HALE AND DORR LLP
Draft of 3/27/98

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

[X] ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the Year Ended December 31, 1997

COMMISSION FILE NO. 0-27352

HYBRIDON, INC.
(Exact name of registrant as specified in its charter)

Delaware	3072298
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)

620 Memorial Drive, Cambridge, Massachusetts	02139
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: (617) 528-7000

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

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes [X] No [ ]

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

On March 13, 1998, the aggregate market value of voting Common Stock held by nonaffiliates of the registrant was $9,066,247, based on the last reported sale price of the registrant's Common Stock on the Nasdaq OTC Bulletin Board on March 13, 1998. There were 5,061,650 shares of Common Stock outstanding as of March 13, 1998.

Documents Incorporated by Reference

Document	Part of Form 10-K into which incorporated
Portions of the Registrant's Proxy Statement with respect to the Annual Meeting of Stockholders to be held on June 15, 1998	Items 10, 11, 12 and 13 of Part III

PART I

ITEM 1. BUSINESS.

OVERVIEW

General

Hybridon, Inc. (the "Company"), established in 1989, is a leader in the discovery and development of novel genetic medicines based on antisense technology. Antisense technology involves the use of synthetic segments of DNA (oligonucleotides) to interact at the genetic level with target messenger RNA, which codes for the production of proteins. In contrast to traditional drugs, which are designed to interact with protein molecules associated with diseases, antisense drugs work at the genetic level to interrupt the process by which disease-causing proteins are produced. The Company believes that drugs based on antisense technology may have broader applicability, greater efficacy and fewer side effects than conventional drugs because antisense compounds are designed to intervene early in the disease process at the genetic level and in highly specific fashion.

The Company's efforts in the antisense field are based on an integrated antisense technology platform combining patented and proprietary medicinal chemistries, synthetic DNA manufacturing technology and analytical processes. The Company's strategy is to leverage this technology platform by applying its oligonucleotides against a range of genetic targets associated with major diseases, by manufacturing oligonucleotides for its own internal use and on a custom contract basis for sale to third parties and by entering into collaborations with large pharmaceutical company partners for the development and commercialization of oligonucleotide drugs directed against these genetic targets.

The Company is focusing its efforts on drug development programs involving second-generation antisense compounds based on the Company's proprietary second-generation mixed backbone chemistries. The Company believes that antisense compounds based on second-generation chemistries will demonstrate a range of favorable pharmaceutical attributes and provide flexibility in addressing many biological targets. In particular, the Company believes that these advanced chemistries provide the potential for enhanced metabolic stability, which may result in less frequent dosing and therefore lower costs per treatment, as well as the potential for oral administration. The Company has three compounds in clinical development (one with two formulations via different routes of administration) and several other compounds in advanced preclinical development. The compounds in the clinical phase of drug development are:

- - GEM 132 for the treatment of systemic cytomegalovirus ("CMV") infections and retinitis, which is now in Phase I/II clinical trials in the U.S. and Canada. The Company believes these clinical trials are the first clinical trials involving administration of a second-generation chemistry oligonucleotide into humans;

- - GEM 92 for the treatment of HIV infection and AIDS, which has completed a pilot Phase I clinical study in Europe;

- - GEM 231 for the treatment of a variety of cancers (gene target is protein kinase A), which is currently in Phase I clinical trials in patients with solid tumors who are no longer benefited by other treatments.

The Company's compounds in advanced preclinical development include a series of antisense oligonucleotides with potential to down regulate the production of vascular endothelial growth factor ("VEGF"), which has been implicated in diseases of the retina (e.g., diabetic retinopathy; age related macular degeneration) related to the abnormal formation of new blood vessels in the eye. The Company is evaluating other antisense compounds targeting VEGF as potential therapies for solid tumors, rheumatoid arthritis and psoriasis.

An important part of the Company's business strategy is to enter into research and development collaborations, licensing agreements and other strategic alliances with third parties, primarily biotechnology and pharmaceutical corporations, for the development and commercialization of its products and to engage in spin-outs of certain technology of the Company to minority-owned subsidiaries in order to obtain alternative financing for such technology. The Company is a party to a corporate collaboration with G.D. Searle & Co. ("Searle"), a subsidiary of Monsanto Company, in the field of inflammation/immunomodulation. In addition, the Company has spun-out certain advanced chemistry compounds based on proprietary genetic targets with respect to DNA methyltransferase to a Quebec company, MethylGene Inc. ("MethylGene") in exchange for a minority equity interest in MethylGene.

The Company's plan is to seek corporate collaborations with respect to each of its compounds in development. The Company generally does not anticipate proceeding with any of its current clinical programs beyond such time as data from Phase II trials becomes available, or with any other drug development programs beyond their current stages of development, without a commitment from a corporate collaborator. The Company is also currently considering the possibility of a spin-out of its hepatitis B and human papilloma virus ("HPV") programs to a minority-owned subsidiary.

In 1996, the Company formed its Hybridon Specialty Products Division (the "HSP Division") to manufacture highly purified oligonucleotide compounds both for the Company's internal use and on a custom contract basis for sale to third parties,

including the Company's collaborative partners. The Company is manufacturing oligonucleotides in compliance with current good manufacturing practices ("GMP") at its 36,000 square foot leased manufacturing facility in Milford, Massachusetts. The HSP Division first began production of oligonucleotide compounds for sale to third parties in June 1996 and had revenues of approximately $1.1 million in 1996 and approximately $1.9 million in 1997. The Company is in discussions regarding a possible joint venture with respect to the HSP Division, which the Company believes would enable it to maximize the potential for third party manufacturing by the HSP Division, while ensuring for the Company and its collaborators a source of oligonucleotides. However, there can be no assurance that the Company will enter into any joint venture with respect to the HSP Division or that the terms of any joint venture will be as

anticipated by the Company.

1997 Restructuring and Certain Other Developments

On April 2, 1997, the Company issued $50.0 million of 9% Convertible Subordinated Notes (the 1997 "9% Notes") with a maturity date of April 1, 2004. Under the terms of the 1997 9% Notes, the Company is required to make semiannual interest payments on the outstanding principal balance of the 1997 9% Notes on April 1 and October 1 of each year during which the 1997 9% Notes are outstanding. The Company made the first interest payment of $2.3 million at the beginning of October 1997. In connection with its ongoing financing effort (described below), holders of the 1997 9% Notes in the aggregate original principal amount of approximately $42.0 million have consented to the deferral by the Company of the interest payment due April 1, 1998 until October 1, 1998. See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations -- 1997 9% Notes."

In July 1997, the Company terminated the development of GEM 91, its first generation antisense drug for the treatment of AIDS and HIV infection, based on a review of new data from an open label Phase II clinical trial of patients with advanced HIV infection. In this Phase II trial, three of the nine subjects tested experienced decreases in platelet counts that required dose interruption. In addition, a review of the data showed inconsistent responses to the treatment and failed to confirm the decrease in cellular viremia observed in an earlier clinical trial. As a result, the Company decided to stop the development of GEM 91 and refocus its efforts on its other most advanced drug development programs described above.

During the second half of 1997, the Company implemented a restructuring plan to reduce expenditures on a phased basis over the balance of 1997 and into the first half of 1998 in an effort to conserve its cash resources. As part of this restructuring plan, in addition to terminating the clinical development of GEM 91, the Company reduced or suspended selected programs unrelated to its core advanced chemistry antisense drug development programs, including its ribozyme program. In

addition, the Company terminated the employment of 84 employees at its Cambridge and Milford, Massachusetts facilities in the second half of 1997 and substantially reduced operations at its Paris, France office and terminated ten employees at that location in August 1997. As part of this restructuring, the Company reviewed all outside testing, public relations, travel and entertainment and consulting arrangements and terminated or renegotiated various of these arrangements.

As part of this restructuring, the Company has subleased one facility in Cambridge, Massachusetts and a substantial portion of its corporate headquarters located at 620 Memorial Drive, Cambridge, Massachusetts. Effective March 31, 1998, the Company has also terminated the lease for its office in Paris, France.

This restructuring of the Company, together with employee attrition, resulted in a reduction in the number of the Company's employees from 213 at June 30, 1997 to 102 at December 31, 1997 and 78 at March 30, 1998 and the subleasing of an aggregate of approximately 61,000 square feet of space. As a result, the Company has significantly scaled back the level and scope of its operations since mid-1997. However, because of the significant costs involved in terminating employees, subleasing its facilities, terminating research contracts, suspending or cancelling research programs and substantially reducing operations, the Company did not begin to experience a material decrease in its expenditure rate until the fourth quarter of 1997. The Company is continuing to explore opportunities to reduce operating expenses in an effort to conserve its cash resources.

In September 1997, the Company received notification from F. Hoffmann-La Roche Ltd. ("Roche") that Roche had decided not to pursue further its antisense collaboration with the Company and was terminating the

collaboration effective February 28, 1998. As part of this termination, Roche has agreed to assign its patent rights to the HPV and hepatitis C programs covered by such collaboration to the Company, subject to the execution of definitive documentation.

In December 1997, because of the Company's failure to satisfy the minimum net tangible assets criteria of the Nasdaq National Market, the Company's Common Stock was delisted from the Nasdaq National Market and began being quoted on the Nasdaq OTC Bulletin Board. In addition, in December 1997, the Company effected a one-for-five reverse stock split of its Common Stock. All per share Common Stock information contained herein (other than in the Exhibit Index) has been adjusted to reflect this reverse split.

Ongoing Financing Effort

In January 1998, the Company commenced a private offering of up to 400 units, each unit consisting of a Note Due 2007 in the original principal amount of $100,000 and warrants to purchase Common Stock. The Company is offering the units at a price of $100,000 per unit. As of March 30, 1998, the Company had received approximately $4.8 million in gross proceeds from the sale of units. The Company has very limited cash resources and substantial obligations to lenders,

equipment lessors, real estate landlords and trade creditors. The Company's ability to continue operations in 1998 depends on its success in raising new funds in this financing or otherwise. If the Company is unable to obtain substantial additional new funding in April 1998, it will be required to terminate its operations or seek relief under applicable bankruptcy laws by the end of April 1998. See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations -- 1998 Financing Activities."

TECHNOLOGY OVERVIEW

Introduction

Proteins play a central role in virtually every aspect of human metabolism. Almost all human diseases are the result of inappropriate protein production or performance. Traditional drugs are designed to interact with protein molecules that support or create diseases. Antisense drugs work at the genetic level to interrupt the process by which disease-causing proteins are produced.

The information necessary to produce a specific protein is encoded in a specific gene. The information required to produce all human proteins is contained in the human genome and its collection of more than 100,000 genes. Each gene is made up of DNA, which is a duplex of entwined strands -- a "double helix." In each duplex, the building blocks of DNA, called nucleotides, are bound or "paired" with complementary nucleotides on the other strand. The precise sequence of a nucleotide chain that is the blueprint for the information that is used during protein production is called the "sense" sequence. The sequence of a nucleotide chain that is precisely complementary to a given sense sequence is called its "antisense" sequence.

Protein synthesis or expression typically involves a two-phase process. First, the information contained in the gene is transcribed from the sense strand of DNA into one or more molecules of messenger RNA. Second, the information encoded in the messenger RNA is translated into the sequence of amino acids that comprise the protein. The information contained in a single gene is often repeatedly transcribed into multiple copies of messenger RNA, which in turn are repeatedly translated, giving rise to multiple copies of the same protein.

Conventional Drugs

Most drugs are chemicals designed to induce or inhibit the function of a target molecule, typically a protein, with as few unwanted side effects as

possible. However, conventional drugs are not available for the treatment of many diseases because of their relatively low level of selectivity. The selectivity of conventional drugs is usually determined by only a few, generally two or three, points of interaction at the binding site of the target molecule. Frequently, sites on other non-

target molecules resemble the target binding site sufficiently to permit the conventional drug to bind to some degree. This lack of selectivity may result in decreased efficacy, unwanted side effects or a need to administer the drug in less than optimal dosages due to toxicity concerns. In addition, the development of conventional drugs is generally time consuming and expensive, as thousands of compounds must be synthesized to find one with the right efficacy and side effect profile.

Gene Expression Modulation

In contrast to conventional drugs, which usually interact with disease-associated proteins after they have been produced, gene expression modulation technology is intended to regulate the production of disease-associated proteins, thus targeting an earlier biochemical process. Advances in genomic science have identified many targets for gene expression modulation products. Once a gene that codes for a disease-associated protein is identified, an oligonucleotide based on the complementary sequence for the selected site can be synthesized and its pharmaceutical properties optimized by chemical modification. These chemically-modified oligonucleotides may be composed of DNA, RNA or a combination of the two.

Chemically-modified oligonucleotides can be designed to attack a disease at the genetic level by binding to messenger RNA or DNA to prevent production of disease-associated proteins. Binding to messenger RNA generally is used in the "antisense" approach to gene expression modulation, while binding to the DNA generally is used in the "triplex" approach to gene expression modulation.

In the antisense approach to gene expression modulation, chemically-modified oligonucleotides, which consist of the antisense sequence to a selected region on a target messenger RNA, are used to inhibit the synthesis of a particular protein. Because the sequence of nucleic acid bases of a chemically-modified antisense oligonucleotide is complementary to its target sequence on a messenger RNA, the antisense oligonucleotide forms a large number of bonds at the target site, typically between 15 and 30, practically assuring that the oligonucleotide will hybridize (bind) tightly to the selected type of messenger RNA. Since a single messenger RNA may be translated repeatedly into a protein, a single chemically-modified antisense oligonucleotide may inhibit the synthesis of many copies of a protein. Moreover, in vitro tests have shown that certain chemically-modified antisense oligonucleotides form complexes with their target messenger RNAs. These complexes activate RNaseH, a cellular enzyme, in a manner that destroys the messenger RNA to which the oligonucleotide is bound, without destroying the oligonucleotide itself, thus freeing the oligonucleotide to bind with another identical messenger RNA.

The triplex approach involves the interaction of oligonucleotides directly with the appropriate region of the double-stranded DNA comprising the target gene, thus

resulting in a triplex structure and physically interfering with the transcription of DNA into messenger RNA. The triplex approach typically does not involve the destruction of the region of DNA to which the oligonucleotides are bound, in contrast with the effects of antisense oligonucleotides on messenger RNA. Constraining factors to the triplex approach to date have been the

difficulty of obtaining access for oligonucleotides to the DNA, the relative weakness of the bonding of the oligonucleotides with the DNA and concerns over compounds that interact directly with the DNA genetic information.

HYBRIDON ANTISENSE TECHNOLOGY

Hybridon has developed an integrated antisense technology platform based on proprietary medicinal chemistries, analytical chemistry and manufacturing technology. The development of Hybridon's antisense chemistry has been directed by Dr. Sudhir Agrawal, the Company's Chief Scientific Officer, and builds on the pioneering work in the antisense field begun in the 1970s by Dr. Paul C. Zamecnik, a founder and director of the Company and Chairman of its Scientific Advisory Board, at the Massachusetts General Hospital ("MGH") and continued by Dr. Zamecnik at the Worcester Foundation for Biomedical Research, Inc., which has since merged into the University of Massachusetts (the "Worcester Foundation").

Medicinal Chemistries. Hybridon's scientists have designed and synthesized over 20 proprietary families of synthetic antisense oligonucleotide chemistries. The Company believes that antisense compounds based on these chemistries may demonstrate a range of favorable pharmaceutical attributes, including: reduced side effects, increased duration of action, increased potency and susceptibility to lower dosing, less frequent dosing, controlled release formulation and alternative routes of administration, including oral administration. Hybridon designed its first generation phosphorothioate oligonucleotides to increase their resistance to enzymatic degradation and their biological activity and to act catalytically by triggering RNase H. GEM 91 was such a phosphorothioate-modified oligonucleotide. Hybridon has used the insights gained by it in the human clinical trials of GEM 91 in the design of its more advanced oligonucleotide chemistries.

Manufacturing Technology. The Company's expertise in the structure, design and analysis of chemically-modified oligonucleotides has served as the foundation of its manufacturing technology and know-how. The Company has developed proprietary technology to increase the purity of oligonucleotide products, enhance the efficiency of the production process and increase the scale of production. In 1996, the Company completed development of two separate commercial scale oligonucleotide synthesizers, one in an internal program and one in a collaboration with Pharmacia Biotech, Inc. The synthesizer developed by Hybridon is capable of producing advanced chemistry antisense oligonucleotides. In addition, the Company has implemented proprietary purification processes, which use water in place of chemical solvents, simplifying environmental compliance and permitting purification of kilogram batches of

oligonucleotides. The Company has also developed proprietary chemical synthesis processes and novel reagents used in the synthesis process, which the Company believes may further decrease the cost of production of its modified oligonucleotides.

Proprietary Analytical Tools and Processes. The Company has established proprietary analytical tools and processes that enable it to analyze oligonucleotide compounds with greater speed and accuracy when compared to traditional methods. Hybridon has developed a novel method of determining antisense purity that is sensitive to a single DNA base difference; this method is significantly more accurate than traditional chromatography methods. The Company uses the information that it obtains with its proprietary analytical tools and processes to improve production quality control, to comply with regulatory requirements and to monitor the pharmacokinetic behavior of its oligonucleotide compounds in preclinical studies and clinical trials.

HYBRIDON DRUG DEVELOPMENT AND DISCOVERY PROGRAMS

The Company is focusing its efforts on drug development programs involving second-generation antisense compounds based on the Company's proprietary mixed backbone chemistries as shown below. The Company's plan is to seek corporate collaborations with respect to each of its compounds in

development. The Company generally does not anticipate proceeding with any of its current clinical programs beyond such time as data from Phase II trials becomes available, or with any of its other drug development programs described below beyond their current stages of development, without a commitment from a corporate collaborator.

TARGET	PRIMARY THERAPEUTIC INDICATION(S)	STATUS(1)
CLINICAL PROGRAMS		
Cytomegalovirus	CMV Retinitis	GEM 132 for Intravitreal Injection - Phase I/II Clinical Trial/Seeking Partner
	CMV (Systemic)	GEM 132 for Systemic Injection - Phase I/II Clinical Trial/Seeking Partner
HIV-1	HIV-1 Infection and AIDS	GEM 92 - (Intravenous and Oral Formulations) - Pilot Phase I Clinical Trial/Seeking Partner
Protein Kinase A	Cancer	GEM 231 - (Intravenous Formulation) - Phase I Clinical Trial/Seeking Partner
PRECLINICAL PROGRAMS		
Vascular Endothelial Growth Factor	Retinopathies (e.g. macular degeneration and diabetic retinopathy)	GEM 220 - Preclinical/Seeking Partner
	Cancer Angiogenesis	Preclinical/Seeking Partner
	Psoriasis	Preclinical/Seeking Partner
Hepatitis C Virus	Hepatitis; Liver Cancer	Lead Compounds/Seeking Partner(2)
Murine Double Minute-2	Cancer	Research Compounds/Seeking Partner
Amyloid Proteins	Alzheimer's	Research Compounds/Seeking Partner
Human Papilloma Viruses	Genital Warts	Preclinical 2)(3)
Hepatitis B Virus	Hepatitis; Liver Cancer	Research Compounds (2)(3)
DRUG DEVELOPMENT PROGRAMS IN HYBRIDON SPINOUT		
DNA Methyltransferase	Cancer	Preclinical/MethylGene(4)

(1) Phase II clinical trials. The product is administered to a limited patient population to (i) evaluate the effectiveness for specific indications and (ii) identify possible short-term adverse effects and safety risks.

Phase I clinical trials. The product is administered to a limited number of healthy human subjects or patients and tested for pharmacokinetics (absorption, metabolism, distribution and excretion), pharmacologic action, dose response, safety and, if possible, early evidence of effectiveness.

Pilot Phase I Study. The product is administered to a small number of patients to assess safety, pharmacokinetics and other data on a preliminary basis.

Preclinical: Compounds are undergoing additional testing and alternative chemistries are being evaluated in biological assays and/or appropriate animal models in order to assess efficacy, toxicology and pharmacokinetics and to select particular chemistries with optimal pharmaceutical attributes. If these procedures are completed satisfactorily and other scientific and financial criteria are met, the Company may initiate IND-enabling Good Laboratory Practices ("GLP") studies and begin preparation of an IND application.

Lead Compounds: One or more antisense compounds have demonstrated biological activity for a particular gene target in a specific and relevant biological assay.

Research Compounds: Appropriate target gene(s) and sequence(s) are being determined; antisense compounds are being synthesized and screened for biological activity.

