HYSEQ INC
Form 424B3
July 24, 2002

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PROSPECTUS

File Pursuant to Rule 424(b)(3)
Registration No. 333-90458

6,948,454 Shares

Hyseq, Inc.

d/b/a Hyseq Pharmaceuticals, Inc.

COMMON STOCK

These shares of common stock are being offered by the selling stockholders identified in this prospectus. The selling stockholders may sell their shares of common stock in a number of different ways and at varying prices. We provide more information about how the selling stockholders may sell their shares in the section entitled Plan of Distribution beginning on page 22.

We are not selling any shares of our common stock under this prospectus and will not receive any proceeds from the sale of these shares.

Our common stock is quoted on the Nasdaq National Market under the symbol HYSQ. On July 23, 2002, the last reported sale price for our common stock on the Nasdaq National Market was $1.96 per share.

Investing in our common stock involves risks. See Risk Factors beginning on page 1.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

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You should rely only on the information provided or incorporated by reference in this prospectus or any prospectus supplement. Neither we nor the selling stockholders have authorized anyone to provide you with additional or different information. The selling stockholders are not making an offer of these securities in any jurisdiction where the offer is not permitted. You should assume that the information in this prospectus and any prospectus supplement is accurate only as of the date on the front of the document and that information incorporated by reference in this prospectus or any prospectus supplement is accurate only as of the date of the document incorporated by reference. In this prospectus and any prospectus supplement, unless otherwise indicated, Hyseq Pharmaceuticals, Hyseq, we, us and our refer to Hyseq, Inc., d/b/a Hyseq Pharmaceuticals, Inc., and its subsidiaries and do not refer to the selling stockholders.

We own or have rights to use trademarks or trade names that we use in conjunction with the operation of our business. Hyseq is a registered trade and service mark of ours. All other trademarks, service marks and trade names referred to in this prospectus are the property of their respective owners.

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RISK FACTORS

An investment in our common stock involves a number of risks. You should carefully consider the following information about these risks, as well as the other information appearing in this prospectus, before buying shares of our common stock.

We must be able to continue to secure additional financing

Our business does not currently generate the cash needed to finance our operations. We will require substantial additional financial resources to conduct the time-consuming and costly research, preclinical development, clinical trials and regulatory approval and marketing activities necessary to commercialize our potential biopharmaceutical products. Also, in pursuing our goal of building a fully integrated biopharmaceutical company, we will need to expand our facilities and hire and train significant numbers of employees to staff these facilities, which will require substantial additional funds. We will need to secure additional financing in order to conduct our research and expand our facilities. However, unanticipated expenses, or unanticipated opportunities that require financial commitments, could give rise to requirements for additional financing sooner than we expect. Financing may be unavailable when we need it or may not be available on acceptable terms. The unavailability of financing may require us to delay, scale back, or eliminate expenditures for our research and development program or our facilities expansion plans. We may also be required to grant rights to third parties to develop and market product candidates that we would prefer to develop and market ourselves. If we were required to grant such rights, the ultimate value of these product candidates to us would be reduced.

We intend to seek additional funding through collaborations and public or private equity or debt financings. We have financed our operations since inception primarily through the sale of equity securities, and revenue from corporate collaborations. We have not generated royalty revenues from product sales, and do not expect to receive significant revenues from royalties in the foreseeable future, if ever.

To execute an operating plan that includes facilities expansion and additional staffing, we will need to secure additional financing. Additional financing, however, may not be available on acceptable terms, if at all. For approximately the past eighteen months, the capital markets have been volatile and uncertain. Given the current state of the markets for public and private offerings of securities, we may have difficulty raising the amount of funds, on reasonable terms, necessary to finance our current operating plan. We have implemented a plan to delay, and scale back some of our operating expenditures, including facilities expansion plans, until we obtain additional funding. This plan includes a hiring freeze, a freeze on capital expenditures and a deferral of as many of our contractual financial commitments as possible. If we are unable to obtain additional financing, we may need to look to our Chairman to provide financing, which he has agreed to do. The planned reduction in operating expenditures may have a negative effect on our business. In addition, the perception in the capital markets that we may not be able to raise the amount of financing we desire, or on terms favorable to us, may have a negative effect on the trading price of our stock. Additional equity financings could result in significant dilution of current stockholders equity interests. If sufficient capital is not available, we will delay, reduce the scope of, eliminate or divest one or more of our subsidiaries, discovery, research or development programs or our facilities expansion. Any such action could significantly harm our business, financial condition and results of operations.

Our future capital requirements and the adequacy of our currently available funds will depend on many factors, including, among others, the following:

- continued scientific progress in our research and development programs, including progress in our research and preclinical studies on our potential therapeutic protein candidates;

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

our ability and the ability of our subsidiary Callida to attract additional financing on favorable terms;

the magnitude and scope of our research and development programs, including development of potential therapeutic protein candidates and Callida technology and applications;

our ability to maintain, and the financial commitments involved in, our existing collaborative and licensing arrangements;

our 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 our intellectual property rights;

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

progress in our clinical studies of alfimeprase;

the time and cost involved in obtaining regulatory approvals;

our need to develop, acquire or license new technologies or products;

competing technological and market developments;

future funding commitments to our subsidiary Callida, and our ability to borrow funds from Affymetrix to fund our commitment, under the terms of the Affymetrix settlement;

our ability to use our common stock to repay our outstanding note to Affymetrix and our line of credit with our Chairman;

legal and Nasdaq restrictions that impede our ability to raise funds from private placements of our common stock;

future funding commitments to our collaborators;

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

the uncertain condition of the capital markets; and

other factors not within our control.

Development of our products will take years; our products will require approval before they can be sold

Because substantially all of our potential products currently are in research or preclinical development, revenues from sales of any products will not occur for at least the next several years, if at all. We cannot be certain that any of our products will be safe and effective or that we will obtain regulatory approvals. In addition, any products that we develop may not be economical to manufacture on a commercial scale. Even if we develop a product that becomes available for commercial sale, we cannot be certain that consumers will accept the product. We cannot predict whether we will be able to develop

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and commercialize any of our protein candidates successfully. If we are unable to do so, our business, results of operations and financial condition will be materially adversely affected.

We do not yet have products in the commercial markets. All of our potential products are in research or preclinical development. We cannot apply for regulatory approval of our potential products until we have performed additional research and development and testing. We cannot be certain that we, or our strategic partners, will be permitted to undertake clinical testing of our potential products and, if we are successful in initiating clinical trials, we may experience delays in conducting them. Our clinical trials may not demonstrate the safety and efficacy of our potential products, and we may encounter unacceptable side effects or other problems in the clinical trials. Should this occur, we may have to delay or discontinue development of the potential product that causes the problem. After a successful clinical trial, we cannot market products in the United States until we receive regulatory approval. Even if we are able to gain regulatory approval of our products after successful clinical trials and then commercialize and sell those products, we may be unable to manufacture enough products to maintain our business, which could have a negative impact on our financial condition.

