required for inventions, including gene-based inventions. The revised guidelines state that a patent application for an invention must disclose a well-established utility or a specific, substantial and credible utility for the isolated and purified gene. There can be no assurance that Hyseq s disclosures in these applications are sufficient to meet the statutory requirements for patentability in all cases. Hyseq cannot

Table of Contents

assure you that any of its currently pending or future applications will issue as patents, or that any patent issued to Hyseq will not be challenged, invalidated, circumvented or held unenforceable by way of an interference proceeding or litigation.

Patent protection for therapeutic protein-based products can include coverage of the composition of matter of a gene and the protein it expresses, methods to generate or manufacture the products and methods of using the products. Prior to the genomics era, there were few patents filed each year that contained DNA sequence information. The development of methods for rapid DNA sequencing and bioinformatics techniques has driven significant growth in the number of patent applications filed on genes and their corresponding proteins.

In part, the filing of so many patents on DNA sequences reflects the importance of patent protection for therapeutic protein-based products. The costs of developing these products can run into the hundreds of millions of dollars and can take up to 10 to 12 years from experimental stage to market. Without patent protection, companies often have little incentive to invest in this important endeavor. Protection through patent exclusivity provides the opportunity for a company to recoup its research and development costs, make a profit on the therapeutic protein-based product, and invest in research and development of additional therapeutic protein-based products.

The growth in the number of patents filed on DNA sequences has spurred continuing reassessment of the related patenting process. Beginning in the early 1990s, many companies filed patent applications primarily covering ESTs or other partial gene sequences, believing that resulting patents would cover the related full-length gene sequences. In the mid-1990s, it became increasingly evident that applications filed with the United States Patent and Trademark Office would need to cover full-length gene sequences to result in broad patent protection. More recently, the Patent and Trademark Office has published guidelines regarding utility of patented gene sequences. These guidelines suggest that many existing patent applications with inadequate utility disclosure may not result in issued patents, even if the applications cover full-length gene sequences. Patents on methods of use for proteins may become more important as more information becomes available about the therapeutic significance of discovered genes and proteins.

Hyseq has also filed United States patent applications on more than 830,000 partial human gene sequences. There can be no assurance that the disclosures in these applications are sufficient to meet the statutory requirements for patentability. Where only a partial sequence is disclosed, the U.S. Patent and Trademark Office may issue patents of a very limited scope that will not cover a full-length gene sequence that includes the partial sequence. Therefore, there is a significant risk that the U.S. Patent and Trademark Office will not issue patents based on patent disclosures limited to partial gene sequences or will issue patents of a very limited scope. The commercial protection provided by any patents issued on the basis of partial gene sequences is uncertain.

Other companies or institutions may have filed patent applications, or may file patent applications in the future, which attempt to patent genes similar to or the same as those covered in Hyseq s patent applications, including applications based on Hyseq s potential products. The U.S. Patent and Trademark Office would decide the priority of competing patent claims in an interference proceeding. Any patent application filed by a third party may have priority over a patent application Hyseq filed, in which event such third party may require Hyseq to stop pursuing a potential product, or negotiate a royalty arrangement to pursue and commercialize the potential product.

Issued patents may not provide freedom to operate with respect to Hyseq s potential products because certain uses of Hyseq s potential products may give rise to claims that such uses infringe the patents of others. This risk will increase as the biotechnology industry expands and as other companies obtain more patents and attempt to discover the utility and function of all known genes. Other persons could bring legal actions against Hyseq to claim damages or to stop Hyseq s manufacturing and marketing of the affected products. If any of these actions are successful, in addition to any potential liability for past damages, these persons may require Hyseq to obtain a license in order to continue to manufacture or market the affected products. Hyseq believes that there will continue to be significant litigation in its industry regarding patent

and other intellectual property rights. If Hyseq becomes involved in patent litigation related to its technology or potential products, it could consume a substantial portion of its resources.

Hyseq pursues patent protection for products and processes where appropriate and it also relies on trade secrets, know-how and continuing technological advancement to develop and maintain its competitive position, Hyseq s policy is to have each employee enter into an agreement that contains provisions prohibiting the disclosure of confidential information to anyone outside the company. Research and development contracts and relationships between Hyseq and its scientific consultants provide access to aspects of Hyseq s know-how that is protected generally under confidentiality agreements with the parties involved. There can be no assurance, however, that these confidentiality agreements will be honored or that Hyseq can effectively protect its rights to its unpatented trade secrets. Moreover, there can be no assurance that others will not independently develop substantially equivalent proprietary information and techniques or otherwise gain access to Hyseq s trade secrets.

Competition

Hyseq s strategy as a biopharmaceutical company is to define and patent human genes that are most likely to be involved in a disease condition and to focus on identifying product candidates from the proteins produced by these genes. There are a finite number of genes in the human genome, virtually all of which have been or will soon be identified. Other active companies include major pharmaceutical and biotechnology 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 Hyseq does. As a result, they may succeed in identifying genes and determining their functions or developing products earlier than Hyseq or its current or future collaboration partners do. They also may obtain patents and regulatory approvals for such products more rapidly than Hyseq or its current or future collaboration partners, or develop products that are more effective than those proposed to be developed by Hyseq or its collaboration partners. Further, any potential products based on genes Hyseq identifies 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 Hyseq identifies. There can be no assurance that research and development by others will not render the products that Hyseq may develop obsolete or uneconomical or result in treatments, cures or diagnostics superior to any therapy or diagnostic developed by Hyseq or that any therapy Hyseq develops will be preferred to any existing or newly developed technologies. Certain of Hyseq s collaboration partners may now be, or could become, competitors.

Hyseq is in a competition to identify, establish uses for and patent as many genes and their corresponding proteins as possible and to commercialize the products it develops from these genes and proteins. Hyseq faces competition from other entities using high-speed gene sequencers and other sophisticated bioinformatics technologies to discover genes, including but not limited to Celera Genomics Corporation, Curagen, Inc., Genentech, Inc., Human Genome Sciences, Inc., Incyte Genomics, Inc., Millennium Pharmaceuticals, Inc., and Zymogenetics, Inc. Hyseq also faces competition from entities using more traditional methods to discover genes related to particular diseases, including other large biotechnology and pharmaceutical companies. Hyseq expects that competition in its field will continue to be intense. Research to identify genes is also being conducted by various institutes and government-financed entities in the United States and in foreign countries, including France, Germany, Japan and the United Kingdom and elsewhere, as well as by numerous smaller laboratories associated with universities or other not-for-profit entities. In addition, a number of pharmaceutical and biotechnology companies and government-financed programs are engaged or have announced their intention to engage in areas of human genome research similar to or competitive with Hyseq s focus on gene discovery, and other entities are likely to enter the field.

Hyseq believes the principal competitive factors affecting its markets are rights to develop and commercialize therapeutic protein-based products, including appropriate patent and proprietary rights; safety and effectiveness of therapeutic protein-based products; the timing and scope of regulatory approvals; the cost and availability of these products; the availability of appropriate third-party reimbursement programs; and the availability of alternative therapeutic products or treatments. Although Hyseq believes that it is well

Table of Contents

positioned to compete adequately with respect to these factors in the future, Hyseq s future success is currently difficult to predict because it is an early stage company; all of its internal product candidates are still in various stages of pre-clinical development and have yet to undergo clinical trials. Also, although Hyseq believes that its bioinformatics technologies and exploratory biology capabilities provide it with a competitive advantage, any of the companies or other entities Hyseq competes with may discover and establish a superior patent position in one or more genes or proteins that Hyseq has identified and designated or considered designating as a product candidate. In addition, any potential products based on genes or proteins Hyseq identifies will face competition both from companies developing gene- or protein-based products and from companies developing other forms of treatment for diseases that may be caused by, or related to, the genes or proteins Hyseq identifies. Furthermore, Hyseq s potential products, if approved and commercialized, may compete against well established existing therapeutic protein-based products, many of which may be currently reimbursed by government health administration authorities, private health insurers and health maintenance organizations. Also, healthcare professionals and consumers may prefer existing or newly developed products to any product Hyseq develops.

Although Hyseq believes that there are significant product development opportunities for both Hyseq and for its collaborators, competition exists to develop and commercialize therapeutic protein-based products. Many of Hyseq s existing and potential competitors have substantially greater research and product development capabilities and financial, scientific, marketing and human resources than Hyseq does. As a result, these competitors may: succeed in identifying genes or proteins, or developing therapeutic protein-based products, earlier than Hyseq does; obtain approvals for products from the FDA or other regulatory agencies more rapidly than Hyseq does; obtain patents that block or otherwise inhibit Hyseq s ability to develop and commercialize its product candidates; develop treatments or cures that are safer or more effective than those Hyseq proposes to develop; devote greater resources to marketing or selling their products; introduce or adapt more quickly to new technologies or scientific advances, which could render Hyseq s high throughput technologies obsolete; introduce products that make the continued development of Hyseq s potential products uneconomical; more effectively negotiate third-party collaborative or licensing arrangements; and take advantage of acquisition or other opportunities more readily than Hyseq can.

With regard to Hyseq s subsidiary, Callida, competition in the area of DNA analysis tools is intense and expected to increase. Technologies in this area are new and rapidly evolving. Applications of Callida s SBH technology compete primarily with Affymetrix and Applied Biosystems. Applied Biosystems presently markets gel sequencers, a well-established sequencing technology, which compete with applications of SBH technology. Other companies also are developing or have developed DNA analysis tools that may compete with applications of SBH technology, including Aclara Biosciences, Inc., Agilent Technologies, Inc., Caliper Technologies, Inc., CuraGen, Inc., IBM, Illumina, Inc., Molecular Devices, Nanogen, Inc., and Sequenom, Inc. Many of these companies have significantly greater research and development, marketing and financial resources than Hyseq does, and therefore represent significant competition.

Government Regulation

Regulation by governmental authorities in the United States and most foreign countries will be a significant factor in manufacturing and marketing Hyseq s potential products and in its ongoing research and product development activities. Virtually all of Hyseq s products and those of its partners, such as Amgen, Aurora Biosciences, Chiron, Deltagen and Kirin, will require regulatory approval by governmental agencies prior to commercialization. In particular, human therapeutic products are subject to rigorous preclinical and clinical testing and other approval requirements by the FDA and comparable agencies in foreign countries. Hyseq is currently collaborating with Amgen to develop alfimeprase, which is a drug candidate that will require regulatory approval. The collaboration is further described in [note 12, Subsequent Events, to the financial statements included in this joint proxy statement/ prospectus]. The time required for completing such testing and obtaining such approvals is uncertain. Unexpected biological activities, some of which may result in safety issues, may arise during preclinical evaluation. Such observations could delay or alter the course of a development program or ultimately result in the termination of a program. Any delay in clinical testing may also delay product development. In addition, delays or rejections may be encountered based on changes in

Table of Contents

FDA or foreign regulatory policy during the period of product development and testing. Various federal statutes and regulations also regulate the manufacturing, safety, labeling, storage, record-keeping and marketing of such products. The lengthy process of obtaining regulatory approvals and ensuring compliance with appropriate federal statutes and regulations requires the expenditure of substantial resources. Any delay or failure by Hyseq or by its collaboration partners to obtain regulatory approval could adversely affect the commercialization of products Hyseq or its collaboration partners are developing, Hyseq s ability to achieve product collaboration milestones or receive royalty revenue and thus negatively impact its liquidity and capital resources.

Preclinical studies are generally conducted in the laboratory to evaluate the potential efficacy and safety of a therapeutic product. The results of these studies are submitted to the FDA as part of an Investigational New Drug application (IND), which must be reviewed by FDA personnel before clinical testing can begin. Typically, clinical evaluation involves three sequential phases, which may overlap. During Phase I, clinical trials are conducted with a relatively small number of subjects to determine the early safety profile of a drug, as well as the pattern of drug distribution and drug metabolism. In Phase II, trials are conducted with groups of patients afflicted by a specific target disease to determine preliminary efficacy, optimal dosages, and dosage tolerance and to gather additional safety data. In Phase III, larger-scale, multi-center comparative trials are conducted with patients afflicted with a specific target disease to provide data for the statistical proof of efficacy and safety as required by the FDA and foreign regulatory agencies. The FDA, the clinical trial sponsor or the investigator may suspend clinical trials at any time if they believe that clinical subjects are being exposed to an unacceptable health risk. Although Hyseq has begun Phase I clinical studies, there is no assurance that the safety profile of alfimeprase will be acceptable and that it will proceed to Phase II or Phase III.

The results of preclinical and clinical testing are submitted to the FDA in the form of a New Drug Application for small molecule products or a Biologic License Application for biological products. In responding to New Drug Application or Biologic License Application it may grant marketing approval, request additional information, or deny the application if the FDA determines that the application does not satisfy its regulatory approval criteria. There can be no assurance that approvals will be granted on a timely basis, if at all. The failure to obtain timely permission for clinical testing or timely approval for product marketing would have a material negative effect on Hyseq. Product approvals may subsequently be withdrawn if compliance with regulatory standards is not maintained or if problems are identified after the product reaches the market. The FDA may require testing and surveillance programs to monitor the effect of a new product and may prevent or limit future marketing of the product based on the results of these post-marketing programs.

Currently one of Hyseq s product candidates, alfimeprase, qualifies as an orphan drug under the Orphan Drug Act of 1983. This act generally provides incentives to manufacturers to undertake development and marketing of products to treat relatively rare diseases or those diseases that affect fewer than 200,000 persons annually in the United States. A drug that receives orphan drug designation by the FDA and is the first product to receive FDA marketing approval for its product claim is entitled to various advantages, including a seven-year exclusive marketing period in the United States for that product claim. However, any drug that is considered by the FDA to be different from or clinically superior to a particular orphan drug, including any orphan drug of Hyseq s that has been so designated by the FDA, will not be precluded from sale in the United States during the seven-year exclusive marketing period. Hyseq cannot assure you that any of its other product candidates will be designated as an orphan drug by the FDA or, if so designated, will have a positive effect on its revenues.

To manufacture Hyseq s potential products, a domestic or foreign drug manufacturing facility must be registered with the FDA as a manufacturing establishment, must submit to periodic inspection by the FDA and must comply with current Good Manufacturing Practices regulations. In addition, the FDA imposes a number of complex regulations on entities that advertise and promote biologics, including, among others, standards and regulations for direct-to-consumer advertising, off-label promotions, industry-sponsored scientific and educational activities, and promotional activities involving the Internet. The FDA has very broad enforcement authority under the Federal Food, Drug and Cosmetic Act, and failure to abide by these

Table of Contents

regulations can result in penalties, including the issuance of a warning letter directing Hyseq to correct deviations from FDA standards, a requirement that future advertising and promotional materials be pre-cleared by the FDA, and civil and criminal penalties.

Whether or not FDA approval has been obtained, approval of a product by comparable foreign regulatory authorities is necessary prior to the commencement of marketing of a product in those countries. The approval procedures vary among countries and can involve additional testing. The time required to obtain approval may differ from that required for FDA approval. Although there are some centralized procedures for filings in the European Union countries, in general each country has its own procedures and requirements, and compliance with these procedures and requirements may be expensive and time-consuming. Accordingly, there may be substantial delays in obtaining required approvals from foreign regulatory authorities after the relevant applications are filed, if Hyseq ultimately receive any approvals at all.

Even if regulatory approval for a product is obtained, the product and the facilities manufacturing the product are subject to continued review and periodic inspection. Each drug-manufacturing establishment in the United States must be registered with the FDA. Domestic manufacturing establishments are subject to biannual inspections by the FDA and must comply with the FDA s cGMP regulations, as well as regulatory agencies in other countries if products are sold outside the United States. If Hyseq s subsidiary Callida manufactures for sale to third parties diagnostic product applications of its SBH technology, it will need to comply with cGMP regulations pertaining to devices. Hyseq will need to spend funds, time and effort to ensure full technical compliance with these regulations. The FDA stringently applies regulatory standards for manufacturing drugs, biologics, and medical devices. The FDA s cGMP regulations require that drugs and medical devices be manufactured and records be maintained in a prescribed manner with respect to manufacturing, testing and control activities.

Hyseq s policy is to conduct research activities in compliance with the National Institute of Health Guidelines for Research Involving Recombinant DNA Molecules. Hyseq also is subject to various federal, state and local laws, regulations and recommendations relating to safe working conditions, laboratory and manufacturing practices, the experimental use of animals and the use and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with its work. The extent and character of governmental regulation that might result from future legislation or administrative action and its effect on Hyseq cannot be accurately predicted.

Hyseq is subject to federal, state and local laws and regulations governing the use, storage, handling and disposal of hazardous materials, including 33P, a low energy radioactive isotope used in labeling some of Hyseq s probes and subsequently present in certain waste products. Although Hyseq believes that its safety procedures for such materials comply with the standards prescribed by local, state, and federal laws and regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of such an accident, Hyseq could be held liable for any damages that result and any liability could exceed its resources.

Human Resources

At November 15, 2002, Hyseq had 155 full-time equivalent employees, including 25 Callida employees, 74 of whom hold Ph.D., M.D., J.D. or other advanced degrees. Approximately 112 of Hyseq s employees are engaged in research and development activities, including 24 in Callida Genomics, and approximately 43 are engaged in business development, finance, operations support, and administration. None of Hyseq s employees are represented by a collective bargaining agreement, nor has Hyseq experienced work stoppages. Hyseq believes that relations with its employees are good.

Table of Contents

Management s Discussion and Analysis of Financial Condition and Results of Operations of Hyseq

This Management s Discussion and Analysis of Financial Condition and Results of Operations of Hyseq contains forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by words including anticipate, believe, intends, estimates, expect, should, may, potential and similar expressions. Such statements are management s current expectations and involve risks and uncertainties. Actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors discussed herein and elsewhere including, in particular, those factors described under Risk Factors set forth on page , and in its other periodic reports filed from time to time with the SEC. Actual results and performance could also differ materially from time to time from those projected in its filings with the SEC.

Company Overview

Hyseq is 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. Hyseq intends to develop and commercialize these types of product candidates on its own or in collaboration with other biotechnology or pharmaceutical companies.

Hyseq believes its signature-by-hybridization platform, which is related to its proprietary SBH technology provides a significant advantage in discovering novel, rarely-expressed genes. Hyseq believes it possesses one of the most important proprietary databases of full-length human gene sequences and has the potential to develop a significant pipeline of product candidates for research and development. Previously, Hyseq s activities have focused primarily on full-length gene sequencing, patenting, bioinformatics, cloning, and early stage research activities to prioritize potential therapeutic protein candidates. As of November 15, 2002, Hyseq had filed patent applications on approximately 10,000 predicted full-length human gene sequences, and had issued 17 gene-related patents. Hyseq is accelerating its research activities to elucidate the role of novel genes in its proprietary database, its encoded proteins and corresponding antibodies. Hyseq s database includes chemokines, growth factors, stem cell factors, interferons, integrins, proteases, hormones, receptors and other potential protein therapeutics or drug targets. Hyseq s focused bioinformatics and screening capabilities have significantly enhanced its understanding of the biological activity of these genes and their corresponding proteins, enabling Hyseq to file strategic patent applications that encompass both composition of matter and method of use claims.

Hyseq is primarily focused on discovering and developing therapeutic protein-based products, as Hyseq believes that naturally occurring therapeutic proteins have several commercial advantages over small molecule drugs.

In the near term, Hyseq is balancing the risks in developing therapeutics from its full-length gene database by also focusing on an early stage clinical product candidate acquired through collaboration with Amgen, Inc. Hyseq entered into this collaboration in January 2002, with the goal of developing and commercializing alfimeprase, a thrombolytic enzyme, for the treatment of peripheral arterial occlusion (or PAO) and other cardiovascular indications. Pre-clinical studies suggest that alfimeprase is a promising agent for dissolving blood clots (clot lysis) and may provide clinically significant advantages for the treatment of patients with PAO and other cardiovascular indications. In June of 2002 Hyseq initiated Phase I clinical trials in a multi-center, open-label, dose-escalation study to evaluate alfimeprase s safety and pharmacokinetics, to be conducted in 20 patients across approximately eight centers in the United States.

Critical Accounting Policies and Estimates

Hyseq s discussion and analysis of its operating results and financial condition is based upon its consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of the financial statements requires Hyseq to make estimates, judgments, and assumptions that affect the reported amounts of assets, liabilities,

revenues and expenses, and related disclosure of contingent amounts. While Hyseq believes its estimates, judgments, and assumptions are reasonable, the inherent nature of estimates is that actual results will likely be different from the estimates made.

Hyseq believes the following critical accounting policies, among others, affect the more significant judgments and estimates used in the preparation of its consolidated financial statements.

Revenue Recognition

Hyseq recognizes revenue when all of the following conditions have occurred:

Persuasive evidence of an arrangement exists;

Delivery has occurred or services have been rendered;

The price is fixed and determinable; and

Collection is reasonably assured.

Hyseq defers and recognizes up-front refundable fees as revenues upon the later of when they become nonrefundable or when performance obligations are completed. In situations where Hyseq has no continuing performance obligations, Hyseq recognizes up-front nonrefundable fees as revenues when receivable. In situations where continuing performance obligations exist, Hyseq defers and amortizes up-front nonrefundable fees over the performance period. The terms of such arrangements may cause Hyseq s operating results to vary considerably from period to period.

Income Taxes

Income taxes are accounted for under the asset and liability method pursuant to Financial Accounting Standards Board Statement of Financial Accounting Standards (SFAS) Statement No. 109. Under SFAS 109, deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

Hyseq records a valuation allowance to reduce deferred income tax assets to an amount that is more likely than not to be realized. Assessment of the realization of deferred income tax assets requires that estimates and assumptions be made as to the taxable income of future periods. Hyseq s deferred tax assets are reduced to zero, as management believes that it is more likely than not that the deferred tax assets will not be realized. Projection of future period earnings is inherently difficult as it involves consideration of numerous factors such as Hyseq s overall strategies and estimates of new product development and acceptance, product lifecycles, selling prices and volumes, responses by competitors, manufacturing costs and assumptions as to operating expenses and other industry specific and macro and micro economic factors. In addition, consideration is also given to ongoing and constantly evolving global tax laws and Hyseq s own tax minimization strategies.

Capitalization of Software Developed for Internal Use

Hyseq accounts for software developed for internal use in accordance with Statement of Position (SOP) 98-1, Accounting for the Costs of Computer Software Developed or Obtained for Internal Use, which requires research and development costs associated with the application development stage to be capitalized for internal use software. Platform and software development costs incurred prior to the application development stage are charged to expense as incurred. Management is required to use professional judgment in determining whether development costs meet the criteria in SOP 98-1 for immediate expense or capitalization. Amortization of the capitalized costs begins when all substantial testing is completed and the software is ready for its intended use. Hyseq s management periodically reviews the carrying value of the

Table of Contents

projects that have been capitalized to determine if impairment may exist. If it is determined that the carrying value of the asset has been impaired, the value would be reduced by a charge to operations in the amount of the impairment.

Selected Quarterly Financial Data (Unaudited)

The following table sets forth certain unaudited financial data for each of the quarters within the twelve months ended December 31, 2001 and 2000 and the quarters in the nine months ended September 30, 2002. This information has been derived from the consolidated financial statements of Hyseq and, in management s opinion, reflects all adjustments (consisting only of normal recurring adjustments) necessary for a fair presentation of the information for the quarters presented. The operating results for any quarter are not necessarily indicative of results for any future period:

Hyseq Pharmaceuticals, Inc.

Selected Quarterly Financial Data (Unaudited)

	Quarter Ended		
	September 30, 2002	**June 30, 2002**	**March 31, 2002**
Contract revenues	$11,022	$ 6,661	$ 5,232
Loss from operations	(988)	(7,854)	(18,840)
Net loss	(1,444)	(8,068)	(18,956)
Basic and diluted net loss per share	(0.06)	(0.37)	(1.01)

	Quarter Ended			
	December 31, 2001	**September 30, 2001**	**June 30, 2001**	**March 31, 2001**
Contract revenues	$ 7,069	$ 5,872	$ 5,981	$ 5,668
Loss from operations	(11,553)	(9,905)	(8,349)	(6,386)
Net loss	(11,357)	(10,008)	(8,427)	(6,679)
Basic and diluted net loss per share	(0.61)	(0.59)	(0.55)	(0.49)

	Quarter Ended			
	December 31, 2000	**September 30, 2000**	**June 30, 2000**	**March 31, 2000**
Contract revenues	$ 4,289	$ 5,936	$ 3,574	$ 1,805
Loss from operations	(6,627)	(4,199)	(5,331)	(6,572)
Net loss	(6,695)	(4,116)	(5,112)	(6,330)
Basic and diluted net loss per share	(0.49)	(0.30)	(0.38)	(0.48)

Results of Operations

Contract Revenues

Comparison of the Three and Nine Months Ended September 30, 2002 and 2001. Revenues were $11.0 million and $22.9 million for the three and nine months ended September 30, 2002, respectively, compared to $5.9 million and $17.5 million for the same periods in 2001. BASF contract revenues were $9.7 million and $19.4 million for the three and nine months ended September 30, 2002, respectively, compared to

$5.6 million and $16.4 million during the three and nine months ended September 30, 2001. Higher BASF contract revenues reflect the fact that in May 2002, Hyseq and BASF announced an agreement to accelerate completion of its agricultural gene discovery collaboration to approximately January 31, 2003.

Table of Contents

Revenues earned during the three and nine months ended September 30, 2002 also included $0.8 million and $2.0 million amortization, respectively, of a $4.0 million license payment received from Affymetrix in October 2001 at the time of settlement of its outstanding litigation and the creation of its majority-owned subsidiary Callida Genomics (Callida). Affymetrix s payment was made in return for a non-exclusive license, without the right to grant sublicenses, under 11 U.S. patents and 30 U.S. patent applications and counterpart foreign patents and applications to make, use, sell, and import products in the non-universal gene array field. This license payment will continue to be amortized to revenue as Callida utilizes its cash in conducting research & development efforts. As of September 30, 2002, $1.2 million of this license payment remains as deferred revenue.

Revenues earned during the three months ended September 30, 2002 also included a one-time upfront non-refundable license payment of $0.5 million received as part of a license agreement with Celera Diagnostics and the University of California, San Francisco. This license grants Celera non-exclusive access to the large-scale patient sample collection and accompanying clinical data associated with Hyseq s collaboration with University of California, San Francisco, to elucidate the molecular genetics of cardiovascular disease.

Its revenues typically vary from quarter to quarter and may result in significant fluctuations in its operating results from year to year. In the future, Hyseq may not be able to maintain existing collaborations, obtain additional collaboration partners or obtain revenue from other sources. The failure to maintain existing collaborations or the inability to enter into additional collaborative arrangements or obtain revenues from other sources could have a material adverse effect on its revenues and operating results. Revenues for 2003 will be reduced substantially as a result of the accelerated completion of its collaboration with BASF Plant Science, which Hyseq expects to occur in January 2003.

Comparison of Years Ended December 31, 2001 and 2000. Hyseq s contract revenues were $24.6 million for 2001 compared to $15.6 million for 2000. The increase was primarily due to higher revenues earned from its collaboration with BASF for gene screening services to target potential agricultural products.

Contract revenues earned during 2001 included $22.4 million under Hyseq s agreement with BASF, $1.2 million under its agreement with Chiron, $0.8 million under its agreement with Affymetrix, and $0.2 million under its agreement with Applied Biosystems.

Revenues recognized under Hyseq s agreement with BASF were $22.4 million for 2001 compared to $11.7 million for 2000. Processing was slightly ahead of contractual levels of 1.1 million average clones per month in 2001, compared to 0.6 million average clones per month in 2000 when processing was ramping up.

Revenues recognized in 2001 under Hyseq s agreement with Chiron consist mainly of $1.0 million minimum annual research funding received for the second year of the two-year extension initiated by Chiron in May of 2000, compared to $3.3 million revenue in 2000 earned in the final months of the initial three year gene screening services portion of its agreement with Chiron.

Hyseq s revenues typically vary from quarter to quarter and may result in significant fluctuations in its operating results from year to year. In the future, Hyseq may not be able to maintain existing collaborations, obtain additional collaboration partners or obtain revenue from other sources. The failure to maintain existing collaborations, the inability to enter into additional collaborative arrangements or obtain revenue from other sources could have a material adverse effect on Hyseq s revenues and operating results.

Comparison of Years Ended December 31, 2000 and 1999. Hyseq s contract revenues increased by $9.2 million to $15.6 million in 2000, compared to $6.4 million for 1999. Contract revenues recognized in 2000 included $11.7 million from BASF and $3.3 million from Chiron. The increase in 2000 was due primarily to the ramp up of gene screening services for BASF, less a $1.6 million decrease in revenues earned from Chiron due the completion in the first half of 2000 of the gene screening services portion of that three year collaboration.

Table of Contents

Operating Expenses

Comparison of the Three and Nine Months Ended September 30, 2002 and 2001. Hyseq s total operating expenses, consisting of research and development expenses and general and administrative expenses, were $12.0 million and $50.6 million for the three and nine months ended September 30, 2002, respectively, compared to $15.8 million and $42.2 million for the same periods in 2001.

Hyseq s research and development expenses were $9.1 million and $40.9 million during the three and nine months ended September 30, 2002, respectively, compared with $11.4 million and $31.5 million during the same periods in 2001. The fluctuation in research and development expenses was due mainly to a $10.0 million non-cash charge for the fair value of warrants granted to Amgen, Inc. in the first quarter as Hyseq began its collaboration to develop and commercialize alfimeprase, a novel acting thrombolytic, for the treatment of peripheral arterial occlusion (PAO) and other indications. Due to the addition of laboratory and office space leased in April 2001, rent expense was $2.7 million and $8.1 million during the three and nine months ended September 30, 2002, respectively, compared to $2.7 million and $5.4 million during the same period last year. Offsetting these increases were lower supply expenses resulting from the acceleration of its collaboration with BASF Plant Science according to an agreement signed in May 2002, as well as lower personnel costs from the associated reduction in force. In addition, Hyseq recorded cost recoveries from Kirin Brewery, Ltd and Intel Corporation in connection with its research collaborations, and lower payments to its collaboration partners University of California, San Francisco and Aurora Biosciences Corporation. During October 2002, Hyseq recorded $1.7 million in collaboration costs related to its agreement with Deltagen, upon achievement of the second major contract milestone by Deltagen.

Its general and administrative expenses were $2.9 million and $9.1 million during the three and nine months ended September 30, 2002, respectively, compared with $3.6 million and $9.8 million during the same periods in 2001. Lower outside legal expenses resulting from the settlement of all outstanding litigation with Affymetrix late in 2001 were partially offset by higher cost of internal patent prosecution as Hyseq actively continues to prosecute and enforce its intellectual property rights. In addition, accrual of a $2.0 million loan for Hyseq s President and CEO was completed in January 2002.

Hyseq expects operating expenses during the remainder of 2002 to decrease as a result of its agreement with BASF Plant Science to accelerate completion of its collaboration, and as a result of its other cost control efforts including a partial hiring freeze, a freeze on capital expenditures, delay of its facilities expansion plans, and deferral of as many of its contractual financial commitments as possible. These savings will be partially offset by higher costs of outside clinical research services for Phase I clinical trials for alfimeprase in the first quarter.

Comparison of Years Ended December 31, 2001 and 2000. Hyseq s total operating expenses, consisting of research and development expenses and general and administrative expenses, increased by $22.5 million to $60.8 million for 2001 compared to $38.3 million for 2000.

For 2001, Hyseq s research and development expenses increased by $17.5 million to $46.5 million compared to $29.0 million for 2000. This increase was primarily due to Hyseq s biopharmaceutical research and development efforts, and includes a $3.3 million increase in costs associated with the addition of scientific personnel, $4.5 million increase in outside contract research services, and a $1.1 million write-off of certain capitalized software development costs. Due to the acquisition of additional facilities for research and development, rent expense increased $5.4 million and depreciation expense of leasehold improvements increased $1.1 million.

Hyseq s general and administrative expenses increased $4.1 million to $13.5 million in 2001 compared to $9.3 million in 2000. The increase in general and administrative expenses during 2001 included $3.4 million increase in personnel expenses in connection with the compensation, recruiting, and relocation of an experienced and accomplished senior management team.

Hyseq expects operating expenses to increase during 2002 as it plans to continue research and development of its therapeutic protein candidates, build out its new facilities to support its research and development efforts, further develop SBH technology applications through its subsidiary, Callida, and

prosecute its intellectual property rights. The magnitude of the increases in Hyseq s operating expenses will be significantly affected by its ability to secure adequate sources of external financing or additional sources of revenue. If Hyseq does not obtain adequate financing or revenue in a timely manner, this could significantly harm its business, financial condition and results of operations, and may require Hyseq to delay or eliminate one or more of its research or development programs and/or delay the build out and occupation of its new leased facilities. See Management s Discussion and Analysis of Financial Condition and Results of Operations of Hyseq Liquidity and Capital Resources.

Comparison of Years Ended December 31, 2000 and 1999. Hyseq s total operating expenses, consisting of research and development expenses and general and administrative expenses, increased by $12.0 million to $38.3 million for 2000 compared to $26.3 million for 1999.

For 2000, Hyseq s research and development expenses increased by $10.8 million to $29.0 million compared to $18.2 million for 1999. This increase in Hyseq s research and development expenses was primarily attributable to the increase in production throughput in its gene discovery and complete gene sequencing programs, including $5.1 million increase in costs associated with the addition of scientific and bioinformatic personnel, $1.9 million increase in outside contract services, $2.5 million increase in supplies purchases related to its collaborations, and a $0.6 million write-off of certain capitalized software development costs.

Hyseq s general and administrative expenses increased $1.2 million to $9.3 million in 2000 compared to $8.1 million in 1999. The increase in general and administrative expenses during 2000 included $0.8 million increase in rent expenses associated with the new leased facilities, $0.5 million increase in recruiting and salary expenses, plus increases in legal expenses related to its patent litigation and settlement with Affymetrix.

Interest Income and Expense

Comparison of the Three and Nine Months Ended September 30, 2002 and 2001. Hyseq s net interest expense was $0.4 million and $0.9 million during the three and nine months ended September 30, 2002, respectively, compared with $0.1 million and $0.5 million during the same periods in 2001. The change in net interest expense was due to interest on its $4.0 million loan from Affymetrix and the $4.0 million line-of-credit from its Chairman, as well as lower interest rates on interest earned on its bank balances. Partially offsetting this was lower interest expense on lower average capital lease balances.

Comparison of Years Ended December 31, 2001 and 2000. Hyseq s interest income and expense, net decreased by $1.1 million to $0.6 million interest expense for 2001 compared to $0.5 million interest income for 2000. This decrease in interest income resulted from lower average cash and investment balances and lower interest rates.

Comparison of Years Ended December 31, 2000 and 1999. Hyseq s interest income and expense, net decreased by $0.8 million to $0.5 million interest income for 2000 compared to $1.3 million interest income for 1999. This decrease in 2000 resulted from lower cash and investment balances, and higher interest expense from Hyseq s increased equipment and leasehold financing activities.

Net Loss

Comparison of the Three and Nine Months Ended September 30, 2002 and 2001. Since its inception, Hyseq has incurred operating losses, and as of September 30, 2002 Hyseq had an accumulated deficit of $136.9 million. Hyseq incurred a net loss for the three and nine months ended September 30, 2002 of $1.4 million and $28.5 million, respectively, compared to a net loss of $10.0 million and $25.1 million in the same periods of 2001. This change in net loss resulted primarily from its continued research and development of its biopharmaceutical product candidates, from accelerated completion of its collaboration with BASF Plant Sciences, and from the $10.0 million non-cash charge for the fair value of warrants granted to Amgen Inc. in the first quarter of 2002, as part of its collaboration to develop and commercialize alfimeprase. Hyseq expects to continue to incur significant operating losses, which may increase substantially

Table of Contents

as Hyseq further expands research and development of its potential biopharmaceutical product candidates and other operations, and as Hyseq prosecutes and enforces its intellectual property rights.

Comparison of Years Ended December 31, 2001 and 2000 and Years Ended December 31, 2000 and 1999. Since its inception, Hyseq has incurred net losses, and as of December 31, 2001, Hyseq had an accumulated deficit of $108.4 million. During 2001, Hyseq incurred a net loss of $36.5 million as compared to a $22.3 million net loss in 2000 and a net loss of $18.5 million in 1999. Hyseq expects to continue to incur significant net losses, which may increase substantially as it pursues research and development of its therapeutic protein candidates and other operations, and prosecutes and enforces its intellectual property rights.

Loss Attributable to Minority Interest

Loss attributable to minority interest of $0.1 million is recorded for the portion of Callida s losses attributable to minority stockholder Affymetrix. As the expected future level of Callida s losses increases, Hyseq anticipates recording additional losses attributable to minority interest up to the point where Affymetrix initial minority interest investment is depleted. Beyond that point, Hyseq will absorb 100% of the net losses until Callida generates net income.

Liquidity and Capital Resources

Hyseq s primary source of liquidity is cash from financing activities and from collaboration receipts. Hyseq generated cash of $17.3 million and $40.3 million from financing activities, and cash of $17.8 million and $16.9 million from collaborations in the first nine months of 2002 and 2001, respectively. Hyseq generated cash of $44.3 million, $1.3 million and $1.6 million from financing activities, and cash of $22.0 million, $15.6 million and $10.8 million from collaboration receipts in 2001, 2000 and 1999 respectively.

Hyseq s primary use of capital resources is to fund operating activities and to acquire capital equipment and make leasehold improvements. Hyseq used cash of $23.5 million and $19.0 million for operating activities, and cash of $1.8 million and $7.5 million to acquire capital equipment and make leasehold improvements in the first nine months of 2002 and 2001, respectively. Hyseq used cash of $21.5 million, $20.3 million and $11.9 million for operating activities, and cash of $12.6 million, $8.3 million and $4.4 million to acquire capital equipment and make leasehold improvements in 2001, 2000 and 1999, respectively.

While Hyseq expects operating expenses during the remainder of 2002 to continue to decrease moderately, Hyseq will need additional funding in 2003 in order to continue its biopharmaceutical research efforts and execution of clinical trials for alfimeprase. If Hyseq does not obtain adequate financing or collaboration receipts in a timely manner, this could significantly harm its business, financial condition, and results of operations, and may require Hyseq to delay and scale back one or more of its research or development programs, or relinquish greater rights to products at an earlier stage of development or on less favorable terms than it would otherwise seek to obtain, which could materially adversely affect its business, financial condition, and operating results.

