UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

For Annual and Transition Reports Pursuant to Sections 13 or 15(d) of the Securities Exchange Act of 1934

☒ **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: 0-27352

HYBRIDON, INC.
(Exact name of Registrant as specified in its certificate of incorporation)

Delaware	**04-3072298**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
345 Vassar Street Cambridge, Massachusetts	**02139**
(Address of principal executive offices)	**(Zip Code)**

(617) 679-5500
(Registrant's telephone number, including area code)

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

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

Common Stock, $.001 par value
Preferred Stock Purchase Rights
(Title of Class)

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 the 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 the 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 approximate aggregate market value of the voting stock held by non-affiliates of the registrant was $54.5 million as of March 27, 2002.

As of March 27, 2002, the registrant had 45,697,637 shares of Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Proxy Statement with respect to the Annual Meeting of Stockholders to be held on June 19, 2002	Items 10, 11, 12 and 13 of Part III.

HYBRIDON, INC.

FORM 10-K

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This annual report on Form 10-K references the following U.S. trademarks owned by us: Hybridon®, GEM®, CpR™, Cyclicon™, IMO™, YpG™, and YpR™. This annual report on Form 10-K also contains trademarks of other companies.

PART I.

Item 1. *Business*

Overview

We are a leading company in the discovery and development of novel therapeutics and diagnostics using synthetic DNA. Our activities are based on four technologies:

- immunomodulatory oligonucleotide, or IMO™, technology, which uses synthetic DNA to modulate responses of the immune system;
- antisense technology, which uses synthetic DNA to inhibit the production of disease-associated proteins at the cellular level;
- cancer therapy potentiation, which uses synthetic DNA to enhance the antitumor activity of certain marketed anticancer drugs; and
- Cyclicon™ technology, which uses novel synthetic DNA structures, which we refer to as Cyclicons, in drug target validation and drug discovery.

Antisense. We were founded in 1989 to explore the pioneering work of Paul Zamecnik, M.D., a member of our board of directors, who is regarded by many as the father of antisense. We remain a leader in antisense to this day, particularly in the key area of developing the novel chemical structures on which advanced, or second generation, antisense drug candidates are based.

The advanced antisense chemistries developed by us serve as the basis for second generation antisense drug candidates, which we believe have the following potential advantages over earlier antisense drug candidates:

- fewer side effects;
- greater stability in the body;
- greater potency; and
- greater potential for multiple routes of administration, including oral delivery.

We believe that our antisense technology is potentially applicable to a wide variety of therapeutic indications. We are currently focusing our antisense efforts on cancer and infectious diseases.

IMOs. Our IMO technology has evolved from our clinical experience with antisense oligonucleotides, segments of DNA, in which we learned that some types of oligonucleotides can act as potent immune modulators. Our early insights and those of others showed that oligonucleotides containing specific nucleotide segments, or motifs, mimic in the human body the immune stimulating effects of bacterial DNA. Using our DNA chemistry, we have designed and are developing a new, proprietary class of IMO compounds. We believe these compounds, which we refer to as second generation IMO compounds, may offer a number of potential advantages over earlier immunomodulatory oligonucleotides including:

- greater potency;
- greater specificity because second generation IMO compounds may be designed to induce different parts of the human immune system;
- reduced manufacturing costs; and
- the possibility of composition of matter patent protection.

We believe that our IMO compounds may be used as monotherapies in the treatment of conditions such as cancer, asthma/allergy and infectious diseases, as well as in combination therapies with antibodies, vaccines and chemotherapeutics.

Cancer Therapy Potentiation. Our cancer therapy potentiation technology is based on our discovery in preclinical studies that when oligonucleotides are administered in combination with certain marketed anticancer drugs, such as irinotecan, the activity of the co-administered anticancer drug is greatly improved. In the case of irinotecan, which is marketed in the United States under the name Camptosar®, we have observed increased antitumor activity in over 10 different animal tumor models. We recently commenced a Phase I/II clinical trial combining our second generation antisense compound GEM 231 with irinotecan to determine whether the effects observed in animals can be achieved in humans.

Strategy. We plan to exploit our therapeutic technologies in several ways. In the near term, we intend to seek collaborations with pharmaceutical or biotechnology companies covering some of our product candidates which will allow us to share in the potential success of the product candidates through upfront payments, development milestones and royalties on net sales, without incurring significant additional development costs. Also, in the near term, we plan to advance the balance of our product pipeline by continuing the clinical development of GEM 231 and by bringing our lead IMO preclinical candidate HYB 2055 into the clinic ourselves. Over the longer term, we plan to continue to exploit our technologies through collaborations, but also to increase the number of products we develop and ultimately market on our own.

Our Product Pipeline

We are developing products based on three of our therapeutic technologies. The table below summarizes these products, the therapeutic use of these products and the development status of these products.

Product Description	Therapeutic Use	Development Status
IMO™		
HYB 2055 — second generation IMO for use as a monotherapy	Cancer	Preclinical candidate
HYB 2055 — second generation IMO for use in combination therapies	In combination with Vaccines, Antibodies	Preclinical candidate
Antisense		
GEM 231 — second generation antisense drug candidate targeted to PKA	Cancer	Phase I/II
GEM 92 — second generation antisense drug candidate targeted to the gag region of HIV-1	HIV	Phase I
ORI-1001 — second generation antisense drug candidate targeted to HPV6[1]	Human Papillomavirus (HPV)	Phase I
GEM 240 — second generation antisense compound targeted to MDM2	Cancer	Preclinical candidate
GEM 220 — second generation antisense compound targeted to Vascular Endothelial Growth Factor (VEGF)	Cancer	Preclinical candidate
Cancer Therapy Potentiation		
GEM 231 — second generation antisense drug used to potentiate the antitumor activity of irinotecan	Cancer	Phase I/II

1. Being developed by OriGenix Technologies, a Canadian company which we formed with an investor group. We owned approximately 25% of the capital of OriGenix as of March 15, 2002.

Developments in 2001 and Early 2002

In 2001 and early 2002, we focused our business activities on obtaining additional cash to fund the continued development of our technologies and product pipeline, reducing our debt, simplifying our capital

structure, strengthening our management team and seeking to enter into licensing and development collaborations.

Increased Cash Resources; Debt Reduction

Through a series of transactions over the course of 2001, we increased our cash resources from $8.5 million at December 31, 2000, which included $5.0 million of restricted cash, to $31.8 million at December 31, 2001 and reduced our debt from $15.3 million at December 31, 2000 to $1.6 million at December 31, 2001.

Collaboration and License Agreement with Isis Pharmaceuticals

In May 2001, we entered into a collaboration and license agreement with Isis Pharmaceuticals, Inc. Under the agreement, we licensed to Isis our antisense chemistry and delivery patents and patent applications. We retained the right to use these patents and patent applications in our own drug discovery and development efforts and in collaborations with third parties. In consideration of the license, Isis agreed to pay us $15.0 million in cash plus shares of Isis common stock in four installments intended to have an aggregate value of $19.5 million based on the stock price of the Isis common stock on the dates of issuance of the shares. In 2001, Isis paid $15.0 million to us in cash and issued to us 857,143 shares of its common stock having an aggregate fair market value on the dates on which title to the shares was received of $17.3 million. The remaining $4.5 million installment is due in 2003, subject to possible acceleration depending on the price of Isis' common stock.

In addition, under the agreement, we licensed from Isis specified antisense patents and patent applications. In return, we agreed to pay Isis a total of $6.0 million in cash or in shares of our common stock in three equal annual installments of $2.0 million beginning in May 2002. The license permits us to use the patents and patent applications licensed to us by Isis in our drug discovery and development efforts and in specified types of collaborations with third parties.

Early Conversion of Convertible Preferred Stock, Warrants and 8% Notes

In 2001, we significantly simplified our capital structure by exchanging shares of our common stock for all of our Series B preferred stock, several classes of our warrants and substantially all of our 8% notes. As a result of the exchange of our common stock for warrants as part of this program, the number of shares of our common stock underlying our outstanding warrants as a percentage of the number of shares of our common stock outstanding declined from 71% at December 31, 2000 to 13% at December 31, 2001.

New Chief Executive Officer

In August 2001, Stephen R. Seiler joined us as our Chief Executive Officer. Prior to joining us, Mr. Seiler served as Executive Vice President, Planning Investment & Development for Elan Corporation plc and was based in Elan's headquarters in Dublin, Ireland. Before joining Elan, Mr. Seiler had served as head of pharmaceutical investment banking at Paribas Capital Markets in London.

Commencement of Clinical Trial Combining GEM 231 with Irinotecan (Camptosar®)

In January 2002, we commenced a Phase I/II clinical trial combining our second generation antisense compound GEM 231 with irinotecan. We are conducting the trial at Vanderbilt University Medical Center and the University of Chicago Medical Center.

EpiGenesis Collaboration

In April 2001, we commenced a collaboration with EpiGenesis Pharmaceuticals, Inc. under which we licensed antisense patents, patent applications and technology to EpiGenesis and agreed to collaborate with EpiGenesis on the development of up to five antisense drugs for the treatment of respiratory diseases. Under the collaboration, EpiGenesis will be responsible for all development and commercialization activities. We

received an upfront license fee from EpiGenesis and are entitled to annual minimum royalties, running royalties on product sales and a portion of any sublicense income.

Immunomodulatory Oligonucleotide (IMO™) Technology

Introduction

The human body's immune system protects the body against viruses, bacteria and other infectious agents. It also acts to identify and eliminate abnormal cells, such as cancer cells. The immune system acts through a variety of white blood cells which recognize pathogens and abnormal cells and initiate a series of interactions that activate specific genes to respond to the pathogens or abnormal cells.

It has been known for over a century that DNA from infectious agents, such as bacteria, is recognized by the immune system and boosts immune protection. In the past few years, scientists have identified the specific sequences in bacterial DNA that are recognized by the immune system. These sequences are recognized by a specific protein receptor called TLR9. Protein receptors are molecules on the surface or inside of cells that are sensitive to foreign entities. Once this recognition occurs, scientists generally believe that TLR9 triggers an immune response against the bacterial DNA through a cascade of cell signals which ultimately leads to the release of cytokines, chemokines, immunoglobulins and additional white blood cells to attack the infection.

IMOs are synthetic DNA that contain the specific sequences recognized by TLR9 alone or with other receptors and mimic bacterial DNA. As such, IMOs are recognized as bacterial DNA by the receptor TLR9, alone or with other receptors. As a result of this recognition by the receptors, IMOs can trigger an immune response similar to the immune response triggered by bacterial DNA.

Therapeutic Potential of IMO™s

Because IMOs generate immune responses in a variety of ways, they may provide therapeutic benefits in a number of areas:

- *Cancer.* Cancer cells are recognized as abnormal cells and trigger an immune response. However, this response is notoriously weak. The benefits of immunostimulation by bacterial DNA in cancer patients have been long recognized. For example, bacterial DNA is currently used to treat bladder cancer. IMOs may strengthen the immune response to cancer cells because they trigger a strong cellular immune response that targets and kills cancerous cells.
- *Vaccines and Antibody Therapies.* IMOs have the potential to be used in combination with vaccines or antibody therapies because the immune response initiated by IMOs increases the production of specific antibodies.
- *Asthma/Allergies.* Certain white blood cells called cytokines are produced as a result of the activation of immune cells by IMOs. Cytokines suppress immune responses that result from asthmatic and allergic conditions while simultaneously promoting an immune response that further alleviates asthmatic and allergic conditions. As a result, IMOs have potential for use in the treatment of asthma, allergies and other diseases which result from an overreaction by the immune system.
- *Infection.* IMOs activate an immune defense against pathogens that is of a general nature and not directed at any specific microorganism. As a result, IMOs have the potential to be used prophylactically to ward off the danger of infection or to boost the immune response to an early-stage or ongoing infection.

IMO™ Chemistry

IMOs increase the expression of many proteins and affect the behavior of several kinds of cells. The profile of changes produced by IMOs is complex and varies somewhat from one oligonucleotide to another. Effects depend on the sequence and structure of the IMO.

Based on our extensive experience with DNA chemistry, we are developing a portfolio of second generation IMOs which have improved immunomodulatory properties compared with first generation IMOs. Our second generation IMOs contain specific sequences which have different effects on the immune system. These specific sequences contain synthetic motifs referred to as YpG and CpR. Studies in cell culture and in mice involving our YpG and CpR IMOs have revealed that certain modifications in the chemical make-up of the IMO can result in increased or decreased immunostimulatory activity. With the knowledge from these DNA medicinal-chemistry studies, we are designing second generation IMOs that induce specific cytokines to target specific disease indications. We are creating a portfolio of these second generation IMOs that can provide custom-designed IMOs as drug candidates for a variety of therapeutic or prophylactic uses.

IMO^{TM} Drug Discovery and Development

As part of our strategy to commercialize our IMOs, we plan to enter into collaborations with other biotechnology and pharmaceutical companies that can use our IMOs, either in combination with other drugs or drug candidates owned by the potential collaborator, or as monotherapies. As a first step in the commercialization process, we have entered into a number of material transfer agreements with potential collaborators. These potential collaborators range in size from small biotechnology companies to global pharmaceutical companies.

Under the material transfer agreements, these companies are allowed to use our IMOs in their own experimental disease models. Once the experiments are complete, these companies share the results with us. Based on the results achieved to date by these third parties in *in vitro* and *in vivo* animal models, we believe our IMO compounds are effective in inducing immune responses. We are working on converting these relationships into collaborations.

In 2002, we selected HYB 2055 as the lead preclinical candidate in our IMO program. We are designing and conducting the preclinical studies necessary to submit an investigational new drug application, or IND, for HYB 2055, and expect to submit the IND by the end of 2002. We selected HYB 2055 because of the potency it demonstrated in *in vitro* and *in vivo* models. We anticipate that the first clinical program for HYB 2055, will be for use as a monotherapy in the treatment of cancer and in combination with vaccines and antibodies. We believe HYB 2055 also may have use as a monotherapy for other therapeutic indications, such as asthma and allergies and infectious diseases, and in combination therapies with chemotherapeutics.

Antisense Technology

Introduction

The heart, brain, liver and other organs in the human body function together to support life. Each microscopic cell within these organs produces proteins that affect how that cell functions within the organ, and ultimately how efficiently each organ functions within the body.

A normal cell produces a given set of normal proteins in the right amount for the body to function properly. A diseased cell produces inappropriate or mutant proteins, or produces the wrong amount of normal proteins. A cell produces inappropriate types or amounts of proteins when its DNA changes, either through mutation, as in many types of cancer cells, or by infection with a virus. In some instances, inappropriate proteins act directly to cause or support a disease. In other instances, inappropriate proteins interfere with proteins that prevent or combat disease. Most traditional drugs are designed to interact with protein molecules that are already present in the body and that cause or support disease. Antisense drugs are designed to work at an earlier stage to inhibit production of disease-causing or disease-supporting proteins.

The full complement of human genes, known as the human genome, contains the information required to produce all human proteins. A copy of the complete human genome is present in each cell, and each cell makes proteins based on its copy of the genome. The information that controls a cell's production of a specific protein is contained in the gene relating to that protein. Each gene is made up of two intertwined strands of DNA that form a structure called a "double helix." Each strand of DNA consists of a string of individual DNA building blocks called nucleotides, arranged in a specific sequence. It is the sequence of nucleotides that

contains genetic information. One of the paired strands of the double helix contains the information that directs the composition of a specific protein, and is called the "coding" strand. The other strand, the "non-coding" strand, contains a different but complementary sequence of nucleotides.

Cells make proteins in a two-stage process. First, the cell creates a molecule of messenger RNA consisting of a string of nucleotides in a sequence that is the exact mirror image of, or complementary to, the sequence of the coding strand of DNA in the double helix. This messenger RNA strand is called the "sense" sequence. In the next step, the cell produces proteins based on the information contained in the messenger RNA.

Conventional Drugs

Most drugs are chemicals that stimulate or suppress the function of a particular molecule, usually a protein, which causes a disease. The drug acts by binding to the target molecule, often at as few as two or three points of contact with the target molecule. Once the binding takes place, the disease-causing activity of the target molecule is stopped.

Frequently, however, sites on other non-target molecules present in the body resemble the target-binding site of a disease-causing molecule enough to permit the conventional drug to bind to some degree to those non-target molecules. Most drug side effects arise due to this drug interaction with molecules other than the target molecule. This lack of selectivity can result in unwanted side effects, potentially requiring lower doses of the drug, and thus, decreased effectiveness.

Another characteristic of conventional drugs is that developing them is a time-consuming and expensive process. For every compound that is found to be effective and have tolerable side effects, thousands may be investigated and rejected. In the traditional drug discovery process, this may take many years and millions of dollars.

Antisense Drugs

A synthetic DNA molecule with a sequence exactly complementary to the sense sequence of the messenger RNA of a specific gene can bind to and inhibit the function of that messenger RNA. This exact complement of the sense messenger RNA sequence is referred to as an "antisense" sequence. By inhibiting the function of the relevant messenger RNA, it is possible to decrease or eliminate the production of disease-causing or disease-supporting proteins. Moreover, the nucleotide sequence of an antisense synthetic DNA complementary to its target sequence on the messenger RNA can be designed in a manner such that the antisense synthetic DNA forms a large number of bonds at the target site, typically 30 or more, as compared to as few as two to three bonds for conventional drugs. This allows it to form a strong bond with the messenger RNA.

Antisense drug development technology involves the design and synthesis of synthetic DNA to bind and inhibit the activity of messenger RNA which codes for the production of disease-associated proteins. We believe that drugs based on antisense technology may be more effective and cause fewer side effects than conventional drugs because antisense drugs are designed to intervene in a highly specific fashion in the production of proteins, rather than after the proteins are made.

Recent years have seen a dramatic increase in the understanding of the role of genes in producing proteins associated with disease. This knowledge has come from many sources, including the human genome project and the work being done by academic institutions and pharmaceutical companies all over the world. As a consequence, we believe that the pharmaceutical industry is increasingly becoming an environment that is rich in potential drug targets. The challenge for the future will be to create drugs effective against these newly discovered gene targets. We believe that the increase in the number of potential targets provides us with increasing opportunities to employ our antisense technology. Once a gene associated with a disease-associated protein is identified, it should be possible to design a synthetic DNA with an antisense mechanism and to improve the pharmaceutical effects of that synthetic DNA by chemical modification.

Hybridon Antisense Technology

Our antisense technology is based on our advanced chemistries, which enable us to alter the chemical makeup of the synthetic DNA backbone in a manner designed to make synthetic DNA safer and more stable without adversely affecting its ability to inhibit the production of disease-associated proteins. A synthetic DNA backbone is the linkage between the nucleosides in a strand of DNA. Oligonucleotides which contain a natural backbone are not suitable for use as drugs because they are rapidly degraded by enzymes before they reach the intended target. To be an effective antisense agent, the oligonucleotide must be chemically modified to increase its stability against these enzymes.

We and other companies have developed oligonucleotides which are chemically modified by replacing certain oxygen atoms on the backbone with sulfur atoms. We refer to oligonucleotides with this modification as first generation antisense compounds. Although one of our competitors in the antisense field currently markets a first generation antisense drug to treat a viral infection through local delivery and two other first generation antisense drugs are in late-stage clinical trials for cancer, we believe that the first generation antisense chemistry in these drugs limits their applicability because first generation antisense compounds are relatively toxic, degrade in the human body quickly and are less suitable for oral administration.

We have designed and created families of advanced synthetic DNA chemistries, including DNA/RNA combinations, called hybrid or mixed backbone chemistries. We believe that antisense compounds based on these advanced chemistries, which we refer to as second generation antisense compounds, will show favorable pharmaceutical characteristics and significantly improved therapeutic utility as compared to first generation antisense compounds. We believe that second generation antisense compounds may exhibit the following desirable characteristics in comparison with first generation compounds:

- fewer side effects;
- greater stability in the body, enabling patients to take doses less frequently;
- greater potency, permitting patients to take lower doses; and
- greater potential for multiple routes of administration, including by injection, orally or topically.

Antisense Drug Development and Discovery

We believe that our antisense technology is potentially applicable to a wide variety of therapeutic indications. We are focusing our drug development and discovery efforts on developing second generation antisense drugs for cancer and infectious diseases. We currently have two antisense compounds in the clinical phase of development and a number of other compounds in preclinical development.