The success of our potential products in preclinical studies does not guarantee that these results will be replicated in humans

Even though some of our therapeutic protein candidates have shown results in preclinical studies, these results may not be replicated in our clinical trials with humans. Human clinical results could be different from our expectations following our preclinical studies. Consequently, there is no assurance that the results in our preclinical studies are predictive of the results that we will see in our clinical trials with humans. Also, while we have demonstrated some evidence that our therapeutic protein candidates have utility in preclinical studies, these results do not mean that the resulting products will be safe and effective in humans. Our therapeutic protein candidates may have undesirable and unintended side effects or other characteristics that may prevent or limit their use.

Our ability to commercialize gene-based products is unproven

We have not developed any therapeutic or diagnostic products using proteins produced by the genes we have discovered. Before we make any products available to the public, we or our collaboration partners will need to conduct further research and development and complete laboratory testing and animal and human studies. Moreover, with respect to biopharmaceutical products, we or our collaboration partners will need to obtain regulatory approval before releasing any such products. With respect to agricultural products, our collaboration partner may need to obtain regulatory approval before releasing any such products. We have spent, and expect to continue to spend, significant amounts of time and money in determining the function of genes and the proteins they produce, using our own capabilities and those of our collaboration partners. Such determination process constitutes the first step in developing commercial products. We also have spent and will continue to spend significant amounts of time and money in developing processes for manufacturing of our recombinant proteins under pre-clinical development, yet we may not be able to produce sufficient protein for preclinical studies. A commercially viable product may never be developed from our gene discoveries.

Our development of gene-based products is subject to several risks, including but not limited to:

the possibility that a product is toxic, ineffective or unreliable;

failure to obtain regulatory approval for the product;

the product may be difficult to manufacture on a large scale, or may not be economically feasible to market;

competitors may develop a superior product; or

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other persons or companies patents may preclude our marketing of a product.

Our biopharmaceutical development programs are currently in the research stage or in preclinical development. None of our potential therapeutic protein candidates have advanced to Phase I clinical trials. Our programs may not move beyond their current stages of development. Even if our research does advance, we will need to engage in certain additional preclinical development efforts to determine whether a product is sufficiently safe and efficacious to enter clinical trials. We have little experience with these activities and may not be successful in developing or commercializing products.

Under our collaboration arrangement with Chiron in the solid tumor cancer field, Chiron maintains responsibility for the development of a product. Under our collaboration arrangement with Kirin Brewery Company, Ltd., Kirin has primary responsibility for clinical development in its territory and we have primary responsibility in our territory. Under our collaboration arrangement with Deltagen, we share responsibility for development of a product. With respect to these arrangements, we run the risk that Chiron or Kirin may not pursue clinical development in a timely or effective manner, if at all, and that Deltagen may not cooperate with us in pursuing clinical development in a timely or effective manner.

If a product receives approval from the FDA to enter clinical trials, Phases I, II, and III of those trials include multi-phase, multi-center clinical studies to determine the products safety and efficacy prior to marketing. We cannot predict the number or extent of clinical trials that will be required or the length of the period of mandatory patient follow-up that will be imposed. Assuming clinical trials of any product are successful and other data appear satisfactory to us, we or our applicable collaboration partner will submit an application to the FDA and appropriate regulatory bodies in other countries to seek permission to market the product. Typically, the review process at the FDA is not predictable and can take up to several years. Upon completion of such review, the FDA may not approve our or our collaboration partners application or may require us to conduct additional clinical trials or provide other data prior to approval. Furthermore, even if our products or our collaboration partners products receive regulatory approval, delays in the approval process could significantly harm our business, financial condition and results of operations.

In addition, we may not be able to produce any products in commercial quantities at a reasonable cost or may not be able to market successfully such products. If we do not develop a commercially viable product, then we would suffer significant harm to our business, financial condition and operating results.

The success of our business depends on patents and other proprietary information

We currently have patents that cover some of our technological discoveries and patent applications that we expect to cover some of our gene, protein and technological discoveries. We have five issued patents relating to our gene and protein discoveries. We will continue to apply for patents for our discoveries. We cannot assure you that any of our currently pending or future applications will issue as patents, or that any patent issued to us 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 we own patents, we cannot be certain that:

our patents will not be challenged;

protection against competitors will be provided by such patents; or

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

We seek patents on:

full-length gene sequences;

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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 our ability to develop and/or manufacture gene-based products.

To obtain a patent, we must identify a utility for the gene or the protein we seek to patent. Identifying a utility may require significant research and development with respect to which we may incur a substantial expense and invest a significant amount of time.

Patent applications we may apply for with respect to human therapeutics could require us to generate data, which may involve substantial costs. Finally, we cannot predict the timing of the grant of a patent.

We also rely on trade secret protection for our confidential and proprietary information. Although our policy is to enforce security measures to protect our assets, trade secrets are difficult to protect. We require all employees to enter into confidentiality agreements with us. However:

competitors may independently develop substantially equivalent proprietary information and techniques;

competitors may otherwise gain access to our trade secrets;

persons with whom we have confidentiality agreements may disclose our trade secrets; or

we may be unable to protect our trade secrets meaningfully.

Certain of the patent applications protecting our subsidiary Callida s SBH technology are filed only in the United States. Therefore, Callida currently is not able to prevent others from practicing SBH technology outside of the United States. Furthermore, although we believe Callida intends to defend its patents, it may not prevail in a court case against others who use similar technology.

Certain of the patent applications protecting our gene-related information are filed only in the United States. Even where we have filed our patents applications internationally, we may choose not to maintain foreign patent protection through failure to enter national phase or failure to pay maintenance annuities.

We may be required to obtain licenses to patents or other proprietary rights of others. These required licenses may not, however, be made available on terms acceptable to us, or at all. If we do not obtain these licenses, we may not be able to develop, manufacture or sell products, or encounter delays in product market introductions, or incur substantial costs while we attempt to design around existing patents. Any of these obstacles could significantly harm our business, financial condition and operating results.

Our business is difficult to evaluate because we have been focused on our current business strategy for only approximately four years

We commenced operations in the fourth quarter of 1994. Our initial business focused on gene discovery using our signature by hybridization platform, and applications of our SBH technology

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including the HyChip system. Not only is our operating history relatively short, but we began to transition our business strategy from gene discovery to research and development of potential therapeutic protein candidates in 1998. Accordingly, we have a limited operating history from which you can evaluate our present business and future prospects. As a relatively new entrant to the business of biopharmaceutical research and development, we face risks and uncertainties relating to our ability to implement our business plan successfully. Our prospects must be considered in light of the risks, expenses and difficulties frequently encountered by companies in their early state of development, particularly companies in new and rapidly evolving markets such as research and development of gene-based products. If we are unsuccessful in addressing these risks and uncertainties, our business, results of operations, financial condition and prospects will be materially adversely affected.