Hyseq s future capital requirements and the adequacy of available funds will depend on many factors. Hyseq may not be able to secure additional financing to meet its funding requirements on acceptable terms, if at all. If Hyseq raises additional funds by issuing equity securities, substantial dilution to its existing stockholders may result. If Hyseq is unable to obtain additional funds it may have to significantly curtail the scope of its operations. Hyseq has implemented a plan to delay, scale back or eliminate some of its operating expenditures, including facilities expansion plans, until it obtains additional funding. This plan includes a hiring freeze, a freeze on capital expenditures and a deferral of as many of its contractual financial commitments as possible. If Hyseq is unable to obtain financing, it may need to look to its Chairman to provide additional financing, which he has agreed to do.

Table of Contents

Cash and Cash Equivalents, Cash on Deposit, and Short-term Investments

As of September 30, 2002, Hyseq had $4.3 million in cash. This amount reflects a net decrease of $8.1 million from the $12.3 million in cash Hyseq had as of December 31, 2001.

In addition, Hyseq has $1.1 million in restricted cash on deposit as security for a $1.0 million letter of credit in conjunction with a facility lease. Provided that no default has occurred under the lease, the letter of credit and the cash collateralizing it may be reduced by $0.5 million per year in July 2003, and July 2004. The cash on deposit at any time in conjunction with this letter of credit is restricted and cannot be withdrawn. Hyseq controls the investment of the cash and receives the interest earned thereon.

Cash inflows from the accelerated completion schedule agreed to by Hyseq and BASF Plant Science in May 2002 will be $5.3 million on December 31, 2002, and $2.0 million on January 31, 2003, provided Hyseq continues to meet its deliverables under the terms of the revised collaboration agreement. Other than net cash inflows in connection with its BASF collaboration, Hyseq does not anticipate receiving significant net cash inflows from any projects during the foreseeable future.

Comparison of the Years Ended December 31, 2001 and 2000. As of December 31, 2001, Hyseq had $12.3 million in cash and cash equivalents. These amounts reflect a net increase of $9.6 million from the $2.7 million in cash and cash equivalents Hyseq had as of December 31, 2000. This increase resulted primarily from the $20.0 million draw down of the first of its two lines of credit from its Chairman which was converted to common stock in March 2001, $20.7 million received from its August private stock offering net of offering expenses, and $8.0 million received from Affymetrix under the terms of its legal settlement and new collaboration, less cash used by operations of $21.5 million and capital spending of $12.6 million.

Comparison of Years Ended December 31, 2000 and 1999. As of December 31, 2000, Hyseq had $2.7 million in cash and cash equivalents. These amounts reflect a net decrease of $27.9 million from the $30.6 million in cash, cash equivalents and short-term investments it had as of December 31, 1999. This decrease resulted primarily from $21.0 million of net cash used in operating activities plus $8.3 million investments in equipment and capitalized software.

Cash Used in Operating Activities

Comparison of the Nine Months Ended September 30, 2002 and 2001. The amount of net cash used in operating activities was $23.5 million during the nine months ended September 30, 2002, increasing from $19.0 million used during the same period of 2001. The increase in cash used by operating activities was due primarily to higher research and development costs resulting from Hyseq s biopharmaceutical development efforts and Phase I clinical trials for alfimeprase, as well as payment of a $2.0 million loan to its President and CEO. These increases were partially offset by lower supplies and personnel spending resulting from the accelerated completion of its collaboration with BASF Plant Science according to an agreement signed in May 2002, and by lower rent payments for its 985 Almanor Avenue building as part of an agreement signed in August 2002 with its landlord to defer some rent amounts for three years, effective June 1, 2002.

Hyseq received cash of $15.7 million from BASF Plant Science in the first nine months of 2002. Hyseq also received cash in the first nine months of $0.5 million, $0.6 million, $0.5 million and $0.5 million from Kirin Brewery, Ltd., Intel Corporation, Agilent Technologies, and Celera Diagnostics, respectively, in connection with research collaborations and license agreements, and made lower payments to its collaboration partner University of California, San Francisco.

After the close of the quarterly period ending September 30, 2002, Hyseq and its landlord entered into agreements to terminate its eleven-year lease of buildings at 225, 249 and 257 Humboldt Court, Sunnyvale, California (originally entered into June 23, 2000) and to grant Hyseq a six-month option to purchase these properties for a purchase price of $15.3 million. These agreements provide that Hyseq s lease is terminated retroactively, effective as of October 1, 2002. Hyseq will pay a lease termination fee of $5.4 million (of which $3.1 million was already held by the landlord for prepaid rent and a security deposit). Also, Hyseq will pay approximately $4.5 million for the option to purchase the building, which is creditable against the

purchase price of the building if the option is ultimately exercised (of which $1.7 million is cash, $2.6 million is in the form of a six-month interest free promissory note guaranteed by its Chairman, Dr. Rathmann (the Option Note), and approximately $200,000 is in the form of warrants granted by Hyseq to the landlord). Also, Hyseq will pay additional option consideration of $95,000 per month commencing November 1, 2002 and ending when the option is exercised or April 30, 2003, whichever occurs first. Hyseq paid the entire lease termination and option fees on November 1, 2002. At the current time Hyseq has not decided whether it will exercise the purchase option.

Termination of the original lease will result in a reduction of future rental commitments under operating leases of approximately $33 million, with an average reduction of $3.7 million per year. Upon the exercise of its option to purchase the properties, the option fee of approximately $4.5 million will be applied towards the $15.3 million purchase price of the properties. The remaining $10.8 million of the purchase price will be financed for five years by the landlord at an annual interest rate of 8.5% and is secured only by the properties (the Purchase Note). At the time of purchase, the $2.6 million Option Note will convert into a five-year note on the same terms as the Purchase Note. Hyseq will make monthly payments on the Notes in the amount of $107,901 collectively for five years, at which time the remaining principal balance will be due to the landlord. Upon exercise of the purchase option the guarantee of the Option Note by its Chairman will terminate and Hyseq will put in place a $2.6 million letter of credit.

Comparison of Years Ended December 31, 2001 and 2000. The amount of net cash used in operating activities increased by $1.2 million to $21.5 million in 2001 from $20.3 million in 2000. This increase in cash used for operations in 2001 compared to 2000 was due primarily to increased research and development expenses related to Hyseq s pharmaceutical product candidates, and the addition of new leased facilities for laboratory expansion, partially offset by an increase in current liabilities including a $2.5 million accrual for major contract services and for $3.2 million deferred revenues related to the Affymetrix collaboration.

Comparison of Years Ended December 31, 2000 and 1999. The amount of net cash used in operating activities increased by $8.4 million to $20.3 million in 2000 from $11.9 million in 1999. This increase in cash used in operations in 2000 compared to 1999 was due primarily to increased research and development expenses related to Hyseq s pharmaceutical product candidates and its complete gene sequencing programs, and the addition of new leased facilities for laboratory expansion and payment of advanced rent for those lease facilities.

Cash Provided by (Used in) Investing Activities

Hyseq s investing activities have consisted primarily of capital expenditures.

Comparison of the Nine Months Ended September 30, 2002 and 2001. Net cash used in investing activities was $1.8 million during the nine months ended September 30, 2002, compared to $7.5 million during the same period of 2001. The decrease was primarily due to a freeze on new capital equipment and leasehold improvement expenditures during 2002. Hyseq expects net cash used in investing activities to stay at low levels for the foreseeable future.

Comparison of Years Ended December 31, 2001 and 2000. Net cash used in investing activities decreased by $21.2 million to $13.1 million used in 2001 by investing activities, compared to $8.1 million provided in 2000 by investing activities. The decrease was primarily due to no new net redemptions of investments in 2001, compared with $17.0 million net redemptions of short-term investments in 2000. Capital expenditures increased by $4.3 million to $12.6 million in 2001, primarily due to leasehold improvements, compared with $8.3 million in 2000.

Comparison of Years Ended December 31, 2000 and 1999. Net cash provided by investing activities increased by $5.7 million to $8.1 million in 2000 compared to $2.4 million in 1999. The increase was primarily due to higher net redemptions of short-term investments in 2000, partially offset by higher purchases of equipment used to support Hyseq s expanding research and development activities and

investment in capitalized software. In 2000, all of Hyseq s short-term investments were reinvested upon maturity into commercial paper with maturities of less than 90 days.

Cash Provided by Financing Activities

Comparison of the Nine Months Ended September 30, 2002 and 2001. Net cash provided by financing activities for the first nine months of 2002 was $17.3 million compared to $40.3 million for the same period of 2001.

On April 5, 2002, Hyseq completed a private placement with proceeds of approximately $14.3 million, net of offering expenses. The comparable period in 2001 included a private placement from which Hyseq received proceeds of approximately $20.7 million, net of offering expenses.

In August 2001, Hyseq received a commitment from Dr. Rathmann to provide a second line of credit of up to $20.0 million in aggregate principal amount, available for draw down through August 5, 2003. From February 2002 through November 1, 2002, Hyseq drew down an aggregate of $10 million under this line of credit, and, as of November 1, 2002, a further $10.0 million remains available for draw down in the future. For further details, see Management s Discussion and Analysis of Financial Condition and Results of Operations of Hyseq Disclosure Regarding Hyseq s Chairman below.

The comparable period in 2001 included a $20.0 million draw down of the first of two lines of credit extended to Hyseq by Dr. Rathmann, as discussed under Disclosure Regarding Hyseq s Chairman below.

In the first nine months of 2002, principal payments of capital leases and loan obligations were $1.9 million compared to the same period last year at $1.6 million. Proceeds from the issuance of common stock upon the exercise of stock options and the Employee Stock Purchase Plan were $0.4 million, compared to $0.7 million during the same period last year.

Its future capital requirements and the adequacy of available funds will depend on many factors. Hyseq may not be able to secure additional financing to meet its funding requirements on acceptable terms, if at all. If Hyseq raises additional funds by issuing equity securities, substantial dilution to its existing stockholders may result. If Hyseq is unable to obtain additional funds Hyseq may have to significantly curtail the scope of its operations. Hyseq has implemented a plan to delay, scale back or eliminate some of its operating expenditures, including facilities expansion plans, until it obtains additional funding. This plan includes a partial hiring freeze, a reduction in capital expenditures and a deferral of as many of its contractual financial commitments as possible. If Hyseq is unable to obtain third party financing, Hyseq may need to look to its Chairman to provide additional financing, which he has agreed to do.

Comparison of Years Ended December 31, 2001 and 2000. Net cash provided by financing activities increased to $44.3 million in 2001 compared to $1.3 million in 2000. The increase was primarily due to the draw down of the first of two $20.0 million lines of credit from the Chairman of Hyseq s Board of Directors, the completion of a private stock placement from which Hyseq received net proceeds of $20.7 million, and a $4.0 loan from Affymetrix as part of the Callida collaboration. The increase was partially offset by payments on existing capital lease and loan obligations.

As of December 31, 2001, minority interest was $0.1 million. Minority interest is related to the establishment of Callida in October 2001, a majority-owned subsidiary, and reflects the initial minority stockholders capitalization less the minority stockholders portion of the net losses incurred to date.

Comparison of Years Ended December 31, 2000 and 1999. Net cash provided by financing activities decreased slightly to $1.3 million in 2000 compared to $1.6 million in 1999. The decrease was primarily due to lower proceeds from financing arrangements, partially offset by higher proceeds from employee stock option exercises and higher payments on loan obligations. In 2000, Hyseq borrowed the remaining $2.0 million of a $5.0 million asset-backed financing commitment obtained in 1999.

Table of Contents

Disclosure Regarding Hyseq s Chairman

In November 2000, Hyseq received a commitment from Dr. Rathmann to provide a line of credit of up to $20.0 million in aggregate principal amount. The promissory note under the line of credit relating to outstanding amounts was convertible at Hyseq s option into shares of Hyseq common stock at fair market value. On March 20, 2001 Hyseq drew down the entire $20.0 million amount and, following ratification of the merger by its stockholders at last year s annual meeting, Hyseq converted the note for the entire amount into 2,237,637 shares of Hyseq common stock.

In August 2001, Hyseq received a commitment from Dr. Rathmann to provide a second line of credit of up to $20.0 million in aggregate principal amount, available for draw down through August 5, 2003. Amounts outstanding under the line of credit bear interest at prime plus 1% and are payable in 48 equal monthly installments beginning upon the expiration date of August 5, 2003. The promissory note issued pursuant to the line of credit may be repaid by converting into shares of Hyseq common stock at any time upon the agreement of Hyseq and Dr. Rathmann at a price based upon the average price of Hyseq common stock over the 20-day period prior to the conversion or, if in connection with an equity financing, at the offering price. In February 2002, Hyseq drew down $4.0 million under the line of credit. On October 21, 2002 Hyseq drew down an additional $2.0 million under the line of credit. On November 1, 2002, Hyseq drew down an additional $4.0 million under the line of credit in connection with agreements executed October 25, 2002 between Hyseq and its landlord to terminate its building leases at each of 225, 249 and 257 Humboldt Court, Sunnyvale, California and grant Hyseq a six-month option to purchase these properties. The balance available as of November 1, 2002 for draw down under the second line of credit from Dr. Rathmann was $10.0 million.

Dr. Rathmann guaranteed to a maximum of $1.5 million and provided the collateral for Hyseq s $4.0 million letter of credit under Hyseq s 985 Almanor lease. Dr. Rathmann also provided collateral for a $250,000 letter of credit under Hyseq s Humboldt Ct. lease termination agreement and guaranteed the $2.6 million note that was part of the option fee.

On February 1, 2000, Hyseq s Board of Directors granted Dr. Rathmann an option to purchase 1,000,000 shares of Hyseq common stock for services as Chairman of the Board, at an exercise price equal to the then-current market price on the day before the date of grant of $31.688 per share, which option vests and becomes exercisable over two years at a rate of one-third upon grant and one-third on each yearly anniversary thereafter. The term of the option is ten years. On August 21, 2001, Hyseq s Board of Directors granted Dr. Rathmann an option to purchase 1,000,000 shares of Hyseq common stock, for services as Chairman of the Board at an exercise price equal to the then-current market price of $8.635 per share. This option has a ten year term, and vests and becomes exercisable over four years at a rate of one-fourth upon the one year anniversary of the date of grant and 1/48th of the total number of shares upon each monthly anniversary thereafter. In the event of a change in control of Hyseq, the option shall become immediately exercisable. Upon the termination of Dr. Rathmann s directorship with Hyseq for any reason or no reason, except as a result of Dr. Rathmann s death or disability, the unvested portion of the option shall be forfeited, and the vested unexercised portion of the option shall be exercisable for a period of thirty days following termination or the expiration of the term of the option if earlier. The option shall be exercisable by Dr. Rathmann or his legal representative, and in the event of his death only by his beneficiary. The option shall not otherwise be transferable by Dr. Rathmann or by operation of law, and any attempted transfer or other disposition of the option shall be void and shall result in the cancellation of the option. Hyseq s Board of Directors has the right to amend or terminate the provisions of the option in any manner it may deem necessary or advisable to carry out the purpose of the grant as the result of, or to comply with, any change in applicable regulations, interpretation or statutory enactment.

Dr. Rathmann receives no cash compensation as an employee and instead receives options to purchase 3,000 shares per month. To date, at Dr. Rathmann s request, Hyseq has not granted him any equity incentives in recognition of the lines of credits that he has made available to Hyseq, his guarantee of Hyseq s real estate leases, his provision of collateral for two of Hyseq s letters of credit under facilities leases, or the occasional use of his private jet for its business purposes. Hyseq believes that the Board is likely to take action in the

Table of Contents

future to provide appropriate incentives to Dr. Rathmann in order to ensure his continued active involvement with Hyseq.

Qualitative and Quantitative Disclosures About Market Risk

Market Rate Risk

Hyseq has exposure to changes in interest rates in its cash equivalents, which are held primarily in money market accounts which earn interest at variable rates. Hyseq does not use derivative financial instruments in its investment portfolio. Hyseq places its investments with high quality issuers and, by policy, limit the amount of credit exposure to any one issuer. Hyseq is averse to principal loss and ensures the safety and preservation of its invested funds by limiting default, market and reinvestment risk. The recorded carrying amounts of Hyseq s cash equivalents approximate fair value due to their short-term maturities.

Hyseq also has exposure to changes in interest rates in its line of credit with its Chairman, which bears interest at the prime rate plus one percentage point. Hyseq s interest rate exposure is mitigated by its ability to repay amounts outstanding under the line of credit with Hyseq common stock.

Changes in interest rates do not affect interest income on Hyseq s restricted cash as it is maintained in commercial paper with fixed rates and maturities of less than 90 days.

Changes in interest rates do not affect interest expense on Hyseq s lease obligations as they bear fixed rates of interest.

Changes in interest rates do not affect Hyseq s note payable as it bears fixed rate of interest.

The table below presents the amounts and related interest rates of Hyseq s cash equivalents, restricted cash, lease obligations, line of credit, and note payable at September 30, 2002, December 31, 2001 and 2000:

	2000		2001		September 30, 2002	
	Average Rate	Carrying Amount	Average Rate	Carrying Amount	Average Rate	Carrying Amount
		(In thousands)		(In thousands)		(In thousands)
Cash equivalents	5.50%	$2,699	3.17%	$12,329	0.97%	$4,272
Restricted cash	6.42%	$2,106	4.52%	$ 1,606	2.37%	$1,106
Lease obligation	11.90%	$7,100	11.60%	$ 4,734	11.64%	$2,799
Line of credit	N/A%	$	N/A%	$	5.75%	$4,000
Note payable	N/A%	$	7.50%	$ 4,000	7.50%	$4,000

Table of Contents

Security Ownership of Certain Beneficial Owners and Management

The following table sets forth certain information regarding the beneficial ownership of Hyseq s common stock as of November 15, 2002 by: (1) each of its directors; (2) each of its named executive officers for the month ended September 30, 2002; (3) by each person known by it to be the beneficial owner of more than 5% of its outstanding common stock; and (4) all of its directors and executive officers as a group. As of November 15, 2002, Hyseq had 23,035,854 shares of its common stock outstanding.

	Shares Beneficially Owned(1)		
Name and Address of Beneficial Owner(1)	Number of Shares	Percentage Before the Merger	Percentage After the Merger
George B. Rathmann(2)	5,051,411	20.4	7.8
Robert D. Weist(3)	305,314	1.3	*
Raymond F. Baddour(4)	69,539	*	*
Thomas N. McCarter, III(5)	77,219	*	*
Mary K. Pendergast(6)	5,000	*	*
Richard B. Brewer(7)	5,000	*	*
Ted W. Love(8)	378,347	1.6	*
William F. Bennett(9)	122,191	*	*
Linda A. Fitzpatrick(10)	46,354	*	*
Peter S. Garcia(11)	83,956	*	*
Li-Hsien Rin-Laures(12)	71,571	*	*
Nina V. Giles(13)	0	*	*
Walter Funk(14)	26,979	*	*
All Directors and Executive Officers as a Group (13 persons)	6,242,881	24.4	9.6

* Represents beneficial ownership of less than 1% of Hyseq s common stock.

(1) Beneficial ownership is determined in accordance with the Rules 13d-3 under the Exchange Act and generally includes voting or investment power with respect to securities. Shares of common stock subject to options and warrants which are currently exercisable, or will become exercisable within 60 days of November 15, 2002, are deemed outstanding for computing the percentage of the person or entity holding such securities but are not outstanding for computing the percentage of any other person or entity. Additionally, for calculating the percentage of shares beneficially owned after the merger, the number of shares of Hyseq common stock issuable in exchange for 24,117,061 shares of Variagenics common stock outstanding as of November 15, 2002 has been included in the calculation of outstanding Hyseq common stock. Except as indicated by footnote, and subject to the community property laws where applicable, to Hyseq s knowledge the persons named in the table above have sole voting and investment power with respect to all shares of common stock shown as beneficially owned by them. Unless otherwise indicated, the address for each person is 675 Almanor Avenue, Sunnyvale, California 94085.

(2) Represents: (i) 3,327,364 shares of common stock held in trust for the benefit of the Rathmann family, for which Dr. Rathmann and his spouse serve as co-trustees; (ii) 1,438,333 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of November 15, 2002; and (iii) 285,714 shares of common stock issuable upon the exercise of warrants held by the Rathmann Family Trust.

(3) Represents: (i) 236,675 shares held in trust for the benefit of the Weist family for which Mr. Weist and his spouse serve as co-trustees, (ii) 53,639 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of November 15, 2002; and (iii) 15,000 shares of common stock issuable upon the exercise of warrants held by the Weist Family Trust.

(4) Represents 69,539 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of November 15, 2002.

(5)

Represents: (i) 19,200 shares of common stock owned by Mr. McCarter, and (ii) 58,019 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of November 15, 2002.

(6) Represents 5,000 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of November 15, 2002.

Table of Contents

(7) Represents 5,000 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of November 15, 2002.

(8) Represents: (i) 19,639 shares of common stock owned by Dr. Love, (ii) 351,563 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of November 15, 2002; and (iii) 7,145 shares of common stock issuable upon the exercise of warrants held by Dr. Love. Excludes 423,437 shares issuable upon the exercise of options which are not currently exercisable and will not be exercisable within 60 days of November 15, 2002.

(9) Represents: (i) 26,504 shares of common stock owned by Dr. Bennett, (ii) 88,542 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of November 15, 2002; and (iii) 7,145 shares of common stock issuable upon the exercise of warrants held by Dr. Bennett. Excludes 236,458 shares issuable upon the exercise of options which are not currently exercisable and will not be exercisable within 60 days of November 15, 2002.

(10) Represents: (i) 46,354 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of November 15, 2002. Excludes 203,646 shares issuable upon the exercise of options which are not currently exercisable and will not be exercisable within 60 days of November 15, 2002.

(11) Represents: (i) 17,957 shares of common stock owned by Mr. Garcia, (ii) 58,854 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of November 15, 2002; and (iii) 7,145 shares of common stock issuable upon the exercise of warrants held by Mr. Garcia. Excludes 241,146 shares issuable upon the exercise of options which are not currently exercisable and will not be exercisable within 60 days of November 15, 2002.

(12) Represents: (i) 738 shares of common stock owned by Dr. Rin-Laures, and (ii) 70,833 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of November 15, 2002. Excludes 179,167 shares issuable upon the exercise of options which are not currently exercisable and will not be exercisable within 60 days of November 15, 2002.

(13) Excludes 175,000 shares issuable upon the exercise of options which are not currently exercisable and will not be exercisable within 60 days of November 15, 2002.

(14) Represents: (i) 26,979 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of November 15, 2002. Excludes 123,021 shares issuable upon the exercise of options which are not currently exercisable and will not be exercisable within 60 days of November 15, 2002.

Table of Contents

Description of Hyseq Capital Stock

The following is a summary of the material terms of Hyseq s capital stock. Because it is only a summary, it does not contain all the information that may be important to you. Accordingly, you should read carefully the more detailed provisions of the articles of incorporation of Hyseq, as amended, the bylaws of Hyseq and the rights agreement between Hyseq and U.S. Stock Transfer Corporation, each of which has been filed with the SEC, as well as applicable Nevada law. See Comparison of Stockholder Rights and Corporate Governance Matters.

General

As of the date of this joint proxy statement/prospectus, Hyseq s authorized capital stock consists of:

100,000,000 shares of common stock, par value $0.001 per share,

3,000,000 shares of Series A Preferred Stock, par value $0.001 per share, and

5,000,000 shares of All Other Series Preferred Stock, par value $0.001 per share.

As of the record date for the Hyseq special meeting, shares of Hyseq common stock were issued and outstanding and no shares of Hyseq preferred stock were issued and outstanding.

Common Stock

Holders of Hyseq common stock are entitled to one vote per share for the election of directors and all other matters submitted for stockholder vote, except matters submitted to the vote of another class or series of shares. Holders of common stock are not entitled to cumulative voting rights. The approval of 66 2/3% of the voting rights of the common stock is required to make certain amendments to Hyseq s articles of incorporation, amend Hyseq s by-laws, and to remove a director from Hyseq s board of directors. The affirmative vote of the holders of a majority of Hyseq s outstanding common stock is required to approve the sale or exclusive license or assignment having the same effect as a sale by Hyseq of U.S. Patent 5,202,231. See Comparison of Stockholder Rights and Corporate Governance Matters.

The holders of common stock are entitled to dividends in such amounts and at such times, if any, as may be declared by the board of directors out of funds legally available therefor. Hyseq has not paid any dividends on its common stock and does not anticipate paying any cash dividends on such stock in the foreseeable future. Upon liquidation, dissolution or winding up of Hyseq, the holders of common stock are entitled to share ratably in all net assets available for distribution to stockholders after payments to creditors and holders of senior securities. The common stock is not redeemable and has no preemptive, conversion or sinking fund rights. The rights of the holders of common stock are subject to the rights of the holders of any Preferred Stock which may, in the future, be issued. All outstanding shares of common stock are, and the shares of common stock to be issued by Hyseq pursuant to the merger when issued will be, duly authorized, validly issued, fully paid and non-assessable.

Preferred Stock

The Hyseq board of directors is authorized to determine the dividend rights, dividend rate, conversion rights, voting rights, rights and terms of redemption, liquidation preferences, sinking fund rights, the number of shares constituting any series of preferred stock, and the designation of any series of preferred stock. The issuance of preferred stock may have the effect of delaying, deferring or preventing a change in control of Hyseq without further action by the stockholders and may adversely affect the voting and other rights of the holders of common stock. The issuance of preferred stock with voting and conversion rights may adversely affect the voting power of the holders of common stock, including the loss of voting control to others. In connection with Hyseq s rights agreement, the Hyseq board of directors has authorized the issuance of up to 20,000 shares of preferred stock as Series B Junior Participating Preferred Stock in connection with the adoption of its right plan discussed below.

Table of Contents

Stockholder Rights Plan

On June 5, 1998, Hyseq adopted a stockholder rights plan pursuant to a rights agreement. The following description of the rights agreement is subject in its entirety to the terms and conditions of the rights agreement. You should read the rights agreement carefully. See Where You Can Find More Information below.

Exercisability of Rights. Pursuant to Hyseq s rights agreement, one whole right attaches to each share of Hyseq common stock outstanding. Each right entitles the registered holder to purchase from Hyseq one one-thousandth (1/1000) of a share of Hyseq Series B Junior Participating Preferred Stock at an initial purchase price of $175.00, subject to customary antidilution adjustments. The rights do not become exercisable until the earlier to occur of:

10 business days following a public announcement that a person or group has acquired beneficial ownership of 15% (or 27.5% in the case of an approved stockholder) or more of Hyseq s outstanding common stock (any such person or group is referred to as an acquiring person), or

10 business days (or a later date as determined by the Hyseq board of directors) following the commencement or announcement of an intention to make a tender offer or exchange offer, that would result in a person or entity becoming an acquiring person

The rights will expire on June 5, 2008, unless they are redeemed or exchanged by Hyseq before that time.

Flip-In Feature. When a person or group becomes an acquiring person (or at such later time as determined by independent directors of Hyseq s board of directors) then each registered holder of a Hyseq right, except for such person or group, will be entitled to purchase, for the exercise price, shares of Hyseq common stock having a then current market value equal to two times the exercise price of the right.

Flip-Over Feature. Subject to specified exemptions, in the event that Hyseq is involved in a merger, or Hyseq sells more than 50% of its assets or earning power to an acquiring company, each right will entitle the holder, other than an acquiring person, to purchase, upon exercise, a number of shares of common stock of the acquiring company having a then current market value of two times the exercise price of the right.

Redemption. Hyseq may, at its option, at any time prior to the close of business on the tenth day following the day a person or group becomes an acquiring person, redeem all of the then-outstanding rights at a redemption price of $.001 per right, subject to certain adjustments.

At any time after a person or group becomes an acquiring person and prior to the acquisition by that person or group of 50% or more of the outstanding common stock, Hyseq s board of directors may cause it to acquire the rights (other than rights owned by the acquiring person) of the outstanding shares of common stock of Hyseq, in whole or in part, in exchange for one share of common stock per right.

No Rights as a Stockholder. Until a right is exercised, the holder thereof, as such, will have no rights as a stockholder of Hyseq and will not have the right to vote or to receive dividends by virtue of the right.

Amendment of the Rights. While the rights are redeemable, Hyseq may supplement or amend any provision of the rights agreement in any respect without the approval of any holders of rights or common shares. When the rights are no longer redeemable, Hyseq may supplement or amend the rights agreement without the approval of any holders of rights certificates as long as the supplement or amendment does not adversely affect the interests of the holders of rights (other than an acquiring person). Any supplement or amendment to the rights agreement shall require the affirmative vote of a majority of Hyseq s independent directors. Any extension of the final expiration date of the rights shall require the affirmative vote of three-quarters of the independent directors.

Anti-takeover Effects. Hyseq s rights agreement is designed to maximize the value of Hyseq s outstanding common stock in the event of an unsolicited attempt to take over Hyseq in a manner or on terms that are not approved by the Hyseq board of directors. Once the Hyseq rights have become exercisable, the rights will cause substantial dilution to a person or group that attempts to acquire or merge with Hyseq in

Table of Contents

most cases. The rights could discourage, delay or prevent certain types of transactions involving an actual or potential change in control of Hyseq, including transactions in which stockholders might otherwise receive a premium for their shares over current market prices. The rights should not interfere with any merger or other business combination approved by the Hyseq board of directors since Hyseq may amend the rights agreement to make it inapplicable to such a transaction or redeem.

The Hyseq rights agreement does not apply to the merger with Variagenics.

Anti-Takeover Effects of Articles and By-Laws

Hyseq s articles of incorporation and by-laws include a number of provisions that may have the effect of encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with Hyseq s board of directors rather than pursue non-negotiated takeover attempts. These provisions include:

that members of the Hyseq board of directors serve staggered terms of up to three years;

that the holders of 66 2/3% of the voting rights of all classes of stock entitled to vote are required to remove directors of Hyseq;

that the board of directors may fill vacancies on the board of directors;

that all stockholder action must be effected at a duly called meeting and not by a consent in writing;

that Hyseq s stockholders may call a special meeting of stockholders only upon a request of stockholders owning not less than 50% of Hyseq s capital stock;

that stockholders must comply with certain notice requirements to nominate directors to serve of Hyseq s board of directors and to bring proposals before annual and special meetings of Hyseq;

that the board of directors is authorized to designate the rights and privileges of Hyseq s authorized and unissued preferred stock; and

that the holders of 66 2/3% of the voting rights of all classes of stock entitled to vote are required to amend the by-laws and certain provisions of the articles of incorporation.

These provisions are intended to enhance the continuity and stability in the composition of Hyseq s board of directors and management and in the policies formulated by them. These provisions are also designed to maximize the value of Hyseq s outstanding common stock in the event of an unsolicited attempt to takeover Hyseq in a manner or on terms that are not approved by the Hyseq board of directors and to discourage certain tactics that may be used in proxy fights.

However, these provisions could discourage, delay or prevent certain types of transactions involving an actual or potential change in control of Hyseq, including transactions in which stockholders might otherwise receive a premium for their shares over current market prices. These provisions should not interfere with any merger or other business combination approved by the Hyseq board of directors.

See Risk Factors Risks Related to the Combined Company Hyseq has implemented anti-takeover provisions that may reduce the market price of the Hyseq common stock and Comparison of Stockholders Rights and Corporate Governance Matters for further discussion of these provisions.

Transfer Agent

The transfer agent and registrar for the Common Stock is U.S. Stock Transfer Corporation, 1745 Gardena Ave., Glendale, California 91204, (818) 502-1404.

Table of Contents

INFORMATION ABOUT VARIAGENICS

Business of Variagenics

Variagenics is a leader in applying pharmacogenomics technology to the discovery, development and commercialization of personalized drugs and molecular diagnostic products. Variagenics primary therapeutic focus is cancer. Pharmacogenomics is the study of the correlation between an individual s genetic differences, or genetic variability, and his or her specific response to a drug. The most common form of this genetic variability is a single nucleotide polymorphism, or SNP. Using a drug pathway approach, Variagenics identifies therapeutically important genetic markers, including SNPs, groups of SNPs called haplotypes, and other markers. Variagenics uses its pharmacogenomics technology to select an optimal set of these genetic markers for clinical testing, and ultimately, the development of high-value molecular diagnostic products which predict patient response to drugs. Variagenics technology, expertise and proprietary data offers pharmaceutical and biotechnology companies a full range of solutions to support key steps of their drug discovery and development process, extending from drug target identification through clinical trials to commercialization. Variagenics also intends to develop its own proprietary molecular diagnostic products. Variagenics has established multiple sources of revenue, including collaboration revenues, milestone payments and license fees, and intends to obtain royalties on products commercialized using its technology.

From its inception in December 1992 through 1996, Variagenics focused on research activities directed toward developing a novel genetic approach to cancer therapy. In 1996, Variagenics significantly broadened its focus to include discovery of SNPs and other genetic markers, and development of pharmacogenomics technologies, including a proprietary NuCleave DNA testing and analysis technology, with applications targeted to several therapeutic areas, including cancer, central nervous system disorders, cardiovascular disease and inflammatory disorders, among others. In 2002, Variagenics implemented a restructuring plan to conserve cash and focus resources on its oncology molecular diagnostic development programs. Variagenics also discontinued its NuCleave product.

Industry Background

The effect that a drug has on an individual is often a function of that individual s unique genetic make-up. Genetic variation may also explain why some individuals contract certain diseases and others do not, and may also determine why some individuals respond differently to the same drug. Typically, drugs are developed to interact with a single version of a given protein in the human body. Accordingly, a drug may only be effective in individuals that carry the specific variant of the protein for which the drug was designed. Individuals who have genetically-caused variation in these drug targets, or in the proteins involved in the metabolism of the drug, may not respond to the drug or may experience adverse side effects.

The methods used by the pharmaceutical industry to develop new drugs and to improve existing drugs are expected to undergo a fundamental transformation to take genetic variation into account. In fact, genetic variation can play a significant role in all stages of drug discovery and development and can also be used to help provide information to a physician to select the best drug for a particular patient.

Genomics

The exact DNA sequence in all the genes of an individual, called a genome, is unique to each individual and forms each individual s genetic make-up. Genomics, broadly defined, is the study of the genome and its importance in human physiology and disease.

The field of genomics is proceeding through the following three interactive phases:

identifying, or sequencing, the approximately 3 billion base pairs of DNA;

defining the functional role of each of the genes within the human genome; and,

most recently, applying pharmacogenomics to drug development and to the development of novel molecular diagnostic products.

Table of Contents

The use of genomics could enable physicians to treat disease prior to the development of clinical symptoms and, in particular, to tailor treatments to the unique genetic make-up of an individual. For this to become a reality, however, the enormous amount of genomics data currently being generated must be sorted and interpreted in a cost-effective fashion and in a method practical for use in clinical testing.

Genetic Variability, SNPs, Genotypes and Haplotypes

A difference in one or more nucleotide base of a DNA sequence, referred to as a genetic variation, can modify the way a gene functions. The most common type of genetic variation is called a single nucleotide polymorphism, or SNP. It is estimated that hundreds of thousands of SNPs contribute to the differences between individuals and among groups of individuals. However, only a small subset of those SNPs is likely to be related to disease susceptibility or to how an individual responds to a drug. The challenge is to prioritize which subset of SNPs can be effectively utilized within the costly clinical trial process.

After a SNP is discovered, a genetic test, or assay, must be developed to allow for rapid and repetitive testing of the occurrence of that SNP in a targeted population. The basic process to identify the presence of a SNP is called genotyping. A patient s genotype contains an analysis of the SNPs identified for that patient for a particular evaluation. Generally, a genotyping analysis will identify the presence of a small subset of the total SNPs in a patient.

A more profound test in many cases is to identify the group of SNPs, or haplotype, that collectively exerts an effect on drug action. Variagenics believes that haplotypes should have far greater predictive value than individual SNPs, and that researchers will be increasingly turning to haplotypes as a better indicator of the potential effects of drugs. Variagenics also believes that haplotyping assays will reduce the total number of possible explanations for SNP variations down to a number that is practical to test in the size of clinical trials commonly conducted in a drug development program.

Pharmacogenomics

It has long been known that people respond differently to the same drug. The field of pharmacogenomics studies these variations in drug response and their relation to genetic differences. Variagenics believes that the emerging ability to correlate drug response with SNPs and other genetic markers should enable doctors to prescribe appropriate drugs to patients with the goal of maximizing drug response and minimizing negative side effects.

Drug Target Identification and Validation

A pharmacogenomic screening capability, introduced early in the drug target development process, could save drug development sponsors significant time and money. Pharmaceutical companies could use targeted pharmacogenomic screening to eliminate non-promising compounds sooner. Compounds that make it through this screening process should have a higher chance of success.

Clinical Trials

Making the clinical trial process more efficient is critical to a pharmaceutical company s ability to manage its costs. The challenge for drug developers is to use meaningful pharmacogenomics data to predict which patients are likely to benefit from a drug or likely to experience negative side effects. Pharmacogenomics information could be used to reduce the number of patients in many clinical trials. Pre-selecting patients for a clinical protocol who are likely to respond to the drug candidate could significantly reduce the required sample size. In addition, demonstrating superior efficacy or reduced toxicity in a defined patient population could hasten or help secure regulatory approval.

Commercialization

Pharmacogenomics data about an individual s potential response to a drug creates opportunities to enhance the commercial value of pharmaceuticals. Given the high cost of drug development, the ability to

Table of Contents

properly market a new drug to its ideal target population is key to maximizing the drug s potential value. In addition, broad usage of a drug in patient segments where the drug is less effective or more toxic could jeopardize overall usage of the drug, even to the point of recall. If the appropriate set of pharmacogenomics data could be identified and the appropriate diagnostic tests were developed for a given drug, patients could be steered more quickly to appropriate therapies. These tests could allow pharmaceutical companies to engage in highly-focused product positioning and marketing campaigns.

How Variagenics Applies Pharmacogenomics

Variagenics offers pharmaceutical and biotechnology companies a broad range of solutions for applying pharmacogenomics to the discovery and development of new drugs and diagnostics, extending from drug target identification through clinical testing to commercialization. Variagenics also intends to develop proprietary molecular diagnostic products by identifying genetic markers associated with response to cancer therapies, with the goal of optimizing patient care.

Variagenics uses an extended candidate gene approach to develop a highly-characterized proprietary database of genetic variation.

Variagenics proprietary ProSNP™ database is a comprehensive collection of genetic variability data specific to pharmacogenomics and relevant to major drugs in development, including drugs for cancer and for cardiovascular, central nervous system and inflammatory disorders. Variagenics has targeted its SNP discovery to extended candidate gene sets considered most likely to affect drug activity. Moreover, Variagenics SNP detection is performed on DNA samples derived from an ethnically and geographically diverse panel of over 100 anonymous individuals. This provides a greater than 99% probability of detecting SNPs with a frequency in the population of 10% or greater. Variagenics database of SNPs is highly-characterized. It includes information on the percentage occurrence of selected SNPs in a target population and information on Variagenics SNPs potential significance to drug response. The database also contains critical information regarding important haplotype groupings. As of November 15, 2002, Variagenics database contains over 31,000 SNPs and over 13,000 haplotypes.

