HYSEQ INC
Form 10-K/A
July 22, 2002

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HYSEQ PHARMACEUTICALS, INC.

Annual Report 2001

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SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K/A

(Amendment No. 2)

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2001

or

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission File Number: 0-22873

HYSEQ, INC.

(Exact Name of Registrant as Specified in Its Charter)

Nevada	**36-3855489**
(State or Other Jurisdiction of Incorporation or Organization)	*(I.R.S. Employer Identification No.)*
670 Almanor Avenue, Sunnyvale, CA	**94085**
(Address of principal executive offices)	*(Zip Code)*

Registrant s telephone number, including area code:

408-524-8100

Securities registered pursuant to Section 12(b) of the Exchange Act: None

Securities registered pursuant to Section 12(g) of the Exchange Act:

Common Stock, $.001

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes þ No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. o

The aggregate market value of the common stock held by non-affiliates of the Registrant on March 15, 2002 was $94,672,151 based on the last sale price of the common stock as reported by the Nasdaq Stock Market.

As of March 15, 2002, the Registrant had 19,371,052 shares of common stock outstanding.

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EXPLANATORY NOTE

This Amendment No. 2 on Form 10-K/ A revises Items 1 and 14(a)(3) and Exhibits 10.16, 10.17, 10.18, 10.20, 10.22 and 10.23 of our Annual Report on Form 10-K for the fiscal year ended December 31, 2001 that was originally filed on April 1, 2002 (the Original Filing), and amended pursuant to Amendment No. 1 on Form 10-K/A filed on May 9, 2002, to respond to comments we received from the Securities and Exchange Commission.

This report revises the disclosure under the Business section to disclose additional information with respect to the aggregate fees that we may receive or be obligated to pay in connection with our Collaboration and License Agreement with Aurora Biosciences Corporation, dated June 29, 2001. This report also updates Item 14(a)(3) and revises Exhibits 10.16, 10.17, 10.18, 10.20, 10.22 and 10.23 filed as exhibits to the Original Filing to disclose additional portions of those exhibits for which we had originally requested confidential treatment. Other than these amendments, Items 1 and 14 remain in the same form as initially filed.

This report continues to speak as of the date of the Original Filing, and we have not updated the disclosure in this report to speak as of a later date. All information contained in this report and the Original Filing is subject to updating and supplementing as provided in our periodic reports filed with the Securities and Exchange Commission.

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PART I

Item 1. *Business*

This Annual Report on Form 10-K contains historical information as well as forward-looking statements that involve risks and uncertainty. Our actual results could differ significantly from discussions and forward-looking statements in this document. Factors that could cause or contribute to such differences include but are not limited to those discussed in this section under the caption Risk Factors, as well as those under Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations and those discussed elsewhere in this Annual Report on Form 10-K.

Company Overview

We were incorporated in Illinois in August 1992 and reincorporated as a Nevada corporation on November 12, 1993. We have being doing business as Hyseq Pharmaceuticals, Inc. since October 2001.

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 March 15, 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.

Scientific and Industry Background

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

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The complete set of genetic information of each organism, known as its genome, is encoded in its deoxyribonucleic acid (or DNA). DNA, which is found in the nucleus of cells, is a molecule comprising two complementary strands entwined in the form of a double helix. Various combinations of four chemical building blocks or bases of DNA, adenine (A), thymine (T), cytosine (C) and guanine (G), are linked together in series to form each DNA strand. The bases of one DNA strand bind to the bases of the other strand in a specific fashion to form base pairs: A pairs with T and G pairs with C. In humans, there are approximately six billion base pairs organized into 23 pairs of DNA structures called chromosomes.

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

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

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

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

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

Strategy

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

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

The third part of our strategy involves strategic relationships to share research and development efforts and marketing opportunities with other biotechnology and pharmaceutical companies. We believe this approach will greatly enhance our chances to move a number of drug candidates into clinical trials over the next several years. We are now focusing on new corporate relationships with other biotechnology and pharmaceutical companies to share costs and expertise of identifying and developing product candidates. This

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focus also includes plans to collaborate with strategic partners with expertise to develop antibodies and small molecules from our proprietary targets.

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

Our strategy also encompasses pursuing comprehensive intellectual property protection. We seek to establish patent priority for our gene and protein discoveries at the earliest possible time. We use data generated from bioinformatics and exploratory biology to enhance our patent applications.