We lack manufacturing experience and we intend to rely initially on contract manufacturers

We do not currently have significant manufacturing facilities. We are 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 IND with the FDA and proceed with clinical trials for any of our potential therapeutic protein candidates. We are 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 our potential therapeutic protein candidates. Our 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 our potential therapeutic protein candidates enter the clinical trial phase, initially we will be dependent on third-party contract manufacturers to produce the volume of current good manufacturing practices materials needed to complete such trials. We will need to enter into contractual relationships with these or other organizations in order to (i) complete the GLP toxicology and other studies necessary to file an IND with the FDA, and (ii) produce a sufficient volume of cGMP material in order to conduct clinical trials of our potential therapeutic protein candidates. We cannot be certain that we will be able to do so on a timely basis or that we 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 our filing for an IND, or our progress through the clinical trial phase. Any significant delay or interruption would have a material adverse effect on our ability to file an IND with the FDA and/or proceed with the clinical trial phase for any of our potential therapeutic protein candidates.

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

We are dependent upon collaborative arrangements

As we have transitioned our business from gene discovery to research and development of biopharmaceutical candidates, we have shifted our focus for new collaborative arrangements. We are now focusing on new collaborative arrangements where we would share costs of identifying, developing and marketing product candidates. There can be no assurance that we will be able to negotiate new collaboration arrangements of this type on acceptable terms, or at all.

Our subsidiary Callida, engaged in the development of SBH technology, is also dependent on the cooperation of its partners in collaborative arrangements and may also need to negotiate new collaborative arrangements in the future.

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

our management team to devote a significant amount of time and effort to the management of these relationships;

effective allocation of our resources to multiple projects; and

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

Our need, including the need of our 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 our business, financial condition and results of operations.

The research we perform in our gene discovery collaborative arrangements is at an early stage of product development. The successful development of products under these collaborations is highly dependent on the performance of our collaboration partners. Under our gene discovery collaborative arrangements, our collaboration partners are generally required to (i) undertake and fund certain research and development activities with us, (ii) make payments to us upon achievement of certain scientific milestones and (iii) pay royalties to us when and if they commercially market a product developed from the collaborative arrangement. We do not directly control the amount or timing of resources devoted to development activities by our collaboration partners. We, therefore, face a risk that our collaboration partners may not commit sufficient resources to our research and development programs or the commercialization of our products or may not perform their obligations as expected. If any collaboration partner fails to conduct its activities to be performed under our collaboration arrangement in a timely manner, or at all, our expectations of royalties and milestone payments related to such collaboration arrangement could be delayed or eliminated. Also, our current or future collaboration partners, if any, may independently pursue existing or other development-stage products or alternative technologies in preference to those they are developing in collaboration with us. Further, disputes may arise with respect to ownership of products developed under any such collaboration arrangement. Finally, any of our current collaboration arrangements may be terminated or not renewed by our collaboration partners, and we may not be able to negotiate additional collaboration arrangements in the future on acceptable terms, or at all.

We are dependent on key personnel

The success of our business is highly dependent on the principal members of our scientific and management staff and including our chairman and senior management team. The loss of the services of any such individual might significantly delay or prevent us from achieving our 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 our success. We 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 our business, financial condition and results of operations.

Management of growth

We expect to increase significantly the number of our employees and the scope of our operations. Such growth may place a significant strain on our management and operations. In order to execute our strategy to build a fully integrated biopharmaceutical company, develop therapeutic or diagnostic products, and obtain regulatory approvals, we will need to:

attract and train skilled employees;

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attract and retain employees with expertise to ensure that we meet FDA and foreign regulatory requirements for conducting clinical trials;

expand our facilities for additional research and development laboratories and offices and acquire additional equipment and supplies;

expand our protein production capacity;

enter into and manage contractual relationships with contract research and manufacturing organizations; and

get additional funding.

Our ability to manage such growth effectively will depend upon our ability to broaden our management team and to attract, hire and retain skilled employees. Our success also will depend on the ability of our officers and key employees to continue to implement and improve our operational, management information and financial control systems and to expand, train and manage our employee base. Inability to manage growth effectively could significantly harm our business, financial condition and operating results.

We must attract and retain qualified employees and consultants

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

Future sales of our common stock may depress our stock price

Sales in the public market of substantial amounts of our common stock could depress prevailing market prices of our common stock. As of July 8, 2002, we had 22,994,366 shares of our common stock outstanding. All of these shares are freely transferable without restriction or further registration under the Securities Act of 1933, as amended, except for shares held by our affiliates and unregistered shares held by non-affiliates. As of July 8, 2002, our affiliates held 4,408,028 shares of our common stock and non-affiliates held 543,027 unregistered shares of our common stock, which are transferable pursuant to Rule 144 as promulgated under the Securities Act of 1933, subject to the volume limitations of Rule 144. Although we do not believe that our affiliates have any present intentions to dispose of any shares of common stock owned by them, there can be no assurance that such intentions will not change in the future. An additional 708,480 shares owned by a Yugoslav entity have been held in a blocked account pursuant to restrictions imposed by the U.S. Department of Treasury arising from the political situation in former Yugoslavia and therefore have not been able to be voted or transferred. We believe that some of these restrictions may have been removed and the remaining restrictions may be removed in the future. There can be no assurance as to how long any such restrictions will remain in effect.

As of July 8, 2002, warrants to purchase 4,043,360 shares of our common stock were outstanding. In addition, under registration statements on Form S-8 under the Securities Act of 1933, we have registered approximately 5,605,572 shares of our common stock for sale upon the exercise of outstanding options under our 1995 Stock Option Plan, Non-Employee Director Stock Option Plan,

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Scientific Advisory Board/ Consultants Stock Option Plan, and stock option agreements entered into outside of any of our stock option plans and under our Employee Stock Purchase Plan and our Non-Qualified Employee Stock Purchase Plan. Shares of our common stock acquired pursuant to these plans and agreements are available for sale in the open market. In addition, we have reserved approximately 1,443,160 shares of our common stock for issuance upon the exercise of outstanding options under stock option agreements entered into outside of any of our stock option plans. As of July 8, 2002, 438,915 of the 1,443,160 shares of these options were exercisable. Although these shares have not been registered under the Securities Act of 1933, and therefore are restricted securities within the meaning of Rule 144 under the Securities Act of 1933, we intend to register these shares on a registration statement on Form S-8 under the Securities Act of 1933. Certain options or warrants may have exercise prices that are substantially below the prevailing market price of our common stock. The exercise of those options or warrants, and the prompt resale of shares of our common stock received, may result in downward pressure on the price of our common stock. The existence of the currently outstanding warrants and options to purchase our common stock may negatively affect our ability to complete future equity financings at acceptable prices and on acceptable terms.