Clinical Development

GEM 231 for the Treatment of Cancer. GEM 231 is a second generation antisense compound for the treatment of cancer. We are currently conducting Phase I/II clinical trials of GEM 231 as both a monotherapy and a combination therapy with currently marketed cancer therapies including irinotecan, which is marketed in the United States under the name Camptosar®, paclitaxel, which is marketed in the United States under the name Taxol®, and docetaxel, which is marketed in the United States under the name Taxotere®. The trials are intended to evaluate the safety and pharmacokinetics of GEM 231 as a monotherapy and as a combination therapy.

GEM 231 is an inhibitor of the RIα subunit of protein kinase A. Protein kinase A is a protein that plays a key role in the control of the growth and differentiation of mammalian cells. Studies have shown that levels of protein kinase A are increased in the cells of many human cancers and that high levels of protein kinase A correlate with unfavorable clinical outcomes in patients with breast and ovarian cancers.

We have previously conducted a Phase I clinical trial of GEM 231 to evaluate its safety in multiple doses in oncology patients. The trial explored the maximum tolerated dose of GEM 231 for both single doses and multiple doses. Even in high doses, GEM 231 did not show the side effects normally associated with most

current cancer treatments or with first generation antisense compounds. We believe that this trial was the first systemic administration of a second generation antisense compound to oncology patients.

GEM 92 for the Treatment of HIV-1. GEM 92 is a second generation antisense compound that is targeted to the gag region of the human immunodeficiency virus HIV-1. Based on the clinical experience we gained with GEM 91, our first generation antisense compound that also targeted the gag region of HIV-1, we created chemical modifications to improve the side effects profile and to enhance the stability of the compound. In 1997, we completed a pilot Phase I clinical study in Europe of GEM 92. All doses given in the pilot study were well tolerated by the patients. Further, GEM 92 was detected in the blood after both oral dosing and injection, suggesting that GEM 92 could be developed as an oral drug. Both GEM 92's medicinal approach and genetic target are unique in that no antisense drug has been approved for the treatment of AIDS, and no other drug has the same target on the HIV-1 genome. We are currently seeking to out-license GEM 92 to a third party for further development and do not plan to continue its development on our own.

Preclinical Development

We have a number of antisense compounds in the preclinical testing phase of development. The two principal antisense compounds which we have in preclinical development are:

- GEM 220 is a second generation antisense compound directed against Vascular Endothelial Growth Factor or VEGF. VEGF is a growth factor that contributes to the growth of new blood vessels, which is a process called angiogenesis. In diseases such as cancer, the growth of new blood vessels is critical to the growth of tumors. Because GEM 220 is designed to inhibit VEGF, we believe GEM 220 can inhibit angiogenesis in malignant tumors and in other disease states such as macular degeneration and psoriasis.
- GEM 240 is a second generation antisense compound designed to inhibit mdm2. Mdm2 is a protein found in increased levels in many human cancers. Mdm2 binds to tumor suppressor protein p53, which results in reduced suppression of tumor cells by p53 and thereby contributes to the growth of cancer cells. In animal studies, GEM 240 has been shown to decrease levels of mdm2 in many types of cancer cells, including colon cancer cells, breast cancer cells and brain cancer cells, and in turn to stabilize p53 levels in these cells.

Cancer Therapy Potentiation

Despite the number of advances that have been made in the treatment of human cancers, currently marketed anticancer therapies often fail to produce sustained antitumor benefits to a cancer patient. In addition, standard therapies available to treat malignancies, such as drugs that work due to their toxicity to cells, and other damaging treatments, like radiation, often produce substantial toxic side effects. To address these problems, oncologists have increasingly employed treatment regimens that include a combination of therapies, each of which has demonstrated antitumor activity.

As part of our efforts to develop antisense drugs which could be used as part of cancer combination therapies, we discovered that the combination of oligonucleotide compounds with certain types of anticancer therapies, such as the anticancer prodrug irinotecan (Camptosar®), could enhance or potentiate the antitumor activity of the anticancer therapy included in the combination. These types of anticancer therapies are known as prodrugs because after administration they are metabolized by the body to produce their most active forms.

We are focusing a significant portion of our antitumor research efforts on the combination of an antisense oligonucleotide with irinotecan. Irinotecan is a prodrug that is altered primarily in the liver to generate an active product designated as SN38. SN38 is considered to be the molecule responsible for most of the antitumor activity of irinotecan. SN38 is also implicated in production of the major side effects encountered clinically with irinotecan. When we tested irinotecan in animals in combination with several different oligonucleotides, we noted both incremental non-antisense and antisense specific tumor activity. In addition, in over ten animal tumor models, the co-administration of GEM 231 with irinotecan resulted in enhanced and prolonged suppression of tumor growth in comparison with irinotecan alone.

As part of our ongoing Phase I/II clinical trials of GEM 231, described under "Antisense Technology — Antisense Drug Discovery and Development — Clinical Development — GEM 231 for the Treatment of Cancer," we are studying the combination of GEM 231 and irinotecan in patients with solid tumors. We are conducting the trials at Vanderbilt University Medical Center and the University of Chicago Medical Center.

Cyclicons

With the advent of the human genome project, researchers have identified thousands of genes whose functions have not yet been established. In order to design drugs targeting these genes, it is important to understand the role of each gene in normal and disease conditions.

We have an established program in which our synthetic DNA can be used to determine if a specific gene is a good target for drugs. Our synthetic DNA, designed as antisense molecules, is especially useful in these studies because of its enhanced ability to interact with very specific targets.

We have developed a novel circular-structured oligonucleotide, which we refer to as a Cyclicon, for use in drug target validation, drug discovery and as a probe and primer in PCR amplification. PCR amplification is an important process that is widely used in academic laboratories and the biopharmaceutical industry to produce many DNA copies from a single strand of DNA. We have designed our Cyclicons so that when the circular-structured oligonucleotide binds to messenger RNA, the circular structure of the oligonucleotide is disrupted and fluorescence is emitted. As a result, drug developers can use our Cyclicons as a tool to measure when and where reactions between an antisense sequence and messenger RNA occur.

Research and Development

For the years ended December 31, 2001, 2000 and 1999, we spent approximately $4.9 million, $3.5 million and $4.8 million, respectively, on company-sponsored research and development activities. In addition, for the years ended December 31, 2000, and 1999, we spent approximately $82,500 and $965,000, respectively, on customer-sponsored research and development activities with funds provided by third parties.

Patents, Proprietary Rights and Licenses

Patents and Proprietary Issues

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

As of March 15, 2002, we owned or exclusively licensed 76 issued U.S. patents and 60 U.S. patent applications and 114 corresponding foreign patents and over 140 corresponding foreign patent applications. The issued patents held or exclusively licensed by us include composition of matter patents on our own advanced DNA chemistries covering the use of these chemistries with various genes or sequences, patents covering therapeutic targets, patents covering immune modulation and patents covering oral and other routes of administering our synthetic DNA. These issued patents expire at various dates ranging from 2006 to 2019.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. Our ability to maintain and solidify our proprietary position for our technology will depend on our success in obtaining effective claims and enforcing those claims once granted. We do not know whether any of our patent applications or those patent applications which we license will result in the issuance of any patents. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, invalidated or circumvented, and the rights granted thereunder may not provide us proprietary protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies or duplicate any technology developed by us. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible

that, before any of our products can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thus reducing any advantage of the patent, which could adversely affect our ability to protect future drug development and, consequently, our operating results and financial position.

Because patent applications in the United States and many foreign jurisdictions are typically not published until eighteen months after filing and because publications of discoveries in the scientific literature often lag behind actual discoveries, we cannot be certain that we were the first to make the inventions claimed in each of our issued patents or pending patent applications, or that we were the first to file for protection of the inventions set forth in these patent applications.

Litigation may be necessary to defend against or assert claims of infringement, to enforce patents issued to us, to protect trade secrets or know-how owned by us, or to determine the scope and validity of the proprietary rights of others. In addition, interference proceedings declared by the U.S. Patent and Trademark Office may be necessary to determine the priority of inventions with respect to our patent applications. Litigation or interference proceedings could result in substantial costs to and diversion of effort by us, and could have a material adverse effect on our business, financial condition and results of operations. These efforts by us may not be successful.

Trade Secrets

We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets are difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, scientific advisors and other contractors. There can be no assurance that these agreements will not be breached, that we will have adequate remedies for any breach, or that our trade secrets will not otherwise become known or be independently discovered by competitors. To the extent that our employees, consultants or contractors use intellectual property owned by others in their work for us, disputes may also arise as to the rights in related or resulting know-how and inventions.

Licenses

We are a party to a number of royalty-bearing license agreements under which we have acquired rights to patents, patent applications and technology of third parties. Our principal license agreement is with University of Massachusetts Medical Center. Under the terms of our license agreement with University of Massachusetts Medical Center, we are the worldwide, exclusive licensee under several U.S. issued patents and various patent applications owned by University of Massachusetts Medical Center relating to antisense oligonucleotides and their production and use. Many of these patents and patent applications have corresponding applications on file or corresponding patents in other major industrial countries.

Seventeen of the issued U.S. patents and 28 of the issued foreign patents licensed by us from University of Massachusetts Medical Center broadly claim the use of our hybrid antisense oligonucleotides and ribozymes. The other issued U.S. patents covered by the license agreement include claims covering composition and uses of oligonucleotides based on advanced chemistries, and compositions of certain modified oligonucleotides that are useful for diagnostic tests or assays. The patents licensed to us by University of Massachusetts Medical Center expire at dates ranging from 2006 to 2019. This license expires upon the expiration of the last to expire of the patents covered by the license.

Other license agreements under which we are the licensee include:

- an exclusive license agreement with McGill University covering patent applications relating to synthetic DNA and DNA Methyltransferase,
- an exclusive license agreement with Massachusetts General Hospital covering patents and patent applications jointly owned by us and Massachusetts General Hospital directed to compositions and use of antisense applied to Alzheimer's disease,
- an exclusive license agreement with Louisiana State University covering patents and patent applications jointly owned by us and Louisiana State University relating to MDM2,

- a non-exclusive license agreement with Genzyme Corporation covering patents and patent applications relating to MDM2,
- a non-exclusive license agreement with Integrated DNA Technologies, Inc., covering patents and patent applications that broadly claim chemical modifications to synthetic DNA, and
- an exclusive license agreement with Dr. Yoon S. Cho-Chung covering patents and patent applications relating to protein kinase A.

Under these licenses we are obligated to pay royalties on net sales by us of products or processes covered by a valid claim of a patent or patent application licensed to us. We also are required in some cases to pay a specified percentage of any sublicense income that we may receive. These licenses impose various commercialization, sublicensing, insurance and other obligations on us. Our failure to comply with these requirements could result in termination of the licenses. Each of these licenses terminates upon the expiration of the last to expire of the patents covered by the license.

Corporate Alliances and Spinouts

An important part of our business strategy is to enter into research and development collaborations, licensing agreements and other strategic alliances, primarily with biotechnology and pharmaceutical corporations, to develop and commercialize drugs based on our technologies. We have also established spinout companies in order to obtain external funding for the continued development of our antisense technology in specific disease fields.

Isis Pharmaceuticals, Inc.

In May 2001, we entered into a collaboration and license agreement with Isis. Under the agreement, we granted Isis a license, with the right to sublicense, to our antisense chemistry and delivery patents and patent applications. We retained the right to use these patents and patent applications in our own drug discovery and development efforts and in collaborations with third parties. In consideration of the license, Isis agreed to pay us $15.0 million in cash plus shares of Isis common stock in four installments intended to have an aggregate value of $19.5 million based on the stock price of the Isis common stock on the dates of issuance of the shares. In 2001, Isis paid $15.0 million to us in cash and issued to us 857,143 shares of its common stock having an aggregate fair market value on the dates on which title to the shares was received of $17.3 million. The remaining $4.5 million is due in 2003, subject to possible acceleration depending on the price of Isis' common stock. Isis has also agreed to pay us a portion of specified sublicense income it receives from specified types of sublicenses of our patents and patent applications.

Under the agreement, we licensed from Isis specified antisense patents and patent applications, principally Isis' suite of Rnase H patents. We have the right under the agreement to use these patents and patent applications in our drug discovery and development efforts and in specified types of collaborations with third parties. In consideration of this license, we agreed to pay Isis a total of $6.0 million in cash or in shares of our common stock in three equal annual installments of $2.0 million beginning in May 2002. We also agreed to pay Isis a nominal annual maintenance fee and a modest royalty on sales of products covered by specified patents and patent applications sublicensed to us by Isis.

The licenses granted under the Isis agreement terminate upon the last to expire of the patents and patent applications licensed under the agreement. We may terminate at any time the sublicense by Isis to us of the patents and patent applications for which we have maintenance fee and royalty obligations.

EpiGenesis Pharmaceuticals, Inc.

In April 2001, we commenced a collaboration with EpiGenesis under which we licensed antisense patents, patent applications and technology to EpiGenesis and agreed to collaborate with EpiGenesis on the

development of up to five antisense compounds for the treatment of respiratory diseases. Under the collaboration, EpiGenesis will be responsible for all development and commercialization activities. We received an upfront license fee from EpiGenesis and are entitled to annual minimum royalties, running royalties on product sales and a portion of any sublicense income. The agreement may be terminated by either party upon a material breach of the agreement or by EpiGenesis at any time upon 90 days prior written notice.

OriGenix Technologies Inc.

In January 1999, we and three Canadian institutional investors formed OriGenix to develop and market drugs for the treatment of infectious diseases, with an initial focus on viral diseases. In connection with the formation of OriGenix, we made a cash investment in OriGenix and granted to OriGenix an exclusive, royalty-free worldwide license to our antisense patents, patent applications and technology for the treatment of human papilloma virus, or HPV, and hepatitis B virus infections. In consideration for the cash investment and the license, we received shares of capital of OriGenix. As of March 15, 2002, we owned approximately 25% of the outstanding shares of OriGenix.

HPV infection can cause a variety of warts, including benign genital warts. HPV infection can also lead to cervical cancer. Hepatitis B infections can lead to liver cirrhosis and cancer of the liver. OriGenix has conducted a Phase I clinical trial of ORI-1001 in 30 human volunteers to evaluate the safety of ORI-1001. The results of the trial indicated that ORI-1001 did not cause irritation in the volunteers.

Prior to the sale of Hybridon Specialty Products, or HSP, to Avecia Biotechnology, we were the sole and exclusive supplier of oligonucleotides to OriGenix. In September 2000, in connection with the sale of HSP to Avecia, we and Avecia agreed that for so long as our supply agreement is in effect with Avecia, OriGenix would have the right to purchase oligonucleotides from Avecia on the same terms as we do.

MethylGene Inc.

In 1996, we and three Canadian institutional investors formed MethylGene Inc. In connection with the formation of MethylGene, we made a cash investment in MethylGene and granted to MethylGene an exclusive, royalty-free worldwide license to antisense patents, patent applications and technology owned or exclusively licensed by us from University of Massachusetts Medical Center and McGill University to develop and market the following:

- antisense compounds which inhibit the production of DNA methyltransferase for any indication;
- other methods of inhibiting DNA methyltransferase for any indication; and
- antisense compounds to inhibit up to two additional molecular targets for any indication.

In consideration for the cash investment and the license, we received shares of capital of MethylGene. In 2001, we sold all of our shares in MethylGene for an aggregate purchase price of $7.2 million.

Prior to the sale of HSP to Avecia, we were the sole and exclusive supplier of oligonucleotides to MethylGene. In September 2000, in connection with the sale of HSP to Avecia, we and Avecia agreed that for so long as our supply agreement is in effect with Avecia, MethylGene would have the right to purchase oligonucleotides from Avecia on the same terms as we do.

Academic and Research Collaborations

We have entered into a number of collaborative research relationships with independent researchers, leading academic and research institutions and U.S. government agencies. These research relationships allow us to augment our internal research capabilities and obtain access to specialized knowledge and expertise.

In general, our collaborative research agreements require us to pay various amounts to support the research. We usually procure the synthetic DNA for the collaboration, which the collaborator then tests. If in the course of conducting research under its agreement with us a collaborator, solely or jointly with us, creates any invention, we generally have an option to negotiate an exclusive, worldwide, royalty-bearing license to the

invention. Inventions developed solely by our scientists in connection with a collaborative relationship generally are owned exclusively by us. Most of these collaborative agreements are nonexclusive and can be cancelled with limited notice.

Government Regulation

The testing, manufacturing, labeling, advertising, promotion, export, and marketing, among other things, of drugs are extensively regulated by governmental authorities in the U.S. and other countries. In the U.S., the FDA regulates pharmaceutical products under the Federal Food, Drug, and Cosmetic Act, or FDCA, and other laws. Both before and after approval is obtained, violations of regulatory requirements may result in various adverse consequences, including the FDA's delay in approving or refusal to approve a drug, suspension or withdrawal of an approved product from the market, operating restrictions, and the imposition of civil or criminal penalties.

The steps required before a product may be approved for marketing in the U.S. generally include (i) preclinical laboratory tests and animal tests, (ii) the submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin, (iii) adequate and well-controlled human clinical trials to establish the safety and efficacy of the product, and (iv) satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is made to assess compliance with the FDA's good manufacturing practices regulations, or GMP.

Preclinical tests include laboratory evaluation of the product, as well as animal studies to assess the potential safety and efficacy of a drug. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which must become effective before human clinical trials may be commenced. The IND will automatically become effective 30 days after its receipt by the FDA, unless the FDA before that time raises concerns or questions about the conduct of the trials as outlined in the IND. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed. We cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined, and certain phases may be eliminated. In Phase I, the initial introduction of the drug into human subjects, the drug is usually tested for safety (adverse effects), dosage tolerance, and pharmacologic action. Phase II usually involves studies in a limited patient population to (i) evaluate preliminarily the efficacy of the drug for specific, targeted conditions, (ii) determine dosage tolerance and appropriate dosage and (iii) identify possible adverse effects and safety risks. Phase III trials generally further evaluate clinical efficacy and test further for safety within an expanded patient population. We, or the FDA, may suspend clinical trials at any time on various grounds, including a finding that the patients are being exposed to an unacceptable health risk.

The results of the preclinical and clinical studies, together with other detailed information, including information on the manufacture and composition of the product, are submitted to the FDA as part of a new drug application for approval prior to the marketing and commercial shipment of the product. The FDA may deny a new drug application if all applicable regulatory criteria are not satisfied or may require additional clinical, toxicology or manufacturing data. Even after a new drug application results in approval to market a product, the FDA may withdraw product approval if compliance with regulatory standards is not maintained or if safety problems occur after the product reaches the market. In addition, the FDA requires surveillance programs to monitor the consistency of manufacturing and the safety of approved products that have been commercialized. The agency has the power to require changes in labeling or to prevent further marketing of a product based on new data that may arise after commercialization. Also, new federal, state, or local government requirements may be established that could delay or prevent regulatory approval of our products under development.

We will also be subject to a variety of foreign regulations governing clinical trials and sales of our products. Whether or not FDA approval has been obtained, approval of a product by the comparable regulatory authorities of foreign countries must be obtained prior to the commencement of marketing of the product in those countries. The approval process varies from country to country and the time may be longer or

shorter than that required for FDA approval. For marketing outside the U.S., we are also subject to foreign regulatory requirements governing human clinical trials and marketing approval for products. The requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary greatly from country to country.

In addition to regulations enforced by the FDA, we are also subject to regulation under the Occupational Safety and Health Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, and other present and potential future federal, state, or local regulations. Our research and development activities involve the controlled use of hazardous materials, chemicals and various radioactive compounds. Although we believe that our safety procedures for handling and disposing of such materials comply with the standards prescribed by state and federal 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 such liability could exceed our resources.

Manufacturing

Until September 2001, when we sold HSP to Avecia, we manufactured on our own all of the oligonucleotide compounds that we needed for research, preclinical and clinical purposes. As part of the sale, we entered into a supply agreement with Avecia under which we may purchase our requirements for oligonucleotide compounds from Avecia at a preferential price until March 2003.

We expect that, following the termination of the supply agreement with Avecia, we will seek to enter into arrangements with Avecia or other third-party manufacturers to supply us with the oligonucleotide compounds that we need for our research, preclinical, clinical and commercial supply purposes.

Competition

We expect that our product candidates will address several different markets defined by the potential indications for which these product candidates are developed and ultimately approved by regulatory authorities. For several of these indications, these product candidates will be competing with products and therapies either currently existing or expected to be developed, including IMO compounds and antisense oligonucleotides developed by third parties.

Competition among these products and therapies will be based, among other things, on

- product efficacy,
- safety,
- reliability,
- availability,
- price, and
- patent position.