(2) Developed as part of the Company's collaboration with Roche, which was terminated by Roche as of February 28, 1998. Roche has agreed to assign all rights to these programs to the Company in connection with such termination, subject to the execution of definitive documentation.

(3) The Company is currently considering the possibility of a spin-out of its hepatitis B and HPV programs to a minority-owned subsidiary.

(4) Technology relating to target has been licensed to and is being developed by MethylGene, a Canadian company co-founded by the Company and in which the Company owns a minority interest. See "Item 1. Business -- Financial Collaborations -- MethylGene Inc."

CLINICAL PROGRAMS

Cytomegalovirus

CMV is a member of the herpes virus family which exists latently in approximately 60% of the general U.S. population, and in approximately 90% of the HIV/AIDS population. Because of their immunocompromised state, AIDS patients often suffer from CMV infection. In this patient population, CMV may be manifested as retinal, gastrointestinal, hepatic, pulmonary and/or neurological disease, although in 75% of patients with CMV, CMV usually manifests itself as retinal disease. CMV retinitis lesions progress rapidly and can result in blindness if left untreated.

Prior to the advent of combination therapy including protease inhibitors (a highly active anti-retroviral therapy ("HAART")), for AIDS, approximately 15% of AIDS patients had active CMV disease and another 25% were considered at risk. Because the introduction of HAART treatment has been effective at delaying progression of AIDS, the introduction of HAART treatment has reduced the incidence of new cases of CMV retinitis in AIDS patients by about three-fold.

The Company believes that aggressive AIDS treatment will prolong the time that patients are living with CMV retinitis. Between 1994 and 1996, the mean time of survival of CMV patients increased from 12 to 18 months. The Company expects such period to increase to 30 months by the end of 1998. As patients live longer and with less evidence of disease, the Company believes there is likely to be a marked decrease in tolerance of cumbersome dosing regimens and adverse side-effects characteristic of present therapies.

Although the market for CMV drugs is relatively small, the Company expects the market to grow due to (i) failures of HAART therapy and (ii) CMV breakthrough during HAART therapy at CD4+ lymphocyte counts above 100. Failures of HAART therapy may occur as a result of development of resistance, intolerance and lack of compliance due to complex dosing regimens involving multiple products. The Company believes that although HAART therapy is effective for a limited period of time, the duration of HAART therapy is highly variable. Several reports presented at the 1997 Interscience Conference on Antimicrobial Agents and Chemotherapy suggest CMV reactivation in protease-experienced patients at CD4+ lymphocyte counts greater than 100 and, in some cases, greater than 200.

The Company is conducting clinical trials of GEM 132, its second-generation antisense oligonucleotide for the treatment of CMV infection. In these trials, the Company is studying two different routes of administration. In an escalating dose, Phase I/II multicenter trial in the U.S. and Canada, in which GEM 132 is

administered by injection into the vitreous of the eye, the Company is studying the safety and activity of GEM 132 in patients with CMV retinitis who are no longer able to benefit from marketed therapies. In Phase I trials in normal volunteers, the Company is administering a series of single and multiple dose regimens, employing two-hour intravenous infusions of up to 150 mg/dose at weekly intervals over four weeks. In Phase I/II studies involving patients infected both with HIV and CMV, the Company is evaluating the effects of multiple two-hour intravenous infusions, given at weekly or biweekly intervals, on the quantities of CMV cultured from the semen as a measure of antiviral activity. All doses studied to date in these clinical trials have been well tolerated. The Company anticipates these trials will result in the identification of one or more promising doses and a schedule of administration for more extended evaluation in patients with CMV infection.

GEM 132 has demonstrated significant inhibition of the replication of CMV in tissue culture assays. GEM 132 has demonstrated activity in cell culture against both clinical isolates and viruses which have become resistant to current therapies, such as ganciclovir. In addition, in cell culture studies, GEM 132 has demonstrated significantly more potent anti-viral activity than the two existing therapies against which it has been tested, ganciclovir and foscarnet.

HIV-1 and AIDS

AIDS is caused by infection with HIV and leads to severe, life-threatening impairment of the immune system. HIV causes immunosuppression by attacking and destroying T-cells, which coordinate much of the network of normal immune responses. HIV infection usually leads to AIDS, although progression to symptomatic disease may take many years. The process of HIV replication involves the integration of a DNA copy of the viral RNA into the human genome, the transcription of the DNA copy into messenger RNA ("reverse transcription") and the synthesis of viral proteins and copies of viral RNA for packaging into new virus particles that may infect other cells.

As of June 30, 1996, approximately 548,100 cases of AIDS had been reported to the U.S. Center for Disease Control and Prevention (CDC), and the current population of surviving AIDS patients in the U.S. was estimated to be approximately 200,000. As of June 30, 1996, AIDS was the second leading cause of death in the U.S. for men between the ages of 25 and 44 and the third leading cause of death in the U.S. for women between the ages of 25 and 44. In 1996, the

U.S. Public Health Service estimated that more than 1,000,000 other people in the U.S. were infected with HIV. As of June 30, 1996, the World Health Organization (the "WHO") reported that approximately 1,394,000 AIDS cases had been reported worldwide, but it estimated that the actual total number of cases was over 7,700,000. The WHO also estimated that, as of June 30, 1996, approximately 21,800,000 individuals were infected with HIV/AIDS worldwide.

A growing number of drugs for the treatment of HIV infection and AIDS have received marketing approval from the FDA, and from other regulatory authorities. All of those approved drugs are either inhibitors of the reverse transcriptase enzyme or the protease enzyme of HIV-1. Although each of these drugs has demonstrated some evidence of antiviral activity as a monotherapy by reducing the quantities of virus in the plasma, any studies which have demonstrated prolonged benefit on the surrogate markers (viral RNA and CD4+ lymphocyte counts) and sustained clinical remission have involved combinations of these agents.

The standard HAART therapy involves treatment with a protease inhibitor in conjunction with two inhibitors of reverse transcriptase. While use of these regimens has been associated with decreased mortality rates and important improvements in the quality of life for patients with AIDS, there are increasing reports of failure of HAART therapy to sustain the initially-achieved viral suppression and clinical benefit. The Company believes that these reports underscore the need for new antiretroviral therapies, preferably active against targets other than protease or reverse transcriptase.

The Company recently completed a pilot Phase I clinical study in Europe of GEM 92, the Company's second-generation compound for the treatment of HIV-1 infection and AIDS. This study was designed to explore the safety and to provide information on the pharmacokinetics of GEM 92 after oral and intravenous dosing. All doses administered in the pilot study were well tolerated.

The Company is developing GEM 92 using insights gained in the development and the clinical trials of GEM 91, which involved over 250 volunteers and patients with HIV-1 infection. The Company elected to discontinue further development of GEM 91 in July 1997 based on preliminary data from a Phase II clinical trial in which three of the nine subjects treated had experienced decreases in platelet counts that required dose interruption. In addition, a review of the virology data showed inconsistent responses to the treatment and failed to confirm the decrease in cellular viremia observed in an earlier trial.

GEM 92 differs from GEM 91 in that GEM 92 is based on the Company's second-generation chemistries, which the Company believes provide the potential for enhanced metabolic stability compared to the Company's first-generation compounds. The Company believes that this improved stability may make it possible to administer lower doses at less frequent intervals and may make the oral route of administration feasible.

Protein Kinase A

Protein Kinase A ("PKA") is a protein that has been shown to be expressed in human cancer cell lines and in primary tumors after cells have been transformed with

various oncogenes or after stimulation of cell growth with cell growth stimulating factors. Based on cell culture studies, the Company believes that

overexpression of PKA may be associated with colon, breast, ovarian and lung cancer. Hybridon has identified specific sequences on the PKA gene as targets for chemically-modified antisense oligonucleotides and has synthesized an advanced chemically-modified antisense compound, GEM 231, that has demonstrated inhibition of the expression of PKA and tumor growth in animal model studies. In these studies, repeated doses of Hybridon's oligonucleotide compound administered either intraperitoneally or orally resulted in reduction of PKA, associated with suppression of tumor growth. GEM 231 has also demonstrated in cell culture tests and in an animal xenograft model that a combination of GEM 231 with cytotoxic drugs or other classes of anticancer agents may enhance the antitumor effect of GEM 231.

In January 1998, the Company initiated a Phase I dose-escalation trial of GEM 231 in patients with refractory solid tumors. In this safety trial, GEM 231 is being administered by two-hour intravenous infusions given twice a week. If treatment is well tolerated and if there is no progression of the tumor at eight weeks, treatment can be continued until there is toxicity or until there is clearly no effect on the tumor. This trial is designed to establish a maximum tolerated dose for GEM 231 when used as a single agent. The study is also intended to assist the Company in selecting one or more doses to evaluate more extensively in Phase II trials.

PRECLINICAL PROGRAMS

Vascular Endothelial Growth Factor. Vascular Endothelial Growth Factor ("VEGF") is a growth factor that stimulates angiogenesis, the process of new blood vessel formation. Angiogenesis plays a major role in wound healing and organ regeneration and also is involved in certain pathological processes, such as tumor growth and metastasis. VEGF has been shown to be overexpressed in developing tumors and is believed to be a key factor in providing new blood supply to feed developing tumors. Hybridon has identified specific sequences on the VEGF messenger RNA as targets for chemically-modified antisense oligonucleotides and has synthesized an advanced chemically-modified antisense oligonucleotide, GEM 220, that has inhibited the expression of the VEGF gene in in vitro and tissue culture assays.

Dermatology. VEGF, in association with its role in angiogenesis, has recently been implicated in psoriasis, which currently afflicts more than 6,000,000 people in the U.S. with between 150,000 and 260,000 new cases in the U.S. each year. Hybridon has identified specific sequences on the VEGF messenger RNA as targets for chemically-modified antisense oligonucleotides and has synthesized chemically- modified antisense oligonucleotides that have inhibited the expression of the VEGF gene in in vitro and tissue culture assays. The Company has explored optimal forms of topical delivery of oligonucleotides to the basal layers of the epidermis, where

VEGF has been found to be overexpressed in psoriasis.

Ophthalmology. Overexpression of VEGF has also been implicated in four major causes of blindness: late stage, age-related macular degeneration, which afflicts approximately 500,000 people in the U.S.; proliferative diabetic retinopathy, the major cause of blindness in diabetics which affects approximately 250,000 people in the U.S.; central retinal vein occlusion, which afflicts approximately 200,000 people in the U.S.; and retinopathy of prematurity, which affects approximately 10,000 premature newborns annually in the U.S. Hybridon has identified specific sequences on the VEGF messenger RNA as targets for chemically-modified antisense oligonucleotides and is synthesizing chemically-modified antisense oligonucleotides designed to inhibit the expression of the VEGF gene in retinal cells. These oligonucleotides have been shown in an animal model of retinopathy to inhibit vascular proliferation and prevent aberrant angiogenesis in the retinas of mice in a model for retinopathy of prematurity. Hybridon's antisense oligonucleotides have also been shown to inhibit neovascularization in a primate animal model of neovascularization.

Oncology. Angiogenesis is a key prerequisite for solid tumor growth and may also constitute an early event in tumorigenesis. In order for tumor cell

masses to grow beyond a few millimeters in size, additional vascularization is needed. In fact, tumor growth will slow or stop in direct proportion to blood supply.

VEGF has been shown to be a tumor angiogenesis factor, contributing to new vessel growth. Several studies in experimental animal model systems have shown that inhibition of VEGF will inhibit tumor vascularization. In addition, VEGF has been shown in in vitro studies to provide an autocrine growth stimulus for some tumor cell lines.

Hepatitis C Virus. There are approximately 3,500,000 people in the U.S. carrying the hepatitis C virus, and approximately 150,000 individuals in the U.S. become infected with hepatitis C each year. Approximately 80% of those who contract the virus each year develop chronic hepatitis C infections and approximately 30,000 cases each year ultimately result in cirrhosis of the liver. Chronic infection due to hepatitis C is a significant disease in Japan and other Pacific Rim countries that has been linked to the development of primary liver cancer. Pursuant to its collaboration with Roche, Hybridon identified through joint research with Roche specific sequences on the messenger RNA as targets for chemically modified antisense oligonucleotides and synthesized a lead compound that inhibited hepatitis C viral gene expression in in vitro and tissue culture assays. In connection with the termination by Roche of the

Company's collaboration with Roche, Roche has agreed to assign all of its rights to the lead compound to the Company, subject to the execution of definitive documentation.

Murine Double Minute-2. MDM-2 is a human oncogene which has been shown in in vitro studies to encode a protein that binds to and inactivates tumor suppressor genes p53 and Rb. Recent studies by a number of academic institutions have suggested that overexpression of the MDM-2 gene is present in approximately 70% of all breast cancers and correlates with increased malignancy as well as drug resistance. The Company, in collaboration with two academic institutions, has identified specific sequences on the messenger RNA as targets for chemically-modified antisense oligonucleotides and have synthesized chemically-modified antisense oligonucleotides that inhibit MDM-2 production in tissue culture assays. Preliminary studies are being conducted in animal models. The Company is in the process of seeking to obtain exclusive rights to these sequences from its academic collaborators.

Amyloid Proteins. Alzheimer's disease is a neurodegenerative disease which is the most common cause of dementia in the elderly. It is estimated to affect approximately 4,000,000 individuals in the U.S. The presence of amyloid precursor protein ("APP") in the brain at abnormal sites and in abnormal amounts has been reported to be associated with Alzheimer's disease. Hybridon has identified a specific sequence on the messenger RNA as a target for chemically-modified antisense oligonucleotides and has synthesized chemically-modified antisense oligonucleotides that inhibit APP production in tissue culture assays.

Human Papilloma Viruses. Human papilloma viruses are associated with a variety of warts, including benign genital warts which, if untreated, can lead to cervical cancer. Each year, condyloma acuminata (genital warts) are diagnosed in approximately 750,000 patients in the U.S. and accounts for more than 2,000,000 visits to health care providers in the U.S. HPV infections are the most common sexually transmitted diseases in the world today, with an estimated 11 to 46 percent of sexually active women having DNA evidence of HPV infection. Traditional therapies include wart removal through cryotherapy, laser therapy or excisional surgery; topical application of formulations of podophyllotoxin, trichloroacetic acid and salicylic acid or 5-flurouracil, or alternatively, direct injections of interferon into the wart. While existing therapies may help eliminate the warts, none of them eradicates the virus. Consequently, recurrence of genital warts, as well as transmission of the virus, remains a significant problem.

Pursuant to its collaboration with Roche, Hybridon identified through joint research with Roche specific sequences on the messenger RNA of the papilloma virus as targets for chemically-modified antisense oligonucleotides and synthesized a lead compound that inhibited human papilloma virus gene expression in tissue culture assays. This compound also has been shown in an animal model to be active in preventing wart-like tissue proliferation. In connection with the termination by

Roche of the collaboration with Roche, Roche has agreed to assign all of its rights to the lead compound to the Company, subject to the execution of definitive documentation. The Company is currently considering the possibility of a spin-out of this program.

Hepatitis B Virus. Hepatitis B is a major health problem throughout the world, with endemic infection in some less developed countries. Hepatitis B infections can lead to liver cirrhosis and cancer of the liver. The WHO estimates there are more than 1,000,000 new cases of hepatitis B infection annually in developed countries and 350 million chronically infected carriers worldwide. Based on data from the CDC, an estimated 30 percent of these will progress to symptomatic acute infections while a total of 10 to 15 percent will become chronic hepatitis B carriers at risk of chronic liver disease and progression to cirrhosis or hepatocellular carcinoma. The Company has acquired an established cell-base assay for selecting compounds targeted to hepatitis B as well as several active oligonucleotide compounds that the Company plans to evaluate as potential pre-clinical candidates. Approximately 1,200,000 individuals in the U.S. carry the hepatitis B virus. There are an estimated 200,000 to 300,000 new hepatitis B infections in the U.S. each year. Pursuant to its collaboration with Roche, Hybridon identified through joint research with Roche specific sequences on the messenger RNA as targets for chemically-modified antisense oligonucleotides and synthesized chemically-modified antisense oligonucleotides that inhibit the expression of hepatitis B virus in cell cultures. Although Roche determined not to pursue this program, the Company is continuing its development efforts. All rights relating to the Roche- sponsored research with respect to hepatitis B reverted to the Company when Roche determined not to pursue the program. The Company is currently considering the possibility of a spin-out of this program to a minority owned subsidiary.

DRUG DEVELOPMENT PROGRAMS IN HYBRIDON SPINOUT

DNA Methyltransferase. DNA methyltransferase is a regulatory protein that has been implicated in the processes of cell growth and differentiation and has been shown to be overexpressed in some tumors, such as small cell lung cancer, colon cancer and breast cancer. Hybridon has identified specific sequences on the messenger RNA as targets for chemically-modified antisense oligonucleotides and has synthesized chemically-modified antisense oligonucleotides that alter DNA methylation of cultured human cancer cells and inhibit the ability of such cells to grow in cell culture and their ability to form tumors in mice. The Company has licensed the technology relating to the development of this compound to MethylGene, which is currently developing this technology. See "Item 1. Business -- Financial Collaborations -- MethylGene Inc."

CORPORATE COLLABORATIONS

An important part of Hybridon's business strategy is to enter into research and development collaborations, licensing agreements or other strategic alliances with third parties, primarily biotechnology and pharmaceutical corporations, for the development and commercialization of certain products. As of the date hereof, the Company is a party to corporate collaborations with Searle and Medtronic, all as summarized below. The Company intends to retain manufacturing rights for many of the products, if any, it may license pursuant to these collaborations.

G.D. Searle & Co.

In January 1996, the Company and Searle entered into a collaboration relating to research and development of therapeutic antisense compounds directed at up to eight molecular targets in the field of inflammation/immunomodulation (the "Searle Field").

Pursuant to the collaboration, the parties are conducting research and development relating to a compound directed at a molecular target in the Searle Field designated by Searle. In this project, Searle is funding certain research and development efforts by the Company, and each of Searle and the Company have committed certain of its own personnel to the collaboration. The initial phase of research and development activities relating to the initial target will be conducted through the earlier of (i) the achievement of certain product candidate milestones and (ii) 36 months after commencement of the collaboration, subject to early termination by Searle. The parties may extend the initial collaboration by mutual agreement, including agreement as to additional research funding by Searle.

In addition, under the collaboration Searle has the right, at its option, to designate up to six additional molecular targets in the Searle Field (the "Additional Targets") for collaborative research and development with Hybridon on terms substantially consistent with the terms of the collaboration applicable to the initial molecular target. This right is exercisable by Searle with respect to each of the Additional Targets upon the payment by Searle of certain research payments (beyond the project specific payments relating to the particular Additional Target) and the purchase of additional Common Stock from the Company by Searle (at the then fair market value). The aggregate amount to be paid by Searle for such research payments and equity investment in order to designate each of the Additional Targets is $10,000,000 per Additional Target. In the event that Searle designates all of the Additional Targets, the aggregate amount to be paid by Searle for research payments will be $24,000,000 and the aggregate amount to be paid by Searle in equity investment will be $36,000,000. If Searle has not designated all of the Additional Targets by the time it advances the product candidate for the initial molecular target to certain stages of preclinical development, Searle will be required to purchase an additional $10,000,000 of Common Stock (at the then fair market value) on specified

dates in order to maintain its right to designate any of the Additional Targets that it has not yet designated. The payment for any such Common Stock will be creditable against the equity investment portion of the payments to be made by Searle with respect to the designation of any of the Additional Targets that Searle has not yet designated.

Searle also has the right, at its option, to designate a molecular target in the Searle Field to develop a therapeutic agent for cancer that acts through immunomodulation (the "Searle Cancer Target") for collaborative research and development with the Company on terms substantially consistent with the terms of the collaboration applicable to the initial molecular target. At the time of such designation, Searle will be required to make certain research payments to the Company and purchase additional Common Stock from the Company (at the then fair market value). The aggregate amount to be paid by Searle for such research payments and equity investment will range from $14,000,000 (comprised of $7,000,000 in research payments and $7,000,000 in equity investment) if the Searle Cancer Target is designated in 1998 to $26,000,000 (comprised of $21,000,000 in research payments and $5,000,000 in equity investment) if the Searle Cancer Target is designated in 2000.