Variagenics performs custom SNP discovery for its collaborators, working jointly to select an extended set of candidate genes. Alternatively, Variagenics can screen for SNPs in the DNA from patients in a clinical trial with a specific disease or drug response.

Variagenics uses its technologies to select an optimal set of genetic markers for clinical testing, including SNPs, haplotypes and other genetic changes unique to cancer.

Variagenics proprietary technologies filter and focus the tremendous volume of SNP and other genetic information into a usable amount of data suitable for clinical research testing. The hundreds of thousands of individual SNP data points now entering the public and private domain have little commercial utility without a process for reducing this information to a manageable set of genetic markers. Variagenics proprietary bioinformatics software allows researchers to compare genetic sequence data with public and proprietary databases to quickly analyze the common haplotypes in key genes. In addition, Variagenics has developed experimental methods to identify haplotypes that are associated with drug action. Variagenics believes that the future effectiveness of pharmacogenomics will largely depend on the ability to experimentally detect haplotypes, and that Variagenics is well positioned to be a leader in this new emerging technology.

Variagenics has also developed a methodology for analyzing the functional consequences of SNPs. This methodology provides a means for predicting which of the subset of SNPs that encode amino acid substitutions are most likely to affect the function or stability of a target protein. Variagenics is using this scientific method to rapidly identify influential genetic variations in patient populations.

To complement its expertise in working with polymorphism, Variagenics also uses a variety of technologies to examine genetic changes unique to cancer. These include methods for:

measuring changes in gene copy number;

analyzing gene expression; and

identifying promoter methylation patterns in tumors.

Combining these approaches with genotyping provides the most comprehensive genetic picture of a tumor to date.

Variagenics is also developing new statistical methods for identifying associations between multiple types of markers and therapeutic outcomes. Such analysis increases the probability that Variagenics will discover marker sets with strong clinical associations, ultimately leading to a molecular diagnostic product.

Variagenics plans to develop new diagnostic products and improved drugs both internally and with its collaborators. Ultimately, Variagenics pharmacogenomics approach should enable the development of improved, targeted therapeutic and diagnostic products. Variagenics anticipates that the application of its technologies will substantially impact the drug development programs of its pharmaceutical collaborators.

Variagenics is funding the internal development of diagnostic programs, as well as establishing research collaborations to co-develop additional diagnostics products. Variagenics has commenced proof-of-principle clinical studies intended to validate genetic markers it has selected for predicting response to cardiovascular drugs. In addition, Variagenics has initiated clinical studies on a family of diagnostic tests to determine optimal treatment for colon cancer.

Variagenics has developed a unique approach to cancer therapy called Variagenic® Targeting, which is based on its understanding of the deterioration of chromosomes in cancer cells, or loss of heterozygosity. Variagenics has identified over 20 potential targets for new drugs.

Business Strategy

Variagenics business strategy focuses on applying pharmacogenomics to the development and commercialization of new pharmaceutical and diagnostic products, based on its proprietary technologies, databases and expertise. The key elements of Variagenics strategy are:

Rapidly commercialize the full range of pharmacogenomics capabilities;

Establish diverse sources of revenue;

Capitalize upon bringing improved pharmaceutical and diagnostic products to market;

Maintain and improve the proprietary technology base; and

Use management s industry expertise in target business segments.

Rapidly commercialize the full range of pharmacogenomics capabilities

Variagenics provides a comprehensive product offering covering key stages of pharmaceutical product development, from discovery through development to commercialization. Variagenics highly characterized proprietary database of SNPs, haplotypes and other genetic variations, and its expertise in applying pharmacogenomics to the development of therapeutics and novel diagnostics offers pharmaceutical and diagnostic companies a complete solution that allows for more cost-effective and improved drug and diagnostic test development.

Establish diverse sources of revenue

Variagenics has targeted several complementary strategic business segments to provide a diverse set of revenue sources. Variagenics works with collaborators to provide pharmacogenomic solutions from drug development through commercialization. Revenues are currently generated from collaboration funding, milestone achievements, and license fees, and Variagenics expects to ultimately earn additional revenues from royalties on drugs and diagnostic products as they are launched.

Table of Contents

Capitalize upon bringing improved pharmaceutical and diagnostic products to market

Variagenics expects to add significant value to its pharmaceutical collaborators drugs. A corresponding part of its strategy is to develop and commercialize the diagnostic tests that will direct the selection of the most appropriate drug regimen for a patient. Commercialization is expected to be accomplished through collaborations in the life sciences, reference laboratories and diagnostics manufacturing fields.

Maintain and improve the proprietary technology base

Variagenics plans to continue to develop technologies for the commercial application of pharmacogenomics. Variagenics has established a proprietary SNP database clustered among genes important to common drug mechanisms and pathways related to drug efficacy, side effects and metabolism. Variagenics will continue to pursue innovation to establish:

proprietary databases and the right to use newly discovered SNPs and genes;

proprietary positions for technologies used to detect genetic variances, including genotyping and haplotyping; and

proprietary rights to genetic pathway targets involved in drug response in major disease categories.

Use management s industry expertise in target business segments

Variagenics has established a management team that has expertise across the genomics, pharmaceutical, diagnostic, life sciences and clinical research industries. Variagenics uses this breadth of industry expertise to target pharmacogenomics opportunities in these industries.

Commercial Collaborations

Variagenics has established, or intends to establish, commercial collaborations with leading companies in each of its targeted market sectors, including pharmaceuticals/ biotechnology, clinical research organizations, life sciences and diagnostics/ laboratory services.

In the pharmaceuticals/ biotechnology sector, Variagenics has entered into collaborations with Novartis Pharmaceuticals Corporation, Amgen Inc., Boehringer Ingelheim Pharmaceuticals, Inc. and Isis Pharmaceuticals, Inc. In May 2002, Variagenics entered into an agreement with Novartis Pharmaceuticals Corporation to identify markers and develop molecular diagnostics to predict patient response to Gleevec and PKI 166, an EGFr antagonist, both in development for prostate cancer. Variagenics is receiving funding from Novartis for applying its integrated suite of cancer genome-specific technologies and performing statistical analyses to associate genetic markers with clinical outcomes. Variagenics also retains the exclusive rights to any resulting molecular diagnostic tests. In August 2000, Variagenics signed a collaborative agreement with Boehringer Ingelheim to utilize its capabilities in the development of a new therapeutic candidate by Boehringer Ingelheim. The goal of the program is to identify genetic markers predictive of therapeutic response, and to use this information in drug development as well as in the development of a diagnostic test. In 2001 and 2002, Variagenics delivered its marker discovery report and assays for potential use in prospective clinical trials. Variagenics entered into agreements with Isis and Amgen in 2000 and 2001, respectively. Variagenics has delivered its marker discovery reports under these agreements. In 2001, Variagenics entered into a research and development collaboration with GeneMatrix, Inc., a Korean biotechnology company, to develop molecular diagnostic products for predicting response to drugs in the treatment of colon and gastric cancer. Under the collaboration, GeneMatrix has rights for products marketed in Korea, and Variagenics has rights for products marketed in the rest of the world. As part of the collaboration, GeneMatrix purchased a NuCleave® system.

In the clinical research organization sector, both Covance, Inc. and Quintiles Transnational Corporation selected Variagenics as their collaborator for complementary segments of the market.

Covance, a world-wide market leader in providing laboratory services for clinical trials, selected Variagenics as their provider of genotyping assays. Variagenics placed a NuCleave® system at Covance s

Table of Contents

largest testing laboratory in Indianapolis, Indiana. The August 1999 alliance agreement with Covance provides funding to Variagenics for assay development and royalties payable for laboratory tests performed at Covance. From the commencement of the collaboration through September 30, 2002, Variagenics has recorded approximately $1.8 million in sponsored research fees ($0.2 million in 2002) and no royalties under its agreement with Covance. Under this agreement, Covance is the only contract research organization which can directly license Variagenics technologies for providing pharmacogenomic lab services in clinical trials. The agreement with Covance is for a five-year term. Covance may terminate the agreement if (i) Variagenics fails to achieve assay production targets, or (ii) Variagenics has a change in control, including if Taylor J. Crouch ceases to serve as the Chief Executive Officer. Following the departure of Mr. Crouch in April, 2002, Covance did not exercise this termination option. Either party may terminate the agreement upon material breach, misconduct or insolvency of the other party. After the five-year term expires, the agreement may be automatically renewed for additional one-year terms.

Variagenics arrangement with Quintiles is a preferred provider co-marketing arrangement under which Quintiles worldwide business development group will incorporate its SNP discovery and clinical design services into the Quintiles selling cycle. The December 1998 agreement with Quintiles is for a five-year term. Variagenics will receive revenues from this marketing agreement based on the types of pharmacogenomic services Variagenics performs under the contract. To date, Variagenics has not received any revenues under its arrangement with Quintiles. The agreement may be terminated by either party upon a material breach of the agreement.

In the life sciences sector, Variagenics has formed collaborations with both Waters Technologies Corporation and Bruker Daltonics, Inc. in connection with the development and marketing of Variagenics NuCleave®DNA testing and analysis technology. In May 2002, Variagenics discontinued the development and marketing of the NuCleave® product.

Variagenics entered into a strategic alliance with Waters in June 2000 to combine its proprietary NuCleave® chemical cleavage genotyping and haplotyping technologies with Waters DNA sample purification technology to create a kit for NuCleave® mass spectrometry applications. Both Waters and Variagenics agreed to develop the market for the NuCleave®technology and kits among pharmaceutical companies and clinical laboratories. As part of the alliance, Variagenics received $3.5 million in fees and milestone payments, and may receive up to $3.5 million upon the achievement of additional milestones, as well as royalties on kit sales. In addition, Variagenics issued to an affiliate of Waters $7.5 million in Variagenics common stock at the initial public offering price of $14.00 in a private placement which closed concurrently with the initial public offering. As part of the private placement, Variagenics issued a warrant to the Waters affiliate to purchase 80,357 shares of Variagenics common stock. The warrant has a five-year term and an exercise price per share equal to the initial public offering price. The alliance will continue until the later of: (i) the expiration of Variagenics patent rights for the technology that are the subject of the alliance, (ii) 15 years after the first commercial sale of kits developed under the alliance or (iii) by mutual consent of Waters and Variagenics to terminate the alliance. Waters may terminate the alliance upon 120 days notice after two years from the formation of the alliance, subject to Waters fulfillment of a supply commitment.

The Waters affiliate has agreed in a standstill agreement to refrain from taking certain actions, including acquiring additional shares of Variagenics stock, soliciting proxies or participating in an election contest with respect to Variagenics, or acting alone or with others to acquire Variagenics. The standstill agreement will terminate upon the earlier to occur of: (i) the termination of the alliance agreement, (ii) approval by Variagenics board of directors of the merger of its company or the acquisition of more than 30% of its securities by a third party, (iii) a publicly-announced tender or exchange offer for its securities and (iv) the third anniversary of the standstill agreement.

In May 2000, Variagenics entered into a collaboration with Bruker Daltonics, Inc., a leading provider of life sciences tools based on mass spectrometry, to manufacture and develop mass spectrometers for its NuCleave™ DNA testing and analysis system. In 2002, Variagenics extended its collaboration with Bruker Daltonics through March 31, 2003. The agreement provides for termination by either party for any reason upon 90 days notice. The parties may agree to renew the agreement for additional one-year terms.

In the diagnostics/laboratory services sector, Variagenics initiated a program to license, on a non-exclusive basis, several of its proprietary genetic markers to diagnostics companies and companies providing reference laboratory services, technologies and supplies. In 2001, Variagenics entered into the first of these agreements by granting a non-exclusive license to its MTHFR patent rights to Nanogen, Inc. in exchange for an upfront fee, milestone payments and royalties. In 2002, Variagenics has entered into similar agreements with Third Wave Technologies, Inc., ARUP Laboratories and Quest Diagnostics.

Sponsored Research and Clinical Research Collaborations

Variagenics has established sponsored research arrangements with academic institutions, as well as consulting agreements with scholars, to keep pace with the rapid development within the pharmacogenomics field. Variagenics has an academic collaboration with a researcher at McGill University to study the pharmacogenomic effects of genetic variation in MTHFR in cardiovascular and cancer applications. In addition, from 2000 to mid-2002, Variagenics funded research at the University of Reading, England, in their Departments of Medical and Pharmaceutical Statistics and Applied Statistics. This sponsored research program was aimed at developing new methods for genetic analysis in clinical trials.

In 2001, Variagenics began a program of clinical research collaborations with leading academic investigators. Variagenics clinical programs include a combination of retrospective and prospective clinical studies in multiple therapeutic areas, primarily cancer, but also cardiovascular and disorders of metabolism. Variagenics is using these studies to validate its pharmacogenomics technologies and genetic markers. In these studies, Variagenics expects to genotype clinical samples from patients treated with a drug, then determine associations between its genetic markers and response to the drug. If the genetic markers can be associated with drug response, Variagenics may proceed to develop a molecular diagnostic product.

Chemotherapy Metabolism Initiative

In July 2002, Variagenics announced the completion of the enrollment phase of a prospective Phase I clinical study, whose objective is to identify the genetic contribution of variation in the CYP3A family of drug metabolizing enzymes. These enzymes account for the clearance of more than 50 percent of all cancer agents, and, together with an understanding of genetic variability, could predict efficacy and tolerability of these drugs in patients. As part of this initiative, Variagenics secured cancer diagnostic rights to a patent application for CYP3A5, a genetic marker that could predict patient responses to chemotherapy, from St. Jude Children s Hospital in Memphis.

PRINCE Study

In July 2002, Variagenics announced the initiation of a large, retrospective study aimed at identifying markers that could predict patients response to pravastatin, a leading cholesterol reducing agent. The study, conducted in collaboration with Brigham & Women s Hospital in Boston, will attempt to identify significant associations between variations in genes relevant to statin activity and the magnitude of reduction for cholesterol and C-reactive protein, which is known to vary widely among patients. Analysis of the nearly 3,000 patient samples will, in the short-term, provide the company with pharmacogenomic proof-of-principle, and longer-term could lead to the development of molecular diagnostic tests.

Colorectal Cancer Diagnostics Program

In September 2002, the company launched its program to develop molecular diagnostic tests predictive of patients response to chemotherapy. The first trial will involve genetic analysis of 120 colorectal cancer patients who have experienced severe side effects following treatment with 5-fluorouracil (5-FU) chemotherapy. The goal of the study is to identify and confirm markers of toxicity through a retrospective analysis of polymorphisms in the normal DNA of these patients.

The Company s long-term goal is to develop a suite of molecular diagnostics to guide optimal treatment for colorectal cancer. In addition to this trial, Variagenics intends to conduct retrospective and prospective clinical studies involving 5-FU, irinotecan and oxaliplatin.

Table of Contents

Technology, Research and Development

Variagenics has developed and plans to continue to develop proprietary technologies to execute the technical steps required to implement the key phases of pharmacogenomic drug development through commercialization. Variagenics is also developing other advanced drug development technologies to meet the needs of the principal stakeholders in the pharmacogenomics field which includes pharmaceutical, diagnostic/laboratory, life sciences and contract clinical research companies. Variagenics spent approximately $8.4 million in 1999, $11.3 million in 2000, $19.1 million in 2001 and $16.6 million in 2002 through September 30 on company-sponsored research and development.

The following areas represent Variagenics comprehensive pharmacogenomic platform capabilities:

identification of genes likely to be relevant to interpatient variation in response to a drug, or candidate genes;

discovery and cataloging of SNPs and haplotypes in and around the candidate genes;

prioritization of the SNPs and haplotypes to be subsequently integrated into clinical trial testing;

development of assays used to analyze the SNPs and other genetic markers in clinical samples, which may include both genotyping and haplotyping assays, as well as loss of heterozygosity assays;

analysis of clinical trial data to determine correlations between the selected genetic markers and patient drug response;

development of diagnostic tests to support pharmacogenomic products; and

development of pharmaceutical products based on the Variagenic® Targeting approach.

Intellectual Property

Variagenics has structured its intellectual property portfolio in order to attempt to develop and maintain a proprietary position in the identification and application of genomic information to the development of current and future drugs and diagnostic tests. Variagenics may not succeed in its attempts.

As of November 21, 2002, Variagenics owned 21 issued U.S. patents, had exclusive licenses to 3 U.S. patents and a non-exclusive licenses to 6 U.S. patents and owned or had rights to 121 U.S. pending patent applications. In addition, Variagenics owned or had rights to 18 issued foreign patents and owned or had rights to 92 pending foreign patent applications. Variagenics patent portfolio has three areas of technology pertinent to the field of pharmacogenomics pharmacogenetics, variance detection, and Variagenic® Targeting.

In its patent portfolio, Variagenics has described candidate genes with likely involvement in drug response for the following disease categories: cancer, neurological, psychiatric, inflammatory, immune, metabolic, endocrine, cardiovascular and renal disease, as well as the effect of genotype on the parameters of response to any drug, including the levels and rates of movement of drugs within biological systems. In addition to the patent applications describing the utility of proprietary SNPs, Variagenics owns rights to gene specific patents for the following genes: ApoE (CNS applications), paraoxonase I (CNS applications), BCHE (CNS applications), GPIIIa/ IIb (CNS applications), MTHFR (cardiovascular and cancer applications), TPMT (cancer, transplant and arthritis applications), methionine synthetase (hyperhomocysteinemia, cardiovascular disease, neural tube defects, cancer applications), UGT1A1 (drug metabolism applications), and P450 3A5 (cancer applications).

In the area of polymorphism detection technologies, Variagenics patent applications describe a DNA analysis platform based on mass spectrometry. Variagenics patent applications in this field describe the use of NuCleave®, a unique mononucleotide chemical cleavage method, as well as additional chemistries and strategies for the rapid resolution and identification of SNPs using mass spectrometry.

In the area of targeting alleles, which are two or more different genes which may occupy the same location on a specific chromosome, Variagenics patents and patent applications describe Variagenic®

Table of Contents

Targeting, a technology involving loss of heterozygosity, profiling and, in particular, differences among alleles. An issued patent broadly describes allelic differences as a result of loss of heterozygosity occurring in cancer. The allele-specific differences observed in cancer can be applied further to other disease indications.

Variagenics strategy is to apply for patent protection on SNPs of known genes and their uses and additional uses for previously identified SNPs discovered by third parties. Variagenics has sought and intends to continue to seek patent protection for additional uses for SNPs that may have initially been patented by third parties. In these cases, Variagenics might need a license from the holders of the patent with respect to the gene in order to make, use or sell products for this use.

Variagenics also relies upon trade secrets, know-how and licensing opportunities to protect its intellectual property. Complex legal and factual determinations and evolving laws make patent protection uncertain. As a result, Variagenics cannot be sure that patents will issue from any of its patent applications or from applications licensed or that any issued patents will have sufficient breadth or terms to offer meaningful protection of its technology. In addition, Variagenics issued patents or patents Variagenics license may be successfully challenged, invalidated, circumvented or rendered unenforceable so that its patent rights would not create an effective competitive barrier. Moreover, the laws of some foreign countries may not protect its proprietary rights to the same extent as do U.S. and Canadian laws. Variagenics attempts to protect its trade secrets by entering into confidentiality agreements with third parties, employees and consultants. Most of Variagenics employees and consultants also sign agreements requiring that they assign to Variagenics their interests in discoveries, inventions, patents and copyrights arising from their work, maintain the confidentiality of its intellectual property, and refrain from unfair competition with Variagenics during their employment and for a period of time after their employment, which includes solicitation of its employees and customers. Variagenics cannot be sure that these agreements will not be breached or invalidated or even held valid by a court. In addition, Variagenics cannot assure you that third parties will not independently discover or invent competing technologies or reverse engineer its trade secrets, or other technologies. If Variagenics intellectual property is not protected from disclosure to, or use by, third parties, its competitive market position will be harmed.

Generally, U.S. patents have a term of 17 years from the date of issue for patents issued from applications filed with the U.S. Patent Office prior to June 8, 1995 and 20 years from the application filing date or earlier claimed priority date in the case of patents issued from applications filed on or after June 8, 1995. Under some circumstances, patent term extensions may be obtained, or disclaimers of some part of the patent term may be required. Patents in most other countries have a term of 20 years from the date of filing the patent application.

Although Variagenics is not a party to any material legal proceedings relating to intellectual property, in the future, third parties may file claims asserting that its technologies or products infringe on their intellectual property. Variagenics cannot predict whether third parties will assert such claims against it or against the licensors of technologies licensed to Variagenics, or whether those claims will harm its business. If Variagenics is forced to defend against such claims, whether they are with or without any merit or whether they are resolved in favor of or against Variagenics or its licensors, Variagenics may face costly litigation and diversion of management s attention and resources. As a result of disputes, Variagenics may have to develop costly non-infringing technologies, or enter into licensing agreements. These agreements, if necessary, may be unavailable on terms acceptable to Variagenics, or at all, which could seriously harm its business and financial condition.

Competition

Variagenics business model exposes it to competition in many of the sectors in which it operates and it expects the intensity of competition to increase. Variagenics is subject to significant competition from pharmaceutical, biotechnology and diagnostic companies, academic and research institutions and government or other publicly-funded agencies that are pursuing products and services that are substantially similar to its proposed products and services, or which otherwise address the needs of its customers and potential customers. Some of Variagenics competitors have greater financial, operational, sales and marketing

Table of Contents

resources, and more experience in research and development than Variagenics has. These competitors may have developed, or could develop in the future, technologies that compete with its products or which could render its products obsolete. Variagenics principal competitors come from three areas: pharmacogenomics, genomics and molecular diagnostics. Genaissance Pharmaceuticals, Inc. is another company exclusively focused on pharmacogenomics. Genomics companies also performing SNP discovery, such as CuraGen Corporation, Celera Genomics Group and Perlegen Sciences, may focus their discovery efforts on providing further characterization of relevant SNPs to drug action and thus begin to compete with its pharmacogenomics model. Companies such as Affymetrix, Inc., Orchid Biosciences, Inc., Sequenom, Inc. and Third Wave Technologies, Inc. supply tools to meet the rapidly increasing workload of research experiments. Molecular diagnostics companies such as Celera Diagnostics and Myriad Genetics may compete by broadening their focus from disease prediction and monitoring to diagnostics which predict drug response. Variagenics cannot assure you that it will be able to make the enhancements to its technologies necessary to compete successfully with newly emerging techniques.

Government Regulation

At the current time, the FDA does not regulate Variagenics or its products. However, many of Variagenics customers and collaborators will be subject to regulation depending on the type of products or services they provide. The FDA and comparable regulatory agencies in foreign countries impose substantial requirements on the clinical development, manufacture and marketing of biopharmaceuticals and in vitro diagnostic products. These agencies regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, advertising and promotion of these products and services. Different centers within the FDA are responsible for regulating these products, depending on whether the product is considered a pharmaceutical, biologic or medical device.

The process required by the FDA before a pharmaceutical or biologic product may be marketed in the U.S. generally requires substantial time, effort and financial resources. Satisfaction of FDA requirements or similar requirements of foreign regulatory agencies typically takes several years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease. Even if a product receives regulatory approval, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market.

The use of genetic information in research and for other purposes raises concerns about the privacy and security of that information. A federal law, the Health Insurance Portability and Accountability Act of 1996 (HIPAA) regulates the disclosure and use of protected health information and creates rights for the subjects of that information. Variagenics is not considered one of the covered entities under the regulations that implement the law and which will go into effect in April 2003. However, some of Variagenics customers and collaborators who send Variagenics clinical samples will have to comply with HIPAA by, among other things, obtaining proper informed consent from the subjects for the transfer and use by Variagenics of those clinical samples.

Because Variagenics testing services are currently used only for research purposes, Variagenics is not registered under the Clinical Laboratory Improvement Act, or CLIA. However, Covance, which uses its technology in clinical trials, is CLIA-certified. CLIA is intended to ensure the quality and reliability of clinical laboratories in the U.S. by mandating specific standards in the areas of personnel qualification, administration, participation in proficiency testing, patient test management, quality control, quality assurance and inspections. Variagenics cannot assure you that the CLIA regulations and future administrative interpretations of CLIA will not have a materially adverse impact on its ability to sell its technology to Covance or any future collaborators that want to use its technology to provide reference laboratory services.

Variagenics is also subject to numerous environmental and safety laws and regulations, including those governing the use and disposal of hazardous materials. Any violation of, and the cost of compliance with, these regulations could have a material adverse effect on its business and results of operations.

Table of Contents

Employees

As of November 19, 2002, Variagenics employed 81 persons (78 full time), of whom 21 hold Ph.D. or M.D. degrees and 22 hold other advanced degrees. Approximately 61 employees are engaged in research and development, and 20 employees are engaged in business development, intellectual property, finance and other administrative functions. None of Variagenics employees are subject to a collective bargaining arrangement and Variagenics considers its relations with its employees to be good.

Properties of Variagenics

Variagenics leases a 39,014 square foot facility in Cambridge, Massachusetts for its headquarters and as the base for marketing, research and development activities. The lease expires in 2008 and is renewable for another five years. Variagenics believes that suitable additional space will be available to it, when needed, on commercially reasonable terms.

Table of Contents

Management s Discussion and Analysis of Financial Condition and Results of Operations of Variagenics

Overview

Variagenics is a leader in applying pharmacogenomics technologies to the discovery, development and commercialization of personalized drugs and molecular diagnostic products. Variagenics primary therapeutic focus is cancer. As a pharmacogenomics company, Variagenics identifies therapeutically important genetic markers, including the most common form of genetic variability, single nucleotide polymorphisms, or SNPs, groups of SNPs called haplotypes, and other genetic markers. Variagenics combines its technology, expertise and proprietary data to offer pharmaceutical and biotechnology companies a full range of solutions to support key steps of their drug discovery and development process. Variagenics also intends to develop its own proprietary molecular diagnostic products. From inception in December 1992 through 1996, Variagenics main focus is on research activities directed toward developing a pharmacogenomic approach to cancer therapy. In 1996 that focus was broadened to include SNP discovery and development of pharmacogenomic technologies. Since its inception in 1992, Variagenics operating activities have been primarily devoted to research and development, recruiting personnel, raising capital, acquiring assets and business development. In 1999, Variagenics recognized revenue from its first commercial collaboration and in March 2001, it recognized its first product sale.

Variagenics has incurred losses since its inception and, as of September 30, 2002, it had an accumulated stockholders deficit of $104.2 million. Variagenics anticipates incurring additional operating losses through at least the end of 2003, as it continues to develop its pharmacogenomic technologies and develop and commercialize proprietary molecular diagnostic products. Payments under contracts, collaborations and licensing arrangements will be subject to significant fluctuation in both timing and amount and, therefore, its results of operations for any period may not be comparable to the results of operations for any other period. In April 2002, Variagenics announced the resignation of its President and Chief Executive Officer and the related promotions of two of its senior officers.

During the three months ended June 30, 2002, Variagenics formulated a restructuring plan in order to conserve cash and focus resources on its oncology molecular diagnostic development programs. Variagenics has also discontinued its NuCleave® product, which had been the source of revenue from product sales.

In connection with this restructure, Variagenics recorded a charge of $2.0 million, which consisted of $1.1 million related to employee separation costs and $0.9 million related to impairment of fixed assets which were taken out of service and held for sale as of June 30, 2002. None of these assets was sold as of September 30, 2002.

The restructuring reduced headcount by 44 positions, representing approximately 30% of Variagenics workforce. Approximately half the reductions were in the high-throughput DNA sequencing group; the other half were spread throughout the organization, representing both research and development positions as well as general and administrative staff.

The employee separation costs were accounted for under EITF 94-3 Liability Recognition for Certain Employee Termination Benefits and Other Costs to Exit an Activity (Including Certain Costs Incurred in a Restructuring) and include amounts to be paid for severance and related benefits. As of September 30, 2002, all the employees to be terminated subject to the restructuring plan had ceased active employment with Variagenics; $1.0 million of severance and related benefits was paid out, with the remaining balance of $0.1 million included in accrued restructure and related charges, which Variagenics expects to be substantially paid out prior to December 31, 2002.

In refocusing the business, Variagenics identified certain laboratory equipment with a net book value of $2.3 million that will no longer be required. Variagenics has decommissioned this equipment and expects to sell it by June 2003. Certain of this equipment was purchased under capital leases, and Variagenics has accrued for costs associated with the early termination of the related obligations. Variagenics has also classified the debt associated with these assets to the current portion of capital lease obligations. Finally, Variagenics recorded an impairment charge of $0.9 million related to this equipment to write the asset down

to its estimated net realizable value in accordance with FAS 144 Accounting for Impairment or Disposal of Long-Lived Assets.

Variagenics expects to substantially complete its restructuring program by the end of 2002. If Variagenics restructuring program is implemented in the manner and on the timeline it intends, Variagenics expects to realize the full benefits of its restructuring program by the first quarter of 2003, and anticipates reducing its quarterly cash burn from approximately $6 million to approximately $4 million. However, Variagenics cannot assure that its restructuring program will achieve all of the cost and expense reductions and other benefits it anticipates or that the plan will be completed in the timetable contemplated.

Critical Accounting Policies

Valuation of Long-Lived and Intangible Assets

Variagenics reviews its long-lived assets for impairment annually or sooner if events or changes in circumstances indicate that the carrying amount may not be recoverable.

During the three months ended June 30, 2002, and concurrent with its restructuring plan, Variagenics decommissioned some of its laboratory equipment and committed to a plan to sell it by June 2003. As a result of this decision, Variagenics measured its assets held for sale at the lower of its carrying amount or fair value less costs to sell and recognized an impairment charge of $0.9 million. Variagenics estimate of the net realizable value of these assets depends on market conditions and the actual results may differ from its estimates. In the event actual net proceeds from these assets are below its expectations, or if Variagenics receives no proceeds at all, Variagenics will record an additional impairment loss up to an amount equal to the remaining carrying value of $1.4 million at September 30, 2002 (plus any related costs of disposal). In the event actual net sales proceeds from these assets exceed its expectations, Variagenics will recognize a gain. In addition, there could be new events and circumstances that would indicate impairment of additional long-lived assets; Variagenics will assess the value of such assets and provide for estimated losses when such impairments are identified.

Sources of Revenue and Revenue Recognition

Variagenics revenue to date has been generated from research funding and milestones from collaborations, research grants from a governmental agency and license fees. In the first quarter of both 2001 and 2002, Variagenics recognized revenue from the sale of its NuCleave® product; this product has been discontinued as a result of its restructuring program. As a result of its restructuring, it expects that future revenues will be derived from collaborations and its oncology molecular diagnostic development programs.

Variagenics recognizes revenue from grants in the period in which related costs are incurred. Variagenics recognizes revenue from collaborations under the percentage of completion method in accordance with SEC Staff Accounting Bulletin No. 101, Revenue Recognition in Financial Statements. Under percentage of completion accounting, revenue is based on the cost of effort from the contract s commencement up to the reporting date, divided by the total expected research and development costs from the contract s commencement to the end of the research and development period, multiplied by the total expected contractual payments under the arrangement. Revenue from product sales is generally recognized upon Variagenics receipt of the customer s signed acceptance of the installed product, provided that there is evidence of arrangement, the fee is fixed or determinable and collection of resulting receivables is probable. Payments received in advance of being earned are recorded as deferred revenue. As of September 30, 2002, Variagenics had approximately $0.3 million of deferred revenue.

Table of Contents

Variagenics, Inc.

Selected Quarterly Financial Data (Unaudited)

	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
(in thousands, except per share amounts)				
2002:				
Revenue	$ 706	$ 158	$ 178	
Restructuring and related charges		1,974		
Loss from operations	(10,287)	(10,088)	(6,772)	
Net loss	(9,870)	(9,797)	(6,533)	
Net loss per share (basic and fully diluted)	$ (0.42)	$ (0.42)	$ (0.27)	
2001:				
Revenue	$ 1,102	$ 915	$ 574	$ 392
Loss from operations	(5,110)	(6,771)	(7,660)	(9,979)
Net loss	(3,704)	(5,566)	(6,624)	(9,409)
Net loss per share (basic and fully diluted)	$ (0.16)	$ (0.24)	$ (0.28)	$ (0.40)
2000:				
Revenue	$ 127	$ 149	$ 763	$ 1,215
Loss from operations	(4,779)	(4,520)	(7,402)	(4,220)
Net loss	(4,730)	(4,301)	(6,163)	(2,606)
Net loss attributable to common stockholders	(25,479)	(5,417)	(6,404)	(2,606)
Net loss attributable to common stockholders per share (basic and fully diluted)	$ (34.85)	$ (5.73)	$ (0.35)	$ (0.11)

Results of Operations

Three Months Ended September 30, 2002 and 2001

Revenues. Revenues decreased to $0.2 million for the three months ended September 30, 2002 from $0.6 million for the comparable period ended September 30, 2001 due to the completion of a major collaboration in the fourth quarter of 2001. Revenues in both periods consisted principally of collaboration revenues.

Research and Development Expenses. Research and development expenses excluding non-cash equity compensation totaled $4.5 million in the three month periods of both 2002 and 2001. In 2002, increased costs in connection with clinical research projects ($0.6 million) and increased facility costs ($0.2 million) were substantially offset by decreased consumption of lab materials and consumables ($0.7 million) and decreased salary and related personnel costs ($0.2 million). Variagenics anticipates reductions in research and development expenses (principally, salary and related personnel costs, depreciation, equipment maintenance and lab materials and consumables) for the remainder of 2002 as the full impact of its restructuring program is realized.

General and Administrative Expenses. General and administrative expenses excluding non-cash equity compensation decreased to $1.8 million for the period ended September 30, 2002 from $2.3 million for the comparable period of 2001. The decrease in general and administrative expense was primarily due to decreased salary and related personnel costs ($0.3 million) and decreased facility costs ($0.2 million). Variagenics anticipates reductions in general and administrative expenses (principally, salary and related personnel costs) for the remainder of 2002 as the full impact of its restructuring program is realized.

Non-Cash Equity Compensation. Variagenics recognizes equity-related charges resulting from grants of options to employees and non-employees; a total of $0.7 million in the third quarter of 2002 versus

$1.4 million in the same period of 2001. These charges are included in research and development expenses ($0.5 million and $0.6 million in the three month periods of 2002 and 2001, respectively) or general and administrative expenses ($0.2 million and $0.8 million in the three month periods of 2002 and 2001, respectively), depending upon the nature of the work performed by the individuals receiving the grants. Variagenics incurred expenses of $0.7 million in the third quarter of 2002 versus $1.4 million in the same period of 2001 related to stock options previously issued to employees. Employee options generally vest over four years, which is expected to result in additional compensation expense of $3.2 million for periods ending subsequent to September 30, 2002. Variagenics recorded a decrease in expense of less than $0.1 million for each of the quarters ended September 30, 2002 and September 30, 2001 related to options granted to non-employees. Non-employee equity grants are subject to remeasurement over the vesting period and Variagenics cannot estimate the expense it will recognize in future periods because the expense will depend on a number of variables, including its stock price.

Interest Income. Interest income, which is earned on cash equivalents and short- and long-term marketable securities, decreased to $0.3 million for the third quarter of 2002 from $1.1 million for the comparable period in 2001. The lower interest income was due to the effect of falling interest rates and the continued use of invested cash to fund operations.

Interest Expense. Interest expense increased to $87,000 for the third quarter of 2002 from $78,000 for the comparable period in 2001 due to an increase in capital lease obligations.

Net Loss. The net loss decreased to $6.5 million for the third quarter of 2002 from $6.6 million for the comparable period in 2001 primarily due to the reasons listed above.

Nine Months Ended September 30, 2002 and 2001

Revenues. Revenues decreased to $1.0 million for the nine months ended September 30, 2002 from $2.6 million for the comparable period ended September 30, 2001 due to the completion of a major collaboration in the fourth quarter of 2001. Revenues for the period ended September 30, 2002 consisted of $0.5 million in collaboration revenues, $0.5 million in product sales, and just under $0.1 million in license fees, while revenues for the period ended September 30, 2001 consisted of $2.4 million in collaboration revenues and $0.2 million in product sales.

Cost of Product Sales. Cost of product sales was $0.2 million for each of the nine month periods ended September 30, 2002 and September 30, 2001.

Research and Development Expenses. Research and development expenses excluding non-cash equity compensation increased to $14.6 million for the nine months ended September 30, 2002 from $11.5 million for the comparable period ended September 30, 2001. The increase was due primarily to increased costs in connection with clinical research projects ($2.3 million), increased salary and related personnel costs ($1.4 million), increased facility costs ($0.7 million), and increased depreciation and amortization due to property and equipment additions ($0.4 million). These increases were partially offset by decreased consumption of lab materials and consumables ($1.6 million). Variagenics anticipates reductions in research and development expenses (principally, salary and related personnel costs, depreciation, equipment maintenance and lab materials and consumables) for the remainder of 2002 as the full impact of its restructuring program is realized.

General and Administrative Expenses. General and administrative expenses excluding non-cash equity compensation decreased to $6.1 million for the period ended September 30, 2002 from $6.6 million for the comparable period of 2001. The decrease in general and administrative expense was primarily due to decreased facility costs ($0.6 million) and decreased salary and related personnel costs ($0.3 million) offset by increased fees relating to outsourced functions ($0.3 million). Variagenics anticipates reductions in general and administrative expenses (principally, salary and related personnel costs) for the remainder of 2002 as the full impact of its restructuring program is realized.

Non-Cash Equity Compensation. Variagenics recognizes equity-related charges resulting from grants of options to employees and non-employees; a total of $5.3 million in the nine month period of 2002 versus

$3.8 million in the same period of 2001. These charges are included in research and development expenses ($2.2 million and $1.4 million in the nine month periods of 2002 and 2001, respectively) or general and administrative expenses ($3.1 million and $2.4 million in the nine month periods of 2002 and 2001, respectively), depending upon the nature of the work performed by the individuals receiving the grants. Variagenics incurred expenses of $5.4 million in the nine month period of 2002 and $4.4 million for the comparable period in 2001 related to stock options previously issued to employees. (The 2002 total includes $3.0 million for the acceleration of option vesting for two executive officers who terminated their employment with Variagenics. Of this amount, $2.4 million is included in general and administrative expenses while $0.6 million is related to research and development.) Employee options generally vest over four years, which is expected to result in additional compensation expense of $3.2 million for periods ending subsequent to September 30, 2002. Employee terminations as a result of Variagenics restructuring resulted in a reversal of $1.5 million of deferred compensation in the equity section of the balance sheet. This reversal will cause a reduction in the amount of non-cash equity compensation expensed in future periods. Variagenics recorded a decrease in expense of $0.1 million for the nine month period of September 30, 2002 and $0.6 million for the nine month period of September 30, 2001 related to options granted to non-employees. Non-employee equity grants are subject to remeasurement over the vesting period and it cannot estimate the expense it will recognize in future periods because the expense will depend on a number of variables, including its stock price.