The timing of market introduction of our products and competitive products will also affect competition among products. We also expect the relative speed with which we can develop products, complete the clinical trials and approval processes and supply commercial quantities of the products to the market to be an important competitive factor. Our competitive position will also depend upon our ability to attract and retain qualified personnel, to obtain patent protection or otherwise develop proprietary products or processes and to secure sufficient capital resources for the often substantial period between technological conception and commercial sales.

There are a number of companies, both privately and publicly held, that are conducting research and development, preclinical and clinical and commercial activities relating to technologies and products that are similar to our technologies and products, including large pharmaceutical companies with programs in IMOs or antisense technology and biotechnology companies with similar programs, such as Isis, Genta Incorporated,

Coley Pharmaceutical Group and Dynavax Technologies Corp. Many of our competitors, particularly the pharmaceutical and large biotechnology companies with which we compete, have substantially greater financial, technical and human resources than we have. In addition, many of our competitors have significantly greater experience than we have in undertaking preclinical studies and human clinical trials of new pharmaceutical products, obtaining FDA and other regulatory approvals of products for use in health care and manufacturing, marketing and selling approved products.

Employees

As of March 15, 2002, we employed 22 individuals full-time, including 14 employees in research and development. Sixteen of our employees had M.D.s and/or Ph.D.s. None of our employees is covered by a collective bargaining agreement, and we consider relations with our employees to be good.

Item 2. ***Properties***

We lease approximately 26,000 square feet of laboratory and office space, including 6,000 square feet of specialized preclinical lab space, in Cambridge, Massachusetts under a lease that expires April 30, 2007. We believe these facilities are adequate to accommodate our needs for the near term.

Item 3. ***Legal Proceedings***

We are not party to any material legal proceedings.

Item 4. ***Submission of Matters to a Vote of Security Holders***

No matters were submitted to a vote of security holders in the quarter ended December 31, 2001.

Executive Officers of Hybridon

The following table sets forth the names, ages and positions of our executive officers and significant employees as of March 15, 2002:

Name	Age	Position
Stephen R. Seiler	45	Chief Executive Officer and Director
Sudhir Agrawal, D. Phil	48	President, Chief Scientific Officer and Director
Robert G. Andersen	51	Chief Financial Officer, Vice President of Operations, Treasurer and Secretary
R. Russell Martin, M.D.	66	Senior Vice President of Drug Development
Jinyan Tang, Ph.D.	58	Vice President of Chemistry

Stephen R. Seiler was appointed our Chief Executive Officer and elected to our board of directors on September 1, 2001. Prior to joining us, Mr. Seiler served as Executive Vice President, Planning Investment & Development at Elan Corporation plc from 1995 to 2001. From 1991 to 1995, Mr. Seiler worked as an Investment Banker at Paribas Capital Markets in both London and New York. He was founder and head of Paribas's pharmaceutical investment banking group. Mr. Seiler received a J. D. from Georgetown University with Honors in 1980 and a B.A. summa cum laude in History from the University of Notre Dame in 1977. He is a member of the bar in New York, Arizona, and Missouri.

Dr. Sudhir Agrawal joined us in 1990 and has served as our Chief Scientific Officer since January 1993, our Senior Vice President of Discovery since March 1994, our President since February 2000 and as a director since March 1993. Prior to his appointment as Chief Scientific Officer, he served as our Principal Research Scientist from February 1990 to January 1993 and as our Vice President of Discovery from December 1991 to January 1993. He served as Acting Chief Executive Officer from February 2000 until September 2001. Prior to joining us, Dr. Agrawal served as a Foundation Scholar at the Worcester Foundation from 1987 through 1991. Dr. Agrawal served as a Research Associate at Research Council Laboratory of Molecular Biology in Cambridge, England from 1985 to 1986, studying synthetic oligonucleotides. Dr. Agrawal received a D. Phil in chemistry in 1980, an M.Sc in organic chemistry in 1975 and a B.Sc. in chemistry, botany and zoology in 1973

from Allahaban University in India. Dr. Agrawal is one of the most published researchers in the field of antisense technology. He is a member of the editorial board of Antisense Research & Development Journal, Trends in Molecular Medicine, Investigational Drug Journal, and Current Cancer Drug Targets, and is associate editor of Molecular Biotechnology.

Robert G. Andersen joined us in November 1996 and has served as our Vice President of Operations since 1997, our Treasurer since March 1998 and our Chief Financial Officer since February 2000. From November 1996 to 1997, he served as our Vice President of Systems Engineering and Management Information Systems. Mr. Andersen also serves as a director of OriGenix, Inc., our spin-off company based in Montreal, Canada. Prior to joining us, Mr. Andersen served in a variety of positions at Digital Equipment Corporation from 1986 to 1996, most recently as Group Manager of the Applied Objects Business Unit. From 1978 to 1986, Mr. Andersen held technical management positions at United Technologies Corporation, most recently as Director of Quality for Otis Elevator Company's European Operations and Worldwide Director of Controls. Mr. Andersen received his B.E.E. magna cum laude in Electrical Engineering from The City College of New York in 1972 and an M.S. in Management from Northeastern University in 1978. He is also a graduate of the United Technologies Advanced Studies Program.

Dr. R. Russell Martin joined us in 1994 and has served as our Senior Vice President of Drug Development since 1998. He served as our Vice President of Drug Development from 1996 through 1998 and our Vice President of Clinical Research from 1994 through 1996. Prior to joining us, Dr. Martin served in a variety of positions at Bristol-Myers Squibb from 1983 to 1993, most recently as Vice President of Infectious Diseases Clinical Research. Dr. Martin received an A.B. degree from Yale University in 1956 and a M.D. degree from the Medical College of Georgia in 1960. From 1971 to 1983, he was on the faculty of Baylor College of Medicine, most recently as Professor of Medicine, Microbiology and Immunology. He is a Fellow of the American College of Physicians and of the Infectious Diseases Society of America.

Dr. Jinyan Tang joined us in 1991 and has served as our Vice President of Chemistry since 2000. Dr. Tang was our Vice President of Process Research and Development from 1995 to 1997 and Vice President of Production from 1997 to 2000. Prior to joining us, Dr. Tang served as Visiting Fellow at the Worcester Foundation from 1988 to 1991. Dr. Tang served as Visiting Research Professor at the University of Colorado in 1988 and Associate Professor at the Shanghai Institute of Biochemistry, Chinese Academy of Sciences from 1985 to 1988 studying oligonucleotide chemistry. Dr. Tang received a B.Sc. in Biochemistry in 1965 and a Ph.D. of Biochemistry in 1978 from the Shanghai Institute of Biochemistry, Chinese Academy of Sciences.

PART II.

Item 5. *Market For Registrant's Common Equity and Related Stockholder Matters*

(a) Market Information

Our common stock is quoted on the OTC Bulletin Board under the symbol "HYBN.OB". Quotes on the OTC Bulletin Board may reflect inter-dealer prices, without retail markups, markdowns or commissions and do not necessarily represent actual transactions.

The following table sets forth, for the periods indicated, the high and low sales prices per share of our common stock during each of the quarters set forth below as reported on the OTC Bulletin Board since January 1, 2000:

	High	Low
2001		
First Quarter	$0.72	$0.41
Second Quarter	1.51	0.41
Third Quarter	1.30	0.70
Fourth Quarter	2.01	0.71
2000		
First Quarter	$6.88	$0.84
Second Quarter	3.44	0.75
Third Quarter	1.31	0.50
Fourth Quarter	1.02	0.28

The reported closing sales price of our common stock on the OTC Bulletin Board on March 15, 2002 was $1.54 per share.

The number of common stockholders of record on March 15, 2002 was 386.

We have never declared or paid cash dividends on our capital stock and we do not expect to pay any cash dividends on our capital stock in the foreseeable future. The indenture under which we issued 9% convertible subordinated notes in April 1997 limits our ability to pay dividends or make other distributions on our common stock or to pay cash dividends on our convertible preferred stock. As of March 15, 2002, $1.3 million in total principal amount of the 9% notes remained outstanding.

Our Series A preferred stock pays dividends at 6.5% per year, payable semi-annually in arrears. These dividends may be paid either in cash or in additional shares of Series A preferred stock, at our discretion subject to the restriction under the indenture described above. As of March 15, 2002, we have only paid these dividends in shares of Series A preferred stock.

(b) Sales of Unregistered Securities

Sales by us during the year ended December 31, 2001 of securities that were not registered under the Securities Act of 1933, as amended, consist of:

- During 2001, holders of 26,079 shares of our Series A preferred stock converted such shares into 613,624 shares of our common stock. We relied upon Section 3(a)(9) of the Securities Act of 1933, as amended, as an exemption from registration for the newly issued common stock.
- On April 9, 2001, we issued 46,429 shares of our common stock to Dr. Paul C. Zamecnik, a member of our board of directors, in lieu of $26,000 in director and consulting fees. On December 17, 2001, we issued 16,765 shares of our common stock to Dr. Zamecnik in lieu of $28,500 in director and consulting fees. We relied upon Section 4(2) of the Securities Act of 1933, as amended, as an exemption from registration for the newly issued common stock.

- Between May 14, 2001 and May 24, 2001,we issued 178,571 shares of our common stock in lieu of $100,000 in consulting fees due to an affiliate of Mr. Youssef El Zein and Mr. Nasser Menhall, two members of our board of directors. We relied upon Section 4(2) of the Securities Act of 1933, as amended, as an exemption from registration for the newly issued common stock.
- On July 27, 2001, holders of 78,259 shares of Series B preferred stock converted such shares of Series B preferred stock into 19,564,500 shares of common stock. We relied upon Section 4(2) of the Securities Act of 1933, as amended, as an exemption from registration for the newly issued common stock.
- Between July 27, 2001 and November 20, 2001, holders of approximately $456,000 of 8% notes converted these notes into 1,140,448 shares of common stock. We relied upon Section 4(2) of the Securities Act of 1933, as amended, as an exemption from registration for the newly issued common stock.
- Between July 27, 2001 and October 17, 2001, holders of warrants to purchase an aggregate of 7,661,893 shares of our common stock with exercise prices ranging between $0.60 and $2.40 per share exercised and/or converted such warrants for 4,669,808 shares of our common stock. We relied upon Section 4(2) of the Securities Act of 1933, as amended, as an exemption from registration for the newly issued common stock.
- On October 2, 2001, we issued 50,000 shares of common stock to Dr. James B. Wyngaarden, a member of our board of directors, for services provided to us. On December 17, 2001, we issued 6,765 shares of common stock to Dr. Wyngaarden in lieu of $11,500 in director and committee meeting fees. We relied upon Section 4(2) of the Securities Act of 1933, as amended, as an exemption from registration for the newly issued common stock.

Item 6. *Selected Financial Data*

The selected financial data presented below have been derived from our consolidated financial statements, as adjusted to reflect the disposition of HSP as discontinued operations, and have been audited by Arthur Andersen LLP, independent public accountants. The financial data should be read along with, and are qualified by reference to, "Management's Discussion and Analysis of Financial Condition and Results of Operations," our consolidated financial statements and notes thereto and the Report of Independent Public Accountants included elsewhere in this annual report on Form 10-K.

	Year Ended December 31,				
	2001	2000	1999	1998	1997
	(In thousands, except per share data)				
Statement of Operations Data:					
Revenues:					
Service revenue	$ —	$ 82	$ 365	$ 375	$ —
License fees	850	—	—	—	—
Research and development	—	179	600	1,100	945
Royalty and other income	134	83	123	—	—
Interest income	577	229	92	148	1,079
Total revenues	1,561	573	1,180	1,623	2,024
Operating expenses:					
Research and development	4,868	3,620	5,783	14,183	35,326
General and administrative	4,914	3,184	3,664	6,573	11,027
Stock-based compensation from repriced options	1,762	—	—	—	—
Interest	1,319	2,154	683	2,820	4,278
Restructuring	—	—	—	—	10,345
Total operating expenses	12,863	8,958	10,130	23,576	60,976
Gain on sale of securities, net	5,217	—	—	—	—
Loss before provision for income taxes	(6,084)	(8,385)	(8,950)	(21,953)	(58,952)
Provision for income taxes	500	—	—	—	—
Loss from continuing operations	(6,584)	(8,385)	(8,950)	(21,953)	(58,952)
Income (loss) from discontinued operations	2,663	5,462	(1,553)	(4,028)	(10,509)
Loss before extraordinary items	(3,921)	(2,923)	(10,503)	(25,981)	(69,461)
Extraordinary item:					
Gain on conversion of 9% convertible subordinated notes payable	—	—	—	8,877	—
Loss on conversion of 8% convertible subordinated notes payable	(1,412)	—	—	—	—
Net loss	(5,333)	(2,923)	(10,503)	(17,104)	(69,461)
Accretion of preferred stock dividend	(8,342)	(4,087)	(4,232)	(2,689)	—
Net loss applicable to common stockholders	$ (13,675)	$ (7,010)	$ (14,735)	$ (19,793)	$ (69,461)
Basic and diluted net loss per common share from:					
Continuing operations	$ (0.21)	$ (0.48)	$ (0.57)	$ (1.85)	$ (11.67)
Discontinued operations	0.09	0.31	(0.10)	(0.34)	(2.08)
Extraordinary gain (loss)	(0.05)	—	—	0.75	—
Net loss per share	(0.17)	(0.17)	(0.66)	(1.44)	(13.76)
Accretion of preferred stock dividends	(0.27)	(0.23)	(0.27)	(0.23)	—
Net loss per share applicable to common stockholders	$ (0.44)	$ (0.40)	$ (0.93)	$ (1.67)	$ (13.76)
Shares used in computing basic and diluted net loss per common share(1)	30,820	17,418	15,811	11,859	5,050
Balance Sheet Data:					
Cash, cash equivalents and short-term investments(2)	$ 31,834	$ 3,532	$ 2,552	$ 5,608	$ 2,202
Working capital (deficit)	27,259	(4,238)	(6,534)	(5,306)	(21,992)
Total assets	32,309	10,001	10,717	15,092	30,480
Restricted cash	—	5,000	—	—	3,051
Long-term debt and capital lease obligations, net of current portion	—	—	—	—	1,328
9% convertible subordinated notes payable	1,306	1,306	1,306	1,306	50,000
8% convertible subordinated notes payable	288	8,046	6,100	—	—
Accumulated deficit	(273,868)	(260,193)	(253,183)	(238,448)	(218,655)
Total stockholders' (deficit) equity	(33)	(7,530)	(6,072)	2,249	(46,048)

(1) Computed on the basis described in Note 2(k) of notes to consolidated financial statements appearing elsewhere in this annual report on Form 10-K.

(2) Short-term investments consisted of U.S. government and corporate bonds with maturities greater than ninety days but less than one year from the balance sheet date.

Quarterly Operating Results (Unaudited)

The following table presents the unaudited statement of operations data for each of the eight quarters in the period ended December 31, 2001. The information for each of these quarters is unaudited, but has been prepared on the same basis as the audited financial statements appearing elsewhere in this annual report on Form 10-K. In the Company's opinion, all necessary adjustments, consisting only of normal recurring adjustments, have been made to present fairly the unaudited quarterly results when read in conjunction with the audited financial statements and the notes thereto appearing elsewhere in this document. These operating results are not necessarily indicative of the results of operations that may be expected for any future period.

	Three Months Ended							
	Dec. 31 2001	Sep. 30 2001	Jun. 30 2001	Mar. 31 2001	Dec. 31 2000	Sep. 30 2000	Jun. 30 2000	Mar. 31 2000
	(In thousands, except per share data)							
Statement of Operations Data:								
Revenues	$ 666	$ 344	$ 388	$ 164	$ 361	$ 60	$ 41	$ 112
Operating Expenses:								
Research and development	1,428	1,080	1,259	1,101	826	761	860	1,173
General and administrative	791	1,523	1,253	1,347	844	562	875	903
Stock-based compensation from repriced options	1,415	(577)	924	—	—	—	—	—
Interest	218	515	272	315	297	952	559	346
Total operating expenses	3,852	2,541	3,708	2,763	1,968	2,275	2,294	2,422
Gain (loss) on sale of securities, net	(502)	(1,171)	6,890	—	—	—	—	—
Income (loss) before provision for income taxes	(3,688)	(3,368)	3,570	(2,598)	(1,607)	(2,215)	(2,253)	(2,310)
Provision for income taxes	100	—	400	—	—	—	—	—
Income (loss) from continuing operations	(3,788)	(3,368)	3,170	(2,598)	(1,607)	(2,215)	(2,253)	(2,310)
Income (loss) from discontinued operations	695	1,968	—	—	170	5,868	(182)	(394)
Loss before extraordinary gain	(3,093)	(1,400)	3,170	(2,598)	(1,437)	3,653	(2,435)	(2,704)
Extraordinary item:								
Loss on conversion of 8% convertible subordinated notes payable	—	—	—	(1,412)	—	—	—	—
Net (loss) income	(3,093)	(1,400)	3,170	(4,010)	(1,437)	3,653	(2,435)	(2,704)
Accretion of preferred stock dividend	(1,040)	(5,113)	(1,181)	(1,008)	(975)	(1,021)	(1,021)	(1,071)
Net (loss) income applicable to common stockholders	$(4,133)	$(6,513)	$ 1,989	$(5,018)	$(2,412)	$ 2,632	$(3,455)	$(3,775)
Basic net (loss) income per share applicable to common stockholders	$ (0.09)	$ (0.16)	$ 0.11	$ (0.27)	$ (0.13)	$ 0.15	$ (0.20)	$ (0.23)
Diluted net (loss) income per share applicable to common stockholders	$ (0.09)	$ (0.16)	$ 0.04	$ (0.27)	$ (0.13)	$ 0.15	$ (0.20)	$ (0.23)
Shares Used in Computing Income (Loss) Per Common Share(1)								
Basic	45,559	40,211	18,854	18,489	18,380	17,923	17,243	16,261
Diluted	45,559	40,211	57,174	18,489	18,380	17,923	17,243	16,261

(1) Computed on the basis described in Note 2(k) of Notes to consolidated financial statements appearing elsewhere in this annual report on Form 10-K.

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

We are a leading company in the discovery and development of novel therapeutics and diagnostics using synthetic DNA. Our activities are based on four technologies:

- immunomodulatory oligonucleotide, or IMO, technology, which uses synthetic DNA to modulate responses of the immune system;
- antisense technology, which uses synthetic DNA to inhibit the production of disease-associated proteins at the cellular level;
- cancer therapy potentiation, which uses synthetic DNA to enhance the antitumor activity of certain marketed anticancer drugs; and
- Cyclicon technology, which uses novel synthetic DNA structures which we refer to as Cyclicons, in drug target validation and drug discovery.

Since we began operations in February 1990, we have been involved primarily in research and development and manufacturing. To date, almost all of our revenues have been from collaborative and license agreements, interest income and manufacturing of synthetic DNA and reagent products by our DNA manufacturing business, known as the Hybridon Specialty Products Division, or HSP, prior to our selling HSP in September 2000.

We have incurred total losses of $273.9 million through December 31, 2001 and expect to incur substantial operating losses in the future. In order to commercialize our therapeutic products, we need to address a number of technological challenges and to comply with comprehensive regulatory requirements. We expect that our research and development and general and administrative expenses will be significant in 2002 as we use the cash resources that we obtained in 2000 and 2001 to advance more rapidly our discovery and development programs.

Developments in 2000 and 2001

During 2000 and 2001 we entered into a series of transactions that resulted in the disposition of some of our assets, a decrease in our outstanding debt from $15.3 million at December 31, 2000 to $1.6 million at December 31, 2001, and an increase in our cash, cash equivalents and short-term investments from $8.5 million at December 31, 2000 to $31.8 million at December 31, 2001.

HSP Sale. In September 2000, we sold HSP and related intellectual property to Avecia Biotechnology for $15.0 million. We received $12.0 million at the closing of the sale and the remaining $3.0 million in September 2001.

Our consolidated financial statements have been restated to reflect the financial results of HSP as a discontinued operation for the years ended December 31, 2000 and 1999. Reported revenues, expenses and cash flows exclude the operating results of the discontinued operations.

Exchange of 8% Notes. In March 2001, holders of $7.6 million of our 8% notes exchanged their notes for 76,046 shares of our Series B preferred stock. As part of the exchange, the 8% note holders released their security interest in $5.0 million of the proceeds from the sale of HSP, which had been held by them as collateral prior to the exchange.