Searle has exclusive rights to commercialize any products resulting from the collaboration. If Searle determines, in its sole discretion, to commercialize a product, Searle will fund and perform preclinical tests and clinical trials of the product candidate and will be responsible for regulatory approvals for and marketing of the product. In certain instances and for specified periods of time, the Company has agreed to perform research and development work in the Searle Field exclusively with Searle. In addition, as to each product candidate, the Company will be entitled to milestone payments from

Searle totalling up to an aggregate of $10,000,000 upon the achievement of certain development benchmarks. The Company also will be entitled to royalties from net sales of products resulting from the collaboration. Subject to satisfying certain conditions relating to its manufacturing capacities and capabilities, Hybridon will retain manufacturing rights, and Searle will be required to purchase its requirements of products from the Company on an exclusive basis at specified transfer prices. Upon a change in control of the Company, Searle would have the right to terminate the Company's manufacturing rights, although the royalty payable in respect of net sales would be increased in such event.

Under the collaboration, in the event that Searle designates (and makes the required payments and equity investments for) all of the Additional Targets or in certain other instances relating to the Company's failure to satisfy certain requirements relating to its manufacturing capacities and capabilities, Searle will have the right, exercisable in its sole discretion, to require the Company to form a joint venture with Searle for the development of products in the Searle Field (other than products relating to molecular targets that have already been designated by Searle) to which each party will contribute $50,000,000 in cash, although the Company's cash contribution

would be reduced by the value of the technology and other rights contributed by Hybridon to the joint venture. The Company and Searle would each own 50% of the joint venture, although Searle's ownership interest in the joint venture would increase based upon a formula to up to a maximum of 75% if the joint venture is established in certain instances relating to the Company's failure to satisfy certain requirements relating to its manufacturing capacities and capabilities.

Under the collaboration, Searle also purchased 200,000 shares of Common Stock in the Company's initial public offering.

Medtronic, Inc.

In May 1994, the Company and Medtronic entered into a collaboration involving the testing of a drug delivery device for use in delivering Hybridon's antisense oligonucleotides for the treatment of Alzheimer's disease. See "Item 1. Business -- Hybridon Drug Development and Discovery Programs -- Preclinical Programs -- Amyloid Proteins." Hybridon will be responsible for the development of, and hold all rights to, any drug developed pursuant to this collaboration, and Medtronic will be responsible for the development of, and hold all rights to, any delivery system developed pursuant to this collaboration. The parties may extend this collaboration by mutual agreement to other neurodegenerative disease targets. The research and development to be conducted is determined and supervised by a committee comprised of an equal number of designees of the Company and Medtronic.

As part of the collaboration, Medtronic purchased an aggregate of 131,667 shares of the Company's Common Stock.

FINANCIAL COLLABORATIONS

In order to maintain financial flexibility, Hybridon considers innovative arrangements to finance certain applications of its GEM technology, particularly applications that it would not develop in the near term without external funding. The Company has entered into one such arrangement, which is summarized below.

MethylGene Inc.

In 1996, the Company and certain Canadian institutional investors formed a

Quebec company, MethylGene, to develop and market (i) antisense compounds to inhibit DNA methyltransferase for the treatment of cancers, (ii) other methods of inhibiting DNA methyltransferase for the treatment of any indications and (iii) antisense compounds to inhibit a second molecular target other than DNA methyltransferase for the treatment of cancers, to be agreed upon by Hybridon and MethylGene (such three product areas being referred to herein as the "MethylGene Fields"). In December 1997, Hybridon and Methylgene expanded the Methylgene Fields to include (a) antisense compounds to inhibit DNA methyltransferase for any indication and (b) antisense compounds to inhibit a second and third molecular target for any indications, as may be selected by Methylgene, so long as such molecular targets are not bona fide targets under investigation by the Company on or prior to the date that Methylgene notifies the Company of the identity of such second or third molecular target.

Hybridon initially acquired a 49% minority interest in MethylGene for approximately CDN$1,000,000, and the Canadian investors acquired a majority interest in MethylGene for a total of approximately CDN$7,500,000. On March 4, 1998, Methylgene raised an additional CDN$15,800,000 from the private placement of securities. As a result of such financing, Hybridon now owns an approximately 30% interest in Methylgene.

The Canadian investors who initially invested in the Company continue to have the right to exchange all (but not less than all) of the shares of stock in MethylGene that they initially purchased for shares of Common Stock of Hybridon on the basis of 37.5 MethylGene shares (for which they paid approximately US $56.25) for one share of Hybridon Common Stock (subject to adjustment for stock splits, stock dividends and the like). This option is exercisable only during a 90-day period commencing on the earlier of the date five years after the closing of the Canadian investors' investment in MethylGene or the date on which MethylGene ceases operations, and terminates sooner if MethylGene satisfies certain conditions.

Hybridon has granted to MethylGene exclusive worldwide licenses and sublicenses in respect of certain technology relating to the MethylGene Fields. In addition, Hybridon and MethylGene have entered into a supply agreement pursuant to which MethylGene is obligated to purchase from Hybridon all required formulated bulk oligonucleotides at specified transfer prices. The Company is currently finalizing a drug development advisory and services agreement pursuant to which the Company will assist Methylgene in preparing an IND for its first compound.

It is anticipated that MethylGene will continue to qualify to receive certain Canadian tax benefits with respect to the research and development activities which it carries on in Canada.

MANUFACTURING TECHNOLOGY AND THE HYBRIDON SPECIALTY PRODUCTS DIVISION

The Company has developed a manufacturing technology platform which integrates key elements of the manufacturing process to increase the purity of oligonucleotide products, enhance the efficiency of the production process and increase the scale of production. The Company has developed two separate commercial scale oligonucleotide synthesizers. One of these machines was developed in an internal program and the other in a collaboration with Pharmacia. Both machines are designed with a capacity of up to 100 millimoles (approximately 300 grams per batch), although the Company believes that these machines may be able to exceed such capacity. Pharmacia has retained the right to sell the machine developed under the collaboration to third parties, subject to an obligation to pay Hybridon royalties on such third party sales. The

Company believes that its machines are the first commercial scale oligonucleotide synthesizers designed for more advanced chemistries. In addition, the Company has implemented proprietary purification processes, which use water in place of chemical solvents, simplifying environmental compliance and permitting purification of kilogram batches of oligonucleotides. The Company has also developed proprietary chemical synthesis processes and novel reagents used in the synthesis process, which the Company believes will further decrease the cost of production of advanced oligonucleotides.

In 1996, Hybridon formed the HSP Division to capitalize on this technology and know-how and manufacture highly purified oligonucleotide compounds both for Hybridon's internal use and for sale to third parties, including the Company's collaborative partners, on a custom contract basis. The Company is manufacturing oligonucleotides at its 36,000 square foot leased manufacturing facility, which the Company believes is the first commercial-scale synthetic DNA production facility with a fully integrated manufacturing technology platform, including large-scale synthesis, purification and proprietary analytical support. The Company first began production of oligonucleotide compounds for sale to third parties in June 1996 and had revenues of approximately $1.1 million in 1996 and approximately $1.9 million in 1997. The Company's principal customers include Genta/JBL Scientific, Aronex Pharmaceuticals, Inc. and Gen-Probe, Inc.

In order to strengthen the marketing of the HSP Division's products, in 1996 the Company entered into a four-year sales and supply agreement with the Applied Biosystems Division of Perkin-Elmer. Under the agreement, Perkin-Elmer agreed to refer potential customers for the custom contract manufacture of oligonucleotides to Hybridon, and Hybridon agreed to purchase amidites from Perkin- Elmer for the manufacture of oligonucleotides sold to such customers and to pay Perkin-Elmer a percentage of the sales price paid by such customers. In addition, Perkin-Elmer licensed to Hybridon its oligonucleotide synthesis patents.

The Company is in discussions regarding a possible joint venture with respect

to the HSP Division, which the Company believes would enable it to maximize the potential for third party manufacturing by the HSP Division, while ensuring for the Company and its collaborators a source of oligonucleotides. However, there can be no assurance that the Company will enter into any joint venture of the HSP Division or that the terms of any joint venture will be as anticipated by the Company.

The production of antisense compounds is similar to the chemical synthesis used in the production of conventional pharmaceuticals, and in contrast with typical biopharmaceuticals, does not involve any fermentation processes or living cells. Moreover, unlike many conventional drugs, antisense compounds targeted at different diseases can be manufactured with the same nucleotide building blocks and using the same manufacturing processes and equipment with minimal adjustments. As a result, the knowledge and experience that the Company obtains in the manufacture of one compound is substantially applicable to the manufacture of other oligonucleotide compounds for the treatment of other diseases and results in other manufacturing efficiencies.

The Company may need to further increase its manufacturing capacity through the purchase or construction of additional large-scale oligonucleotide synthesizers in order to satisfy its anticipated future requirements for its product candidates and in order to manufacture oligonucleotides on a custom contract basis for sale to third parties. In addition, in order to successfully commercialize its product candidates or achieve satisfactory margins on sales, the Company may be required to reduce further the cost of production of its oligonucleotide compounds. See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations -- Certain Factors That May Affect Future Results -- Limited Manufacturing Capability."

The Company believes that it is currently manufacturing

oligonucleotides in substantial compliance with FDA requirements for manufacturing in compliance with GMP, although its facility and procedures have not been formally inspected by the FDA and the procedures and documentation followed may have to be enhanced in the future as the Company expands its oligonucleotide production activities. Failure to establish to the FDA's satisfaction compliance with GMP can result in the FDA denying authorization to initiate or continue clinical trials, to receive approval of a product or to begin or to continue commercial marketing.

In addition, the Company's manufacturing processes are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of certain materials and waste products.

MARKETING STRATEGY

Hybridon plans to market the pharmaceutical products it is developing either directly or through co-marketing, licensing, distribution or other arrangements with pharmaceutical and biotechnology companies. Hybridon's current strategy with respect to these products in development is to build a hospital-targeted direct sales group for products for market areas that can be accessed with a small to medium size sales force. Implementation of this strategy will depend on many factors, including the market potential of any such products the Company develops as well as on the Company's financial resources. The Company does not expect to establish a direct sales capability with respect to such products until such time as one or more of such products approach marketing approval. To market those products that will serve a large, geographically diverse patient population, the Company expects to enter into licensing, distribution or partnering agreements with pharmaceutical and biotechnology companies that have large, established sales organizations. To the extent the Company enters into marketing arrangements with third parties, any revenues received by the Company will be dependent on the efforts of such third parties, and there can be no assurance that such efforts will be successful. While the Company has developed general marketing strategies, it has not begun the implementation of any of these strategies with respect to any of these potential products.

ACADEMIC AND RESEARCH COLLABORATIONS

Hybridon enters into collaborative research agreements relating to specific disease targets and other research activities in order to augment its internal research capabilities and to obtain access to the specialized knowledge or expertise of its collaborative partners. With respect to certain of the Company's drug development programs, the Company relies primarily upon outside collaborators. Accordingly, termination of the Company's collaborative research agreements with any of these collaborators could result in the termination of the related research program.

In general, the Company's collaborative research agreements require the payment by Hybridon of various amounts in support of the research to be conducted. The Company usually provides the collaborator with selected oligonucleotides, which the collaborator then tests in his or her assay systems. If the collaborator creates any invention during the course of his or her efforts, solely or jointly with the Company, Hybridon generally has an option to negotiate an exclusive, worldwide, royalty-bearing license of the collaborator's rights in the invention for the purpose of commercializing any product incorporating such invention. Inventions developed solely by Hybridon's scientists as part of the collaboration generally are owned exclusively by Hybridon. Most of these collaborative agreements are non-exclusive and can be cancelled on relatively short notice.

Since July 1997, the Company has allowed a number of its collaborative research agreements to expire and has terminated certain others. The Company has, however, maintained the research agreements which it has determined are appropriate to support its current drug development programs.

PATENTS, TRADE SECRETS AND LICENSES

Proprietary protection for the Company's product candidates, processes and know-how is important to Hybridon's business. Thus, the Company plans to prosecute and enforce aggressively its patents and proprietary technology. The Company's policy is to file patent applications to protect technology, inventions and improvements that are considered important to the development of its business. Hybridon seeks to establish a comprehensive proprietary position through a "layered" patent strategy covering the Company's families of oligonucleotide chemistries, the antisense sequences of the Company's oligonucleotide compounds and the overall chemical compositions of these oligonucleotide compounds. The Company believes that this approach may provide it with at least three independent levels of protection. Hybridon also seeks to protect its proprietary analytical and manufacturing processes. The patents and patent applications owned or exclusively licensed by the Company also are directed to many aspects of the Company's proprietary oligonucleotide production and analysis technology and ribozyme technology. The Company also relies upon trade secrets, know-how, continuing technological innovation and licensing opportunities to develop and maintain its competitive position.

As of February 28, 1998, Hybridon owned or exclusively licensed 55 issued U.S. patents, seven issued foreign patents, 22 allowed U.S. patent applications, two allowed European applications and 62 other U.S. and 105 other non-U.S. patent applications. The patents and applications owned or exclusively licensed by the Company cover various chemically advanced oligonucleotides, proprietary target sequences, specific preferred oligonucleotide products, methods for making and purifying oligonucleotides, analytical methods and methods for oligonucleotide-based therapeutic treatment of various diseases. The U.S. patents owned or exclusively licensed by Hybridon expire at various dates ranging from 2006 to 2015.

Under the terms of a license agreement with the Worcester Foundation (the "Foundation License"), Hybridon is the worldwide, exclusive licensee under several U.S. issued or allowed patents and various patent applications owned by the Worcester Foundation relating to 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.

One of the issued U.S. patents (the "HIV Patent") and one of the issued European patents licensed from the Worcester Foundation broadly claim antisense

oligonucleotides as new compositions of matter for inhibiting the replication of HIV. The other issued U.S. patents include claims covering composition and uses of oligonucleotides based on the Company's advanced chemistries, methods of oligonucleotide synthesis that are potentially applicable to large-scale commercial production, compositions of certain modified oligonucleotides that are useful for diagnostic tests or assays and methods of purifying full-length oligonucleotides after synthesis. The earliest expiration of the patents licensed to the Company by the Worcester Foundation is 2006, when the HIV Patent expires.

The Company also is the exclusive licensee under various other U.S. and foreign patents and patent applications, including two U.S. patents jointly owned by the Worcester Foundation and the Mount Sinai Medical Center of New York claiming the use of antisense oligonucleotides for the inhibition of influenza viruses and two U.S. patent applications owned by McGill University relating to oligonucleotides and DNA methyltransferase. The Company and Massachusetts

General Hospital ("MGH") jointly own one issued U.S. patent directed to compositions of antisense oligonucleotides applicable to Alzheimer's disease. The Company holds an exclusive license to MGH's interests under such patent.

The Company is a non-exclusive licensee of certain patents held by the NIH relating to oligonucleotide phosphorothioates and a non-exclusive licensee of an NIH patent covering the phosphorothiolation of oligonucleotides. The field of each of these licenses extends to a wide variety of genetic targets. If certain of the claims of the NIH patents non-exclusively licensed to Hybridon are valid, certain of the Company's products in development would infringe these patents in the absence of the license.

The U.S. Patent and Trademark Office ("the U.S. PTO") has informed Hybridon that certain otherwise allowable patent applications exclusively licensed by the Company from the Worcester Foundation have been submitted to the Board of Patent Appeals and Interferences to determine whether an interference should be declared with issued U.S. patents held by the NIH relating to oligonucleotide phosphorothioates. An interference proceeding is an inter-parties proceeding in the U.S. PTO to determine who is the first to invent a claimed invention, and thus who is entitled to a patent for the claimed invention. McDonnell Boehnen Hulbert & Berghoff, the Company's U.S. patent counsel, is of the opinion that the Worcester Foundation patent application has a prima-facie case for priority against the NIH for an invention that includes phosphorothioate-modified oligonucleotides. However, there can be no assurance an interference can be declared, or if declared, as to the outcome thereof. An adverse outcome in the interference would not affect the non-exclusive license from the NIH to Hybridon of the NIH phosphorothioate patents. The U.S. PTO has also declared a four-way interference involving two additional U.S. patents relating to the Company's chimeric oligonucleotides which Hybridon exclusively licenses from the Worcester Foundation. There can be no assurance as to the outcome of this interference.

Under the licenses to which it is a party, the Company is obligated to pay royalties on net sales by the Company of products or processes covered by a valid claim of a patent or patent application licensed to it. The Company also is required in some cases to pay a specified percentage of any sublicense income that the Company may receive. These licenses impose various commercialization, sublicensing, insurance and other obligations on the Company. Failure of the Company to comply with these requirements could result in termination of the license. The Foundation License also grants the Company a right of first refusal to certain technology developed by the Worcester Foundation.

The patent positions of pharmaceutical and biotechnology firms, including Hybridon, are generally uncertain and involve complex legal and factual questions. Consequently, even though Hybridon and its licensors are currently prosecuting their respective patent applications with the U.S. Patent and Trademark Office and certain foreign patent authorities, the Company does not know whether any of its applications or those of third parties under which the Company has or may obtain a license will result in the issuance of any patents or, if any patents are issued, whether they will provide significant proprietary protection or will be circumvented or invalidated. Since patent applications in the U.S. are maintained in secrecy until patents issue, and since publication of discoveries in the scientific or patent literature tend to lag behind actual discoveries by several months, Hybridon cannot be certain that it, or any licensor of patents to it, as the case may be, was the first creator of inventions claimed by pending patent applications or that Hybridon or any licensor, as the case may be, was the first to file patent applications for such inventions. See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations -- Certain Factors That May Affect Future Results -- Patents and Proprietary Rights."

Competitors of the Company and other third parties hold issued patents and pending patent applications relating to antisense and other gene expression modulation technologies, and it is uncertain whether these patents and patent applications will require the Company to alter its products or processes, pay

licensing fees or cease certain activities. See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations -- Certain Factors That May Affect Future Results -- Patents and Proprietary Rights." In particular, the Company is aware of a European patent granted to a third party relating to certain types of stabilized synthetic oligonucleotides for use as therapeutic agents for selectively blocking the translation of a messenger RNA into a targeted protein by binding with a portion of the messenger RNA to which the stabilized synthetic oligonucleotide is substantially complementary. This European patent was revoked in entirety in an opposition proceeding before the European Patent Office in September 1995. The holder of this patent has appealed such decision.

Hybridon's practice is to require its employees, consultants, members of its Scientific and Clinical Advisory Boards, outside scientific collaborators and sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with the Company. These agreements provide that all confidential information developed or made known to the individual during the course of the individual's relationship with Hybridon is to be kept confidential and not disclosed to third parties, subject to a right to publish certain information in the scientific literature in certain circumstances and subject to other specific exceptions. In the case of employees, the agreements provide that all inventions conceived by the individual shall be the exclusive property of the Company. There can be no assurance, however, that these agreements will provide meaningful protection for the Company's trade secrets or adequate remedies in the event of unauthorized use or disclosure of such information.

Hybridon engages in collaborations and sponsored research agreements and enters into preclinical and clinical testing agreements with academic and research institutions and U.S. government agencies, such as the NIH, to take advantage of their technical expertise and staff and to gain access to clinical evaluation models, patients, and related technology. Consistent with pharmaceutical industry and academic standards, and the rules and regulations under the Federal Technology Transfer Act of 1986, these agreements may provide that developments and results will be freely published, that information or materials supplied by Hybridon will not be treated as confidential and that Hybridon may be required to negotiate a license to any such developments and results in order to commercialize products incorporating them. There can be no assurance that the Company will be able successfully to obtain any such license at a reasonable cost or that such developments and results will not be made available to competitors of the Company on an exclusive or nonexclusive basis. See "Item 1. Business -- Academic and Research Collaborations."

GOVERNMENT REGULATION

The production and marketing of the Company's products and its research and development activities are subject to regulation for safety, effectiveness and quality by numerous governmental authorities in the U.S. and other countries. The Company believes that it is in material compliance with all federal, state and foreign legal and regulatory requirements under which it operates. However, there can be no assurance that such legal or regulatory requirements will not be amended or that new legal or regulatory requirements will not be adopted, any one of which could have a material adverse effect on the Company's business or results of operations.

FDA Approval

In the U.S., pharmaceutical products intended for therapeutic or diagnostic use in humans are subject to rigorous FDA regulation. The process of completing clinical

trials and obtaining FDA approvals for a new drug is likely to take a number of years and requires the expenditure of substantial resources. There can be no assurance that any product will receive such approval on a timely basis, if at all. See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations -- Certain Factors That May Affect Future Results -- No Assurance of Regulatory Approval; Government Regulation."