Our subsidiary Callida Genomics, Inc. may not be able to raise third party financing

In October 2001, we formed Callida Genomics, Inc. to develop and commercialize our SBH technology. We recognize 90% of Callida s operating losses in our consolidated results of operations up to the point where Affymetrix s initial minority interest investment is depleted. Beyond that point, the Company will absorb 100% of the net losses until Callida generates net income. There is no guarantee, however, that Callida will meet its technical milestone and other requirements to obtain additional funding through Affymetrix and Hyseq. There is also no assurance that Callida will be able to obtain any third party financing or that any such financing that Callida obtains will be on favorable terms or that the funding from outside sources will be sufficient to fund Callidas operations. We cannot assure the success of Callida and if Callida is unable to obtain sufficient funding from outside sources, we may abandon their projects or bear the costs of financing Callida ourselves, which will divert our resources from other biopharmaceutical projects.

We have a history of operating losses and may never be profitable

For the years ended December 31, 2001, 2000 and 1999, we had net losses of $36.5 million, $22.3 million and $18.5 million, respectively. As of December 31, 2001, we had an accumulated deficit of $108.4 million. For the quarter ended March 31, 2002, we had an accumulated deficit of $127.4 million. The process of developing our therapeutic protein candidates will require significant additional research and development, preclinical testing, clinical trials and regulatory approvals. These activities, together with general administrative expenses, are expected to result in operating losses for the foreseeable future. We may never generate profits, and if we do become profitable, we may be unable to sustain or increase profitability on a quarterly or annual basis. As a result, the trading price of our stock could decline.

We may face fluctuations in operating results

Our operating results may rise or fall significantly as a result of many factors, including:

- the amount of research and development we engage in;
- the progress we make with research and preclinical studies on our therapeutic protein candidates, and the number of candidates in research and preclinical studies;
- our ability to expand our facilities to support our operations;
- our ability to enter into new strategic relationships;

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the nature, effectiveness, size, timing or termination of our collaborative arrangements;

the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;

the possibility that others may have or obtain patent rights that are superior to ours;

changes in government regulation; and

competitors release of successful products into the market.

Because substantially all of our potential products currently are in research or preclinical development, revenues from sales of any products will not occur for at least the next several years, if at all. We also have a high percentage of fixed costs such as lease obligations. As a result, we may experience fluctuations in our operating results from quarter to quarter and continue to generate losses. Quarterly comparisons of our financial results may not necessarily be meaningful and investors should not rely upon such results as an indication of our future performance.

We face potential volatility of our stock price

Our common stock has been traded on the Nasdaq National Market since August 1997. The market price of our common stock may fluctuate substantially because of a variety of factors, including:

volatility and uncertainty in the capital markets in general;

fluctuations in our results of operations;

sales of our 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 our potential products;

changes in our earnings estimates;

changes in accounting principles;

lack of trading volume in our stock;

fluctuations within the biotechnology sector;

announcements by competitors; and

other factors not within our 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 significant effect on the market prices of securities issued by many companies for reasons unrelated to the operating performance of these companies. 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 us could result in substantial costs and a

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diversion of managements attention and resources, which could significantly harm our business, financial condition and operating results.

FDA regulatory approval of our products is uncertain; we face heavy government regulation

Products such as those proposed to be developed by us or our collaboration partners, typically will be subject to an extensive regulatory process by federal, state and local governmental authorities, including the FDA, and comparable agencies in other countries before we may market and sell such products. In order to obtain regulatory approval of a drug product, we or our 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, we must show that the manufacturing facilities used to produce the products are in compliance with cGMP requirements. In the event we or our collaboration partners, develop products classified as drugs, we and our collaboration partners will be required to obtain appropriate approvals as well.

If our subsidiary Callida sells applications of our SBH technology for clinical diagnostics, it will need to comply with appropriate cGMP regulations pertaining to devices. The new Quality System Regulation imposes design controls and makes other significant changes in the requirements applicable to manufacturers. Callida must also demonstrate that a Biologic License Application or New Drug Application for any biological products would be approved by the applicable government agency. In addition, if Callida markets applications of our SBH technology as diagnostic products, they may be considered to be medical devices and Callida or its collaboration partners will be required to show that the diagnostic product is substantially equivalent to a legally marketed product not requiring FDA approval. In addition, Callida must demonstrate that it is capable of manufacturing the product in accordance with the relevant standards. To obtain FDA approval for such products, Callida must submit extensive data to the FDA, including pre-clinical and clinical trial data to prove the safety and efficacy of the device. Clinical trials are normally conducted over a two- to five-year period, but may take longer to complete as a result of many factors, including:

slower than anticipated patient enrollment;

difficulty in finding a sufficient number of patients fitting the appropriate inclusion criteria;

difficulty in acquiring a sufficient supply of clinical trial materials; or

adverse events occurring during the trials.

Furthermore, data obtained from preclinical and clinical activities are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval or clearance for a product.

The process of obtaining FDA and other required regulatory approvals and clearances is lengthy and will require us to expend substantial capital and resources. We may not ultimately be able to obtain the necessary approvals and clearances. Moreover, if and when our 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;

injunctions;

civil penalties;

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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.

We also are 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 our discovery, research and development work, including radioactive compounds and infectious disease agents. In addition, we cannot predict the extent of government regulations or the impact of new governmental regulations that might significantly harm the discovery, development, production and marketing of our products. We may be required to incur significant costs to comply with current or future laws or regulations and we may be adversely affected by the cost of such compliance.

If we market therapeutic and 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. We or our collaboration partners may not be successful in obtaining the necessary approvals.

Any delay or failure by us or our collaboration partners to obtain regulatory approvals for our products:

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

could impose significant additional costs on us or our collaboration partners;

could diminish competitive advantages that we may attain; and

would adversely affect the marketing of our products.

We face intense competition

The genomics and biopharmaceutical industries are intensely competitive. Our strategy as a biopharmaceutical company is 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. Our competitors 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 we do. As a result, they may succeed in identifying genes and determining their functions or developing products earlier than we or our current or future collaboration partners do. They also may obtain patents and regulatory approvals for such products more rapidly than we or our current or future collaboration partners, or develop products that are more effective than those proposed to be developed by us or our collaboration partners. Further, any potential products based on genes we 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 we identify.

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Many of the companies developing competing products have significantly greater financial resources than we have. Many such companies also have greater expertise than we or our collaboration partners 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 our products. These companies and institutions compete with us in recruiting and retaining qualified scientific and management personnel as well as in acquiring technologies complementary to our programs. We 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 we may develop obsolete or uneconomical, or result in treatments, cures or diagnostics superior to any therapy or diagnostic developed by us or that any therapy we develop will be preferred to any existing or newly developed technologies. While we believe that our technology provides a significant competitive advantage, any one of our competitors may discover and establish a patent position in one or more genes which we designate as a product candidate, before we do. Competition in this field is expected to intensify. Certain of our collaboration partners may now be, or could become, competitors.

Competition in the area of DNA analysis tools is intense and expected to increase. Technologies in this area are new and rapidly evolving. Other companies also are developing or have developed DNA analysis tools that may compete with applications of Callidas SBH technology. Many of these companies have significantly greater research and development, marketing and financial resources than we do, and therefore represent significant competition.

