

HYSEQ INC  
Form 10-K/A  
May 09, 2002

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**SECURITIES AND EXCHANGE COMMISSION**

**Washington, D.C. 20549**

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**Form 10-K/A**  
**(Amendment No. 1)**

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**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**

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

**Commission File Number: 0-22873**

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**HYSEQ, INC.**

*(Exact Name of Registrant as Specified in Its Charter)*

**Nevada**  
*(State or Other Jurisdiction of  
Incorporation or Organization)*

**670 Almanor Avenue, Sunnyvale, CA**  
*(Address of principal executive offices)*

**36-3855489**  
*(I.R.S. Employer  
Identification No.)*

**94085**  
*(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**

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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  No

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.

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.

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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. 1 on Form 10-K/ A amends Items 1, 7, 8, 10, 11, 12, 13 and 14 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 ) to respond to comments we received from the Securities and Exchange Commission.

This report revises the risk factors section under Item 1 to include an additional risk factor regarding influence and control by our executive officers and directors. This report revises the disclosure under Management s Discussion and Analysis to disclose additional information for each of our major research and development projects. Our Statement of Stockholders Equity has been revised to define the term PIPE issuances. Note 7 of our Consolidated Financial Statements under Collaborative Agreements has been revised to (i) disclose when amounts were received by us under the agreements and when such amounts were recognized as revenue, (ii) disclose the term and termination provisions of each agreement to the extent such information is not confidential and (iii) specifically quantify the amounts exchanged with Aurora Biosciences Corporation. In addition, the disclosure in Note 7 of our Consolidated Financial Statements under Collaborative Agreements has been revised to clarify our disclosure relating to Affymetrix. Items 10, 11, 12, and 13 have been revised to delete language incorporating information by reference and disclose information required under each item. Item 14 has been revised to incorporate new consents by our auditors and the form of non-stockholder approved stock option agreement as exhibits to this Amendment No. 1 on Form 10-K/ A. Other than these amendments, Items 1, 7, 8, 9, 10, 11, 12, 13 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

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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 been 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 genes.

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.

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.

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

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

## Strategy

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 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-clinical 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 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 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 Applied Biosystems 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. Aurora may receive performance milestones, as well as development milestones and royalties on our products that result from the collaboration. In addition, as part of the agreement, we will provide Aurora access to selected novel targets from our database of proprietary full-length cDNAs. We will receive a database access fee and licensing fees and may receive development milestones and royalties on Aurora's small molecule products that result from the collaboration.

### *Deltagen*

In October 2001, 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 Oceania. 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.

***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 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 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.

## **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.

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 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 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.

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;

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.

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.

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.

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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 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.

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.

***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 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;

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 marketing, distribution and manufacture of such products would remain subject to extensive ongoing regulatory requirements. Failure to comply with applicable regulatory requirements can result in:

warning letters;

finest;

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.

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 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 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 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.

***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.

**Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations**

We have included or incorporated by reference into this Management's Discussion and Analysis of Financial Condition and Results of Operations and elsewhere in this Annual Report on Form 10-K, and from time to time our management may make, statements that constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by words including anticipate, believe, intends, estimates, expect, should, may, potential and similar expressions. Such statements are based on our management's current expectations and involve risks and uncertainties. Actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors discussed in this Annual Report, including those set forth in Item 7 as well as under Item 1. Business, including Risk Factors.

**Critical Accounting Policies and Estimates**

Our discussion and analysis of our operating results and financial condition is based upon our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of the financial statements requires us to make estimates, judgments, and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent amounts. While we believe our estimates, judgments, and assumptions are reasonable, the inherent nature of estimates is that actual results will likely be different from the estimates made.

We believe the following critical accounting policies, among others, affect the more significant judgments and estimates used in the preparation of our consolidated financial statements.

**Revenue Recognition**

We recognize revenue when all of the following conditions have occurred:

Persuasive evidence of an arrangement exists,

Delivery has occurred or services have been rendered,

The price is fixed and determinable, and

Collectibility is reasonably assured.

We defer and recognize up-front refundable fees as revenues upon the later of when they become nonrefundable or when performance obligations are completed. In situations where we have no continuing performance obligations, we recognize up-front nonrefundable fees as revenues when receivable. In situations where continuing performance obligations exist, we defer and amortize up-front nonrefundable fees over the performance period. The terms of such arrangements may cause our operating results to vary considerably from period to period.

**Income Taxes**

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

We record a valuation allowance to reduce deferred income tax assets to an amount that is more likely than not to be realized. Assessment of the realization of deferred income tax assets requires that estimates and assumptions be made as to the taxable income of future periods. Our deferred tax assets are reduced to zero,



as management believes that it is more likely than not that the deferred tax assets will not be realized. Projection of future period earnings is inherently difficult as it involves consideration of numerous factors such as our overall strategies and estimates of new product development and acceptance, product lifecycles, selling prices and volumes, responses by competitors, manufacturing costs and assumptions as to operating expenses and other industry specific and macro and micro economic factors. In addition, consideration is also given to ongoing and constantly evolving global tax laws and our own tax minimization strategies.

#### ***Capitalization of Software Developed for Internal Use***

Hyseq accounts for software developed for internal use in accordance with Statement of Position ( SOP ) 98-1, Accounting for the Costs of Computer Software Developed or Obtained for Internal Use, which requires research and development costs associated with the application development stage to be capitalized for internal use software. Platform and software development costs incurred prior to the application development stage are charged to expense as incurred. Management is required to use professional judgment in determining whether development costs meet the criteria in SOP 98-1 for immediate expense or capitalization. Amortization of the capitalized costs begins when all substantial testing is completed and the software is ready for its intended use. Management periodically reviews the carrying value of the projects that have been capitalized to determine if impairment may exist. If it is determined that the carrying value of the asset has been impaired, the value would be reduced by a charge to operations in the amount of the impairment.

#### **Results of Operations**

##### ***Contract Revenues***

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

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

Revenues recognized under our agreement with BASF were \$22.4 million for 2001 compared to \$11.7 million for 2000. Processing was slightly ahead of contractual levels of 1.1 million average clones per month in 2001, compared to 0.6 million average clones per month in 2000 when processing was ramping up. We anticipate that revenues and clone processing levels will stay about the same during 2002 and will be reduced during 2003 as we wind down our activities and eventually terminate the agreement in June 2003.

Revenues recognized in 2001 under our agreement with Chiron consist mainly of \$1.0 million minimum annual research funding received for the second year of the two-year extension initiated by Chiron in May of 2000, compared to \$3.3 million revenue in 2000 earned in the final months of the initial three year gene screening services portion of our agreement with Chiron. Chiron has the right to extend the agreement for one additional two-year period in May 2002 for a minimum of \$1.0 million each year.

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

Our biopharmaceutical research and development, or R&D, efforts are currently at the stage of cloning and screening hundreds of genes from our databases, coupled with initial exploratory research to evaluate their biological activity. All of this research is at a relatively early stage and, other than Alfineprase, for which we plan to commence Phase I clinical trials in the second quarter of 2002, we have no R&D projects that would be classified at present as drug product candidates or otherwise likely to generate revenues in the foreseeable future. The process of selecting and evaluating genes, their encoded proteins and/or antibodies to these

proteins for their potential as drug candidates is a long-term process, which is described under *Research and Development* in Item 1, above.

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

### ***Operating Expenses***

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

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

Research and development costs under our collaboration with BASF were \$9.1 million for 2001, compared with \$7.6 million for 2000 when production was ramping up in the early part of the year. As of December 31, 2001 research and development costs related to BASF were \$16.7 million. Gene screening services provided to BASF are scheduled under the contract for completion in the second quarter of 2003, with BASF having an option to extend the contract for up to an additional four years in annual increments. We anticipate costs and service levels for the BASF collaboration to continue for the remainder of the contract at a rate that is slightly less than the current year.

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

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

We expect operating expenses to increase during 2002 as we plan to continue research and development of our therapeutic protein candidates, build out our new facilities to support our research and development efforts, further develop SBH technology applications through our subsidiary Callida, and prosecute our intellectual property rights. The magnitude of the increases in our operating expenses will be significantly affected by our ability to secure adequate sources of external financing or additional sources of revenue. If we do not obtain adequate financing or revenue in a timely manner, this could significantly harm our business, financial condition and results of operations, and may require us to delay or eliminate one or more of our

research or development programs and/or delay the build out and occupation of our new leased facilities. See **Liquidity and Capital Resources.**

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

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

Research and development costs under our collaboration with BASF were \$7.6 million for 2000, compared with a negligible amount in 1999 following the contract signing in December 1999.

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

#### ***Interest Income and Expense, Net***

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

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

#### ***Net Loss***

Since our inception, we have incurred net losses, and as of December 31, 2001, we had an accumulated deficit of \$108.4 million. During 2001, we incurred a net loss of \$36.5 million as compared to a \$22.3 million net loss in 2000 and a net loss of \$18.5 million in 1999. We expect to continue to incur significant net losses, which may increase substantially as we pursue research and development of our therapeutic protein candidates and other operations, and prosecute and enforce our intellectual property rights.

#### ***Loss Attributable To Minority Interest***

Loss attributable to minority interest of \$0.3 million is recorded for the portion of Callida's losses attributable to minority stockholder Affymetrix. As the expected future level of Callida's losses increases, we anticipate recording additional losses attributable to minority interest up to the point where Affymetrix' initial minority interest investment is depleted. Beyond that point, the Company will absorb 100% of the net losses until Callida generates net income.

#### **Liquidity and Capital Resources**

Our primary source of liquidity is cash from financing activities and from collaboration receipts. We generated cash of \$44.3 million and \$1.3 million from financing activities, and cash of \$22.0 million and \$15.6 million from collaboration receipts in 2001 and 2000, respectively. Other than net cash inflows in connection with our BASF collaboration, we do not anticipate receiving net cash inflows from any significant projects at any time during the foreseeable future.

Our primary use of capital resources is to fund operating activities and to acquire capital equipment and make leasehold improvements. We used cash of \$21.5 million and \$20.3 million for operating activities, and cash of \$12.6 million and \$8.3 million to acquire capital equipment and make leasehold improvements in 2001 and 2000, respectively. We expect operating expenses to increase during 2002, and will need additional funding in order to finance the expansion of our biopharmaceutical research and the build out of our new leased facilities to support such research. If we do not obtain adequate financing or collaboration receipts in a timely manner, this could significantly harm our business, financial condition, and results of operations, and may require us to delay and scale back one or more of our research or development programs, discontinue the build out of our new leased facilities, or relinquish greater rights to products at an earlier stage of development or on less favorable terms than we would otherwise seek to obtain, which could materially adversely affect our business, financial condition, and operating results.