The steps required before a new oligonucleotide-based pharmaceutical product for use in humans may be marketed in the U.S. include (i) preclinical tests, (ii) submission to the FDA of an IND application, which must become effective before human clinical trials commence, (iii) adequate and well-controlled human clinical trials to establish the safety and effectiveness of the product, (iv) submission of a New Drug Application ("NDA") to the FDA, and (v) FDA approval of the NDA prior to any commercial sale or shipment of the product.

Preclinical tests include laboratory evaluation of product chemistry and formulation, as well as animal studies, to assess the potential safety and effectiveness of the product. Compounds must be manufactured according to GMP and preclinical safety tests must be conducted by laboratories that comply with FDA regulations regarding GLP. See "Item 1. Business -- Manufacturing." The results of the preclinical tests are submitted to the FDA as part of an IND and are reviewed by the FDA prior to the commencement of human clinical trials. Unless the FDA objects to, or makes comments or raises questions concerning, an IND, the IND will become effective 30 days following its receipt by the FDA. There can be no assurance that submission of an IND will result in FDA authorization to commence clinical trials.

Clinical trials involve the administration of the investigational new drug to healthy volunteers and to patients, under the supervision of a qualified principal investigator. Clinical trials are conducted in accordance with Good Clinical Practices under protocols that detail the objectives of the study, the parameters to be used to monitor safety and the effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND. Further, each clinical study must be conducted under the auspices of an independent Institutional Review Board (an "IRB"). The IRB will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution.

Clinical trials are typically conducted in three sequential phases, although the phases may overlap. In Phase I, the investigational new drug usually is administered to healthy human subjects and is tested for safety (adverse effects), dosage, tolerance, metabolism, distribution, excretion and pharmacodynamics (clinical pharmacology). Phase II involves studies in a limited patient population to (i) determine the effectiveness of the investigational new drug for specific indications, (ii) determine dosage tolerance and optimal dosage, and (iii) identify possible adverse effects and safety risks. When an investigational new drug is found to be effective and to have

an acceptable safety profile in Phase II evaluation, Phase III trials are undertaken to further evaluate clinical effectiveness and to further test for safety within an expanded patient population at geographically dispersed clinical study sites. There can be no assurance that Phase I, Phase II or Phase III testing will be completed successfully within any specified time period, if at all, with respect to any of the Company's products subject to such testing. Furthermore, the Company, an IRB or the FDA may suspend clinical trials at any time if it is felt that the participants are being exposed to an unacceptable health risk.

The results of the pharmaceutical development, preclinical studies and clinical studies are submitted to the FDA in the form of an NDA for approval of

the marketing and commercial shipment of the product. The FDA may require additional testing or information before approving the NDA. In any event, the FDA may deny an NDA if applicable regulatory criteria are not satisfied. Moreover, if regulatory approval of a product is granted, such approval may require postmarketing testing and surveillance to monitor the safety of the product or may entail limitations on the indicated uses for which it may be marketed. Finally, product approvals may be withdrawn if compliance with regulatory standards is not maintained or if problems occur following initial marketing.

In addition to product approval, the Company may be required to obtain a satisfactory inspection by the FDA covering the Company's manufacturing facilities before a product manufactured by the Company can be marketed in the U.S. The FDA will review the Company's manufacturing procedures and inspect its facilities and equipment for compliance with GMP and other applicable rules and regulations. Any material change by the Company in its manufacturing process, equipment or location would necessitate additional FDA review and approval.

Foreign Regulatory Approval

Whether or not FDA approval has been obtained, approval of a pharmaceutical product by comparable governmental regulatory authorities in foreign countries must be obtained prior to the commencement of clinical trials and subsequent marketing of such product in such countries. The approval procedure varies from country to country, and the time required may be longer or shorter than that required for FDA approval.

Under European Union ("EU") law, either of two approval procedures may apply to the Company's products: a centralized procedure, administered by the EMEA (the European Medicines Evaluation Agency); or a decentralized procedure, which requires approval by the medicines agency in each EU Member State where the Company's products will be marketed. The centralized procedure is mandatory for certain biotechnology products and available at the applicant's option for certain other products. Whichever procedure is used, the safety, efficacy and quality of the

Company's products must be demonstrated according to demanding criteria under EU law and extensive nonclinical tests and clinical trials are likely to be required. In addition to premarket approval requirements, national laws in EU Member States will govern clinical trials of the Company's products, adherence to good manufacturing practice, advertising and promotion and other matters. In certain EU Member States, pricing or reimbursement approval may be a legal or practical precondition to marketing.

Other Regulation

In addition to regulations enforced by the FDA, the Company also is subject to regulation under the Occupational Safety and Health Act and other present and potential future federal, state or local regulations. Furthermore, because the Company's research and development involves the controlled use of hazardous materials, chemicals, viruses and various radioactive compounds, the Company's operations are subject to U.S. Department of Transportation and Environmental Protection Agency requirements and other federal, state and foreign laws and regulations regarding hazardous waste disposal, air emissions and wastewater discharge, including without limitation the Environmental Protection Act, the Toxic Substances Control Act and the Resource Conservation and Recovery Act. Although the Company believes that its procedures for handling and disposing of such materials comply with the standards prescribed by applicable regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of such an accident, the Company could be held liable for any damages that result and any such liability could have a material adverse effect on the Company.

COMPETITION

The Company's products under development are expected to address

several different markets defined by the potential indications for which such products are developed and ultimately approved by regulatory authorities. For several of these indications, the Company's proposed products will be competing with products and therapies either currently existing or expected to be developed, including antisense oligonucleotides developed by third parties. Competition among these products will be based, among other things, on product efficacy, safety, reliability, availability, price and patent position. An important factor will be the timing of market introduction of the Company's or competitive products. Accordingly, the relative speed with which Hybridon can develop products, complete the clinical trials and approval processes and supply commercial quantities of the products to the market is expected to be an important competitive factor. The Company's competitive position will also depend upon its 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 activities on technologies and products aimed at therapeutic modulation of gene expression. The Company believes that the industry-wide interest in these technologies and products will continue and will accelerate as the techniques which permit their application to drug development become more widely understood. There can be no assurance that the Company's competitors will not succeed in developing products based on oligonucleotides or other technologies that are more effective than any which are being developed by the Company or which would render the Company's technology and products obsolete and noncompetitive prior to recovery by the Company of the research, development and commercialization expenses incurred with respect to those products. Furthermore, because of the fundamental differences between gene expression modulation and other technologies, there may be indications for which such other technologies are superior to gene expression modulation. The development by others of new treatment methods not based on gene expression modulation technology for those indications for which the Company is developing compounds could render the Company's compounds noncompetitive or obsolete.

Competitors of the Company engaged in all areas of drug discovery in the U.S. and other countries are numerous and include, among others, major pharmaceutical and chemical companies, biotechnology firms, universities and other research institutions. Many of these competitors have substantially greater financial, technical and human resources than the Company. In addition, many of these competitors have significantly greater experience than the Company in undertaking preclinical studies and human clinical trials of new pharmaceutical products and obtaining FDA and other regulatory approvals of products for use in health care. Accordingly, the Company's competitors may succeed in obtaining FDA or other regulatory approvals for products more rapidly than the Company. Furthermore, if the Company is permitted to commence commercial sales of products, it will also be competing with respect to manufacturing efficiency and marketing capabilities, areas in which it has limited or no experience.

In its HSP Division operations, the Company competes against a number of third parties, and there is the possibility of internal production by the Company's customers. Many of these third parties and customers have greater financial, technical and human resources than the Company. Key competitive factors will include the price and quality of the products as well as manufacturing capacity and ability to comply with specifications and to fulfill orders on a timely basis. The Company may be required to reduce the cost of its product offerings to meet competition. See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations -- Certain Factors That May Affect Future Results -- Competition."

EMPLOYEES

As of March 30, 1998, Hybridon employed 78 individuals full-time, of whom 40 held advanced degrees. Sixty-three of these employees are engaged in research and development activities and 15 are employed in finance, corporate development and legal and general administrative activities. In addition, 27 of these employees are employees of the HSP Division, of whom eight are employed in process development and quality control. Many of the Company's management and professional employees have had prior experience with pharmaceutical, biotechnology or medical products companies. None of the Company's employees is covered by collective bargaining agreements, and management considers relations with its employees to be good.

SCIENTIFIC ADVISORY BOARD

The Company's Scientific Advisory Board consists of individuals with recognized expertise in gene expression modulation technology, antisense oligonucleotides, oligonucleotide biochemistry, human genetics, medicine and related fields who advise the Company about current and long-term scientific planning, research and development. The Scientific Advisory Board holds approximately three or four formal meetings annually. All members of the Scientific Advisory Board are employed by employers other than the Company, primarily academic institutions, and may have commitments to or consulting or advisory agreements with other entities that may limit their availability to the Company. These companies may also be competitors of Hybridon. Several members of the Scientific Advisory Board have, from time to time, devoted significant time and energy to the affairs of the Company. However, except for Drs. Zamecnik and Wyngaarden, who are parties to consulting agreements with the Company, no members are regularly expected to devote more than a small portion of their time to Hybridon.

As part of its efforts to reduce expenditures, the Company plans to reduce the size of the Scientific Advisory Board and rely in part on individual consultants.

The following persons are currently members of the Scientific Advisory Board:

Paul C. Zamecnik, M.D. (Chairman) is a founder of Hybridon and serves as a director of the Company. Dr. Zamecnik has served as a Principal Scientist of the Worcester Foundation and as the Collis P. Huntington Professor of Oncologic Medicine Emeritus at the Harvard Medical School since 1979.

Daniel M. Brown, Sc.D., F.R.S. has been a Fellow of King's College, University of Cambridge, since 1953, and currently serves as Vice-Provost of King's College and as an Attached Scientific Worker in the Medical Research Council Laboratory of Molecular Biology at the University of Cambridge. Dr. Brown is also an Emeritus

Reader in Organic Chemistry at the University of Cambridge and became a Fellow of the Royal Society in 1982.

Har Gobind Khorana, Ph.D. has served as a Sloan Professor in the Departments of Biology and Chemistry at the Massachusetts Institute of Technology since 1970. Dr. Khorana has been awarded numerous prestigious honors, including the Nobel Prize in Medicine or Physiology in 1968 and the National Medal of Science in 1987.

Roger E. Monier, Ph.D. has served as Director of Molecular Oncology at the Institute Gustave Roussy in Paris since 1985. From 1980 to 1985, Dr. Monier served as the Director of Life Sciences at the Centre Nationale de Recherches

Scientifiques in Paris. Dr. Monier was elected to the French Academy of Science in 1992.

Peter Palese, Ph.D. has served as a Professor in the Department of Microbiology at Mount Sinai School of Medicine in New York since 1978 and has served as Chairman of the Department of Microbiology since 1987.

Thoru Pederson, Ph.D. is a Principal Scientist of Cell Biology at the Worcester Foundation and has served as its President and Director since 1985. Dr. Pederson is also a Professor of Biochemistry and Molecular Biology at the University of Massachusetts Medical School. From February 1990 to November 1993, Dr. Pederson served as a director of the Company.

Jerry A. Weisbach, Ph.D. is an independent consultant to biotechnology and pharmaceutical companies. Dr. Weisbach served as Director of Technology Transfer and as an Adjunct Professor at The Rockefeller University from 1988 to 1994. Dr. Weisbach served as Corporate Vice President of Warner-Lambert Company, an international pharmaceutical company, from 1981 to 1987 and President of the Parke- Davis Pharmaceutical Research Division of Warner-Lambert Company from 1979 to 1987.

James B. Wyngaarden, M.D. a director of the Company, served as the Foreign Secretary of the National Academy of Sciences and the Institute of Medicine of the National Academy of Sciences from 1990 to 1994. Dr. Wyngaarden also served as the Director of the NIH from 1982 to 1989 and as a council member of the Human Genome Organization from 1990 to 1993 and as its Director from 1990 to 1991.

Members of the Company's Scientific Advisory Board are paid $2,500 per calendar quarter for their services in such capacity and are reimbursed for their expenses incurred in connection with attendance at its meetings. Members of the Scientific Advisory Board also have received options to purchase Common Stock of the Company under the Company's stock option plans.

CLINICAL ADVISORY BOARD

The Company's Clinical Advisory Board was formally established in November 1993 to advise the Company with respect to clinical trials of the Company's product candidates. The Clinical Advisory Board holds approximately three or four formal meetings annually. The Clinical Advisory Board consists of individuals with recognized expertise in the conduct of clinical trials and the regulatory approval process. All members of the Clinical Advisory Board are employed by employers other than the Company, primarily academic institutions, and may have commitments to or consulting or advisory agreements with other entities that may limit their availability to the Company. These companies may also be competitors of Hybridon. Several members of the Clinical Advisory Board have, from time to time, devoted significant time and energy to the affairs of the Company. However, except for Drs. Wyngaarden, who is a director of and a consultant to the Company, and Drs. Groopman and Weisbach, who are consultants to the Company, no members are regularly expected to devote more than a small portion of their time to Hybridon.

As part of its efforts to reduce expenditures, the Company plans to reduce the size of the Clinical Advisory Board and rely in part on individual consultants.

The following persons are currently members of the Clinical Advisory Board:

Dr. Wyngaarden's (Chairman) background and experience are described above under "Item 1. Business -- Scientific Advisory Board."

Robert M. Chanock, M.D. has served as an infectious disease epidemiologist and laboratory virologist at the NIH since 1957. Prior to that Dr. Chanock held academic appointments at the University of Cincinnati College of Medicine and the Johns Hopkins University School of Hygiene and Public

Health. Dr. Chanock has been awarded numerous prestigious honors, including the ICN International Prize in Virology in 1990, the Bristol-Myers Squibb Award for Distinguished Achievement in Infectious Diseases Research in 1993 and the Albert B. Sabin Foundation award.

Vincent T. DeVita, Jr., M.D. has served as Director of the Yale Cancer Center since 1993. Dr. DeVita served as an attending physician and member of the Program of Molecular Pharmacology and Therapeutics from 1988 to 1993, and as Physician-in- Chief from 1988 to 1991, at Memorial Sloan Kettering Cancer Center. From 1980 to 1988, Dr. DeVita served as Director of the National Cancer Institute, NIH. In 1995, he was honored with the City of Medicine Award.

Jerome Groopman, M.D. has served as Chief of the Division of Hematology/Oncology at the New England Deaconess Hospital since 1985. He has also served as a Professor of Medicine at Harvard Medical School since 1993. Dr. Groopman is a member of the AIDS Advisory Committee, the Biologics Committee of the FDA, the AIDS Clinical Trials Group of the NIH and the AIDS Basic Science

Research Study Section A, NIAID.

Paul Meier, Ph.D. has served as Professor and Chairman of the Department of Statistics and Division of Biological Sciences at Columbia University since 1985. Dr. Meier has served as an advisor to the FDA on the statistical analysis of clinical trials since 1991.

Dr. Weisbach's background and experience are described under "Item 1. Business -- Scientific Advisory Board."

Members of the Company's Clinical Advisory Board are paid $2,500 per calendar quarter for their services in such capacity and are reimbursed for their expenses incurred in connection with attendance at its meetings.

ITEM 2. PROPERTIES.

The Company's executive, administrative and research and development facilities, comprising approximately 91,500 square feet (a portion of which is subleased as described below), currently are located in Cambridge, Massachusetts. These facilities are held under a lease which expires in 2012, but may be extended at Hybridon's option for two additional five-year terms. The lease provides for an annual rent of approximately $38.00 per square foot for the first five years, approximately $42.00 per square foot for the second five years and approximately $47.00 per square foot for the third five years.

A substantial portion of the Cambridge headquarters facility (approximately 41,500 square feet of office and laboratory space) has been subleased to a third party under an agreement extending to September 1, 1999. The Company is evaluating several long term options for the Cambridge facility, including a possible transfer of its leases or a sale of its ownership interest in the Cambridge facility. In either case, such transaction would require the Company to relocate its headquarters.

In addition, the Company leases additional space in Cambridge, Massachusetts comprising approximately 26,000 square feet for a term expiring April 30, 2007 at an annual rent of approximately $23 per square foot. The Company is currently subleasing approximately 20,000 square feet of this facility to a third party under a sublease expiring September 30, 2000.

The Company leases its 36,000 square foot manufacturing facility in Milford, Massachusetts under a lease which expires in 2004. The term of the lease may be extended at Hybridon's option for two additional five-year terms. In addition to its manufacturing operations, the Company conducts process and analytical chemistry operations at this facility.

Effective March 31, 1998, the Company has terminated the lease for its offices in Paris, France.

For a description of various arrangements relating to the Cambridge headquarters facility

and the Paris facility, see "Certain Relationships and Related Transactions -- Transactions with Pillar S.A. and Certain Affiliates" in the Company's 1998 Proxy Statement (as defined in "Item 10. Directors and Executive Officers of the Registrant").

ITEM 3. LEGAL PROCEEDINGS.

The Company is not a party to any litigation that it believes could have a material adverse effect on the Company or its business.

ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS.

At a Special Meeting of Stockholders held on November 18, 1997, the Company's stockholders, by the vote specified below, approved an amendment to the Company's Certificate of Incorporation to effect a reverse split of the Company's Common Stock, pursuant to which each five shares of Common Stock then outstanding were converted into one share of Common Stock.

For	Against	Abstain	Broker Non-Votes
14,652,634	77,698	13,563	0

EXECUTIVE OFFICERS AND SIGNIFICANT EMPLOYEES OF THE COMPANY

The executive officers and significant employees of the Company and their ages as of March 13, 1998 are as follows:

NAME	AGE	POSITION
Executive Officers		
E. Andrews Grinstead, III.....	52	Chairman of Board of Directors, President and Chief Executive Officer
Sudhir Agrawal, D. Phil.....	44	Senior Vice President of Discovery, Chief Scientific Officer and Director
Significant Employees		
Robert G. Andersen.....	47	Vice President of Operations and Planning and Treasurer
Jose E. Gonzalez, Ph.D.....	51	Vice President of Manufacturing and General Manager, Hybridon Specialty Products Division
Philippe Guinot, M.D., Ph.D....	48	Vice President of Drug Development and General Manager, Hybridon Europe

NAME	AGE	POSITION
R. Russell Martin, M.D.....	62	Vice President of Drug Development
Jin-Yan Tang, Ph.D.....	52	Vice President of Production
Mark C. Wiggins.....	42	Vice President of Business Development and Marketing

Mr. Grinstead joined the Company in June 1991 and was appointed Chairman of the Board and Chief Executive Officer in August 1991 and President in January 1993. He has served on the Board of Directors since June 1991. Prior to joining the Company, Mr. Grinstead served as Managing Director and Group Head of the life sciences group at Paine Webber, Incorporated, an investment banking firm, from 1987 to October 1990; Managing Director and Group Head of the life sciences group at Drexel Burnham Lambert, Inc., an investment banking firm, from 1986 to 1987; and Vice President at Kidder, Peabody & Co. Incorporated, an investment banking firm, from 1984 to 1986, where he developed the life sciences corporate finance specialty group. Mr. Grinstead served in a variety of operational and executive positions with Eli Lilly and Company ("Eli Lilly"), an international pharmaceutical company, from 1976 to 1984, most recently as General Manager of Venezuelan Pharmaceutical, Animal Health and Agricultural Chemical Operations and at Lilly Corporate Staff as Administrator, Strategic Planning and Acquisitions. Since 1991, Mr. Grinstead has served as a director of EcoScience Corporation, a development stage company engaged in the development of biopesticides, and as a director of Pharmos Corporation, a development stage company engaged in the development of novel pharmaceutical compounds and drug delivery systems. Mr. Grinstead also serves as a director of Meridian Medical Technologies, Inc., a pharmaceutical and medical device company. Mr. Grinstead was appointed to The President's Council of the National Academy of Sciences and the Institute of Medicine in January 1992 and the Board of the Massachusetts Biotech Council in 1997. Since 1994, Mr. Grinstead has served as a member of the Board of Trustees of the Albert B. Sabin Vaccine Foundation, a charitable foundation dedicated to disease prevention. Mr. Grinstead received an A.B. from Harvard College in 1967, a J.D. from the University of Virginia School of Law in 1974 and an M.B.A. from the Harvard Graduate School of Business Administration in 1976.

Dr. Agrawal joined the Company in February 1990 and served as Principal Research Scientist from February 1990 to January 1993 and as Vice President of Discovery from December 1991 to January 1993 prior to being appointed Chief Scientific Officer in January 1993 and Senior Vice President of Discovery in March 1994. He has served on the Board of Directors since March 1993. Prior to joining the Company, Dr. Agrawal served as a Foundation Scholar at the Worcester Foundation from 1987 through 1991. Dr. Agrawal served as a Research Associate at the Medical

Research Council Laboratory of Molecular Biology in Cambridge, England, from 1985 to 1986, studying synthetic oligonucleotides. Dr. Agrawal received a B.Sc. in chemistry, botany and zoology in 1973, an M.Sc. in organic chemistry in 1975 and a D. Phil. in chemistry in 1980 from Allahabad University in India.