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

We intend to develop our own manufacturing capabilities in the future, but in the near term we expect to use third-party manufacturers. We have initiated the design phase for a pilot manufacturing plant, which we intend to use as a source of clinical product supply. We plan to subsequently develop larger-scale commercial manufacturing facilities as our products progress through clinical development.

Research and Development

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

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

We use a diverse set of tools to evaluate the biological functions of the genes and proteins we discover. In our collaboration with Kirin Brewery Company, Ltd., we conduct screens in which the gene of interest has

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been introduced into genetically modified mice (transgenic mice) such that the encoded human protein is expressed in the adult animal. Through our collaboration with Deltagen Inc., we can identify the function of our genes by developing knockout mice, in which the corresponding mouse gene has been inactivated by genetic manipulation. We use dozens of independent assays to investigate the biological and biochemical activities of our novel proteins. To obtain additional information, our scientists have adapted or created in vivo laboratory models that mimic human diseases to determine the cause of disease and response to treatment. For certain ligands, we clone the receptors for the ligand present in a tissue or cell. In addition to providing a marker for tissues that should respond to the protein, the receptors themselves can have therapeutic potential. We also rely on an external network of collaborators to investigate biology and conduct additional tests that we do not perform in-house.

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

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

Alfimeprase: Product Candidate for Clot Lysis

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

To date none of our other therapeutic protein product candidates has progressed beyond pre-clinical testing, aside from alfimeprase. Recently, we have refocused our efforts from previously identified pre-clinical stage product candidates, IL1Hy1 and CD39L4, to other more promising pre-clinical candidates, the results of testing to date may not be indicative of results that will be obtained in further pre-clinical studies or in clinical trials. However, as we have not begun human testing of alfimeprase or any other product candidates, human

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clinical results could be different from our expectations following our pre-clinical studies. Consequently, there is no assurance that the results in our pre-clinical testing are predictive of the results that we will see in our clinical trials with humans. As further results of tests are received, we may abandon or reduce our efforts regarding particular projects. Additionally, there can be no assurance that clinical trials as to any particular product candidate, if commenced, will be successful, that the proposed disease indication will prove true, or that any product can be successfully commercialized. See Risk Factors Development of Our Products Will Take Years; Our Products Will Require Approval Before They Can Be Sold and Risk Factors The Success of Our Potential Products in Preclinical Studies Does Not Guarantee that these Results Will Be Replicated in Humans.

Intellectual Property

We seek patent protection on isolated partial and full-length gene sequences, as well as their encoded protein products, antibodies that bind to these proteins, and methods of using these genes, proteins or antibodies. As of March 15, 2002, we had filed patent applications on approximately 10,000 full-length gene sequences and their corresponding proteins and antibodies. Subsequent bioinformatics analyses of our proprietary collection indicate that these putative full-length gene sequences represent approximately 10,000 different genes. We have also filed patent applications on more than 830,000 partial gene sequences. We hold five United States patents relating to our proprietary gene sequences with claims covering the genes, their encoded protein products, corresponding antibodies, or methods of use.

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

Our success will depend in large part on our ability to: obtain patent and other proprietary protection for genes and proteins we discover; defend patents once obtained; operate without infringing the patents and proprietary rights of third parties; and preserve our trade secrets.

Research and Development Collaborations

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

Aurora

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

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of such milestones). As part of the agreement, we will provide Aurora access to selected novel targets from our database of proprietary full-length cDNAs. The agreement calls for Aurora to make payments to Hyseq of up to $1,825,000 over approximately two years, which includes technology and target access fees, license fees, and milestone payments. In addition, Hyseq may receive up to $1,150,000 in clinical milestone payments on the first Aurora product developed under the agreement (contingent upon achievement of such milestones). If none of the clinical milestones are achieved, then none of the milestone payments will be made or received by either party.