Our future capital requirements and the adequacy of available funds will depend on many factors, including those set forth under Item 1, Risk Factors We Must Be Able to Continue to Secure Additional Financing above. We may not be able to secure additional financing to meet our funding requirements on acceptable terms, if at all. If we raise additional funds by issuing equity securities, substantial dilution to our existing stockholders may result. If we are unable to obtain additional funds we may have to significantly curtail the scope of our operations. We have implemented a plan to delay, scale back or eliminate 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 financing, we may need to look to our Chairman to provide additional financing, which he has agreed to do.

#### ***Cash and Cash Equivalents and Short-Term Investments***

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

#### ***Sources and Uses of Capital***

All of our investments in marketable securities have had maturities of less than one year, have been considered available-for-sale, and as such have been classified as short-term investments. We have held our cash equivalents and investments in investment-grade commercial paper, bank certificates of deposit and other interest-bearing securities. We make our investments in accordance with our investment policy. The primary objectives of our investment policy are liquidity, safety of principal and diversity of investments. At December 31, 2001, we did not hold any marketable securities.

In October 2001, as part of our reorganization and litigation settlement, Affymetrix gave us a total of \$8.0 million in cash, which was comprised of two pieces: a license payment of \$4.0 million dollars for granting Affymetrix a non-exclusive license under various U.S. patents and patent applications; and a loan to us of \$4.0 million (interest rate of 7.5%, 5 year term) for Hyseq to invest in Callida. In lieu of repayment of this loan, we have the right, at any time, to exchange the note in whole or in part into such number of shares of our common stock (based on a price per share equal to 90% of the ten day trailing average price) equal to the aggregate amount of principal and interest to be exchanged. Our right to exchange the note into shares of common stock is subject to a number of conditions set forth in the note, including the requirements that the exchange of the note into our common stock does not cause Affymetrix to hold more than 19% of our outstanding common stock, and that there shall be an effective registration statement relating to the resale of the common stock issuable upon exchange of the note.

Both we and Affymetrix committed to invest additional amounts in N-Mer, contingent on Callida achieving certain milestones. Affymetrix has committed to lend us the additional amount that we have committed to invest in Callida, and we have the option to repay this loan with common stock. All outstanding principal and interest under the Affymetrix loan (and future loans) may become due and payable under specified conditions, including: upon the exercise by Affymetrix of its option to acquire N-Mer; upon a change in control of us; if our common stock ceases to be approved for quotation on Nasdaq or listed on a national securities exchange; in certain customary cases involving insolvency, bankruptcy or similar proceedings; that the aggregate amount outstanding under all loans exceeds 10% of our equity market capitalization; or if we end up in litigation with Affymetrix in the future.

In August 2001, we completed a private placement of approximately 3.04 million newly issued shares of common stock at \$7.00 per share, together with warrants to purchase approximately 1.52 million shares of common stock, for aggregate gross proceeds of approximately \$21.3 million (\$20.7 million, net of offering expenses). The warrants are exercisable at any time through and including August 28, 2006 at \$10.50 per share, a 50 percent premium to the per unit purchase price on the closing date, which may be adjusted to \$7.95 per share based on certain future issuances. We may seek to raise funds through additional private placements in the future but cannot guarantee that we will be successful.

In August 2001, the Company received a commitment from the Chairman of its Board of Directors to provide a second line of credit of up to \$20.0 million. A line of credit agreement was executed on August 6, 2001, and makes available the principal amount of \$20.0 million, for draw down through August 5, 2003. Amounts outstanding under the line of credit are secured by a promissory note which bears interest at a rate equal to one percent (1%) above the prime rate, and will be payable in 48 equal monthly installments beginning August 5, 2003. Amounts outstanding may be repaid by conversion into shares of our common stock at any time upon the agreement of us and Dr. Rathmann at a price based upon the average price of the our common stock over the 20-day period prior to the conversion, or, if in connection with an equity financing, at the offering price. We may not repay more than \$20 million in the form of shares of common stock. Under certain specified conditions, including (1) a change in control (based on a 50% ownership test), (2) insolvency or bankruptcy, or (3) a material adverse effect on our business, properties, assets or condition, we may not be able to borrow any further amounts under the line of credit. If any of the following events of default occurs, all payments under the promissory note may be accelerated: we shall fail to make payments within five business days of the date due; the breach by us of a representation or warranty made to Dr. Rathmann; the uncured breach by us of an obligation under the credit agreement; a material default by us under any other agreement with Dr. Rathmann; and customary defaults related to our bankruptcy or insolvency. As of March 15, 2002, \$16.0 million was available under this line of credit.

In April 2001, we leased an additional 138,698 square feet of space at 985 Almanor Avenue in Sunnyvale, California, adjacent to our current operating facilities. Lease payments over the ten-year term of the lease total approximately \$54.1 million. Pursuant to the terms of the lease, we provided a letter of credit in the amount of \$4.0 million as additional security for the lease; this letter of credit terminates after 5 years if we have not been in monetary default under the lease. Our Chairman provided the collateral for our letter of credit under this lease. This lease, as well as some of our other leases, contain customary event of default provisions, including that all payments due under the leases, such as amounts for unpaid rent and payments for future rent up to an amount of loss that we prove could have been reasonably avoided, will be accelerated upon the occurrences of events of default. Our lease obligations are further described in Item 2 Properties, and in Notes to Consolidated Financial Statements, Note 5 Capital Lease and Loan Obligations.

In August 2001, the terms of our Humboldt Court lease required us to provide a \$2.0 million letter of credit. This letter of credit was provided in March 2002 and must be increased by \$1.0 million annually in each of August 2002 and August 2003, after which it can decrease by \$2.0 million in 2007.

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

shares of common stock to our Chairman in satisfaction of \$20.0 million of outstanding principal under the line of credit.

We have \$1.6 million in restricted cash on deposit as security for a \$2.0 million letter of credit in conjunction with the 675 Almanor lease. Provided that no event of default under the lease occurs, the letter of credit and the cash collateralizing it will be reduced by \$0.5 million per year in July 2002, July 2003, and July 2004. The cash on deposit at any time in conjunction with this letter of credit is restricted and cannot be withdrawn. We control the investment of the cash and receive the interest earned thereon.

As of December 31, 2001, our contractual payment obligations consist principally of lease payments as described in Item 2 Properties above and in the Notes to the Consolidated Financial Statements Note 5 Capital Lease and Loan Obligations and Note 6 Commitments and Contingencies; the loan repayment to Affymetrix and our contingent obligation to provide future funding to Callida described in the Notes to the Consolidated Financial Statements Note 7 Collaborative Agreements; and collaboration payments. Under the terms of our collaboration agreement with Deltagen, we will be obligated to pay \$10.0 million over the next two years to fund the research work under the agreement. Under the terms of our collaboration agreement with Aurora, we may be obligated to pay up to \$2.6 million over the next two years for work performed under that agreement.

#### ***Cash Used in Operating Activities***

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

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

#### ***Cash Provided by Investing Activities***

Our investing activities, other than purchases and sales of short-term investments, have consisted primarily of capital expenditures.

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

*Comparison of Years Ended December 31, 2000 and 1999.* Net cash provided by investing activities increased by \$5.7 million to \$8.1 million in 2000 compared to \$2.4 million in 1999. The increase was primarily due to higher net redemptions of short-term investments in 2000, partially offset by higher purchases of equipment used to support our expanding research and development activities and investment in capitalized software. In 2000, all of our short-term investments were reinvested upon maturity into commercial paper with maturities of less than 90 days.

***Cash Provided by Financing Activities***

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

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

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

***Disclosure Regarding Our Chairman***

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

In August 2001, we received a commitment from Dr. Rathmann to provide a second line of credit of up to \$20.0 million in aggregate principal amount, available for draw down through August 5, 2003. Amounts outstanding under the line of credit bear interest at prime plus 1% and are payable in 48 equal monthly installments beginning upon the expiration date of August 5, 2003. The promissory note issued pursuant to the line of credit may be repaid by converting into shares of our common stock at any time upon the agreement of us and Dr. Rathmann at a price based upon the average price of our common stock over the 20-day period prior to the conversion or, if in connection with an equity financing, at the offering price. In February 2002, we drew down \$4.0 million under the line of credit.

Dr. Rathmann guaranteed to a certain maximum amount and provided the collateral for our \$4.0 million letter of credit under our 985 Almanor lease, and our \$2.0 million letter of credit under our Humboldt Court lease.

On February 1, 2000, our Board of Directors granted Dr. Rathmann an option to purchase 1,000,000 shares of our common stock for services as Chairman of the Board, at an exercise price equal to the then-current market price on the day before the date of grant of \$31.688 per share, which option vests and becomes exercisable over two years at a rate of one-third upon grant and one-third on each yearly anniversary thereafter. The term of the option is ten years. On August 21, 2001, our Board of Directors granted Dr. Rathmann an option to purchase 1,000,000 shares of our common stock, for services as Chairman of the Board at an exercise price equal to the then-current market price of \$8.635 per share. This option has a ten year term, and vests and becomes exercisable over four years at a rate of one-fourth upon the one year anniversary of the date of grant and 1/48th of the total number of shares upon each monthly anniversary thereafter. In the event of a change in control of our company, the option shall become immediately exercisable. Upon the termination of Dr. Rathmann's directorship with us for any reason or no reason, except as a result of Dr. Rathmann's death or disability, the unvested portion of the option shall be forfeited, and the vested unexercised portion of the option shall be exercisable for a period of thirty days following termination or the expiration of the term of the option if earlier. The option shall be exercisable by Dr. Rathmann or his legal representative, and in the event of his death only by his beneficiary. The option shall not otherwise be

transferable by Dr. Rathmann or by operation of law, and any attempted transfer or other disposition of the option shall be void and shall result in the cancellation of the option. Our Board of Directors has the right to amend or terminate the provisions of the option in any manner it may deem necessary or advisable to carry out the purpose of the grant as the result of, or to comply with, any change in applicable regulations, interpretation or statutory enactment.

Dr. Rathmann receives no cash compensation as an employee and instead receives options to purchase 3,000 shares per month. To date, at Dr. Rathmann's request, we have not granted him any equity incentives in recognition of the lines of credits that he has made available to us, his guarantee of our real estate leases, his provision of collateral for two of our letters of credit under facilities leases, or the occasional use of his private jet for our business purposes. We believe that the Board is likely to take action in the future to provide appropriate incentives to Dr. Rathmann in order to ensure his continued active involvement with us.

#### ***Recent Accounting Pronouncements***

In June 2001, the Financial Accounting Standards Board (or FASB) issued Statement of Financial Accounting Standards (or SFAS) No. 141, *Business Combinations*, which requires that all business combinations be accounted for under the purchase method of accounting. This statement is effective for all business combinations initiated after June 30, 2001. Implementation of SFAS No. 141 will not have a material effect on the Company's results of operations or financial position.