Sale of MethylGene Shares and Payment of Loan. In April and May 2001, we sold our shareholdings in MethylGene which, at the time, represented 22% of the capital of MethylGene. We received total proceeds of $7.2 million from the sale. We used $3.0 million of the proceeds to reduce a $6.0 million loan from six of our stockholders. In September 2001, we paid off the remaining $3.0 million of this loan. In connection with the payoff of the $6.0 million loan, $0.8 million previously deposited to secure the loan was released.

Collaboration and License Agreement with Isis Pharmaceuticals. In May 2001, we entered into a collaboration and license agreement with Isis Pharmaceuticals, Inc. In consideration of the license, Isis agreed to pay us $15.0 million in cash plus shares of Isis common stock in four installments intended to have an

aggregate value of $19.5 million based on the stock price of the Isis common stock on the dates of issuance of the shares. In 2001, Isis paid $15.0 million to us in cash and issued to us 857,143 shares of its common stock having an aggregate fair market value on the dates on which title to the shares was received of $17.3 million. The remaining $4.5 million is due in 2003, subject to possible acceleration depending on the price of Isis' common stock. In addition, under the agreement, we licensed from Isis specified antisense patents and patent applications. In return, we agreed to pay Isis a total of $6.0 million in cash or in shares of our common stock in three equal annual installments of $2.0 million beginning in May 2002. In accordance with terms of our license agreement with University of Massachusetts Medical Center, we paid the University of Massachusetts Medical Center $1.2 million in respect of the consideration we received from Isis and have agreed to pay University of Massachusetts Medical Center an additional $0.2 million upon our receipt of the last $4.5 million installment from Isis.

Completion of Early Exercise Program. In the second half of 2001, we completed an "early exercise" program in which we exchanged shares of our common stock for shares of our Series B preferred stock, outstanding warrants and 8% notes. As part of this program:

- holders of our Series B preferred stock exchanged their shares of Series B preferred stock for 19,564,500 shares of our common stock;
- holders of warrants to purchase our common stock with exercise prices per share ranging between $0.60 and $2.40 exchanged their warrants for 4,669,808 shares of our common stock; and
- holders of $456,000 of our 8% notes exchanged such notes for 1,140,448 shares of our common stock.

Critical Accounting Policies

This management's discussion and analysis of financial condition and results of operations presents our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. On an ongoing basis, management evaluates its estimates and judgments, including those related to revenue recognition. Management bases its estimates and judgments on historical experience and on various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We believe the most critical accounting policy affecting the portrayal of our financial condition is revenue recognition. We recognize revenue in accordance with SEC Staff Accounting Bulletin (SAB) No. 101. SAB 101 requires that four basic criteria be met before revenue can be recognized:

- persuasive evidence of an arrangement exists;
- delivery has occurred, services have been rendered or obligations have been satisfied;
- the fee is fixed and determinable; and
- collectibility is reasonably assured.

Determination of the last three criteria are based on management's judgments regarding the fixed nature of the fee charged for services rendered or products delivered and the collectibility of these fees. Should changes in conditions cause management to determine these criteria are not met for any future transactions, revenues recognized for any reporting period could be adversely affected.

During 2001, we received a total of $32.3 million in cash and stock under our collaboration and license agreement with Isis Pharmaceuticals, Inc. This amount and future amounts due under this license agreement are non-refundable. We are recognizing the revenue on a straight-line basis over the 10-year term of the agreement. This deferral of revenue recognition is based on a combination of rights retained by us and a

continuing obligation contained in the license agreement which has been interpreted as neither inconsequential nor perfunctory according to SAB 101. The Company believes that the cost of performing the continuing obligation is not material.

Note 2 to our consolidated financial statements included in this report contains a full description of all our significant accounting policies.

Results of Operations

Years ended December 31, 2001, 2000 and 1999

Revenues

Total revenues increased by $1.0 million, or 180%, from $0.6 million in 2000 to $1.6 million in 2001. The increase was primarily due to license revenues from agreements entered into in 2001 with Isis and EpiGenesis. In connection with the Isis agreement, we recorded $0.8 million in revenues which is net of related costs. The service and research and development revenues in 2000 resulted from services performed by us under a license agreement with MethylGene, which terminated in that year. The increase in total revenues in 2001 also reflected increased interest income from higher cash balances as a result of the payments from Isis and EpiGenesis, the sale of our interest in MethylGene and the sale of HSP.

Total revenues decreased by $0.6 million, or 50%, from $1.2 million in 1999 to $0.6 million in 2000. The decrease was primarily due to a reduction in the services performed by us under our agreements with MethylGene and OriGenix and the termination of a collaboration agreement. These decreases were offset in part by higher interest income from higher cash balances as a result of the sale of HSP.

Research and Development Expenses

Research and development expenses increased by $1.3 million, or 36%, from $3.6 million to $4.9 million in 2001 compared to 2000 and decreased $2.2 million, or 38%, from $5.8 million to $3.6 million in 2000 compared to 1999. The increase in 2001 was primarily attributable to higher payroll costs associated with, among other things, additional personnel hired as we expanded our drug development efforts and higher patent prosecution costs. The decrease in 2000 from 1999 reflected reduced research and development activities as part of a company-wide program to conserve cash. The consolidation of our office and laboratory space into a single facility in Cambridge, Massachusetts and the sale of our Milford, Massachusetts facility, also contributed to the decrease in research and development expenses in 2000.

In 2001, our research and development expenses related primarily to the preclinical development of our IMO technology, including the development of HYB 2055. Although we participated in several clinical trials for GEM 231 in 2001, the trials were hospital-sponsored and the costs for these trials were primarily borne by third parties whose drugs were being tested in the trials in combination with GEM 231. In 2000 and 1999, our research and development expenses also related primarily to the preclinical development of our IMO technology. Given the technological and regulatory hurdles likely to be encountered in the development and commercialization of our products, the future timing and costs of our various research and development programs are uncertain.

General and Administrative Expenses

General and administrative expenses increased $1.7 million, or 53%, from $3.2 million to $4.9 million in 2001 compared to 2000 and decreased $0.5 million, or 16%, from $3.7 million to $3.2 million in 2000 compared to 1999. The increase in 2001 was primarily due to increased professional fees associated with our Early Exchange Program and additional licensing transactions and to increased payroll expenses. The decrease

in 2000 was primarily a result of the consolidation of our office and laboratory space as well as a reduction in business development, public relations, legal and accounting expenses.

Stock-Based Compensation

As a result of a repricing of our stock options in September 1999, some of our outstanding stock options are subject to variable plan accounting. As a result, we incurred a stock-based compensation expense of $1.8 million in 2001. We did not have a stock-based compensation charge prior to 2001 because the fair market value of our common stock at December 31, 2000 was below the exercise price of the repriced options and the accounting rules on repriced options were not effective in 1999.

Interest Expense

Interest expense decreased by $0.9 million, or 41%, from $2.2 million to $1.3 million in 2001 compared to 2000 and increased $1.5 million, or 214%, from $0.7 million to $2.2 million in 2000 compared to 1999. The 2001 decrease was primarily attributable to the conversion of $7.6 million of our 8% notes into Series B preferred stock and the repayment of a $6.0 million note payable to six stockholders. The increase in 2000 was primarily due to the issuance of the 8% notes in December 1999 and our borrowing of $1.0 million under a credit facility in 2000.

Gain on Sale of Securities

In May 2001, we received $7.2 million from the sale of our MethylGene shares and recorded a related gain of $6.9 million, which was net of $0.3 million in direct transaction costs. Also in 2001, we recorded a realized loss of $1.4 million attributable to a loss in the value of the Isis shares received under our agreement with Isis and a loss of $0.3 million relating to direct expenses associated with the agreement. This loss was primarily due to a decline in the value of the shares of Isis common stock following the dates of issuance of the shares to us.

Income (Loss) from Discontinued Operations

We realized gains from discontinued operations of $2.7 million and $5.5 million for 2001 and 2000, respectively, and incurred a loss from discontinued operations of $1.6 million in 1999. The 2001 gain primarily represents the receipt of a $3.0 million contingent payment from Avecia under the terms of the HSP sales agreement. The 2000 gain includes gain on the sale of HSP of $6.3 million and operating losses of $0.8 million.

Income Tax Expense

Income tax expense increased from zero in 2000 to $0.5 million in 2001 as a result of income subject to the Alternative Minimum Tax. During 1999, we did not have any income subject to the Alternative Minimum Tax. In March 2002, the National Economic Stabilization and Recovery Act temporarily rescinded the Alternative Minimum Tax as it applies to us. As a result, we will receive a $450,000 refund and recognize a $0.5 million credit to operations during 2002.

Extraordinary Gain (Loss)

We had an extraordinary loss of $1.4 million in 2001 resulting from the exchange of our Series B preferred stock for 8% notes. As a result, our net loss after extraordinary item was $5.3 million in 2001.

Preferred Stock Dividends

We pay dividends on our Series A preferred stock of 6.5% per annum. Between March and July 2001, when all of the Series B preferred stock was exchanged for our common stock, we paid dividends in the form of additional shares of Series B preferred stock of 8.0% per annum. Dividends paid increased from $4.1 million in 2000 to $8.3 million in 2001 mainly due to a $4.1 million charge to retained earnings related to the exchange of our Series B preferred stock for our common stock as part of our Early Exchange Program. The charge is

equal to the fair value of the common stock issued less the fair value of common stock that would have been issued pursuant to the original conversion terms of the Series B preferred stock.

Net Operating Loss Carryforwards

As of December 31, 2001, we had approximately $210.0 million and $4.0 million of net operating loss and tax credit carryforwards, respectively. The Tax Reform Act of 1986 contains provisions that may limit our ability to utilize net operating loss and tax credit carryforwards in any given year if certain events occur, including cumulative changes in ownership interests in excess of 50% over a three-year period. We have completed several financings since the effective date of the Tax Act, which, as of December 31, 2001, have resulted in ownership changes, as defined under the Tax Act, which will limit our ability to utilize all of our net operating loss carryforwards.

Liquidity and Capital Resources

We require cash to fund our operating expenses, to make capital expenditures and to pay debt service. We expect that our cash requirements for these uses will be substantial and will increase as we expand our operations. Historically, we have funded our operations with revenues from the sources described above, particularly in 2001 from our agreement with Isis, as well as from a variety of debt and equity financings, lease financings and the sale of our shareholdings in MethylGene. Our only committed external sources of funds are a $450,000 tax refund expected from the U.S. government in the first half of 2002 and the final $4.5 million payment due to us from Isis under our agreement with it based on relevant market conditions. This payment from Isis is due no later than May 2003 and may be made by Isis, at its option, in cash or with its common stock having a fair market value intended to approximate $4.5 million.

Cash Resources and Cash Flows

We had available cash, cash equivalents and short-term investments of $31.8 million at December 31, 2001, an increase of $28.3 million, from December 31, 2000.

During 2001, we increased our available cash resources through the following:

- $15.5 million in cash received from licensing transactions;
- $15.6 million in net proceeds from the sale of Isis stock obtained in the Isis transaction;
- $7.2 million from the sale of our MethylGene shares;
- $5.0 million in restricted cash that became available for general corporate purposes upon the exchange of our Series B preferred stock for 8% notes; and
- a contingent payment of $3.0 million from the sale of HSP.

During 2000, we increased our cash resources through the sale of HSP, from which we received $12.0 million, although $5.0 million of the $12.0 million was restricted under the terms of our loan agreement. We also borrowed $1.0 million under a credit facility which we subsequently repaid in 2000. During 1999, we raised cash through the issuance of $7.6 million in convertible notes. Principal uses of cash by us in all three years included funding of our operating loss. We also used $6.0 million of cash in 2001 to repay a loan to us from six of our stockholders.

We believe that our existing cash resources will be sufficient to fund our cash requirements through the end of 2003. Our actual cash requirements will depend on many factors, including particularly the scope and pace of our research and development efforts and our success in entering into strategic alliances.

We do not expect to generate significant additional funds internally until we successfully complete development and obtain marketing approval for products, either alone or in collaboration with third parties, which we expect will take many years. We expect to seek additional external funds periodically from collaborations with other biotechnology companies or pharmaceutical companies and from additional debt,

equity and lease financings. We believe that the key factors that will affect our internal and external sources of cash are:

- the success of our clinical and preclinical development programs;
- the receptivity of the capital markets to financings by biotechnology companies; and
- our ability to enter into strategic collaborations with biotechnology and pharmaceutical companies and the success of such collaborations.

We may not be successful in generating funds internally or from external sources. Lack of necessary funds may require us to delay, scale back or eliminate some or all of our research and development programs.

Contractual Obligations

As of December 31, 2001, our outstanding indebtedness consisted of $0.3 million in principal amount of 8% notes maturing in November 2002 and $1.3 million in principal amount of 9% notes maturing in April 2004. These notes are unsecured. Our only lease commitment relates to our facility in Cambridge, Massachusetts. The $29.2 million in deferred revenue that we are amortizing over the 10-year term of the Isis agreement will not require that we expend any significant cash. We expect to make capital expenditures of approximately $500,000 in 2002, principally for leasehold improvements and for purchases of laboratory and computer equipment.

As of December 31, 2001, our contractual obligations were as follows:

	Payments Due by Period				
Contractual Obligations	**Total**	**Less than 1 year**	**1-3 years**	**4-5 years**	**After 5 years**
Debt	$1,594,000	$ 288,000	$1,306,000	—	—
Lease Commitments	$3,268,000	$ 620,000	$1,833,000	$815,000	—
External Collaborations	$ 293,000	$ 116,000	$ 177,000	—	—
Employment Agreements	$1,800,000	$ 360,000	$ 720,000	$720,000	—
Consulting Agreements	$ 98,000	$ 68,000	$ 30,000	—	—
Payments to Isis (1)	$6,000,000	$2,000,000	$4,000,000	—	—

(1) We have the option to make some or all of the payments to Isis in cash or in shares of our common stock.

RISK FACTORS THAT MAY AFFECT RESULTS

This annual report contains forward-looking statements, including statements about our growth and future operating results, discovery and development of drugs, strategic alliances and intellectual property. For this purpose, any statement that is not a statement of historical fact should be considered a forward-looking statement. We often use the words "believes," "anticipates," "plans," "expects," "intends" and similar expressions to help identify forward-looking statements.

There are a number of important factors that could cause our actual results to differ materially from those indicated or implied by forward-looking statements. Factors that could cause or contribute to such differences include those discussed below, as well as those discussed elsewhere in this annual report. We disclaim any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

Risks Relating to Our Business, Strategy and Industry

If our clinical trials are unsuccessful, or if they are significantly delayed, we may not be able to develop and commercialize our products.

In order to obtain regulatory approvals for the commercial sale of our products, we will be required to complete extensive clinical trials in humans to demonstrate the safety and efficacy of our drug candidates. We may not be able to obtain authority from the FDA or other equivalent foreign regulatory agencies to commence or complete these clinical trials.

The results from preclinical testing of a drug candidate that is under development may not be predictive of results that will be obtained in human clinical trials. In addition, the results of early human clinical trials may not be predictive of results that will be obtained in larger scale, advanced stage clinical trials. Furthermore, we, one of our collaborators, or a regulatory agency with jurisdiction over the trials, may suspend clinical trials at any time if the subjects or patients participating in such trials are being exposed to unacceptable health risks, or for other reasons. As an example, in 1997, after reviewing the results from the most recent clinical trial of GEM 91, our lead antisense compound at the time, we determined not to continue the development of GEM 91 and suspended clinical trials of this product candidate.

The rate of completion of clinical trials is dependent in part upon the rate of enrollment of patients. Patient accrual is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the study, the nature of the study, the existence of competitive clinical trials and the availability of alternative treatments. Delays in planned patient enrollment may result in increased costs and prolonged clinical development.

We may not be able to successfully complete any clinical trial of a potential product within any specified time period. In some cases, we may not be able to complete the trial at all. Moreover, clinical trials may not show our potential products to be both safe and efficacious. Thus, the FDA and other regulatory authorities may not approve any of our potential products for any indication.

We face substantial competition which may result in others discovering, developing or commercializing drugs before or more successfully than us.

The field of drug discovery is highly competitive and characterized by rapid and significant technological change. Many of our competitors are substantially larger than us and have substantially greater capital resources, research and development staffs and facilities than us. Furthermore, many of our competitors are more experienced than us in drug discovery, development and commercialization, obtaining regulatory approvals and drug manufacturing and marketing. As a result, our competitors may discover, develop and commercialize drugs based on synthetic DNA before us. In addition, our competitors may discover, develop and commercialize drugs that render non-competitive or obsolete the drugs that we or our collaborators are seeking to develop and commercialize.

Because the products that we may develop will be based on new technologies and therapeutic approaches, the market may not be receptive to these products upon their introduction.

The commercial success of any of our products for which we may obtain marketing approval from the FDA or other regulatory authorities will depend upon their acceptance by the medical community and third party payors as clinically useful, cost-effective and safe. Many of the products that we are developing are based upon new technologies or therapeutic approaches that are relatively new and unproven. As a result, it may be more difficult for us to achieve market acceptance of our products. Our efforts to educate the medical community on these potentially unique approaches may require greater resources than would be typically required for products based on conventional technologies or therapeutic approaches. The safety, efficacy, convenience and cost-effectiveness of our products as compared to competitive products will also affect market acceptance.

Competition for technical and management personnel is intense in our industry and we may not be able to sustain our operations or grow if we are unable to attract and retain key personnel.

Our success is highly dependent on the retention of principal members of our technical and management staff, including Stephen Seiler and Sudhir Agrawal. Furthermore, our future growth will require hiring a significant number of qualified technical and management personnel. Accordingly, recruiting and retaining such personnel in the future will be critical to our success. There is intense competition from other companies and research and academic institutions for qualified personnel in the areas of our activities. If we are not able to continue to attract and retain, on acceptable terms, the qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or grow.

Regulatory Risks

We may not be able to obtain marketing approval for products resulting from our development efforts.

All of the products that we are developing will require additional research and development, extensive preclinical studies and/or clinical trials and regulatory approval prior to any commercial sales. This process is lengthy, often taking a number of years, and expensive.

We may need to successfully address a number of technological challenges in order to complete development of our products. Moreover, these products may not be effective in treating any disease or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining regulatory approval or prevent or limit commercial use.

If we fail to comply with the extensive regulatory requirements to which our products are subject, we could be subject to adverse consequences and penalties.

The testing, manufacturing, labeling, advertising, promotion, export, and marketing, among other things, of our products are subject to extensive regulation by governmental authorities in Europe, the United States, and elsewhere throughout the world.

In general, there can be no assurance that submission of materials requesting permission to conduct clinical trials will result in authorization by the FDA or equivalent foreign regulatory agency to commence clinical trials, or that once clinical trials have begun, testing will be completed successfully within any specific time period, if at all, with respect to any of our products. Once trials are complete and an application for marketing approval has been submitted to the relevant regulatory agency, the regulatory agency may deny the application if applicable regulatory criteria are not satisfied, or may require additional testing or information.

If regulatory approval of a product is granted, such approval may be subject to limitations on the indicated uses for which the product may be marketed or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. As to any product for which we obtain marketing approval, the product, the facilities at which the product is manufactured, any post-approval clinical data and our promotional activities will be subject to continual review and periodic inspections by the FDA and other regulatory agencies.

Both before and after approval is obtained, violations of regulatory requirements may result in various adverse consequences, including the regulatory agency's delay in approving, or refusal to approve a product, suspension or withdrawal of an approved product from the market, operating restrictions, or the imposition of civil or criminal penalties.

We have only limited experience in regulatory affairs and our products are based on new technologies; these factors may affect our ability or the time we require to obtain necessary regulatory approvals.

We have only limited experience in filing and prosecuting the applications necessary to gain regulatory approvals. Moreover, the products that result from our research and development programs will likely be based on new technologies and new therapeutic approaches that have not been extensively tested in humans. The

regulatory requirements governing these types of products may be more rigorous than for conventional drugs. As a result, we may experience a longer regulatory process in connection with any product that we develop based on these new technologies or new therapeutic approaches.

Risks Relating to Our Financial Results and Need for Financing

We have incurred substantial losses and expect to continue to incur losses. We will not be successful unless we reverse this trend.

We have incurred losses in every year since our inception. As of December 31, 2001, we had incurred operating losses of approximately $273.9 million. We expect to continue to incur substantial operating losses in future periods. We have received no revenues from the sale of drugs. To date, almost all of our revenues have been from collaborative and license agreements, interest income and manufacturing of synthetic DNA and reagent products by HSP prior to our selling HSP in September 2000.