Deltagen

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

Kirin

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

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

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

BASF

In December 1999, we entered into a collaboration with American Cyanamid Company in which we use our signature-by-hybridization platform to target potential agricultural products. During 2000, BASF Aktiengesellschaft acquired the crop protection business of American Cyanamid Company and subsequently assigned our collaboration with American Cyanamid to BASF Plant Sciences GmbH. The collaboration provides for funding of $60 million over its initial term of three and one half years. The collaboration can be extended by mutual agreement, for up to four additional one-year terms. BASF has the exclusive right to commercialize any agricultural products resulting from the collaboration. We will receive royalties on any such products. The agreement requires us to generate data at a specified level per year which, if not met, could result in our breach of the agreement. Revenues from our collaboration with BASF represented less than 10% of total revenue for fiscal year ended December 31, 1999, 75% of total revenue for fiscal year ended December 31, 2000, and 91% of total revenue for fiscal year ended December 31, 2001.

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Chiron

In May 1997, we entered into a collaboration with Chiron in which we used our signature-by-hybridization platform to target solid tumor cancer therapeutics, diagnostic molecules and vaccines. The collaboration had an initial term of three years ending in May 2000, and has been extended by Chiron for an additional two-year period ending in May 2002. At its option, Chiron may extend the collaboration for one more two-year period before the current extension ends in May 2002. Our gene sequencing obligations under the original term of the agreement are substantially completed. Chiron has the exclusive right to commercialize any solid tumor products resulting from the collaboration. We will receive royalties on any such products. In addition to research funding payments, in 1997 Chiron made an equity investment in us of $7.5 million in conjunction with the collaboration. Revenues from our collaboration with Chiron represented 76% of total revenue for fiscal year ended December 31, 1999, 21% of total revenue for fiscal year ended December 31, 2000, and less than 10% of total revenue for fiscal year ended December 31, 2001.

University of California, San Francisco

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

Applied Biosystems

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

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

Affymetrix

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

Our Subsidiary Callida Genomics, Inc.

In October 2001, we formed a new majority-owned subsidiary, Callida Genomics, Inc., to carry out the Company s business relating to our proprietary SBH technology. At the same time, Callida formed a wholly owned subsidiary, N-Mer, Inc. to collaborate with Affymetrix, Inc. on developing and commercializing a high speed DNA sequencing chip. Affymetrix has an initial 10% equity interest in Callida which may increase or

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decrease upon further third party financing of Callida. We and Affymetrix have agreed to each make additional investments in Callida, which will be conditioned on N-Mer s attainment of a specified technical milestone and the procurement of third-party financing. Callida granted Affymetrix an option to purchase a majority interest in N-Mer, which will be exercisable at any time over the next five years.

We contributed all of our SBH patents and patent applications to Callida. A team of approximately 30 Hyseq scientists, including one of our founders, Dr. Radoje Drmanac, who pioneered our DNA chip and SBH technology, are now full-time employees of Callida. Our Chairman Dr. George Rathmann will also serve as Chairman, Interim President and Chief Executive Officer of Callida. As of March 15, 2002, Hyseq has a 90% equity position in Callida.

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

Licensed Technology

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

Patents and Trade Secrets

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

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

In part, the filing of so many patents on DNA sequences reflects the importance of patent protection for therapeutic protein-based products. The costs of developing these products can run into the hundreds of

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millions of dollars and can take up to 10 to 12 years from experimental stage to market. Without patent protection, companies often have little incentive to invest in this important endeavor. Protection through patent exclusivity provides the opportunity for a company to recoup its research and development costs, make a profit on the therapeutic protein-based product, and invest in research and development of additional therapeutic protein-based products.

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

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

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

Issued patents may not provide freedom to operate with respect to our potential products because certain uses of our potential products may give rise to claims that such uses infringe the patents of others. This risk will increase as the biotechnology industry expands and as other companies obtain more patents and attempt to discover the utility and function of all known genes. Other persons could bring legal actions against us to claim damages or to stop our manufacturing and marketing of the affected products. If any of these actions are successful, in addition to any potential liability for past damages, these persons may require us to obtain a license in order to continue to manufacture or market the affected products. We believe that there will continue to be significant litigation in our industry regarding patent and other intellectual property rights. If we become involved in patent litigation related to our technology or potential products, it could consume a substantial portion of our resources.

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

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Competition

Our strategy as a biopharmaceutical company is to define and patent human genes that are most likely to be involved in a disease condition and to focus on identifying product candidates from the proteins produced by these genes. There are a finite number of genes in the human genome, virtually all of which have been or will soon be identified. Other active companies include major pharmaceutical and biotechnology firms, not-for-profit entities and United States and foreign government-financed programs, many of which have substantially greater research and product development capabilities and financial, scientific, marketing and human resources than 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. 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. Certain of our collaboration partners may now be, or could become, competitors.