Restructuring and Related Charges. During the three months ended June 30, 2002, Variagenics formulated a restructuring plan in order to conserve cash and focus resources on its oncology molecular diagnostic development programs. Variagenics has also discontinued its NuCleave® product, which had been the source of its revenue from product sales. In connection with this restructure, Variagenics recorded a charge of $2.0 million, which consisted of $1.1 million related to employee separation costs and $0.9 million related to impairment of fixed assets which were taken out of service and held for sale as of June 30, 2002. None of these assets was sold as of September 30, 2002.

Interest Income. Interest income, which is earned on cash equivalents and short- and long-term marketable securities, decreased to $1.2 million for the nine month period of 2002 from $3.8 million for the comparable period in 2001. The lower interest income was due to the effect of falling interest rates and the continued use of invested cash to fund operations.

Interest Expense. Interest expense increased to $259,000 for the nine month period of 2002 from $156,000 for the comparable period in 2001 due to an increase in capital lease obligations.

Net Loss. The net loss increased to $26.2 million for the nine month period of 2002 from $15.9 million for the comparable period in 2001 primarily due to the reasons listed above.

Years Ended December 31, 2001 and 2000

Revenues. Revenues totaled $3.0 million for the year ended December 31, 2001, versus $2.3 million in 2000. Revenues for both periods consisted principally of collaboration revenues and milestone achievements under current contracts. Revenue for the year ended December 31, 2001 included $0.2 million from product sales and $0.2 million from license fees.

Cost of Product Sales. Cost of product sales was $0.2 million for the year ended December 31, 2001. There were no product sales in the comparable period of 2000.

Research and Development Expenses. Research and development expenses consist primarily of salaries and related personnel costs, consumable laboratory supplies, facilities and equipment expenses, license fees and fees paid to scientific advisors, consultants and sponsored research providers. Variagenics expenses its research and development costs as they are incurred. Research and development expenses excluding non-cash equity compensation increased to $16.9 million for the year ended December 31, 2001 from $8.9 million for the year ended December 31, 2000. The increase was due primarily to increased salary and related personnel costs as Variagenics expanded its research and technology development activities ($3.7 million), increased consumption of lab materials and consumable supplies ($1.7 million), costs of

clinical research programs ($1.2 million) and increased depreciation and amortization due to property and equipment additions ($0.6 million). Variagenics expects research and development spending to increase over the next several years as Variagenics expand its clinical research programs.

General and Administrative Expenses. General and administrative expenses consist primarily of salaries and related expenses for executive, business development, finance and other administrative personnel, facility operations and equipment costs, legal expenses for general legal activities and preparation of intellectual property filings, recruiting and marketing. General and administrative expenses excluding equity compensation increased to $8.6 million for the year ended December 31, 2001 from $5.7 million for the comparable period of 2000. This increase was due primarily to increases in general and administrative expense, including increased salary and personnel costs of $1.0 million, increased facility and administrative expenses of $0.4 million, increased marketing and business development expenditures of $0.1 million, and increased legal costs related to patent filings of $0.8 million.

Non-Cash Equity Compensation. Variagenics recognized equity-related charges resulting from grants of options and stock to employees and options and restricted stock to non-employees; a total of $6.8 million in 2001 versus $8.6 million in 2000. These charges are included in research and development expenses ($2.9 million in 2001 and $3.0 million in 2000) or general and administrative expenses ($3.9 million in 2001 and $5.6 million in 2000) depending upon the nature of the work performed by the individuals receiving the grants. Variagenics incurred expenses of $7.0 million in 2001 and $7.2 million in 2000 related to the issuance of stock options to employees. These employee options generally vest over four years, which will result in additional compensation expense of $10.2 million for periods ending subsequent to December 31, 2001. Variagenics also incurred expenses of $1.4 million in 2000 and a reduction of expenses of $0.2 million in 2001 related to restricted stock and options granted to non-employees. Non-employee equity grants are subject to remeasurement over the vesting period and Variagenics cannot estimate the expense it will recognize in future periods because the expense will depend on a number of variables, including its stock price.

Interest Income. Interest income, which is earned on cash equivalents and short- and long-term marketable securities, increased to approximately $4.5 million for the year ended December 31, 2001 from approximately $3.4 million for the year ended December 31, 2000. The higher interest income was due to the increase in cash during 2000 from the net proceeds of the initial public offering and concurrent private placement of common stock in July 2000 (approximately $80.3 million) and the sale of the Series F redeemable convertible preferred stock in March 2000 (approximately $19.9 million). The increase in interest income due to this increase in cash was somewhat offset in 2001 due to the effect of falling interest rates and the use of cash for operations.

Interest Expense. Interest expense was $0.2 million for both the years ended December 31, 2001 and December 31, 2000. The year 2000 figure included the remaining interest on obligations repaid with the proceeds of Variagenics initial public offering. The year 2001 figure reflects increased financing of capital additions through leasing arrangements.

Net Loss and Net Loss Attributable to Common Stockholders. The net loss increased to $25.3 million for the year ended December 31, 2001 from $17.8 million for the year ended December 31, 2000 primarily due to the reasons listed above. In March 2000, Variagenics issued redeemable convertible preferred stock at $4.29 per share for net proceeds of $19.9 million. The issuance of these shares resulted in a beneficial conversion feature, which Variagenics recorded as a dividend of $19.9 million to the preferred stockholders. Coupled with the accretion of dividends on redeemable convertible preferred stock of $2.2 million for the first seven months of 2000, this increased the loss attributable to common stockholders for 2000 to $39.9 million. There were no such dividends in 2001, as the convertible preferred stock converted to common stock at Variagenics initial public offering in July 2000.

Years Ended December 31, 2000 and 1999

Revenues. Revenues totaled $2.3 million for the year ended December 31, 2000, versus $0.4 million in 1999. Revenues for the year ended December 31, 2000 consisted principally of collaboration revenues and milestone achievements under current contracts.

Table of Contents

Research and Development Expenses. Research and development expenses consist primarily of salaries and related personnel costs, consumable laboratory supplies, facilities and equipment expenses, license fees and fees paid to scientific advisors, consultants and sponsored research providers. Variagenics expenses its research and development costs as they are incurred. Research and development expenses excluding non-cash equity compensation increased to $8.9 million for the year ended December 31, 2000 from $6.7 million for the year ended December 31, 1999. The increase was due primarily to increased salary and related personnel costs as Variagenics expanded its research and technology development activities ($0.4 million), increased consumption of lab materials, consumable supplies and small equipment ($1.1 million) and increased depreciation and amortization due to property and equipment additions ($0.3 million).

General and Administrative Expenses. General and administrative expenses consist primarily of salaries and related expenses for executive, business development, finance and other administrative personnel, facility operations and equipment costs, legal expenses for general legal activities and preparation of intellectual property filings, recruiting and marketing. General and administrative expenses excluding equity compensation decreased to $5.7 million for the year ended December 31, 2000 from $5.9 million for the comparable period of 1999. General and administrative expenses for 1999 included a charge of $1.8 million recorded in connection with the cancellation of Variagenics agreements with Nova Molecular, Inc. as described below. There was no comparable charge in 2000. This decrease was offset by increases in general and administrative expense, including increased salary and personnel costs of $0.6 million, increased marketing and business development expenditures of $0.4 million, and increased legal costs related to patent filings of $0.2 million.

Non-cash Equity Compensation. Variagenics recognized equity-related charges resulting from grants of options and stock to employees and options and restricted stock to non-employees; a total of $8.6 million in 2000 versus $3.0 million in 1999. These charges are included in research and development expenses ($3.0 million in 2000 and $1.9 million in 1999) or general and administrative expenses ($5.6 million in 2000 and $1.1 million in 1999) depending upon the nature of the work performed by the individuals receiving the grants. Variagenics incurred expenses of $7.2 million in 2000 and $0.6 million in 1999 related to the issuance of stock options to employees. These employee options generally vest over four years, which will result in additional compensation expense of $19.0 million for periods ending subsequent to December 31, 2000. Variagenics also incurred expenses of $1.4 million in 2000 and $1.7 million in 1999 related to restricted stock and options granted to non-employees.

Interest Income. Interest income, which is earned on cash equivalents and short- and long-term marketable securities, increased to approximately $3.4 million for the year ended December 31, 2000 from approximately $0.2 million for the comparable period in 1999. The higher interest income was due to the increase in cash from the net proceeds of the initial public offering and concurrent private placement of common stock in July 2000 (approximately $80.3 million) and the sale of the Series F redeemable convertible preferred stock in March 2000 (approximately $19.9 million).

Interest Expense. Interest expense decreased to $0.2 million for the year ended December 31, 2000 from $1.5 million for the comparable period in 1999 due to interest from convertible notes and warrants recorded in the 1999 period. These obligations were no longer outstanding in the year 2000 period.

Net Loss and Net Loss Attributable to Common Stockholders. The net loss increased to $17.8 million for the year ended December 31, 2000 from $16.7 million for the comparable period in 1999 primarily due to the reasons listed above, partially offset by the equity in loss of affiliate ($0.3 million) and charges in connection with the cancellation of certain affiliate agreements ($1.8 million) in 1999. In March 2000, Variagenics issued redeemable convertible preferred stock at $4.29 per share for net proceeds of $19.9 million. The issuance of these shares resulted in a beneficial conversion feature, which Variagenics recorded as a dividend of $19.9 million to the preferred stockholders. Coupled with the accretion of dividends on redeemable convertible preferred stock of $2.2 million for the first seven months of 2000, this increased the loss attributable to common stockholders for the period to $39.9 million.

Table of Contents

Liquidity and Capital Resources

Nine Months Ended September 30, 2002

Cash and cash equivalents totaled $32.6 million at September 30, 2002, an increase of $7.5 million from the December 31, 2001 balance of $25.1 million. The increase in cash is principally due to the maturity of marketable securities. For the nine-month period, cash, cash equivalents, and short- and long-term marketable securities combined decreased by $19.2 million. For the first nine months of 2002, Variagenics used $17.7 million for operations, which consisted of the net loss of $26.2 million offset by non-cash compensation expense of $5.3 million, depreciation and amortization of $1.5 million and restructuring and related charges of $1.0 million. Variagenics used $30.6 million to purchase marketable securities and $1.4 million to purchase property and equipment, and received $57.3 million from the maturity of marketable securities and $0.7 million from the sale and leaseback of equipment. Variagenics used $0.8 million for its financing activities, which included net proceeds of $0.5 million from the exercise of common stock options offset by the repayment of $1.3 million of capital lease obligations.

Variagenics cash, cash equivalents, and short- and long-term marketable securities totaled $60.8 million at September 30, 2002 versus $80.0 million at December 31, 2001. Variagenics believes that its cash reserves and its expected short term revenue will be sufficient to fund its operations at least through the year 2003. During or after this period, or in the event of acquisitions or extraordinary events, if cash generated by operations is insufficient to satisfy its liquidity requirements, Variagenics may need to issue additional equity or debt securities or obtain additional credit arrangements. Additional financing may not be available on terms acceptable to it or at all. The sale of additional equity or convertible debt securities may result in additional dilution to its stockholders.

Variagenics has incurred losses since its inception and, as of September 30, 2002, had an accumulated stockholders deficit of $104.2 million. Management anticipates incurring additional operating losses through at least the end of 2003. Variagenics future viability is dependent upon its ability to:

develop pharmacogenomic technologies;

develop and commercialize proprietary molecular diagnostic products; and

commence generating cash from operations.

Years Ended December 31, 2001 and 2000

Cash and cash equivalents totaled $25.1 million at December 31, 2001, a decrease of $25.2 million from December 31, 2000. Variagenics used $17.9 million for operations in 2001, which consisted of the net loss of $25.3 million offset by non-cash compensation expense of $6.8 million and depreciation and amortization of $1.8 million. Variagenics used $69.2 million to purchase marketable securities and $2.3 million to purchase property and equipment. Variagenics received $63.9 million from the maturity of marketable securities and $1.2 million from the sale and leaseback of property and equipment. Variagenics used $0.8 million for its financing activities, which included repayments of capital lease obligations totaling $1.2 million and the issuance of a promissory note to an affiliate offset by the proceeds from exercise of stock options of $0.3 million and the release of restricted cash of $0.3 million.

Cash, cash equivalents, and short- and long-term marketable securities totaled $80.0 million at December 31, 2001.

Years Ended December 31, 2000 and 1999

Cash and cash equivalents totaled $50.3 million at December 31, 2000, an increase of $48.5 million from December 31, 1999. Variagenics used $6.4 million for operations in 2000, which consisted of the net loss of $17.8 million offset by non-cash compensation expense of $8.6 million and depreciation and amortization of $1.1 million. Variagenics used $51.0 million to purchase marketable securities and $1.0 million to purchase property and equipment, and received $5.0 million from the maturity of marketable securities. Variagenics received $101.9 million from its financing activities, which included net proceeds of

$73.1 million from the initial public offering, $7.2 million from the concurrent private placement of common stock, $19.9 million from the sale of Series F redeemable convertible preferred stock and $2.6 million from the exercise of warrants. These financing proceeds were offset in part by repayments of capital lease obligations totaling $0.7 million and a bank line of credit of $0.2 million.

Variagenics cash, cash equivalents, and short- and long-term marketable securities totaled $99.0 million at December 31, 2000.

Recent Developments

On July 25, 2002, Variagenics announced that it completed a license agreement with St. Jude Children s Research Hospital in Memphis under which it obtained exclusive rights in the field of oncology to develop diagnostic test products predictive of drug response. The license agreement covers a patent application claiming CYP3A5 genotyping methods and diagnostic test kits predictive of variable expression of CYP3A5. Variagenics also announced the completion of the patient enrollment phase of a related pharmacogenomic research study.

On July 30, 2002, Variagenics announced that it entered into a research collaboration with Brigham & Women s Hospital and Paul M. Ridker, M.D., M.P.H., Director of Brigham & Women s Center for Cardiovascular Disease Prevention. Under the collaboration, Variagenics will apply its genotyping and haplotyping platforms and statistical analysis methodology to the PRINCE (Pravastatin Inflammation CRP Evaluation) study to explore the contribution of genetic variability to variations in patients therapeutic responses to pravastatin, a major cholesterol-lowering agent. Variagenics will receive an exclusive option to license intellectual property resulting from the research, which may lead to the future development of cardiovascular diagnostic tests.

On July 30, 2002, Variagenics announced that it granted a worldwide license for its RNA targeting patent (PCT/US00/05271) to Renegade Therapeutics, a novel drug discovery company. Under the terms of the agreement, Variagenics granted Renegade Therapeutics worldwide exclusive rights to all non-allele specific applications for the research, development, and commercialization of small molecule drugs that target RNA. The terms of the agreement include up-front fees, milestone payments, reimbursement for patent related expenses, and royalties on sales of any compounds developed using the licensed technology.

On September 26, 2002, Variagenics announced the launch of its program to develop molecular diagnostic tests predictive of the response of solid tumors to chemotherapy. The first clinical study will involve genetic analysis of over 100 patients who have experienced severe side effects following 5-fluorouracil (5-FU) chemotherapy for colorectal cancer. A retrospective study has been started with Dr. Andre van Kuilenburg from the Laboratory of Genetic Metabolic Diseases at the Academic Medical Center in Amsterdam.

On October 10, 2002, Variagenics announced licensing agreements under its MTHFR (methylenetetrahydrofolate reductase) patent rights with ARUP Laboratories, a leading full-service clinical reference laboratory. Under the terms of these agreements, Variagenics granted ARUP non-exclusive rights to commercialize home brew tests for MTHFR allele testing associated with increased thrombo-embolic disease risk and other disorders.

On October 16, 2002, Variagenics announced that it granted an option to a worldwide license to Strida Pharma, Inc., a new privately-held cancer therapeutics company, relating to certain or its MTHFR patent rights. Under the terms of the agreement, Variagenics granted Strida an option to a license granting worldwide exclusive rights to commercialize therapeutic inhibitors of the MTHFR gene. The terms of the agreement include an up-front fee, and may lead to milestone payments and royalties on sales of any compounds that are developed using the technology. Variagenics gains the right to use Strida s data in support of its own patent applications.

On October 29, 2002, Variagenics announced that it signed a licensing agreement under its MTHFR patent rights with Quest Diagnostics, Inc. Under the terms of the agreement, Variagenics granted Quest

Table of Contents

Diagnostics non-exclusive rights to commercialize laboratory developed tests for MTHFR allele testing associated with increased thrombo-embolic disease risk and other disorders.

Special Note Regarding Forward-Looking Statements

The Variagenics Management s Discussion and Analysis of Financial Condition and Results of Operations Section contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act that involve risks and uncertainties. Discussions containing forward-looking statements may be found in the material set forth under Management s Discussion and Analysis of Financial Condition and Results of Operations as well as in this joint proxy statement/prospectus generally. Variagenics generally uses words such as believe, may, could, will, intend, expect, anticipate, plan, and similar expressions to identify forward-looking statements. Y place undue reliance on these forward-looking statements. Variagenics actual results could differ materially from those anticipated in the forward-looking statements for many reasons, including the risks described above and elsewhere in this joint proxy statement/prospectus. Variagenics discusses these risks in detail in its Annual Report on Form 10-K filed with the Securities and Exchange Commission on April 1, 2002.

Although Variagenics believes the expectations reflected in the forward-looking statements are reasonable, they relate only to events as of the date on which the statements are made, and it cannot assure you that its future results, levels of activity, performance or achievements will meet these expectations. Moreover, neither Variagenics nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. Variagenics does not intend to update any of the forward-looking statements after the date of this joint proxy statement/prospectus to conform these statements to actual results or to changes in its expectations, except as required by law.

Quantitative and Qualitative Disclosures About Market Risk

Any exposure to market risk is principally confined to Variagenics cash equivalents and marketable securities, all of which have maturities of less than eighteen (18) months. Variagenics maintains a non-trading investment portfolio of investment grade, liquid debt securities that limits the amount of credit exposure to any one issue, issuer or type of instrument.

Table of Contents

Security Ownership of Certain Beneficial Owners and Management

The following table sets forth certain information regarding the beneficial ownership of shares of the Variagenics common stock as of November 15, 2002 by (i) each stockholder known by Variagenics to own beneficially 5% or more of its outstanding shares of common stock, (ii) each current director and executive officer of Variagenics and (iii) all directors and executive officers of Variagenics as a group. The information in this table is based on the most recent SEC filings by these stockholders or other information obtained by Variagenics as to their ownership of Variagenics stock.

	Shares Beneficially Owned(2)		
Name and Address of Beneficial Owner(1)	Number of Shares	Percentage Before the Merger	Percentage After the Merger
Wells Fargo Bank Indiana, N.A.(3) P.O. Box 960 Fort Wayne, IN 46801	3,419,015	13.9%	8.9%
Atlas Venture(4) 890 Winter St. Waltham, MA 02154	2,564,151	10.6%	6.7%
Oxford Bioscience Partners(5) 315 Post Road West Westport, CT 06880	2,092,863	8.6%	5.5%
CIBC(6) 425 Lexington Avenue, 9th Floor New York, NY 10017	2,099,118	8.7%	5.5%
Forward Ventures(7) 9255 Towne Centre Drive, Suite 300 San Diego, CA 92121	1,242,324	5.1%	3.2%
Joseph S. (Jay) Mohr(8)	65,302	*	*
Taylor J. Crouch	86,962	*	*
Anne L. Bailey(9)	178,502	*	*
Alan C. Houston, M.D.(10)	81,431	*	*
Richard P. Shea(11)	160,307	*	*
Vincent P. Stanton Jr., M.D.(12)	172,849	*	*
Colin W. Dykes, Ph.D.	91,909	*	*
David Housman, Ph.D.(13)	304,901	1.3%	*
Philippe O. Chambon, M.D., Ph.D.(14)	3,985,363	16.3%	10.3%
Jean-Francois Formela, M.D.(15)	2,602,847	10.7%	6.8%
William A. Scott, Ph.D.(16)	32,173	*	*
Martin A. Vogelbaum(17)	154,303	*	*
Ellen M. Zane(18)	28,892	*	*
All directors and current executive officers as a group (10 persons)	7,685,439	30.1%	19.4%

* Represents beneficial ownership of less than one percent of Variagenics outstanding shares of common stock.

(1) Addresses are given for beneficial owners of more than 5% of the outstanding common stock only. Unless otherwise indicated, the address of each shareholder is c/o Variagenics, Inc., 60 Hampshire Street, Cambridge, Massachusetts 02139.

(2) The number of shares of Variagenics common stock issued and outstanding on November 15, 2002 was 24,117,061. Shares of common stock that an individual or group has the right to acquire within sixty days of November 15, 2002, pursuant to the exercise of options and warrants or pursuant to stock

purchase agreements, are deemed outstanding for the purpose of computing the percentage ownership of such individual or group, but are not deemed to be outstanding for the purpose of computing the percentage ownership of any other person shown in the table. Additionally, for calculating the percentage of shares beneficially owned after the merger, the number of shares of Hyseq common stock issuable in exchange for shares of Variagenics common stock outstanding as of September 30, 2002 has been included in the calculation of percentage ownership.

(3) This information, except the percentage beneficially owned, is based solely on a Schedule 13G filed by Wells Fargo & Company with the Securities and Exchange Commission on March 26, 2001. Includes 2,979,815 shares of common stock and warrants to purchase 439,200 shares of common stock held by Wells Fargo Bank Indiana, N.A. (the Bank), as trustee, pursuant to a voting trust agreement by and among the Bank, Sprout Capital VIII, L.P., Sprout Venture Capital, L.P., DLJ Capital Corporation, DLJ ESC II, L.P. and Donaldson, Lufkin & Jenrette, Inc. Philippe O. Chambon, M.D., Ph.D. is a general partner of the general partner of Sprout Capital VIII, L.P.

(4) This information, except the percentage beneficially owned, is based solely on a Schedule 13G filed by Atlas Venture Fund III, L.P. with the Securities and Exchange Commission on February 8, 2002. Includes 2,332,891 shares of common stock and warrants to purchase 188,470 shares of common stock held by Atlas Venture Fund III, L.P. and 38,691 shares of common stock and warrants to purchase 4,099 shares of common stock held by Atlas Venture Entrepreneurs Fund III L.P. Jean-Francois Formela, M.D., is a general partner of Atlas Venture.

(5) This information is based solely on a Schedule 13G filed by Oxford Bioscience with the Securities and Exchange Commission on February 13, 2002. Includes 800,492 shares of common stock and warrants to purchase 62,468 shares of common stock held by Oxford Bioscience Partners II, L.P., 599,897 shares of common stock and warrants to purchase 46,815 shares of common stock held by Oxford Bioscience Partners (Bermuda) II, L.P., 172,827 shares of common stock and warrants to purchase 16,206 shares of common stock held by Oxford Bioscience Partners (Adjunct) II, L.P., and 357,583 shares of common stock and warrants to purchase 36,575 shares of common stock held by Oxford Bioscience Partners (GS-Adjunct) II, L.P.

(6) This information, except the percentage beneficially owned, is based solely on a Schedule 13G filed by Canadian Imperial Bank of Commerce (CIBC) with the Securities and Exchange Commission on February 14, 2001. Includes 1,574,339 shares of common stock held by CIBC WMV Inc., a wholly-owned indirect subsidiary of CIBC, and 524,779 shares of common stock held by CIBC Employee Private Equity Fund Partners, a vehicle owned by partnerships established for the benefit of employees of CIBC to which CIBC serves as an advisor.

(7) This information is based solely on a Schedule 13G filed by Forward Ventures III, L.P. with the Securities and Exchange Commission on February 12, 2002. Includes 216,155 shares of common stock and warrants to purchase 43,364 shares of common stock held by Forward Ventures III, L.P. and 818,587 shares of common stock and warrants to purchase 164,218 shares of common stock held by Forward Ventures III Institutional Partners, L.P.

(8) Includes 65,002 shares issuable upon the exercise of options to purchase common stock.

(9) Includes 134,155 shares issuable upon the exercise of options to purchase common stock.

(10) Includes 79,298 shares issuable upon the exercise of options to purchase common stock.

(11) Includes 153,328 shares issuable upon the exercise of options to purchase common stock.

(12) Includes 122,550 shares issuable upon the exercise of options to purchase common stock.

(13) Includes 115,467 shares issuable upon the exercise of options to purchase common stock.

(14) Includes 31,534 shares of common stock issuable upon the exercise of options to purchase common stock. Includes 2,442,751 shares of common stock and warrants to purchase 381,796 shares of common stock held by Wells Fargo Bank Indiana, N.A. (the Bank), as trustee, pursuant to a voting trust agreement by and among the Bank, Sprout Capital VIII, L.P., Sprout Venture Capital, L.P., DLJ Capital Corporation, DLJ ESC II, L.P. and Donaldson, Lufkin & Jenrette, Inc. and 1,129,282 shares of common stock held by Sprout Capital VIII, L.P. Dr. Chambon is a general partner of the general partner of

Sprout Capital VIII, L.P. and disclaims beneficial ownership of such shares and warrants, except to the extent of his pecuniary interest in the shares and warrants.

(15) Includes 33,696 shares issuable upon the exercise of options to purchase common stock. Includes 2,371,582 shares of common stock and warrants to purchase 192,569 shares of common stock held by Atlas Venture. Dr. Formela is a general partner of Atlas Venture and disclaims beneficial ownership of such shares and warrants, except to the extent of his pecuniary interest in the shares and warrants.

(16) Includes 30,673 shares issuable upon the exercise of options to purchase common stock.

(17) Includes 152,303 shares issuable upon the exercise of options to purchase common stock.

(18) Consists of 28,892 shares issuable upon the exercise of options to purchase common stock.

Legal Proceedings of Variagenics

On or about December 6, 2001, Variagenics was sued in a complaint filed in the United States District Court for the Southern District of New York naming as defendants Variagenics and certain of its officers and its underwriters. The complaint purportedly is filed on behalf of persons purchasing Variagenics stock between July 21, 2000 and December 6, 2000, and alleges violations of Sections 11, 12(a)(2) and 15 of the Securities Act of 1933, as amended, and Section 10(b) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder.

The complaint alleges that, in connection with Variagenics July 21, 2000 initial public offering, the defendants failed to disclose additional and excessive commissions purportedly solicited by and paid to the underwriter defendants in exchange for allocating shares of Variagenics stock to preferred customers and alleged agreements among the underwriter defendants and preferred customers tying the allocation of IPO shares to agreements to make additional aftermarket purchases at pre-determined prices. Plaintiffs claim that the failure to disclose these alleged arrangements made Variagenics registration statement on Form S-1 filed with the SEC in July 2000 and the prospectus, a part of the registration statement, materially false and misleading. Plaintiffs seek unspecified damages. On or about April 19, 2002, an amended complaint was filed which makes essentially the same allegations. On or about July 15, 2002, Variagenics and the individuals filed a motion to dismiss. Plaintiffs have recently voluntarily dismissed their claims against the individual defendants.

Variagenics believes that the allegations are without merit, however, Variagenics, along with most of the other issuers, has begun settlement discussions with the plaintiffs. Variagenics believes that any loss or settlement amount, if any, will not be material to its financial condition, however, Variagenics cannot predict the outcome of this matter.

Other than the litigation disclosed above, Variagenics is not involved in any legal proceedings that are material to its business or financial condition.

Table of Contents

COMPARISON OF STOCKHOLDER RIGHTS AND CORPORATE GOVERNANCE MATTERS

Hyseq is incorporated under the laws of the State of Nevada, while Variagenics is incorporated under the laws of the State of Delaware. Before the completion of the merger, the rights of holders of Variagenics common stock are governed by Delaware law, the certificate of incorporation of Variagenics and the by-laws of Variagenics. After the completion of the merger, Variagenics stockholders will become stockholders of Hyseq, and their rights will be governed by Nevada law, the articles of incorporation of Hyseq, as amended, the by-laws of Hyseq and the Rights Agreement between Hyseq and U.S. Stock Transfer.

While there are substantial similarities between Delaware law and Nevada law as well as between the charters and by-laws of Hyseq and Variagenics, a number of differences do exist. The following is a summary of the material differences between the rights of Hyseq stockholders and the rights of Variagenics stockholders. While Hyseq and Variagenics believe that this summary covers the material differences between the two, this summary may not contain all of the information that is important to you. This summary is not intended to be a complete discussion of the respective rights of Hyseq and Variagenics stockholders and it is qualified in its entirety by reference to Delaware law, Nevada law and the various documents of Hyseq and Variagenics referenced in this summary. You should carefully read this entire joint proxy statement/ prospectus and the other documents referenced in this joint proxy statement/ prospectus for a more complete understanding of the differences between being a stockholder of Hyseq and being a stockholder of Variagenics. Hyseq and Variagenics have filed with the SEC their respective documents referred to herein and will send copies of these documents to you upon your request. See the section entitled Where You Can Find More Information.

	Hyseq	**Variagenics**
Authorized Capital Stock	The authorized capital stock of Hyseq consists of 100,000,000 shares of common stock, par value of $.001 per share, 3,000,000 shares of Series A preferred stock, par value of $.001 per share, and 5,000,000 shares of Other Series preferred stock. No shares of preferred stock are outstanding.	The authorized capital stock of Variagenics consists of 70,000,000 shares of common stock, $.01 par value per share, and 5,000,000 shares of preferred stock, $.01 par value per share. No shares of preferred stock are outstanding.
Number of Directors	Nevada law provides that a corporation must have at least one director and may provide in its articles of incorporation or its by-laws for a fixed number of directors or a variable number of directors within a fixed maximum and minimum. Hyseq s by-laws provide that its board of directors will consist of at least two and at most nine directors and that the exact number of directors will be determined by the board of directors. The number of directors of Hyseq currently is fixed at 7.	Delaware law provides that a corporation must have at least one director and that the number of directors shall be fixed by or in the manner provided in the by-laws unless the certificate of incorporation fixes the number of directors. Variagenics certificate of incorporation does not fix the number of directors and its by-laws provide that its number of directors shall be fixed from time to time exclusively by the board of directors. The number of directors of Variagenics currently is fixed at 6.
Cumulative Voting	Nevada law allows for a corporation s articles of incorporation to permit stockholders to cumulate their votes for directors. However, the articles of	Delaware law allows for a corporation s certificate of incorporation to permit stockholders to cumulate their votes for directors. However, the certificate of

Table of Contents

	Hyseq	Variagenics
	incorporation of Hyseq do not so provide, and accordingly, holders of Hyseq common stock have no cumulative voting rights in connection with the election of directors.	incorporation of Variagenics does not so provide, and accordingly, holders of Variagenics common stock have no cumulative voting rights in connection with the election of directors.
Classification of Board of Directors	Nevada law provides that the articles of incorporation or the by-laws may provide for a classified board of directors, but at least one-fourth of the directors must be elected annually. Hyseq s by-laws provide for three classes of directors that serve staggered terms of one, two or three years as is designated at the time of a director s election.	Delaware law permits, but does not require, a classified board of directors, divided into as many as three classes with staggered terms under which one-half or one-third of the directors are elected to terms of two or three years, as applicable. Variagenics certificate of incorporation provides that the board of directors shall be divided into three classes that serve staggered terms of one, two or three years as is designated at the time of the director s election.
Removal of Directors	Under Nevada law, directors may be removed from office by a two-thirds stockholder vote, or if provided for in the articles of incorporation, by the vote of a larger percentage of shares. However, if a corporation s articles of incorporation provide for cumulative voting to elect directors, such directors may not be removed other than by a vote or a sufficient number of shares to have prevented their election in the first instance. Hyseq s by-laws provide that any director or the entire board of directors may be removed, with cause, by the holders of 66 2/3% of the voting rights of the shares then entitled to vote at an election of directors.	Under Delaware law, directors may be removed from office by a majority stockholder vote and in the case of the corporation whose board is classified, stockholders may effect such removal only for cause. Variagenics certificate of incorporation provides that any director or the entire board of directors may be removed from office for cause by the holders of a majority of the outstanding shares of capital stock entitled to vote at an election of directors.
Vacancies on the Board of Directors	Nevada law provides that all vacancies on a corporation s board of directors, including those caused by an increase in the number of directors, may be filled by a majority of the remaining directors, though less than a quorum, unless the articles of incorporation provide otherwise. Hyseq s articles of incorporation provide that vacancies occurring on the board of directors other than by expiration of the director s term may	Delaware law provides that all vacancies on a corporation s board of directors, including those caused by an increase in the number of directors, may be filled by a majority of the remaining directors, though less than a quorum, unless the certificate of incorporation provides otherwise. Variagenics certificate of incorporation provides that newly created directorships resulting from

Table of Contents

	Hyseq	Variagenics
	be filled only by the board of directors and not by the stockholders. Hyseq s by-laws provide that vacancies caused by reason of death, resignation or removal will be filled by a majority of the directors then in office, although less than a quorum, or by a sole remaining director, and vacancies and newly created directorships resulting from an increase in the authorized number of directors elected by all of the stockholders having the right to vote as a single class may be filled by a majority of the directors then in office, although less than a quorum, or by a sole remaining director.	any increase in the authorized number of directors or any vacancy resulting from death, resignation, retirement disqualification, removal from office or other cause may be filled only by a majority vote of the directors then in office, even though less than a quorum, or by a sole remaining director.
Stockholder Action by Written Consent	Nevada law provides that unless otherwise provided in a corporation s articles of incorporation or by-laws, any action required or permitted to be taken at a meeting of stockholders may be taken without a meeting if a written consent to the action is signed by stockholders holding at least a majority of the voting power. If a different proportion of voting power is required for an action at a meeting, then that proportion of written consents is also required. Hyseq s articles of incorporation and by-laws provide that no stockholder action may be taken by written consent.	Delaware law provides that unless otherwise provided in a corporation s certificate of incorporation or by- laws, any action required or permitted to be taken at a meeting of stockholders may be taken without a meeting if a written consent to the action is signed by stockholders holding at least a majority of the voting power. If a different proportion of voting power is required for an action at a meeting, then that proportion of written consents is also required. Variagenics certificate of incorporation and by-laws provide that no stockholder action may be taken by written consent.
Amendment of Articles of Incorporation or Certificate of Incorporation	Under Nevada law and Hyseq s articles of incorporation, the articles of incorporation may be amended by the affirmative vote of the holders of a majority of the voting rights of all classes of stock entitled to vote. However, the affirmative vote of the holders of 66 2/3% of the voting rights is required to amend, repeal or adopt any provision inconsistent with the provisions of the articles of incorporation relating to: stockholder action only being allowed at a duly called annual or special meeting; the authority and power of Hyseq s	Under Delaware law and Variagenics certificate of incorporation, the certificate of incorporation may be amended by the affirmative vote of the holders of a majority of the voting rights of all classes of stock entitled to vote. However, the affirmative vote of the holders of 70% of the voting power of all of the outstanding shares of capital stock of the corporation entitled to vote generally in the election of directors, voting together as a single class, is required to: a) reduce the number of authorized shares of common stock and the number of authorized shares of

Table of Contents

	Hyseq	Variagenics
	board of directors and the procedure required to amend Hyseq s by-laws; the authority of the Hyseq s board of directors to consider factors other than price when evaluating whether to accept an offer to acquire Hyseq or its assets; the percentage of the shares necessary to amend the articles of incorporation; the elimination of directors personal liability for monetary damages arising from their negligence and gross negligence; and indemnification of directors, officers and other persons.	preferred stock; b) amend, alter, repeal or adopt any provision inconsistent with the provisions of the certificate of incorporation related to: stockholder action only being allowed at an annual or special meeting duly called by the board of directors; the provisions related to the election, nomination and removal of directors; the authority and power of Variagenics board of directors and the procedure required to amend Variagenics by-laws; the percentage of shares necessary to amend the certificate of incorporation; and indemnification of officers, directors and other persons.
Amendment of Bylaws	Nevada law provides that subject to the by-laws adopted by the stockholders, if any, the directors may amend the by-laws of the corporation. Hyseq s articles of incorporation and by-laws provide that the by-laws may be amended by Hyseq s board of directors or by an affirmative vote of the holders of 66 2/3% of the voting rights of all classes of stock entitled to vote.	Delaware law provides that a corporation s stockholders entitled to vote have the power to amend by- laws, although the corporation s certificate of incorporation may give the board of directors the power to amend the by-laws. Variagenics certificate of incorporation provides that the by-laws may be amended, altered or repealed, and new by-laws may be adopted, by the board of directors. The stockholders of Variagenics also have the power to adopt, amend or repeal the by-laws, but only if the affirmative vote of 70% of the voting power of all outstanding shares of capital stock entitled to vote generally in the election of directors, voting together as a single class, is obtained.
Special Meeting of Stockholders	Under Nevada law, meetings may be held in the manner provided by the by-laws of the corporation. Hyseq s by-laws provide that special meetings of the stockholders may be called by the Chief Executive Officer, president, the board of directors or by holders of common stock who	Under Delaware law, meetings may be held in the manner provided by the by- laws of the corporation. Variagenics certificate of incorporation and by-laws provide that special meetings of the stockholders may be called only by the board of directors pursuant to a resolution adopted by the majority of