Mr. Andersen joined the Company and was appointed Vice President of Systems Engineering and Management Information Systems in November 1996 prior to being appointed Vice President of Operations and Planning in 1997 and Treasurer of the Company in January 1998. Prior to joining the Company, Mr. Andersen served in a variety of positions at Digital Equipment Corporation, a computer company, from 1986 to 1996, most recently as Group Manager of the Applied Objects Group. From 1978 to 1986, Mr. Andersen served in a variety of positions at United Technologies Corporation, an aviation technology company, most recently as Director of Quality. Mr. Andersen received his B.E.E. in Electrical Engineering from The City College of New York in 1972 and a M.S. from Northeastern University in 1978.

Dr. Gonzalez joined the Company and was appointed Vice President of Manufacturing in August 1995 and was appointed General Manager, Hybridon Specialty Products Division, in September 1997. Prior to joining the Company, Dr. Gonzalez served as Vice President of Manufacturing Operations at Enzon Corporation, a biotechnology company, from 1993 to 1995. From 1977 to 1993, Dr. Gonzalez served in a variety of positions at The Upjohn Company, a pharmaceutical company, most recently as Associate Director of Bioprocess Development. Dr. Gonzalez received a B.S. in chemistry from the University of Miami in 1969 and a Ph.D. in biochemistry from Purdue University in 1974.

Dr. Guinot joined the Company and was appointed Vice President of European Drug Development and General Manager of Hybridon Europe in September 1995. Prior to joining the Company, Dr. Guinot served as a consultant to the Laboratoire Francais du Fractionnemant et des Biotechnologies (the "LFB") from 1994 to 1995, where he was responsible for conducting audits of all of the LFB's research and development programs. From 1981 to 1994, Dr. Guinot served in a variety of positions at the Beaufour-Ipsen Group, a group of affiliated pharmaceutical companies, most recently as General Manager of the Institute Henri Beaufour where he was responsible for the planning, strategy, budget and coordination of the Beaufour-Ipsen Group's product development efforts. In addition, Dr. Guinot has served as an Adjunct Professor of Medicine at the University of California, Davis since 1992, an Adjunct Professor of Physiology at New York Medical College since 1991 and Consultant Physician in Internal Medicine at Broussais Hospital in Paris. Dr. Guinot received an M.D. from the University of Paris in 1975 and a Ph.D. in biophysics from Clermont Ferrand in 1994.

Dr. Martin joined the Company and served as Vice President of Clinical Research from April 1994 to February 1997 prior to being appointed Vice President of

Drug Development in February 1997. Prior to joining the Company, Dr. Martin served in a variety of positions at Bristol Myers Squibb from 1983 to 1994, most recently as Vice President of Clinical Research (Infectious Diseases). During such period, he served as an Adjunct Associate Professor of Medicine and Associate Clinical Professor at Yale University School of medicine from 1987 to 1994, Clinical Professor at University of Connecticut School of Medicine from 1986 to 1993 and Adjunct Professor of Medicine at Baylor College of Medicine from 1993 to 1994. Prior to joining Bristol Myers Squibb, Dr. Martin served as Professor of Medicine, Microbiology and Immunology at Baylor College from 1975 to 1983. Dr. Martin received an A.B. in American studies from Yale University in 1956 and an M.D. from the Medical College of Georgia in 1960.

Dr. Tang joined the Company in 1991 and served as Senior Research Scientist from 1991 to 1993, Director of Oligonucleotide Chemistry from 1993 to 1994 and Executive Director of Process Chemistry from 1994 to April 1995 prior to being appointed Vice President of Process Development in April 1995. In November of 1997, Dr. Tang was appointed Vice President of Production. Prior to joining the Company, Dr. Tang served as a Visiting Fellow at the Worcester Foundation from 1988 to 1991. He also served as a Visiting Professor at the University of Colorado in 1988. Dr. Tang received a B.S. in biochemistry from Shanghai University of Sciences and Technology in 1965 and a Ph.D. from the Shanghai Institute of biochemistry in 1978.

Mr. Wiggins joined the Company and was appointed Vice President of Business Development and Marketing in November 1996. Prior to joining the Company, Mr. Wiggins served in a variety of positions at Schering-Plough Corporation, a pharmaceutical company, from 1986 to 1996, most recently as the Director of Business Development. From 1980 to 1986, Mr. Wiggins held various marketing positions at Ortho Pharmaceuticals, Inc., a pharmaceutical company, and Pfizer, Inc., a pharmaceutical company. Mr. Wiggins received his B.S. in Finance from Syracuse University in 1978 and a M.B.A. from the University of Arizona in 1980.

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PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS.

From January 24, 1996 until December 2, 1997, the Company's Common Stock was traded on the Nasdaq National Market under the symbol "HYBN." Prior to January 24, 1996, there was no established public trading market for the Company's Common Stock.

On December 2, 1997, the Company's Common Stock was delisted from the Nasdaq National Market and began being quoted on the Nasdaq OTC Bulletin Board. Prices reflected on the Nasdaq OTC Bulletin Board may reflect inter-dealer prices, without retail mark-up, mark-downs or commissions and may not necessarily represent actual transactions.

On December 10, 1997 the Company effected a one-for-five reverse stock split of its Common Stock. As a result of the reverse stock split, each five shares of Common Stock was automatically converted into one share of Common Stock, with cash paid in lieu of any fractional shares.

The following table sets forth for the periods indicated the high and low sales prices per share of the Common Stock during each of the quarters set forth below as reported on the Nasdaq National Market and the Nasdaq OTC Bulletin Board since January 24, 1996 and as adjusted to reflect the December 1997 reverse stock split.

	HIGH	LOW
1996		
First Quarter (from January 24, 1996).....	$71.250	$43.750
Second Quarter.....	59.375	25.625
Third Quarter.....	59.375	33.125
Fourth Quarter.....	43.125	26.250
1997		
First Quarter.....	$43.125	$28.125
Second Quarter.....	35.625	25.000
Third Quarter.....	28.125	7.500
Fourth Quarter.....	4.859	2.609

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The reported closing bid price of the Common Stock on the Nasdaq OTC Bulletin Board on March 13, 1998 was $2.4375 per share. The number of stockholders of record on March 13, 1998 was 297.

The Company has never declared or paid cash dividends on its capital stock, and the Company does not expect to pay any cash dividends on its Common Stock in the foreseeable future. The indenture under which the Company issued $50.0 million of the 1997 9% Notes on April 2, 1997 limits the Company's ability

to pay dividends or make other distributions on its Common Stock. In addition, the Company is currently prohibited from paying cash dividends under a credit facility with a commercial bank (the "Bank Credit Facility").

Recent Sales of Unregistered Securities

During the quarterly period ended December 31, 1997, the Company did not sell any securities that were not registered under the Securities Act of 1933, as amended (the "Securities Act").

ITEM 6. SELECTED FINANCIAL DATA.

The selected financial data presented below for each of the years ended December 31, 1993, 1994, 1995, 1996 and 1997 have been derived from the Company's Consolidated Financial Statements that have been audited by Arthur Andersen LLP, independent public accountants. This financial data should be read in conjunction with the Management's Discussion and Analysis of Financial Condition and Results of Operations, the Consolidated Financial Statements and the Notes thereto and the other financial information appearing elsewhere in this Annual Report on Form 10-K.

	Years Ended December 31,				
	1993	1994	1995	1996	1997
	(In thousands, except per share data)				
Statement of Operations Data:					
Revenues					
Research and development	$ 917	$ 1,032	$ 1,186	$ 1,419	$ 945
Product revenue	--	--	--	1,080	1,877
Royalty income	--	--	--	62	48
Interest income	267	135	219	1,447	1,079
	1,184	1,167	1,405	4,008	3,949
Operating Expenses					
Research and development	16,168	20,024	29,685	39,390	46,828
General and administrative	4,372	6,678	6,094	11,347	11,026
Interest	380	69	173	124	4,536
Restructuring	--	--	--	--	11,020
Total operating expenses	20,920	26,771	35,952	50,861	73,410
Net Loss	$(19,736)	$(25,604)	$(34,547)	$(46,853)	$(69,461)
Basic and Diluted Net Loss per Common Share(1)	(55.80)	(70.77)	$ (94.70)	$ (10.24)	$ (13.76)
Shares Used in Computing Basic and Diluted Net Loss per Common Share(1)	354	362	365	4,576	5,050
Pro Forma Net Loss per Common Share(1)	(11.71)	(11.04)	$ (11.02)	$ (9.67)	$ (13.76)
Shares Used in Computing Pro Forma Net Loss per Common Share(1)	1,686	2,320	3,135	4,843	5,050

	December 31,				
	1993	1994	1995	1996	1997
	(In thousands)				
Balance Sheet Data:					
Cash, cash equivalents and short-term investments(2)	$ 8,767	$ 3,396	$ 5,284	$ 16,419	$ 2,202
Working capital (deficit)	8,357	(1,713)	210	8,888	(24,100)
Total assets	15,243	11,989	19,618	41,537	35,072
Long-term debt and capital lease obligations, net of current portion	79	1,522	1,145	9,032	3,282
9% Convertible Subordinated Notes Payable	--	--	--	--	50,000
Deficit accumulated in the development stage	(42,190)	(67,794)	(102,341)	(149,194)	(218,655)
Total stockholders' equity (deficit)	12,178	4,774	12,447	22,855	(46,048)

(1) Computed on the basis described in Note 2(b) of Notes to Consolidated Financial Statements attached as APPENDIX A hereto.

(2) Short-term investments consisted of U.S. government securities with maturities greater than three months but less than one year from the purchase date.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS.

GENERAL

The Company is engaged in the discovery and development of genetic medicines based on antisense technology. The Company commenced operations in February 1990 and since that time has been engaged primarily in research and development efforts, development of its manufacturing capabilities and organizational efforts, including recruitment of scientific and management personnel, and raising capital. To date, the Company has not received revenue from the sale of biopharmaceutical products developed by it. In order to commercialize its own products, the Company will need to address a number of technological challenges and comply with comprehensive regulatory requirements. Accordingly, it is not possible to predict the amount of funds that will be required or the length of time that will pass before the Company receives revenues from sales of any of these products. All revenues received by the Company to date have been derived from collaborative agreements, interest on invested funds and revenues from the custom contract manufacturing of synthetic DNA and reagent products by the Company's HSP Division.

The Company has very limited cash resources and substantial obligations to lenders, equipment lessors, real estate landlords and trade creditors. The Company's ability to continue operations in 1998 depends on its success in raising new funds. If the Company is unable to raise substantial additional new funding beginning in April 1998, it will be required to terminate its operations or seek relief under applicable bankruptcy laws by the end of April 1998.

In the Report of Independent Public Accountants set forth in Appendix A attached to this Annual Report on Form 10-K, Arthur Andersen LLP, the Company's independent public accountants, states that there is substantial doubt about the Company's ability to continue as a going concern.

As part of its efforts to seek new funding, in January 1998, the Company commenced a private offering (the "1998 Unit Financing") of up to 400 units, each unit (a "Unit") consisting of a Note Due 2007 (the "1998 Unit

Notes") in the original principal amount of $100,000 and warrants to purchase Common Stock. The Company is offering the Units at a price of $100,000 per Unit. As of March 30, 1998, the Company had sold 48 Units for an aggregate purchase price of $4.8 million. There can be no assurance as to whether the Company will be able to sell any additional Units or as to the timing of the Company's sale of additional Units. See "1998 Financing Activities" below.

The Company has incurred cumulative losses from inception through

December 31, 1997 of approximately $218.7 million. The Company implemented a restructuring plan in the second half of 1997 which it expects will significantly reduce the Company's operating expenses and cost requirements in 1998 from 1997 levels. However, the Company expects that its research and development expenses will continue to be significant in 1998 and future years as it pursues its core drug development programs and expects to continue to incur operating losses and have significant capital requirements that it will not be able to satisfy with internally generated funds. The Company continues to explore opportunities to reduce operating expenses in an effort to conserve its cash resources.

This Annual Report on Form 10-K contains forward-looking statements. For this purpose, any statements contained herein that are not statements of historical fact may be deemed to be forward-looking statements. Without limiting the foregoing, the words "believes," "anticipates," "plans," "expects" and similar expressions are intended to identify forward-looking statements. There are a number of important factors that could cause the Company's actual results to differ materially from those indicated by such forward-looking statements. These factors include, without limitation, those set forth below under the caption "Certain Factors That May Affect Future Results."

RESTRUCTURING PLAN

During the second half of 1997, the Company implemented a restructuring plan to reduce expenditures on a phased basis over the balance of 1997 and into the first half of 1998 in an effort to conserve its cash resources. As part of this restructuring plan, in addition to terminating the clinical development of GEM 91, the Company reduced or suspended selected programs unrelated to its core advanced chemistry antisense drug development programs, including its ribozyme program. In connection with the reduction and suspension of programs, the Company has accrued termination fees related to research contracts and has incurred restructuring charges relating to programs that have been suspended or canceled. In addition, the Company terminated the employment of 84 employees at its Cambridge and Milford, Massachusetts facilities in the second half of 1997 and substantially reduced operations at its Paris, France office and terminated ten employees at that location in August 1997. As part of the restructuring, the Company reviewed all outside testing, public relations, travel and entertainment and consulting arrangements and terminated or renegotiated various of these arrangements.

As part of the restructuring, the Company subleased one facility in Cambridge, Massachusetts and a substantial portion of its corporate headquarters located at 620 Memorial Drive, Cambridge, Massachusetts. The Company incurred expenses relating to these subleases for broker fees and renovation expenses incurred in preparing the Memorial Drive space for the new tenant. In addition, the Company has accrued the estimated lease loss of subleasing the remaining space at its corporate

headquarters. The Company has accrued the remaining lease costs prior to

terminating the lease for its offices in Paris, France effective March 31, 1998.

Because of the significant costs involved in terminating employees, subleasing its facilities, terminating research contracts, suspending or cancelling research programs and substantially reducing operations, the Company did not begin to experience a material decrease in its expenditure rate until the fourth quarter of 1997. The Company recorded a restructuring charge of $11.0 million for the actions that occurred in 1997.

RESULTS OF OPERATIONS

Years ended December 31, 1997, 1996 and 1995

Revenues

The Company had total revenues of $3.9 million in 1997, $4.0 million in 1996 and $1.4 million in 1995. During 1997, 1996 and 1995, the Company received revenues from research and development collaborations of $945,000, $1.4 million and $1.2 million, respectively. Research and development collaboration revenues decreased in 1997 from 1996 because the research funding, which the Company had been receiving under the Company's collaboration with Roche in 1996 and 1995, was terminated by Roche as of March 31, 1997. Research and development collaboration revenues increased in 1996 from 1995 because collaboration revenues in 1996 included revenues earned under a collaborative agreement with Searle, which the Company entered into in January 1996.

Revenues from the custom contract manufacturing of synthetic DNA and reagent products by the HSP Division were $1.9 million in 1997 and $1.1 million in 1996. The increase in revenues in 1997 resulted from a full year of operations for the HSP Division, which commenced operations in the third quarter of 1996. This increase in revenues in 1997 was significantly lower than the Company had anticipated. As of December 31, 1997, the HSP Division had a backlog of $1,200,000. The Company anticipates filling this backlog in the first half of 1998.

Revenues from interest income were $1.1 million in 1997, $1.4 million in 1996 and $219,000 in 1995. The decrease in interest income in 1997 from 1996 was the result of lower cash balances available for investment in 1997 than in 1996. The increase in interest income in 1996 from 1995 was the result of substantially higher cash balances available for investment as a result of the Company's initial public offering, which was completed on February 2, 1996.

Research and Development Expenses

During 1997, 1996 and 1995, the Company expended $46.8 million, $39.4 million and $29.7 million, respectively, on research and development activities. The increases in research and development expenses in 1997 and 1996 reflected increasing expenses related primarily to ongoing clinical trials of the Company's product candidates, including clinical trials of two different formulations of GEM 132, which were first initiated during the third quarter of 1996 and the first quarter of 1997, clinical trials of GEM 92, which were initiated in the third quarter of 1997 and clinical trials of GEM 91, which were initiated in France in October 1993 and in the U.S. in May 1994 and terminated in July 1997. Clinical expenses related to GEM 91 decreased significantly during the second half of 1997 after the Company elected to terminate development of this compound.

Research and development expenses also increased in 1997 and 1996 due to significant increases in preclinical expenses incurred to meet the filing requirements to initiate the domestic clinical trials of the Company's product candidates.

The facilities expense related to the research and development area increased significantly in 1997 as a result of the relocation of the corporate offices to Cambridge, Massachusetts.

Research and development salaries and related costs remained at approximately the same level in 1997 as 1996 because of the costs involved in terminating employees in 1997. Research and development salaries and related costs increased significantly in 1996 over 1995 as the number of employees engaged in research and development increased to 206 at December 31, 1996 from 124 at December 31, 1995.

Patent expenses also remained at approximately the same level in 1997 as 1996 as the Company limited the scope of patent protection that it sought as part of its effort to conserve its cash resources. Patent expenses increased in 1996 as compared to 1995, as the Company continued to develop a patent portfolio both domestically and internationally.

General and Administrative Expenses

The Company incurred general and administrative expenses of $11.0 million in 1997, $11.3 million in 1996, and $6.1 million in 1995, respectively.

The facilities expense related to the general and administrative area increased significantly in 1997 as a result of the relocation of the corporate offices to Cambridge, Massachusetts. However, as a result of the implementation of the restructuring plan in the second half of 1997, such increase was offset by decreases in

general and administrative salaries and related costs and in consulting expenses in the second half of 1997. As part of the restructuring, approximately 11 general and administrative positions were eliminated. General and administrative expenses related to business development, public relations and legal expenses remained at approximately the same level in 1997 as 1996.

The increase in general and administrative expenses in 1996 from 1995 was primarily attributable to an increase in expenses for business development activity, public relations and legal expenses incurred primarily as a result of being a public company and salaries and related costs.

Interest Expense

Interest expense was $4.5 million in 1997, $124,000 in 1996 and $173,000 in 1995. The increase in interest expense in 1997 from 1996 reflected an increase in the Company's debt outstanding associated with the Company's issuance of $50,000,000 of 1997 9% Notes and interest incurred on borrowings to finance the purchase of property and equipment. The decrease in interest expense in 1996 from 1995 reflected a decrease in the outstanding balance of borrowings to finance the purchase of property and equipment.

Restructuring Charge

In connection with the implementation of the restructuring plan in the second half of 1997, the Company recorded a restructuring charge of $11.0 million for the actions that occurred in 1997. The Company made cash payments of approximately $1.5 million in 1997 and expects to make additional cash payments of approximately $3.7 million in 1998 in connection with the restructuring.

Net Loss

As a result of the above factors, the Company incurred net losses of $69.5 million in 1997, $46.9 million in 1996 and $34.5 million in 1995.

LIQUIDITY AND CAPITAL RESOURCES

General

From inception through December 31, 1997, the Company financed its operations, including capital expenditures, through a public offering of common stock, private placements of equity securities and the 1997 9% Notes and the

exercise of stock options and warrants with aggregate gross proceeds totalling $212.6 million, as well as through bank and other borrowings of $10.1 million, capital leases of $5.6

million, research and development and milestone payments from corporate collaborators totalling $5.5 million and sales of synthetic DNA and reagent products by the HSP Division totalling $3.0 million. Through December 31, 1997, the Company utilized approximately $179.0 million to fund operating activities and $29.3 million to finance capital expenditures, including leasehold improvements at the Company's Cambridge, Massachusetts corporate headquarters and at its manufacturing facility in Milford, Massachusetts.

During the year ended December 31, 1997, the Company utilized approximately $51.1 million to fund operating activities and approximately $7.5 million for capital expenditures. The primary use of cash for operating activities was to fund the Company's cash operating loss of $63.4 million. Capital expenditures during 1997 included amounts expended for the build-out and equipping of the Company's corporate headquarters and primary research and development laboratories in Cambridge, Massachusetts and of its leased manufacturing facility in Milford, Massachusetts. The Company expects to purchase a minimal amount of capital equipment in 1998 as part of its effort to conserve cash resources.