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

We believe the principal competitive factors affecting our markets are rights to develop and commercialize therapeutic protein-based products, including appropriate patent and proprietary rights; safety and effectiveness of therapeutic protein-based products; the timing and scope of regulatory approvals; the cost and availability of these products; the availability of appropriate third-party reimbursement programs; and the availability of alternative therapeutic products or treatments. Although we believe that we are well positioned to compete adequately with respect to these factors in the future, our future success is currently difficult to predict because we are an early stage company; all of our internal product candidates are still in various stages of pre-clinical development and have yet to undergo clinical trials. Also, although we believe that our bioinformatics technologies and exploratory biology capabilities provide us with a competitive advantage, any of the companies or other entities we compete with may discover and establish a superior patent position in one or more genes or proteins that we have identified and designated or considered designating as a product candidate. In addition, any potential products based on genes or proteins we identify will face competition both from companies developing gene- or protein-based products and from companies developing other forms of treatment for diseases that may be caused by, or related to, the genes or proteins we identify. Furthermore, our potential products, if approved and commercialized, may compete against well established existing therapeutic protein-based products, many of which may be currently reimbursed by government health administration authorities, private health insurers and health maintenance organizations. Also, healthcare professionals and consumers may prefer existing or newly developed products to any product we develop.

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

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

Government Regulation

Regulation by governmental authorities in the United States and most foreign countries will be a significant factor in manufacturing and marketing our potential products and in our ongoing research and product development activities. Virtually all of our products and those of our partners, such as Amgen, Aurora Biosciences, Chiron, Deltagen and Kirin, will require regulatory approval by governmental agencies prior to commercialization. In particular, human therapeutic products are subject to rigorous preclinical and clinical testing and other approval requirements by the FDA and comparable agencies in foreign countries. We are currently collaborating with Amgen to develop alfimeprase, which is a drug candidate that will require regulatory approval. The collaboration is further described in note 12, Subsequent Events, to the financial statements included in this Annual Report on Form 10-K. The time required for completing such testing and obtaining such approvals is uncertain. Unexpected biological activities, some of which may result in safety issues, may arise during preclinical evaluation. Such observations could delay or alter the course of a development program or ultimately result in the termination of a program. Any delay in clinical testing may also delay product development. In addition, delays or rejections may be encountered based on changes in FDA or foreign regulatory policy during the period of product development and testing. Various federal statutes and regulations also regulate the manufacturing, safety, labeling, storage, record-keeping and marketing of such products. The lengthy process of obtaining regulatory approvals and ensuring compliance with appropriate federal statutes and regulations requires the expenditure of substantial resources. Any delay or failure by us or by our collaboration partners to obtain regulatory approval could adversely affect the commercialization of products we or they are developing, our ability to achieve product collaboration milestones or receive royalty revenue and thus negatively impact our liquidity and capital resources.

Preclinical studies are generally conducted in the laboratory to evaluate the potential efficacy and safety of a therapeutic product. The results of these studies are submitted to the FDA as part of an Investigational New Drug application (IND), which must be reviewed by FDA personnel before clinical testing can begin. Typically, clinical evaluation involves three sequential phases, which may overlap. During Phase I, clinical trials are conducted with a relatively small number of subjects to determine the early safety profile of a drug, as well as the pattern of drug distribution and drug metabolism. In Phase II, trials are conducted with groups of patients afflicted by a specific target disease to determine preliminary efficacy, optimal dosages, and dosage

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tolerance and to gather additional safety data. In Phase III, larger-scale, multi-center comparative trials are conducted with patients afflicted with a specific target disease to provide data for the statistical proof of efficacy and safety as required by the FDA and foreign regulatory agencies. The FDA, the clinical trial sponsor or the investigator may suspend clinical trials at any time if they believe that clinical subjects are being exposed to an unacceptable health risk. Although the IND has been filed for alfimeprase, we may change the clinical study design, which may require further review by the FDA. Once we begin Phase I clinical studies, there is no assurance that the safety profile of alfimeprase will be acceptable and that it will proceed to Phase II or Phase III.