Table of Contents

	Hyseq	Variagenics
	hold, in the aggregate, not less than 50% of the outstanding shares of common stock for the purpose or purposes stated in the call of the meeting.	the directors.
Notice of Stockholder Meetings	Under Nevada law and Hyseq s by- laws, written notice of any meeting of the stockholders must be given not less than ten nor more than 60 days before the date of the meeting to each stockholder entitled to vote at the meeting. Nevada law also provides that the articles of incorporation or by-laws may require that the notice be published in one or more newspapers. Neither Hyseq s by-laws nor its articles of incorporation contain such a requirement.	Under Delaware law and Variagenics by-laws, written notice of any meeting of the stockholders must be given to each stockholder entitled to vote at the meeting not less than ten nor more than 60 days before the date of the meeting.
Delivery and Notice Requirements of Stockholder Nominations and Proposals	Nevada corporate law does not specify how stockholders may nominate directors or bring other business before a stockholder meeting. Hyseq s by-laws provide that for nominations or other business to be properly brought before an annual meeting by a stockholder, the stockholder must notify Hyseq s secretary not less than 60 days nor more than 90 days prior to the first anniversary of the preceding year s annual meeting. However, if the date of the annual meeting is advanced by more than 30 days or delayed by more than 60 days from that anniversary date, then notice must be delivered no earlier than 90 days before the annual meeting and no later than 60 days before the annual meeting, or no later than 10 days after the day on which public announcement of the date of the annual meeting is first made by Hyseq. Hyseq s by-laws also provide that in the event that the number of directors to be elected is increased and there is no public announcement naming all of the nominees for director or specifying the size of the increased board of directors made by Hyseq at least 70 days before the first anniversary of the preceding year s annual meeting, a	Variagenics by-laws provide that for a stockholder proposal to be brought properly before an annual meeting, the stockholder must notify the corporate secretary of Variagenics not less than 60 days nor more than 90 days prior to the first anniversary of the preceding year s annual meeting. However, if the actual date of the annual meeting is more than 30 days before or more than 60 days after that anniversary date, then notice must be delivered no earlier than the 90th day prior to the annual meeting and no later than the 60th day prior to the annual meeting, or no later than ten days after the day on which public announcement of the date of the annual meeting is first made by Variagenics. Variagenics by-laws also provide that for a stockholder to nominate a director in the event that the number of directors to be elected has increased and there is no public announcement by Variagenics naming all of the nominees for director or specifying the size of the increase to the board of directors at least 70 days prior to the first anniversary of the preceding year s annual meeting (or if the annual meeting is held more than 30 days before or 60 days after such anniversary date,

Table of Contents

	Hyseq	Variagenics
	stockholder s notice will be timely, with respect to nominees for any new positions created by that increase, if it is delivered to Hyseq s secretary not later than 10 days after the first public announcement by Hyseq of the increase. Hyseq s by-laws also provide that in the event of a special meeting called by Hyseq to elect directors, a Hyseq stockholder may nominate a person for election if it delivers notice to the secretary not earlier than 90 days before that special meeting and not later than 60 days before that special meeting or 10 days after the day the first public announcement by Hyseq of the date of the special meeting and of the nominees proposed by the board of directors to be elected.	at least 70 days prior to such annual meeting), such notice will be timely if delivered to the secretary of Variagenics no later than the 10th day following the day in which public announcement is first made by Variagenics. Variagenics by-laws also provide that in the event Variagenics calls a special meeting of stockholders for the purpose of electing directors, a stockholder may nominate a person for election if it delivers notice to the secretary of Variagenics no earlier than the 90th day prior to the special meeting and no later than the 60th day prior to such special meeting, or the 10th day following the day in which public announcement of the special meeting is first made by Variagenics.
Proxy	Under Nevada law, at any meeting of the stockholders of a corporation, a stockholder may designate another person to act as a proxy. A proxy is effective only for a period of six months, unless it is coupled with an interest or unless otherwise provided in the proxy. No proxy shall be valid for more than seven years. Hyseq s by-laws provide that no proxy shall be valid after three years from its date of execution, unless the proxy provides for a longer period.	Under Delaware law, at any meeting of the stockholders of a corporation, a stockholder may designate another person to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period.
Preemptive Rights	Under Nevada law, absent an express provision in a corporation s articles of incorporation, a stockholder does not, by operation of law, possess preemptive rights to subscribe to additional issuances of its stock. Hyseq s articles of incorporation provide that no stockholder shall be entitled as a matter of right to subscribe for any additional stock or other securities.	Under Delaware law, absent express provision in a corporation s certificate of incorporation, a stockholder does not, by operation of law, possess preemptive rights to subscribe to additional issuances of the corporation s stock. Variagenics certificate of incorporation does not provide that stockholders possess any preemptive right to subscribe to additional issuances of its capital stock.
Dividends	Under Nevada law, the board of directors may make distributions to	Under Delaware law, a corporation may pay dividends out of surplus or

Table of Contents

	Hyseq	Variagenics
	stockholders, unless otherwise provided in the articles of incorporation. However, no distribution may be made if it would cause: the corporation to be unable to pay its debts as they become due; or except as otherwise specifically allowed by the articles of incorporation, the corporation s assets to be less than the sum of its liabilities plus the amount that would be needed, if the corporation were to be dissolved at the time of the distribution, to satisfy the preferential stockholders whose rights are superior to those receiving the distribution.	net profits for the current or preceding fiscal year, provided that the capital of the corporation is not less than the aggregate liquidation preference of the corporation s outstanding stock having a preference upon distribution of assets. Variagenics board of directors may declare and pay dividends on common stock only from legally available funds for the payment of such dividends. Under Variagenics certificate of incorporation holders of common stock are treated equally for the purpose of dividend rights. Variagenics has never paid cash dividends on its common stock.
Limitation of Personal Liability of Directors and Officers	In accordance with Nevada law, Hyseq s articles of incorporation provide that none of its directors or officers shall be personally liable to it or any of its stockholders for damages for breach of fiduciary duty as a director or officer. However, this provision excludes any limitation on liability for: acts or omissions which involve intentional misconduct, fraud or a knowing violation of law, or the payment of distributions in violation of Nevada law.	Variagenics certificate of incorporation does not limit the personal liability of its officers and directors or any of its stockholders for damages for breach of fiduciary duty as a director or officer.
Indemnification of Officers and Directors	In accordance with Nevada law, Hyseq s by-laws provide that it shall indemnify any person who was or is a party or is threatened to be made a party to, or otherwise becomes involved in, any proceeding (other than an action by or in the right of the corporation) by reason of the fact that he is or was an officer, director or agent of Hyseq against losses actually and reasonably incurred by that person if they acted in good faith and in a manner they reasonably believed to be in or not opposed to the best interests of Hyseq. Losses are the total amount that the officer, director or agent becomes legally obligated to pay, including judgments, fines, amounts	Variagenics certificate of incorporation provides that Variagenics shall, to the fullest extent permitted by Delaware law, as amended from time to time, indemnify each director, officer or other person serving as an agent of the corporation who is made party or is otherwise involved in a suit or proceeding by reason of that fact. Variagenics shall not be required to indemnify any director, officer or other person in connection with any proceeding initiated by such person against Variagenics, its officers, directors, employees or other agents unless (i) such indemnification is expressly required to be made by law or (ii) the proceeding was authorized

Table of Contents

	Hyseq	Variagenics
	paid in settlement, attorneys fees, expenses of establishing a right to indemnification and other expenses. If the proceeding is a criminal proceeding, the person to be indemnified must have had no reasonable cause to believe their conduct was unlawful. Hyseq will provide similar indemnification to a person for expenses, resulting from an action by or in the right of Hyseq, except that no indemnification will be made if that person is adjudged by a court of competent jurisdiction after exhaustion of all appeals to be liable to the corporation or for amounts paid in settlement to the corporation unless the court determines that the person is fairly and reasonably entitled to indemnity for expenses. Expenses of officers, directors and agents include attorneys fees, any expenses of establishing a right to indemnification and amounts paid in settlement. Expenses incurred by an officer, director or agent of Hyseq shall be paid by it as they are incurred and before the final disposition of the proceeding upon receipt of an undertaking by or on behalf of that person to repay the amount if it is ultimately be determined by a court that he or she is not entitled to be indemnified by the corporation. The indemnification and advancement of expenses provided by Hyseq s by-laws is not exclusive of any other similar rights a person may have. Hyseq has the power to purchase and maintain insurance on behalf of any person who is or was an officer, director or agent of the corporation against any liability resulting from that person s relationship to the Hyseq.	by the board of directors. Variagenics will provide similar indemnification to a person for expenses, except that no indemnification will be made if that person is adjudged by a court of competent jurisdiction after exhaustion of all appeals to be liable to the corporation. Expenses incurred by such person shall be paid by Variagenics as incurred and before final disposition of the proceeding upon receipt of an undertaking by or on behalf of such person to repay the amount if it is ultimately determined by a court, after exhaustion of all appeals, that such person is not entitled to be indemnified by the corporation. Delaware law and Variagenics by- laws provide that Variagenics has the power to purchase and maintain insurance on behalf of any person who is or was an agent of it against any liability resulting from that person s relationship to the corporation, regardless of whether Variagenics would have the power to indemnify such person against losses under the Delaware General Corporation Law.
Stockholder Rights Plan	Hyseq has adopted a stockholder rights plan. Pursuant to the stockholder rights plan, holders of Hyseq common stock become entitled to purchase shares of common stock of Hyseq or of an	

Table of Contents

	Hyseq	Variagenics
	acquiring entity for half price upon a person or group acquiring a threshold percentage of Hyseq common stock. The rights could discourage, delay or prevent certain types of transactions involving an actual or potential change in control of Hyseq, including transactions in which stockholders might otherwise receive a premium for their shares over current market prices. The Hyseq rights agreement does not apply to the merger with Variagenics. See Information About Hyseq Description of Hyseq Capital Stock for a more complete description of the stockholder rights plan.	
Appraisal Rights	Nevada law provides that stockholders have the right, in some circumstances, to dissent from certain corporate reorganizations and to instead demand payment of the fair cash value of their shares. Unless a corporation s articles of incorporation provide otherwise, dissenters do not have rights of appraisal with respect to a merger or consolidation by a corporation, if the shares of the corporation are either: listed on a national securities exchange, designated as a national market system security on an interdealer quotation system by the National Association of Securities Dealers, Inc., or held by at least 2,000 stockholders of record, unless the stockholders receive in exchange for their shares anything other than cash, shares, or cash and shares. In each case, the shares must be of the surviving corporation or of another corporation that is publicly listed or held by more than 2,000 stockholders. Stockholders of a corporation surviving a merger do not have appraisal rights if no vote of the	Delaware law provides that stockholders have the right, in some circumstances, to dissent from certain corporate reorganizations and to instead demand payment of the fair cash value of their shares. Unless a corporation s articles of incorporation provide otherwise, dissenters do not have rights of appraisal with respect to a merger or consolidation by a corporation, if the shares of the corporation are either: listed on a national securities exchange, designated as a national market system security on an interdealer quotation system by the National Association of Securities Dealers, Inc., or held by at least 2,000 stockholders of record, unless the stockholders receive in exchange for their shares anything other than cash in lieu of fractional shares, shares, or a combination of the foregoing. In each case, the shares must be of the surviving corporation or of another corporation that are publicly listed or held by more than 2,000 stockholders. Stockholders of a corporation surviving a merger do not have

Table of Contents

	Hyseq	Variagenics
	stockholders of the surviving corporation is required to approve the merger. Appraisal rights are not available to Hyseq stockholders with respect to the merger.	appraisal rights if no vote of the stockholders of the surviving corporation is required to approve the merger. Appraisal rights are not available to Variagenics stockholders with respect to the merger.
Certain Business Combination Restrictions	Nevada law prohibits certain business combinations between a corporation and an interested stockholder (one beneficially holding, directly or indirectly, at least 10% of the outstanding voting stock) for three years after such person became an interested stockholder unless such interested stockholder, prior to becoming an interested stockholder, obtained the approval of the board of directors of either the business combination or the transaction that resulted in such person becoming an interested stockholder. Nevada law will permit, however, business combinations that meet all requirements of the corporation s articles of incorporation and either: are approved by the board of directors before the interested stockholder became an interested stockholder (or as to which the purchase of shares made by the interested stockholder had been approved by the board of directors before the date of purchase), are approved by the affirmative vote of the holders of stock representing a majority of the voting stock (excluding voting stock of the interested stockholder and its affiliates and associates) at a meeting called for such purpose no earlier than three years after the interested stockholder became an interested stockholder, or the form and amount of consideration to be received by stockholders (excluding the interested stockholder) of the corporation satisfies certain tests and, with limited exceptions, the interested stockholder has not become	Section 203 of the Delaware General Corporation Law provides that if a person acquires 15% or more of the voting stock of a Delaware corporation such person is an interested stockholder and may not engage in certain business combinations with the corporation for a period of three years from the time such person acquired 15% or more of the corporation s voting stock. The statute contains certain exceptions to this prohibition. If, for example, the board of directors approves the acquisition of stock or the transaction prior to the time that the person becomes an interested stockholder, or if the interested stockholder acquires at least 85% of the voting stock of the corporation (excluding voting stock owned by directors who are also officers and certain employee stock plans) in one transaction, or if the transaction is approved by the board of directors and the affirmative vote of 2/3 of the holders of the outstanding voting stock which is not owned by the interested stockholder at a meeting of the stockholders, then the prohibition of a business combination is not applicable. A Delaware corporation can elect in its certificate of incorporation or by- laws not to be governed by Section 203. Variagenics has not made that election.

Table of Contents

	Hyseq	Variagenics
	the beneficial owner of additional voting shares of the corporation after becoming an interested stockholder and before the business combination is consummated. A corporation may expressly exclude itself from application of the foregoing business combination provisions of Nevada law, but Hyseq has not done so.	
Vote on Certain Issues	Hyseq s articles of incorporation provide that the affirmative vote of the holders of shares representing a majority of Hyseq s outstanding common stock is required to approve (a) the sale of U.S. Patent 5,202,231, or (b) an exclusive license or assignment to a single person or entity, other than a wholly owned subsidiary of Hyseq, that has the same effect as a sale of all rights, title and interest in U.S. Patent 5,202,231.	
Constituency Provision	Nevada law provides that in considering the interests of the corporation in a possible acquisition, the directors and officers of the corporation may consider the interests of the corporation s employees, suppliers, creditors and customers, the economy of the state and nation, the interests of the community and of society and the long- and short-term interests of the corporation and its stockholders.	

Table of Contents

CHAPTER TWO INFORMATION ABOUT THE SPECIAL MEETINGS AND VOTING

THE HYSEQ SPECIAL MEETING

Date, Time, Place and Purpose of the Hyseq Special Meeting

The special meeting of Hyseq stockholders will be held at .m. local time on , 2003 at , , California. The purpose of the Hyseq special meeting is to consider and vote on a proposal to approve the issuance of Hyseq common stock in connection with the merger and a proposal to amend the Hyseq, Inc. 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.

Recommendation of the Hyseq Board of Directors

The Hyseq board of directors has unanimously approved the merger agreement, and unanimously recommends that Hyseq stockholders vote **FOR** approval of the issuance of Hyseq common stock to Variagenics stockholders in the merger and **FOR** the amendment to the Hyseq, Inc. 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.

Record Date; Outstanding Shares; Shares Entitled to Vote

Only holders of record of Hyseq common stock at the close of business on the record date, , 2002, are entitled to notice of and to vote at the special meeting. As of the record date, there were shares of Hyseq common stock issued and outstanding, including shares beneficially owned by its executive officers and directors, or % of the outstanding shares of Hyseq common stock as of . A list of Hyseq stockholders will be available for review at Hyseq s executive offices during regular business hours for a period of ten days before the special meeting. Each share of Hyseq common stock is entitled to one vote.

Quorum and Vote Required

A quorum of stockholders is necessary to hold a valid special meeting. The presence, in person or by proxy, of shares of Hyseq common stock representing a majority of shares of Hyseq common stock issued and outstanding on the Hyseq record date will constitute a quorum. Abstentions and broker non-votes, discussed below, count as present for establishing a quorum.

The issuance of the Hyseq common stock in connection with the merger and the amendment to the Hyseq, Inc. 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 requires the affirmative vote of a majority of the shares of Hyseq common stock represented and entitled to vote at the Hyseq special meeting.

Voting; Proxies; Revocation

A proxy card is enclosed for your use. Hyseq asks that you sign, date and return the proxy card in the accompanying envelope, which is postage prepaid if you mail it in the United States.

You have choices on each of the matters to be voted upon at the special meeting. Concerning the issuance of Hyseq common stock in connection with the merger you may:

approve the issuance;

disapprove the issuance; or

abstain from voting for or against the issuance.

Table of Contents

Concerning the amendment to the Hyseq, Inc. Employee Stock Purchase Plan to increase the number of shares of Hyseq common stock available for issuance under the plan by 500,000 to 750,000 shares you may:

approve the amendment;

disapprove the amendment; or

abstain from voting for or against the amendment.

Unless there are different instructions on the proxy, all shares represented by valid proxies (and not revoked before they are voted) will be voted at the meeting *FOR* (1) the issuance of Hyseq common stock in connection with the merger and (2) the amendment to the Hyseq, Inc. Employee Stock Purchase Plan to increase the number of shares of Hyseq common stock available for issuance under the plan by 500,000 to 750,000 shares. With respect to any other business that may properly come before the special meeting and be submitted to a vote of stockholders, proxies will be voted in accordance with the best judgment of the designated proxy holders.

Stockholders of record may vote by either completing and returning the enclosed proxy card prior to the special meeting, voting in person at the special meeting, or submitting a signed proxy card at the special meeting.

Your vote is important. Accordingly, please sign and return the accompanying proxy card whether or not you plan to attend the special meeting in person.

You may revoke your proxy at any time before it is actually voted at the meeting by:

delivering written notice of revocation to Hyseq s Secretary at 670 Almanor Avenue, Sunnyvale, California 94085;

submitting a later dated proxy; or

attending the meeting and voting in person.

Your attendance at the special meeting will not, by itself, constitute revocation of your proxy. You may also be represented by another person present at the meeting by executing a form of proxy designating that person to act on your behalf. Shares may only be voted by or on behalf of the record holder of shares as indicated in Hyseq s stock transfer records. If you are a beneficial owner but your shares are held of record by another person, such as a stock brokerage firm or bank, that person must vote the shares as the record holder in accordance with the beneficial holder s instructions.

All votes cast at the special meeting will be tabulated by the persons appointed by Hyseq to act as inspectors of election for the special meeting.

Abstentions and Broker Non-Votes

Shares represented by proxies that reflect abstentions or broker non-votes (*i.e.*, shares held by a broker or nominee which are represented at the meeting, but with respect to which the broker or nominee is not empowered to vote on a particular proposal) will be counted as shares that are present and entitled to vote for purposes of determining the presence of a quorum but are counted as votes against a particular proposal in determining whether a matter has been approved. The issuance of Hyseq common stock in connection with the merger and the amendment to the Hyseq, Inc. Employee Stock Purchase Plan to increase the number of shares of Hyseq common stock available for issuance under the plan by 500,000 to 750,000 shares, each requires the affirmative vote of the holders of a majority of the shares of its stock entitled to vote, present in person or represented by proxy.

Proxy Solicitation

This solicitation is made on behalf of Hyseq s board of directors and Hyseq will pay the costs of solicitation except that Hyseq and Variagenics have each agreed to pay one-half of the costs of filing, printing and mailing this joint proxy statement/prospectus and related proxy materials. Hyseq s directors, officers and

148

Table of Contents

employees may also solicit proxies by telephone, telegraph, fax or personal interview. Hyseq will not pay any additional compensation to directors, officers or other employees for such services, but may reimburse them for reasonable out-of-pocket expenses in connection with such solicitation. Hyseq will reimburse banks, brokerage firms and other custodians, nominees and fiduciaries for reasonable expenses incurred by them in sending proxy material to its stockholders. Hyseq has retained U.S. Stock Transfer Corporation to assist in the solicitation of proxies with respect to shares of Hyseq common stock held of record by brokers, nominees and institutions for a customary fee, estimated to be approximately $15,000, plus reimbursement of expenses.

Other Business; Adjournments

As of the date of this joint proxy/prospectus, the Hyseq board of directors does not know of any matter that will be presented for consideration at the Hyseq special meeting other than as described in this joint proxy/prospectus.

Adjournments may be made for the purpose of, among other things, soliciting additional proxies. An adjournment may be made from time to time by approval of the holders of shares representing a majority of the votes present in person or by proxy at the special meeting, whether or not a quorum exists, without further notice other than by an announcement made at the special meeting. Hyseq does not currently intend to seek an adjournment of the special meeting.

Assistance

If you need assistance in completing your proxy card or have questions regarding the special meeting, please call (818) 502-1404 or write to the following address:

U.S. Stock Transfer Corporation
1745 Gardena Avenue
Glendale, California 91204

Table of Contents

THE VARIAGENICS SPECIAL MEETING

Date, Time, Place and Purpose of the Variagenics Special Meeting

The special meeting of Variagenics stockholders will be held at .m. local time on , 2003 at , , Massachusetts. The purpose of the Variagenics special meeting is to consider and vote on a proposal to adopt a merger agreement between Hyseq, Vertical Merger Corp., which is a wholly-owned subsidiary of Hyseq, and Variagenics and to transact any other business that properly comes before the Variagenics special meeting or any adjournment or postponement of it. Adoption of the merger agreement will also constitute approval of the merger and the other transactions contemplated by the merger agreement.

Recommendation of the Variagenics Board of Directors

The Variagenics board of directors has approved the merger agreement, and recommends that Variagenics stockholders vote **FOR** adoption of the merger agreement. See The Merger Reasons for the Merger Variagenics.

Record Date; Outstanding Shares; Shares Entitled to Vote

Only holders of record of Variagenics common stock at the close of business on the record date, , 2002, are entitled to notice of and to vote at the special meeting. As of the record date, there were shares of Variagenics common stock outstanding and entitled to vote at the special meeting, held by approximately holders of record. A list of Variagenics stockholders will be available for review at Variagenics executive offices during regular business hours for a period of ten days before the special meeting.

Quorum and Vote Required

A quorum of stockholders is necessary to hold a valid special meeting. The presence, in person or by proxy, of shares of Variagenics common stock representing a majority of shares of Variagenics common stock outstanding and entitled to vote on the Variagenics record date is necessary to constitute a quorum at the Variagenics special meeting. Abstentions and broker non-votes, discussed below, count as present for establishing a quorum.

The affirmative vote of the holders of a majority of the shares of Variagenics common stock outstanding as of the record date is required to adopt the merger agreement.

As of the record date for the special meeting, the directors and executive officers of Variagenics as a group beneficially owned approximately shares of Variagenics common stock, including exercisable options, or approximately % of the outstanding shares of Variagenics on that date.

Voting; Proxies; Revocation

You may vote by proxy or in person at the special meeting.

Voting by Proxy

You should vote your proxy even if you plan to attend the special meeting. You can always change your vote at the special meeting. Voting instructions are included on your proxy card. If you properly give your proxy and submit it to Variagenics in time to vote, one of the individuals named as your proxy will vote your shares as you have directed.

If other matters properly come before the Variagenics special meeting, the shares represented by proxies will be voted, or not voted, by the individuals named in the proxies in their discretion. No proxy that is voted against adoption of the merger agreement will be voted in favor of any adjournment or postponement of the Variagenics special meeting for the purpose of soliciting additional proxies.

Table of Contents

How to vote by proxy:

In Writing: Variagenics stockholders of record may grant their proxies through the mail by completing their proxy card, and signing, dating and returning it in the enclosed, pre-addressed postage-paid envelope. To be valid, a returned proxy card must be signed and dated.

By Telephone: Variagenics stockholders of record will be able to use the telephone to submit their proxies. In order to submit your proxy by telephone, you must dial the toll-free number 1- - - , enter the Control Number located on your proxy card and follow the recorded instructions.

The laws of the state of Delaware, where Variagenics is incorporated, permit a stockholder to grant a proxy in each of these ways. However, if you are not the record holder of your shares, you must provide the record holder of your shares with instructions on how to vote your shares. Variagenics stockholders whose shares are held by a bank, broker or other institution should refer to their voting instruction card forwarded by the bank, broker or other institution holding their shares. If your voting instruction card does not include telephone voting instructions, please complete and return your voting instruction card by mail.

Revocation of Proxies

Variagenics stockholders of record may revoke their proxies at any time before they are voted at the Variagenics special meeting by:

delivering to the corporate Secretary of Variagenics a signed notice of revocation;

granting a later-dated signed proxy; or

attending the special meeting and voting in person, however, attendance at the special meeting will not, by itself, revoke a proxy.

If you submit your proxy or voting instructions by telephone, you can change your vote by submitting a proxy at a later date, using the same procedures, in which case your later submitted proxy will be recorded and your earlier proxy revoked. Variagenics stockholders whose shares are held in the name of a broker or nominee may change their votes by submitting new voting instructions to their brokers or nominees.

Written notices of revocation and other communications with respect to the revocation of Variagenics proxies should be addressed to:

Variagenics
60 Hampshire Street
Cambridge, MA 02139
Attention: Secretary

Voting in Person

If you plan to attend the special meeting and wish to vote in person, you will be given a ballot at the special meeting. Please note, however, that if your shares are held of record by a broker, bank or other institution and you wish to vote at the special meeting, you must bring to the special meeting a proxy from the record holder of the shares authorizing you to vote at the special meeting.

Abstentions and Broker Non-Votes

Shares of Variagenics common stock held by persons attending the Variagenics special meeting but not voting, and shares of Variagenics common stock for which Variagenics has received proxies but with respect to which holders of those shares have abstained from voting, will be counted as present at the Variagenics special meeting for purposes of determining the presence or absence of a quorum for the transaction of business at the Variagenics special meeting, and will be counted as votes cast against adoption of the merger agreement at the Variagenics special meeting for purposes of determining whether stockholder approval of the merger agreement has been obtained.

Table of Contents

Brokers that hold shares of Variagenics common stock in nominee or street name for customers who are the beneficial owners of those shares are prohibited from giving a proxy to vote shares held for those customers on the matters to be considered and voted upon at the Variagenics special meeting without specific instructions from those customers. Accordingly, if your broker holds your Variagenics common stock in nominee or street name, your broker will vote your shares only if you provide instructions on how to vote by filling out the voting instruction form sent to you by your broker with this joint proxy statement/prospectus. If you do not provide your broker with voting instructions, your unvoted shares, so-called broker non-votes, will be counted for purposes of determining whether a quorum exists, and will be counted as votes cast against adoption of the merger agreement at the Variagenics special meeting for purposes of determining whether stockholder approval of the merger agreement has been obtained.

Other Business; Adjournments

As of the date of this joint proxy/prospectus, the Variagenics board of directors does not know of any matter that will be presented for consideration at the Variagenics special meeting other than as described in this joint proxy/prospectus.

Adjournments may be made for the purpose of, among other things, soliciting additional proxies. An adjournment may be made from time to time by approval of the holders of shares representing a majority of the votes present in person or by proxy at the special meeting, whether or not a quorum exists, without further notice other than by an announcement made at the special meeting. Variagenics does not currently intend to seek an adjournment of the special meeting.

Assistance

If you need assistance in completing your proxy card or have questions regarding the special meeting, please contact Variagenics Investor Relations at (617) 588-5300 or write to the following address:

Variagenics, Inc.
60 Hampshire Street
Cambridge, MA 02139
Attn: Investor Relations

Table of Contents

CHAPTER THREE ADDITIONAL HYSEQ SPECIAL MEETING PROPOSAL

AMENDMENT TO HYSEQ, INC. EMPLOYEE STOCK PURCHASE PLAN

Hyseq stockholders are being asked to approve an amendment to the Hyseq, Inc. Employee Stock Purchase Plan (the Purchase Plan) to increase the number of shares of common stock available for issuance under the Purchase Plan from 250,000 shares to 750,000 shares. This proposal is not related to the merger. Even if the merger is not approved, Hyseq will still seek approval of this proposal. The Hyseq board of directors approved the proposed amendment described above on November 3, 2002.

Below is a summary of the principal provisions of the Purchase Plan, assuming approval of the proposed amendment, which summary is qualified in its entirety by reference to the full text of the Purchase Plan. A copy of the proposed amendment is attached as Annex E and is incorporated into this proxy statement by reference. Hyseq will provide, without charge, to each person to whom a proxy statement is delivered, upon request of such person and by first class mail within one business day of receipt of such request, a copy of the Purchase Plan. Any such request should be directed as follows: Nicole Estrin, Manager of Corporate Communications and Investor Relations, 675 Almanor Avenue, Sunnyvale, California 94085, (408) 746-4572.

General Information

The Purchase Plan, which is intended to qualify under the provisions of Section 423 of the Internal Revenue Code of 1986 (the Code), provides for the grant to employees of rights to purchase shares of Hyseq common stock at reduced prices through payroll deductions. Hyseq believes that the Purchase Plan is an effective means of aligning employees interests, through their purchases of common stock, with the interests of stockholders. The Purchase Plan is an integral part of Hyseq s over-all employee benefits package, which Hyseq relies on to help attract and retain motivated and talented employees.

Reasons for the Amendment

The Purchase Plan currently provides that the aggregate number of shares of Hyseq common stock available for purchase under the Purchase Plan is 250,000. As of the record date, of those originally available shares of Hyseq common stock have already been purchased through the Purchase Plan, leaving only shares available for future purchases. The Purchase Plan has been so successful that the number of shares available for purchase were depleted sooner than originally anticipated. As the number of Hyseq s employees grows, Hyseq expects the demand for shares under the Purchase Plan to grow as well. Considering the growing number of employees who are expected to participate in the Purchase Plan, Hyseq expects the shares made available by the amendment will meet its needs until . Because the Purchase Plan is a key benefit for employees and is part of what Hyseq believes is a very competitive compensation package, which allows Hyseq to attract and retain high-quality employees, Hyseq feels strongly that the Purchase Plan should be amended so that there is a sufficient number of shares available for future purchases.

Description of the Purchase Plan

Shares Available for Issuance. If the amendment is approved, the total number of shares of Hyseq common stock that have been purchased under the Purchase Plan, plus the number of shares that will be available for purchase by employees upon the exercise of purchase rights granted under the Purchase Plan, will equal 750,000. If any purchase right granted under the Purchase Plan expires or terminates for any reason without having been exercised in full or ceases for any reason to be exercisable in whole or in part, the unpurchased shares subject to that grant will be added back to the number of shares available for purchase. The aggregate maximum number of shares available for issuance under the Purchase Plan will be subject to appropriate adjustment in the event of stock dividends, stock splits, recapitalization, or similar changes affecting the outstanding shares of Hyseq common stock.

Administration. The Purchase Plan is administered by the Compensation Committee of Hyseq s board of directors. The Compensation Committee has full authority to construe and interpret the Purchase Plan and

correct any defect or omission or reconcile any inconsistency in the Purchase Plan, and its decisions are final, conclusive and binding upon all employees and all persons claiming under or through any employee.

Offering Periods and Purchase Dates. The Purchase Plan is implemented by consecutive offering periods (which we refer to as an offering period) of six months each, with the exact time period to be determined by the Compensation Committee (in no event to exceed twenty-seven months). On the last day of each offering period, Hyseq will apply the participants accumulated payroll deductions to purchase shares of its common stock at the purchase price described below (which we refer to as a purchase date).

Eligibility and Enrollment. All of Hyseq s employees and, if designated by its board of directors, the employees of its subsidiaries, that customarily work more than twenty hours a week are eligible to participate in the Purchase Plan on the first day of the first offering period coincident with or next following the employee s completion of 90 days of continuous service. However, no employee is eligible to participate in the Purchase Plan if, immediately after the election to participate, such employee would own 5% or more of the voting power or value of all classes of Hyseq capital stock or that of any of its affiliates, or if the employee s rights to purchase Hyseq common stock under the Purchase Plan or any other plans qualified under Section 423 of the Internal Revenue Code, would result during any calendar year in the purchase of shares having an aggregate fair market value of more than $25,000.

An eligible employee may become a participant in the Purchase Plan effective the first day of an offering period following the submission of an enrollment form that authorizes deductions from the employee s paycheck, so long as the enrollment form is submitted to the plan s administrator at least 15 days prior to the first day of the applicable offering period. If an enrollment form is submitted less than 15 days before the first day of an offering period, it shall become effective on the first day of the next offering period.

Payroll Deductions. A participant may elect to have deductions made from his or her pay on each payday at a whole number percentage rate of at least 1% but less than 10% of the compensation that he or she is entitled to receive. A participant may increase the rate of his or her payroll deductions effective as of any subsequent offering period by filing a new authorization form with the plan s administrator at least 15 days before the first day of the next offering period. A request for a decrease in payroll deductions becomes effective as soon as practicable after it is filed with the plan s administrator.

Purchase of Stock; Price. On each purchase date, each participant s accumulated payroll deductions are applied to the purchase of whole shares of Hyseq common stock at a price which is the lower of (i) 85% of the fair market value per share of Hyseq common stock on the first trading day of the offering period or (ii) 85% of the fair market value per share of Hyseq common stock on the applicable purchase date. The fair market value of Hyseq common stock on a given date is defined as the closing price on such day as reported by the Nasdaq National Market. In the event that the aggregate number of shares which all participants elect to purchase on a purchase date exceeds the number of shares remaining for issuance under the Purchase Plan, the available shares will be ratably divided and any excess cash will be refunded to the participants.

Participants are notified by statements of account as soon as practicable following each purchase date as to the amount of payroll deductions, the number of shares purchased, the purchase price and the remaining cash balance of their plan account. Certificates representing whole shares are delivered to a brokerage account in the name of each participant.

Withdrawal from the Purchase Plan. A participant may elect to withdraw from participation under the Purchase Plan at any time by filing the prescribed form with the plan s administrator. If a participant withdraws from participation under the Purchase Plan, terminates his or her employment or otherwise becomes ineligible to participate in the Purchase Plan, any unused payroll deductions will be returned to him or her without interest. A participant must wait six months from the date of his or her withdrawal from the Purchase Plan before he or she may reenter the Purchase Plan as a participant.

Amendment and Termination of the Purchase Plan. Hyseq s board of directors may amend or terminate the Purchase Plan at any time, provided that stockholder approval shall be obtained when required by applicable laws, regulations or rules.

Table of Contents

Nontransferability. The rights or interests of any participant in the Purchase Plan or in any shares or cash to which such participant may be entitled, are not transferable, except as permitted by the Code, by will or by the laws of descent and distribution.

Adjustments Upon Changes in Capitalization. Appropriate adjustments in the aggregate number of shares of Hyseq common stock available for issuance under the Purchase Plan will be made to give effect to any merger, consolidation, acquisition, reorganization, stock split, stock dividend or other relevant change in the capitalization of Hyseq.

Certain Federal Income Tax Information

The following is a general summary as of the date of this joint proxy statement/ prospectus of the federal income tax consequences to Hyseq and employees participating in the Purchase Plan. The federal tax laws may change and the federal, state and local tax consequences for any participating employee will depend upon his or her individual circumstances. Each participating employee is encouraged to seek the advice of a qualified tax advisor regarding the tax consequences for participation in this Purchase Plan.

The Purchase Plan, and the right of participants to make purchases thereunder, is intended to qualify under the provisions of Section 423 of the Code. The Purchase Plan is not subject to any provisions of the Employees Retirement Income Security Act of 1974. Under the applicable Code provisions, no income will be taxable to a participant until the sale or other disposition of the shares purchased under the Purchase Plan. Upon such sale or disposition, the participant will generally be subject to tax in an amount that depends upon the holding period. If the shares are sold or disposed of more than two years from the first day of the offering period and one year from the purchase date, the participant will recognize ordinary income measured as the lesser of (i) the excess of the fair market value of the shares at the time of such sale or disposition over the purchase price or (ii) an amount equal to 15% of the fair market value of the shares as of the first day of the offering period. Any additional gain will be treated as long-term capital gain. If the shares are held for the periods described above, are sold and the sale price is less than the purchase price, there is no ordinary income and the participating employee has a long-term capital loss for the difference between the sale price and the purchase price. If the shares are sold or otherwise disposed of before the expiration of the holding periods described above, the participant will recognize ordinary income generally measured as the excess of the fair market value of the shares on the date the shares are purchased over the purchase price. Any additional gain or loss on such sale or disposition will be long-term or short-term capital gain or loss, depending on the holding period. Hyseq is not entitled to a deduction for amounts taxed as ordinary income or capital gain to a participant except to the extent of ordinary income recognized upon a sale or disposition of shares prior to the expiration of the holding periods described above. Hyseq will treat any transfer of record ownership of shares as a disposition, unless it is notified to the contrary. In order to enable it to learn of disqualifying dispositions and ascertain the amount of the deductions to which it is entitled, participating employees will be required to notify Hyseq in writing of the date and terms of any disposition of shares purchased under the Purchase Plan.

New Plan Benefits

The amounts of future stock purchases under the Purchase Plan are not determinable because, under the terms of the Purchase Plan, purchases are based upon elections made by participants. Future purchase prices are not determinable because they are based upon fair market value of Hyseq common stock.

Vote Required and Board of Directors Recommendation

You may vote for approval of the amendment, vote against approval, or abstain from voting altogether by completing, signing and returning the enclosed proxy card or by attending the meeting. IF YOU SIGN AND RETURN THE PROXY CARD BUT NEGLECT TO COMPLETE THE FOR/ AGAINST/ ABSTAIN SECTION, THE PROXIES WILL VOTE YOUR SHARES FOR APPROVAL OF THE AMENDMENT TO THE EMPLOYEE STOCK PURCHASE PLAN.

Table of Contents

Approval of the amendment requires the affirmative vote of the holders of a majority of the shares of its stock entitled to vote, present in person or represented by proxy.

THE BOARD OF DIRECTORS RECOMMENDS THAT YOU VOTE FOR APPROVAL OF THE AMENDMENT TO THE EMPLOYEE STOCK PURCHASE PLAN, WHICH INCREASES THE NUMBER OF SHARES ISSUABLE UNDER THE PLAN FROM 250,000 TO 750,000.

Table of Contents

Information Regarding Compensation

Executive Compensation

The following table sets forth the compensation paid or accrued by Hyseq for the three fiscal years ended December 31, 2001, to or on behalf of Hyseq s Chief Executive Officer, the four other most highly compensated executive officers and two former highly compensated officers (collectively referred to as Hyseq s named executive officers).

Summary Compensation Table

		Annual Compensation($)			Long Term Compensation	
Name and Principal Position	Year	Salary	Bonus	Other Annual Compensation(1)	Securities Underlying Options/SAR(#)(2)	All Other Compensation ($)
George B. Rathmann(3)	2001				1,036,000	
Chairman of the Board and Chief Executive Officer	2000				1,033,000	
Ted W. Love(4)	2001	491,221			575,000	
President and Chief Executive Officer						
David M. Rosen(5)	2001	189,792			13,000	
Vice President of Operations	2000	170,961			4,200	
	1999	120,398			58,630	
Peter S. Garcia(6)	2001	159,167	34,000		225,000	
Senior Vice President and Chief Financial Officer						
Linda A. Fitzpatrick(7)	2001	130,449	26,250		175,000	
Senior Vice President of Human Resources						
William F. Bennett(8)	2001	126,042	41,250		250,000	
Senior Vice President of Research and Development						
Radoje T. Drmanac(9)	2001	265,000				
Chief Scientific Officer	2000	253,750	65,000		6,020	
	1999	215,000	53,250		30,290	
Snezana Drmanac(10)	2001	189,167				
Vice President of SBH	2000	173,000			4,200	
Biochemistry	1999	154,125			19,990	

(1) Excludes perquisites and other personal benefits, securities or property aggregating less than $50,000 or 10% of the total annual salary and bonus reported for each named executive officer.

(2) The securities underlying the options are shares of Hyseq s common stock.