In June 2001, the FASB issued SFAS No. 142, *Goodwill and Other Intangible Assets*. This statement applies to intangibles and goodwill acquired after June 30, 2001, as well as goodwill and intangibles previously acquired. Under this statement, goodwill, as well as other intangibles determined to have an infinite life, will no longer be amortized; however, these assets will be reviewed for impairment on a periodic basis. This statement became effective January 1, 2002. Implementation of SFAS No. 142 will not have a material effect on the Company's results of operations or financial position.

In June 2001, the FASB issued SFAS No. 143, *Accounting for Asset Retirement Obligations*. SFAS No. 143 requires liability recognition for obligations associated with the retirement of tangible long-lived asset and the associated asset retirement costs. The Company is required to adopt the provisions of SFAS No. 143 effective January 1, 2003, with earlier application encouraged. Implementation of SFAS 143 will not have a material effect on the Company's results of operations or financial position.

In August 2001, the FASB issued SFAS No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets*. SFAS No. 144 supersedes SFAS No. 121, *Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to Be Disposed Of*, in that it removes goodwill from its impairment scope and allows for different approaches in cash flow estimation. However, SFAS No. 144 retains the fundamental provisions of SFAS No. 121 for (a) recognition and measurement of long-lived assets to be held and used and (b) measurement of long-lived assets to be disposed of. SFAS No. 144 also supersedes the business segment concept in APB Opinion No. 30, *Reporting the Results of Operations-Reporting the Effects of Disposal of a Segment of a Business, and Extraordinary, Unusual and Infrequently Occurring Events and Transactions*, in that it permits presentation of a component of an entity, whether classified as held for sale or disposed of, as a discontinued operation. However, SFAS No. 144 retains the requirement of APB Opinion No. 30 to report discontinued operations separately from continuing operations. The Company was required to adopt the provision of SFAS No. 144 effective January 1, 2002. Implementation of SFAS 144 is not expected to have a material effect on the Company's results of operations or financial position.

**Item 8. Financial Statements and Supplementary Data**

Hyseq, Inc.'s financial statements and notes thereto appear on pages 40 to 61 of this Form 10-K/A.

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**INDEPENDENT AUDITORS REPORT**

The Board of Directors and Stockholders of

Hyseq, Inc.:

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

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

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

/s/ KPMG LLP

San Francisco, California  
February 5, 2002

**REPORT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS**

The Board of Directors and Stockholders

Hyseq, Inc.:

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

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

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

/s/ ERNST & YOUNG LLP

Palo Alto, California  
February 2, 2000

## HYSEQ PHARMACEUTICALS, INC.

## CONSOLIDATED BALANCE SHEETS

(In thousands, except share information)

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

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Total stockholders' equity	<u>15,421</u>	<u>8,362</u>
Total liabilities and stockholders' equity	<u>\$ 39,904</u>	<u>\$ 21,288</u>

See accompanying Notes to Consolidated Financial Statements.

## HYSEQ PHARMACEUTICALS, INC.

## CONSOLIDATED STATEMENTS OF OPERATIONS

(In thousands, except per share data)

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

See accompanying Notes to Consolidated Financial Statements.

## HYSEQ PHARMACEUTICALS, INC.

## CONSOLIDATED STATEMENTS OF STOCKHOLDERS EQUITY

For the Years Ended December 31, 2001, 2000 and 1999

(In thousands, except share data)

	Common Stock		Additional	Notes	Deferred	Accumulated	Accumulated	Total
	Shares	Amount	Paid-in	Receivable	Compensation	Other	Deficit	Stockholders
			Capital	from		Comprehensive		Equity
				Stockholders		Loss		
(In thousands, except share data)								
<b>Balance at December 31, 1998</b>	12,931	\$ 13	\$ 82,328	\$ (3,503)	\$ (126)	\$ (14)	\$ (31,122)	\$ 47,576
Issuance of common stock upon exercise of stock options and under Employee Stock Purchase Plan	152		122					122
Amortization of deferred compensation					89			89
Comprehensive loss:								
Net loss							(18,547)	(18,547)
Other comprehensive income (loss)						(18)		(18)
Comprehensive loss								(18,565)
<b>Balance at December 31, 1999</b>	13,083	\$ 13	\$ 82,450	\$ (3,503)	\$ (37)	\$ (32)	\$ (49,669)	\$ 29,222
Issuance of common stock upon exercise of stock options and under Employee Stock Purchase Plan	560	1	1,481					1,482
Issuance of common stock upon cash exercise of warrants	1		6					6
Issuance of common stock upon cashless exercise of warrants	149							
Compensation expense related to SAB option grants			157					157
Notes receivable from stockholders repaid by surrendering shares of stock	(71)		(3,816)	3,503				(313)
Amortization of deferred compensation					29			29
Comprehensive loss:								
Net loss							(22,253)	(22,253)
Other comprehensive income (loss)						32		32
Comprehensive loss								(22,221)
<b>Balance at December 31, 2000</b>	13,722	\$ 14	\$ 80,278	\$	\$ (8)	\$	\$ (71,922)	\$ 8,362
Issuance of common stock upon exercise of stock options and under Employee Stock Purchase Plan	140		848					848
Compensation expense related to vesting acceleration			30					30
Issuance of common stock upon cash exercise of warrants	167		574					574
	3,040	3	20,734					20,737

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Issuance of common stock through private placement in August, 2001, net issuance cost of \$548								
Conversion of line of credit into common stock	2,238	2	19,998					20,000
Gain on sale of 10% interest in Callida			1,308					1,308
Deferred compensation related to SAB option grants			79		(79)			
Amortization of deferred compensation					34			34
Net loss							(36,472)	(36,472)
<b>Balance at December 31, 2001</b>	<b>19,307</b>	<b>\$ 19</b>	<b>\$ 123,849</b>	<b>\$</b>	<b>\$ (53)</b>	<b>\$</b>	<b>\$ (108,394)</b>	<b>\$ 15,421</b>

See accompanying Notes to Consolidated Financial Statements.

## HYSEQ PHARMACEUTICALS, INC.

## CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)

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

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

See accompanying Notes to Consolidated Financial Statements.

**HYSEQ PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**1. Organization and Summary of Significant Accounting Policies**

***Organization***

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

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

***Principles of Consolidation and Basis of Presentation***

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

***Use of Estimates***

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

***Cash and Cash Equivalents***

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

***Equipment, Leasehold Improvements, and Capitalized Software***

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

## HYSEQ PHARMACEUTICALS, INC.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

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

**Impairment of Long-Lived Assets**

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

**Revenue Recognition**

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

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

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

\* less than 10%

**Revenues by Geographic Area**

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

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

**Stock-Based Compensation**

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In accordance with the provisions of Statement of Financial Accounting Standards No. 123 (SFAS No. 123), Accounting for Stock-Based Compensation the Company has elected to account for stock-based

**HYSEQ PHARMACEUTICALS, INC.****NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

compensation to employees under the provisions of Accounting Principles Board Opinion No. 25, Accounting for Stock Issued to Employees, and its related interpretations, and to adopt the disclosure only alternative described in SFAS No. 123. Stock options granted to non-employees are accounted for in accordance with SFAS No. 123 and Emerging Issues Task Force No. 96-18, Accounting for Equity Instruments that Are Issued to Other than Employees for Acquiring, or in Conjunction with Selling, Goods or Services.

***Research and Development***

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

***Net Loss per Share***

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

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

***Segment Reporting***

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

**2. Equipment, Leasehold Improvements and Capitalized Software**

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

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

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



**HYSEQ PHARMACEUTICALS, INC.****NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

of certain capitalized software aggregating \$1.1 million. These write-offs are included in research and development expenses in the accompanying Statement of Operations.

**3. Accumulated Other Comprehensive Losses**

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

**4. Patents, Licenses and Other Assets***Patents and Licenses*

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

*Patent License Agreement*

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

**5. Capital Lease and Loan Obligations**

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

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

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



## HYSEQ PHARMACEUTICALS, INC.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

## 6. Commitments and Contingencies

*Operating Leases*

The Company leases three facilities under operating lease agreements, two that expire in June 2005 and one that expires in July 2011. In April 2001 the Company leased an additional approximately 138,698 square feet of space at 985 Almanor Avenue in Sunnyvale, California, adjacent to our current operating facilities. The lease on this new space requires base lease payments on average of approximately \$451,000 per month and extends through May 2011. Rental expense was approximately \$8.1 million in 2001, \$2.1 million in 2000, and \$1.4 million in 1999. The leases provide for scheduled rent increases annually over the terms of the leases. The rent is being recognized as expense on a straight-line basis.

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

Year Ended December 31,	Minimum Rental Commitments
2002	\$ 9,569
2003	9,975
2004	10,394
2005	9,986
2006	9,583
2007 and thereafter	43,780
	<hr style="width: 10%; margin: 0 auto;"/> \$93,287

*Letters of Credit*

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

## 7. Collaborative Agreements

*Aurora*

In July 2001, the Company entered into a two-year collaboration and license agreement with Aurora Biosciences Corporation, under which Aurora will screen over 200 secreted proteins from the Company's proprietary collection, using Aurora's proprietary CellSensor Panel, and also granted the Company a non-exclusive license to certain fluorescent protein technologies. Aurora will use its technology on behalf of the

Company to identify proteins of interest as potential therapeutics and will receive upfront payments, licensing

**HYSEQ PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

fees and technology access fees. Aurora may receive performance milestones, as well as development milestones and royalties on the Company's products that result from the collaboration. In addition, as part of the agreement, the Company will provide Aurora access to selected novel targets from the Company's database of proprietary full-length cDNAs. The Company will receive a database access fee and licensing fees and may receive development milestones and royalties on Aurora's small molecule products that result from the collaboration. The Company paid Aurora \$0.75 million in nonrefundable upfront technology access and license fees and \$0.20 million for screening services in July and December 2001, respectively, which was recognized as research and development expense in these periods. In addition, in July 2001, Aurora paid the Company \$0.25 million in nonrefundable database access fees, and a \$0.25 million nonrefundable license fee, which the Company recognized as a reduction in research and development expense in that period. The agreement terminates upon the later of the last to expire of the patents covered under the agreement or the last royalty obligation due under the agreement is paid. Either party has the right to terminate sooner in the event of an uncured material breach by the other party or in connection with the bankruptcy, insolvency, dissolution or winding up of the other party.