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

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

To manufacture our potential products, a domestic or foreign drug manufacturing facility must be registered with the FDA as a manufacturing establishment, must submit to periodic inspection by the FDA and must comply with current Good Manufacturing Practices regulations. In addition, the FDA imposes a number of complex regulations on entities that advertise and promote biologics, including, among others, standards and regulations for direct-to-consumer advertising, off-label promotions, industry-sponsored scientific and educational activities, and promotional activities involving the Internet. The FDA has very broad enforcement authority under the Federal Food, Drug and Cosmetic Act, and failure to abide by these regulations can result in penalties, including the issuance of a warning letter directing us to correct deviations from FDA standards, a requirement that future advertising and promotional materials be pre-cleared by the FDA, and civil and criminal penalties.

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

Even if regulatory approval for a product is obtained, the product and the facilities manufacturing the product are subject to continued review and periodic inspection. Each drug-manufacturing establishment in the United States must be registered with the FDA. Domestic manufacturing establishments are subject to biannual inspections by the FDA and must comply with the FDA s cGMP regulations, as well as regulatory

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agencies in other countries if products are sold outside the United States. If our subsidiary Callida manufactures for sale to third parties diagnostic product applications of its SBH technology, it will need to comply with cGMP regulations pertaining to devices. We will need to spend funds, time and effort to ensure full technical compliance with these regulations. The FDA stringently applies regulatory standards for manufacturing drugs, biologics, and medical devices. The FDA s cGMP regulations require that drugs and medical devices be manufactured and records be maintained in a prescribed manner with respect to manufacturing, testing and control activities.

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

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

Human Resources

At December 31, 2001, we had 224 full-time equivalent employees including Callida employees, 92 of whom hold Ph.D., M.D., J.D., or other advanced degrees. Approximately 186 of our employees are engaged in research and development activities, including 29 in Callida Genomics, and approximately 38 are engaged in business development, finance, operations support, and administration. None of our employees are represented by a collective bargaining agreement, nor have we experienced work stoppages. We believe that relations with our employees are good.

Risk Factors

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.

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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;

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;

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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 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.

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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

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 product s 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 partner s 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 partner s 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.

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We seek patents on:

full-length gene sequences;

partial gene sequences;

proteins produced by those genes;

antibodies to those proteins;

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

processes, devices and other technology that enhance 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 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

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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.

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.

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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;

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.

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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 March 15, 2002, we had 19,371,052 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 March 15, 2002, our affiliates held 4,414,946 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 March 15, 2002, warrants to purchase 3,149,433 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, 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 1,268,160 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 March 15, 2002, 229,540 of the 1,268,160 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 majority 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

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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 Callida s 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. 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;

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;

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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 diversion of management s 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

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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;

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 Callida s 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 others. The degree of market

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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 Callida s 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 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

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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 33.8% of our common stock outstanding as of May 2, 2002, and Dr. Rathmann will beneficially own approximately 23.7% of our common stock outstanding as of May 2, 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 22.7% of our common stock outstanding as of May 2, 2002, and Dr. Rathmann will beneficially own approximately 16.0% of our common stock outstanding as of May 2, 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

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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.

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 corporation s voting stock or an affiliate or associate of a corporation who at any time within the prior three years beneficially owned, directly or indirectly, 10% or more of a corporation s voting stock. According to the statute, 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 corporation s stock after crossing certain threshold ownership percentages, unless the acquirer obtains the approval of the target corporation s stockholders. This statute only applies to Nevada corporations that do business directly or indirectly in Nevada. 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.

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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.

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.

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PART IV

Item 14. ***Exhibits, Financial Statement Schedules, and Reports on Form 8-K***

(a)(3) *Exhibits*

The following documents are filed as part of this annual report on Form 10-K. The Company will furnish a copy of any exhibit listed to requesting stockholders upon payment of the Company s reasonable expenses in furnishing those materials.