(3) Dr. Rathmann served as Hyseq s Chief Executive Officer from May 2000 to March 2001. Salary and bonus information for the year 2001 represents compensation paid to Dr. Rathmann through March 2001. Dr. Rathmann received a grant of options to purchase 3,000 shares of Hyseq s common stock each month, with an exercise price per share equal to the fair market value of its common stock on date of each grant, in lieu of cash compensation for his services as an employee. Salary and bonus information for the year 2001 represents compensation paid to Dr. Rathmann since February 2000, when he joined Hyseq.

(4)

Dr. Love has served as Hyseq s President since January 2001 and as Chief Executive Officer and a director since March 2001. Salary and bonus information for the year 2001 represents compensation paid since January 2001.

(5) David M. Rosen resigned as Hyseq s Vice President of Operations on June 21, 2002.

(6) Mr. Garcia joined Hyseq in May 2001 as its Senior Vice President and Chief Financial Officer. Salary and bonus information for the year 2001 represents compensation paid since May 2001.

(7) Ms. Fitzpatrick joined Hyseq in April 2001 as its Senior Vice President of Human Resources. Salary and bonus information for the year 2001 represents compensation paid since April 2001.

(8) Dr. Bennett joined Hyseq in July 2001 as its Senior Vice President of Research and Development. Salary and bonus information for the year 2001 represents compensation paid since July 2001.

Table of Contents

(9) Dr. R. Drmanac resigned as Hyseq s Chief Scientific Officer to become Chief Scientific Officer of its subsidiary Callida in October 2001 and remained employed with Callida through December 2001. Salary and bonus information for the year 2001 represents compensation paid through December 2001.

(10) Dr. S. Drmanac resigned as Hyseq s Vice President of SBH Biochemistry to become Vice President of SBH and Research and Development of its subsidiary Callida in October 2001 and remained employed with Callida through December 2001. Salary and bonus information for the year 2001 represents compensation paid through December 2001.

During the periods indicated above, none of the named executive officers received any awards under any long-term incentive plan, and Hyseq does not have a pension plan.

Employment Agreements

In February 2000, Hyseq entered into its standard form of Employment and Confidential Information Agreement with Dr. Rathmann, providing for his services in capacities to be determined. Dr. Rathmann served as Hyseq s President from May 2000 to January 2001, as its Chief Executive Officer from May 2000 to March 2001, and as its Chairman and a director since February 2000. Pursuant to that agreement, and as determined by Hyseq s Board, Dr. Rathmann receives a monthly stock option grant to purchase 3,000 shares of Hyseq common stock with an exercise price per share equal to the fair market value of Hyseq common stock on the date of each grant in lieu of cash compensation for his services.

In January 2001, Hyseq entered into an employment agreement with Dr. Love. Pursuant to the agreement, Hyseq is obligated to pay Dr. Love an initial annual salary of $485,000. In addition, Dr. Love is entitled to participate in Hyseq s management bonus pool, employee benefit plans maintained by Hyseq and in other benefits provided to Hyseq s senior executives, including retirement and 401(k) plans, deferred compensation, medical and dental, annual vacation, paid holidays, sick leave and similar benefits. In connection with Dr. Love s employment agreement, Hyseq also granted him options to purchase an aggregate of 500,000 shares of Hyseq common stock. 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 in connection with this agreement or otherwise 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 the event of Dr. Love s death, the benefits described above shall be paid to his heirs. In the event Dr. Love is disabled for at least six consecutive months while employed by Hyseq, Hyseq may terminate Dr. Love, but must pay him the benefits described above.

As provided by the terms of Dr. Love s employment agreement, Hyseq has entered into a loan agreement with Dr. Love, pursuant to which he may borrow up to $2.0 million from Hyseq. The loan agreement with Dr. Love provides for interest on outstanding balances to accrue at the lowest applicable federal interest rate or such other higher rate of interest, if required, to constitute a market rate of interest as contemplated by the Rules and Regulations of the Financial Accounting Standards Board and the U.S. Securities and Exchange Commission. Interest accrues but is deferred and all interest and principal is due in January 2006. The employment agreement also provided that, at any time following his first year of employment but before the third anniversary of beginning his employment, Dr. Love may forfeit the option to

purchase 150,000 of the 500,000 shares of the option granted to him in exchange for $2.0 million plus the accrued interest under the loan agreement, and the loan then becomes immediately due and payable.

In July 2002, pursuant to the loan agreement, Hyseq loaned Dr. Love $2.0 million to repay a pre-existing loan from Dr. Rathmann to Dr. Love that had been made February 1, 2001 in the amount of $2.0 million. The $2.0 million payment was made directly to Dr. Love and is considered a loan from Hyseq to Dr. Love under the same terms and conditions as the $2.0 million loan provided for in Dr. Love s employment agreement.

Directors Plan

Hyseq grants options to purchase shares of Hyseq common stock to its directors under its Directors Plan. Under the Directors Plan, each non-employee director receives an initial grant of options when they join Hyseq s Board, and annual grants thereafter on the day of each annual meeting of stockholders. The initial grant, and each annual grant, gives each non-employee director the right to purchase up to 10,000 shares of Hyseq common stock. At each grant, the number of shares is determined by the lesser of (i) the number determined by dividing $200,000 by the fair market value of Hyseq common stock on the date of grant or (ii) 10,000 shares. A non-employee director s initial award vests as to one-half of the underlying shares on the date of grant, and one-half of the remaining portion of the award vests on the dates of the next two annual stockholders meetings. If a new non-employee director has not been a director for a year at the time of his or her first subsequent grant, then it becomes exercisable on the first anniversary of the date he or she joined Hyseq s Board. All other subsequent option grants are exercisable in full on the date of grant. In the event of a change of control (as defined below), all of the options granted under Hyseq s Directors Plan shall become immediately exercisable.

Management Stock Option Agreements

In connection with Dr. Love s employment agreement, Hyseq granted him options to purchase an aggregate of 500,000 shares of Hyseq common stock. Specifically, Hyseq granted Dr. Love (i) an option under its 1995 Stock Option Plan to purchase 31,840 shares at an exercise price of $12.56 per share, the fair market value of Hyseq common stock on the date of grant as determined under that plan, which shares become exercisable in four equal annual installments commencing one year after the date of grant, and (ii) an option to purchase 468,160 shares at an exercise price of $12.50 per share, the closing price on the date of grant, of which 150,000 shares became exercisable immediately and the remainder become exercisable in four equal annual installments commencing one year after the date of grant. Hyseq s employment agreement with Dr. Love also provides that, at any time following his first year of employment but before the third anniversary of the beginning of his employment, so long as Dr. Love has not exercised his option to purchase 150,000 of the 500,000 shares, he may forfeit that option, in exchange for $2.0 million plus the accrued interest under the loan agreement and the loan then becomes immediately due and payable. The guaranteed value of the 150,000 options at $2.0 million was recognized ratably as compensation expense over the service period of one year.

Option Grants in 2001

Hyseq granted options to its executive officers under its 1995 Stock Option Plan, with the exception of the following option grants, which were granted pursuant to separate option agreements:

grant on February 1, 2000 to Dr. Rathmann of an option to purchase 1,000,000 shares of Hyseq common stock at an exercise price equal to the then-current market price on the day before the date of grant of $31.688 per share;

grant on August 21, 2001 to Dr. Rathmann of an option to purchase 1,000,000 shares of Hyseq common stock with an exercise price equal to the then-current market price of $8.635 per share;

grant on January 11, 2001 to Dr. Love of an option to purchase 468,160 shares of Hyseq common stock with an exercise price equal to the then-current market price of $12.500 per share;

Table of Contents

grant on July 16, 2001 to Dr. Bennett of an option to purchase 250,000 shares of Hyseq common stock with an exercise price equal to the then-current market price of $10.400 per share;

grant on May 1, 2001 to Mr. Garcia of an option to purchase 200,000 shares of Hyseq common stock with an exercise price equal to the then-current market price of $11.665 per share;

grant on August 1, 2001 to Dr. Rin-Laures of an option to purchase 200,000 shares of Hyseq common stock with an exercise price equal to the then-current market price of $10.440 per share; and

grant on April 24, 2001 to Ms. Fitzpatrick of an option to purchase 150,000 shares of Hyseq common stock with an exercise price equal to the then-current market price of $9.955 per share.

grant on June 24, 2002 to Ms. Giles of an option to purchase 175,000 shares of Hyseq common stock with an exercise price equal to the then-current market price of $1.89 per share.

In the event of a change of control, all of the options granted to Hyseq s executive officers under its 1995 Stock Option Plan and those options granted pursuant to separate option agreements as set forth above shall become immediately exercisable. Change of Control under the Directors Plan, 1995 Stock Option Plan and the separate option agreements described above means:

an acquisition by any entity or group of beneficial ownership of more than 50% of Hyseq s outstanding securities entitled to vote for the election of directors, or voting securities;

the commencement by an entity or group of a tender offer (other than by Hyseq or one of its subsidiaries) for more than 50% of Hyseq s outstanding voting securities;

a merger or consolidation in which the holders of Hyseq s outstanding voting securities immediately prior to the merger hold less than 50% of the outstanding voting securities of the surviving or resulting corporation;

a transfer of all or substantially all of Hyseq s assets other than to an entity of which Hyseq holds at least 80% of the voting securities; and

the election of the lesser of three directors or directors constituting a majority of Hyseq s Board of Directors without the approval of the incumbent Board of Directors.

The following tables show for the fiscal year ended December 31, 2001, certain information regarding options granted to, exercised by, and held at year end by Hyseq s named executive officers:

	Individual Grants				Potential Realizable Value At Assumed Annual Rates of Stock Price Appreciation for Option Term(2)	
Name	Number of Securities Underlying Options Granted(#)	% of Total Options Granted To Employees in 2001	Exercise of Base Price($/Sh)(1)	Expiration Date	5%($)	10%($)
George B. Rathmann	1,036,000	45.3	(3)	(4)	5,655,628	14,331,344
Ted W. Love	575,000	25.1	(5)	(6)	4,470,391	11,283,071
William F. Bennett	250,000	10.9	10.40	7/15/11	1,634,560	4,141,970
Linda A. Fitzpatrick	175,000	7.6	(9)	(10)	1,102,857	2,794,635
Peter S. Garcia	225,000	9.8	(7)	(8)	1,630,788	4,132,411
David M. Rosen	13,000	0.6	10.44	7/31/11	85,324	216,211
Radoje T. Drmanac						
Snezana Drmanac						

(1) All options have a per share exercise price equal to the fair market value of Hyseq s common stock on the date of grant, with the exception of the initial option granted to Dr. Rathmann to purchase 1,000,000 shares of its common stock, which has a per share exercise price equal to

the closing price of a share of its common stock on the day prior to the date of the grant.

Table of Contents

(2) Reflects the value of the stock option on the date of grant assuming (i) for the 5% column, a five-percent annual rate of appreciation in its common stock over the ten-year term of the option, and (ii) for the 10% column, a ten-percent annual rate of appreciation in its common stock over the ten-year term of the option, in each case without discounting to net present value and before income taxes associated with the exercise. The 5% and 10% assumed rates of appreciation are based on the rules of the Securities and Exchange Commission and do not represent Hyseq s estimate or projection of the future price of its common stock. The amounts in this table may not be achieved.

(3) On August 21, 2001, Hyseq granted an option to purchase 1,000,000 shares of its common stock to Dr. Rathmann with an exercise price of $8.635 per share. He received a monthly option grant of 3,000 shares at exercise prices ranging from $6.0825 to $15.125 per share.

(4) The option granted on August 21, 2001 will expire August 20, 2011. The monthly options granted will expire on January 30, 2011, February 27, 2011, March 29, 2011, April 29, 2011, May 30, 2011, June 28, 2011, July 30, 2011, August 30, 2011, September 27, 2011, October 30, 2011, November 29, 2011 and December 30, 2011, respectively.

(5) On January 11, 2001, Hyseq granted an option to purchase 468,160 shares of its common stock to Dr. Love with an exercise price of $12.50 per share; an option to purchase 31,480 shares with an exercise price of $12.5625 per share. On August 1, 2001, Dr. Love received an option grant to purchase 75,000 shares of its common stock at exercise price of $10.44 per share.

(6) The options granted will expire on January 10, 2011 and July 31, 2011, respectively.

(7) On May 1, 2001, Hyseq granted an option to purchase 200,000 shares of its common stock to Mr. Garcia with an exercise price of $11.665 per share. On August 1, 2001, Mr. Garcia received an option grant to purchase 25,000 shares of its common stock at exercise price of $10.44 per share.

(8) The options granted will expire on April 30, 2011 and July 31, 2011, respectively.

(9) On April 24, 2001, Hyseq granted an option to purchase 150,000 shares of its common stock to Ms. Fitzpatrick with an exercise price of $9.955 per share. On August 1, 2001, Ms. Fitzpatrick received an option grant to purchase 25,000 shares of its common stock at exercise price of $10.44 per share.

(10) The options granted will expire on April 23, 2011 and July 31, 2011, respectively.

Aggregate Option Exercises in 2001; 2001 Year-End Option Values

Name	Shares Acquired at Exercise(#)	Value Realized($)	Number of Securities Underlying Unexercised Options at Fiscal Year End(#)(1)		Value of Unexercised In-the-Money Options at Fiscal Year End($)	
			Exercisable	Unexercisable	Exercisable	Unexercisable
George B. Rathmann			735,666	1,333,334	5,903	
Ted W. Love			150,000	425,000		
William F. Bennett				250,000		
Linda A. Fitzpatrick				175,000		
Peter S. Garcia				225,000		
David M. Rosen			15,708	45,464	66,163	132,318
Radoje T. Drmanac			167,199	25,659	822,146	84,757
Snezana Drmanac			92,034	16,144	395,145	53,084

(1) The securities underlying the options are shares of Hyseq s common stock.

Table of Contents

The following table sets forth information as of December 31, 2001 for all of Hyseq s equity compensation plans:

Equity Compensation Plan Information

Plan Category	No. of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights (a)	Weighted Average Exercise Price of Outstanding Options, Warrants and Rights (b)	No. of Securities Remaining Available for Future Issuance Under Equity Compensation Plans Excluding Securities Reflected in Column (a) (c)
Equity compensation plans approved by security holders	4,356,181	$15.18	125,109
Equity compensation plans not approved by security holders	1,268,160	$11.33	0
Total	5,624,341	$14.32	125,109

Non-Stockholder Approved Equity Arrangements

In 2001, Hyseq granted options to purchase shares of Hyseq common stock to certain of its officers in connection with and as an inducement to their commencement of employment with Hyseq. These option grants were not approved by Hyseq s stockholders. Specifically, on January 11, 2001, Hyseq granted an option to purchase 468,160 shares of Hyseq common stock at an exercise price of $12.50 per share to Dr. Love, Hyseq s President and Chief Executive Officer. On April 24, 2001, Hyseq granted an option to purchase 150,000 shares of Hyseq common stock at an exercise price of $9.955 per share to Ms. Fitzpatrick, Hyseq s Senior Vice President of Human Resources. On May 1, 2001, Hyseq granted an option to purchase 200,000 shares of Hyseq common stock at an exercise price of $11.665 per share to Mr. Garcia, Hyseq s Senior Vice President and Chief Financial Officer. On July 15, 2001, Hyseq granted an option to purchase 250,000 shares of Hyseq common stock at an exercise price of $10.40 per share to Mr. Bennett, Hyseq s Senior Vice President of Research and Development. On August 1, 2001, Hyseq granted an option to purchase 200,000 shares of Hyseq common stock at an exercise price of $10.44 per share to Dr. Rin-Laures, Hyseq s General Counsel. On June 24, 2002, Hyseq granted an option to purchase 175,000 shares of Hyseq common stock at an exercise price of $1.89 per share to Nina Giles. The option exercise prices for these option grants are equal to the closing sales price for Hyseq common stock on the last trading day prior to the date of grant. These options may be exercised for 30 days following an officer s termination of employment (or one year in the event an officer s employment is terminated as a result of his or her death or disability). Each of these options has a 10 year term.

These options vest in cumulative annual installments of 25%. In the event of a change of control (as defined above), all of these options will become 100% vested and exercisable immediately.

These options are not required to be and have not been approved by Hyseq s stockholders.

Compensation Committee Interlocks and Insider Participation

During fiscal 2001, the compensation committee consisted of Dr. Baddour and Mr. Weist, neither of whom is (i) a present or former officer or employee of Hyseq, or (ii) is engaged in any transactions described under the heading Certain Transactions, with the exception of Mr. Weist, who is Hyseq s Vice Chairman, who was Hyseq s Chairman from March 1994 to February 1, 2000 and Hyseq s President from May 1993 until March 1994, and who participated in Hyseq s private placement in April 2002. Mr. Weist, Trustee of the Weist Family Trust, purchased 30,000 shares of Hyseq common stock and was issued a warrant for the

Table of Contents

purchase of 15,000 shares of Hyseq common stock. Of the $21,285,131 Hyseq received in gross proceeds from the private placement, Hyseq received approximately $210,000 from Mr. Weist.

Compensation Committee Report

The compensation committee of Hyseq s Board of Directors comprises Dr. Baddour, as Chairperson, and Mr. Weist. The compensation committee s responsibilities include recommending to the Board the compensation for Hyseq s executive officers, grants of stock options to Hyseq s employees, and administering Hyseq s stock option and employee stock purchase plans. The compensation committee bases its decisions on Hyseq s executive compensation philosophy, which seeks to relate salaries, bonuses and stock option awards to Hyseq s success in meeting annual and long-term performance goals, to reward individual achievement and to attract and retain qualified executives.

Hyseq previously set its executive officers salaries in the low to mid-range compared to those with similar management positions in peer companies consisting primarily of other genomics and biotechnology companies. In an effort to attract additional executive officers with specific experience that Hyseq believes is necessary for its development as a biopharmaceutical company, Hyseq is setting new executive officer salaries in the mid to high salary range, as compared to similarly situated companies. The level of salaries paid to Hyseq s executive officers also takes into account Hyseq s technological achievements during the year, Hyseq s success in entering into significant technology agreements with collaborators, as well as an evaluation of the individual performance and contribution of each executive to Hyseq s performance for the year. Particular emphasis is placed on the individual officer s level of responsibility for and role in meeting Hyseq s strategic, technological and financial objectives. Because of Hyseq s stage of development, the compensation committee has not used either the profitability or the market value of Hyseq common stock as a significant factor in consideration for setting executive officer salaries.

Bonuses

Hyseq awards bonuses for accomplishments achieved during the past year. The compensation committee recommends to the Board the amount of the bonus, with advice from Hyseq s management. The compensation committee makes its recommendations based upon an assessment of the individual s contributions during the year, compared to (but not restricted to) a list of goals previously approved by management and the compensation committee. The compensation committee also considers general business and economic factors relating to Hyseq in recommending the size of the bonus pool and adjusts bonuses based on those factors as well. Hyseq did not pay any bonuses for the fiscal year ended December 31, 2001.

Stock Options

Stock options awards are intended to align the interests of executives with the interests of the stockholders in Hyseq s long-term performance. The compensation committee developed guidelines for executive stock option awards, in consultation with Hyseq s management. The guidelines are based upon:

analysis of long-term incentive awards based on each individual executive s position;

responsibilities, performance and contribution to the achievement of Hyseq s long-term goals; and

competitive stock option data from other genomics and biotechnology companies.

In addition, the compensation committee reviews the equity position of all executive officers on an annual basis and awards stock options to executive officers periodically.

Chief Executive Officer s Compensation

Dr. Rathmann was Hyseq s Chief Executive Officer from May 2000 to March 2001. In lieu of cash compensation for his services as Hyseq s employee, Dr. Rathmann receives a monthly grant of options to purchase 3,000 shares of Hyseq common stock, with a per share exercise price equal to the fair market value of a share of Hyseq common stock on the date of each grant.

Table of Contents

Dr. Love has been Hyseq s Chief Executive Officer since March 2001. Dr. Love s annual salary is $585,000. Dr. Love s salary is not directly tied to Hyseq s performance. However, his compensation, including stock options, takes into account Hyseq s success in meeting its strategic, technological and financial objectives. Because of Hyseq s stage of development, Hyseq has not used either the profitability or the market value of Hyseq common stock as significant factors to be considered in setting Chief Executive Officer compensation.

Internal Revenue Code Section 162(m)

Under Section 162(m) of the Internal Revenue Code, the amount of compensation paid to certain executives that is deductible with respect to Hyseq s corporate taxes is limited to $1,000,000 annually. It is the current policy of the compensation committee to maximize, to the extent reasonably possible, Hyseq s ability to obtain a corporate tax deduction for compensation paid to Hyseq s executive officers to the extent consistent with the best interests of Hyseq and its stockholders.

COMPENSATION COMMITTEE

RAYMOND F. BADDOUR, SC.D., *Chairperson*
ROBERT D. WEIST

Table of Contents

STOCK PERFORMANCE GRAPH

The following graph compares the annual percentage change in Hyseq s cumulative total stockholder return on Hyseq common stock, for the period from August 7, 1997 (the date of Hyseq s initial public offering) through December 31, 2001, with the comparable return of three indexes: the Hambrecht & Quist Biotechnology Index, The Nasdaq Market Index and the Nasdaq Pharmaceuticals Index. Hyseq has not paid any dividends on Hyseq common stock, and no dividends are included in the representation of Hyseq s performance. The graph assumes you invested $100 in Hyseq common stock and in each of the indices on August 8, 1997 (the date Hyseq common stock was first publicly traded). The stock price performance on the graph below is not necessarily indicative of future price performance.

Assumes $100 invested on Aug. 8, 1997. Assumes dividend reinvested fiscal year ending Dec. 31, 2001.

	8/08/97	12/31/97	12/31/98	12/31/99	12/31/00	12/31/01
Hyseq Inc.	100.00	64.71	35.29	114.29	96.64	51.90
Hambrecht & Quist Biotechnology Index	100.00	98.21	149.55	319.68	343.68	285.84
Nasdaq Market Index	100.00	98.95	139.56	246.14	154.71	123.32
Nasdaq Pharmaceuticals Index	100.00	96.87	123.23	230.23	288.06	244.71

At December 31, 2001, the closing price of Hyseq common stock was $7.72 per share.

Table of Contents

CHAPTER FOUR ADDITIONAL INFORMATION

LEGAL MATTERS

Kummer Kaempfer Bonner & Renshaw of Las Vegas, Nevada will issue an opinion about certain legal matters with respect to the Hyseq common stock being offered in this prospectus. Certain United States federal income tax consequences of the merger will be passed upon for Hyseq by Latham & Watkins and for Variagenics by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.

EXPERTS

The consolidated financial statements of Hyseq and subsidiaries as of December 31, 2001 and 2000 and for each of the years then ended have been included herein and in the registration statement in reliance upon the report of KPMG LLP, independent auditors, included herein, and upon the authority of said firm as experts in accounting and auditing.

Ernst & Young LLP, independent auditors, have audited Hyseq s consolidated statements of operations, stockholders equity and cash flows for the year ended December 31, 1999, as set forth in their report, which is included in this prospectus and incorporated by reference elsewhere in the registration statement. Hyseq s financial statements are included herein in reliance on the report of Ernst & Young LLP given on their authority as experts in accounting and auditing.

The consolidated financial statements of Variagenics and subsidiaries as of December 31, 2001 and 2000 and for each of the three years in the period ended December 31, 2001 have been included herein and in the registration statement in reliance upon the report of PriceWaterhouseCoopers LLP, independent auditors, included herein, and upon the authority of said firm as experts in accounting and auditing.

Future Stockholder Proposals

Hyseq. Pursuant to Rule 14a-8 under the Exchange Act, stockholders may present proper proposals for inclusion in Hyseq s proxy statement and for consideration at the next annual meeting of its stockholders by submitting their proposals to Hyseq in a timely manner. In order to be so included for the 2003 Annual Meeting, stockholder proposals must comply with the requirements of Rule 14a-8 and must be received by Hyseq no later than February 28, 2003, unless the meeting date is before July 7, 2003 or after September 5, 2003, in which case a reasonable time before Hyseq begins to print and mail its proxy materials. In addition, Hyseq s By-laws establish an advance notice procedure with regard to certain matters, including stockholder proposals not included in Hyseq s proxy statement, to be brought before an annual meeting of stockholders. In general, notice must be received by the Secretary of Hyseq not less than 60 days nor more than 90 days prior to the anniversary date of the immediately preceding annual meeting and must contain specified information concerning the matters to be brought before such meeting and concerning the stockholder proposing such matters. Therefore, to be presented at Hyseq s 2003 Annual Meeting, such a proposal must be received by Hyseq after May 8, 2003 but no later than June 7, 2002. If the date of the annual meeting is more than 30 days earlier or more than 60 days later than such anniversary date, notice must be received not earlier than the 90th day prior to such annual meeting and not later than the close of business on the later of the 60th day prior to such annual meeting or the 10th day following the day on which public announcement of the date of such meeting is first made. If a stockholder who has notified Hyseq of his or her intention to present a proposal at an annual meeting does not appear or send a qualified representative to present his proposal at such meeting, Hyseq need not present the proposal for a vote at such meeting.

Variagenics. Variagenics has already held its 2002 Annual Meeting of Stockholders on May 29, 2002. Variagenics will hold an annual meeting in 2003 only if the merger has not already been completed. In order to be considered for inclusion in the proxy statement for Variagenics s 2003 Annual Meeting of Stockholders, stockholder proposals must be received by Variagenics on or before December 31, 2002. For stockholder proposals which are not to be included in proxy materials for the 2003 Annual Meeting, in order for a stockholder to nominate a person or persons for election to the Board of Directors or to properly bring other business before an annual meeting of stockholders, notice of such business proposal or of such nomination

Table of Contents

must be delivered to the Secretary of Variagenics not earlier than February 28, 2003 and not later than March 31, 2003. Proposals received after that date will not be voted on at the Annual Meeting.

WHERE YOU CAN FIND MORE INFORMATION

Hyseq and Variagenics file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, statements or other information filed by either Hyseq or Variagenics at the SEC s Public Reference Room at 450 Fifth Street, N.W., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference rooms. The SEC filings of Hyseq and Variagenics are also available to the public from commercial document retrieval services and at the web site maintained by the SEC at http://www.sec.gov.

Hyseq has filed a registration statement on Form S-4 to register with the SEC the Hyseq common stock to be issued to Variagenics stockholders in the merger. This joint proxy statement/prospectus is a part of that registration statement and constitutes a proxy statement and a prospectus of Hyseq, in addition to being a proxy statement of Variagenics for the Variagenics special meeting. The registration statement, including the attached exhibits and schedules, contains additional relevant information about Hyseq and Variagenics and Hyseq common stock. As allowed by SEC rules, this joint proxy statement/prospectus does not contain all the information you can find in the registration statement or the exhibits to the registration statement.

The SEC allows Hyseq and Variagenics to incorporate by reference information into this joint proxy statement/prospectus. This means that Hyseq and Variagenics can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is considered to be a part of this joint proxy statement/prospectus, except for any information that is superseded by information that is included directly in this joint proxy statement/prospectus or incorporated by reference subsequent to the date of this joint proxy statement/prospectus.

This joint proxy statement/prospectus incorporates by reference the documents listed below that Hyseq and Variagenics have previously filed with the SEC. They contain important information about Hyseq and Variagenics and their financial condition. The following documents, which were filed by Hyseq with the SEC, are incorporated by reference into this joint proxy statement/prospectus:

annual report of Hyseq on Form 10-K for the fiscal year ended December 31, 2001, filed with the SEC on April 1, 2002, as amended on Form 10-K/A filed with the SEC on May 9, 2002 and Form 10-K/A filed with the SEC on July 22, 2002;

quarterly report on Form 10-Q for the quarter ended March 31, 2002, filed with the SEC on May 15, 2002 as amended on Form 10-Q/A filed with the SEC on July 22, 2002;

quarterly report on Form 10-Q for the quarter ended June 30, 2002, filed with the SEC on August 14, 2002;

quarterly report on Form 10-Q for the quarter ended September 30, 2002, filed with the SEC on November 8, 2002;

current report of Hyseq on Form 8-K, filed with the SEC on January 11, 2002;

current report of Hyseq on Form 8-K, filed with the SEC on January 28, 2002;

current report of Hyseq on Form 8-K, filed with the SEC on April 9, 2002;

current report of Hyseq on Form 8-K, filed with the SEC on May 16, 2002;

current report of Hyseq on Form 8-K, filed with the SEC on August 14, 2002;

current report of Hyseq on Form 8-K, filed with the SEC on September 6, 2002;

current report of Hyseq on Form 8-K, filed with the SEC on November 1, 2002;

Table of Contents

current report of Hyseq on Form 8-K, filed with the SEC on November 12, 2002; and

the description of Hyseq s common stock set forth in its Registration Statement on Form 8-A, filed with the SEC on July 23, 1997.

The following documents, which were filed by Variagenics with the SEC, are incorporated by reference into this joint proxy statement/prospectus:

annual report of Variagenics on Form 10-K for the fiscal year ended December 31, 2002, filed with the SEC on April 1, 2002;

quarterly report on Form 10-Q for the quarter ended March 31, 2002, filed with the SEC on May 14, 2002;

quarterly report on Form 10-Q for the quarter ended June 30, 2002, filed with the SEC on August 14, 2002;

quarterly report on Form 10-Q for the quarter ended September 30, 2002, filed with the SEC on November 14, 2002;

current report of Variagenics on Form 8-K, filed with the SEC on June 27, 2002;

current report of Variagenics on Form 8-K, filed with the SEC on November 12, 2002; and

current report of Variagenics on Form 8-K, filed with the SEC on November 15, 2002.

In addition, Hyseq and Variagenics incorporate by reference additional documents that either may file with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of this joint proxy statement/prospectus and the dates of the Hyseq special meeting and the Variagenics special meeting, respectively. These documents include periodic reports, such as annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, as well as proxy statements.

Hyseq and Variagenics also incorporate by reference the following additional documents:

the merger agreement attached to this joint proxy statement/prospectus as Annex A; and

the stockholder voting agreement attached to this joint proxy statement/prospectus as Annex B;

Hyseq has supplied all information contained or incorporated by reference into this joint proxy statement/prospectus relating to Hyseq, and Variagenics has supplied all the information relating to Variagenics.

You can obtain any of the documents incorporated by reference into this joint proxy statement/prospectus through Hyseq or Variagenics, as the case may be, or from the SEC through the SEC s Internet Web site at the address described above. Documents incorporated by reference are available from Hyseq and Variagenics without charge, excluding any exhibits to those documents, unless the exhibit is specifically incorporated by reference as an exhibit in this joint proxy statement/prospectus.

Hyseq stockholders and Variagenics stockholders may request a copy of information incorporated by reference into this joint proxy statement/prospectus by contacting the investor relations department for each of Hyseq and Variagenics at:

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

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 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.phx.

Table of Contents

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 , 2002.

Hyseq and Variagenics have not authorized anyone to give any information or make any representation about the merger or the companies that is different from, or in addition to, that contained in this joint proxy statement/prospectus or in any of the materials that they have incorporated into this joint proxy statement/prospectus. Therefore, if anyone does give you information of this sort, you should not rely on it. If you are in a jurisdiction where offers to exchange or sell, or solicitations of offers to exchange or purchase, the securities offered by this joint proxy statement/prospectus or the solicitation of proxies is unlawful, or if you are a person to whom it is unlawful to direct these types of activities, then the offer presented in this joint proxy statement/prospectus does not extend to you. The information contained in this joint proxy statement/prospectus is accurate only as of the date of this document unless the information specifically indicates that another date applies.

Table of Contents

INDEX TO FINANCIAL STATEMENTS

Table of Contents

HYSEQ PHARMACEUTICALS, INC.

Condensed Consolidated Balance Sheets
As Of September 30, 2002 And December 31, 2001

	September 30, 2002	December 31, 2001
	(in thousands, except share data) (unaudited)	
ASSETS		
Current Assets:		
Cash	$ 4,272	$ 12,329
Accounts receivable	183	53
Other current assets	7,558	3,919
Total Current Assets	12,013	16,301
Cash on deposit	1,106	1,606
Equipment, leasehold improvements and capitalized software, net	16,357	18,988
Patents, licenses and other assets, net	2,667	3,009
Total Assets	$ 32,143	$ 39,904
LIABILITIES AND STOCKHOLDERS EQUITY		
Current Liabilities:		
Accounts payable	$ 2,425	$ 3,210
Accrued professional fees	808	928
Line of credit	4,000	
Other current liabilities	5,217	7,672
Deferred revenue	1,204	3,702
Current portion of capital lease and loan obligations	1,510	2,506
Total Current Liabilities	15,164	18,018
Noncurrent portion of capital lease and loan obligations	1,289	2,228
Other noncurrent liabilities		125
Note payable	4,000	4,000
Total Liabilities	20,453	24,371
Commitments and contingencies		
Minority interest		112
Stockholders Equity:		
Preferred stock, par value $0.001; 8,000,000 shares authorized; none issued and outstanding as of September 30, 2002 and December 31, 2001		
Common stock, par value $0.001; 100,000,000 shares authorized; 23,035,854 and 19,307,735 shares issued and outstanding as of September 30, 2002 and December 31, 2001, respectively	23	19
Additional paid-in capital	148,547	123,849
Deferred stock compensation	(18)	(53)
Accumulated deficit	(136,862)	(108,394)
Total stockholders equity	11,690	15,421
Total liabilities and stockholders equity	$ 32,143	$ 39,904

See accompanying notes to condensed consolidated financial statements.

Table of Contents

HYSEQ PHARMACEUTICALS, INC.

Condensed Consolidated Statements Of Operations
For The Three And Nine Months Ended September 30, 2002 And 2001

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2002	2001	2002	2001
	(in thousands, except per share data) (unaudited)			
Contract revenues	$11,022	$ 5,872	$ 22,915	$ 17,522
Operating expenses:				
Research and development	9,131	11,350	40,885	31,532
General and administrative	2,879	3,602	9,102	9,805
Restructuring		825	610	825
Total operating expenses	12,010	15,777	50,597	42,162
Loss from operations	(988)	(9,905)	(27,682)	(24,640)
Gain/(loss) on sale or disposal of fixed assets	(47)		(34)	
Interest income	13	38	70	217
Interest expense	(422)	(141)	(934)	(692)
Net loss before minority interest	(1,444)	(10,008)	(28,580)	(25,115)
Loss attributable to minority interest			112	
Net loss	$ (1,444)	$ (10,008)	$ (28,468)	$ (25,115)
Basic and diluted net loss per share	$ (0.06)	$ (0.59)	$ (1.34)	$ (1.64)
Shares used in computing basic and diluted net loss per share	22,767	16,911	21,197	15,351

See accompanying notes to condensed consolidated financial statements.

Table of Contents

HYSEQ PHARMACEUTICALS, INC.

Condensed Consolidated Statements Of Cash Flow
For The Nine Months Ended September 30, 2002 And 2001

	Nine Months Ended September 30,	
	2002	**2001**
	(in thousands) (unaudited)	
NET CASH USED IN OPERATING ACTIVITIES	$(23,510)	$(18,956)
Cash flows from investing activities:		
Purchases of property and equipment	(1,865)	(7,504)
Proceeds from sale of fixed assets	53	
NET CASH USED IN INVESTING ACTIVITIES	(1,812)	(7,504)
Cash flows from financing activities:		
Payment on capital lease and loan obligations	(1,935)	(1,630)
Proceeds from release of cash on deposit	500	500
Proceeds from drawdown on line of credit	4,000	
Proceeds from issuance of common stock, net of issuance costs	14,267	40,744
Proceeds from issuance of common stock upon exercise of options/ESPP	433	681
NET CASH PROVIDED BY FINANCING ACTIVITIES	17,265	40,295
Net increase (decrease) in cash	(8,057)	13,835
Cash at beginning of period	12,329	2,699
Cash at end of period	$ 4,272	$ 16,534

See accompanying notes to condensed consolidated financial statements.

Table of Contents

HYSEQ PHARMACEUTICALS, INC.

NOTES TO UNAUDITED CONDENSED CONSOLIDATED FINANCIAL STATEMENTS

September 30, 2002
(Unaudited)

1. Basis of Presentation

The accompanying unaudited condensed consolidated financial statements have been prepared by Hyseq, Inc. d/b/a Hyseq Pharmaceuticals, Inc. (Hyseq, the Company, we, us, or our) in accordance with accounting principles generally accepted in the United States of America for interim financial information and with the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, they do not include all of the information and footnotes required by accounting principles generally accepted in the United States of America for complete financial statements. The accompanying financial information is unaudited, but includes all adjustments (consisting of normal recurring adjustments) which the Company considers necessary for a fair presentation of the financial position, operating results and cash flows for the periods presented. The condensed consolidated balance sheet as of December 31, 2001 is derived from the Company s audited financial statements. The condensed consolidated financial statements include the accounts of the Company s majority-owned subsidiary Callida Genomics, Inc. The results of operations for the interim period shown herein are not necessarily indicative of operating results expected for the entire year.

2. Segment Information

In October 2001, the Company created majority-owned subsidiary Callida Genomics, Inc. to develop and commercialize the Company s sequencing-by-hybridization (SBH) technology, including a high-speed DNA sequencing chip developed in collaboration with Affymetrix, Inc. Management has chosen to organize Callida as a separate entity to provide DNA analysis solutions useful to businesses engaged in the genomic sciences. This stands in contrast to the business goal of Hyseq Pharmaceuticals, which is to develop and market therapeutic drugs for the treatment of human diseases. The Company anticipates that in the future the two segments will grow in different business directions, will require different skills of their key employees and different business practices, and will exist within different regulatory environments.

In the first quarter of 2002, the Company began reporting Callida as a separate segment for internal management reporting purposes. Total assets for Callida were $9.2 million and $14.1 million, as of September 30, 2002 and December 31, 2001, respectively. There is no comparative data for the quarter ended September 30, 2001.