We lack marketing experience for biopharmaceuticals

We currently have no sales, marketing or distribution capability. For the foreseeable future, we intend to rely primarily on our current and future collaboration partners or licensors, if any, to market our products. Such collaboration partners, however, may not have effective sales forces and distribution systems. If we are unable to maintain or establish such relationships and are required to market any of our products directly, we will have to develop our own marketing and sales force with the appropriate technical expertise and with supporting distribution capabilities. We 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 we depend on our collaboration partners or third parties for marketing and distribution, any revenues we receive will depend upon the efforts of such collaboration partners or third parties. Such efforts may not be successful.

Our products may not be accepted in the marketplace

Even if they are approved for marketing, products we develop may never achieve market acceptance. Our products, if successfully developed, will compete with a number of traditional drugs and therapies manufactured and marketed by major pharmaceutical and other biotechnology companies. Our products will also compete with new products currently under development by such companies and

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others. The degree of market acceptance of any products developed by us, alone, or in conjunction with our collaboration partners, will depend on a number of factors, including:

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

our 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 we alone, or in conjunction with our collaboration partners, develop. The lack of such market acceptance would significantly harm our business, financial condition and results of operations.

We may develop diagnostic testing products in the future. Our success in diagnostics will depend in large part upon our ability to obtain customers and upon the ability of these customers to market genetic tests performed with our technology properly. Genetic tests, including any performed using applications of Callidas SBH technology, may be difficult to interpret and may lead to misinformation or misdiagnosis. Even when a genetic test identifies the existence of a mutation in a person, the test cannot determine with absolute certainty whether the tested individual will develop the disease or condition for which the test is performed. The prospect of broadly available genetic predisposition testing has raised societal and governmental concerns regarding the appropriate use and the confidentiality of information provided by such testing. Government authorities could limit the use of genetic testing or prohibit testing for genetic predisposition to certain conditions. Ethical concerns about genetic testing may adversely affect market acceptance of our technology for diagnostic applications. Impaired market acceptance of our technology could significantly harm our business, financial condition and operating results.

We face uncertainties related to SBH technology applications

We have developed applications of our SBH technology, currently in our subsidiary, Callida, including the chip component to be used with the HyChip system. As Callida continues development of SBH technology applications, it may discover problems in the functioning of these applications, including the HyChip system. Callida may be unable to improve applications of our SBH technology enough to be able to market them successfully. Further, SBH technology applications compete against other DNA analysis tools and well-established technologies. We cannot predict the outcome of these uncertainties.

We face uncertainty with respect to pricing, third-party reimbursement and health care reform

Our ability to collect significant royalties from our products may depend on our ability, and the ability of our 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

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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, we may not be able to market our products effectively. We also face the risk that we will have to offer our diagnostic products at low prices 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 our products. The cost containment measures that health care providers are instituting and the results of potential health care reforms may prevent us from maintaining prices for our products that are sufficient for us to realize profits and may otherwise significantly harm our business, financial condition and operating results.

We face product liability exposure and potential unavailability of insurance

We risk financial exposure to product liability claims in the event that the use of products developed by us or our collaboration partners, if any, result in personal injury. We may experience losses due to product liability claims in the future. We have obtained limited product liability insurance coverage. Such coverage, however, may not be adequate or may not continue to be available to us in sufficient amounts or at an acceptable cost, or at all. We 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 our business, financial condition and results of operations.

We use hazardous materials

Our research and development activities involve the controlled use of hazardous materials. Although we believe that our safety procedures for handling and disposing of these materials comply with applicable laws and regulations, we cannot eliminate the risk of accidental contamination or injury from hazardous materials. If a hazardous material accident occurred, we would be liable for any resulting damages. This liability could exceed our financial resources. Additionally, hazardous materials are subject to regulatory oversight. If our access to hazardous materials necessary for our operations is limited by federal, state or local regulatory agencies, we could experience delays in our research and development programs. Paying damages or experiencing delays caused by restricted access to necessary materials could reduce our ability to generate revenues and make it more difficult to fund our operations.

Many corporate actions will be controlled by our officers and directors regardless of the opposition of other stockholders or the desire of other stockholders to pursue an alternative course of action

If our stockholders ratify the proposals included in our proxy statement for our 2002 annual meeting, our executive officers and directors, including Dr. Rathmann, will, in the aggregate, beneficially own approximately 27.3% of our common stock outstanding as of July 8, 2002, and Dr. Rathmann will beneficially own approximately 23.9% of our common stock outstanding as of July 8, 2002. Even if our stockholders do not ratify the proposals included in our proxy statement for our 2002 annual meeting, our executive officers and directors will, in the aggregate, beneficially own approximately 19.9% of our common stock outstanding as of July 8, 2002, and Dr. Rathmann will beneficially own approximately 16.4% of our common stock outstanding as of July 8, 2002. For purposes of this paragraph, beneficial ownership is determined in accordance with Rule 13d-3 under the Exchange Act. In either case, these stockholders will, if they act together, be able to exercise substantial influence and control over all matters requiring approval by our stockholders, including the election of directors and approval of significant corporate transactions. This concentration of ownership may also have the effect of delaying or preventing a change in our control.

We have implemented anti-takeover provisions that may reduce the market price of our common stock

Our Amended and Restated By-Laws provide that members of our board of directors serve staggered three-year terms. Our Amended and Restated Articles of Incorporation provide that all stockholder action must be effected at a duly called meeting and not by a consent in writing. The Amended and Restated By-Laws provide, however, that our stockholders may call a special meeting of stockholders only upon a request of stockholders owning at least 50% of our capital stock. These provisions of our Amended and Restated Articles of Incorporation and our Amended and Restated 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 our board of directors and in the policies formulated by our board of directors. We also intended these provisions to discourage certain types of transactions that may involve an actual or threatened change of control. We designed these provisions to reduce our 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 our shares. As a consequence, they also may inhibit fluctuations in the market price of our shares that could result from actual or rumored takeover attempts. Such provisions also may have the effect of preventing changes in our management.

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We are permitted to issue shares of our preferred stock without stockholder approval upon such terms as our board of directors determines. Therefore, the rights of the holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of our 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 our current stockholders.

On June 5, 1998, our board of directors adopted a rights plan and declared a dividend with respect to each share of our 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 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 our 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 our outstanding common stock. The adoption of the rights plan makes it more difficult for a third party to acquire control of us without the approval of our board of directors.

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 corporations voting stock or an affiliate or associate of a corporation who at any time within the prior three years beneficially owned, directly or indirectly, 10% or more of a corporations voting stock. According to the statute, we may not engage in a combination within three years after an interested stockholder acquires our shares, unless (i) our 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 corporations stock after crossing certain threshold ownership percentages, unless the acquirer obtains the approval of the target corporations stockholders. This statute only applies to Nevada corporations that do business directly or indirectly in Nevada. We do not intend to do business in Nevada within the meaning of the statute. Therefore, it is unlikely that the statute will apply to us.