Exhibit Number	Description
3.1	Amended and Restated Articles of Incorporation of the Company, as amended(1)
3.2	Amended and Restated By-Laws of the Company(9)
3.3	Amendment No. 3 to Amended and Restated Articles of Incorporation of Hyseq, Inc.(10)
4.1	Specimen Common Stock certificate(1)
4.2	Form of Registration Rights Agreement(1)
4.3	Form of Warrant Agreement(1)
4.4	Rights Agreement between Hyseq, Inc. and U.S. Stock Transfer dated June 5, 1998(2)
4.5	Form of Securities Purchase Agreement, dated as of August 28, 2001, by and among Hyseq, Inc. and the investors party thereto.(10)
4.6	Form of Registration Rights Agreement, dated as of August 28, 2001, by and among Hyseq, Inc. and the investors party thereto.(10)
4.7	Form of Warrant, dated as of August 28, 2001(10)
4.8	Hyseq Promissory Note, dated as of November 13, 2001, in the principal amount of $4,000,000(12)
4.9	Registration Rights Agreement, dated as of November 13, 2001, by and between Hyseq, Inc. and Affymetrix, Inc.(12)
4.10	Pledge and Security Agreement, dated as of November 13, 2001, by and between Hyseq, Inc. and Affymetrix, Inc.(12)
10.1	Form of Indemnification Agreement between the Company and each of its directors and officers(1)
10.2	Stock Option Plan, as amended (3)
10.3	Non-Employee Director Stock Option Plan, as amended (4)
10.4	Patent License Agreement between Arch Development Corporation and Hyseq, Inc. dated June 7, 1994(1)
10.5	Stock Purchase Agreement for Series B Convertible Preferred Stock dated May 28, 1997(1)
10.6	Collaboration and License Agreement between Hyseq Inc. and Chiron Corporation dated May 30, 1997(1)
10.7	Collaboration Agreement between Hyseq Inc. and The Perkin-Elmer Corporation dated May 30, 1997(1)
10.8	Employee Stock Purchase Plan (5)
10.9	Non-Qualified Employee Stock Purchase Plan(8)
10.10	Scientific Advisory Board/ Consultants Stock Option Plan(8)
10.11	Collaboration and License Agreement between Hyseq, Inc. and American Cyanamid Company dated December 10, 1999(6)
10.12	Line of Credit Agreement between Hyseq, Inc. and Dr. George B. Rathmann dated November 10, 2000(7)
10.13	Employment and Confidential Information Agreement between Hyseq, Inc. and Ted W. Love dated January 11, 2001(9)
10.14	Industrial Multi-Tenant Lease by and between AMB Property, L.P. and Hyseq, Inc. dated June 23, 2000, as amended(9)
10.15	Lease between The Irvine Company and Hyseq, Inc. dated as of April 30, 2001(11)

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Exhibit Number	Description
10.16	Collaboration and License Agreement, dated as of June 29, 2001, by and between Hyseq, Inc. and Aurora Biosciences Corporation*
10.17	Collaboration Agreement, dated as of August 21, 2001, by and between Hyseq, Inc. and Kirin Brewery Company, Ltd.*
10.18	Secreted Protein Development and Collaboration Agreement, dated as of October 9, 2001, by and between Hyseq, Inc. and Deltagen, Inc.*
10.19	Line of Credit Agreement, dated as of August 6, 2001, by and between Hyseq, Inc. and Dr. George B. Rathmann(12)
10.20	Settlement Agreement, dated as of October 24, 2001, by and between Hyseq, Inc. and Affymetrix, Inc.*
10.21	Interference Settlement Agreement, dated as of October 24, 2001, by and between Hyseq, Inc. and Affymetrix, Inc.(12)
10.22	Product Development and Supply Agreement, dated as of October 24, 2001, by and between N-Mer, Inc. and Affymetrix, Inc.*
10.23	Product Solicitation Agreement, dated as of October 24, 2001, by and between N-Mer, Inc. and Affymetrix, Inc.*
10.24	Option Agreement, dated as of October 24, 2001, by and among Affymetrix, Inc, Hyseq, Inc., Callida Genomics, Inc., and N-Mer, Inc.(12)
10.25	Stock Option Agreement, dated as of February 1, 2000 by and between Hyseq, Inc. and Dr. George B. Rathmann(12)
10.26	Stock Option Agreement, dated as of August 21, 2001 by and between Hyseq, Inc. and Dr. George B. Rathmann(12)
10.27	Form of Non-Stockholder Approved Stock Option Agreement for Officers(13)
21.1	Subsidiaries of Hyseq, Inc. as of December 31, 2001: Callida Genomics, Inc., a Delaware corporation; N-Mer, Inc., a Delaware corporations; Hyseq Diagnostics, Inc., a Nevada corporation(12)
23.1	Consent of KPMG LLP, Independent Auditors(13)
23.2	Consent of Ernst & Young LLP, Independent Auditors(13)

(1) Previously filed with the Commission as an Exhibit to and incorporated herein by reference from the Company s Registration Statement filed on Form S-1, as amended, File No. 333-29091.