RECONCILIATION OF REPORTABLE SEGMENTS FINANCIAL INFORMATION

(in thousands)

	Three Months Ended September 30, 2002			Nine Months Ended September 30, 2002		
	Hyseq	Callida	Total	Hyseq	Callida	Total
Contract revenues	$11,022	$	$11,022	$ 22,400	$ 515	$ 22,915
Loss from operations	625	(1,613)	(988)	(23,375)	(4,307)	(27,682)
Net income/(loss)	$ 169	$(1,613)	$ (1,444)	$(24,161)	$(4,307)	$(28,468)

3. Collaboration with Amgen, Inc.

The Company is currently focusing on the development of alfimeprase, an early stage clinical product candidate that it began developing in collaboration with Amgen, Inc. in January 2002. Alfimeprase is a thrombolytic agent that dissolves blood clots. It was originally identified through Amgen s research program and is a novel recombinant derivative of fibrolase, a naturally occurring enzyme. Unlike other thrombolytic plasminogen activators, alfimeprase can directly and rapidly degrade the network of fibrin protein that

captures red blood cells to form blood clots. The first target medical indication is Peripheral Arterial Occlusion (or PAO). In PAO, a clot blocks blood flow to a distant body part, usually in the leg. It is estimated that more than 100,000 cases of PAO are reported in the United States per year. Pre-clinical studies indicate that alfimeprase is a promising agent for dissolving clots (clot lysis), and may be particularly well suited for the PAO indication. An IND has been filed in the PAO indication and the Company initiated Phase I human studies for this indication in the second quarter of 2002. The Phase I trial is a multi-center, open-label, dose-escalation study to evaluate alfimeprase s safety and pharmacokinetics that is being conducted in twenty patients across approximately eight centers in the United States. If the early safety profile of alfimeprase is acceptable after the phase I study, alfimeprase will proceed to phase II human studies in 2003 to gather additional safety data and to evaluate preliminary efficacy and dosages, to be followed by phase III studies to provide the statistical proof of efficacy and safety required by regulatory agencies.

Under the terms of the collaboration agreement with Amgen, the Company will lead development and be responsible for all clinical development activities, while Amgen will be responsible for manufacturing activities. Amgen will have the option to lead commercialization efforts in which both companies may participate. The Company will fund all development costs up to an agreed amount, after which costs as well as eventual profits will be shared equally. The Company can terminate the agreement at any time with notice. For a limited time period, Amgen may opt out of the collaboration by converting it to an exclusive licensing arrangement. Amgen also has the right to terminate the agreement if we do not begin human clinical trials within a certain time period, upon our uncured material breach or material default, upon a materially adverse clinical development, or upon our bankruptcy. In January of 2002, the Company recorded a $10.0 million non-cash charge as research and development expense for the fair value of warrants granted to Amgen under the terms of the collaboration, as determined using the Black-Scholes option pricing model. No cash has changed hands to date under the agreement.

Research and development expenses for the third quarter of 2002 for the alfimeprase project were $0.9 million, and research and development expenses for the nine months ended September 30, 2002 were $1.9 million.

The Company expects research and development costs for our alfimeprase clinical studies to be approximately $3.0 million in 2002. The Company expects its research and development expenses to increase substantially in 2003 and beyond if the Company proceeds beyond Phase I clinical trials with alfimeprase. It is not unusual for the clinical development of these types of products to take in excess of 5 years and to cost well in excess of $100 million. The time and cost of completing the clinical development of any product candidate will depend on a number of factors, including the disease or medical condition to be treated, clinical trial design and endpoints, availability of patients to participate in trials and the relative efficacy of the product versus treatments already approved. Due to these uncertainties, the Company is unable to estimate the length of time or the costs that will be required to complete the development of this product candidate.

4. Lease Amendment

In August 2002 the Company and its landlord entered into an amendment of its lease on the property at 985 Almanor Ave, Sunnyvale, California. The amendment provides for a rent deferral of approximately $4.9 million over the next three years, retroactive to June 1, 2002. The deferred rent liability will be forgiven if the Company completes its planned building improvements, which are budgeted for at least $9.8 million, by May 31, 2005. Otherwise the Company will be required to repay the deferred rent liability, plus interest, over a four-year period beginning June 1, 2005 in equal monthly installments of $0.1 million. Other terms of the amendment include extending the term of the Company s existing $4 million letter of credit until the end of the lease term, and early reinstatement of the original rental rates if the Company raises $75 million in cash as a result of a single public or private offering, with the amount of rent deferred up to that date coming due immediately. In addition, Dr. Rathmann agreed to continue his existing $1.5 million guarantee of the Company s obligations under the lease for three years.

Until the Company completes the building improvements, the Company will record a deferred rent liability recalculated on a straight-line basis for the remainder of the lease term beginning on the amendment

Table of Contents

date of June 1, 2002, including the additional rent payments of $0.1 million in the calculation. At such time as the Company completes the building improvements and receives the rental credits, the Company will again recalculate on a straight-line basis the rental payments over the remaining term of the lease, including the rental credits.

5. Employment Agreement

In January 2001, the Company entered into an employment agreement with an officer and director of the Company. Pursuant to the employment agreement, the officer was granted an option to purchase 500,000 shares of common stock as an inducement to become an employee of the Company. Of the 500,000 shares, the officer was granted (i) an option under the Company s 1995 Employee Stock Option Plan to purchase 31,840 shares at an exercise price of $12.56 per share, the fair market value on the date of grant as determined under the 1995 Plan, which shares become exercisable in four equal annual installments commencing one year after the date of grant, and (ii) an option to purchase 468,160 shares at an exercise price of $12.50 per share, the closing price on the date of grant, of which 150,000 shares became exercisable immediately and the remainder become exercisable in four equal annual installments commencing one year after the date of grant. These option agreements provide for the acceleration of vesting of options upon certain specified events.

Also pursuant to the employment agreement, the Company entered into a loan agreement with the officer, whereby the officer may borrow up to $2.0 million from the Company. The employment agreement also provided that, at any time following his first year of employment but before the third anniversary of beginning his employment, this officer may forfeit the option to purchase 150,000 of the 500,000 shares of the option granted to him in exchange for $2.0 million plus the accrued interest under the loan agreement, and the loan then becomes immediately due and payable. The Company accrued the guaranteed value of the 150,000 options of $2.0 million, recognized ratably as compensation expense over the service period of one year.

In July 2002, pursuant to the loan agreement, the Company loaned the officer $2.0 million to repay a pre-existing loan from the Chairman to the officer that had been made February 1, 2001 in the amount of $2.0 million. The $2.0 million payment was made directly to the Chairman and is considered a loan from the Company to the officer under the same terms and conditions as the $2.0 million loan provided for in the officer s employment agreement. To record the loan, the Company reduced the $2.0 million previously accrued to zero. The interest rate on the loan is 5.07%, the lowest applicable federal interest rate in effect at the time the loan was originated. Interest accrues but is deferred and all interest and principal is due in January 2006.

6. Recent Accounting Pronouncements

In July 2002, the FASB issued Statement of Financial Accounting Standards No. 146, Accounting for Costs Associated with Exit or Disposal Activities (SFAS 146). SFAS 146 requires recording costs associated with exit or disposal activities at their fair values when a liability has been incurred. Under previous guidance, certain exit costs were accrued upon management s commitment to an exit plan, which is generally before an actual liability is incurred. Adoption of this statement is required for exit or disposal activities initiated after December 31, 2002. We do not expect the adoption of SFAS 146 to have a material impact on our financial position or results of operations.

7. Subsequent Events

On October 1, 2002 the Company announced the collaboration of its Callida Genomics subsidiary with SurroMed, Inc. of Mountain View, California for the development of a high throughput universal genotyping system. The collaboration will be funded in part by a National Institute of Standards and Technology (NIST) Advanced Technology Program (ATP) grant, providing approximately $3.2 million funding for Callida over three years.

Table of Contents

On October 21, 2002 the Company drew down an additional $2.0 million from our Chairman s second line of credit to the Company.

On October 25, 2002, the Company and its landlord entered into agreements to terminate the Company s eleven-year lease of buildings at 225, 249 and 257 Humboldt Court, Sunnyvale, California (originally entered into June 23, 2000) and to grant the Company a six-month option to purchase these properties for a purchase price of $15.3 million. These agreements provide that the Company s lease is terminated retroactively, effective as of October 1, 2002. The Company will pay a lease termination fee of $5.4 million (of which $3.1 million was already held by the landlord for prepaid rent and a security deposit). Also, the Company will pay approximately $4.5 million for the option to purchase the building, which is creditable against the purchase price of the building if the option is ultimately exercised (of which $1.7 million is cash, $2.6 million is in the form of a six-month interest free promissory note guaranteed by Company s Chairman, Dr. Rathmann (the Option Note), and approximately $200,000 is in the form of warrants granted by the Company to the landlord). Also, the Company will pay additional option consideration of $95,000 per month commencing November 1, 2002 and ending when the option is exercised by the Company or April 30, 2003, whichever occurs first. The Company paid the entire lease termination and option fees on November 1, 2002. At the current time the Company has not decided whether it will exercise the purchase option.

Termination of the original lease will result in a reduction of future rental commitments under operating leases of approximately $33 million, with an average reduction of $3.7 million per year. Upon the Company s exercise of its option to purchase the properties, the option fee of approximately $4.5 million will be applied towards the $15.3 million purchase price of the properties. The remaining $10.8 million of the purchase price will be financed for five years by the landlord at an annual interest rate of 8.5% and is secured only by the properties (the Purchase Note). At the time of purchase, the $2.6 million Option Note will convert into a five-year note on the same terms as the Purchase Note. The Company will make monthly payments on the Notes in the amount of $107,901 collectively for five years, at which time the remaining principal balance will be due to the landlord. Upon exercise of the purchase option the guarantee of the Option Note by the Company s Chairman will terminate and the Company will put in place a $2.6 million letter of credit.

On November 1, 2002 the Company drew down an additional $4.0 million from our Chairman s second line of Credit to the Company in connection the Company s agreements with its landlord to terminate its lease for the Humboldt Court buildings, leaving a balance of $10.0 million available for draw down through August 5, 2003.

Table of Contents

INDEPENDENT AUDITORS REPORT

The Board of Directors and Stockholders of

Hyseq, Inc.:

We have audited the accompanying consolidated balance sheets of Hyseq, Inc. and subsidiary as of December 31, 2001 and 2000 and the related consolidated statements of operations, stockholders equity and cash flows for the years then ended. These consolidated financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Hyseq, Inc. and subsidiary as December 31, 2001 and 2000 and the consolidated results of their operations and their cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

/s/ KPMG LLP

San Francisco, California
February 5, 2002

Table of Contents

REPORT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

The Board of Directors and Stockholders

Hyseq, Inc.:

We have audited the accompanying consolidated statements of operations, stockholders equity and cash flows of Hyseq, Inc. for the year ended December 31, 1999. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audit.

We conducted our audit in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, based on our audit, the consolidated financial statements referred to above present fairly, in all material respects, the consolidated results of operations and cash flows for Hyseq, Inc. for the year ended December 31, 1999, in conformity with accounting principles generally accepted in the United States.

/s/ Ernst & Young LLP

Palo Alto, California
February 2, 2000

Table of Contents

HYSEQ PHARMACEUTICALS, INC.

Consolidated Balance Sheets
As Of December 31, 2001 And 2000

	At December 31,	
	2001	2000
	(In thousands, except share information)	
ASSETS		
Cash and cash equivalents	$ 12,329	$ 2,699
Accounts receivable	53	22
Prepaid rent	1,890	2,224
Contract revenue receivable	1,037	
Other current assets	992	682
Total current assets	16,301	5,627
Cash on deposit	1,606	2,106
Equipment, leasehold improvements and capitalized software, net	18,988	12,465
Patents, licenses and other assets, net	3,009	1,090
Total assets	$ 39,904	$ 21,288
LIABILITIES AND STOCKHOLDERS EQUITY		
Accounts payable	$ 3,210	$ 1,979
Accrued professional fees, other	928	833
Accrued bonus	1,833	
Accrued license fee	2,500	
Deferred rent	1,608	231
Deferred revenue	3,702	1,798
Current portion of capital lease and loan obligations	2,506	2,379
Other current liabilities	1,731	984
Total current liabilities	18,018	8,204
Noncurrent portion of capital lease and loan obligations	2,228	4,722
Other noncurrent liabilities	125	
Note Payable	4,000	
Total liabilities	24,371	12,926
Minority interest	112	
Commitments and contingencies		
Stockholders equity:		
Preferred stock, par value $0.001; 8,000,000 shares authorized; none issued and outstanding as of December 31, 2001 and 2000		
Common stock, par value $0.001; 100,000,000 shares authorized; 19,307,735 and 13,722,388 issued and outstanding as of December 31, 2001 and 2000, respectively	19	14
Additional paid-in capital	123,849	80,278
Deferred stock compensation	(53)	(8)
Accumulated deficit	(108,394)	(71,922)
Total stockholders equity	15,421	8,362

Total liabilities and stockholders equity	$ 39,904	$ 21,288

See accompanying Notes to Consolidated Financial Statements.

Table of Contents

HYSEQ PHARMACEUTICALS, INC.

Consolidated Statements Of Operations
For The Years Ended December 31, 2001, 2000 And 1999

	Year Ended December 31,		
	2001	**2000**	**1999**
	(In thousands, except per share data)		
Contract revenues	$ 24,590	$ 15,604	$ 6,397
Operating expenses:			
Research and development	46,506	29,018	18,157
General and administrative	13,452	9,315	8,101
Restructuring	825		
Total operating expenses	60,783	38,333	26,258
Loss from operations	(36,193)	(22,729)	(19,861)
Interest income	319	1,347	2,004
Interest expense	(891)	(871)	(690)
Loss before minority interest	(36,765)	(22,253)	(18,547)
Loss attributable to minority interest	293		
Net loss	$(36,472)	$(22,253)	$(18,547)
Basic and diluted net loss per share	$ (2.26)	$ (1.65)	$ (1.43)
Weighted average shares used in computing basic and diluted net loss per share	16,158	13,449	13,004

See accompanying Notes to Consolidated Financial Statements.

Table of Contents

HYSEQ PHARMACEUTICALS, INC.

Consolidated Statements Of Stockholders Equity
For The Years Ended December 31, 2001, 2000 And 1999

	Common Stock		Additional Paid-in Capital	Notes Receivable from Stockholders	Deferred Compensation	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders Equity
	Shares	Amount						
				(In thousands, except share data)				
Balance at December 31, 1998	12,931	$ 13	$ 82,328	$ (3,503)	$ (126)	$ (14)	$ (31,122)	$ 47,576
Issuance of common stock upon exercise of stock options and under Employee Stock Purchase Plan	152		122					122
Amortization of deferred compensation					89			89
Comprehensive loss:								
Net loss							(18,547)	(18,547)
Other comprehensive income (loss)						(18)		(18)
Comprehensive loss								(18,565)
Balance at December 31, 1999	13,083	$ 13	$ 82,450	$ (3,503)	$ (37)	$ (32)	$ (49,669)	$ 29,222
Issuance of common stock upon exercise of stock options and under Employee Stock Purchase Plan	560	1	1,481					1,482
Issuance of common stock upon cash exercise of warrants	1		6					6
Issuance of common stock upon cashless exercise of warrants	149							
Compensation expense related to SAB option grants			157					157
Notes receivable from stockholders repaid by surrendering shares of stock	(71)		(3,816)	3,503				(313)
Amortization of deferred compensation					29			29
Comprehensive loss:								
Net loss							(22,253)	(22,253)
Other comprehensive income (loss)						32		32
Comprehensive loss								(22,221)
Balance at December 31, 2000	13,722	$ 14	$ 80,278	$	$ (8)	$	$ (71,922)	$ 8,362
Issuance of common stock upon exercise of stock options and under Employee Stock Purchase Plan	140		848					848
Compensation expense related to vesting acceleration			30					30

Issuance of common stock upon cash exercise of warrants	167		574					574
Issuance of common stock through PIPE in August, 2001, net issuance cost of ($548)	3,040	3	20,734					20,737
Conversion of line of credit into common stock	2,238	2	19,998					20,000
Gain on sale of 10% interest in Callida			1,308					1,308
Deferred compensation related to SAB option grants			79		(79)			
Amortization of deferred compensation					34			34
Net loss							(36,472)	(36,472)
Balance at December 31, 2001	19,307	$ 19	$123,849	$	$ (53)	$	$(108,394)	$ 15,421

See accompanying Notes to Consolidated Financial Statements.

Table of Contents

HYSEQ PHARMACEUTICALS, INC.

Consolidated Statements Of Cash Flows
For The Years Ended December 31, 2001, 2000 And 1999

	Year Ended December 31,		
	2001	2000	1999
		(In thousands)	
Cash flows from operating activities:			
Net loss	$(36,472)	$(22,253)	$(18,547)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	5,070	3,095	2,876
Loss attributable to minority interest	(293)		
Stock compensation expense	30	157	
Amortization of deferred stock compensation	34	29	89
Non-cash change in deferred revenue	(24,195)	(11,954)	
Loss on disposal of assets		578	
Loss on impairment of capitalized software	1,087		
Realized gain (loss) on short-term investments			(18)
Other non-cash items	238		
Changes in operating assets and liabilities:			
Accounts receivable	(31)	1,228	(599)
Prepaid rent	334	(2,107)	(11)
Contract revenue	(1,037)		
Other current assets	(310)	17	18
Deferred revenue	26,099	10,666	5,000
Accounts payable	1,231	506	(432)
Accrued professional fees	95	(945)	203
Accrued bonus	1,833	(145)	145
Accrued license fee	2,500		
Deferred rent	1,377	84	69
Other current liabilities	747	696	(659)
Other non-current liabilities	125		
Net cash used in operating activities	(21,538)	(20,348)	(11,866)
Cash flows from investing activities:			
Purchases of property and equipment	(12,582)	(8,269)	(4,374)
Purchases of short-term investments		(57,101)	(16,382)
Maturities of short-term investments		74,095	24,300
Intangible and other assets	(542)	(639)	(1,158)
Proceeds from sale of fixed assets		9	
Net cash (used in) provided by investing activities	(13,124)	8,095	2,386
Cash flows from financing activities:			
Proceeds from financing arrangements and loans	4,000	2,073	3,001
Proceeds from release of cash on deposit	500		
Payment on capital lease and loan obligations	(2,367)	(2,283)	(1,523)
Repurchases of common stock			(115)
Proceeds from line of credit	20,000		
Proceeds from issuance of common stock (PIPE), net of issuance costs	20,737		
Proceeds from issuance of common stock upon the exercise of options, warrants and Employee Stock	1,422	1,487	237

Purchase Plan			
Net cash provided by financing activities	44,292	1,277	1,600
Net decrease in cash	9,630	(10,976)	(7,880)
Cash and cash equivalents at beginning of year	2,699	13,675	21,555
Cash and cash equivalents at end of year	$ 12,329	$ 2,699	$ 13,675
Supplemental disclosures of cash flow information:			
Interest paid	$ 739	$ 868	$ 690
Noncash investing and financing activities:			
Cashless exercise of stock options	$	$ 687	$
Cashless exercise of warrants	$	$ 745	$ 206
Sale of interest in subsidiary in exchange for intellectual property	$ 1,713	$	$
Conversion of line of credit to common stock	$ 20,000	$	$

See accompanying Notes to Consolidated Financial Statements.

Table of Contents

HYSEQ PHARMACEUTICALS, INC.

Notes To Consolidated Financial Statements

1. Organization and Summary of Significant Accounting Policies

Organization

Hyseq, Inc. (the Company or Hyseq) was established in August 1992 as an Illinois corporation and subsequently reincorporated as a Nevada corporation on November 12, 1993. On October 24, 2001 the Company began doing business as Hyseq Pharmaceuticals, Inc. The Company s wholly owned subsidiary, Hyseq Diagnostics, Inc., was formed as a Nevada corporation on July 18, 1995 and is inactive. The Company s prior wholly owned subsidiary, GeneSolutions Inc., was formed as a Nevada corporation on July 23, 1999 and was merged into the Company on January 8, 2002. The Company s majority-owned subsidiary, Callida Genomics, Inc., was formed as a Delaware corporation on October 24, 2001 to carry out the Company s business relating to sequencing-by-hybridization (SBH) technology. Callida Genomics wholly owned subsidiary, N-Mer, Inc., was formed as a Delaware corporation on October 24, 2001 to collaborate with Affymetrix, Inc (See Note 8).

Hyseq researches and develops biopharmaceutical products from its collection of novel genes discovered using its high-throughput screening signature-by-hybridization platform, related to its proprietary sequencing-by-hybridization technology. Hyseq has collaborations for conducting research and development on gene-based products and collaboration with Amgen to develop alfimeprase, a thrombolytic enzyme for PAO and other indications.

Principles of Consolidation and Basis of Presentation

The consolidated financial statements include the accounts of Hyseq Pharmaceuticals and Callida Genomics, our majority owned subsidiary. All significant intercompany transactions and accounts have been eliminated in consolidation. Upon consolidation, 10% of the losses in Callida are excluded from Hyseq s consolidated results and are allocated to the minority interest holder Affymetrix up to the point where Affymetrix s initial investment is depleted. Beyond that point, the Company will absorb 100% of the net losses until Callida generates net income.

Use of Estimates

The preparation of the financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

Cash and Cash Equivalents

Cash equivalents consist primarily of money market accounts, commercial paper and certificates of deposit with original maturities of three months or less. This is consistent with the Company s policy to maintain high liquidity and ensure safety of principal.

Equipment, Leasehold Improvements, and Capitalized Software

Equipment, leasehold improvements, and capitalized software are recorded at cost. Equipment under capital leases is recorded at the lower of the net present value of the minimum lease payments required over the term of the lease or the fair value of the assets at the inception of the lease. Additions, renewals and betterments that significantly extend the life of an asset are capitalized. Minor replacements, maintenance, and repairs are charged to operations as incurred. Equipment is depreciated over the estimated useful lives of the related assets, ranging from three to five years, using the straight-line method. Equipment under capital leases is amortized over the shorter of the estimated useful life or the terms of the lease, using the straight-line method. Leasehold improvements are amortized over the shorter of the estimated life or the term of the lease, using the straight-line method. Capitalized software is amortized over the shorter of the estimated useful life

or two years, using the straight-line method. When assets are retired or otherwise disposed of, the assets and related accumulated depreciation or amortization are eliminated from the accounts and any resulting gain or loss is reflected in income.

Impairment of Long-Lived Assets

Periodically, management determines whether any property and equipment or any other assets have been impaired based on the criteria established in Statement of Financial Accounting Standards No. 121, Accounting for the Impairment of Long-Lived Assets and Long-Lived Assets to be Disposed Of (SFAS No. 121).

Revenue Recognition

Revenues are recognized when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed and determinable and collectibility is reasonably assured. Revenues related to collaborative research agreements and government grants are generally recognized over the related funding periods for each contract as the services are performed. Nonrefundable up-front payments received in connection with collaborative research agreements where the Company has no continuing performance obligation are recognized when receivable and collectibility is reasonably assured. When a continuing performance obligation exists, these revenues are deferred and recognized over the relevant periods of service, generally the research term.

Revenues from collaborative agreements representing 10% or more of total revenue are as follows:

	Year Ended December 31,		
	2001	2000	1999
Source:			
BASF Plant Sciences GmbH	91%	75%	*
Chiron Corporation	*	21%	76%
Kirin Brewery Co. Ltd.	*	*	19%

* less than 10%

Revenues by Geographic Area

Revenues by geographic area are based on customers country of domicile rather than customer s shipping locations:

	Year Ended December 31,		
	2001	2000	1999
	(In thousands)		
Revenues:			
Domestic	$ 2,230	$ 3,639	$5,178
Germany	22,360	11,665	19
Japan		300	1,200
Total revenues	$24,590	$15,604	$6,397

Stock-Based Compensation

In accordance with the provisions of Statement of Financial Accounting Standards No. 123 (SFAS No. 123), Accounting for Stock-Based Compensation the Company has elected to account for stock-based compensation to employees under the provisions of Accounting Principles Board Opinion No. 25, Accounting for Stock Issued to Employees, and its related interpretations, and to adopt the disclosure

only alternative described in SFAS No. 123. Stock options granted to non-employees are accounted for in accordance with SFAS No. 123 and Emerging Issues Task Force No. 96-18, Accounting for Equity Instruments that Are Issued to Other than Employees for Acquiring, or in Conjunction with Selling, Goods or Services.

Research and Development

Research and development costs are expensed to operations as incurred and include costs related to the Company s collaborations. Research costs related to collaborations were approximately $13.0 million, $10.4 million and $7.0 million in 2001, 2000 and 1999, respectively.

Net Loss per Share

Basic and diluted net loss per share are presented in conformity with the Statement of Financial Accounting Standards No. 128 (SFAS No. 128), Earnings Per Share for all periods presented. In accordance with SFAS No. 128, basic and diluted net loss per share has been computed using the weighted average number of shares of common stock outstanding during the period.

In 2001, 2000 and 1999, outstanding options and warrants of 730,051, 1,513,000 and 369,000 shares, respectively, (as determined using the treasury stock method) were not included as they were antidilutive.

Segment Reporting

To date, the Company has viewed its operations as principally one segment. Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker in making decisions how to allocate resources and assess performance. The Company s chief operating decision maker is the Chief Executive Officer. As a result, the financial information disclosed herein materially represents all of the financial information related to the Company s principal operating segment.

2. Equipment, Leasehold Improvements and Capitalized Software

Equipment, leasehold improvements and capitalized software, net consist of the following (in thousands):

	December 31,	
	2001	**2000**
Machinery, equipment and furniture	$ 11,044	$ 8,535
Computers and capitalized software	9,890	7,633
Leasehold improvements	13,006	5,191
	33,940	21,359
Less: accumulated depreciation	(14,952)	(8,894)
Equipment, leasehold improvements and capitalized software, net	$ 18,988	$12,465

Depreciation expense totaled $6.1 million, $3.1 million and $2.8 million for the years ended December 31, 2001, 2000 and 1999, respectively. Equipment and leasehold improvements at December 31, 2001 and 2000 include items under capitalized leases in the amount of $0.6 million and $0.7 million, respectively, and related accumulated depreciation of $0.5 million and $0.5 million at December 31, 2001 and 2000, respectively. These leases are secured by the equipment leased thereunder. During 2001, there were write-offs of certain capitalized software aggregating $1.1 million. These write-offs are included in research and development expenses in the accompanying Statement of Operations.

Table of Contents

3. Accumulated Other Comprehensive Losses

Accumulated other comprehensive income or loss consists entirely of unrealized gains and losses on securities. The change in accumulated other comprehensive loss was $0, $32,000 and ($18,000) in 2001, 2000 and 1999, respectively. This change consisted entirely of unrealized losses on securities.

4. Patents, Licenses and Other Assets

Patents and Licenses

Patent costs are incurred in connection with obtaining certain patents and filing of related patent applications. Patent and license amortization expense was $99,008, $27,633 and $27,633 for the years ended December 31, 2001, 2000 and 1999, respectively. Patent amortization expense is recorded on a straight-line basis over the patent s estimated useful life which approximates 17 years.

Patent License Agreement

In 1994, the Company entered into a patent license agreement with an affiliate of the University of Chicago for an exclusive license to use certain proprietary technology developed by the Company s former Chief Scientific Officer and to develop, use, and sell licensed products or processes. The Company issued 15,244 shares of Series A preferred stock (which converted to common stock in connection with the Company s initial public offering in 1997). The Company began paying minimum royalties of $25,000 per annum beginning in 1997 and increasing to $100,000 per annum in 1999, and will continue to pay minimum royalties at the rate of $100,000 per annum over the term of the agreement, which terminates upon the later to occur of (a) fifteen years after the date of the agreement or (b) the expiration of the last-to-expire patents of the licensed patent rights.

5. Capital Lease and Loan Obligations

The Company has financed equipment purchases through capital lease and loan agreements. The capital lease and loan obligations are to be repaid over terms of 48 to 60 months at interest rates ranging from 8.10% to 14.98% and are secured by the related equipment.

Future minimum payments under the capital lease and loan agreements are as follows (in thousands):

Years Ending December 31:	
2002	$ 2,941
2003	1,435
2004	875
2005	201
2006	4
Total loan payments	5,456
Less: Amount representing interest	(722)
Present value of future loan payments	4,734
Less: Current portion	(2,506)
Noncurrent portion	$ 2,228

6. Commitments and Contingencies

Operating Leases

The Company leases three facilities under operating lease agreements, two that expire in June 2005 and one that expires in July 2011. In April 2001 the Company leased an additional approximately 138,698 square feet of space at 985 Almanor Avenue in Sunnyvale, California, adjacent to our current operating facilities. The lease on this new space requires base lease payments on average of approximately $451,000 per month and extends through May 2011. Rental expense was approximately $8.1 million in 2001, $2.1 million in

Table of Contents

2000, and $1.4 million in 1999. The leases provide for scheduled rent increases annually over the terms of the leases. The rent is being recognized as expense on a straight-line basis.

Minimum future rental commitments under non-cancelable operating leases at December 31, 2001 are as follows (in thousands):

	Minimum Rental Commitments
Year Ended December 31,	
2002	$ 9,569
2003	9,975
2004	10,394
2005	9,986
2006	9,583
2007 and thereafter	43,780
	$93,287

Letters of Credit

In accordance with the terms of the 675 Almanor facility lease agreement signed in the fourth quarter of 1997, the Company was required to obtain an irrevocable standby letter of credit in the amount of $2.0 million as partial security for the Company s lease obligations. In connection with obtaining the letter of credit, the Company was required to place $2.1 million restricted cash on deposit with the Company s primary bank as security for the letter of credit. The letter of credit and the cash collateralizing it was reduced by $0.5 million commencing in July 2001 and will be further reduced by $0.5 million each year thereafter to a certain minimum amount provided that no default under the lease occurs. The cash on deposit at any time in conjunction with this letter of credit is restricted and cannot be withdrawn. The Company controls the investment of the cash and receives interest earned thereon. The Company was also required to provide a letter of credit in the amount of $4.0 million as additional security for the lease of 985 Almanor Avenue, which requirement terminates after 5 years if the Company has not been in monetary default under the lease. Under the terms of the Humboldt Court lease, the Company was required to provide a $2.0 million letter of credit. This letter of credit was provided in March 2002 and must be increased by $1.0 million annually in each of August 2002 and August 2003, after which it can decrease by $2.0 million in 2007.

7. Collaborative Agreements

Aurora

In July 2001, the Company entered into a two-year collaboration and license agreement with Aurora Biosciences Corporation, under which Aurora will screen over 200 secreted proteins from the Company s proprietary collection, using Aurora s proprietary CellSensor™ Panel, and also granted the Company a non-exclusive license to certain fluorescent protein technologies. Aurora will use its technology on behalf of the Company to identify proteins of interest as potential therapeutics and will receive upfront payments, licensing fees and technology access fees. Aurora may receive performance milestones, as well as development milestones and royalties on the Company s products that result from the collaboration. In addition, as part of the agreement, the Company will provide Aurora access to selected novel targets from the Company s database of proprietary full-length cDNAs. The Company will receive a database access fee and licensing fees and may receive development milestones and royalties on Aurora s small molecule products that result from the collaboration.

Deltagen

In October 2001, the Company entered into a collaboration with Deltagen, Inc. to undertake research and development activities on approximately 200 novel secreted proteins. The Company will provide gene

Table of Contents

sequences encoding for the secreted proteins, and Deltagen will utilize its in vivo mammalian gene knockout technology to identify and validate potential commercially relevant biopharmaceutical drug targets. Deltagen and the Company will each have certain joint development and commercialization rights around potential biopharmaceutical drug targets discovered through the collaboration. Deltagen and the Company will share the collaboration s costs; Hyseq will provide Deltagen with approximately $10.0 million in research and development payments over two years.

Kirin

In August 2001, the Company entered into a collaboration with Kirin Brewery Co. Ltd., in which Kirin will fund three years of collaborative research work at Hyseq and both companies will conduct research directed toward discovering proteins and antibodies for a variety of diseases, including hematopoietic and inflammatory diseases. Discoveries during the collaboration will be jointly owned by Kirin and Hyseq, and will be jointly developed and marketed with costs, efforts, and revenues shared by both companies. The Company will have marketing rights in North America on all products discovered and developed under the collaboration. Kirin will have marketing rights in Asia, New Zealand, and Australia. Marketing rights will be shared by both companies in the rest of the world.

In October 1998, the Company entered into a collaboration with Kirin Brewery Co. Ltd., in which the Company used its proprietary gene discovery technologies to target novel genes relating to a specific growth factor activity from certain cell lines provided by Kirin. The Company retains exclusive rights to develop and market pharmaceutical products resulting from the collaboration in North America, subject to milestone and royalty payments to Kirin. Kirin retains equivalent rights and obligations in Asia and Oceania. The Company and Kirin share such rights equally in Europe and the rest of the world. Under the terms of the agreement, Kirin paid the Company $3.0 million for the initial phase of the collaboration. Total revenue recognized in 2000, 1999 and 1998 under the agreement was $0.3 million, $1.2 million and $1.5 million, respectively. The agreement was extended once and expired March 31, 2001.

BASF

In December 1999, the Company entered into a collaboration with American Cyanamid Company in which the Company uses its signature-by-hybridization technology to target agricultural products. During 2000, BASF Aktiengesellschaft acquired the crop protection business of American Cyanamid Company and subsequently assigned our collaboration with American Cyanamid to BASF Plant Sciences GmbH (or BASF). The collaboration provides for funding of $60 million over its initial term of three and one half years. The collaboration can be extended by mutual agreement for up to four additional one-year terms. Subject to compliance with the terms of the contract, the Company expects to recognize revenue from this collaboration over the term of the agreement as services are performed. Total revenue recognized in 2001 and 2000 under the agreement was $22.4 million and $11.7 million respectively. BASF has the exclusive right to commercialize any agricultural products resulting from the collaboration. The Company will receive royalties on any such products.

Chiron

In May 1997, the Company entered into a collaboration with Chiron Corporation. Pursuant to the terms of the collaboration agreement, the Company and Chiron are collaborating to develop solid tumor therapeutics, diagnostic molecules and vaccines. The collaboration had an initial term of three years and has been extended by Chiron for an additional two-year period. Chiron may extend the collaboration for one more two-year period. Chiron has the exclusive right to commercialize solid tumor therapeutics, diagnostic molecules and vaccines resulting from the collaboration. The Company will receive royalties on any such products. Concurrent with execution of the collaboration agreement in 1997, Chiron made an equity investment of $5.0 million in return for shares of the Company s preferred stock, which subsequently converted into common stock upon the Company s initial public offering in 1997. Chiron also purchased shares of common stock directly from the Company in a private placement concurrent with the Company s initial public offering in 1997 for an aggregate purchase price of $2.5 million. Total revenue recognized in

Table of Contents

2001, 2000, and 1999 under the agreement with Chiron was $1.2 million, $3.3 million, and $4.9 million, respectively, which the Company received as research funding payments and recognized as revenue as earned. The Company has no future performance obligations related to the revenue recognized in 2001, 2000, and 1999 and no portions of such revenues are refundable.

UCSF

In February 1998, the Company entered into a collaborative agreement with the University of California San Francisco (or UCSF) to conduct research on genes that may have important roles in the development of cardiovascular and related diseases. Under the terms of the five-year agreement, the Company makes quarterly payments of approximately $0.1 million to UCSF in connection with the agreement to reimburse UCSF for direct and indirect expenses incurred in clinical sample collection and for research conducted.

Applied Biosystems

In May 1997, the Company entered into an agreement with the Applied Biosystems Stock Group of Applera Corporation to combine certain of the Company s chip technology and Applied Biosystems life science system capabilities to commercialize the HyChip system. Pursuant to the terms of the agreement, the Company committed $5.0 million to further development of the Company s chip component of the HyChip system. The Company spent approximately $2.0 million for the development of the chip component of the HyChip system from June 1997 through December 1997. Of this amount, $0.5 million was reimbursed to the Company under its NIST grant. As of December 31, 1998, the Company had satisfied the $5.0 million obligation under its agreement with Applied Biosystems. In October 2001, Applied Biosystems and the Company amended the collaboration to facilitate the settlement with Affymetrix. Significant components of this amendment include the conversion of the prior exclusive marketing arrangement with Applied Biosystems into a non-exclusive arrangement and the conclusion of all further collaboration obligations. In June 1997 Applied Biosystems made an equity investment of $5.0 million in return for shares of the Company s preferred stock, which subsequently converted into common stock upon the Company s initial public offering in 1997. Applied Biosystems also purchased shares of common stock directly from the Company in a private placement concurrent with the initial public offering in 1997 for an aggregate purchase price of $5.0 million. The Company recognized approximately $0.3 million in revenue in each of 2001, 2000, and 1999 from Applied Biosystems from research funding reimbursement under the collaboration and from an expansion of the existing relationship as services were performed.

Affymetrix

In October 2001, the Company and Affymetrix Inc. resolved all outstanding litigation and entered into a collaboration to accelerate development and commercialization of a high speed universal DNA sequencing chip. This collaboration with Affymetrix is through a newly created venture, N-Mer, Inc., that is a wholly owned subsidiary of Callida, which in turn is a newly formed majority-owned subsidiary of the Company. N-Mer will have access to both SBH technology from the Company, through Callida, and to Affymetrix GeneChip technology, a platform for array-based experiments. Affymetrix will be the exclusive array and system supplier and is initially authorized to be the exclusive agent for the distribution of any potential N-Mer products.

Hyseq contributed cash, certain assets consisting primarily of equipment, capitalized software, and SBH intellectual property to Callida upon its formation in exchange for a 90% interest in Callida, in the form of Series A convertible preferred stock (See Note 8). In exchange for a contribution of certain intellectual property (a non-exclusive license to 12 U.S. patents or patent applications and counterpart foreign applications in a limited field of use) to Callida, Affymetrix received a 10% equity interest in Callida, in the form of Series A-1 convertible preferred stock (See Note 8). The Company accounts for the Affymetrix 10% ownership share as minority interest in Callida, recognizing a portion of Callida s losses attributable to Affymetrix as a gain on the statement of operation, up to the point where Affymetrix initial minority interest investment is depleted. Beyond that point, the Company will absorb 100% of the net losses until Callida generates net income.

Table of Contents

Affymetrix gave a total of $8.0 million in cash to Hyseq at the close of the settlement. The $8.0 million payment is comprised of two pieces. First, Affymetrix made a license payment of $4.0 million dollars in return for a non-exclusive license, without the right to grant sublicenses, under 11 U.S. patents and 30 U.S. patent applications and counterpart foreign patents and applications to make, use, sell, and import products in the non-universal array field. Universal arrays are DNA arrays designed without reference to specific gene sequences that can be used to sequence any gene. This license payment will be recognized as revenue as Callida utilizes its cash in conducting R&D efforts.

Second, Affymetrix made a loan to Hyseq of $4.0 million (interest rate of 7.5%, 5 year term) for Hyseq s cash investment in Callida. In lieu of cash repayment of this loan, Hyseq has the right, at any time, to exchange the note in whole or in part into such number of shares of Hyseq common stock (based on a price per share equal to 90% of the ten day trailing average price) equal to the aggregate amount of principal and interest to be exchanged.

Callida capitalized the intellectual property contributed by Affymetrix at its fair value of $1.7 million, based on its estimate of future royalty payments on potential Callida and N-Mer products, and based upon its determination that the intellectual property contributed has a future alternative use. The intellectual property will be amortized on a straight-line basis over its estimated useful life of four years.