***Deltagen***

In October 2001, the Company entered into a collaboration with Deltagen, Inc. to undertake research and development activities on approximately 200 novel secreted proteins. The Company will provide gene sequences encoding for the secreted proteins, and Deltagen will utilize its in vivo mammalian gene knockout technology to identify and validate potential commercially relevant biopharmaceutical drug targets. Deltagen and the Company will each have certain joint development and commercialization rights around potential biopharmaceutical drug targets discovered through the collaboration. Deltagen and the Company will share the collaboration's costs; Hyseq will provide Deltagen with approximately \$10.0 million in research and development payments over two years, beginning in April 2002. As of December 31, 2001, the Company had made no cash payments to Deltagen. The agreement terminates upon the later of the expiration of the last valid claim relating to a gene or secreted protein candidate covered under the agreement or October 9, 2006. Either party has the right to terminate sooner in the event of an uncured material breach by the other party, and Deltagen has the right to terminate sooner in the event the Company fails to pay Deltagen amounts owed to Deltagen under the agreement within 90 days' written notice of such failure to pay by Deltagen.

***Kirin***

In August 2001, the Company entered into a collaboration with Kirin Brewery Co. Ltd., in which Kirin will fund three years of collaborative research work at Hyseq and both companies will conduct research directed toward discovering proteins and antibodies for a variety of diseases, including hematopoietic and inflammatory diseases. Discoveries during the collaboration will be jointly owned by Kirin and Hyseq, and will be jointly developed and marketed with costs, efforts, and revenues shared by both companies. The Company will have marketing rights in North America on all products discovered and developed under the collaboration. Kirin will have marketing rights in Asia, New Zealand, and Australia. Marketing rights will be shared by both companies in the rest of the world. Beginning April 2002, for the first year of the agreement, at the end of each quarter, Kirin will reimburse the Company at the rate of \$0.25 million per full-time equivalent employee (FTE) performing research under the agreement, up to four FTEs. Thereafter, each quarter the Company and Kirin will compare the number of FTEs performing research at their respective companies, and the company performing more research will be reimbursed by the other at the above-mentioned FTE rate. Payments received will be recognized as a reduction in research and development expense in the period received, and payments made will be recognized as a research and development expense in the period paid. As of December 31, 2001, no cash payments had been made under the agreement. The agreement provides that either party has the right to terminate prior to the end of its three year term in the event of an uncured material breach by the other party, upon a change of control of the other party, or in connection with the bankruptcy, insolvency, dissolution or winding up of the other party.

**HYSEQ PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

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

***BASF***

In December 1999, the Company entered into a collaboration with American Cyanamid Company in which the Company uses its signature-by-hybridization technology to target agricultural products. During 2000, BASF Aktiengesellschaft acquired the crop protection business of American Cyanamid Company and subsequently assigned our collaboration with American Cyanamid to BASF Plant Sciences GmbH (or BASF). The collaboration provides for funding of \$60 million over its initial term of three and one half years. The collaboration can be extended by mutual agreement for up to four additional one-year terms. Subject to compliance with the terms of the contract, the Company expects to recognize revenue from this collaboration over the term of the agreement as services are performed. Total revenue recognized in 2001 and 2000 under the agreement was \$22.4 million and \$11.7 million respectively. BASF has the exclusive right to commercialize any agricultural products resulting from the collaboration. The Company will receive royalties on any such products. Unless otherwise terminated, the agreement shall continue through June 30, 2003 and thereafter until expiration of the last patent covering the composition, use or manufacture of a product developed under the agreement. The agreement provides that either party has the right to terminate sooner in the event of an uncured material breach by the other party or in connection with the bankruptcy, insolvency, dissolution or winding up of the other party. In addition, BASF may terminate the agreement if Hyseq sells all or substantially all of its assets, is acquired by a third party or there is a change of control, is no longer generally engaged in gene discovery and sequencing as a primary business activity or is generally unable to perform the types of obligations set forth in the agreement, or if Hyseq fails to meet or comply with certain milestones set forth in the agreement.

In 2001, the Company received \$20.0 million from BASF, with a \$5.0 million payment in each of the four quarters of the year, which was recorded as deferred revenue. Deferred revenue is recognized monthly based on the actual levels of gene screening services performed.

***Chiron***

In May 1997, the Company entered into a collaboration with Chiron Corporation. Pursuant to the terms of the collaboration agreement, the Company and Chiron are collaborating to develop solid tumor therapeutics, diagnostic molecules and vaccines. The collaboration had an initial term of three years and has been extended by Chiron for an additional two-year period. Chiron may extend the collaboration for one more two-year period. Chiron has the exclusive right to commercialize solid tumor therapeutics, diagnostic molecules and vaccines resulting from the collaboration. The Company will receive royalties on any such products. Concurrent with execution of the collaboration agreement in 1997, Chiron made an equity investment of \$5.0 million in return for shares of the Company's preferred stock, which subsequently converted into common stock upon the Company's initial public offering in 1997. Chiron also purchased shares of common stock directly from the Company in a private placement concurrent with the Company's initial public offering in 1997 for an aggregate purchase price of \$2.5 million. Total revenue recognized in 2001, 2000, and 1999 under the agreement with Chiron was \$1.2 million, \$3.3 million, and \$4.9 million, respectively, which the Company received as research funding payments and recognized as revenue as earned. The Company has no future performance obligations related to the revenue recognized in 2001, 2000, and 1999 and no portions of such revenues are refundable. The agreement

**HYSEQ PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

provides that either party may terminate in the event of an uncured material breach by the other party or in connection with the bankruptcy, insolvency, dissolution or winding up of the other party.

The Company receives \$1.0 million per year for any additional two-year periods Chiron decides to extend the agreement, plus approximately \$0.1 million for gene storage, with the 2001 payment received in June 2001. Each payment is recognized ratably as revenue over the related twelve-month extension period. The current extension ends May 31, 2002, at which time Chiron has an option to extend the agreement for two more years at \$1.0 million per year.

***UCSF***

In February 1998, the Company entered into a collaborative agreement with the University of California at San Francisco (or UCSF) to conduct research on genes that may have important roles in the development of cardiovascular and related diseases. Under the terms of the five-year agreement, the Company makes quarterly payments of approximately \$0.1 million to UCSF in connection with the agreement to reimburse UCSF for direct and indirect expenses incurred in clinical sample collection and for research conducted. The agreement may be extended past the five-year term by mutual agreement of the Company and UCSF. The agreement may be terminated by either party upon 30 days written notice if the research program is no longer technically or commercially feasible or by the Company if milestones or deliverables are not met. In addition, the agreement may be terminated by either party upon an uncured material breach by the other party.

***Applied Biosystems***

In May 1997, the Company entered into an agreement with the Applied Biosystems Stock Group of Applera Corporation to combine certain of the Company's chip technology and Applied Biosystems' life science system capabilities to commercialize the HyChip system. Pursuant to the terms of the agreement, the Company committed \$5.0 million to further development of the Company's chip component of the HyChip system. The Company spent approximately \$2.0 million for the development of the chip component of the HyChip system from June 1997 through December 1997. Of this amount, \$0.5 million was reimbursed to the Company under its NIST grant. As of December 31, 1998, the Company had satisfied the \$5.0 million obligation under its agreement with Applied Biosystems. In October 2001, Applied Biosystems and the Company amended the collaboration to facilitate the settlement with Affymetrix. Significant components of this amendment include the conversion of the prior exclusive marketing arrangement with Applied Biosystems into a non-exclusive arrangement and the conclusion of all further collaboration obligations. In June 1997 Applied Biosystems made an equity investment of \$5.0 million in return for shares of the Company's preferred stock, which subsequently converted into common stock upon the Company's initial public offering in 1997. Applied Biosystems also purchased shares of common stock directly from the Company in a private placement concurrent with the initial public offering in 1997 for an aggregate purchase price of \$5.0 million. The Company recognized approximately \$0.3 million in revenue in each of 2001, 2000, and 1999 from Applied Biosystems from research funding reimbursement under the collaboration and from an expansion of the existing relationship as services were performed. The agreement has a term of five years and shall remain in effect until the last-to-expire of the valid claims within the patents and patent applications licensed by either party under the agreement. The agreement provides that either party may terminate in the event of an uncured material breach by the other party or in connection with the bankruptcy, insolvency, dissolution or winding up of the other party. In addition, the agreement is terminable by either party upon a change of control.

***Affymetrix***

In October 2001, the Company and Affymetrix Inc. resolved all outstanding litigation and entered into a collaboration to accelerate development and commercialization of a high speed universal DNA sequencing chip. This collaboration with Affymetrix is through a newly created venture, N-Mer, Inc., that is a wholly

**HYSEQ PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

owned subsidiary of Callida, which in turn is a newly formed majority-owned subsidiary of the Company. N-Mer will have access to both SBH technology from the Company, through Callida, and to Affymetrix GeneChip technology, a platform for array-based experiments. Affymetrix will be the exclusive array and system supplier and is initially authorized to be the exclusive agent for the distribution of any potential N-Mer products. The collaboration terminates upon dissolution of N-Mer, subject to the right of either party to terminate sooner in the event of an uncured material breach by the other party.

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

Affymetrix gave a total of \$8.0 million in cash to Hyseq at the close of the settlement. The \$8.0 million payment is comprised of two pieces. First, Affymetrix made a license payment of \$4.0 million in return for a non-exclusive license, without the right to grant sublicenses, under 11 U.S. patents and 30 U.S. patent applications and counterpart foreign patents and applications to make, use, sell, and import products in the non-universal array field. Universal arrays are DNA arrays designed without reference to specific gene sequences that can be used to sequence any gene. This license payment will be recognized as revenue as Callida utilizes its cash in conducting R&D efforts. During 2001, revenue of \$0.8 million was recognized by the Company, leaving \$3.2 million in deferred revenue to be recognized in future periods.

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

Callida capitalized the intellectual property contributed by Affymetrix at its fair value of \$1.7 million, given the alternative future use of the intellectual property in multiple micro-array products currently being developed for use in the fields of diagnostics and DNA sequencing. The fair value of the intellectual property licensed was determined using discounted cash flow techniques based upon a previously established contractual royalty arrangement over an 8 year period, at a discount rate of 25%, which reflects the high level of risk associated with these types of research projects. The intellectual property will be amortized on a straight-line basis over its estimated useful life of four years.

The N-mer collaboration is still in the early stages and currently has access to \$4 million in funding from Callida. The companies have begun the process of testing universal arrays produced by Affymetrix for DNA sequencing capabilities. Both Hyseq and Affymetrix committed to invest additional amounts in N-Mer, contingent on the N-Mer project achieving certain milestones. If these milestones are met at the end of 2002 or start of 2003, funding of the project will continue and a product could be launched in 2003 or 2004. Affymetrix received an option to purchase from Callida a majority interest of the outstanding common stock of N-Mer, exercisable at any time over the next five years. The exercise price varies, based on the amount by which the indebtedness of N-Mer at the time of exercise exceeds \$1 million, and, if the option is exercised after October 24, 2004, the amount of cumulative operating expenses incurred and recognized by N-Mer prior to the date of exercise. The exercise price is subject to a maximum of \$32 million if the option is exercised during the first 3 years, and a maximum of \$48 million if exercised thereafter. Upon exercise, Affymetrix must

**HYSEQ PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

relinquish all Callida securities then held by it that were purchased pursuant to its obligation to fund Callida and, if any such securities have been transferred, Affymetrix must remit to Callida the proceeds from such transfer.