We expect to increase our spending significantly in order to expand our infrastructure and research and development programs. As a result, we will need to generate significant revenues to fund this spending. We cannot be certain whether or when we will become profitable because of the significant uncertainties with respect to our ability to generate revenues from the sale of products and from any potential strategic alliances.

We may need additional financing, which may be difficult to obtain. Our failure to obtain necessary financing or doing so on unattractive terms could adversely affect our discovery and development programs and other operations.

We will require substantial funds to conduct research and development, including preclinical testing and clinical trials of our drugs. We will also require substantial funds to conduct regulatory activities and to establish commercial manufacturing, marketing and sales capabilities. Additional financing may not be available when we need it or may not be available on favorable terms.

If we are unable to obtain adequate funding on a timely basis, we may be required to significantly curtail one or more of our discovery or development programs. For example, we significantly curtailed expenditures on our research and development programs during 1999 and 2000 because we did not have sufficient funds available to advance these programs at planned levels. We could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to certain of our technologies, drug candidates or drugs which we would otherwise pursue on our own.

If we raise additional funds by issuing equity securities, further dilution to our then existing stockholders will result. In addition, the terms of the financing may adversely affect the holdings or the rights of such stockholders.

Risks Relating to Collaborators

We need to establish collaborative relationships in order to succeed.

An important element of our business plan is entering into collaborative relationships for the development and commercialization of products based on our discoveries. We face significant competition in seeking appropriate collaborators. Moreover, these arrangements are complex to negotiate and time-consuming to document. We may not be successful in our efforts to establish collaborative relationships or other alternative arrangements.

Reliance on collaborative relationships poses a number of risks, including the following:

- we cannot effectively control whether our collaborators will devote sufficient resources to our programs or products;

- disputes may arise in the future with respect to the ownership of rights to technology developed with collaborators;
- disagreements with collaborators could delay or terminate the research, development or commercialization of products, or result in litigation or arbitration;
- contracts with our collaborators may fail to provide sufficient protection;
- we may have difficulty enforcing the contracts if one of these collaborators fails to perform;
- our collaborators may terminate their collaborations with us, which could make it difficult for us to attract new collaborators or adversely affect the perception of us in the business or financial communities;
- collaborators have considerable discretion in electing whether to pursue the development of any additional drugs and may pursue technologies or products either on their own or in collaboration with our competitors; and
- collaborators with marketing rights may choose to devote fewer resources to the marketing of our products than they do to products that they develop.

Given these risks, it is possible that any collaborative arrangements into which we enter may not be successful. Previous collaborative arrangements to which we were a party with F. Hoffmann-La Roche and G.D. Searle & Co. both were terminated prior to the development of any product. Failure of these efforts could delay our drug development or impair commercialization of our products.

Risks Relating to Intellectual Property

If we are unable to obtain patent protection for our discoveries, the value of our technology and products will be adversely affected. If we infringe patent or other intellectual property rights of third parties, we may not be able to develop and commercialize our products or the cost of doing so may increase.

Our patent positions, and those of other drug discovery companies, are generally uncertain and involve complex legal, scientific and factual questions.

Our ability to develop and commercialize drugs depends in significant part on our ability to:

- obtain patents;
- obtain licenses to the proprietary rights of others on commercially reasonable terms;
- operate without infringing upon the proprietary rights of others;
- prevent others from infringing on our proprietary rights; and
- protect trade secrets.

Third parties may own or control patents or patent applications and require us to seek licenses, which could increase our development and commercialization costs, or prevent us from developing or marketing products.

We may not have rights under some patents or patent applications related to our products. Third parties may own or control these patents and patent applications in the United States and abroad. Therefore, in some cases, to develop, manufacture, sell or import certain of our products, we or our collaborators may choose to seek, or be required to seek, licenses under third party patents issued in the United States and abroad or those that might issue from United States and foreign patent applications. In such event, we would be required to pay license fees or royalties or both to the licensor. If licenses are not available to us on acceptable terms, we or our collaborators may not be able to develop, manufacture, sell or import these products.

We may become involved in expensive patent litigation or other proceedings, which could result in our incurring substantial costs and expenses or substantial liability for damages or require us to stop our development and commercialization efforts.

There has been substantial litigation and other proceedings regarding the patent and other intellectual property rights in the biotechnology industry. We may become a party to patent litigation or other proceedings regarding intellectual property rights. The cost to us of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the cost of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. If a patent litigation or other proceeding is resolved against us, we or our collaborators may be enjoined from developing, manufacturing, selling or importing our drugs without a license from the other party and we may be held liable for significant damages. We may not be able to obtain any required license on commercially acceptable terms or at all.

Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Patent litigation and other proceedings may also absorb significant management time.

Risks Relating to Product Manufacturing, Marketing and Sales

We have no experience selling, marketing or distributing products and no internal capability to do so.

If we receive regulatory approval to commence commercial sales of any of our products, we will face competition with respect to commercial sales, marketing and distribution. These are areas in which we have no experience. To market any of our products directly, we would need to develop a marketing and sales force with technical expertise and with supporting distribution capability. Alternatively, we could engage a pharmaceutical or other healthcare company with an existing distribution system and direct sales force to assist us. There can be no assurance that we will successfully establish sales and distribution capabilities or gain market acceptance for our products. To the extent we enter co-promotion or other licensing arrangements, any revenues we receive will depend on the efforts of third parties and there can be no assurance that our efforts will succeed. If in the future we elect to perform sales, marketing and distribution functions for such types of products ourselves, we would face a number of additional risks, including the need to recruit a large number of additional experienced marketing and sales personnel.

Because we have limited manufacturing experience, we will be dependent on third-party manufacturers to manufacture products for us or will be required to incur significant costs and devote significant efforts to establish our own manufacturing facilities and capabilities.

We have limited manufacturing experience and no commercial scale manufacturing capabilities. In order to continue to develop our products, apply for regulatory approvals and commercialize products, we will need to develop, contract for or otherwise arrange for the necessary manufacturing capabilities.

We currently rely upon third parties to produce material for preclinical and clinical testing purposes and expect to continue to do so in the future. We also expect to rely upon third parties to produce materials required for clinical trials and for the commercial production of our products.

There are a limited number of manufacturers that operate under the FDA's good manufacturing practices regulations capable of manufacturing our products. As a result, we may have difficulty finding manufacturers for our products with adequate capacity for our needs. If we are unable to arrange for third party manufacturing of our products on a timely basis, or to do so on commercially reasonable terms, we may not be able to complete development of our products or market them.

Reliance on third party manufacturers entails risks to which we would not be subject if we manufactured products ourselves, including reliance on the third party for regulatory compliance and quality assurance, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control

and the possibility of termination or nonrenewal of the agreement by the third party, based on its own business priorities, at a time that is costly or inconvenient for us.

If we fail to obtain an adequate level of reimbursement for our products by third party payors, there may be no commercially viable markets for our products.

The availability and levels of reimbursement by governmental and other third party payors affect the market for healthcare products. These third party payors continually attempt to contain or reduce the costs of healthcare by challenging the prices charged for medical products and services. We may not be able to sell our products profitably if reimbursement is unavailable or limited in scope or amount.

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the healthcare system. Further proposals are likely. The potential for adoption of these proposals affects or will affect our ability to raise capital, obtain collaborators and market our products.

We expect to experience pricing pressures in connection with the sale of our drugs due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative proposals.

We face a risk of product liability claims and may not be able to obtain insurance.

Our business exposes us to the risk of product liability claims that is inherent in the manufacturing, testing and marketing of human therapeutic drugs. Although we have product liability and clinical trial liability insurance that we believe is appropriate, this insurance is subject to deductibles and coverage limitations. We may not be able to obtain or maintain adequate protection against potential liabilities. If we are unable to obtain insurance at acceptable cost or otherwise protect against potential product liability claims, we will be exposed to significant liabilities, which may materially and adversely affect our business and financial position. These liabilities could prevent or interfere with our commercialization efforts.

Risks Relating to an Investment in Our Common Stock

Certain provisions of our charter documents, our rights agreement and Delaware law could delay or prevent the sale of our company.

Provisions of our charter documents, our rights agreement and Delaware law may make it more difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change in control would result in the purchase of shares of our common stock at a premium to the market price. In addition, these provisions may limit the ability of stockholders to approve transactions that they may deem to be in their best interest.

Our common stock is considered a "penny stock" and may be difficult to sell.

The SEC has adopted regulations which generally define "penny stock" to be an equity security that has a market price of less than $5.00 per share or an exercise price of less than $5.00 per share, subject to specific exemptions. Presently, the market price of our common stock is substantially less than $5.00 per share and therefore is designated as a "penny stock" according to SEC rules. This designation requires any broker or dealer selling these securities to disclose certain information concerning the transaction, obtain a written agreement from the purchaser and determine that the purchaser is reasonably suitable to purchase the securities. These rules may restrict the ability of brokers or dealers to sell our common stock and may affect the ability of investors to sell their shares. In addition, since our common stock is traded on the OTC Bulletin Board, investors may find it difficult to obtain accurate quotations of our common stock.

Item 7A. ***Quantitative and Qualitative Disclosures About Market Risk***

Historically, our primary exposures have been related to nondollar-denominated operating expenses in Europe. As of December 31, 2001, we have no assets and liabilities related to nondollar-denominated currencies.

We maintain investments in accordance with our investment policy. The primary objectives of our investment activities are to preserve principal, maintain proper liquidity to meet operating needs and maximize yields. Although our investments are subject to credit risk, our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure from any single issue, issuer or type of investments. We do not own derivative financial investment instruments in our investment portfolio.

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

All financial statements required to be filed hereunder are filed as listed under Item 14(a) immediately after the signature page to this report on Form 10-K, and are incorporated herein by this reference.

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

None.

PART III.

The response to the Part III items incorporate by reference certain sections of Hybridon's Proxy Statement for the Annual Meeting of Stockholders to be held on June 19, 2002 (the "2002 Proxy Statement"). The 2002 Proxy Statement will be filed with the Securities and Exchange Commission (the "Commission") on or before April 30, 2002.

Item 10. ***Directors and Executive Officers of Hybridon***

The response to this item is contained under the following captions in the 2002 Proxy Statement: "Election of Directors," "Executive Officers" and "Section 16(a) Beneficial Ownership Reporting Compliance," which sections are incorporated herein by this reference.

Item 11. ***Compensation of Executive Officers***

The response to this item is contained in the 2002 Proxy Statement under the captions: "Certain Transactions," "Compensation of Executive Officers and Directors" and "Report of the Compensation Committee on Executive Compensation," which sections are incorporated herein by this reference

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

The response to this item is contained in the 2002 Proxy Statement under the caption "Security Ownership of Certain Beneficial Owners and Management," which section is incorporated herein by this reference

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

The response to this item is contained in the 2002 Proxy Statement under the captions "Certain Transactions" and "Compensation of Executive Officers and Directors," which sections are incorporated herein by this reference.

PART IV.

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

(a)(1) *Financial Statements.*

(2) We are not filing any financial statement schedules as part of this Annual Report on Form 10-K because they are not applicable or the required information is included in the financial statements or notes thereto.

(3) The list of Exhibits filed as a part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately preceding such Exhibits, and is incorporated herein by this reference.

(b) *Reports on Form 8-K.* On December 21, 2001, Hybridon filed a Current Report on Form 8-K, reporting the adoption of a shareholder rights plan by its board of directors.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, on this 26th day of March 2002.

Hybridon, Inc.

By: /s/ STEPHEN R. SEILER
Stephen R. Seiler
Chief Executive Officer

POWER OF ATTORNEY AND SIGNATURES

We, the undersigned officers and directors of Hybridon, Inc., hereby severally constitute and appoint Stephen R. Seiler and Robert G. Andersen, and each of them singly, our true and lawful attorneys, with full power to them and each of them singly, to sign for us in our names in the capacities indicated below, all amendments to this Annual Report on Form 10-K, and generally to do all things in our names and on our behalf in such capacities to enable Hybridon, Inc. to comply with the provisions of the Securities Exchange Act of 1934, as amended, and all requirements of the Securities and Exchange Commission.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ JAMES B. WYNGAARDEN, M.D. James B. Wyngaarden, M.D.	Chairman of the Board of Directors	March 28, 2002
/s/ STEPHEN R. SEILER Stephen R. Seiler	Chief Executive Officer and Director (Principal Executive Officer)	March 26, 2002
/s/ SUDHIR AGRAWAL, D. PHIL Sudhir Agrawal, D. Phil	President, Chief Scientific Officer and Director	March 28, 2002
/s/ ROBERT G. ANDERSEN Robert G. Andersen	Chief Financial Officer and Vice President of Operations, Treasurer and Secretary (Principal Financial Officer)	March 29, 2002
/s/ ARTHUR W. BERRY Arthur W. Berry	Director	March 26, 2002
/s/ CAMILLE CHEBEIR Camille Chebeir	Director	March 29, 2002
/s/ YOUSSEF EL-ZEIN Youssef El-Zein	Director	March 29, 2002

Signature	Title	Date
/s/ C. KEITH HARTLEY C. Keith Hartley	Director	March 29, 2002
/s/ NASSER MENHALL Nasser Menhall	Director	March 29, 2002
/s/ PAUL C. ZAMECNIK, M.D. Paul C. Zamecnik, M.D.	Director	March 29, 2002

Exhibit Index

Exhibit No.	Description
3.1(1)	Restated Certificate of Incorporation of the Registrant, as amended.
3.2(2)	Amended and Restated Bylaws of the Registrant.
4.1(2)	Specimen Certificate for shares of Common Stock, $.001 par value, of the Registrant.
4.2(3)	Indenture dated as of March 26, 1997 between Forum Capital Markets LLC and the Registrant.
4.3(4)	Certificate of Designation of Series A Preferred Stock, par value $.01 per share, dated May 5, 1998.
4.4(4)	Class A Warrant Agreement dated May 5, 1998.
4.5(4)	Class B Warrant Agreement dated May 5, 1998.
4.6(4)	Class C Warrant Agreement dated May 5, 1998.
4.7(5)	Rights Agreement dated December 10, 2001 by and between the Registrant and Mellon Investor Services LLC, as rights agent.
†10.1(2)	License Agreement dated February 21, 1990 and restated as of September 8, 1993 between the Registrant and University of Massachusetts Medical Center.
†10.2(2)	Patent License Agreement effective as of October 13, 1994 between the Registrant and McGill University.
†10.3(2)	License Agreement effective as of October 25, 1995 between the Registrant and the General Hospital Corporation.
†10.4(2)	License Agreement dated as of October 30, 1995 between the Registrant and Yoon S. Cho-Chung.
†10.5(2)	System Design and Procurement Agreement dated as of December 16, 1994 between the Registrant and Pharmacia Biotech, Inc.
10.6(2)	Registration Rights Agreement dated as of February 21, 1990 between the Registrant, the Worcester Foundation for Biomedical Research, Inc. and Paul C. Zamecnik.
10.7(2)	Registration Rights Agreement dated as of June 25, 1990 between the Registrant and Nigel L. Webb.
10.8(2)	Registration Rights Agreement dated as of February 6, 1992 between the Registrant and E. Andrews Grinstead, III.
10.9(2)	Registration Rights Agreement dated as of February 6, 1992 between the Registrant and Anthony J. Payne.
††10.10(2)	1990 Stock Option Plan, as amended.
††10.11(2)	1995 Stock Option Plan.
††10.12(2)	1995 Director Stock Plan.
††10.13(2)	1995 Employee Stock Purchase Plan.
††10.14(7)	Employment Agreement dated March 1, 1997 between the Registrant and Dr. Sudhir Agrawal.
††10.15(2)	Consulting Agreement dated as of February 21, 1990 between the Registrant and Dr. Paul C. Zamecnik.
10.16(6)	Registration Rights Agreement dated as of January 24, 1996 between the Registrant and G.D. Searle & Co.
10.17(8)	Registration Rights Agreement dated as of March 26, 1997 between Forum Capital Markets LLC and the Registrant.
10.18(8)	Warrant Agreement dated as of March 26, 1997 between Forum Capital Markets LLC and the Registrant.

Exhibit No.	Description
†10.19(9)	Amendment No. 1 to License Agreement, dated as of February 21, 1990 and restated as of September 8, 1993, by and between University of Massachusetts Medical Center and the Registrant, dated as of November 26, 1996.
†10.20(10)	Licensing Agreement dated March 12, 1999 by and between Hybridon, Inc. and Integrated DNA Technologies, Inc.
†10.21(11)	Licensing Agreement dated September 7, 1999 by and between Hybridon, Inc. and Genzyme Corporation.
10.22(12)	Form of Subscription Agreements dated as of December 13, 1999, by and among Hybridon and the purchasers of notes due 2002.
10.23(12)	License Agreement dated September 20, 2000 by and between Hybridon and Boston Biosystems, Inc.
10.24(12)	Assignment of Coexclusive License dated September 20, 2000 by and between Hybridon and the Public Health Service.
10.25(12)	Oligonucleotide Purification Patent License Agreement dated September 20, 2000 by and between Hybridon and Boston Biosystems, Inc.
10.26(13)	Asset Purchase Agreement dated June 29, 2000 by and between Hybridon and Boston Biosystems, Inc.
†10.27(12)	Assignment of Patent Rights dated September 20, 2000 by and between Hybridon and Boston Biosystems, Inc.
†10.28(12)	PNT Monomer Patent License and Option Agreement dated September 20, 2000 by and between Hybridon and Boston Biosystems, Inc.
†10.29(12)	Agreement Relating to Patents Forming Part of Acquired Assets but to be Licensed Back to Hybridon for the Purposes of OriGenix Agreements dated September 20, 2000 by and between Hybridon and Boston Biosystems, Inc.
10.30(14)	Agreement dated March 28, 2001 by and between Hybridon, Founders Financial Group, Pecks Management Partners L.T.D. and General Motors Investment Management Corporation, in its capacity as Trustee for the General Motors Employees Global Trust Group.
10.31(14)	Stock Purchase Agreement by and between Paul Capital Partners L.P. and PCP Associates and Hybridon dated March 30, 2001.
10.32(14)	Agreement and Mutual Release between Hybridon and MethylGene, Inc. dated March 21, 2001.
10.33(14)	Offer to Exchange Series B Preferred Stock of Hybridon, Inc. dated March 5, 2001.
10.34(15)	Amended and Restated 1997 Stock Incentive Plan.
†10.35(16)	Collaboration and License Agreement by and between Isis Pharmaceuticals, Inc., and Hybridon, Inc., dated May 24, 2001.
10.36(16)	Master Agreement relating to the Cross License of Certain Intellectual Property and Collaboration by and between Isis Pharmaceuticals, Inc. and Hybridon, Inc., dated May 24, 2001.
10.37(16)	Share Purchase Agreement between Hybridon, Inc. and Royal Bank Ventures, Inc., Fonds De Solidarite Des Travailleurs Du Quebec (F.T.Q.), and Ontario Teacher's Pension Plan Board, dated May 11, 2001.
††10.38(17)	Employment Agreement by and between Stephen R. Seiler the Company effective as of July 25, 2001.
10.39	Unit Purchase Agreement by and among Registrant and certain persons and entities listed therein, dated April 1, 1998.

Exhibit No.	Description
10.40	Offer to Exchange Hybridon Warrants and Shares of Series B Convertible Preferred Stock, dated July 29, 2001.
21.1	Subsidiaries of the Registrant.
23.1	Consent of Arthur Andersen LLP.
99.1	Letter to Securities and Exchange Commission from Hybridon pursuant to temporary Note 3T.

(1) Incorporated by reference to Exhibits to the Registrant's Amendment No. 1 to Form 8-A dated December 21, 2001. (File No. 0-27352)

(2) Incorporated by reference to Exhibits to the Registrant's Registration Statement on Form S-1 (File No. 33-99024).

(3) Incorporated by reference to Exhibits to the Registrant's Current Report on Form 8-K dated April 2, 1997. (File No. 0-27352)

(4) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended March 31, 1998. (File No. 0-27352)

(5) Incorporated by reference to Exhibits to the Registrant's Current Report on Form 8-K filed on December 21, 2001. (File No. 0-27352)

(6) Incorporated by reference to Exhibits to the Registrant's Annual Report on Form 10-K for the year ended December 31, 1995. (File No. 0-27352)

(7) Incorporated by reference to Exhibits to the Registrant's Annual Report on Form 10-K for the year ended December 31, 1996. (File No. 0-27352)

(8) Incorporated by reference to Exhibits to Registrant's Current Report on Form 8-K, dated April 2, 1997. (File No. 0-27352)

(9) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended June 30, 1997. (File No. 0-27352)

(10) Incorporated by reference to Exhibits to the Registrant's Annual Report on Form 10-K for the year ended December 31, 1998. (File No. 0-27352)

(11) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended September 30, 1999. (File No. 0-27352)

(12) Incorporated by reference to Exhibits to the Registrant's Registration Statement on Form S-1 (File No. 333-69649).