The provisions of our governing documents, our existing agreements and current Nevada law may, collectively:

- lengthen the time required for a person or entity to acquire control of us through a proxy contest for the election of a majority of our board of directors;
- discourage bids for our common stock at a premium over market price; and
- generally deter efforts to obtain control of us.

Risk of natural disasters and power blackouts

Our facilities are located in Sunnyvale, California. In the event that a fire or other natural disaster (such as an earthquake) prevents us from operating our production line, our business, financial condition and operating results would be materially, adversely affected. Some of our landlords maintain earthquake coverage for our facilities. Although we maintain personal property and business interruption coverage, we do not maintain earthquake coverage for personal property or resulting business interruption.

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The State of California has experienced natural gas and electricity problems, which have resulted in rolling power blackouts, some of which have affected our facilities. In addition, we, like others, have experienced large fluctuation in our natural gas rates and may experience steep fluctuations in our electric rates. Although we have an auxiliary generator, it is intended for emergency backup in the event of a power outage and is not capable of powering our entire operations. Future power blackouts and/or large increases in our utility costs could harm our business, financial condition and results of operations.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

Some of the statements in the section entitled Risk Factors and elsewhere in this prospectus constitute 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 based on our mar 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 in this prospectus, including those set forth in the section entitled Risk Factors above.

ABOUT HYSEQ PHARMACEUTICALS

We are engaged in research and development of novel biopharmaceutical protein-based products for the treatment of human disease from our collection of proprietary genes discovered using our high-throughput signature-by-hybridization platform. We are 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. We intend to develop and commercialize these types of product candidates on our own or in collaboration with other biotechnology or pharmaceutical companies.

We believe our signature-by-hybridization platform, which is related to our proprietary sequencing-by-hybridization (or SBH) technology, gives us a significant advantage in discovering novel, rarely-expressed genes. We believe we possess one of the most important proprietary databases of full-length human gene sequences and have the potential to develop a significant pipeline of product candidates for research and development. Previously, our 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 July 8, 2002, we had filed patent applications on approximately 10,000 full-length human gene sequences. We are accelerating our research activities to elucidate the role of novel genes in our proprietary database, their encoded proteins and corresponding antibodies. Our database includes chemokines, growth factors, stem cell factors, interferons, integrins, hormones, receptors and other potential protein therapeutics or drug targets. Our focused bioinformatics and screening capabilities have significantly enhanced our understanding of the biological activity of these genes and their corresponding proteins, enabling us to file strategic patent applications that encompass both composition of matter and method of use claims.

We are primarily focused on discovering and developing therapeutic protein-based products, as we believe that naturally occurring therapeutic proteins have several commercial advantages over small molecule drugs.

In the near term, we are balancing the risks in developing therapeutics from our full-length gene database by also focusing on an early stage clinical product candidate acquired through collaboration with Amgen, Inc. We 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.

Under the terms of our collaboration agreement with Amgen, we 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. We will fund all development costs up to an agreed amount, after which costs as well as eventual profits will be shared equally. We 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. Under the collaboration agreement, we may be obligated to make a one-time milestone payment of $10 million upon obtaining regulatory approval for the collaboration product in a major market. If Amgen exercises its license option pursuant to the collaboration, we may, upon the occurrence of specified conditions, be obligated to make milestone payments in an aggregate amount of up to $40 million. The $10 million milestone payment under the collaboration agreement is creditable against the $40 million aggregate milestone payments under the license agreement described above. We may also be obligated to pay Amgen an amount of up to $10 million in the event that a clinical trial is not timely commenced.

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We were incorporated in Illinois in August 1992 and reincorporated in Nevada in November 1993. We have being doing business as Hyseq Pharmaceuticals, Inc. since October 2001. Our executive offices are located at 670 Almanor Avenue, Sunnyvale, California 94085 and our telephone number is (408) 524-8100. Our World Wide Web address is http://www.hyseq.com. Information contained in our World Wide Web site should not be considered to be part of this prospectus.

USE OF PROCEEDS

We will not receive any of the proceeds from the sale of the shares of common stock offered by the selling stockholders.

SELLING STOCKHOLDERS

On April 5, 2002, we sold an aggregate of 3,575,691 shares of our common stock to some of the selling stockholders in a private placement and issued those selling stockholders warrants to purchase an aggregate of 893,927 shares of common stock. In connection with this sale, we agreed to file a registration statement with the SEC covering the resale of the shares, including the shares issuable upon exercise of the warrants.

On November 13, 2001, Affymetrix, Inc., a Delaware corporation, purchased from us a promissory note in the principal amount of $4,000,000. At any time prior to payment in full of the principal balance of, and all interest accrued on, the promissory note, the promissory note may, at our election, be exchanged, in full or in part, into shares of our common stock. No portion of the promissory note may be exchanged into shares of common stock to the extent that such exchange would cause the holder or any of its affiliates to beneficially own more than 19% of the shares of our common stock outstanding as of the date of exchange. The number of shares of common stock deliverable upon exchange of the promissory note will equal the amount of principal and interest to be exchanged divided by the exchange price. The exchange price of the promissory note is determined by multiplying 90% by the average of the per share closing prices of our common stock for ten consecutive trading days immediately preceding and including the second trading day prior to the date of the exchange. In connection with the purchase and sale of the promissory note, we agreed to file a registration statement with the SEC covering the resale by the holder of the shares of our common stock issuable upon exchange of the promissory note.

This prospectus also covers 166,241 shares of common stock held by The Donald G. Brungard Living Trust UTD 11/28/92. We sometimes refer to such stockholder as the Brungard trust.

The promissory note sold to Affymetrix and the warrants issued to the selling stockholders were not and will not be registered under the Securities Act of 1933, as amended.

The following table sets forth the names of the selling stockholders, the number of shares of our common stock that each selling stockholder beneficially owns as of July 23, 2002 and the number of shares which may be offered pursuant to this prospectus. Beneficial ownership is determined in accordance with Rule 13d-3 under the Securities Exchange Act of 1934. Each selling stockholder offering shares of common stock to be issued upon the exercise of a warrant may not exercise its warrant if such exercise would result in the selling stockholder owning more than 4.999% of our outstanding shares of common stock (including for such purpose the shares of common stock issuable upon such exercise), unless the less than 4.999% requirement is waived by the selling stockholder holding the warrant (as to itself only) upon not less than 61 days prior notice to us. Other holders of warrants shall be unaffected by any such waiver. In addition, each selling stockholder offering shares of common stock to be issued upon the exercise of a

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warrant may not exercise the warrant into shares of our common stock if, after the exercise, such holder, together with any of its affiliates, would beneficially own over 9.999% of the outstanding shares of our common stock. However, the 9.999% limitation would not prevent the holder from acquiring and selling in excess of 9.999% of our common stock through a series of exercises. Percentage ownership is based on 22,994,366 shares of common stock outstanding as of July 23, 2002. Each selling stockholder may sell all, some or none of the common stock being offered.