The Company believes that Affymetrix's purchase option has no material fair value, until such point that research reaches a technical milestone and product feasibility is achieved, and has no accounting implications as of the date of inception of Callida or as of December 31, 2001. The Company will periodically evaluate the value of N-Mer to determine whether Affymetrix's purchase option has value. If so, such value will be recorded through earnings and on Hyseq's balance sheet.

**8. Stockholders' Equity**

***Preferred Stock***

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

As of December 31, 2001 and 2000, there were no issued and outstanding shares of preferred stock. On June 5, 1998, Hyseq's Board of Directors adopted a rights plan and declared a dividend with respect to each share of common stock then outstanding. This dividend took the form of a right that entitles the holders to purchase one one-thousandth of a share of our Series B junior participating preferred stock at a purchase price of \$175, subject to adjustment from time to time. These rights have also been issued in connection with each share of common stock issued after June 5, 1998. The rights are exercisable only if a person or entity or affiliated group of persons or entities acquires, or has announced its intention to acquire, 15% (27.5% in the case of certain approved stockholders) or more of the Company's outstanding common stock. The adoption of the rights plan makes it more difficult for a third party to acquire control of the Company without the approval of the Board of Directors.

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

***Common Stock***

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

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

**HYSEQ PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

***Deferred Compensation***

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

***Warrants***

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

***Stock Option Plans***

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

The Company granted options to purchase common stock to several key employees, directors, scientific advisory board members and scientists prior to adoption of the employee plan. Each option gives the holder the right to purchase common stock at prices between \$0.78 and \$1.82 per share. In 1998, the Company granted options outside of any of the Company's stock option plans to purchase a total of 9,500 shares of common stock to three non-employee directors and a scientific advisory board member at prices between \$4.75 and \$10.06 per share. The options vest over periods up to four years. In February 2000, an officer and director of the Company was granted an option to purchase 1,000,000 shares of common stock at \$31.69 per share, the closing price on the day prior to the grant, as an inducement to become an employee of the Company. This option becomes exercisable one-third upon the date of grant, one-third on the one-year anniversary and one third on the two-year anniversary of the date of grant. In 2001, the Company granted options outside of any of the Company's stock option plans to purchase a total of 1,268,160 shares to five employee officers at prices between \$9.96 and \$12.56 per share as inducements to become employees of the company. In August 2001, a director of the Company was granted an option, contingent upon shareholder approval, to purchase 1,000,000 shares of common stock at \$8.63 per share, the closing price on the day prior to the grant. As of December 31, 2001, 3,537,966 options issued outside of any of the Company's stock option plans were outstanding.

In 1997, the Company's stockholders adopted the Non-Employee Director Stock Option Plan, or directors plan, providing for periodic stock option grants to non-employee directors of the Company. Under the directors plan, each new, non-employee director receives a one-time grant of options to purchase 23,040 shares of common stock, of which options to purchase 11,520 shares vest immediately, with the balance vesting in two equal allotments on the first and second anniversaries of joining the Board. All non-employee directors automatically receive options to purchase up to 5,760 shares each year (such that the amount

## HYSEQ PHARMACEUTICALS, INC.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

received under the directors plan when added to all prior options granted to a director which vest in that year total 5,760) on the date of the annual meeting of the stockholders commencing in 1997. Options under the directors plan are granted at the fair market value of the Company's common stock on the date of the grant. In 2000, the Company's stockholders approved an amendment to the directors plan that changed the method for determining the number of shares granted under the plan, and lengthened the vesting date for the new director's initial and first annual grants of options. Under the amendment, the number of shares that are granted will be equal to the lesser of the number determined by dividing \$200,000 by the fair market value of our common stock on the date of grant, or 10,000 shares. The amendment also revised the vesting date for initial options that are granted when a new director joins our Board such that 50% of a new director's option will vest one year after the grant date and the other 50% will vest two years after the grant date. A total of 438,240 shares of common stock have been reserved for issuance under the directors plan, of which options to purchase 147,155 shares were outstanding at December 31, 2001.

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

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

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

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

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

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

## HYSEQ PHARMACEUTICALS, INC.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

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

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

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

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

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

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

Options Outstanding				Options Exercisable	
Range of Exercise Price	Number of Shares	Weighted-Average Remaining Contractual Life	Weighted-Average Exercise Price	Number of Shares	Weighted-Average Exercise Price
\$ 1.56 - \$ 4.17	600,256	5.26	\$ 2.92	449,814	\$ 2.80
4.44 - 7.82	312,108	7.58	5.54	174,058	5.33
8.02 - 8.64	1,114,476	9.32	8.60	86,676	8.33

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8.67	10.40	456,266	9.44	10.14	10,666	9.45
10.44	10.44	985,320	9.58	10.44	0	0.00
10.49	12.50	747,460	9.14	12.23	209,000	12.42
12.56	29.81	345,380	8.77	25.44	122,039	26.19
31.69	31.69	1,000,000	8.08	31.69	666,666	31.69
32.03	95.19	60,075	8.52	43.67	28,875	46.55
101.44	101.44	3,000	8.16	101.44	750	101.44
		<u>5,624,341</u>	<u>8.56</u>	<u>\$ 14.32</u>	<u>1,748,544</u>	<u>\$ 17.93</u>

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

## HYSEQ PHARMACEUTICALS, INC.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

**Employee Stock Purchase Plan**

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

**9. Income Taxes**

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

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

As of December 31, 2001, the Company had federal and state net operating loss carryforwards of approximately \$107.7 million and \$23.0 million, respectively. The Company also had federal and California research and development tax credit carryforwards of approximately \$2.5 million and \$2.3 million, respectively. The federal net operating loss and credit carryforwards will expire at various dates beginning in the year 2008 through 2021, if not utilized. The State of California net operating losses will expire at various dates beginning in 2001 through 2011, if not utilized. The California Research Credits carryforward indefinitely.

Utilization of the Company's net operating loss carryforwards and credits may be subject to an annual limitation due to the change in ownership provisions of the Internal Revenue Code of 1986 and similar state provisions. The annual limitation may result in the expiration of net operating losses and credits before utilization.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets for financial reporting and the amount used for income tax purposes. Significant components of the Company's deferred tax assets for federal and state income taxes are as follows (in thousands):

	Year Ended December 31,	
	2001	2000
Deferred Tax Assets:		
Net operating loss carryforwards	\$ 37,970	\$ 28,971
Research and other credits	4,422	6,564
Capitalized research expenses	2,446	856
Accrued expenses and reserves	3,921	1,362
Deferred revenue	1,475	
	<hr/>	<hr/>
Total deferred tax assets	50,234	37,753

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Valuation allowance	<u>(50,234)</u>	<u>(37,753)</u>
Net deferred tax assets	\$ <u>          </u>	\$ <u>          </u>

## HYSEQ PHARMACEUTICALS, INC.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Deferred tax assets are reduced by a valuation allowance as management believes that it is more likely than not that the deferred tax assets will not be realized. The net valuation allowance increased by \$12.5 million, \$15.7 million and \$8.3 million for the fiscal years ended December 31, 2001, 2000 and 1999, respectively.

Approximately \$12.2 million of the federal net operating losses and \$6.6 million of the state net operating losses relate to deductions from stock based compensation. No income statement benefit will result from the realization of these losses.

**10. Transactions with Related Parties**

As of December 31, 2001, 2000 and 1999, the Company had outstanding accounts payable balances of approximately \$3,000, \$45,000, and \$86,000 respectively, for professional services rendered by a law firm of which the spouse of the Company's former President and Chief Executive Officer was a member. The Company incurred legal fees and costs to this law firm of approximately \$57,000, \$400,000, and \$441,000 for the years ended December 31, 2001, 2000 and 1999, respectively.

In August 2001, the Company received a commitment from its Chairman to provide a second line of credit of up to \$20.0 million in aggregate principal amount, secured by a promissory note and available for draw down through August 5, 2003. The Chairman has also agreed to provide financing to fund operating activities as needed through 2001. Amounts outstanding under the line of credit bear interest at prime plus 1% and are payable in 48 equal monthly installments beginning upon the expiration date of August 5, 2003. The promissory note issued pursuant to such line of credit may be converted into shares of its common stock at any time upon the agreement of us and Dr. Rathmann at a price based upon the average price of our common stock over the 20-day period prior to such conversion or, if in connection with an equity financing, at the offering price. In February 2002, we drew down \$4.0 million of the \$20.0 million line of credit.

Our Chairman guaranteed our 985 Almanor lease (up to a certain maximum amount) and provided the collateral for the Company's \$4.0 million letter of credit under this lease. Our Chairman also guaranteed our Humboldt Court lease (to a certain maximum amount) and provided the collateral for the Company's \$2.0 million letter of credit under this lease.

The Chairman receives no cash compensation as an employee and instead receives options to purchase 3,000 shares per month. In August 2001, the Board also granted the Chairman an option to purchase an additional 1,000,000 shares. However, to date, at the request of the Chairman, the Company has not granted the Chairman any equity incentives in recognition of the lines of credits that the Chairman made available to the Company, the Chairman's guarantee of the Company's real estate leases, the Chairman's provision of collateral for two of the Company's letters of credit under facilities leases, or the occasional use of the Chairman's private jet for Company business. The Company believes that the Board is likely to take action in the future to provide appropriate incentives to the Chairman in order to ensure his continued active involvement in the Company.

**11. Selected Quarterly Financial Data (Unaudited)**

Summarized selected quarterly financial data is as follows (in thousands):

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



## HYSEQ PHARMACEUTICALS, INC.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

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

\* The sum of earnings per share for the four quarters of 2001 is different from the full year amount as a result of computing the quarterly and full year amounts on the weighted average number of common shares outstanding in the respective periods.

Historically, the Company's revenues have varied considerably from period to period due to the nature of the Company's collaborative arrangements. As a consequence, the Company's results in any one quarter are not necessarily indicative of results to be expected for a full year.

The third quarter of 2001 included a reclass of restructuring cost of \$ 825,000 from other income expenses to operations.

The fourth quarter of 2001 included (i) an adjustment to increase contract revenues of approximately \$402,000 and (ii) the write-off of certain capitalized software costs of approximately \$1,087,000.