(13) Incorporated by reference to the Registrant's Proxy Statement dated August 8, 2000. (File No. 0-27352)

(14) Incorporated by reference to Exhibits to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2000. (File No. 0-27352)

(15) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended March 31, 2001. (File No. 0-27352)

(16) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended June 30, 2001. (File No. 0-27352)

(17) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended September 30, 2001. (File No. 0-27352)

† Confidential treatment granted as to certain portions, which portions are omitted and filed separately with the Commission.

†† Management contract or compensatory plan or arrangement required to be filed as an Exhibit to the Annual Report on Form 10-K.

HYBRIDON, INC. AND SUBSIDIARIES

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS
December 31, 2001

REPORT OF INDEPENDENT PUBLIC ACCOUNTANTS

To Hybridon, Inc.:

We have audited the accompanying consolidated balance sheets of Hybridon, Inc. (a Delaware corporation) as of December 31, 2001 and 2000, and the related consolidated statements of operations, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2001. These financial statements are the responsibility of Hybridon, Inc.'s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits 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 audits provide a reasonable basis for our opinion.

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

/s/ ARTHUR ANDERSEN LLP

Boston, Massachusetts
February 21, 2002

HYBRIDON, INC. AND SUBSIDIARIES

CONSOLIDATED BALANCE SHEETS

	December 31, 2001	December 31, 2000
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 20,923,295	$ 1,532,155
Short-term investments	10,910,987	2,000,000
Receivables	274,863	368,915
Prepaid expenses and other current assets	56,992	40,104
Total current assets	32,166,137	3,941,174
Property and equipment, net	143,298	90,678
Other assets:		
Deferred financing costs	—	969,631
Restricted cash	—	5,000,000
	$ 32,309,435	$ 10,001,483
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 498,642	$ 1,084,330
Accrued expenses	1,021,660	1,094,735
Current portion of long-term debt	288,028	6,000,000
Current portion of deferred revenue	3,098,654	—
Total current liabilities	4,906,984	8,179,065
9% convertible subordinated notes payable	1,306,000	1,306,000
8% convertible notes payable	—	8,046,420
Deferred revenue, net of current portion	26,129,725	—
Commitments and Contingencies (Note 10)		
Stockholders' equity (deficit):		
Preferred stock, $0.01 par value Authorized — 5,000,000 shares Series A convertible preferred stock Designated — 1,500,000 shares Issued and outstanding — 640,166 and 626,170 shares at December 31, 2001 and 2000, respectively	6,402	6,262
Common stock, $0.001 par value Authorized — 100,000,000 shares Issued and outstanding — 45,632,525 and 18,382,237 shares at December 31, 2001 and 2000, respectively	45,632	18,382
Additional paid-in capital	273,870,458	252,645,636
Accumulated deficit	(273,868,184)	(260,193,046)
Deferred compensation	(87,582)	(7,236)
Total stockholders' deficit	(33,274)	(7,530,002)
	$ 32,309,435	$ 10,001,483

The accompanying notes are an integral part of these consolidated financial statements.

HYBRIDON, INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF OPERATIONS

	Years Ended December 31,		
	2001	2000	1999
Revenues:			
Service revenue	$ —	$ 82,500	$ 365,000
License fees	849,866	—	—
Research and development	—	179,277	600,000
Royalty and other income	134,225	82,826	122,544
Interest income	577,267	228,695	92,202
Total revenues	1,561,358	573,298	1,179,746
Operating expenses:			
Research and development	4,868,035	3,620,203	5,783,092
General and administrative	4,913,654	3,184,017	3,663,811
Stock-based compensation from repriced options (1)	1,761,657	—	—
Interest	1,319,387	2,153,831	683,134
Total operating expenses	12,862,733	8,958,051	10,130,037
Gain on sale of securities, net	5,217,451	—	—
Loss before provision for income taxes	(6,083,924)	(8,384,753)	(8,950,291)
Provision for income taxes	500,000	—	—
Loss from continuing operations	(6,583,924)	(8,384,753)	(8,950,291)
Income (loss) from discontinued operations	2,662,597	5,462,154	(1,552,751)
Loss before extraordinary item	(3,921,327)	(2,922,599)	(10,503,042)
Extraordinary item:			
Loss on conversion of 8% convertible subordinated notes payable	(1,411,876)	—	—
Net loss	(5,333,203)	(2,922,599)	(10,503,042)
Accretion of preferred stock dividends	(8,341,935)	(4,087,317)	(4,232,251)
Net loss applicable to common stockholders	$(13,675,138)	$(7,009,916)	$(14,735,293)
Basic and diluted net loss per share (Note 14)	$ (0.44)	$ (0.40)	$ (0.93)
Shares used in computing basic and diluted net loss per common share	30,820,098	17,418,233	15,810,664
(1) The following summarizes the allocation of stock based compensation from repriced options			
Research and development	$ 1,060,404	$ —	$ —
General and administrative	701,253	—	—
Total	$ 1,761,657	$ —	$ —

The accompanying notes are an integral part of these consolidated financial statements.

HYBRIDON, INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock					
	Number Of Shares	$0.01 Par Value	Number Of Shares	$0.01 Par Value	Number Of Shares	$0.001 Par Value	Additional Paid-In Capital	Accumulated Deficit	Deferred Compensation	Total Stockholders' Equity (Deficit)
Balance, December 31, 1998	641,259	$6,413	—	—	15,304,825	$15,305	$241,632,024	$(238,447,837)	$(957,127)	$ 2,248,778
Issuance of common stock to placement agents	—	—	—	—	460,000	460	999,540	—	—	1,000,000
Conversion of preferred into common stock	(21,076)	(211)	—	—	495,897	496	(285)	—	—	—
Issuance of warrants in connection with notes payable	—	—	—	—	—	—	547,328	—	—	547,328
Preferred stock dividends	41,673	416	—	—	—	—	4,231,835	(4,232,251)	—	—
Issuance of stock options to non-employees	—	—	—	—	—	—	402,889	—	—	402,889
Amortization of deferred compensation	—	—			—	—	—	—	231,744	231,744
Net loss	—	—	—	—	—	—	—	(10,503,042)	—	(10,503,042)
Balance, December 31, 1999	661,856	6,618	—	—	16,260,722	16,261	247,813,331	(253,183,130)	(725,383)	(6,072,303)
Exercise of common stock options	—	—	—	—	335,240	336	167,287	—	—	167,623
Retirement of common stock	—	—	—	—	(250,000)	(250)	—	—	—	(250)
Cancellation of stock options	—	—	—	—	—	—	(50,781)	—	50,781	—
Revaluation of stock options issued to non-employees	—	—	—	—	—	—	(449,665)	—	449,665	—
Preferred stock dividends	41,363	414	—	—	—	—	4,086,903	(4,087,317)	—	—
Issuance of stock options to non-employees	—	—	—	—	—	—	117,523	—	—	117,523
Issuance of warrants in connection with line of credit	—	—	—	—	—	—	731,136	—	—	731,136
Conversion of debt into common stock	—	—	—	—	214,043	214	230,953	—	—	231,167
Conversion of preferred into common stock	(77,049)	(770)	—	—	1,822,232	1,821	(1,051)	—	—	—
Amortization of deferred compensation	—	—	—	—	—	—	—	—	217,701	217,701
Net loss	—	—	—	—	—	—	—	(2,922,599)	—	(2,922,599)
Balance, December 31, 2000	626,170	6,262	—	—	18,382,237	18,382	252,645,636	(260,193,046)	(7,236)	(7,530,002)
Exercise of common stock options and warrants	—	—	—	—	4,965,715	4,966	312,228	—	—	317,194
Sale of common stock	—	—	—	—	510,000	510	427,890	—	—	428,400
Issuance of stock, stock options and warrants for services	—	—	—	—	298,530	298	898,269	—	(10,756)	887,811
Issuance of stock bonus	—	—	—	—	157,471	157	88,419	—	—	88,576
Issuance of stock options to employees	—	—	—	—	—	—	112,192	—	(112,192)	—
Amortization of deferred compensation	—	—	—	—	—	—	—	—	42,602	42,602
Conversion of 8% notes into stock	—	—	76,046	760	1,140,448	1,140	9,301,791	—	—	9,303,691
Preferred stock dividends	40,075	401	2,213	22	—	—	8,341,512	(8,341,935)	—	—
Conversion of preferred into common stock	(26,079)	(261)	(78,259)	(782)	20,178,124	20,179	(19,136)	—	—	—
Stock-based compensation from repriced options	—	—	—	—	—	—	1,761,657	—	—	1,761,657
Net Loss	—	—	—	—	—	—	—	(5,333,203)	—	(5,333,203)
Balance, December 31, 2001	640,166	$6,402	—	—	45,632,525	$45,632	$273,870,458	$(273,868,184)	$ (87,582)	$ (33,274)

The accompanying notes are an integral part of these consolidated financial statements.

HYBRIDON, INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Years Ended December 31,		
	2001	2000	1999
Cash Flows From Operating Activities:			
Net loss	$(5,333,203)	$(2,922,599)	$(10,503,042)
Income (loss) from discontinued operations	2,662,597	5,462,154	(1,552,751)
Loss from continuing operations, including extraordinary item	(7,995,800)	(8,384,753)	(8,950,291)
Adjustments to reconcile net loss to net cash used in operating activities —			
Extraordinary loss on exchange of 8% convertible subordinated notes payable	1,411,876	—	—
Gain on sale of property and equipment	(45,560)	—	—
Realized loss on trading securities	1,664,810	—	—
Stock-based compensation	1,850,233	117,523	—
Depreciation and amortization expense	37,703	115,403	394,381
Amortization of deferred compensation	42,602	217,701	634,633
Amortization of deferred financing costs	162,465	456,919	123,140
Issuance of common stock warrants	—	731,136	—
Non cash interest expense	912,224	151,077	65,485
Issuance of common stock for services rendered	177,786	—	—
Changes in operating assets and liabilities —			
Receivables	(243,351)	(140,875)	114,694
Prepaid expenses and other current assets	(6,301)	30,298	209,341
Note receivable from officer	—	—	(11,400)
Accounts payable and accrued expenses	(506,387)	(935,000)	(1,153,013)
Deferred revenue	12,654,116	—	—
Net cash provided by (used in) continuing operating activities	10,116,416	(7,640,571)	(8,573,030)
Net cash provided by (used in) discontinued operations	3,000,000	11,563,672	(130,581)
Cash Flows From Investing Activities:			
Increase in other assets	—	(101,401)	—
Purchases of marketable securities	(13,653,578)	(2,000,000)	—
Proceeds from sale and maturities of securities	20,227,470	—	—
Purchases of property and equipment	(90,322)	(35,572)	(8,303)
Proceeds from sale of property and equipment	45,560	—	—
Net cash provided by (used in) investing activities	6,529,130	(2,136,973)	(8,303)
Cash Flows From Financing Activities:			
Net proceeds from sale of common stock	428,400	167,623	—
Net borrowings under line of credit	—	231,167	—
Proceeds from exercise of common stock options and warrants	317,194	—	—
Proceeds from issuance of convertible notes payable and warrants	—	1,795,566	4,534,290
Proceeds from related party notes payable	—	—	1,500,000
Payments on long-term debt	(6,000,000)	—	—
Decrease (increase) in restricted cash and other assets	5,000,000	(5,000,000)	—
Increase in deferred financing costs	—	—	(378,587)
Net cash (used in) provided by financing activities	(254,406)	(2,805,644)	5,655,703
Net increase (decrease) in cash and cash equivalents	19,391,140	(1,019,516)	(3,056,211)
Cash and cash equivalents, beginning of period	1,532,155	2,551,671	5,607,882
Cash and cash equivalents, end of period	$20,923,295	$ 1,532,155	$ 2,551,671

The accompanying notes are an integral part of these consolidated financial statements.

(1) Organization

Hybridon, Inc. (the Company) was incorporated in the State of Delaware on May 25, 1989. The Company is engaged in the discovery and development of novel therapeutics and diagnostics using synthetic DNA. The Company's activities are based on four technologies: immunomodulatory oligonucleotide (IMO™) technology, which uses synthetic DNA to modulate responses of the immune system; antisense technology, which uses synthetic DNA to inhibit the production of disease-associated proteins at the cellular level; cancer therapy potentiation, which uses synthetic DNA to enhance the antitumor activity of certain marketed anticancer drugs; and Cyclicon™ technology, which uses novel synthetic DNA structures, which we refer to as Cyclicons, in drug target validation and drug discovery.

Since inception, the Company has been primarily engaged in research and development and manufacturing. To date, all revenues received by the Company have been from collaboration and licensing agreements, interest income on investment funds, and manufacturing of synthetic DNA and reagent products by the Company's Hybridon Specialty Products or HSP, business prior to its disposal in September 2000 (see Note 13).

(2) Summary of Significant Accounting Policies

(a) Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

The Company is subject to a number of risks and uncertainties similar to those of other companies of the same size within the biotechnology industry, such as uncertainty of clinical trial outcome, uncertainty of additional funding and history of operating losses.

(b) Principles of Consolidation

In 1999, the consolidated financial statements also reflect the results of the Company's subsidiary, Hybridon S.A. (Europe), a French corporation, prior to dissolution. All material intercompany balances and transactions have been eliminated in consolidation.

(c) Cash Equivalents and Short-Term Investments

The Company considers all highly liquid investments with maturities of 90 days or less when purchased to be cash equivalents. Cash and cash equivalents at December 31, 2001 and 2000 consist of cash and money market funds. The balance at December 31, 2000 excludes restricted cash of $5,000,000 that is included in other assets (see Note 4(c)).

Short-term investments have maturities of greater than three months and mature within one year of the balance sheet date. At December 31, 2001, the Company's short-term investments consisted of corporate and government bonds of approximately $8,929,000 and $1,982,000, respectively. All of the short-term investments mature prior to December 31, 2002. At December 31, 2000, short-term investments consisted of corporate bonds, which matured in January 2001. There were no long-term investments as of December 31, 2001 and 2000, respectively.

The Company accounts for investments in accordance with Statement of Financial Accounting Standards (SFAS) No. 115, *Accounting for Certain Investments in Debt and Equity Securities.* In accordance with

SFAS No. 115, investments that the Company has the positive intent and ability to hold to maturity are classified as "held to maturity" and reported at amortized cost, which approximates fair market value. Management determines the appropriate classification of marketable securities at the time of purchase and reevaluates such designation at each balance sheet date. All of the Company's short-term investments as of December 31, 2001 and 2000 are classified as "held-to-maturity."

Shares received in connection with the license agreement discussed in Note 5 were classified as trading securities in accordance with SFAS No. 115, as the Company's intent was to sell the securities in the short-term. Trading securities are reported at fair value with the changes to the fair value being reported in earnings. Upon execution of the hedging contracts discussed in Note 5, the gains or losses on these securities were offset completely by the losses or gains on the hedging contracts. The Company recorded approximately $306,000 in hedging contract expenses which were included in the gain on sale of securities. The Company also recognized $1,359,000 in losses on trading securities during 2001. There were no unrealized gains or losses at December 31, 2001.

(d) Depreciation and Amortization

Depreciation and amortization are computed using the straight-line method based on the estimated useful lives of the related assets, as follows:

Asset Classification	Estimated Useful Life
Leasehold improvements	Life of lease
Laboratory equipment and other	3 – 5 years

(e) Accrued Expenses

At December 31, 2001 and 2000, accrued expenses consist of the following:

	December 31	
	2001	2000
Payroll and related costs	$ 153,551	$ 127,856
Accrued expenses related to issuance of stock (Note 5)	362,561	—
Other	505,548	966,879
	$1,021,660	$1,094,735

(f) Reclassifications

Amounts in the prior-period consolidated financial statements have been reclassified to conform with the current period's presentation.

(g) Revenue Recognition

Service and research and development revenue is recognized when the services are performed. These revenue categories include drug development, clinical research, bio-analytical work and information services, which include access to research, pre-clinical and clinical information and data from the Company.

In December 1999, the Securities and Exchange Commission issued Staff Accounting Bulletin (SAB) No. 101, *Revenue Recognition*. This bulletin summarizes views of the Staff on applying accounting principles generally accepted in the United States to revenue recognition in financial statements. The Company's current revenue recognition policy complies with SAB No. 101.

During 2001, Hybridon received a total of $32.3 million in cash and stock from its collaboration and license agreement with Isis Pharmaceuticals, Inc. This amount and future amounts due under this license agreement are non-refundable. The Company is recognizing the revenue on a straight-line basis over the 10-year term of the agreement. This deferral of revenue recognition is based on a combination of rights retained by the Company and a continuing obligation contained in the license agreement which has been interpreted as neither inconsequential nor perfunctory according to SAB 101. The Company believes that the cost of performing the continuing obligation is not material. See Notes 5 and 6.

(h) Financial Instruments

SFAS No. 107, *Disclosures About Fair Value of Financial Instruments,* requires disclosure of the estimated fair values of financial instruments. The Company's financial instruments consist of cash and cash equivalents, receivables and debt obligations. The estimated fair values of these financial instruments approximates their carrying values as of December 31, 2001 and 2000, respectively. The estimated fair values have been determined through information obtained from market sources and management estimates. As of December 31, 2001, the Company does not have any material derivative or any other financial instruments as defined by SFAS No. 133, *Accounting for Derivative and Hedging Instruments.*

(i) Concentration of Credit Risk and Significant Customers

As of December 31, 2000, financial instruments that subject the Company to the potential for concentrations of credit risk primarily consisted of receivables of approximately $337,000 relating to Avecia's minimum purchase requirement (see Note 13). As of December 31, 2001, all amounts due from Avecia were received in full. Receivables at December 31, 2001, primarily consisted of approximately $174,000 of interest receivable.

(j) Comprehensive Loss

The Company applies SFAS No. 130, *Reporting Comprehensive Income.* Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from nonowner sources. The Company's comprehensive loss is the same as the reported net loss for all periods presented.

(k) Net Loss per Common Share

The Company applies SFAS No. 128, *Earnings per Share.* Under SFAS No. 128, basic net loss per common share is computed using the weighted average number of shares of common stock outstanding during the period. Diluted net loss per common share is the same as basic net loss per common share for all periods presented as the effects of the Company's potential common stock equivalents are antidilutive (see Note 14).

(l) Segment Reporting

The Company applies SFAS No. 131, *Disclosures About Segments of an Enterprise and Related Information.* SFAS No. 131 establishes standards for reporting information regarding operating segments in annual financial statements and requires selected information for those segments to be presented in interim financial reports issued to stockholders. SFAS No. 131 also establishes standards for related disclosures about products and services and geographic areas. To date, the Company has viewed its operations and manages its business as principally one operating segment. As a result, the financial information disclosed herein represents all of the material financial information related to the Company's principal operating segment. For all of the periods presented, all of the Company's revenues were generated in the United States. As of December 31, 2001 and 2000, all assets were located in the United States.

(m) Derivative Instruments and Hedging

The Company applies SFAS No. 133, *Accounting for Derivative Instruments and Hedging Activities,* as amended by SFAS Nos. 137 and 138. These statements establish accounting and reporting standards for derivative instruments, including derivative instruments embedded in other contracts and for hedging activities. In addition, the Emerging Issues Task Force (EITF) has issued a number of derivative-related tentative and final consensuses. The Company did not own any derivative instruments at December 31, 2001. During 2001, the Company did enter into hedging contracts, all of which expired prior to December 31, 2001 (see Note 5).

(n) Stock-Based Compensation

Effective January 1, 1996, the Company adopted the provisions of SFAS No. 123, *Accounting for Stock-Based Compensation*. The Company has elected to continue to account for employee stock options at intrinsic value, in accordance with Accounting Principles Board (APB) Opinion No. 25, Accounting for Stock Issued to Employees, with disclosure of the effects of fair value accounting on net loss and loss per share on a pro forma basis.