(2) Previously filed with the Commission as an Exhibit to and incorporated herein by reference from the Company s Form 8-K, filed on July 31, 1998, File No. 00-22873.

(3) Previously filed with the Commission as an Exhibit to and incorporated herein by reference from the Company s Registration Statement on Form S-8, File No. 333-41663.

(4) Previously filed with the Commission as an Exhibit to and incorporated herein by reference from the Company s Registration Statement on Form S-8, File No. 333-53089.

(5) Previously filed with the Commission as an Exhibit to and incorporated herein by reference from the Company s Registration Statement on Form S-8, File No. 333-53087.

(6) Previously filed with the Commission as an Exhibit to and incorporated herein by reference from the Company s report on Form 8-K/ A, filed on March 17, 2000, File No. 00-22873.

(7) Previously filed with the Commission as an Exhibit to and incorporated herein by reference from the Company s report on Form 8-K, filed on December 14, 2000, File No. 000-22873.

(8) Previously filed with the Commission as an Exhibit to and incorporated herein by reference from the Company s Annual Report on Form 10-K for the year ended December 31, 1999, File No. 000-22873.

(9) Previously filed with the Commission as an Exhibit to and incorporated herein by reference from the Company s Annual Report on Form 10-K for the year ended December 31, 2000, File No. 000-22873.

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(10) Previously filed with the Commission as an Exhibit to and incorporated herein by reference from the Company s Registration Statement on Form S-3, as amended, filed on September 25, 2001, File No. 333-70134.

(11) Previously filed with the Commission as an Exhibit to and incorporated herein by reference from the Company s report on Form 8-K, filed on May 21, 2001, File No. 000-22873

(12) Previously filed with the Commission as an Exhibit to and incorporated herein by reference from the Company s report on Form 10-K for the year ended December 31, 2001, filed on April 1, 2002, File No. 000-22873

(13) Previously filed with the Commission as an Exhibit to and incorporated herein by reference from the Company s report on Form 10-K/A for the year ended December 31, 2001, filed on May 9, 2002, File No. 000-22873.

* Previously filed with the Commission as an Exhibit to the Company s report on Form 10-K for the year ended December 31, 2001, filed on April 1, 2002. Pursuant to a confidential treatment request filed with the Commission, certain portions of this exhibit were omitted from our prior filing. The current filing reflects comments of the Commission regarding our confidential treatment request.

Denotes compensation plan in which an executive officer or director participates.

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Sunnyvale, State of California, on July 22, 2002.

HYSEQ, INC.
d/b/a HYSEQ PHARMACEUTICALS, INC.

By: /s/ PETER S. GARCIA

Peter S. Garcia
Senior Vice President and Chief Financial Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of Hyseq, Inc. in the capacities indicated on July 22, 2002.

Signature	Title
/s/ TED W. LOVE Ted W. Love	President and Chief Executive Officer (Principal Executive Officer), Director
/s/ PETER S. GARCIA Peter S. Garcia	Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)
/s/ GEORGE B. RATHMANN George B. Rathmann	Chairman of the Board
/s/ ROBERT D. WEIST Robert D. Weist	Vice Chairman of the Board of Directors
/s/ RAYMOND F. BADDOUR Raymond F. Baddour	Director
Richard B. Brewer	Director
Thomas N. McCarter III	Director
/s/ MARY K. PENDERGAST Mary K. Pendergast	Director
Ernst Schweizer	Director

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EXHIBIT INDEX*

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10.23	Product Solicitation Agreement, dated as of October 24, 2001, by and between N-Mer, Inc. and Affymetrix, Inc.

* Only exhibits actually filed on this Form 10-K/A are listed. Exhibits previously filed on the Form 10-K, as amended, or incorporated by reference are set forth in the exhibit listing included in Item 14 of this Form 10-K/A. These exhibits were previously filed with the Commission as an Exhibit to the Company s report on Form 10-K for the year ended December 31, 2001, filed on April 1, 2002. Pursuant to a confidential treatment request filed with the Commission, certain portions of these exhibits were omitted from our prior filing. The current filing reflects comments of the Commission regarding our confidential treatment request.