## 12. Subsequent Events (Unaudited)

In January 2002, the Company entered into collaboration with Amgen, Inc. to develop and commercialize alfimeprase, a novel acting thrombolytic, for the treatment of PAO and other cardiovascular indications. Under the terms of the agreement, Hyseq will lead development and be responsible for all clinical development activities, while Amgen will be responsible for manufacturing activities. Alfimeprase, a product candidate that was identified through Amgen's research program, is a derivative of the fibrolase enzyme and is being developed for the treatment of PAO. PAO of the lower extremity is a significant cause of morbidity and amputation in the United States with over 100,000 cases reported annually. Pre-clinical studies indicate that alfimeprase is a promising agent for dissolving clots (clot lysis), and may be particularly well suited for the PAO indication. An IND for alfimeprase has been filed, and Hyseq anticipates initiating clinical studies in the second quarter of 2002.

In January 2002, the Company, through its subsidiary Callida, entered into a collaborative agreement with Intel Corporation to develop technology for the detection, identification, and analysis of DNA or other biomolecules. The goal of this research collaboration is to explore new technologies for biomolecule detection and identification. Callida will focus on developing novel approaches to DNA sequencing, and Intel will focus on developing devices and protocols for detecting and reading the data.

In February 2002, the company drew down \$4.0 million of the \$20.0 million line of credit that it received from its Chairman in August 2001.

In February 2002, the Company entered into a research agreement with Genetastix, a privately held biotechnology company, to use Genetastix's HuMYTech technology to generate fully human monoclonal antibodies against a proprietary antigen.

**Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure**

Not applicable.

**PART III****Item 10. Directors and Executive Officers of the Registrant**

Set forth below is information regarding each of our directors and executive officers as of May 1, 2002.

**Directors**

Name of Nominee or Director	Age	Position	Director Since
George B. Rathmann, Ph.D.(1)	74	Chairman of the Board	2000
Thomas N. McCarter, III(2)	72	Director	1996
Ted W. Love, M.D.	43	President and Chief Executive Officer, Director	2001
Robert D. Weist(1)(2)(3)	62	Vice Chairman of the Board	1993
Raymond F. Baddour, Sc.D.(2)(3)	77	Director	1993
Ernst Schweizer, Ph.D.	67	Director	1999

(1) member of nominating committee

(2) member of audit committee

(3) member of compensation committee

**Directors nominated to hold office until the Annual Meeting of Stockholders in 2005**

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

*Thomas N. McCarter, III* has served as a director since October 1996. Mr. McCarter currently serves as Chairman of the Ramapo Land Company, a real estate company, and is a general partner of Miles Timber Properties, a land company, positions he has held for more than five years. Mr. McCarter was a former Chairman of Stillrock Management, Inc., an investment company, was a director of Parock Group, a diversified investment company, and is currently a director of other closely held companies. Mr. McCarter attended Princeton University from 1948 to 1951 and has been a certified investment counselor since 1972.

**Directors continuing in office until the Annual Meeting of Stockholders in 2003.**

*Ted W. Love, M.D.* has served as our President since January 2001, our Chief Executive Officer since March 2001, and as a director since February 2001. Dr. Love served as our President and Chief Operating Officer from January 2001 until March 2001. Prior to joining us, Dr. Love served as Senior Vice President of Development at Advanced Medicine, Inc. Dr. Love served as a Research Physician and Vice President of



Product Development at Genentech from 1992 to 1998. Dr. Love holds a B.A. in Molecular Biology from Haverford College and a M.D. from Yale Medical School.

*Robert D. Weist* has served as a director since May 1993 and as Vice Chairman since February 2000. Mr. Weist served as Chairman from March 1994 until February 2000 and as President from May 1993 until March 1994. Mr. Weist has been President of Weist Associates, a management consulting firm, since April 1992. Prior to joining us, from January 1986 to April 1992, Mr. Weist was a consultant to Amgen, Inc., a publicly-held biotechnology company, and served as Senior Vice President, Administration, General Counsel and Secretary, and from May 1982 to January 1986, he served as Amgen's Vice President, General Counsel and Secretary. Mr. Weist also serves as a director of BioSource International Inc., a biological products supplier. Mr. Weist holds a B.S. in chemical engineering from Purdue University, a J.D. from New York University and an M.B.A. from the University of Chicago.

**Directors continuing in office until the Annual Meeting of Stockholders in 2004.**

*Raymond F. Baddour, Sc.D.* has served as a director since December 1993. Since July 1989, Dr. Baddour has served as the Lamot du Pont Professor of Chemical Engineering, Emeritus, at the Massachusetts Institute of Technology where he formerly served as the Lamot du Pont Professor of Chemical Engineering from 1973 to 1989. Dr. Baddour also serves as a director of ActivBiotics, Inc., a pharmaceutical company, Scully Signal Co., an equipment manufacturing company, and MatTek Corporation, a bio-materials company. He was a director of Amgen from 1980 to 1997. Dr. Baddour holds a B.S. in chemical engineering from Notre Dame University and an M.S. and Sc.D. from the Massachusetts Institute of Technology.

*Ernst Schweizer, Ph.D.* has served as a director since March 1999. Since January 2002, Dr. Schweizer has been Head of Business Development and a director of Genmab A/S, a company also focused on the development of antibodies. In addition, he is a director of Speedel Holding and of the Biopharma Fund. In January 1999, Dr. Schweizer joined Medarex, Inc., a biopharmaceutical company focused on the development of antibodies, as President of Medarex Europe and Managing Director of Medarex, Inc., positions he held until the end of 2001. Formerly, Dr. Schweizer served as the Deputy Head of Business Development and Licensing at Novartis, a pharmaceutical company, and was the Chief Scientific and Technical Officer in Business Development and Licensing at CIBA-Geigy, before its consolidation into Novartis in 1997, during a 37 year tenure with these companies. Dr. Schweizer received his Ph.D. from the University of Stuttgart and holds numerous patents.

**Executive Officers**

Name	Age	Position
George B. Rathmann	74	Chairman of the Board of Directors
Ted W. Love	43	President, Chief Executive Officer and Director
William F. Bennett	53	Senior Vice President of Research and Development
Linda A. Fitzpatrick	45	Senior Vice President of Human Resources
Peter S. Garcia	41	Senior Vice President and Chief Financial Officer
Li-Hsien Rin-Laures	35	Senior Vice President, General Counsel and Secretary
Walter Funk	42	Vice President of Research
David M. Rosen	46	Vice President of Operations

*William F. Bennett, Ph.D.* joined us in July 2001 as our Senior Vice President of Research and Development. Dr. Bennett has twenty years experience in drug development, having served as Senior Vice President, Research and Manufacturing at Sensus Drug Development Corporation from 1996 to 2000, Senior Vice President, Product Development at BigBearBio, Inc. from 2000 to 2001, and Vice President, Research at COR Therapeutics from 1995 to 1996. Before holding those positions, Dr. Bennett worked at Genentech, Inc. for thirteen years where he held various positions in Research and Development, including research and development project team leader of the TNKase project. Dr. Bennett received his Ph.D. from University of

Texas Southwestern Medical School, is the author of fifty scientific publications, and holds nineteen issued U.S. patents.

*Linda A. Fitzpatrick* joined us in April 2001 as our Senior Vice President of Human Resources. Prior to joining us, Ms. Fitzpatrick served as Senior Advisor at Advanced Medicine, Inc from April 1999 to January 2001 and Vice President, Human Resources, Corporate Communications and Operations at Gilead Sciences, Inc. from 1992 to 1998. Prior to her tenure at Gilead Sciences, Ms. Fitzpatrick served eight years at Genentech, Inc. where her positions included Director, Investor Relations and Director, Compensation, Benefits and Systems. Ms. Fitzpatrick graduated with honors with a Bachelor of Science degree in Sociology and Psychology from San Francisco State University.

*Peter S. Garcia* joined us in May 2001 as our Senior Vice President and Chief Financial Officer. Prior to joining us, Mr. Garcia served as Chief Financial Officer at Novacept, Inc., from May 2000 to April 2001, Chief Financial Officer and Consultant at IntraBiotics Pharmaceuticals, Inc. from January 1999 to April 2000 and Chief Financial Officer at Dendreon Corporation from July 1996 to December 1998. Prior to this experience, Mr. Garcia worked at Amgen Inc. from 1990 to 1996 in a variety of financial executive positions, including Assistant Corporate Controller. Mr. Garcia graduated with honors with a Bachelor of Arts degree in Economics and Sociology from Stanford University, and earned his Master of Business Administration from the University of California at Los Angeles.

*Li-Hsien Rin-Laures* joined us in August 2001 as our Senior Vice President and General Counsel. Prior to joining us, Dr. Rin-Laures was a partner from 1999 to 2001 in the law firm of Marshall, Gerstein and Borun, which she joined in 1993 after completing a judicial clerkship at the Court of Appeals for the Federal Circuit. Dr. Rin-Laures graduated with honors from Johns Hopkins University with a Bachelors of Arts in Chemistry, received an M.D. from Northwestern University Medical School and received her J.D., cum laude, from Harvard Law School.

*Walter Funk, Ph.D.* joined us in August 2000 and currently holds the position of Vice President of Research. Prior to joining us, Dr. Funk was a founding scientist at Geron Corp. from 1993 to 2000 where he was project leader on molecular biology projects focused on telomerase biology, cell immortalization and senescence. He later led the company's genomics efforts in human stem cell biology. Dr. Funk did post-doctoral work at the University of Texas Southwestern Medical Center at Dallas in the labs of Woodring Wright and Jerry Shay and received his Ph.D. and B.Sc. (Hon) degrees in Biochemistry from the University of British Columbia. He has published over thirty journal papers and is an assignee on 7 U.S. patents.

*David M. Rosen, Ph.D.* joined us in March 1999 as Vice President of Operations. Prior to joining us, Dr. Rosen was Vice President, and then Senior Vice President of Research and Development, responsible for product development and manufacturing operations at Celtrix Pharmaceuticals from May 1995 to October 1998. During his seven years at Celtrix, and an additional nine years at Celtrix's parent company, Collagen Corporation, Dr. Rosen held several other managerial positions in research and development, including Director of Research and Project Leader for a variety of biopharmaceutical projects involving the evaluation of protein therapeutics in the areas of osteoporosis and orthopedics. Dr. Rosen holds a Ph.D. and B.S. in biochemistry from the University of California, Riverside.

#### **Section 16(a) Beneficial Ownership Reporting Compliance**

Section 16(a) of the Securities Exchange Act of 1934 (the Exchange Act) requires our directors and officers and persons who beneficially own more than 10% of our common stock to file with the Securities and Exchange Commission initial reports of beneficial ownership and reports of changes in beneficial ownership of our common stock and other equity securities of ours. Officers, directors and greater than 10% beneficial owners are required by Securities and Exchange Commission regulation to furnish us with copies of all Section 16(a) forms they file.

Based solely on review of the copies of such reports furnished to us and written representations from certain reporting persons, we believe that during the fiscal year ended December 31, 2001, all Section 16(a) filing requirements applicable to our officers, directors and greater than 10% beneficial owners were met.