Cash Resources

The Company had cash and cash equivalents of $2.2 million at December 31, 1997. Since such date, the Company has received $4.8 million in gross proceeds from the 1998 Unit Financing. However, the Company has expended substantially all of the cash resources that it had available at December 31, 1997 and that it received subsequent to that date and continues to have substantial obligations to lenders, equipment lessors, real estate landlords and trade creditors. On March 30, 1998, the Company's obligations included $50.0 million principal amount of 1997 9% Notes, $4.8 million principal amount of 1998 Unit Notes, a $5.0 million Note payable to Silicon Valley Bank (the "Bank"), $3.2 million of capital leases and approximately $7.7 million of accounts payable. Because of the Company's financial condition, many trade creditors are only willing to provide the Company with products and services on a cash on delivery basis.

The Company's ability to continue operations in 1998 depends on its success in raising new funds in the 1998 Unit Financing or otherwise. The Company believes that if the Company raises approximately an additional $25.0 million in gross proceeds from the 1998 Unit Financing by April 30, 1998, and at least $40 million principal amount of 1997 9% Notes are exchanged for preferred stock of the Company pursuant to the 1998 Unit Financing, then such $25 million, together with the committed collaborative research and development payments from Searle for 1998 and anticipated sales of DNA products and reagents to third parties by the HSP Division and margins on such sales, will be adequate to fund the Company's capital requirements through 1998. However, there can be no assurance that the Company will receive any additional proceeds from the 1998 Unit Financing or as to the timing thereof or obtain funds from other sources. If the Company is unable to obtain substantial additional new funding in April 1998, it will be required to terminate its operations or seek relief under applicable bankruptcy laws by the end of April 1998.

Even if the Company obtains sufficient cash to fund its operations in 1998, it will be required to raise substantial additional funds through external sources, including through collaborative relationships and public or private financings, to support its operations beyond 1998. Except for research and development funding from Searle under Hybridon's collaborative agreement with Searle (which is subject to early termination in certain circumstances),

Hybridon has no committed external sources of capital, and, as discussed above, expects no product revenues for several years from sales of the products that it is developing (as opposed to sales of DNA products and reagents manufactured on a custom contract basis by the HSP Division).

No assurance can be given that additional funds will be available to fund the Company's operations for the balance of 1998 or in future years, or, if available, that such funds will be available on acceptable terms. If additional funds are raised by issuing equity securities, further dilution to then existing stockholders will result. Additionally, the terms of any such additional financing may adversely affect the holdings or rights of then existing stockholders.

If adequate funds are not available, the Company may be required to curtail significantly one or more of its core drug development programs, obtain funds through arrangements with collaborative partners or others that may require the Company to relinquish rights to certain of its technologies, product candidates or products which the Company would otherwise pursue on its own or terminate operations or seek relief under applicable bankruptcy laws. It is also possible that creditors of the Company may seek to commence involuntary bankruptcy proceedings against the Company.

The Company's future capital requirements will depend on many factors, including continued scientific progress in its research, drug discovery and development programs, the magnitude of these programs, progress with preclinical and clinical trials, sales of DNA products and reagents to third parties by the HSP Division and the margins on such sales, the time and costs involved in obtaining regulatory approvals, the costs involved in filing, prosecuting and enforcing patent claims, competing technological and market developments, the ability of the Company to establish and maintain collaborative academic and commercial research, development and marketing relationships, the ability of the Company to obtain third-party financing for leasehold improvements and other capital expenditures and the costs of manufacturing scale-up and commercialization activities and arrangements.

1998 Unit Financing

On January 22, 1998, the Company commenced the 1998 Unit Financing. For a description of this financing, see

"1998 Financing Activities" below.

1997 9% Notes

On April 2, 1997, the Company issued $50.0 million of the 1997 9% Notes with a maturity date of April 1, 2004. Under the terms of the 1997 9% Notes, the Company is required to make semiannual interest payments on the outstanding principal balance of the Notes on April 1 and October 1 of each year during which the 1997 9% Notes are outstanding. The outstanding principal balance of the 1997 9% Notes will become due on the maturity date. The Company made the first interest payment of $2.3 million at the beginning of October 1997. On February 6, 1998, in connection with the 1998 Unit Financing, the Company commenced an exchange offer to the holders of the 1997 9% Notes offering to issue to such holders shares of Series A Convertible Preferred Stock and warrants to purchase shares of Common Stock in exchange for such Notes, as described below under the caption "1998 Financing Activities". In addition, as of March 30, 1998, holders of approximately $42.0 million of the outstanding aggregate principal amount of the 1997 9% Notes have agreed to defer the interest payment due to them on April 1, 1998 to October 1, 1998.

Bank Facility

In December 1996, the Company entered into a five-year $7.5 million credit facility with the Bank to finance the leasehold improvements of the

Company's manufacturing facility. The Bank Credit Facility is payable in equal monthly payments of $62,500 plus interest with a balloon payment of $3.8 million due on January 1, 2002. The Bank Credit Facility contains certain financial covenants that

require the Company to maintain minimum tangible net worth (as defined) and minimum liquidity (as defined) and prohibits the payment of dividends. The Company has secured its obligations to the Bank with a lien on all of its assets. If, at specified times, the Company's minimum liquidity is less than $15.0 million, $10.0 million or $5.0 million, the Company is required to make prepayments of the Bank Credit Facility equal to 25%, 50% and 100%, respectively, of the then outstanding balance due under the Bank Credit Facility. On January 15, 1998 the Bank granted the Company a waiver of compliance with the minimum liquidity requirement at December 31, 1997, January 31, 1998 and February 28, 1998. As part of this waiver certain terms of the Bank Credit Facility were amended to increase the interest rate on the Borrower's obligations under the Bank Credit Facility to the institution's prime rate plus 5%. Prior to the amendment interest was payable at the lesser of (i) such financial institution's prime rate plus 1%, or (ii) such financial institution's LIBOR rate plus 3.5%. On March 30, 1998 the Bank granted the Company a waiver of compliance with the minimum tangible net worth requirement at December 31, 1997 and March 31, 1998 and the minimum liquidity requirement at March 31, 1998. As of March 30, 1998, the outstanding principal balance of the Bank Credit Facility is approximately $5.0 million. For an additional description of the Bank Credit Facility see "Note 6(a) of the Notes to Consolidated Financial Statements."

Equipment Leases

In 1997, the Company financed the purchase of furniture for the Cambridge facility through a lease line transaction of approximately $1.2 million. These borrowings are payable in 60 monthly payments of approximately $26,000.

In 1996, the Company financed the purchase of manufacturing equipment and other equipment at the Milford manufacturing facility through a sale/leaseback transaction of approximately $1.7 million under a $2.9 million lease line with a leasing company in the fourth quarter of 1996. These borrowings are payable in 48 monthly payments ranging from $36,000 to $50,000. In June 1997, the Company used the remaining $1.2 million under the lease line to finance the purchase of equipment through a sale/leaseback transaction. These borrowings are payable in 48 monthly payments ranging from $24,000 to $34,000.

Facility Leases

The Company entered into a lease for its corporate headquarters and primary research and development laboratories in Cambridge, Massachusetts and moved its operations to this facility in the first quarter of 1997. The Company's facilities costs increased significantly upon occupying the Cambridge facility. As part of the lease agreement, the Company elected to treat $5.5 million of payments to the landlord (primarily related to tenant improvements) as contributions to the capital of the Cambridge landlord in exchange for a limited partnership interest in the Cambridge landlord. All other expenses incurred to equip and build-out the facility in excess of $5.5 million are included in leasehold improvements and are not exchangeable for a partnership interest under the lease. The Cambridge landlord is an affiliate of three directors of the Company. The Company also is a party to leases for its facilities in

Milford, Massachusetts and the ancillary facility in Cambridge, Massachusetts, under which it has significant payment obligations. Effective March 31, 1998, the Company has terminated the lease for its office space in Paris, France. As discussed in Note 15 to the Consolidated Financial Statements, at December 31,

1997 the Company had facility lease commitments amounting to approximately $59.6 million.

As of December 31, 1997, the Company had approximately $206 million and $3.4 million of net operating loss and tax credit carryforwards, respectively. The Tax Reform Act of 1986 (the "Tax Act") contains certain provisions that may limit the Company's 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. The Company has completed several financings since the effective date of the Tax Act, which, as of December 31, 1997, have resulted in ownership changes in excess of 50%, as defined under the Tax Act.

1998 FINANCING ACTIVITIES

On January 22, 1998, the Company commenced the 1998 Unit Financing referred to above under the caption "General." The 1998 Unit Notes bear interest at a rate of 14% per annum; provided that if the 1998 Unit Financing is terminated before the Mandatory Conversion Event (as defined below) has occurred, the interest rate shall increase to 18% per annum. The Company is required to make semi-annual interest payments on the outstanding principal balance of the 1998 Unit Notes on April 1 and October 1 of each year during which such 1998 Unit Notes are outstanding, with the first such payment being due on April 1, 1998, which interest payment obligation may be satisfied through the issuance of additional 1998 Unit Notes valued at their principal amount. The Company plans to satisfy the interest payment due April 1, 1998 by issuing 1998 Unit Notes. The outstanding principal balance of the 1998 Unit Notes will become due on December 31, 2007. The 1998 Unit Notes are secured by substantially all of the Company's assets, subject to the lien on the Company's assets held by the Bank, are subordinate to the Company's existing indebtedness to the Bank, are senior to approximately 80% of the 1997 9% Notes to the extent provided in a subordination agreement executed by certain holders of the 1997 9% Notes and, except as otherwise provided in this sentence, rank on a parity with the 1997 9% Notes.

The 1998 Unit Notes are not convertible at the option of the holder, but will automatically convert into a new issue of Series B Convertible Preferred Stock of the Company if the aggregate net proceeds from the 1998 Unit Financing exceeds $20.0 million and the holders of at least 80% of the aggregate principal amount of the 1997 9% Notes have exchanged such Notes for a new issue of Series A Convertible Preferred Stock of the Company pursuant to the exchange offer (the "Exchange Offer") described in the following paragraph (such two conditions, the "Mandatory Conversion Event"). The Series B Convertible Preferred Stock underlying the 1998 Unit Notes would rank as to liquidation junior to the Series A Convertible Preferred Stock issuable in the Exchange Offer.

Each Unit includes warrants to purchase 15% (or, in certain circumstances, 20%) of the number of shares of Common Stock underlying the Series B Convertible Preferred Stock underlying the 1998 Unit Notes included in such Unit and may include additional warrants in certain circumstances described below. The Series B Convertible Preferred Stock, if issued, and warrants are convertible into, and exercisable for, Common Stock at a conversion or exercise price equal to the lowest of (i) 80% of the average closing bid price of the Company's Common Stock for the 30 consecutive trading days immediately preceding any closing in the 1998 Unit Financing or (ii) 80% of the average closing bid price of the Company's Common Stock for the five consecutive trading dates immediately preceding any closing in the 1998 Unit Financing; provided, however, that if on the termination date of the 1998 Unit Financing the Company has not received least $20,000,000 in net proceeds from the 1998 Unit Financing or the holders of less than $40,000,000 in principal amount of the 1997 9% Notes accept the Exchange Offer, holders of Units will be entitled to receive additional warrants to purchase, at an exercise price of $0.001 per share, a number of shares of Common Stock equal to 100% of the Common Stock then issuable upon conversion of the Series B Convertible Preferred Stock then issuable upon conversion of the 1998 Unit Notes purchased by such investors, in which case the 1998 Unit Notes will not be convertible into equity securities. If the market price of the Common Stock is less than 125% of the conversion price of the Series B Preferred Stock on the one-year anniversary of the final closing date of the 1998 Unit Financing, the conversion price of the Series B Convertible Preferred Stock will be further adjusted (the "Series B Reset") to the greater of (a) the market price of the Common Stock at such time divided by 1.25 and (b) 50% of the conversion price of the Series B Convertible Preferred Stock at such time, and holders of the Series B Convertible Preferred Stock will also be entitled to receive additional warrants to purchase a number of shares of Common

Stock equal to 50% of the additional number of shares of Common Stock issuable upon conversion of the Series B Convertible Preferred Stock following the Series B Reset.

On February 6, 1998, the Company commenced an Exchange Offer to the holders of its 1997 9% Notes to exchange such 1997 9% Notes for Series A Convertible Preferred Stock and certain warrants of the Company. In the Exchange Offer, each $1,000 of principal amount and accrued but unpaid interest on the 1997 9% Notes may be exchanged, upon the terms and subject to the conditions set forth in the Exchange Offer documents, for 10 shares of Series A Convertible Preferred Stock, stated value $100 per share, and warrants to purchase such a number of shares of Common Stock of the Company equal to 15% of the number of shares of Common Stock into which such Series A Convertible Preferred Stock would be convertible at 212.5% of the initial conversion price of the Series B Convertible Preferred Stock (the "Stated Price"). Such Series A Convertible Preferred Stock would have a liquidation preference of $100 per share plus accrued but unpaid dividends and would bear a dividend of the 6.5% per annum, payable on April 1 and October 1 of each year in cash or additional Series A Preferred Stock, at the option of the Company. The conversion price would be $35 per share of Common Stock through April 1, 2000 and the Stated Price thereafter, which conversion price would be reset upon the occurrence of any Series B Reset to 212.5% of the re-set Series B conversion price. Exchanging holders of 1997 9% Notes will be granted the right to designate a nominee to the Board of Directors of the Company (the "Designated Director"). There can be no assurance that the Exchange Offer will be successful.

On March 30, 1998, the Company amended its Exchange Offer to provide that the terms of the Series A Convertible Preferred Stock and warrants issuable in the Exchange Offer would be revised as described below if the following conditions (the "Equity Conditions") had been met no later than the date the Company accepts for exchange in the Exchange Offer at least $40 million principal amount of 1997 9% Notes: (i) the Company consummates an offering, the size of which is acceptable to the Designated Director, of units consisting of Common Stock priced (the "Common Stock Offering Price") at the greater of $2.00 and 85% of the Market Price (as defined below) of the Common Stock and warrants to purchase a number of shares of Common Stock equal to 25% of such Common Stock sold at an exercise price equal to 120% of the Common Stock Offering Price (the "120% Exercise Price"); (ii) the Company consummates an offering, with gross proceeds of at least $10 million, of Units consisting of shares of preferred stock having the same terms as the preferred stock issuable in the amended Exchange Offer, and warrants with the same 25% coverage as the warrants issuable in the amended Exchange Offer, as described in the following paragraph, but at the 120% Exercise Price (which shares are expected to be sold at a 30% discount from stated value); and (iii) all 1998 Note Units previously sold and accrued interest thereon are exchanged for Common Stock and warrants to purchase a number of shares of Common Stock equal to 30% of the Common Stock issued in such 1998 Note Unit exchange, such Common Stock and Warrants to be valued, and to have the terms, described in clause (i) above. "Market Price" means the average reported closing bid price of the Common Stock for the five consecutive trading days immediately preceding the closing date.

The amended Exchange Offer provides that if the Equity Conditions are met, (a) the conversion terms of the Series A Convertible Preferred Stock will be revised as follows: (i) the conversion price will be 212.5% of the Common Stock Offering Price described above, (ii) such Series A Convertible Preferred Stock will not be convertible for one year following the closing; and (iii) such Series A Convertible Preferred Stock will have no conversion price reset mechanism and (b) the warrant coverage will increase from 15% to 25% of the number of shares of Common Stock underlying the Series A Convertible Preferred Stock (such warrants being exercisable at 212.5% of the Common Stock Offering Price) and will not have any conversion price reset provisions.

The Company intends to use its best efforts to achieve the Equity Conditions, although no assurance can be given that such attempt will be successful. If the same cannot be accomplished in a timely manner, the Company will continue to proceed with the original financing plan.

CERTAIN FACTORS THAT MAY AFFECT FUTURE RESULTS

The following important factors, among others, could cause actual results to differ materially from those contained in forward-looking statements made in this Annual Report on Form 10-K and presented elsewhere by management from time to time.

Capital Needs; Uncertainty of Additional Funding; Risk of Insolvency

The Company has very limited cash resources and substantial obligations to lenders, equipment lessors, real estate landlords and trade creditors. The Company commenced the 1998 Unit Financing in January 1998 and to date has received aggregate gross proceeds of approximately $4.8 million at closings held in the first quarter of 1998. The Company's ability to continue operations in 1998 depends on its success in raising new funds in the 1998 Unit Financing or otherwise. The Company believes that if it raises approximately an additional $25.0 million in gross proceeds from the 1998 Unit Financing by April 30, 1998, and at least $40 million principal amount of 1997 9% Notes are exchanged for preferred stock of the Company pursuant to the 1998 Unit Financing, then such $25 million, together with the committed collaborative research and development payments from Searle for 1998 and anticipated sales of DNA products and reagents to third parties by the HSP Division and margins on such sales, will be adequate to fund the Company's capital requirements through 1998. However, there can be no assurance that the Company will receive any additional proceeds from the 1998 Unit Financing or obtain funds from other sources. If the Company is unable to obtain substantial additional new funding in April 1998, it will be required to terminate its operations or seek relief under applicable

bankruptcy laws by the end of April 1998. See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations -- Liquidity and Capital Resources."

The Company anticipates that, even if it obtains sufficient cash to fund its operations in 1998, it will be required to raise substantial additional funds through external sources, including through collaborative relationships and public or private financings, to support the Company's operations beyond 1998. No assurance can be given that additional financing will be available, or, if available, that it will be available on acceptable terms. If additional funds are raised by issuing equity securities, further dilution to then existing stockholders will result. Additionally, the terms of any such additional financing may adversely affect the holdings or rights of then existing stockholders.

If adequate funds are not available, the Company may be required to curtail significantly one or more of its research, drug discovery or development programs, or obtain funds through arrangements with collaborative partners or others that may require the Company to relinquish rights to certain of its technologies, product candidates or products which the Company would otherwise pursue on its own, sell the HSP Division or terminate operations or seek relief under applicable bankruptcy laws. It is also possible that creditors of the Company may seek to commence involuntary bankruptcy proceedings against the Company.

The Company's future capital requirements will depend on many factors, including continued scientific progress in its research, drug discovery and development programs, the magnitude of these programs, progress with preclinical and clinical trials, sales of DNA products and reagents to third parties manufactured on a custom contract basis by the HSP Division and the margins on such sales, the time and costs involved in obtaining regulatory approvals, the costs involved in filing, prosecuting and enforcing patent claims, competing technological and market developments, the ability of the Company to establish and maintain collaborative academic and commercial research, development and marketing relationships, the ability of the Company to obtain third-party financing for leasehold improvements and other capital expenditures and the costs of manufacturing scale-up and commercialization activities and arrangements.

Early Stage of Development; Technological Uncertainty

The Company's potential pharmaceutical products are at various stages of research, preclinical testing or clinical development. There are a number of technological challenges that the Company must successfully address to complete any of its development efforts. To date, most of the Company's resources have

been dedicated to applying oligonucleotide chemistry and cell biology to the research and development of potential pharmaceutical products based upon antisense technology.

As in most drug discovery programs, the results of in vitro, tissue culture and preclinical studies by the Company may be inconclusive and may not be indicative of results that will be obtained in human clinical trials. In addition, results attained in early human clinical trials by the Company may not be indicative of results that will be obtained in later clinical trials. Neither the Company, nor to its knowledge, any other company has successfully completed human clinical trials of a product based on antisense technology, and there can be no assurance that any of the Company's products will be successfully developed.

The success of any of the Company's potential pharmaceutical products depends in part on the molecular target on the genetic material chosen as the site of action of the oligonucleotide. There can be no assurance that the Company's choice will be appropriate for the treatment of the targeted disease indication in humans or that mutations in the genetic material will not result in a reduction in or loss of the efficacy or utility of a Company product.

Uncertainty Associated with Clinical Trials

Before obtaining regulatory approvals for the commercial sale of any of its pharmaceutical products under development, the Company must undertake extensive and costly preclinical studies and clinical trials to demonstrate that such products are safe and efficacious. The results from preclinical studies and early clinical trials are not necessarily predictive of results that will be obtained in later stages of testing or development, and there can be no assurance that the Company's clinical trials will demonstrate the safety and efficacy of any pharmaceutical products or will result in pharmaceutical products capable of being produced in commercial quantities at reasonable cost or in a marketable form.