In March 2000, the Financial Accounting Standards Board (FASB) issued Interpretation No. 44 (FIN 44), *Accounting for Certain Transactions Involving Stock Compensation — an Interpretation of APB Opinion No. 25*. This interpretation clarified the application of Accounting Principles Board (APB) Opinion No. 25, *Accounting for Stock Issued to Employees* in specified situations, as defined. The interpretation was effective July 1, 2000, but covers specified events that occurred during the period between December 15, 1998 and July 1, 2000. The adoption of this interpretation did not have any effect on the Company's consolidated financial position or results of operations for the year ended December 31, 2000. See Note 9(f) for the effects of FIN 44 on the Company's 2001 financial statements.

(o) New Accounting Pronouncements

In August 2001, the FASB issued SFAS No. 144, Accounting *for the Impairment or Disposal of Long-Lived Assets*. This statement supercedes SFAS No. 121, *Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to Be Disposed Of*, and the accounting and reporting provisions of 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*. Under this statement, it is required that one accounting model be used for long-lived assets to be disposed of by sale, whether previously held and used or newly acquired, and it broadens the presentation of discontinued operations to include more disposal transactions. The provisions of this statement are effective for financial statements issued for fiscal years beginning after December 15, 2001, and interim periods within those fiscal years, with early adoption permitted. The Company believes this pronouncement will not impact its consolidated financial statements.

(3) Note Receivable from Officer

At December 31, 1999, the Company had a note receivable and accrued interest from a former officer of approximately $270,000, with an interest rate of 6.0% per annum. The Company forgave the note in 2000 and charged this amount to general and administrative expense.

(4) Long-Term Debt

(a) Note Payable

During 1998, the Company entered into a $6.0 million note payable with Founders Financial Group, L.P. (Founders), formerly Forum Capital Markets, L.L.C. and several other investors. The terms of the note

payable were as follows: (i) the maturity was November 30, 2003; (ii) the interest rate was 8%; (iii) interest was payable monthly in arrears, with the principal due in full at maturity of the loan; (iv) the note payable was convertible, at the holders' option, in whole or in part, into shares of common stock at a conversion price equal to $2.40 per share, a premium to fair value at date of issuance, and (v) the note required minimum liquidity, as defined, of $2.0 million. At December 31, 2000, the Company classified the $6.0 million outstanding balance as a current liability because it did not have the financing to remain in compliance with the financial covenants at that time.

On March 28, 2001, the Company entered into an agreement with the note holders whereby it paid, out of the proceeds of the sale of its MethylGene shares discussed in Note 7, $3.0 million to the note holders in partial satisfaction of the note. In addition, the Company deposited the sum of $821,250 in a money market fund for the purpose of securing payment of the balance remaining on notes. This arrangement was made to encourage the holders of these notes to release their security interest in the shares of MethylGene, Inc.

In addition, the Company agreed to reduce the conversion price of the note from $2.40 to $1.50 upon completion of the sale of 60% of the Company's holdings in MethylGene. The Company also agreed to further reduce the conversion price from $1.50 to $0.50 if the balance of the note was not paid in full by the Company before September 30, 2001. Pursuant to Emerging Issues Task Force Issue No. 98-5 (EITF 98-5) *Accounting for Convertible Securities with Beneficial Conversion Features or Contingently Adjustable Conversion Ratios* and EITF 00-27, *Application of Issue No. 98-5 to Certain Convertible Instruments*, since the Company had both the intent and ability to pay the remaining notes prior to September 30, 2001, the Company would measure and recognize any potential beneficial conversion amount only if the Company surrendered its unilateral right to avoid the reduction in the conversion price to $0.50. On September 27, 2001, the Company paid off the remaining $3.0 million to the holders in full satisfaction of the notes. The sum of $821,250 previously deposited to secure the notes held was released to the Company.

(b) 9% Convertible Subordinated Notes Payable

Under the terms of the 9% Convertible Subordinated Notes Payable (the 9% Notes), the Company must make semi-annual interest payments on the outstanding principal balance through the maturity date of April 1, 2004. The 9% Notes are subordinate to substantially all of the Company's existing indebtedness. The 9% Notes are convertible at any time prior to the maturity date at a conversion price equal to $35.0625 per share. Upon a change of control of the Company, as defined, the Company will be required to offer to repurchase the 9% Notes at 150% of the original issue price. As of December 31, 2001, $1,306,000 of the 9% Notes are outstanding.

(c) 8% Convertible Notes Payable

In March 2000, the Company completed an offering of 8% Convertible Notes Payable (the 8% Notes). As of December 31, 2000, the Company had received approximately $7.6 million with respect to the 8% Notes. Under the terms of the 8% Notes, the Company must make semiannual interest payments on the outstanding principal balance through the maturity date of November 30, 2002. If the 8% Notes are prepaid before the maturity date, all noteholders are entitled to receive a warrant to purchase the number of shares of common stock equal to the number of shares of common stock that would be issued using the Conversion Ratio. The 8% Notes are convertible at any time prior to the maturity date at a conversion price equal to $0.60 per share of common stock, subject to adjustment under specified circumstances, as defined.

In addition, in connection with the issuance of the 8% Notes, the holders of the $6.0 million note payable (see Note 4(a)) received a warrant to purchase 2,750,000 shares of the Company's common stock at $0.60 per share. The warrant was granted as consideration to the holders of the $6.0 million note for relinquishing their seniority upon liquidation of the Company to the holders of the 8% Notes. The Company computed the

value of the warrants to be $547,328, using the Black-Scholes option-pricing model. The Company recorded the $547,328 as a deferred financing cost, which was being amortized to interest expense over the term of the 8% Notes.

On July 10, 2000, the holders of the 8% Notes entered into an amendment to the Subordination and Intercreditor Agreement whereby all parties agreed to release their lien on the assets that were conveyed in the HSP sale (see Note 13). In return for this partial release, the Company agreed that it would set aside $5.0 million from the proceeds with which it would purchase a money market instrument and pledge the same as collateral to secure its obligation to the holders of the 8% Notes. The amount of the pledge was to be reduced as the Company's obligations were converted to equity or repaid.

On March 5, 2001, the Company made an offer to the holders of its 8% Notes to exchange their notes in a ratio of one share of a newly-designated class of Series B Convertible Preferred Stock (Series B Preferred Stock) for each $100 in principal amount of notes tendered. On March 30, 2001, holders of $7.6 million of the Company's 8% Notes exchanged their notes for 76,046 shares of Series B Preferred Stock. The Company recorded an extraordinary loss of $1.4 million related to the early extinguishment of the 8% Notes. The extraordinary loss represents the difference between the carrying value of the 8% Notes and the fair value of the Series B Preferred Stock, as determined by the fair market value of the common stock into which the Series B Preferred Stock was convertible and the write-off of deferred financing costs and related legal fees.

As a result of the exchange, the holders of the 8% Notes released their claim on $5.0 million of the HSP Sale proceeds, which was held as collateral prior to the exchange.

Prior to December 31, 2001, approximately $456,000 of the remaining 8% Notes were converted into 1,140,448 shares of common stock and all of the 78,259 shares of Series B Preferred Stock were converted into 19,564,500 shares of common stock. These conversions were based on a reduced conversion price of $0.40 per share which was agreed to with the holders of Series B Preferred Stock and 8% Note holders as part of the Company's early exercise program discussed in Note 9. In accordance with SFAS No. 84, *Induced Conversions of Convertible Debt*, the Company recorded a charge to interest expense of approximately $353,000. The charge was equal to the fair value of the common stock received less the fair value of common stock that would have been received pursuant to the original conversion terms of the 8% Notes.

As of December 31, 2001, $288,028 of the 8% Notes remained outstanding.

(d) Related Party Notes Payable

In connection with the exchange of shares of Series B preferred stock for 8% Notes, the Company converted a promissory note payable to a former officer of the Company with a balance of $196,897 into shares of Series B Preferred Stock and subsequently into shares of common stock on terms identical to those described above.

(e) $2.0 Million Line of Credit

On May 30, 2000, the Company entered into a $2.0 million line of credit agreement in order to provide working capital until the closing of the HSP sale. The Company drew down approximately $1.0 million through August 10, 2000.

The Company agreed to issue the following warrants to purchase common stock at an exercise price of $1.08 per share: (i) 500,000 shares to persons designated by Pillar, (ii) 1,000,000 shares to the lenders, proportionate to their respective interests in the $2.0 million line of credit. The Company computed the value of the warrants to be $731,136, using the Black-Scholes option-pricing model. The Company has amortized this amount to interest expense over the term of the $2.0 million line of credit.

Following the close of the HSP sale, the Company repaid approximately $0.8 million in cash and $0.2 million with 214,043 shares of common stock at $1.08 per share pursuant to the terms of the original agreement. The Company has no additional borrowing capacity under this line of credit.

(5) Collaboration and License Agreement with Isis Pharmaceuticals, Inc.

On May 24, 2001, the Company and Isis Pharmaceuticals, Inc. (Isis) entered into a Collaboration and License Agreement (the Agreement). Under the Agreement, the Company granted Isis a license, with the right to sublicense, the Company's antisense chemistry and delivery patents and patent applications. Isis also agreed to pay the Company a portion of specified sublicense income it receives from specified types of sublicenses of our patents and patent applications. The Company has retained the right to use the patents and patent applications in its own drug discovery and development efforts and in collaboration with third parties. In consideration of the license granted by the Company, Isis has paid $15.0 million to us in cash and issued to us 857,143 shares of its common stock having an aggregate fair market value on the dates on which title to the shares was received of $17.3 million. The remaining $4.5 million installment is due in 2003, subject to possible acceleration depending on the price of Isis' common stock.

Under the terms of EITF 00-8, *Accounting by a Grantee for an Equity Instrument to Be Received in Conjunction with Providing Goods or Services*, the Company values the shares of common stock received from Isis at the time of entitlement. During 2001, 857,143 shares of Isis common stock were issued to Hybridon. The Company recorded $17.3 million once title to those shares was received, which represented the fair value of stock on the date title was received, as deferred revenue. The remaining number of shares of Isis stock issuable to Hybridon is based on specified market conditions, as defined in the Agreement and based on current market conditions, would have a fair market value of $4.5 million. If the stock is trading above or below defined ranges, the fair value of the stock could be materially different. The remaining shares of Isis common stock are payable in 2003, subject to possible acceleration depending on the price of Isis' common stock.

Following the receipt of 357,143 of these shares, the Company entered into a number of hedging contracts to protect against a decline in value of the Isis stock while the Company was awaiting registration of these shares which was necessary before the Company could sell the Isis stock. In accordance with SFAS No. 133, these hedging contracts were derivative instruments and were marked to fair market value with the corresponding changes in fair value recognized in earnings. In accordance with SFAS No. 115, the Company recorded an unrealized loss on the shares of approximately $902,000 prior to entering into these hedging contracts. On November 1, 2001, the Company received an additional 500,000 shares of Isis common stock. The Company did not enter into any hedging contracts in connection with the receipt of these shares and recorded realized loss of approximately $457,000 on the sale of these shares. In addition, the $306,000 in fees associated with the execution of the hedging contracts was also charged to expenses during 2001.

Isis has granted the Company a license to use specified antisense patents and patent applications, principally Isis' suite of RNase H patents. The Company has the right under the agreement to use these patents and patent applications in its drug discovery and development efforts and in specified types of collaborations with third parties. In consideration of this license, the Company agreed to pay Isis a total of $6.0 million in cash or in shares of its common stock in three equal annual installments of $2.0 million beginning in May 2002. The Company also agreed to pay Isis a nominal annual maintenance fee and a modest royalty on sales of products covered by specified patents and patent applications sublicensed to the Company by Isis. The number of shares of Hybridon stock issuable to Isis is based on certain market conditions, as defined in the Agreement, and, based on current market conditions, would have a fair market value of $6.0 million, if the stock remains in a certain price range as defined in the Agreement. If the stock is trading above or below these ranges the fair value of the stock could be materially different.

The Company will recognize revenue related to the Agreement ratably over the 10-year term of the license agreement. "Deferred revenue" on the accompanying consolidated balance sheet relates to the unrecognized portion of the $32.3 million of cash and Isis stock received in 2001, as discussed above. While the amounts received are not refundable under any circumstances and the Company does not believe that it will be required to expend any significant future resources under the Agreement, this revenue has been deferred based on SAB 101, which precludes revenue recognition in cases where future obligations are not interpreted to be "inconsequential and perfunctory". The combination of significant rights retained by the Company and an ongoing obligation of the Company to make two representatives available to attend semi-annual telephonic meetings of a collaboration committee with the licensee, led to the accounting treatment described above. Direct expenses related to the Agreement of approximately $2.4 million consist of professional fees, the fair value of warrants issued to a consultant (see Note 9(b)), and royalties (see Note 6). These expenses will be recognized over the term of the Agreement as a reduction in revenue. The Company will also amortize, as a reduction to revenue over the term of the Agreement, the estimated fair value of the Company's stock that will be paid to Isis, as discussed above. In addition, $343,000 in direct expenses were charged to operations prior to closing the agreement in 2001.

During the year ended December 31, 2001, the Company recognized approximately $781,000 of revenues under the Agreement. The amount recognized is net of approximately $138,000 and $363,000, which represent the amortization of direct costs and the amortization of the estimated value of the stock to be issued to Isis, respectively.

(6) Licensing Agreement

In 1993, the Company entered into a licensing agreement with the Worcester Foundation for Biomedical Research, Inc., which has merged with the University of Massachusetts Medical Center, under which the Company has received exclusive licenses to technology in specified patents and patent applications. The Company is required to make royalty payments based on future sales of products employing the technology or falling under claims of a patent, as well as a specified percentage of sublicense income received related to the licensed technology. Additionally, the Company is required to pay an annual maintenance fee through the life of the patents. As a result of the Agreement with Isis Pharmaceuticals, Inc. (Note 5), the Company paid the University of Massachusetts Medical Center approximately $1,177,000 based on the cash received from Isis and the fair market value at the date of the agreement of the first three installments of stock issued to the Company in 2001, less the fair value of the Hybridon stock to be issued to Isis. In addition, the Company is obligated to pay approximately $177,000 upon the issuance of the fourth installment of Isis stock to the Company.

(7) Investment in MethylGene Inc.

In January 1996, the Company and institutional investors formed a Quebec company, MethylGene Inc., to develop and market specified compounds and procedures to be agreed upon by the Company and MethylGene.

The Company granted to MethylGene exclusive, royalty-free worldwide licenses to the Company's antisense patents, patent applications and technology to develop and market the following: (i) antisense compounds which inhibit the production of DNA methyltransferase for any indication; (ii) other methods of inhibiting DNA methyltransferase for any indication and (iii) antisense compounds to inhibit up to two additional molecular targets for any indication.

The Company acquired a 49% interest in MethylGene for approximately $734,000 and the Canadian investors acquired a 51% interest in MethylGene for a total of approximately $5,500,000. Subsequently, MethylGene raised additional proceeds from outside investors that reduced the Company's ownership interest to 22%.

In May 1998, the agreement between the Company and MethylGene was amended to grant MethylGene a nonexclusive right to use any and all antisense chemistries discovered by the Company or any of its affiliates for a period commencing on May 5, 1998 and ending on the earlier of (i) the effective date of termination by MethylGene of its contract for development services to be provided by the Company; (ii) May 5, 1999, unless MethylGene exercises its option to continue contracting for development services provided by the Company or (iii) May 5, 2000. The amendment expired on May 5, 2000. As additional consideration for this nonexclusive right, MethylGene was required to pay the Company milestone amounts, as defined, and transfer 300,000 shares of MethylGene's Class B shares to the Company. The Company has placed no value on these shares. During 2000 and 1999, the Company recognized $72,500 and $285,000, respectively, of revenue related to this agreement.

Prior to the sale of its HSP business (Note 13), the Company supplied MethylGene with synthetic DNA supply needs and recognized during 2000 and 1999 approximately $26,000 and $1,642,000, respectively, of product revenue from sales to MethylGene in discontinued operations. The Company also sold MethylGene a worldwide, royalty free, paid-up license to manufacture their compounds. The Company recognized approximately $179,000 of revenue in 2000 related to this license sale.

On April 27, 2001, the Company closed the sale of 60% of its holding of shares of Class A and Class B stock of MethylGene to a group of private United States institutional investors. The Company had a 22% interest in MethylGene prior to the sale of its investment. On May 14, 2001, the Company closed the sale of the remaining 40% of its holding with three of MethylGene's other shareholders on terms similar to those agreed to by the institutional investors ($2.85 Canadian or approximately $1.84 US per share as of April 27, 2001). The Company received total proceeds of approximately $7.2 million (US), which was reduced by approximately $300,000 in professional fees. The Company recorded a net gain of approximately $6.9 million on these sales. This gain is included in other income on the accompanying consolidated statement of operations.

(8) OriGenix Technologies, Inc.

In January 1999, the Company and institutional investors formed a Quebec company, OriGenix, to develop and market drugs for the treatment of infectious diseases.

Hybridon received a 49% interest in OriGenix in exchange for specified research and development efforts previously undertaken by the Company that were made available to OriGenix and licensed specified antisense compounds and other technology to OriGenix. Subsequently, OriGenix has raised additional funds from institutional investors that reduced the Company's ownership interest to 28%. The institutional investors acquired a 51% interest in OriGenix for approximately $4.0 million. The Company accounted for its investment in OriGenix under the equity method, and the Company's investment has been reduced to zero at December 31, 2001. During 2000 and 1999, the Company recognized $10,000 and $80,000, respectively, of service revenue from sales of DNA products to OriGenix.

Prior to the sale of its HSP business (Note 13), the Company supplied OriGenix with its synthetic DNA needs. During 2000 and 1999, the Company recognized approximately $90,000 and $16,000, respectively, of product revenue from sales to OriGenix in discontinued operations. Also, the Company sold OriGenix a worldwide, royalty-free, paid-up license to manufacture their compounds.

(9) Stockholders' Equity

(a) Common Stock

The Company has 100,000,000 authorized shares of common stock, $.001 par value, of which 45,632,525 shares were issued and outstanding at December 31, 2001.

Pursuant to the terms of a unit purchase agreement dated as of May 5, 1998, the Company issued and sold a total of 9,597,476 shares of common stock (the "Put Shares") at a price of $2.00 per share. Under the terms of the unit purchase agreement, the initial purchasers (the "Put Holders") of the Put Shares have the right (the "Put Right") to require the Company to repurchase the Put Shares. The Put Right may not be exercised by any Put Holder unless: 1) the Company liquidates, dissolves or winds up its affairs pursuant to applicable bankruptcy law, whether voluntarily or involuntarily; 2) all of the Company's indebtedness and obligations, including without limitation the indebtedness under the Company's then outstanding notes, has been paid in full; and 3) all rights of the holders of any series or class of capital stock ranking prior and senior to the common stock with respect to liquidation, including without limitation the Series A convertible preferred stock, have been satisfied in full.

The Company may terminate the Put Right upon written notice to the Put Holders if the closing sales price of its common stock exceeds $4.00 per share for the twenty consecutive trading days prior to the date of notice of termination. Because the Put Right is not transferable, in the event that a Put Holder has transferred Put Shares since May 5, 1998, the Put Right with respect to those shares has terminated. As a consequence of the Put Right, in the event the Company is liquidated, holders of shares of common stock that do not have Put Rights with respect to such shares may receive smaller distributions per share upon the liquidation than if there were no Put Rights outstanding.

As of December 31, 2001, 5,467,578 of the Put Shares continued to be held in the name of Put Holders. The Company cannot determine at this time whether the Put Rights with respect to the balance of the Put Shares have terminated.

(b) Early Exercise Program

In 2001, the Company began an "early exercise" program (the Early Exercise Program) to exchange its Series B Preferred Stock, several classes of its warrants, and its remaining 8% Notes for shares of the Company's common stock, in order to simplify the Company's capital structure and to reduce the number of outstanding securities which are exercisable for or convertible into shares of its common stock. The Company offered the holders of its Series B shares the right to convert such shares into common stock at a lower conversion price than that set forth in the Certificate of Designation governing the terms of their Series B shares. The Company offered the holders of various warrants the opportunity to immediately exercise their warrants for the purchase of shares covered by such warrants at a reduced exercise price, either by paying the lower exercise price for such shares in cash or by engaging in a "cashless" transaction, whereby they could receive a reduced number of shares of common stock in exchange for warrants of equivalent value. The value of the warrants was determined by the Company based on advice from the Company's investment bankers. The Company offered the holders of its remaining 8% Notes the opportunity to exchange the 8% Notes for shares of the Company's common stock at a reduced conversion price. As of December 31, 2001, the results of the program were as follows:

All holders of the Company's Series B Convertible Preferred Stock have exchanged their shares for 19,564,500 shares of the Company's common stock;

Holders of warrants priced between $0.60 and $2.40 have exchanged their warrants for approximately 4,669,808 shares of the Company's common stock; and

$456,221 in 8% notes was exchanged for 1,140,448 shares of common stock.