Name of Selling Stockholder	Shares Beneficially Owned Prior to the Offering	Shares Offered by This Prospectus(1)	Shares Beneficially Owned Subsequent to the Offering (1)	
			Shares	Percent
Affymetrix, Inc.		2,175,075(2)		*
The Donald G. Brungard Living Trust UTD 11/28/92	390,640	166,241	224,399	*
Cleveland Overseas Ltd.	74,404(3)	74,404		*
BankAmerica Investment Corporation	193,455(4)	193,455		*
Ursus Offshore Ltd.	235,125(5)	160,625	74,500	*
Ursus Capital, L.P.	206,575(6)	139,375	67,200	*
Sabalon Investments Inc.	104,167(7)	104,167		*
JB Partners	125,000(8)	125,000		*
Smithfield Fiduciary LLC	297,619(9)	297,619		*
CLSP	992,857(10)	892,857	100,000	*
XMark, L.P.	21,578(11)	21,578		*
XMark, Ltd.	52,828(12)	52,828		*
Brooks Industries of Long Island Inc.	125,000(13)	125,000		*
Vulcan Ventures Inc.	1,544,615(14)	794,615	750,000	3.2
Narragansett Offshore Ltd.	1,050,979(15)	422,269	628,710	2.7
Narragansett I, L.P.	454,047(16)	172,969	281,078	*
Cranshire Capital, L.P.	272,767(17)	148,809	123,958	*
Pine Ridge Financial Inc.	965,963(18)	744,048	221,915	*

* Less than 1% of the outstanding shares of common stock.

(1) Assumes the sale of all shares of common stock offered by this prospectus.(2) The shares offered consist of shares of common stock issuable upon exchange of the promissory note issued by us in the principal amount of $4,000,000, plus 7.5% interest per

annum, based on a 360-day year. No portion of the promissory note may be exchanged into shares of our common stock to the extent that such exchange would cause the holder or any of its affiliates to beneficially own more than 19% of the shares of our common stock outstanding on the date of the exchange. We are listing in this prospectus 125% of the number of shares into which the promissory note, including accrued interest, would be exchanged if it were exchanged as of June 13, 2002. Therefore, the number of shares set forth herein and which Affymetrix may sell pursuant to this prospectus may exceed the number

of shares of common stock that we have calculated pursuant to the preceding sentence.

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(3) The number of shares listed includes 14,881 shares of common stock issuable to Cleveland Overseas Ltd. upon the exercise of a warrant issued by us to Cleveland Overseas Ltd., and 59,523 shares of common stock held by Cleveland Overseas Ltd.

(4) The number of shares listed includes 38,691 shares of common stock issuable to BankAmerica Investment Corporation upon the exercise of a warrant issued by us to BankAmerica Investment Corporation, and 154,764 shares of common stock held by BankAmerica Investment Corporation.(5) The number of shares listed includes 32,125 shares of common stock issuable to Ursus Offshore Ltd. upon the exercise of a warrant issued by us to Ursus Offshore Ltd., and 128,500 shares of common stock held by Ursus Offshore Ltd.(6) The number of shares listed includes 27,875 shares of common stock issuable to Ursus Capital, L.P. upon the exercise of a warrant issued by us to Ursus Capital, L.P., and 111,500

shares of common stock held by Ursus Capital, L.P.(7) The number of shares listed includes 20,834 shares of common stock issuable to Sabalon Investments Inc. upon the exercise of a warrant issued by us to Sabalon Investments Inc., and 83,333 shares of common stock held by Sabalon Investments Inc.(8) The number of shares listed includes 25,000 shares of common stock issuable to JB Partners upon the exercise of a warrant issued by us to JB Partners, and 100,000 shares of common stock held by JB Partners.(9) The number of shares listed includes 59,524 shares of common stock issuable to Smithfield Fiduciary LLC upon the exercise of a warrant issued by us to Smithfield Fiduciary LLC, and 238,095 shares of common stock held by

Smithfield Fiduciary LLC.(10) The number of shares listed includes: (i) 30,600 shares of common stock issuable to CLSP Overseas Ltd. upon the exercise of a warrant issued by us to CLSP Overseas Ltd., (ii) 122,400 shares of common stock held by CLSP Overseas Ltd., (iii) 13,598 shares of common stock issuable to CLSP SBS-II, L.P. upon the exercise of a warrant issued by us to CLSP SBS-II, L.P., (iv) 54,392 shares of common stock held by CLSP SBS-II, L.P., (v) 27,415 shares of common stock issuable to CLSP SBS-I, L.P. upon the exercise of a warrant issued by us to CLSP SBS-I, L.P., (vi) 109,660 shares of common stock held by CLSP SBS-I, L.P., 13,563 shares of common stock issuable to CLSP II, L.P. upon the exercise of a warrant issued by us to CLSP II, L.P., (vii) 54,252

shares of common stock held by CLSP II, L.P., (viii) 93,396 shares of common stock issuable to CLSP, L.P. upon the exercise of a warrant issued by us to CLSP, L.P. and (ix) 373,581 shares of common stock held by CLSP, L.P.(11) The number of shares listed includes 4,316 shares of common stock issuable to XMark, L.P. upon the exercise of a warrant issued by us to XMark, L.P., and 17,262 shares of common stock held by XMark, L.P.(12) The number of shares listed includes 10,566 shares of common stock issuable to XMark, Ltd. upon the exercise of a warrant issued by us to XMark, Ltd., and 42,262 shares of common stock held by XMark, Ltd.(13) The number of shares listed includes 25,000 shares of common stock issuable

to Brooks Industries of Long Island Inc. upon the exercise of a warrant issued by us to Brooks Industries of Long Island Inc., and 100,000 shares of common stock held by Brooks Industries of Long Island Inc.	

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(14) The number of shares listed includes: (i) 250,000 shares of common stock issuable to Vulcan Ventures Inc. upon the exercise of a warrant issued by us to Vulcan Ventures Inc. on August 28, 2001 not being offered by this prospectus, (ii) 158,923 shares of common stock issuable to Vulcan Ventures Inc. upon the exercise of a warrant issued by us to Vulcan Ventures Inc. on April 5, 2002 being offered by this prospectus, (iii) 635,692 shares of common stock held by Vulcan Ventures Inc. being offered by this prospectus and (iv) 500,000 shares of common stock not being offered by this prospectus.