In July 1997, the Company discontinued the development of GEM 91, its first- generation antisense drug for the treatment of AIDS and HIV infection, based on a review of data from an open label Phase II clinical trial of patients with advanced HIV infection. In the Phase II trial, three of the nine subjects tested experienced decreases in platelet counts that required dose interruption. In addition, a review of the data showed inconsistent responses to the treatment and failed to confirm the decrease in cellular viremia observed in an earlier clinical trial. The Company had devoted significant funding and development efforts in GEM 91, and GEM 91 was the Company's most advanced product candidate.

Although the Company is conducting clinical trials on certain oligonucleotide compounds and is developing several oligonucleotide compounds on which it plans to file IND applications with the FDA and equivalent filings outside of the U.S., there can be no assurance that necessary preclinical studies on these compounds will be completed satisfactorily or that the Company otherwise will be able to make its intended filings. Further, there can be no assurance that the Company will be

permitted to undertake and complete human clinical trials of any of the Company's potential products, either in the U.S. or elsewhere, or, if permitted, that such products will not have undesirable side effects or other characteristics that may prevent or limit their commercial use.

The rate of completion of the Company's human clinical trials, if

permitted, will be dependent upon, among other factors, the rate of patient enrollment. Patient enrolment is a function of many factors, including the size of the patient population, the nature of the protocol, the availability of alternative treatments, the proximity to clinical sites and eligibility criteria for the study. Delays in planned patient enrollment might result in increased costs and delays, which could have a material adverse effect on the Company. The Company or the FDA or other regulatory agencies may suspend clinical trials at any time if the subjects or patients participating in such trials are being exposed to unacceptable health risks.

History of Operating Losses and Accumulated Deficit

The Company has incurred net losses since its inception. At December 31, 1997, the Company's accumulated deficit was approximately $218.7 million. Such losses have resulted principally from costs incurred in the Company's research and development programs and from general and administrative costs associated with the Company's development. No revenues have been generated from sales of pharmaceutical products developed by the Company and no revenues from the sale of such products are anticipated for a number of years, if ever. The Company expects to incur additional operating losses over the next several years and expects cumulative losses to increase significantly as the Company's research and development and clinical trial efforts expand. The Company expects that losses will fluctuate from quarter to quarter and that such fluctuations may be substantial. Although the HSP Division has begun to generate revenues from the sale of synthetic DNA products and reagents manufactured by it on a custom contract basis, there can be no assurance that demand for and margins on these products will not be lower than anticipated. In 1997, revenues generated from the sale of synthetic DNA products and reagents were significantly lower than anticipated. The Company's ability to achieve profitability is dependent in part on obtaining regulatory approvals for its pharmaceutical products and entering into agreements for drug discovery, development and commercialization. There can be no assurance that the Company will obtain required regulatory approvals, enter into any additional agreements for drug discovery, development and commercialization or ever achieve drug sales or profitability.

Patents and Proprietary Rights

The Company's success will depend in part on its ability to develop patentable products and obtain and enforce patent protection for its products both in the U.S.

and in other countries. The Company has filed and intends to file applications as appropriate for patents covering both its products and processes. However, the patent positions of pharmaceutical and biotechnology firms, including Hybridon, are generally uncertain and involve complex legal and factual questions. No assurance can be given that patents will issue from any pending or future patent applications owned by or licensed to Hybridon. Since patent applications in the U.S. are maintained in secrecy until patents issue, and since publication of discoveries in the scientific or patent literature tend to lag behind actual discoveries by several months, the Company cannot be certain that it was the first creator of inventions covered by pending patent applications or that it was the first to file patent applications for such inventions. Further, there can be no assurance that the claims allowed under any issued patents will be sufficiently broad to protect the Company's technology. In addition, no assurance can be given that any issued patents owned by or licensed to the Company will not be challenged, invalidated or circumvented, or that the rights granted thereunder will provide competitive advantages to the Company.

The commercial success of the Company will also depend in part on its neither infringing patents issued to competitors or others nor breaching the technology licenses upon which the Company's products might be based. The Company's licenses of patents and patent applications impose various commercialization, sublicensing, insurance and other obligations on the Company. Failure of the Company to comply with these requirements could result in termination of the applicable license. The Company is aware of patents and patent applications belonging to competitors, and it is uncertain whether these

patents and patent applications will require the Company to alter its products or processes, pay licensing fees or cease certain activities. In particular, competitors of the Company and other third parties may hold pending patent applications relating to antisense and other gene expression modulation technologies which may result in claims of infringement against the Company or other patent litigation. There can be no assurance that the Company will be able successfully to obtain a license to any technology that it may require or that, if obtainable, such technology can be licensed at a reasonable cost or on an exclusive basis.

The pharmaceutical and biotechnology industries have been characterized by extensive litigation regarding patents and other intellectual property rights. Litigation, which could result in substantial cost to the Company, may be necessary to enforce any patents issued or licensed to the Company and/or to determine the scope and validity of other parties' proprietary rights. The Company also will have to participate in interference proceedings declared by the U.S. Patent and Trademark Office, which could result in substantial cost to the Company, to determine the priority of inventions. Furthermore, the Company may have to participate at substantial cost in International Trade Commission proceedings to abate importation of products which would compete unfairly with products of the Company.

Hybridon engages in collaborations, sponsored research agreements and other agreements with academic researchers and institutions and government agencies. Under the terms of such agreements, third parties may have rights in certain inventions developed during the course of the performance of such collaborations and agreements.

The Company relies on trade secrets and proprietary know-how which it seeks to protect, in part, by confidentiality agreements with its collaborators, employees and consultants. There can be no assurance that these agreements will not be breached, that the Company would have adequate remedies for any breach or that the Company's trade secrets will not otherwise become known or be independently developed by competitors.

Attraction and Retention of Key Employees and Scientific Collaborators; Employment Agreements

The Company is highly dependent on the principal members of its management and scientific staff, including E. Andrews Grinstead, III, the Company's Chairman of the Board, President and Chief Executive Officer, and Sudhir Agrawal, the Company's Senior Vice President of Discovery and Chief Scientific Officer, the loss of whose services could have material adverse effect on the Company. The Company has executed Employment Agreements with Messrs. Grinstead and Agrawal. Mr. Grinstead's agreement provides for an employment term ending on June 30, 2001 (unless sooner terminated in accordance with the provisions of the agreement), and Mr. Agrawal's agreement provides for an employment term ending on June 30, 2000 (unless sooner terminated in accordance with the agreement). For further information, see "Compensation of Executive Officers" in the Company's Proxy Statement for the Annual Meeting of Stockholders to be held on June 15, 1998.

From June 30, 1997 to March 30, 1998, the number of employees of the Company has decreased from 213 to 78. As a result, the Company has lost significant expertise and will be required to recruit and retain new personnel in order to perform its operations. In addition, any growth or expansion of the Company will require recruiting and retaining qualified scientific personnel to perform research and development work. There can be no assurance that under either circumstance the Company will be able to attract and retain such personnel on acceptable terms given the competition for experienced scientists among numerous pharmaceutical, biotechnology and health care companies, universities and non-profit research institutions. In addition, the Company's growth and expansion into areas and activities requiring additional expertise, such as clinical testing, governmental approvals, production and marketing, would be expected to require the addition of new management personnel and the development of additional expertise by existing management personnel. The failure to acquire such services or to develop such expertise could have a

material adverse effect on the Company.

The Company's success will depend in part on its continued ability to develop and maintain relationships with independent researchers and leading academic and research institutions. The competition for such relationships is intense, and there can be no assurance that the Company will be able to develop and maintain such relationships on acceptable terms. The Company has entered into a number of such collaborative relationships relating to specific disease targets and other research activities in order to augment its internal research capabilities and to obtain access to the specialized knowledge or expertise of its collaborative partners. The loss of any such collaborative relationship could have an adverse effect on the Company's ability to conduct research and development in the area targeted by such collaboration.

Risks Associated with Hybridon Specialty Products Division

Through its Hybridon Specialty Products Division, the Company manufactures oligonucleotide compounds on a custom contract basis for third parties. The results of operations of the HSP Division will be dependent upon the demand for and margins on these products. Demand for such products was significantly lower than anticipated in 1997. The results of operations of the HSP Division also may be affected by the price and availability of raw materials. It is possible that Hybridon's manufacturing capacity may not be sufficient for production of oligonucleotides both for the Company's internal needs and for sale to third parties. The Company's manufacturing facility must comply with GMP and other FDA regulations. See "Certain Factors That May Affect Future Results -- Limited Manufacturing Capability."

The Company believes that it is currently manufacturing oligonucleotides in substantial compliance with FDA requirements for manufacturing in compliance with GMP, although its facility and procedures have not been formally inspected by the FDA and the procedures and documentation followed may have to be enhanced in the future as the Company expands its oligonucleotide production activities. Failure to establish to the FDA's satisfaction compliance with GMP can result in the FDA denying authorization to initiate or continue clinical trials, to receive approval of a product or to begin or to continue commercial marketing.

The Company will be competing against a number of third parties, as well as the possibility of internal production by the Company's customers, in connection with the operations of the HSP Division. Many of these third parties are likely to have greater financial, technical and human resources than the Company. Key competitive factors will include the price and quality of the products as well as manufacturing capacity and ability to comply with specifications and to fulfill orders on a timely basis. The Company may be required to reduce the cost of its product offerings to meet competition. See "Certain Factors That May Affect Future Results -- Competition." Failure to manufacture oligonucleotide compounds in accordance with the purchaser's specifications could expose the Company to breach of contract and/or product liability claims from the purchase or the purchaser's customers. The

Company has limited experience in sales, marketing and distribution and is relying in part upon the efforts of a third party, Perkin-Elmer, in connection with the marketing and sale of products by the HSP Division. See "Certain Factors That May Affect Future Results -- Absence of Sales and Marketing Experience."

Need to Establish Collaborative Commercial Relationships; Dependence on Partners

Hybridon's business strategy includes entering into strategic alliances or licensing arrangements with corporate partners, primarily pharmaceutical and biotechnology companies, relating to the development and commercialization of certain of its potential products. Although the Company is party to a corporate collaboration with Searle, a subsidiary of Monsanto Company, in the field of inflammation/immunomodulation and Medtronic relating to Alzheimers, there can be no assurance that these collaborations will be scientifically or commercially successful, that the Company will be able to negotiate additional collaborations, that such collaborations will be available to the Company on acceptable terms or that any such relationships, if established, will be scientifically or commercially successful. For example, in 1997, Roche terminated the collaborative relationship with the Company that was established in 1992 without selecting any compounds for further development.

The Company expects that under certain of its collaborations, the collaborative partner will have the responsibility for conducting human clinical trials and the submission for regulatory approval of the product candidate with the FDA and certain other regulatory agencies. Should the collaborative partner fail to develop a marketable product, the Company's business may be materially adversely affected. There can be no assurance that the Company's collaborative partners will not be pursuing alternative technologies or developing alternative compounds either on their own or in collaboration with others, including the Company's competitors, as a means for developing treatments for the diseases targeted by these collaborative programs. The Company's business will also be affected by the performance of its corporate partners in marketing any successfully developed products within the geographic areas in which such partners are granted marketing rights. The Company's plan is to retain manufacturing rights for many of the products its may license pursuant to arrangements with corporate partners. However, there can be no assurance that the Company will be able to retain such rights on acceptable terms, if at all, or that the Company will have the ability to produce the quantities of product required under the terms of such arrangements.

Risks of Low-Priced Stock; Possible Effect of "Penny Stock" Rules on Liquidity for the Company's Securities.

Since the Common Stock is not listed on a national securities exchange or on a qualified automated quotation system, it is subject to Rule 15g-9 under the Securities

Exchange Act of 1934, as amended (the "Exchange Act"), which imposes additional sales practice requirements on broker-dealers that sell such securities. Rule 15g-9 defines a "penny stock" to be any equity security that has a market price (as therein defined) of less than $5.00 per share or with an exercise price of less than $5.00 per share, subject to certain exceptions including the securities being quoted on the Nasdaq National Market or SmallCap Market. For transactions covered by this rule, a broker-dealer must make a special suitability determination for the purchaser and have received the purchaser's written consent to the transaction prior to sale.

The foregoing required penny stock restrictions would not apply to the Company's securities if the Company's Common Stock was listed on the Nasdaq National Market or SmallCap Market or met certain minimum net tangible assets or average revenue criteria. The Company's securities, however, do not qualify for exemption from the penny stock restrictions. There can be no assurance that the Common Stock will qualify for listing on the Nasdaq National Market or SmallCap Market in the foreseeable future, if at all. In any event, even if the Company's securities are exempt from such restrictions, the Company would remain subject to Section 15(b)(6) of the Exchange Act, which gives the Securities and Exchange Commission (the "Commission") the authority to restrict any person from participating in a distribution of penny stock, if the Commission finds that such a restriction would be in the public interest.

The market liquidity for the Company's securities is likely to be

materially adversely affected by these requirements. In addition, such rules are likely to adversely affect the Company's ability to raise funds and the ability of broker-dealers to sell the Company's securities in the secondary market.

No Assurance of Regulatory Approval; Government Regulation

The Company's preclinical studies and clinical trials, as well as the manufacturing and marketing of the potential products being developed by it and the products sold by the HSP Division, are subject to extensive regulation by numerous federal, state and local governmental authorities in the U.S. Similar regulatory requirements exist in other countries where the Company intends to test and market its drug candidates. Satisfaction of these requirements, which include demonstrating to the satisfaction of the FDA and foreign regulatory agencies that the product is both safe and effective, typically takes several years or more and can vary substantially based upon the type, complexity and novelty of the product. There can be no assurance that such testing will show any product to be safe or efficacious. Preclinical studies of the Company's product development candidates are subject to Good Laboratory Practices ("GLP") requirements and the manufacture of any products by the Company, including products developed by the Company and products manufactured for third parties on a custom contract basis by the HSP Division, will be subject to GMP requirements prescribed by the FDA.

The regulatory process, which includes preclinical studies, clinical trials and post-clinical testing of each compound to establish its safety and effectiveness, takes many years and requires the expenditure of substantial resources. Delays may also be encountered and substantial costs incurred in foreign countries. There can be no assurance that, even after the passage of such time and the expenditure of such resources, regulatory approval will be obtained for any drugs developed by the Company. Data obtained from preclinical and clinical activities are subject to carrying interpretations which could delay, limit or prevent regulatory approval by the FDA or other regulatory agencies. The Company, an independent Institutional Review Board (an "IRB"), the FDA or other regulatory agencies may suspend clinical trials at any time if the participants in such trials are being exposed to unacceptable health risks. Moreover, if regulatory approval of a drug is granted, such approval may entail limitations on the indicated uses for which it may be marketed. Failure to comply with applicable regulatory requirements can, among other things, result in fines, suspension of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecutions. FDA policy may change and additional government regulations may be established that could prevent or daily regulatory approval of the Company's potential products.

Even if initial regulatory approvals for the Company's product candidates are obtained, the Company, its products and its manufacturing facilities would be subject to continual review and periodic inspection. Moreover, additional government regulations from future legislation or administrative action may be established which could prevent or delay regulatory approval of the Company's products or further regulate the prices at which the Company's proposed products may be sold. The regulatory standards for manufacturing are applied stringently by the FDA. In addition, a marketed drug and its manufacturer are subject to continual review and any subsequent discovery of previously unknown problems with a product or manufacturer may result in restrictions on such product or manufacturer, including withdrawal of the product from the market and withdrawal of the right to manufacture the product.

All of the foregoing regulatory matters also will be applicable to development, manufacturing and marketing undertaken by any strategic partners or licensees of the Company.

Competition

There are many companies, both private and publicly traded, that are conducting research and development activities on technologies and products similar to or competitive with the Company's antisense technologies and proposed

products. For example, many other companies are actively seeking to develop products, including antisense oligonucleotides, with disease targets similar to those being pursued by the Company. Some of these competitive products are in clinical trials.

The Company believes that the industry-wide interest in investigating the potential of gene expression modulation technologies will continue and will accelerate as the techniques which permit the design the development of drugs based on such technologies become more widely understood. There can be no assurance that the Company's competitors will not succeed in developing products based on oligonucleotides or other technologies, existing or new, which are more effective than any that are being developed by the Company, or which would render Hybridon's antisense technologies obsolete and noncompetitive. Moreover, there currently are commercially available products for the treatment of many of the disease targets being pursued by the Company.

Competitors of the Company engaged in all areas of biotechnology and drug discovery in the U.S. and other countries are numerous and include, among others, pharmaceutical and chemical companies, biotechnology firms, universities and other research institutions. Many of the Company's competitors have substantially greater financial, technical and human resources than the Company. In addition, many of these competitors have significantly greater experience than the Company in undertaking preclinical studies and human clinical trials of new pharmaceutical products and obtaining FDA and other regulatory approvals of products for use in health care. Furthermore, if the Company is permitted to commence commercial sales of products, it will also be competing with respect to manufacturing efficiency and marketing capabilities, areas in which it has limited or no experience. Accordingly, the Company's competitors may succeed in obtaining FDA or other regulatory approvals for products or in commercializing such products more rapidly than the Company.

Limited Manufacturing Capability

While the Company believes that its existing production capacity will be sufficient to enable it to satisfy its current research needs and to support the Company's preclinical and clinical requirements for oligonucleotide compounds, the Company will need to purchase additional equipment to expand its manufacturing capacity in order to satisfy its future requirements (subject to obtaining regulatory approvals) for commercial production of its product candidates. In addition, the HSP Division is using the Company's existing production capacity to custom contract manufacture synthetic DNA products for commercial sale. As a result, depending on the level of sales by the HSP Division, and the success of the Company's product development programs, Hybridon's manufacturing capacity may not be sufficient for production for both its internal needs and sales to third parties. In addition, in order successfully to commercialize its product candidates or achieve satisfactory margins on sales, the Company may be required to reduce further the cost of production of its oligonucleotide compounds, and there can be no assurance that the Company will be able to do so.

The manufacture of the Company's products is subject to GMP requirements prescribed by the FDA or other standards prescribed by the appropriate regulatory agency in the country of use. To the Company's knowledge, therapeutic products based on chemically-modified oligonucleotides have never been manufactured on a commercial scale. There can be no assurance that the Company will be able to manufacture products in timely fashion and at acceptable

quality and price levels, that it or its suppliers can manufacture in compliance with GMP or other regulatory requirements or that it or its suppliers will be able to manufacture an adequate supply of product. The Company has in the past relied in part, and may in the future rely, upon third party contractors in connection with the manufacture of some compounds. Reliance on such third parties entails a number of risks, including the possibility that such third parties may fail to perform on an effective or timely basis or fail to abide by regulatory or contractual restrictions applicable to the Company.

There are three sources of supply for the nucleotide building blocks used by the Company in its current oligonucleotide manufacturing process. This process is covered by issued patents either held by or licensed to these three companies. Therefore, these companies are likely the sole suppliers to Hybridon of these nucleotide building blocks. There can be no assurance that nucleotide building blocks will be obtainable at acceptable costs, if at all. The inability of Hybridon to obtain these nucleotide building blocks from one of these suppliers, or to obtain them at an acceptable cost, could have a material adverse effect on Hybridon.

Absence of Sales and Marketing Experience

The Company expects eventually to market and sell certain of its prospective products directly and certain of its products through co-marketing or other licensing arrangements with third parties. The Company has limited experience in sales, marketing and distribution, and does not expect to establish a sales and marketing plan or direct sales capability with respect to the products being developed by it until such time as one or more of such products approaches marketing approval, if at all. In addition, although the Company does have a limited direct sales capability with respect to the sales of custom contract manufactured DNA products to third parties by the HSP Division, the Company has entered into a sales and marketing arrangement with Perkin-Elmer with respect to such products and is reliant in part on the efforts of Perkin-Elmer to promote these products.

In order to market the products being developed by it directly, the Company will be required to develop a substantial marketing staff and sales force with technical expertise and with supporting distribution capability. There can be no assurance that the Company will be able to build such a marketing staff or sales force, that the cost of establishing such a marketing staff or sales force will be justifiable in light of any product revenues or that the Company's direct sales and marketing efforts will be successful. In addition, if the Company succeeds in

bringing one or more products to market, it may compete with other companies that currently have extensive and well-funded marketing and sales operations. There can be no assurance that the Company's marketing and sales efforts would enable it to compete successfully against such other companies. To the extent the Company enters into co-market or other licensing arrangements, any revenues received by the Company will be dependent in part on the efforts of third parties and there can be no assurance that such efforts will be successful.