In accordance with SFAS No. 84, *Induced Conversions of Convertible Debt,* the Company recorded a charge to retained earnings of approximately $4,100,000 in connection with the conversion of Series B Preferred Stock. The charge was equal to the fair value of the common stock received less the fair value of common stock that would have been received pursuant to the original conversion terms of the Series B

Preferred Stock. This charge was recorded as accretion of preferred stock dividends on the accompanying statement of operations and as a component of the net loss available to common stockholders.

In accordance with SFAS No. 123, *Accounting for Stock-Based Compensation,* the Company did not record any charges related to the warrant exchange as the fair value of the warrants immediately prior to the exchange was equal to the fair value of the common stock issued to the holders as settlement of the warrants. For a discussion of the accounting for the conversion of the 8% Notes see Note 4(c).

(c) Warrants

The Company has the following warrants outstanding and exercisable for the purchase of common stock at December 31, 2001:

Expiration Date	Outstanding and Exercisable	Weighted Exercise Price Per Share
April 2, 2002	588,235	$4.25
December 31, 2002	1,997,188	0.60
May 4, 2003	3,260,731	4.10
November 30, 2003	173,333	3.00
March 31, 2006	500,000	0.50
	6,519,487	
Weighted average exercise price per share		2.74

Substantially all of such warrants expiring in 2002 and 2003 were issued in connection with various equity and debt financings described herein. During 2001, the Company issued warrants to purchase 500,000 shares of common stock to an individual who provided consulting services to the Company. The Company valued these warrants using the Black Sholes pricing model. The warrants' fair value of approximately $570,000 was accounted for as a direct cost of the Isis Agreement (see Note 5). Pursuant to EITF Issue 00-19, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock,* the Company believes that equity classification is appropriate for all outstanding warrants.

(d) Stock Options

In 1990, the Company established the 1990 Stock Option Plan which provides for the grant of incentive stock options and nonqualified stock options. Options granted under this plan vest over various periods and expire no later than 10 years from the date of grant. Under the 1990 Option Plan, in the event of a change in control, as defined, the exercise dates of all options then outstanding shall be accelerated in full and any restrictions on exercising outstanding options issued pursuant to the 1990 Option Plan shall terminate. In October 1995, the Company terminated the issuance of additional options under the 1990 Option Plan. As of December 31, 2001, options to purchase a total of 179,357 shares of common stock remained outstanding under the 1990 Option Plan.

In 1995, the Company established the 1995 Stock Option Plan which provides for the grant of incentive stock options and nonqualified stock options. Options granted under this plan vest over various periods and

expire no later than 10 years from the date of grant. A total of 700,000 shares of common stock may be issued upon the exercise of options granted under this plan. The maximum number of shares with respect to which options may be granted to any employee under the 1995 Option Plan shall not exceed 500,000 shares of common stock during any calendar year. The Compensation Committee of the Board of Directors has the authority to select the employees to whom options are granted and determine the terms of each option, including (i) the number of shares of common stock subject to the option; (ii) when the option becomes exercisable; (iii) the option exercise price, which in the case of incentive stock options must be at least 100% and 110% in the case of incentive stock options granted to a stockholder owning in excess of 10% of the Company's common stock, of the fair market value of the common stock as of the date of grant and (iv) the duration of the options which in the case of incentive stock options may not exceed 10 years. As of December 31, 2001, options to purchase a total of 504,350 shares of common stock remained outstanding under the 1995 Stock Option Plan.

In 1995, the Company adopted the 1995 Director Stock Option Plan. A total of 400,000 shares of common stock may be issued upon the exercise of options granted under the Director Plan. Under the terms of the Director Plan, as amended by shareholders at the 1999 Annual Meeting, options to purchase 5,000 shares of common stock are granted to each eligible director on May 1 of each year and upon appointment to the Board. All options vest on the first anniversary of the date of grant or, in the case of annual options, on April 30 of each year with respect to options granted in the previous year. As of December 31, 2001, options to purchase a total of 155,000 shares of common stock remained outstanding under the Director Plan.

In 1997, the Company adopted the 1997 Stock Incentive Plan which has since been amended, most recently at the 2001 Annual Meeting. A total of 13,500,000 shares of common stock may be issued upon the exercise of options granted under the plan. The maximum number of shares with respect to which options may be granted during any calendar year to any employee under the 1997 Stock Incentive Plan is determined by dividing 1,500,000 by the fair market value of a share of the Company's common stock at the time of grant, and not to exceed an overall per participant annual limit of 5,000,000 shares. The Compensation Committee of the Board of Directors has the authority to select the employees to whom options are granted and determine the terms of each option, including (i) the number of shares of common stock subject to the option; (ii) when the option becomes exercisable; (iii) the option exercise price, which in the case of incentive stock options must be at least 100% (110% in the case of incentive stock options granted to those holding 10% or more of the voting power of the Company) of the fair market value of the common stock as of the date of grant and (iv) the duration of the option, which in the case of incentive stock options may not exceed 10 years. As of December 31, 2001, options to purchase a total of 7,399,229 shares of common stock remained outstanding under the 1997 Stock Incentive Plan.

As of December 31, 2001, 5,280,912 options remain available for grant under the 1995 Stock Option Plan, the 1995 Director Plan and the 1997 Stock Incentive Plan.

SFAS No. 123 requires the measurement of the fair value of stock options or warrants granted to employees to be included in the statement of operations or disclosed in the notes to financial statements. The Company has determined that it will continue to account for stock-based compensation for employees under APB Opinion No. 25 and elect the disclosure-only alternative under SFAS No. 123.

Stock option activity for the years ended December 31, 2001, 2000, and 1999 is summarized as follows:

	Number of Shares	Exercise Price Per Share	Weighted Average Price Per Share
Outstanding, December 31, 1998	3,460,732	$1.25 – $65.60	$11.25
Granted	7,640,650	0.44 – 2.00	0.85
Terminated	(5,711,832)	0.44 – 65.60	7.53
Outstanding, December 31, 1999	5,389,550	0.50 – 2.00	0.50
Granted	1,351,026	0.50 – 3.75	1.18
Exercised	(335,240)	0.50	.50
Terminated	(1,003,503)	0.50 – 57.85	.82
Outstanding, December 31, 2000	5,401,833	0.50 – 2.00	0.67
Granted	9,515,987	0.50 – 1.18	0.78
Exercised	(295,907)	0.50 – 0.56	0.50
Terminated	(144,799)	0.50 – 0.56	0.51
Outstanding, December 31, 2001	14,477,114	$0.50 – $ 2.00	$ 0.74
Exercisable, December 31, 1999	2,772,099	$0.50 – $ 2.00	$ 0.50
Exercisable, December 31, 2000	3,980,476	$0.50 – $ 1.25	$ 0.60
Exercisable, December 31, 2001	6,913,118	$0.50 – $ 2.00	$ 0.71

	Options Outstanding			Options Exercisable	
Exercise Prices	Number	Weighted Average Remaining Contractual Life (Years)	Weighted Average Exercise Price Per Share	Number	Weighted Average Exercise Price Per Share
$ 0.50	3,734,680	6.46	$0.50	3,574,751	$0.50
0.56	2,538,697	9.24	0.56	625,255	0.56
0.71 – 0.83	2,800,000	9.56	0.80	690,000	0.81
0.84	3,150,000	9.56	0.84	126,000	0.84
0.93 – 2.00	2,253,737	8.65	1.14	1,897,112	1.13
	14,477,114	8.56	0.74	6,913,118	0.71

In accordance with EITF No. 96-18, *Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling Goods or Services,* the Company measures the fair value of non-employee options as they vest using the Black-Scholes option pricing model. The Company has recorded compensation expense of $13,516, $217,701 and $231,744 in 2001, 2000 and 1999, respectively, related to grants to non-employees.

The Company has computed the pro forma disclosures required by SFAS No. 123 for all stock options and warrants granted to employees after January 1, 1995, using the Black-Scholes option-pricing model. The assumptions used for the years ended December 31, 2001, 2000, and 1999 are as follows:

	2001	2000	1999
Average risk free interest rate	4.77%	6.39%	6.12%
Expected dividend yield	—	—	—
Expected lives	6 years	6 years	6 years
Expected volatility	90%	90%	60%
Weighted average grant date fair value of options granted during the period (per share)	$0.59	$0.98	$0.37

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. In addition, option-pricing models require the input of highly subjective assumptions including expected stock price volatility. 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.

The pro forma effect of applying SFAS No. 123 for the three years ended December 31, 2001 would be as follows:

	2001	2000	1999
Net loss applicable to common stockholders, as reported	$(13,675,138)	$(7,009,916)	$(14,735,293)
Pro forma net loss applicable to common stockholders, as adjusted for the effect of applying SFAS No. 123.	$(15,890,397)	$(8,389,005)	$(18,647,864)
Basic and diluted net loss per common shares —			
As reported	$ (0.44)	$ (0.40)	$ (0.93)
Pro forma	$ (0.52)	$ (0.48)	$ (1.18)

(e) Employee Stock Purchase Plan

In October 1995, the Company adopted the 1995 Employee Stock Purchase Plan, under which up to 100,000 shares of common stock may be issued to participating employees of the Company, as defined, or its subsidiaries.

On the first day of a designated payroll deduction period, the "Offering Period", the Company will grant to each eligible employee who has elected to participate in the Stock Purchase Plan an option to purchase shares of common stock as follows: the employee may authorize an amount, a whole percentage from 1% to 10% of such employee's regular pay, to be deducted by the Company from such pay during the Offering Period. On the last day of the Offering Period, the employee is deemed to have exercised the option, at the option exercise price, to the extent of accumulated payroll deductions. Under the terms of the Stock Purchase Plan, the option price is an amount equal to 85% of the fair market value per share of the common stock on either the first day or the last day of the Offering Period, whichever is lower. In no event may an employee purchase in any one Offering Period a number of shares that is more than 15% of the employee's annualized base pay divided by 85% of the market value of a share of common stock on the commencement date of the Offering Period. The Compensation Committee may, in its discretion, choose an Offering Period of 12 months or less for each of the Offerings and choose a different Offering Period for each Offering. No shares have been issued under the Plan.

(f) Repricing

In September 1999, the Company's Board of Directors authorized the repricing of options to purchase 5,251,827 shares of common stock to $0.50 per share, which represented the market value on the date of the repricing. These options are subject to variable plan accounting (see Note 2(n)), as defined in FIN 44. The repriced options have been reflected as grants and cancellations in the stock option activity for the year ended December 31, 1999. FIN 44 became effective on July 1, 2000. The Company is following the provisions of FIN 44 and will remeasure the intrinsic value of the repriced options, through the earlier of the date of exercise, cancellation or expiration, at each reporting date. For the year ended December 31, 2001, the Company recognized approximately $1,762,000 as stock compensation from repriced options. The Company

had not recognized any compensation expense related to the repriced options as of December 31, 2000, as the fair market value of the Company's common stock at December 31, 2000 was below the exercise price of the repriced option.

(g) Preferred Stock

The Restated Certificate of Incorporation of the Company permits its Board of Directors to issue up to 5,000,000 shares of preferred stock, par value $0.01 per share, in one or more series, to designate the number of shares constituting such series, and fix by resolution, the powers, privileges, preferences and relative, optional or special rights thereof, including liquidation preferences and dividends, and conversion and redemption rights of each such series. During 1998, the Company designated 1,500,000 shares as Series A convertible preferred stock. During 2001, the Company designated 85,000 shares as Series B convertible preferred stock. As of December 31, 2001, there were no shares of Series B convertible preferred stock authorized or outstanding.

(h) Series A Convertible Preferred Stock

The rights and preferences of the Series A convertible preferred stock are as follows:

Dividends

The holders of the Series A convertible preferred stock, as of March 15 or September 15, are entitled to receive dividends payable at the rate of 6.5% per annum, payable semi-annually in arrears. Such dividends shall accrue from the date of issuance of such shares and shall be paid semi-annually on April 1 and October 1 of each year. Such dividends shall be paid, at the election of the Company, either in cash or additional duly authorized, fully paid and non assessable shares of Series A convertible preferred stock. In calculating the number of shares to be paid with respect to each dividend, the Series A convertible preferred stock shall be valued at $100.00 per share. During 2001 and 2000, respectively, total Series A dividend accretion was approximately $4,242,000 and $4,087,000, representing 40,075 and 41,363 shares, respectively.

Liquidation

In the event of a liquidation, dissolution or winding up of the Company, whether voluntary or involuntary, after payment or provision for payment of debts and other liabilities of the Company, the holders of the Series A convertible preferred stock then outstanding shall be entitled to be paid out of the assets of the Company available for distribution to its stockholders, an amount equal to $100.00 per share plus all accrued but unpaid dividends. If the assets to be distributed to the holders of the Series A convertible preferred stock shall be insufficient to permit the payment of the full preferential amounts, then the assets of the Company shall be distributed ratably to the holders of the Series A convertible preferred stock on the basis of the number of shares of Series A convertible preferred stock held. All shares of Series A convertible preferred stock shall rank as to payment upon the occurrence of any liquidation event senior to the common stock.

Conversion

Shares of Series A convertible preferred stock are convertible, in whole or in part, at the option of the holder into fully paid and nonassessable shares of common stock at $4.25 per share, subject to adjustment as defined.

During 2001, holders of 26,079 shares of Series A convertible preferred stock converted their shares into 613,624 shares of the Company's common stock.

During 2000, holders of 77,049 shares of Series A convertible preferred stock converted their shares into 1,822,232 shares of the Company's common stock.

During 1999, holders of 21,076 shares of Series A convertible preferred stock converted their shares into 495,897 shares of the Company's common stock.

Conversion and Redemption

The Company, at its option, may cause the Series A convertible preferred stock to be converted in whole or in part, on a pro rata basis, into fully paid and nonassessable shares of common stock using a conversion price equal to $4.00 if the closing bid price, as defined, of the common stock shall have equaled or exceeded 250% of the conversion price, $4.25, subject to adjustment as defined, for at least 20 trading days in any 30 consecutive trading day period ending three days prior to the date of notice of conversion, such event is referred to as the "Market Trigger."

The Company, at its option, may redeem the Series A convertible preferred stock for cash equal to $100.00 per share plus all accrued and unpaid dividends if the Market Trigger has occurred in the period ending three days prior to the date of notice of redemption.

(i) Series B Convertible Preferred Stock

As discussed in Note 4(c), the holders of $7.6 million of the Company's 8% notes converted their notes into 76,046 shares of Series B Preferred Stock in March 2001. All outstanding shares of Series B convertible preferred stock were converted into common stock during July 2001.

(10) Commitments and Contingencies

(a) Facilities

The Company leases its facility on Vassar Street in Cambridge, Massachusetts, under a lease that has a 10-year term, which commenced on May 1, 1997.

The Company vacated its Milford, Massachusetts facility in September 2000, following the HSP Sale (see Note 13) and moved its corporate facilities to the Vassar Street facility.

Future approximate minimum rent payments as of December 31, 2001, under existing lease agreements through 2007, are as follows:

December 31,	Amount
2002	$ 620,000
2003	611,000
2004	611,000
2005	611,000
2006	611,000
Thereafter	204,000
	$3,268,000

During 2001, 2000, and 1999, facility rent expense for continuing operations net of sublease revenue was approximately $293,000, $246,000 and $67,000, respectively.

(b) External Collaborations

The Company funds research efforts of various academic collaborators in connection with its research and development programs. Total future fixed commitments under these agreements approximate $124,000 and 177,000 in 2002 and 2003, respectively.

(c) Related-Party Agreements with Affiliates of Stockholders and Directors

The Company has entered into consulting agreements, stock placement agreements and an advisory agreement with several companies that are controlled by shareholders and directors of the Company including Founders Financial Group, L.P., Pillar S.A., and Pillar Investment Limited. During 2001, 2000 and 1999, the Company paid $460,000, $74,000 and $336,000, respectively, under these agreements with related parties.

(d) Employment Agreements

The Company has entered into employment agreements with several of its executive officers that provide for, among other things, each officer's annual salary, cash bonus, fringe benefits and vacation and severance arrangements. Under the agreements, the officers are generally entitled to receive severance payments of two to three year's base salary.

On September 1, 2001, the Company appointed a new Chief Executive Officer, whose employment agreement provides for the purchase of 510,000 shares of the Company's stock at a market value of $428,400. The agreement also provides for the grant of (1) 3,150,000 stock options that are exercisable at a market value of $0.84 per share, and vest over a five-year period, and (2) 490,000 stock options that are exercisable at $0.71 per share, and vest over a one-year period. The Company recorded deferred compensation of approximately $60,000 for the $0.71 stock option granted at an exercise price that was below market value. The Company is amortizing this amount as compensation expense over the vesting period.

(e) Contingencies

From time to time, the Company may be exposed to various types of litigation. The Company is not engaged in any legal proceedings that are expected, individually or in the aggregate, to have a material adverse effect on the Company's financial condition or results of operations.

(11) Income Taxes

During 2001, the Company accrued $500,000 for Alternative Minimum Tax (AMT) of which $450,000 was paid prior to December 31, 2001. The National Economic Stabilization and Recovery Act, enacted in March 2002, has temporarily rescinded the AMT as it applies to the Company. The Company will receive a $450,000 refund and recognize a $500,000 credit to operations during 2002 in accordance with SFAS No. 109, *Accounting for Income Taxes.*

The Company applies SFAS No. 109, *Accounting for Income Taxes*. Accordingly, a deferred tax asset or liability is determined based on the difference between the financial statement and tax basis of assets and liabilities, as measured by the enacted tax rates expected to be in effect when these differences reverse. At December 31, 2001, the Company had net operating loss and tax credit carryforwards for federal income tax purposes of approximately $210.0 million and $3.9 million, respectively, available to reduce federal taxable income and federal income taxes, respectively. The Tax Reform Act of 1986 limits the amount of net operating loss and credit carryforwards that companies may utilize in any one year in the event of cumulative changes in ownership over a three-year period in excess of 50%. The Company has completed several financings since the effective date of the Tax Reform Act of 1986, which as of December 31, 2000, have resulted in ownership changes in excess of 50%, as defined under the Act and which will limit the Company's

ability to utilize its net operating loss carryforwards. Ownership changes in future periods may place additional limits on the Company's ability to utilize net operating loss and tax credit carryforwards.

The federal net operating loss carryforwards and tax credit carryforwards expire approximately as follows:

Expiration Date	Net Operating Loss Carryforwards	Tax Credit Carryforwards
December 31,		
2007	$ —	$ 136,000
2008	7,921,000	627,000
2009	25,670,000	689,000
2010	36,134,000	496,000
2011	44,947,000	493,000
2012	60,810,000	750,000
2018	21,366,000	500,000
2019	7,567,000	250,000
2020	5,544,000	50,000
	$209,959,000	$3,991,000

As of December 31, 2001 and 2000, the components of the deferred tax assets are approximately as follows:

	2001	2000
Operating loss carryforwards	$ 84,551,000	$ 94,177,000
Temporary differences	704,000	329,942
Tax credit carryforwards	3,991,000	4,186,000
	89,246,000	98,692,942
Valuation allowance	(89,246,000)	(98,692,942)
	$ —	$ —

The Company has provided a valuation allowance for its deferred tax asset due to the uncertainty surrounding the ability to realize this asset.

(12) Employee Benefit Plan

The Company has an employee benefit plan under Section 401(k) of the Internal Revenue Code. The plan allows employees to make contributions up to a specified percentage of their compensation. Under the plan, the Company may, but is not obligated to, match a portion of the employees' contributions up to a defined maximum. The Company is currently contributing up to 3% of employee base salary, by matching 50% of the first 6% of annual base salary contributed by each employee. Approximately $44,000, $47,000, and $54,000 of 401(k) benefits were charged to continuing operation during 2001, 2000, and 1999, respectively.

(13) Sale of Hybridon Specialty Products

In September 2000, the Company completed the sale of its Hybridon Specialty Products (HSP) business, which manufactured and marketed oligonucleotides to Avecia Biotechnology, a subsidiary of Avecia, Inc. of Manchester, United Kingdom, for up to $15.0 million. In 2000, the Company recorded a gain of approximately $6.3 million on the HSP sale, comprised of net proceeds received during 2000 of approximately $12.0 million less transaction and other costs of approximately $1.2 million and the book value