(15) The number of shares listed includes: (i) 222,536 shares of common stock issuable to Narragansett Offshore, Ltd. upon the exercise of a warrant issued by us to Narragansett Offshore, Ltd. on August 28, 2001 not being offered by this prospectus, (ii) 84,454 shares of common stock issuable to Narragansett Offshore, Ltd. upon the exercise of a warrant issued by us to Narragansett Offshore, Ltd. on April 5, 2002 being offered by this prospectus and (iii) 337,815 shares of common stock held by Narragansett Offshore, Ltd. being offered by this prospectus.(16) The number of

shares listed includes: (i) 109,607 shares of common stock issuable to Narragansett I, L.P. upon the exercise of a warrant issued by us to Narragansett I, L.P. on August 28, 2001 not being offered by this prospectus, (ii) 34,594 shares of common stock issuable to Narragansett I, L.P. upon the exercise of a warrant issued by us to Narragansett I, L.P. on April 5, 2002 being offered by this prospectus and (iii) 138,375 shares of common stock held by Narragansett I, L.P. being offered by this prospectus.(17) The number of shares listed includes: (i) 117,858 shares of common stock issuable to Cranshire Capital, L.P. upon the exercise of a warrant issued by us to Cranshire

Capital, L.P. on August 28, 2001 not being offered by this prospectus, (ii) 6,100 shares of common stock held by Cranshire Capital, L.P. not being offered by this prospectus, (iii) 29,762 shares of common stock issuable to Cranshire Capital, L.P. upon the exercise of a warrant issued by us to Cranshire Capital, L.P. on April 5, 2002 being offered by this prospectus and (iv) 119,047 shares of common stock held by Cranshire Capital, L.P. being offered by this prospectus.(18) The number of shares listed includes: (i) 189,286 shares of common stock issuable to Pine Ridge Financial Inc. upon the exercise of a warrant issued by us to Pine Ridge Financial Inc. on

August 28, 2001 not being offered by this prospectus, (ii) 148,810 shares of common stock issuable to Pine Ridge Financial Inc. upon the exercise of a warrant issued by us to Pine Ridge Financial Inc. on April 5, 2002 being offered by this prospectus and (ii) 595,238 shares of common stock held by Pine Ridge Financial Inc. being offered by this prospectus.

In connection with the issuance of the promissory note to Affymetrix, we granted Affymetrix a non-exclusive license to our array-related patents in the field of non-universal probe arrays, and Affymetrix granted us an internal use license under certain Affymetrix array-related patents for pharmaceutical research. We also entered into a BiotechAccess supply agreement with Affymetrix for Affymetrix GeneChip® technology. Affymetrix paid us a one-time license fee for the non-exclusive license.

Except as stated above, we are unaware of any material relationship between the selling stockholders and us in the past three years.

We are registering the shares of our common stock offered by the selling stockholders (other than the Brungard trust) pursuant to contractual registration rights we granted to the selling stockholders. We have filed a registration statement related to the shares offered by this prospectus and, with respect to the shares offered by Affymetrix, we have agreed to use commercially reasonable efforts to keep such registration statement continuously effective under the Securities Act for so long as there shall remain outstanding any shares of common stock issued in exchange for amounts due under the promissory note sold to Affymetrix, except shares that have been effectively registered under the Securities Act and sold in a manner contemplated by the registration statement or that have been

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transferred in compliance with Rule 144 or are transferable pursuant to paragraph (k) of Rule 144, or any principal or interest is outstanding under the promissory notes. With respect to the shares offered by the other selling stockholders (other than the Brungard trust), we have agreed to keep the registration statement effective until the earlier of (1) the date on which all the shares have been sold or may be sold without volume restrictions pursuant to Rule 144(k) under the Securities Act, and (2) two years after the registration statement is declared effective.

PLAN OF DISTRIBUTION

The selling stockholders and any of their pledges, assignees and successors-in-interest may, from time to time, sell any or all of their shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or negotiated prices. The selling stockholders may use any one or more of the following methods when selling shares:

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by broker-dealer as principal and resale by the broker-dealer for its account;

an exchange distribution in accordance with the rules of the applicable exchange;

privately negotiated transactions;

short sales;

broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;

a combination of any such methods of sale; and

any other method permitted pursuant to applicable law.

The selling stockholders may also sell shares under Rule 144 under the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by the selling stockholders may arrange for other broker-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholders (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. The selling stockholders do not expect these commissions and discounts to exceed what is customary in the types of transactions involved.

The selling stockholders may from time to time pledge or grant a security interest in some or all of the common stock or warrants owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act of 1933 amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

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The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for the purposes of this prospectus.

The selling stockholders and any broker-dealers or agents that are involved in selling the shares may be deemed to be underwriters within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. The selling stockholders have informed the Company that they do not have any agreement or understanding, directly or indirectly, with any person to distribute the Common Stock.

We have advised the selling stockholders that they are required to comply with Regulation M promulgated under the Securities and Exchange Act during such time as they may be engaged in a distribution of the shares. With some exceptions, Regulation M precludes any selling stockholder, any affiliated purchaser and any broker-dealer or other person who participates in such distribution from bidding for or purchasing, or attempting to induce any person to bid for or purchase any security that is the subject of the distribution until the entire distribution is complete. Regulation M also prohibits any bids or purchases made in order to stabilize the price of a security in connection with the distribution of that security. All of the foregoing may affect the marketability of the common stock.

We are required to pay all fees and expenses incident to the registration of the shares, including $10,000 of fees and disbursements of counsel to the selling stockholders. We have agreed to indemnify the selling stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

LEGAL MATTERS

Kummer Kaempfer Bonner & Renshaw of Las Vegas, Nevada will issue an opinion about certain legal matters with respect to the common stock being offered in this prospectus.

EXPERTS

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

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

WHERE YOU CAN FIND MORE INFORMATION

We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission, or the SEC. You may read and copy these reports, proxy statements and other information at the SEC s public reference rooms at 450 Fifth Street, N.W., Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference rooms. Our SEC filings are also available at the SEC s Web site at http://www.sec.gov. In addition, you can read and copy our SEC filings at the office of the National Association of Securities Dealers, Inc. at 1735 K Street, Washington, D.C. 20006.

The SEC allows us to incorporate by reference information that we file with them, which means that we can disclose important information to you by referring you to those documents. The

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information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. Further, all filings we make under the Securities Exchange Act after the date of the initial registration statement and prior to effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus. We incorporate by reference the documents listed below and any future filings we will make with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934:

1. Our Annual Report on Form 10-K for the 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;

2. Our 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;

3. Our Current Report on Form 8-K, filed with the SEC on January 11, 2002;

4. Our Current Report on Form 8-K, filed with the SEC on January 28, 2002;

5. Our Current Report on Form 8-K, filed with the SEC on April 9, 2002;

6. Our Current Report on Form 8-K, filed with the SEC on May 16, 2002; and

7. The description of our common stock set forth in our Registration Statement on Form 8-A, filed with the SEC on July 23, 1997.

We will provide to you at no cost a copy of any and all of the information incorporated by reference in this prospectus. You may make a request for copies of this information in writing or by telephone. Requests should be directed to:

Hyseq Pharmaceuticals, Inc.
Attention: Peter S. Garcia
675 Almanor Avenue
Sunnyvale, CA 94085
(408) 524-8100