**Item 11. Executive Compensation**

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

**Summary Compensation Table**

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

- (1) Excludes perquisites and other personal benefits, securities or property aggregating less than \$50,000 or 10% of the total annual salary and bonus reported for each named executive officer.
- (2) The securities underlying the options are shares of our common stock.
- (3) Dr. Rathmann served as our Chief Executive Officer from May 2000 to March 2001. Salary and bonus information for the year 2001 represents compensation paid to Dr. Rathmann through March 2001. Dr. Rathmann received a grant of options to purchase 3,000 shares of our common stock each month, with an exercise price per share equal to the fair market value of our common stock on date of each grant, in lieu of cash compensation for his services as our employee. Salary and bonus information for the year 2000 represents compensation paid to Dr. Rathmann since February 2000, when he joined our company.
- (4) Dr. Love has served as our President since January 2001 and as Chief Executive Officer and a director since March 2001. Salary and bonus information for the year 2001 represents compensation paid since January 2001.
- (5) Mr. Garcia joined us in May 2001 as our Senior Vice President and Chief Financial Officer. Salary and bonus information for the year 2001 represents compensation paid since May 2001.

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- (6) Ms. Fitzpatrick joined us in April 2001 as our Senior Vice President of Human Resources. Salary and bonus information for the year 2001 represents compensation paid since April 2001.
- (7) Dr. Bennett joined us in July 2001 as our Senior Vice President of Research and Development. Salary and bonus information for the year 2001 represents compensation paid since July 2001.

- (8) Dr. R. Drmanac resigned as our Chief Scientific Officer to become Chief Scientific Officer of our subsidiary Callida in October 2001 and remained employed with us through December 2001. Salary and bonus information for the year 2001 represents compensation paid through December 2001.
- (9) Dr. S. Drmanac resigned as our Vice President of SBH Biochemistry to become Vice President of SBH and Research and Development of our subsidiary Callida in October 2001 and remained employed with us through December 2001. Salary and bonus information for the year 2001 represents compensation paid through December 2001.

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

### Employment Agreements

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

In January 2001, we entered into an employment agreement with Dr. Love. Pursuant to the agreement, we are obligated to pay Dr. Love an initial annual salary of \$485,000. In addition, Dr. Love is entitled to participate in our management bonus pool, employee benefit plans maintained by us and in other benefits provided to our senior executives, including retirement and 401(k) plans, deferred compensation, medical and dental, annual vacation, paid holidays, sick leave and similar benefits. In connection with Dr. Love's employment agreement, we also granted him options to purchase an aggregate of 500,000 shares of our common stock. In the event Dr. Love's employment with us terminates other than for cause or there exists good reason for Dr. Love to terminate his employment with us:

any options granted to Dr. Love in connection with this agreement or otherwise over the first four years of his employment, beginning January 11, 2001, will immediately become vested and exercisable;

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

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

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

In the event of Dr. Love's death, the benefits described above shall be paid to his heirs. In the event Dr. Love is disabled for at least six consecutive months while employed by us we may terminate Dr. Love, but must pay him the benefits described above. In the event of a change of control, if Dr. Love is not employed as the surviving entity's Chief Executive Officer and President for at least one year, beginning the with the effective date of the change of control and ending on the one-year anniversary thereof, unless Dr. Love is terminated for cause, he shall receive the benefits described above.

As provided by the terms of Dr. Love's employment agreement, we have entered into a loan agreement with Dr. Love, pursuant to which he may borrow up to \$2.0 million from us. The loan agreement with Dr. Love provides for interest on outstanding balances to accrue at the lowest applicable federal interest rate or such other higher rate of interest, if required, to constitute a market rate of interest as contemplated by the Rules and Regulations of the Financial Accounting Standards Board and the U.S. Securities and Exchange Commission. Interest accrues but is deferred and all interest and principal is due in January 2006.

## Management Stock Option Agreements

In connection with Dr. Love's employment agreement, we granted him options to purchase an aggregate of 500,000 shares of our common stock. Specifically, we have granted Dr. Love (i) an option under our 1995 Plan to purchase 31,840 shares at an exercise price of \$12.56 per share, the fair market value of our common stock on the date of grant as determined under that plan, which shares become exercisable in four equal annual installments commencing one year after the date of grant, and (ii) an option to purchase 468,160 shares at an exercise price of \$12.50 per share, the closing price on the date of grant, of which 150,000 shares became exercisable immediately and the remainder become exercisable in four equal annual installments commencing one year after the date of grant. Our employment agreement with Dr. Love also provides that, at any time following his first year of employment but before the third anniversary of beginning his employment, so long as Dr. Love has not exercised his option to purchase 150,000 of the 500,000 shares, he may forfeit that option, in exchange for \$2.0 million plus the accrued interest under the loan agreement and the loan then becomes immediately due and payable. The guaranteed value of the 150,000 options at \$2.0 million will be recognized ratably as compensation expense over the service period of one year. As of May 2, 2002, no amounts were outstanding under the loan agreement.

## Option Grants in 2001

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

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

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

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

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

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

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

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

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

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

- (1) All options have a per share exercise price equal to the fair market value of our common stock on the date of grant, with the exception of the initial option granted to Dr. Rathmann to purchase 1,000,000 shares of our common stock, which has a per share exercise price equal to the closing price of a share of our common stock on the day prior to the date of the grant.
- (2) Reflects the value of the stock option on the date of grant assuming (i) for the 5% column, a five-percent annual rate of appreciation in our common stock over the ten-year term of the option, and (ii) for the 10% column, a ten-percent annual rate of appreciation in our common stock over the ten-year term of the option, in each case without discounting to net present value and before income taxes associated with the exercise. The 5% and 10% assumed rates of appreciation are based on the rules of the Securities and Exchange Commission and do not represent our estimate or projection of the future price of our common stock. The amounts in this table may not be achieved.
- (3) On August 21, 2001, we granted an option to purchase 1,000,000 shares of our common stock to Dr. Rathmann with an exercise price of \$8.635 per share. He received a monthly option grant of 3,000 shares at exercise prices ranging from \$6.0825 to \$15.125 per share.
- (4) The option granted on August 21, 2001 will expire August 20, 2011. The monthly options granted will expire on January 30, 2011, February 27, 2011, March 29, 2011, April 29, 2011, May 30, 2011, June 28, 2011, July 30, 2011, August 30, 2011, September 27, 2011, October 30, 2011, November 29, 2011 and December 30, 2011, respectively.
- (5) On January 11, 2001, we granted an option to purchase 468,160 shares of our common stock to Dr. Love with an exercise price of \$12.50 per share; an option to purchase 31,480 shares with an exercise price of \$12.5625 per share. On August 1, 2001, Dr. Love received an option grant to purchase 75,000 shares of our common stock at exercise price of \$10.44 per share.
- (6) The options granted will expire on January 10, 2011 and July 31, 2011, respectively.
- (7) On May 1, 2001, we granted an option to purchase 200,000 shares of our common stock to Mr. Garcia with an exercise price of \$11.665 per share. On August 1, 2001, Mr. Garcia received an option grant to purchase 25,000 shares of our common stock at exercise price of \$10.44 per share.
- (8) The options granted will expire on April 30, 2011 and July 31, 2011, respectively.
- (9) On April 24, 2001, we granted an option to purchase 150,000 shares of our common stock to Ms. Fitzpatrick with an exercise price of \$9.955 per share. On August 1, 2001, Ms. Fitzpatrick received an option grant to purchase 25,000 shares of our common stock at exercise price of \$10.44 per share.

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

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

<b>Option Values at December 31, 2001</b>						
<b>Name</b>	<b>Shares</b>		<b>Number of Securities Underlying Unexercised Options at Fiscal Year End(#)(1)</b>		<b>Value of Unexercised In-The-Money Options at Fiscal Year End(\$)</b>	
	<b>Acquired at Exercise(#)</b>	<b>Value Realized(\$)</b>	<b>Exercisable</b>	<b>Unexercisable</b>	<b>Exercisable</b>	<b>Unexercisable</b>
George B. Rathmann			735,666	1,333,334	5,903	
Ted W. Love			150,000	425,000		
William F. Bennett				250,000		
Linda A. Fitzpatrick				175,000		
Peter S. Garcia				225,000		
David M. Rosen			15,708	45,464	66,163	132,318
Radoje T. Drmanac			167,199	25,659	822,146	84,757
Snezana Drmanac			92,034	16,144	395,145	53,084

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

**Compensation Committee Interlocks and Insider Participation**

During fiscal 2001, the compensation committee consisted of Dr. Baddour and Mr. Weist, neither of whom is (i) a present or former officer or employee of our company, or (ii) is engaged in any transactions described under the heading Certain Transactions, with the exception of Mr. Weist, who is our Vice Chairman, who was our Chairman from March 1994 to February 1, 2000 and our President from May 1993 until March 1994, and who participated in our private placement for which we are requesting ratification at the 2002 Annual Meeting of Stockholders. Mr. Weist, Trustee of the Weist Family Trust, purchased 30,000 shares of our common stock and was issued a warrant for the purchase of 15,000 shares of our common stock. Of the \$21,285,131 we received in gross proceeds from the private placement, we received approximately \$210,000 from Mr. Weist.

**COMPENSATION COMMITTEE REPORT**

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

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

## **Bonuses**

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

## **Stock Options**

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

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

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

competitive stock option data from other genomics and biotechnology companies.

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

## **Chief Executive Officer's Compensation**

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

Dr. Love has been our Chief Executive Officer since March 2001. Dr. Love's annual salary is \$485,000. Dr. Love's salary is not directly tied to our performance. However, his compensation, including stock options, takes into account our success in meeting our strategic, technological and financial objectives. Because of our stage of development, we have not used either the profitability or the market value of our stock as significant factors to be considered in setting Chief Executive Officer compensation.

## **Internal Revenue Code Section 162(m)**

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

### COMPENSATION COMMITTEE

Raymond F. Baddour, Sc.D., Chairperson

Robert D. Weist

**STOCK PERFORMANCE GRAPH**

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

**(PERFORMANCE GRAPH)**

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

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

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

**Item 12. Security Ownership of Certain Beneficial Owners and Management**

The following table sets forth certain information regarding the beneficial ownership of our common stock as of May 2, 2002 by: (1) each of our directors; (2) each of our named executive officers (as listed on page 23); (3) by each person known by us to be the beneficial owner of more than 5% of our outstanding common stock; and (4) all of our directors and executive officers as a group. As of May 2, 2002, we had 22,949,987 shares of our common stock outstanding.