Both Hyseq and Affymetrix committed to invest additional amounts in N-Mer, contingent on Callida achieving certain milestones. Affymetrix received an option to purchase a majority interest of the outstanding common stock of N-Mer at a predetermined sum, exercisable at any time over the next five years. The Company believes that Affymetrix s purchase option has no material fair value, until such point that research reaches a technical milestone and product feasibility is achieved, and has no accounting implications as of the date of inception of Callida or as of December 31, 2001. The Company will periodically evaluate the value of N-Mer to determine whether Affymetrix s purchase option has value. If so, such value will be recorded through earnings and on Hyseq s balance sheet.

8. Stockholders Equity

Preferred Stock

The Company is authorized to issue 8,000,000 shares of preferred stock. The Company s Board of Directors may set the rights and privileges of any preferred stock issued.

As of December 31, 2001 and 2000, there were no issued and outstanding shares of preferred stock. On June 5, 1998, Hyseq s Board of Directors adopted a rights plan and declared a dividend with respect to each share of common stock then outstanding. This dividend took the form of a right that entitles the holders to purchase one one-thousandth of a share of our 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 common stock issued after June 5, 1998. The rights are exercisable only if 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 the Company s outstanding common stock. The adoption of the rights plan makes it more difficult for a third party to acquire control of the Company without the approval of the Board of Directors.

In October 2001, the Company settled all outstanding litigation with Affymetrix, and created a new subsidiary, Callida Genomics, Inc. The authorized capital stock of Callida consists of 10,000,000 shares, of which 6,000,000 shares are common stock, par value $0.001 per share, and 4,000,000 shares are preferred stock, par value $0.001 per share. The preferred stock is divided into a Series A preferred stock, which consists of 3,600,000 shares, and Series A-1 preferred stock, which consists of 400,000 shares. Each of the Series A preferred stock and the Series A-1 preferred stock have aggregate liquidation preferences equal to $4.0 million, with no participation rights to future dividends and no redemption rights. The Series A preferred stock (held by Hyseq) has voting rights; the Series A-1 preferred stock (held by Affymetrix) has no voting rights. Callida classifies these preferred stock as permanent equity on its consolidated balance sheet.

Table of Contents

Common Stock

In March 2001, we completed the draw down of the balance of the $20.0 million available under the first line of credit from our Chairman and paid off the outstanding principal balance in shares of our common stock as provided in the agreement. As a consequence, we issued 2,237,637 shares of common stock to our Chairman in satisfaction of $20.0 million in outstanding principal under the line of credit.

In August 2001, the Company announced the completion of a private stock placement of 3,040,734 newly issued shares of common stock at $7.00 per share, together with warrants to purchase 1,520,369 shares of common stock. The warrants are exercisable at any time through and including August 28, 2006 at $10.50 per share, a 50% premium to the per unit purchase price on the closing date, which may be adjusted to $7.95 per share based on certain future issuances. After August 28, 2003, the warrants may only be exercised on a cashless exercise basis.

Deferred Compensation

The Company recorded deferred compensation of $695,000 in 1997 representing the difference between the issuance and exercise prices related to stock awards and options and the fair value for financial reporting purposes of the Company s common stock. The deferred compensation is being amortized to expense over the vesting period of the options and over the two-year repurchase period for the stock awards. The amortization of deferred compensation was $34,000, $29,000, and $89,000 in 2001, 2000, and 1999, respectively. At December 31, 2001, the deferred compensation balance was approximately $53,000.

Warrants

As of December 31, 2001, warrants to purchase 1,657,889 shares of common stock were outstanding at exercise prices ranging from $4.17 to $10.50 ($9.97 weighted average exercise price) per share. These warrants are held by certain investors and executive officers and expire at various times between July 2002 and August 2006.

Stock Option Plans

In 1995, the Company s stockholders adopted the 1995 Employee Stock Option Plan, or employee plan. The Company initially reserved a total of 1,152,000 common shares for issuance under the employee plan. At the 1998 annual meeting, the Company s stockholders approved a proposal to increase the number of shares authorized for issuance under the Plan to 2,152,000. Options granted under the employee plan may be either incentive stock options or nonstatutory stock options. Incentive stock options may be granted to employees with exercise prices of not less than fair market value and nonstatutory options may be granted to employees at exercise prices of not less than par value of the common stock on the date of grant as determined by the board of directors. Options vest as determined by the board of directors (generally in four equal annual installments commencing one year after the date of grant), and expire 10 years from the date of grant. At December 31, 2001, 1,922,220 options were outstanding under the employee plan.

The Company granted options to purchase common stock to several key employees, directors, scientific advisory board members and scientists prior to adoption of the employee plan. Each option gives the holder the right to purchase common stock at prices between $0.78 and $1.82 per share. In 1998, the Company granted options outside of any of the Company s stock option plans to purchase a total of 9,500 shares of common stock to three non-employee directors and a scientific advisory board member at prices between $4.75 and $10.06 per share. The options vest over periods up to four years. In February 2000, an officer and director of the Company was granted an option to purchase 1,000,000 shares of common stock at $31.69 per share, the closing price on the day prior to the grant, as an inducement to become an employee of the Company. This option becomes exercisable one-third upon the date of grant, one-third on the one-year anniversary and one third on the two-year anniversary of the date of grant. In 2001, the Company granted options outside of any of the Company s stock option plans to purchase a total of 1,268,160 shares to five employee officers at prices between $9.96 and $12.56 per share as inducements to become employees of the company. In August 2001, a director of the Company was granted an option, contingent upon shareholder

Table of Contents

approval, to purchase 1,000,000 shares of common stock at $8.63 per share, the closing price on the day prior to the grant. As of December 31, 2001, 3,537,966 options issued outside of any of the Company s stock option plans were outstanding.

In 1997, the Company s stockholders adopted the Non-Employee Director Stock Option Plan, or directors plan, providing for periodic stock option grants to non-employee directors of the Company. Under the directors plan, each new, non-employee director receives a one-time grant of options to purchase 23,040 shares of common stock, of which options to purchase 11,520 shares vest immediately, with the balance vesting in two equal allotments on the first and second anniversaries of joining the Board. All non-employee directors automatically receive options to purchase up to 5,760 shares each year (such that the amount received under the directors plan when added to all prior options granted to a director which vest in that year total 5,760) on the date of the annual meeting of the stockholders commencing in 1997. Options under the directors plan are granted at the fair market value of the Company s common stock on the date of the grant. In 2000, the Company s stockholders approved an amendment to the directors plan that changed the method for determining the number of shares granted under the plan, and lengthened the vesting date for the new director s initial and first annual grants of options. Under the amendment, the number of shares that are granted will be equal to the lesser of the number determined by dividing $200,000 by the fair market value of our common stock on the date of grant, or 10,000 shares. The amendment also revised the vesting date for initial options that are granted when a new director joins our Board such that 50% of a new director s option will vest one year after the grant date and the other 50% will vest two years after the grant date. A total of 438,240 shares of common stock have been reserved for issuance under the directors plan, of which options to purchase 147,155 shares were outstanding at December 31, 2001.

In 1999, the Company adopted a Scientific Advisory Board/ Consultants Stock Option Plan that provides for periodic grants of non-qualified stock options to members of the Company s scientific advisory board and allows the Board of Directors to approve grants of stock options to consultants. A total of 30,000 shares of common stock have been reserved for issuance under the Scientific Advisory Board/ Consultants Stock Option Plan, of which options to purchase 17,000 shares were outstanding at December 31, 2001.

During 2001, the Company granted 12,000 stock options under the Scientific Advisory Board/ Consultants Stock Option Plan all of which become exercisable in April 2002. In connection with these grants, the Company recorded deferred compensation of $79,265 representing the fair value of the options granted in accordance with SFAS 123. This deferred compensation is periodically re-measured until the underlying options vest in accordance with EITF 96-18. The fair value of these options was estimated at the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions: 1 year for the expected life of the option, 5.07% risk-free interest rate, and .8518 volatility rate. During 2001, the Company recorded $26,422 in amortization of deferred compensation related to grants to non-employees.

The directors plan, the employee plan, and the options granted to an officer and director to purchase 2,000,000 shares (as described above) provide for the acceleration of vesting of options upon certain specified events.

The Company values employee stock options using the intrinsic method of APB 25, rather than the fair value method of SFAS 123. Nevertheless, the Company is required for purposes of comparison to present net loss and loss per share on a pro forma basis as if the fair value method had been used. The fair value for employee stock options was estimated at the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Year Ended December 31,		
	2001	2000	1999
Volatility	1.17	1.38	1.64
Risk-free interest rate	5.13%	6.14%	6.25%
Dividend yield			
Expected life of option	2.3 years	2.6 years	2.5 years

Table of Contents

The Black-Scholes option pricing model was developed for use in estimating the fair value of traded options, which have no vesting restrictions and are fully transferable. Because the Company s employee stock options have characteristics significantly different from those of traded options, and because changes in the subjective input assumptions can materially affect the fair value estimate, in management s opinion, the existing models do not necessarily provide a reliable single measure of the fair value of its employee stock options.

For purposes of pro forma disclosures, the estimated fair value of the options is amortized to expense over the options vesting period. Because SFAS 123 is applicable only to options granted subsequent to December 15, 1994, the pro forma adjustment to net income was not fully reflected until fiscal year 1999.

The Company s pro forma information follows (in thousands, except for per share information):

	Year Ended December 31,		
	2001	2000	1999
Net loss as reported	$(36,472)	$(22,253)	$(18,547)
Pro forma net loss	(52,894)	(42,717)	(19,484)
Basic and diluted net loss per share as reported	(2.26)	(1.65)	(1.43)
Pro forma basic and diluted net loss per share	(3.27)	(3.18)	(1.50)

A summary of the Company s stock option activity, and related information follows:

	Year Ended December 31,					
	2001		2000		1999	
	Number of Shares	Weighted-Average Exercise Price	Number of Shares	Weighted-Average Exercise Price	Number of Shares	Weighted-Average Exercise Price
Options outstanding at beginning of period	2,566,379	$20.10	1,779,324	$ 3.80	1,583,558	$4.03
Options granted	3,387,750	$10.25	1,500,275	$31.80	776,720	$3.77
Options exercised	(71,860)	$ 3.87	(562,722)	$ 3.29	(144,466)	$1.96
Options canceled	(257,928)	$21.31	(150,498)	$ 7.19	(436,488)	$5.18
Options outstanding at end of period	5,624,341	$14.32	2,566,379	$20.10	1,779,324	$3.80

Table of Contents

The following table summarizes information about stock options outstanding and exercisable at December 31, 2001:

		Options Outstanding			Options Exercisable	
Range of Exercise Price		Number of Shares	Weighted-Average Remaining Contractual Life	Weighted-Average Exercise Price	Number of Shares	Weighted-Average Exercise Price
$ 1.56	$ 4.17	600,256	5.26	$ 2.92	449,814	$ 2.80
4.44	7.82	312,108	7.58	5.54	174,058	5.33
8.02	8.64	1,114,476	9.32	8.60	86,676	8.33
8.67	10.40	456,266	9.44	10.14	10,666	9.45
10.44	10.44	985,320	9.58	10.44	0	0.00
10.49	12.50	747,460	9.14	12.23	209,000	12.42
12.56	29.81	345,380	8.77	25.44	122,039	26.19
31.69	31.69	1,000,000	8.08	31.69	666,666	31.69
32.03	95.19	60,075	8.52	43.67	28,875	46.55
101.44	101.44	3,000	8.16	101.44	750	101.44
		5,624,341	8.56	$ 14.32	1,748,544	$ 17.93

The weighted-average grant-date fair value of options granted during the years ended December 31, 2001, 2000 and 1999 was $8.23, $22.90 and $3.52, respectively.

Employee Stock Purchase Plan

In 1998, the Company s stockholders approved an Employee Stock Purchase Plan, covering an aggregate of 50,000 shares of the Company s common stock. Each quarter, an eligible employee may elect to purchase shares of the Company s stock through payroll deductions at a price equal to the lower of 85% of the fair value of the stock as of the first business day of the quarter or the last business day. In 1999, the Company s stockholders approved an amendment to the Company s Employee Stock Purchase Plan that increased the maximum number of shares of common stock available for purchase under the Plan from 50,000 to 250,000. In the year ended December 31, 2001, 67,674 shares of the Company s stock were sold under the Employee Stock Purchase Plan at a weighted-average price of $8.20 per share.

9. Income Taxes

The reconciliation between the amount computed by applying the U.S. federal statutory tax rate of 34% to income taxes and the actual provision for income taxes as of December 31, 2001 follows (in thousands):

Income tax at statutory rate (34%)	(12,500)
Net losses and temporary differences for which no current benefit is recognized	12,580
Permanent differences	(80)
Income tax expense reported	

As of December 31, 2001, the Company had federal and state net operating loss carryforwards of approximately $107.7 million and $23.0 million, respectively. The Company also had federal and California research and development tax credit carryforwards of approximately

$2.5 million and $2.3 million, respectively. The federal net operating loss and credit carryforwards will expire at various dates beginning in the year 2008 through 2021, if not utilized. The State of California net operating losses will expire at various dates beginning in 2001 through 2011, if not utilized. The California Research Credits carryforward indefinitely.

Table of Contents

Utilization of the 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 provisions. The annual limitation may result in the expiration of net operating losses and credits before utilization.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets for financial reporting and the amount used for income tax purposes. Significant components of the Company s deferred tax assets for federal and state income taxes are as follows (in thousands):

	Year Ended December 31,	
	2001	2000
Deferred Tax Assets:		
Net operating loss carryforwards	$ 37,970	$ 28,971
Research and other credits	4,422	6,564
Capitalized research expenses	2,446	856
Accrued expenses and reserves	3,921	1,362
Deferred revenue	1,475	
Total deferred tax assets	50,234	37,753
Valuation allowance	(50,234)	(37,753)
Net deferred tax assets	$	$

Deferred tax assets are reduced by a valuation allowance as management believes that it is more likely than not that the deferred tax assets will not be realized. The net valuation allowance increased by $12.5 million, $15.7 million and $8.3 million for the fiscal years ended December 31, 2001, 2000 and 1999, respectively.

Approximately $12.2 million of the federal net operating losses and $6.6 million of the state net operating losses relate to deductions from stock based compensation. No income statement benefit will result from the realization of these losses.

10. Transactions with Related Parties

As of December 31, 2001, 2000 and 1999, the Company had outstanding accounts payable balances of approximately $3,000, $45,000, and $86,000 respectively, for professional services rendered by a law firm of which the spouse of the Company s former President and Chief Executive Officer was a member. The Company incurred legal fees and costs to this law firm of approximately $57,000, $400,000, and $441,000 for the years ended December 31, 2001, 2000 and 1999, respectively.

In August 2001, the Company received a commitment from its Chairman to provide a second line of credit of up to $20.0 million in aggregate principal amount, secured by a promissory note and available for draw down through August 5, 2003. The Chairman has also agreed to provide financing to fund operating activities as needed through 2001. Amounts outstanding under the line of credit bear interest at prime plus 1% and are payable in 48 equal monthly installments beginning upon the expiration date of August 5, 2003. The promissory note issued pursuant to such line of credit may be converted into shares of its common stock at any time upon the agreement of us and Dr. Rathmann at a price based upon the average price of our common stock over the 20-day period prior to such conversion or, if in connection with an equity financing, at the offering price. In February 2002, we drew down $4.0 million of the $20.0 million line of credit.

Our Chairman guaranteed our 985 Almanor lease (up to a certain maximum amount) and provided the collateral for the Company s $4.0 million letter of credit under this lease. Our Chairman also guaranteed our Humboldt Court lease (to a certain maximum amount) and provided the collateral for the Company s $2.0 million letter of credit under this lease.

Table of Contents

The Chairman receives no cash compensation as an employee and instead receives options to purchase 3,000 shares per month. In August 2001, the Board also granted the Chairman an option to purchase an additional 1,000,000 shares. However, to date, at the request of the Chairman, the Company has not granted the Chairman any equity incentives in recognition of the lines of credits that the Chairman made available to the Company, the Chairman s guarantee of the Company s real estate leases, the Chairman s provision of collateral for two of the Company s letters of credit under facilities leases, or the occasional use of the Chairman s private jet for Company business. The Company believes that the Board is likely to take action in the future to provide appropriate incentives to the Chairman in order to ensure his continued active involvement in the Company.

11. Selected Quarterly Financial Data (Unaudited)

Summarized selected quarterly financial data is as follows (in thousands):

	Quarter Ended			
	December 31, 2001	September 30, 2001	June 30, 2001	March 31, 2001
Contract revenues	$ 7,069	$ 5,872	$ 5,981	$ 5,668
Loss from operations	(11,553)	(9,905)	(8,349)	(6,386)
Net loss	(11,357)	(10,008)	(8,427)	(6,679)
Basic and diluted net loss per share*	(0.61)	(0.59)	(0.55)	(0.49)

	Quarter Ended			
	December 31, 2000	September 30, 2000	June 30, 2000	March 31, 2000
Contract revenues	$ 4,289	$ 5,936	$ 3,574	$ 1,805
Loss from operations	(6,627)	(4,199)	(5,331)	(6,572)
Net loss	(6,695)	(4,116)	(5,112)	(6,330)
Basic and diluted net loss per share	(0.49)	(0.30)	(0.38)	(0.48)

* The sum of earnings per share for the four quarters of 2001 is different from the full year amount as a result of computing the quarterly and full year amounts on the weighted average number of common shares outstanding in the respective periods.

Historically, the Company s revenues have varied considerably from period to period due to the nature of the Company s collaborative arrangements. As a consequence, the Company s results in any one quarter are not necessarily indicative of results to be expected for a full year.

The third quarter of 2001 included a reclass of restructuring cost of $825,000 from other income expenses to operations.

The fourth quarter of 2001 included (i) an adjustment to increase contract revenues of approximately $402,000 and (ii) the write-off of certain capitalized software costs of approximately $1,087,000.

12. Subsequent Events (Unaudited)

In January 2002, the Company entered into collaboration with Amgen, Inc. to develop and commercialize alfimeprase, a novel acting thrombolytic, for the treatment of PAO and other cardiovascular indications. Under the terms of the agreement, Hyseq will lead development and be responsible for all clinical development activities, while Amgen will be responsible for manufacturing activities. Alfimeprase, a product candidate that was identified through Amgen s research program, is a derivative of the fibrolase enzyme and is being developed for the treatment of PAO. PAO of the lower extremity is a significant cause of morbidity and amputation in the United States with over 100,000 cases reported annually. Pre-clinical studies indicate that alfimeprase is a promising agent for dissolving clots (clot lysis), and may be particularly well suited for the PAO indication. An IND for alfimeprase has been filed, and Hyseq anticipates initiating clinical studies in the second quarter of 2002.

Table of Contents

In January 2002, the Company, through its subsidiary Callida, entered into a collaborative agreement with Intel Corporation to develop technology for the detection, identification, and analysis of DNA or other biomolecules. The goal of this research collaboration is to explore new technologies for biomolecule detection and identification. Callida will focus on developing novel approaches to DNA sequencing, and Intel will focus on developing devices and protocols for detecting and reading the data.

In February 2002, the company drew down $4.0 million of the $20.0 million line of credit that it received from its Chairman in August 2001.

In February 2002, the Company entered into a research agreement with Genetastix, a privately held biotechnology company, to use Genetastix s HuMYTech technology to generate fully human monoclonal antibodies against a proprietary antigen.

Table of Contents

UNAUDITED CONSOLIDATED FINANCIAL STATEMENTS

VARIAGENICS, INC. AND SUBSIDIARY

Consolidated Balance Sheets

	December 31, 2001	September 30, 2002
	(in thousands, except per share amounts) (Unaudited)	
ASSETS		
Current assets:		
Cash and cash equivalents	$ 25,142	$ 32,594
Short-term marketable securities	47,776	23,104
Assets held for sale		1,380
Prepaid expenses and other current assets	2,225	1,077
Total current assets	75,143	58,155
Restricted cash	750	750
Property and equipment, net	7,785	5,531
Long-term marketable securities	7,111	5,085
Other assets	143	109
Total assets	$ 90,932	$ 69,630
LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable	$ 1,566	$ 1,213
Accrued expenses and other liabilities	2,081	1,948
Accrued restructure and related charges		116
Deferred revenue	229	286
Current portion of capital lease obligations	1,558	2,136
Total current liabilities	5,434	5,699
Capital lease obligations	2,515	1,348
Total liabilities	7,949	7,047
Commitments and contingencies		
Stockholders Equity:		
Preferred stock, $.01 par value; 5,000 shares authorized, 0 shares issued and outstanding		
Common stock, $.01 par value; 70,000 shares authorized, 23,371 and 24,105 shares issued and outstanding	234	241
Additional paid-in capital	171,035	169,847
Accumulated deficit	(77,998)	(104,198)
Promissory note from scientific advisor	(110)	(118)
Deferred compensation	(10,178)	(3,183)
Less treasury stock, at cost, 0 and 2 shares, respectively		(6)
Total stockholders equity	82,983	62,583
Total liabilities and stockholders equity	$ 90,932	$ 69,630

The accompanying notes are an integral part of these unaudited consolidated financial statements.

Table of Contents

VARIAGENICS, INC. AND SUBSIDIARY

Consolidated Statements of Operations

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2001	2002	2001	2002
	(in thousands, except per share amounts) (Unaudited)			
Revenue:				
Research and development collaborations and other	$ 574	$ 178	$ 2,381	$ 592
Product sales			210	450
Total revenue	574	178	2,591	1,042
Costs and expenses:				
Cost of product sales			186	236
Research and development:				
Non-cash equity compensation	563	501	1,417	2,180
All other research and development expenses	4,519	4,450	11,477	14,612
General and administrative:				
Non-cash equity compensation	840	181	2,426	3,123
All other general and administrative expenses	2,312	1,818	6,626	6,064
Restructure and related charges				1,974
Loss from operations	(7,660)	(6,772)	(19,541)	(27,147)
Other income (expense):				
Interest income	1,114	326	3,803	1,206
Interest expense	(78)	(87)	(156)	(259)
Net loss	$ (6,624)	$ (6,533)	$ (15,894)	$ (26,200)
Net loss per share (basic and diluted)	$ (0.28)	$ (0.27)	$ (0.68)	$ (1.11)
Weighted average common shares outstanding (basic and diluted)	23,346	24,076	23,272	23,688

The accompanying notes are an integral part of these unaudited consolidated financial statements.

Table of Contents

VARIAGENICS, INC. AND SUBSIDIARY

Consolidated Statements of Cash Flows

	Nine Months Ended September 30,	
	2001	**2002**
	(in thousands) (Unaudited)	
Cash flows from operating activities:		
Net loss	$(15,894)	$(26,200)
Adjustments to reconcile net loss to net cash used for operating activities:		
Depreciation and amortization	1,248	1,512
Non-cash compensation expense	3,843	5,303
Restructure and related charges		999
Amortization of premium and accretion of discount on marketable securities	(781)	62
Changes in assets and liabilities:		
Prepaid expenses and other current assets	(696)	1,089
Accounts payable	208	(353)
Accrued expenses	186	(133)
Deferred revenue	(1,444)	57
Net cash used for operating activities	(13,330)	(17,664)
Cash flows from investing activities:		
Maturity of marketable securities	41,623	57,283
Purchase of marketable securities	(43,706)	(30,647)
Acquisition of property and equipment	(1,614)	(1,444)
Proceeds from sale/leaseback of equipment	746	702
Proceeds from sale of equipment		16
Net cash provided by (used for) investing activities	(2,951)	25,910
Cash flows from financing activities:		
Repayment of capital lease obligations	(811)	(1,291)
Proceeds from issuance of common stock	307	511
Promissory note secured by common stock	(107)	
Release of restricted cash for facility lease	250	
Acquisition of treasury stock		(6)
Interest on promissory note from scientific advisor		(8)
Net cash used for financing activities	(361)	(794)
Net increase (decrease) in cash and cash equivalents	(16,642)	7,452
Cash and cash equivalents at beginning of period	50,317	25,142
Cash and cash equivalents at end of period	$ 33,675	$ 32,594

The accompanying notes are an integral part of these unaudited consolidated financial statements.

Table of Contents

VARIAGENICS, INC. AND SUBSIDIARY

Notes to Consolidated Financial Statements
(Unaudited)

1. Nature of the Business and Basis of Presentation

Variagenics, Inc. (the Company) was incorporated in Delaware on December 7, 1992. The Company was originally formed to develop a pharmacogenomic approach to cancer therapy. The Company has broadened that focus to discover genetic variations characterized by single nucleotide polymorphisms (SNPs) and other genetic differences. The Company will use this information to optimize drugs in development, develop new drug targets and bring diagnostic products to market. The consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary, Variagenics Securities Corporation. All intercompany balances and transactions have been eliminated.

The accompanying unaudited consolidated financial statements have been prepared on a basis which contemplates the realization of assets and the satisfaction of liabilities and commitments in the normal course of business. The Company has incurred losses since its inception and, as of September 30, 2002, had an accumulated stockholders deficit of $104.2 million. Management anticipates incurring additional operating losses through at least the end of 2003. The future viability of the Company is dependent upon its ability to: develop pharmacogenomic technologies, develop and commercialize proprietary molecular diagnostic products and commence generating cash from operations.

The Company is subject to risks common to companies in the industry including, but not limited to, uncertainty of product development and commercialization, lack of marketing and sales history, dependence on key personnel, market acceptance of products, competition, product liability, protection of proprietary technology, ability to raise additional financing, and compliance with FDA and other governmental regulations.

The accompanying unaudited consolidated financial statements have been prepared in accordance with generally accepted accounting principles for interim financial information and pursuant to the instructions to Form 10-Q and Article 10 of Regulation S-X of the Securities and Exchange Commission. Accordingly, they do not include all of the information and footnotes required by generally accepted accounting principles for complete annual financial statements. In the opinion of management, all adjustments (consisting of normal recurring adjustments) considered necessary for a fair presentation of these financial statements have been included. Interim results are not necessarily indicative of results that may be expected for a full year. These unaudited consolidated financial statements and notes should be read in conjunction with the financial statements and notes thereto included in the Company s Annual Report on Form 10-K for the fiscal year ended December 31, 2001, which was filed with the Securities and Exchange Commission on April 1, 2002.

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ materially from those estimates.

Certain reclassifications have been made to the unaudited consolidated financial statements for the nine months ended September 30, 2001 to conform to the current year presentation.

2. Summary of Significant Accounting Policies

Net Loss Per Share and Comprehensive Loss

Net loss per share is computed under SFAS No. 128 Earnings Per Share. Basic net loss per share is computed using the weighted average number of shares of common stock outstanding. Diluted net loss per share does not differ from basic net loss per share since potential common shares are antidilutive for all periods presented and, therefore, are excluded from the calculation of diluted net loss per share. Comprehensive loss is equal to net loss for all periods presented.

Table of Contents

The following potentially dilutive common shares were excluded from the calculation of net loss per share because their effect was antidilutive (in thousands):

	September 30, 2001	September 30, 2002
Stock options	3,360	3,371
Warrants	1,277	1,270
Employee stock purchase plan	10	22

New Accounting Pronouncements

In June 2002, the Financial Accounting Standards Board issued SFAS No. 146, Accounting for Costs Associated with Exit or Disposal Activities (FAS 146), which requires that a liability for a cost associated with an exit or disposal activity be recognized when the liability is incurred. FAS 146 is effective for exit or disposal activities initiated after December 31, 2002. The Company will adopt this statement effective January 1, 2003, and does not expect the adoption of this statement to have a material impact on its financial statements.

3. Supplemental Cash Flow Information (in thousands)

	Nine Months Ended September 30,	
	2001	2002
Acquisition of property and equipment under capital lease agreements (excluding sale/ leaseback transactions)	$2,409	$

4. Capital Lease

In March 2002 the Company entered into a lease arrangement with a financing company for the sale and leaseback of $0.7 million of equipment.

5. Restructuring Charges and Asset Impairments

During the three months ended June 30, 2002, management formulated a restructuring plan in order to conserve cash and focus resources on the Company s oncology molecular diagnostic development programs. The Company has also discontinued its NuCleave® product, which had been the source of revenue from product sales.

In connection with this restructure, a charge of $2.0 million was recorded, which consisted of $1.1 million related to employee separation costs and $0.9 million related to impairment of fixed assets which were taken out of service and held for sale as of June 30, 2002. None of these assets was sold as of September 30, 2002.

The restructuring reduced headcount by 44 positions, representing approximately 30% of the Company s workforce. Approximately half the reductions were in the high-throughput DNA sequencing group; the other half were spread throughout the organization, representing both research and development positions as well as general and administrative staff.

The employee separation costs were accounted for under EITF 94-3 Liability Recognition for Certain Employee Termination Benefits and Other Costs to Exit an Activity (Including Certain Costs Incurred in a Restructuring) and include amounts to be paid for severance and related benefits. As of September 30, 2002, all the employees to be terminated subject to the restructuring plan had ceased active employment with the Company; $1.0 million of severance and related benefits was paid out, with the remaining balance of $0.1 million included in accrued restructure and related charges and is expected to be substantially paid out prior to December 31, 2002.

Table of Contents

In refocusing the business, management identified certain laboratory equipment with a net book value of $2.3 million that will no longer be required by the Company. This equipment has been decommissioned and is expected to be sold by June 2003. Certain of this equipment was purchased under capital leases, and costs associated with the early termination of the related obligations have been accrued. The debt associated with these assets has been reclassified to the current portion of capital lease obligations. Finally, an impairment charge of $0.9 million related to this equipment has been recorded to write the asset down to its estimated net realizable value in accordance with FAS 144 Accounting for Impairment or Disposal of Long-Lived Assets .

6. Related Party Transaction

In July 2002, the Company entered into an exclusive license agreement with Renegade Therapeutics, Inc. (Renegade). Under this agreement, the Company will license to Renegade certain of the Company s 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 the Company s 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 the Company. In addition the scientific advisor to whom the Company has extended a promissory note is also an officer and stockholder of Renegade.

7. Subsequent Event

On November 9, 2002, the Company and Hyseq, Inc. (Hyseq) signed a definitive agreement whereby the Company will merge with and into Hyseq in a stock-for-stock transaction. Under the terms of the agreement, which have been approved by the Boards of Directors of both the Company and Hyseq, each share of the Company will be exchanged for shares of Hyseq common stock at an exchange ratio of 1.6451 shares of Hyseq common stock for each share of the Company s common stock. This exchange ratio implies a purchase price for the Company s shareholders of $2.22 per common share of the Company, or approximately $55.9 million (including in-the-money options and warrants), based on the closing price of Hyseq shares on November 8, 2002. The merger will be completed through a reverse triangular, stock-for-stock merger in which Hyseq will form a new wholly-owned subsidiary that will merge into the Company. The surviving entity will then be merged upstream into Hyseq. Subsequently, Hyseq will change its legal name to a yet-to-be determined name. The merger, which is structured as a tax-free reorganization for federal income tax purposes, is subject to approval by the shareholders of both the Company and Hyseq and other closing conditions, and is expected to close by the end of February of 2003.

8. Litigation

On or about December 6, 2001, the Company was sued in a complaint naming as defendants the Company and certain of its officers and its underwriters. The complaint purportedly is filed on behalf of persons purchasing the Company s stock between July 21, 2000 and December 6, 2000, and alleges violations of certain sections of the Securities Act of 1933, as amended, and Section 10(b) and the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder.

The complaint alleges that, in connection with the Company s July 21, 2000 initial public offering, the defendants failed to disclose additional and excessive commissions purportedly solicited by and paid to the underwriter defendants in exchange for allocating shares of the Company s stock to preferred customers and alleged agreements among the underwriter defendants and preferred customers tying the allocation of IPO shares to agreements to make additional aftermarket purchases at pre-determined prices. Plaintiffs claim that the failure to disclose these alleged arrangements made the Company s registration statement on Form S-1 filed with the SEC in July 2000 and the prospectus, a part of the registration statement, materially false and misleading. Plaintiffs seek unspecified damages. On or about April 19, 2002, an amended complaint was filed which makes essentially the same allegations. On or about July 15, 2002, the Company and the individuals

Table of Contents

filed a motion to dismiss. Plaintiffs have recently voluntarily dismissed their claims against the individual defendants.

The Company believes that the allegations are without merit, however, the Company, along with most of the other issuers, has begun settlement discussions with the plaintiffs. The Company believes that any loss or settlement amount, if any, will not be material to its financial statements, however, the Company cannot predict the outcome of this matter.

Table of Contents

REPORT OF INDEPENDENT ACCOUNTANTS

To the Board of Directors and

Stockholders of Variagenics, Inc.

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations, stockholders equity (deficit) and cash flows present fairly, in all material respects, the financial position of Variagenics, Inc. and its subsidiary at December 31, 2000 and 2001, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2001 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company s management; our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with auditing standards generally accepted in the United States of America, which require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

/s/ PRICEWATERHOUSECOOPERS LLP

Boston, Massachusetts
February 13, 2002, except for
Note 20 as to which the date
is November 25, 2002

Table of Contents

VARIAGENICS, INC. AND SUBSIDIARY

Consolidated Balance Sheets As of December 31,

	2000	2001
	(in thousands, except per share amounts)	
ASSETS		
Current assets:		
Cash and cash equivalents	$ 50,317	$ 25,142
Short-term marketable securities	40,646	47,776
Prepaid expenses and other current assets	1,300	2,225
Total current assets	92,263	75,143
Restricted cash	1,000	750
Property and equipment, net	4,831	7,785
Long-term marketable securities	8,062	7,111
Other assets	88	143
Total assets	$106,244	$ 90,932
LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable	$ 580	$ 1,566
Accrued expenses and other liabilities	1,031	2,081
Deferred revenue	1,612	229
Capital lease obligations, current portion	859	1,558
Total current liabilities	4,082	5,434
Capital lease obligations	880	2,515
Total liabilities	4,962	7,949
Commitments and contingencies		
Stockholders Equity:		
Preferred stock, $.01 par value; 5,000 shares authorized, 0 shares issued and outstanding		
Common stock, $.01 par value; 70,000 shares authorized, 23,116 and 23,371 shares issued and outstanding	231	234
Additional paid-in capital	172,757	171,035
Accumulated deficit	(52,695)	(77,998)
Promissory note		(110)
Deferred compensation	(19,011)	(10,178)
Total stockholders equity	101,282	82,983
Total liabilities and stockholders equity	$106,244	$ 90,932

The accompanying notes are an integral part of these consolidated financial statements.

Table of Contents

VARIAGENICS, INC. AND SUBSIDIARY

Consolidated Statements of Operations
For the Years Ended December 31,

	1999	2000	2001
		(in thousands, except per share amounts)	
Revenue:			
Research and development collaborations	$ 200	$ 2,254	$ 2,773
Research grants	199		
Product sales			210
Total revenue	399	2,254	2,983
Costs and expenses:			
Cost of product sales			186
Research and development:			
Non-cash equity compensation	1,949	2,950	2,926
All other research and development expenses	6,653	8,886	16,942
General and administrative:			
Non-cash equity compensation	1,051	5,616	3,876
All other general and administrative expenses	5,894	5,723	8,573
Loss from operations	(15,148)	(20,921)	(29,520)
Other income (expense):			
Interest income	167	3,362	4,465
Interest expense	(1,497)	(241)	(248)
Equity in loss of affiliate	(250)		
Net loss	$(16,728)	$(17,800)	$(25,303)
Dividends on redeemable convertible preferred stock	(1,437)	(22,106)	
Net loss attributable to common stockholders	$(18,165)	$(39,906)	$(25,303)
Net loss attributable to common stockholders per share (basic and diluted)	$ (29.96)	$ (3.69)	$ (1.09)
Weighted average common shares outstanding (basic and diluted)	606	10,816	23,295

The accompanying notes are an integral part of these consolidated financial statements.

Table of Contents

VARIAGENICS, INC. AND SUBSIDIARY

Consolidated Statements of Stockholders Equity (Deficit)
For the Three Years Ended December 31, 2001

	Convertible Preferred Stock		Common Stock						
	Shares	Par Value	Shares	Par Value	Additional Paid-in Capital	Accumulated Deficit	Promissory Note	Deferred Compensation	Total
					(in thousands)				
Balance at December 31, 1998	92	$ 1	618	$ 6	$ 757	$ (18,167)	$	$	$ (17,403)
Issuance of common stock			132	2	783				785
Adjustment to redeemable convertible preferred as a result of change in redemption value					9,045				9,045
Reclassification of Series C preferred stock to redeemable convertible preferred stock	(92)	(1)			(251)				(252)
Issuance of warrants					1,418				1,418
Accretion of issuance costs for redeemable preferred stock					(394)				(394)
Dividend on redeemable preferred stock					(1,043)				(1,043)
Deferred compensation resulting from the grant of options					8,507			(8,507)	
Amortization of deferred compensation								2,182	2,182
Net loss for the year ended December 31, 1999						(16,728)			(16,728)
Balance at December 31, 1999			750	8	18,822	(34,895)		(6,325)	(22,390)
Issuance of common stock			538	5	1,458				1,463
Issuance of common stock in Initial Public Offering			5,750	58	73,001				73,059
Issuance of common stock in private placement			536	5	7,211				7,216
Issuance of warrants					500				500
Conversion of redeemable convertible preferred stock to common stock			15,542	155	52,714				52,869
Accretion of issuance costs for redeemable preferred stock					(95)				(95)
Dividend on redeemable preferred stock					(2,106)				(2,106)
Proceeds from redeemable preferred stock allocated to beneficial conversion feature					19,905				19,905
Dividend on redeemable preferred stock attributable to beneficial conversion feature					(19,905)				(19,905)
Deferred compensation resulting from the grant of options					19,626			(19,626)	
Compensation expense related to stock options					1,626			6,940	8,566
						(17,800)			(17,800)

Net loss for the year ended December 31, 2000								
Balance at December 31, 2000		23,116	231	172,757	(52,695)		(19,011)	101,282
Issuance of common stock		255	3	309				312
Deferred compensation resulting from the grant of options				517			(145)	372
Compensation expense related to stock options				(2,548)			8,978	6,430
Promissory note from scientific advisor						(110)		(110)
Net loss for the year ended December 31, 2001					(25,303)			(25,303)
Balance at December 31, 2001	$	23,371	$234	$171,035	$(77,998)	$(110)	$(10,178)	$ 82,983

The accompanying notes are an integral part of these consolidated financial statements.

Table of Contents

VARIAGENICS, INC. AND SUBSIDIARY

Consolidated Statements of Cash Flows
For the Years Ended December 31,