Name and Address of Beneficial Owner(1)	Shares Beneficially Owned(1)	
	Number of Shares	Percentage
George B. Rathmann(2)	3,836,935	16.0
Robert D. Weist(3)	250,314	1.1
Raymond F. Baddour(4)	59,539	*
Thomas N. McCarter, III(5)	67,219	*
Ernst Schweizer(6)	40,759	*
David M. Rosen(7)	32,866	*
Ted W. Love(8)	242,409	1.1
William F. Bennett(9)	7,511	*
Linda A. Fitzpatrick(10)	37,500	*
Peter S. Garcia(11)	51,217	*
Radoje T. Drmanac(12)	990,209	4.3
Snezana Drmanac(12)	990,209	4.3
All Directors and Executive Officers as a Group (12 persons)	5,616,478	22.7

\* Represents beneficial ownership of less than 1% of our common stock.

- (1) Beneficial ownership is determined in accordance with Rule 13d-3 under the Exchange Act and generally includes voting or investment power with respect to securities. Shares of common stock subject to options and warrants which are currently exercisable, or will become exercisable within 60 days of May 2, 2002, are deemed outstanding for computing the percentage of the person or entity holding such securities but are not outstanding for computing the percentage of any other person or entity. Excludes shares and warrants issued to certain of our executive officers and directors in connection with the August 2001 private placement for which we require stockholder ratification at our 2002 Annual Meeting of Stockholders. Except as indicated by footnote, and subject to the community property laws where applicable, to our knowledge the persons named in the table above have sole voting and investment power with respect to all shares of common stock shown as beneficially owned by them. Unless otherwise indicated, the address for each person is our address at 670 Almanor Avenue, Sunnyvale, California 94085.
- (2) Represents: (i) 2,755,935 shares of common stock held in trust for the benefit of the Rathmann family, for which Dr. Rathmann and his spouse serve as co-trustees; and (ii) 1,081,000 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of May 2, 2002. Excludes 1,000,000 shares issuable upon the exercise of options which are not currently exercisable and will not be exercisable within 60 days of May 2, 2002, and shares of our common stock issuable in repayment of Dr. Rathmann's line of credit to us and which issuance our stockholders are being asked to approve at our 2002 Annual Meeting of Stockholders.
- (3) Represents: (i) 206,675 shares held in trust for the benefit of the Weist family for which Mr. Weist and his spouse serve as co-trustees, and (ii) 43,639 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of May 2, 2002.
- (4) Represents 59,539 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of May 2, 2002.

- (5) Represents: (i) 19,200 shares of common stock owned by Mr. McCarter, and (ii) 48,019 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of May 2, 2002.
- (6) Represents: (i) 23,040 shares of common stock owned by Dr. Schweizer, and (ii) 17,719 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of May 2, 2002.
- (7) Represents: (i) 4,658 shares of common stock owned by Dr. Rosen, and (ii) 28,208 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of May 2, 2002. Excludes 32,964 shares issuable upon the exercise of options which are not currently exercisable and will not be exercisable within 60 days of May 2, 2002.
- (8) Represents: (i) 4,909 shares of common stock owned by Dr. Love, and (ii) 237,500 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of May 2, 2002. Excludes 337,500 shares issuable upon the exercise of options which are not currently exercisable and will not be exercisable within 60 days of May 2, 2002.
- (9) Represents: (i) 7,511 shares of common stock owned by Dr. Bennett. Excludes 250,000 shares issuable upon the exercise of options which are not currently exercisable and will not be exercisable within 60 days of May 2, 2002.
- (10) Represents 37,500 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of May 2, 2002. Excludes 137,500 shares issuable upon the exercise of options which are not currently exercisable and will not be exercisable within 60 days of May 2, 2002.
- (11) Represents: (i) 1,217 shares of common stock owned by Mr. Garcia, and (ii) 50,000 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of May 2, 2002. Excludes 175,000 shares issuable upon the exercise of options which are not currently exercisable and will not be exercisable within 60 days of May 2, 2002.
- (12) Represents: (i) 100,000 shares of common stock held in trust for the benefit of one of the Drmanac children for which the Drs. Drmanac serve as co-trustees; (ii) 100,000 shares of common stock held in trust for the benefit of one of the Drmanac children for which the Drs. Drmanac serve as co-trustees; (iii) 122,496 shares of common stock held in trust for the benefit of the Drmanac family for which the Drs. Drmanac serve as co-trustees; (iv) 413,667 shares of common stock held individually by Dr. R. Drmanac; (v) 162,012 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of May 2, 2002 held by Dr. R. Drmanac; (vi) 4,998 shares of common stock held individually by Dr. S. Drmanac; and (vii) 87,036 shares of common stock issuable upon the exercise of options that are currently exercisable or exercisable within 60 days of May 2, 2002 held by Dr. S. Drmanac. Excludes 41,803 shares issuable upon the exercise of options held by the Drs. Drmanac which are not currently exercisable and will not be exercisable within 60 days of May 2, 2002.

**Item 13. *Certain Relationships and Related Transactions***

On August 6, 2001, we received a commitment from Dr. George B. Rathmann, our Chairman, to provide a line of credit to us of up to \$20.0 million in aggregate principal amount, available for draw down through July 24, 2003. The line of credit agreement was amended and restated as of April 3, 2002. For a description of the line of credit, see the discussion set forth under "Disclosure Regarding our Chairman" in Item 7 of this report. Amounts outstanding under this agreement as of December 31, 2001 and May 2, 2002 are zero and \$4.0 million, respectively.

On August 21, 2001, our Board of Directors granted Dr. Rathmann an option to purchase 1,000,000 shares of our common stock with an exercise price equal to the fair market value of our common

stock on the date of grant. For a description of the option, see the discussion set forth under "Disclosure Regarding our Chairman" in Item 7 of this report.

As provided by the terms of his employment agreement with us, we have entered into a loan agreement with Dr. Ted W. Love, our President, Chief Executive Officer and a director, pursuant to which he may borrow up to \$2.0 million from us. The loan agreement with Dr. Love provides for interest on outstanding balances to accrue at the lowest applicable federal interest rate or such other higher rate of interest, if required, to constitute a market rate of interest as contemplated by the Rules and Regulations of the Financial Accounting Standards Board and the U.S. Securities and Exchange Commission. Interest accrues but is deferred and all interest and principal is due in January 2006. As of May 2, 2002, no amounts were outstanding under the loan agreement.

On August 28, 2001, George B. Rathmann and Frances Joy Rathmann, Co-Trustees of The Rathmann Family 1989 Revocable Trust U/A dated 08/04/89 purchased 571,428 shares of our common stock and were issued a warrant for the purchase of 285,714 shares of our common stock in our private placement for which we are requesting ratification at our 2002 Annual Meeting of Stockholders. Dr. Rathmann is our Chairman of the Board. Of the \$21,285,131 we received in gross proceeds from the private placement, we received approximately \$3,999,996 from Dr. Rathmann.

On August 28, 2001, Ted W. Love, our President and Chief Executive Officer and a director, purchased 14,290 shares of our common stock and was issued a warrant for the purchase of 7,145 shares of our common stock in our private placement for which we are requesting ratification at our 2002 Annual Meeting of Stockholders. Of the \$21,285,131 we received in gross proceeds from the private placement, we received approximately \$100,030 from Dr. Love.

On August 28, 2001, Peter S. Garcia, our Senior Vice President and Chief Financial Officer, purchased 14,290 shares of our common stock and was issued a warrant for the purchase of 7,145 shares of our common stock in our private placement for which we are requesting ratification at our 2002 Annual Meeting of Stockholders. Of the \$21,285,131 we received in gross proceeds from the private placement, we received approximately \$100,030 from Mr. Garcia.

On August 28, 2001, William F. Bennett, our Senior Vice President of Research, and Development purchased 14,290 shares of our common stock and was issued a warrant for the purchase of 7,145 shares of our common stock in our private placement for which we are requesting ratification at our 2002 Annual Meeting of Stockholders. Of the \$21,285,131 we received in gross proceeds from the private placement, we received approximately \$100,030 from Dr. Bennett.

On August 28, 2001, Mr. Weist, Trustee of the Weist Family Trust, purchased 30,000 shares of our common stock and was issued a warrant for the purchase of 15,000 shares of our common stock in our private placement for which we are requesting ratification at our 2002 Annual Meeting of Stockholders. Mr. Weist is a director and a member of our Compensation Committee. Of the \$21,285,131 we received in gross proceeds from the private placement, we received approximately \$210,000 from Mr. Weist.

## PART IV

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

(a)(1) The Financial Statements and report of independent auditors required by this Item are submitted in a separate section, beginning on page 40 of this Report.

	<b>Page No.</b>
Independent Auditors Report KPMG LLP	40
Report of Ernst & Young LLP, Independent Auditors	41
Consolidated Balance Sheets as of December 31, 2001 and 2000	42
Consolidated Statements of Operations for the years ended December 31, 2001, 2000 and 1999	43
Consolidated Statements of Stockholders Equity for the years ended December 31, 2001, 2000 and 1999	44
Consolidated Statements of Cash Flows for the years ended December 31, 2001, 2000 and 1999	45
Notes to Consolidated Financial Statements	46

(a)(2) The schedules have been omitted because they are not applicable or are not required or the information required to be set forth therein is included in the Financial Statements or notes thereto.

(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.

<b>Exhibit Number</b>	<b>Description</b>
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)

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Exhibit Number	Description
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)
10.16	Collaboration and License Agreement, dated as of June 29, 2001, by and between Hyseq, Inc. and Aurora Biosciences Corporation(12)
10.17	Collaboration Agreement, dated as of August 21, 2001, by and between Hyseq, Inc. and Kirin Brewery Company, Ltd.(12)
10.18	Secreted Protein Development and Collaboration Agreement, dated as of October 9, 2001, by and between Hyseq, Inc. and Deltagen, Inc.(12)
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.(12)
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.(12)
10.23	Product Solicitation Agreement, dated as of October 24, 2001, by and between N-Mer, Inc. and Affymetrix, Inc.(12)
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
21.1	Subsidiaries of Hyseq, Inc. as of December 31, 2001: Callida Genomics, Inc., a Delaware corporation; N-Mer, Inc., a Delaware corporation; Hyseq Diagnostics, Inc., a Nevada corporation(12)
23.1	Consent of KPMG LLP, Independent Auditors
23.2	Consent of Ernst & Young LLP, Independent Auditors

(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.

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- (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.
- (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.

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



**EXHIBIT INDEX\***

<b>Exhibit Number</b>	<b>Description</b>
10.27	Form of Non-Stockholder Approved Stock Option Agreement for Officers
23.1	Consent of KPMG LLP, Independent Auditors
23.2	Consent of Ernst & Young LLP, Independent Auditors

\* Only exhibits actually filed on this Form 10-K/A are listed. Exhibits previously filed on the Form 10-K or incorporated by reference are set forth in the exhibit listing included in Item 14 of this Form 10-K/A.