No Assurance of Market Acceptance

Pharmaceutical products, if any, resulting from the Company's research and development programs are not expected to be commercially available for a number of years. There can be no assurance that, if approved for marketing, such products will achieve market acceptance. The degree of market acceptance will depend upon a number of factors, including the receipt of regulatory approvals, the establishment and demonstration in the medical community of the clinical efficacy and safety of the Company's products and their potential advantages over existing treatment methods and reimbursement policies of government and third-party payors. There is no assurance that physicians, patients, payors or the medical community in general will accept or utilize any products that may be developed by the Company.

Product Liability Exposure and Insurance

The use of any of the Company's potential products in clinical trials and the commercial sale of any products, including the products being developed by it and the DNA products and reagents manufactured and sold on a custom contract basis by the HSP Division, may expose the Company to liability claims. These claims might be made directly by consumers, health care providers or by pharmaceutical and biotechnology companies or others selling such products. Hybridon has product liability insurance coverage, and such coverage is subject to various deductibles. Such coverage is becoming increasingly expensive, and no assurance can be given that the Company will be able to maintain or obtain such insurance at reasonable cost or in sufficient amounts to protect the Company against losses due to liability claims that could have a material adverse effect on the Company.

Hazardous Materials

The Company's research and development and manufacturing activities involves the controlled use of hazardous materials, chemicals, viruses and various radioactive compounds. Although the Company believes that its safety procedures for handling and disposing of such materials comply with the standards prescribed by federal, state and local regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of such an accident, the Company could be held liable for any damages that result and any such

liability could have a material adverse effect on the Company.

Uncertainty of Pharmaceutical Pricing and Adequate Reimbursement

The Company's ability to commercialize its pharmaceutical products successfully will depend in part on the extent to which appropriate reimbursement levels for the cost of such products and related treatment are obtained from government authorities, private health insurers and other organizations, such as health maintenance organizations ("HMOs"). Third-party payors are increasingly challenging the prices charged for medical products and services. There can be no assurance that any of the Company's potential products will be considered cost-effective or that adequate third-party reimbursement will be available to enable the Company to maintain price levels sufficient to realize an appropriate return on its investment. Also the trend towards managed health care in the U.S. and the concurrent growth of organizations such as HMOs, which could control or significantly influence the purchase of health care services and products, as well as legislative proposals to reduce government insurance programs, may all result in lower prices for the Company's products. The cost containment measures that health care providers are instituting could affect the Company's ability to sell its products and may have a material adverse effect on the Company.

Uncertainty of Health Care Reform Measures

Federal, state and local officials and legislators (and certain foreign government officials and legislators) have proposed or are reportedly considering proposing a variety of reforms to the health care systems in the U.S. and abroad. The Company cannot predict what health care reform legislation, if any, will be enacted in the U.S. or elsewhere. Significant changes in the health care system in the U.S. or elsewhere are likely to have a substantial impact over times on the manner in which the Company conducts its business. Such changes could have a material adverse effect on the Company. The existence of pending health care reform proposals could have a material adverse effect on the Company's ability to raise capital. Furthermore, the Company's ability to commercialize its potential products may be adversely affected to the extent that such proposals have a material adverse effect on the business, financial condition and profitability of other companies that are prospective corporate partners with respect to certain of the Company's proposed products.

Concentration of Ownership by Directors and Executive Officers

The Company's directors and executive officers and their affiliates beneficially own a significant percentage of the Company's outstanding Common Stock. As a result, these stockholders, if acting together, may have the ability to influence the outcome of corporate actions requiring stockholder approval. This concentration of ownership may have the effect of delaying or preventing a change in control of the

Company.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA.

All financial statements required to be filed hereunder are filed as APPENDIX A hereto, are listed under Item 14(a), and are incorporated herein by this reference.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE.

None.

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT.

The response to this item is contained in part under the caption "Executive Officers and Significant Employees of the Company" in Part I of this Annual Report on Form 10-K and in part in the Company's Proxy Statement for the Annual Meeting of Stockholders to be held on June 15, 1998 (the "1998 Proxy Statement") under the caption "Proposal 1--Election of Directors," which section is incorporated herein by this reference.

Officers are elected on an annual basis and serve at the discretion of the Board of Directors.

ITEM 11. EXECUTIVE COMPENSATION.

The response to this item is contained in the 1998 Proxy Statement under the caption "Proposal 1--Election of Directors," which section is incorporated herein by this reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT.

The response to this item is contained in the 1998 Proxy Statement under the caption "Stock 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 1998 Proxy Statement under the caption "Certain Relationships and Related Transactions," which section is incorporated herein by this reference.

PART IV

ITEM 14. EXHIBITS, FINANCIAL STATEMENT SCHEDULES, AND REPORTS ON FORM 8-K.

(a) The following documents are filed as APPENDIX A hereto and are included as part of this Annual Report on Form 10-K:

Financial Statements:
Report of Independent Public Accountants
Consolidated Balance Sheets
Consolidated Statements of Operations
Consolidated Statements of Stockholders' Equity (Deficit)
Consolidated Statements of Cash Flows
Notes to Consolidated Financial Statements

(b) The Company is 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.

(c) 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.

(d) REPORTS ON FORM 8-K. The following reports on Form 8-K were filed during the last quarter of the Company's fiscal year ended December 31, 1997.

On November 19, 1997, the Company filed a Current Report on Form 8-K, dated October 18, 1997, announcing that the Company planned to commence a private offering of up to $50.0 million of its Common Stock.

On December 10, 1997, the Company filed a Current Report on Form 8-K, dated December 3, 1997, announcing that, effective as of the close of business on December 2, 1997, the Company's Common Stock was delisted from the Nasdaq National Market and the Company's Common Stock would be quoted on the OTC Bulletin Board commencing on December 3, 1997.

SIGNATURES

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

HYBRIDON, INC.

By: /s/ E. Andrews Grinstead, III

E. Andrews Grinstead, III
Chairman of the Board, President and Chief Executive Officer

Date: March 30, 1998

Pursuant to the requirements of the Securities Exchange Act of 1934, 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/ E. Andrews Grinstead, III - ---------- E. Andrews Grinstead, III	Chairman of the Board, President and Chief Executive Officer and Director (Principal Executive Officer)	March 30, 1998
/s/ Robert G. Andersen - ---------- Robert G. Andersen	Treasurer (Principal Financial and Accounting Officer)	March 30, 1998
/s/ Sudhir Agrawal - ---------- Sudhir Agrawal	Director	March 30, 1998
/s/ Mohamed El-Khereiji - ---------- Mohamed El-Khereiji	Director	March 30, 1998
/s/ Youssef El-Zein - ---------- Youssef El-Zein	Director	March 30, 1998
/s/ Nasser Menhall - ---------- Nasser Menhall	Director	March 30, 1998
/s/ James B. Wyngaarden - ---------- James B. Wyngaarden	Director	March 28, 1998
/s/ Paul C. Zamecnik - ---------- Paul C. Zamecnik	Director	March 30, 1998

Appendix A

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REPORT OF INDEPENDENT PUBLIC ACCOUNTANTS

To Hybridon, Inc.:

We have audited the accompanying consolidated balance sheets of Hybridon, Inc. (a Delaware corporation in the development stage) and subsidiaries as of

December 31, 1996 and 1997, 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, 1997 and for the period from inception (May 25, 1989) to December 31, 1997. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with generally accepted auditing standards. 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, 1996 and 1997 and the results of their operations and their cash flows for each of the three years in the period ended December 31, 1997, and for the period from inception (May 25, 1989) to December 31, 1997 in conformity with generally accepted accounting principles.

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. Since inception, the Company has incurred significant losses which it has funded through the issuance of equity securities, debt issuances and through research and development collaborations and licensing agreements. As of December 31, 1997, the Company had a working capital deficit of $(24.1) million and a stockholders' deficit of $(46.0) million. Subsequent to December 31, 1997, the Company has raised $4.8 million through the equity financing discussed in Note 1, as of March 30, 1998. The Company expects such resources to fund operations through March 1998. There is substantial doubt about the Company's ability to continue as a going concern. The financial statements do not include any adjustments that might result from the outcome of this uncertainty. See Note 1 for management's plans.

ARTHUR ANDERSEN LLP

Boston, Massachusetts
March 18, 1998 (except
with respect to the matters
discussed in Note 1 and Note 6(a)
as to which date is March 30, 1998)

HYBRIDON, INC. AND SUBSIDIARIES
(A DEVELOPMENT STAGE COMPANY)

CONSOLIDATED BALANCE SHEETS

ASSETS

	DECEMBER 31, 1996	DECEMBER 31, 1997
CURRENT ASSETS:		
Cash and cash equivalents	$ 12,633,742	$ 2,202,202
Short-term investments	3,785,146	--
Accounts receivable	573,896	529,702
Prepaid expenses and other current assets	1,545,324	1,005,825
Total current assets	18,538,108	3,737,729
PROPERTY AND EQUIPMENT, AT COST:		
Leasehold improvements	9,257,516	16,027,734
Laboratory equipment	5,884,861	6,770,402
Equipment under capital leases	2,904,688	4,879,190
Office equipment	1,496,639	1,947,818
Furniture and fixtures	499,957	645,264

Construction-in-progress	2,193,400	45,409
	22,237,061	30,315,817
Less--Accumulated depreciation and amortization	6,596,293	11,085,013
	15,640,768	19,230,804
OTHER ASSETS:		
Restricted cash	437,714	3,050,982
Notes receivable from officers	317,978	247,250
Deferred financing costs and other assets	1,152,034	3,354,767
Investment in real estate partnership	5,450,000	5,450,000
	7,357,726	12,102,999
	$ 41,536,602	$ 35,071,532
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
CURRENT LIABILITIES:		
Current portion of long-term debt and capital lease obligations	$ 1,308,511	$ 7,868,474
Accounts payable	4,064,419	8,051,817
Accrued expenses	4,190,766	11,917,298
Deferred revenue	86,250	--
Total current liabilities	9,649,946	27,837,589
LONG-TERM DEBT AND CAPITAL LEASE OBLIGATIONS, NET OF CURRENT PORTION	9,031,852	3,282,123
9% CONVERTIBLE SUBORDINATED NOTES PAYABLE	--	50,000,000
COMMITMENTS (Notes 10 and 15)		
STOCKHOLDERS' EQUITY (DEFICIT):		
Preferred stock, $.01 par value- Authorized--5,000,000 shares Issued and outstanding--None	--	--
Common stock, $.001 par value- Authorized--100,000,000 shares Issued and outstanding--5,029,315 and 5,059,650 at December 31, 1996 and 1997, respectively	5,029	5,060
Additional paid-in capital	173,247,476	173,695,698
Deficit accumulated during the development stage	(149,193,775)	(218,655,101)
Deferred compensation	(1,203,926)	(1,093,837)
Total stockholders' equity (deficit)	22,854,804	(46,048,180)
	$ 41,536,602	$ 35,071,532

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

HYBRIDON, INC. AND SUBSIDIARIES
(A DEVELOPMENT STAGE COMPANY)

CONSOLIDATED STATEMENTS OF OPERATIONS

	YEARS ENDED DECEMBER 31,			CUMULATIVE FROM INCEPTION (MAY 25, 1989) TO DECEMBER 31,
	1995	1996	1997	1997
REVENUES:				

Research and development	$ 1,186,124	$ 1,419,389	$ 945,000	$ 5,499,263
Product revenue	--	1,080,175	1,876,862	2,957,037
Royalty income	--	62,321	48,000	110,321
Interest income	218,749	1,446,762	1,079,122	3,220,739
	1,404,873	4,008,647	3,948,984	11,787,360
OPERATING EXPENSES:				
Research and development	29,684,707	39,390,525	46,827,915	165,459,815
General and administrative	6,094,085	11,346,670	11,026,748	47,816,616
Interest	172,757	124,052	4,535,647	6,146,030
Restructuring	--	--	11,020,000	11,020,000
	35,951,549	50,861,247	73,410,310	230,442,461
Net loss	$(34,546,676)	$(46,852,600)	$ (69,461,326)	$(218,655,101)
Basic and Diluted Net Loss per Common Share	$ (94.70)	$ (10.24)	$ (13.76)	
Shares Used in Computing Basic and Diluted Net Loss per Common Share	364,810	4,575,555	5,049,840	
Pro Forma Net Loss per Common Share (Note 2(b))	$ (11.02)	$ (9.67)	$ (13.76)	
Shares Used in Computing Pro Forma Net Loss per Common Share (Note 2(b))	3,134,854	4,843,414	5,049,840	

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

HYBRIDON, INC. AND SUBSIDIARIES
(A DEVELOPMENT STAGE COMPANY)

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)

	CONVERTIBLE PREFERRED STOCK		COMMON STOCK	
	NUMBER OF SHARES	$.01 PAR VALUE	NUMBER OF SHARES	$.001 PAR VALUE
Initial Issuance of Common Stock	--	$ --	133,700	$ 134
Issuance of Series A convertible preferred stock, net of cash issuance costs of $18,000	175,000	1,750	--	--
Issuance of Series B convertible preferred stock, net of cash issuance costs of $11,900	129,629	1,296	--	--
Issuance of common stock	--	--	133,460	133
Net loss	--	--	--	--
Balance, December 31, 1990	304,629	3,046	267,160	267
Issuance of Series C convertible preferred stock, net of cash issuance costs of $23,197	104,000	1,040	--	--
Repurchase of common stock	--	--	(52,500)	(53)
Deferred compensation related to restricted stock awards	--	--	--	--
Amortization of deferred compensation	--	--	--	--
Compensation expense related to stock option grants	--	--	--	--
Net loss	--	--	--	--
Balance, December 31, 1991	408,629	4,086	214,660	214
Issuance of Series C convertible preferred stock, net of cash issuance costs of $20,291	184,000	1,840	--	--
Issuance of common stock related to restricted stock awards	--	--	100,053	100
Issuance of common stock related to the exercise of stock options	--	--	34,615	35
Issuance of warrants	--	--	--	--
Deferred compensation related to stock options and restricted stock awards	--	--	--	--
Amortization of deferred compensation	--	--	--	--
Net loss	--	--	--	--
Balance, December 31, 1992	592,629	5,926	349,328	349
Issuance of Series D convertible preferred stock in exchange for convertible promissory notes payable,				

including accrued interest, net of cash issuance costs of $113,955	378,351	3,784	--	--
Issuance of Series E convertible preferred stock, net of cash issuance costs of $61,251	275,862	2,759	--	--
Issuance of Series F convertible preferred stock, net of cash issuance costs of $2,097,604	407,800	4,078	--	--
Issuance of common stock related to the exercise of stock options	--	--	8,725	9
Reduction in deferred compensation due to stock option termination prior to vesting	--	--	--	--
Amortization of deferred compensation	--	--	--	--
Net loss	--	--	--	--

	ADDITIONAL PAID-IN CAPITAL	DEFICIT ACCUMULATED DURING THE DEVELOPMENT STAGE	DEFERRED COMPENSATION	TOTAL STOCKHOLDERS' EQUITY (DEFICIT)
Initial Issuance of Common Stock	$ 535	$ --	$ --	$ 669
Issuance of Series A convertible preferred stock, net of cash issuance costs of $18,000	855,250	--	--	857,000
Issuance of Series B convertible preferred stock, net of cash issuance costs of $11,900	1,736,801	--	--	1,738,097
Issuance of common stock	534	--	--	667
Net loss	--	(1,110,381)	--	(1,110,381)
Balance, December 31, 1990	2,593,120	(1,110,381)	--	1,486,052
Issuance of Series C convertible preferred stock, net of cash issuance costs of $23,197	2,575,763	--	--	2,576,803
Repurchase of common stock	(210)	--	--	(263)
Deferred compensation related to restricted stock awards	2,328,764	--	(2,328,764)	--
Amortization of deferred compensation	--	--	727,738	727,738
Compensation expense related to stock option grants	669,433	--	--	669,433
Net loss	--	(6,648,899)	--	(6,648,899)
Balance, December 31, 1991	8,166,870	(7,759,280)	(1,601,026)	(1,189,136)
Issuance of Series C convertible preferred stock, net of cash issuance costs of $20,291	4,577,869	--	--	4,579,709
Issuance of common stock related to restricted stock awards	122,644	--	--	122,744
Issuance of common stock related to the exercise of stock options	3,303	--	--	3,338
Issuance of warrants	2,776,130	--	--	2,776,130
Deferred compensation related to stock options and restricted stock awards	2,249,428	--	(2,249,428)	--
Amortization of deferred compensation	--	--	1,332,864	1,332,864
Net loss	--	(14,694,693)	--	(14,694,693)
Balance, December 31, 1992	17,896,244	(22,453,973)	(2,517,590)	(7,069,044)
Issuance of Series D convertible preferred stock in exchange for convertible promissory notes payable, including accrued interest, net of cash issuance costs of $113,955	9,596,767	--	--	9,600,551
Issuance of Series E convertible preferred stock, net of cash issuance costs of $61,251	9,935,988	--	--	9,938,747
Issuance of Series F convertible preferred stock, net of cash issuance costs of $2,097,604	18,288,318	--	--	18,292,396
Issuance of common stock related to the exercise of stock options	26,679	--	--	26,688
Reduction in deferred compensation due to stock option termination prior to vesting	(290,287)	--	290,287	--
Amortization of deferred compensation	--	--	1,124,839	1,124,839
Net loss	--	(19,736,365)	--	(19,736,365)

HYBRIDON, INC. AND SUBSIDIARIES
(A DEVELOPMENT STAGE COMPANY)

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)

	CONVERTIBLE PREFERRED STOCK		COMMON STOCK	
	NUMBER OF SHARES	$.01 PAR VALUE	NUMBER OF SHARES	$.001 PAR VALUE
BALANCE, DECEMBER 31, 1993	1,654,642	16,547	358,053	358
Issuance of Series F convertible preferred stock, net of cash issuance costs of $79,677	116,900	1,169	--	--
Issuance of Series G convertible preferred stock, net of cash issuance costs of $1,006,841	318,302	3,183	--	--
Issuance of common stock related to the exercise of				

stock options	--	--	4,800	5
Cancellation of warrants	--	--	--	--
Reduction in deferred compensation due to stock option termination prior to vesting	--	--	--	--
Amortization of deferred compensation	--	--	--	--
Net loss	--	--	--	--
BALANCE, DECEMBER 31, 1994	2,089,844	20,899	362,853	363
Issuance of Series G convertible preferred stock, net of cash issuance costs of $2,409,926	1,106,591	11,066	--	--
Issuance of common stock related to the exercise of stock options	--	--	5,880	6
Amortization of deferred compensation	--	--	--	--
Net loss	--	--	--	--
BALANCE, DECEMBER 31, 1995	3,196,435	31,965	368,733	369
Issuance of common stock related to initial public offering, net of issuance costs of $5,268,756	--	--	1,150,000	1,150
Conversion of convertible preferred stock to common stock	(3,196,435)	(31,965)	3,371,330	3,371
Issuance of common stock related to the exercise of stock options	--	--	57,740	58
Issuance of common stock related to the exercise of warrants	--	--	81,512	81
Deferred compensation related to grants of common stock options to nonemployees	--	--	--	--
Amortization of deferred compensation relating to grants of common stock options to nonemployees	--	--	--	--
Net loss	--	--	--	--
BALANCE, DECEMBER 31, 1996	--	--	5,029,315	5,029
Issuance of common stock related to the exercise of stock options	--	--	25,005	26
Issuance of common stock related to the exercise of warrants	--	--	330	--
Issuance of common stock for services rendered	--	--	5,000	5
Deferred compensation related to grants of common stock options to nonemployees	--	--	--	--
Amortization of deferred compensation relating to grants of common stock options to nonemployees	--	--	--	--
Net loss	--	--	--	--
BALANCE, DECEMBER 31, 1997	--	$ --	5,059,650	$ 5,060

	ADDITIONAL PAID-IN CAPITAL	DEFICIT ACCUMULATED DURING THE DEVELOPMENT STAGE	DEFERRED COMPENSATION	TOTAL STOCKHOLDERS' EQUITY (DEFICIT)
BALANCE, DECEMBER 31, 1993	55,453,709	(42,190,338)	(1,102,464)	12,177,812
Issuance of Series F convertible preferred stock, net of cash issuance costs of $79,677	5,764,154	--	--	5,765,323
Issuance of Series G convertible preferred stock, net of cash issuance costs of $1,006,841	11,722,072	--	--	11,725,255
Issuance of common stock related to the exercise of stock options	13,395	--	--	13,400
Cancellation of warrants	(68,000)	--	--	(68,000)
Reduction in deferred compensation due to stock option termination prior to vesting	(14,062)	--	14,062	---
Amortization of deferred compensation	--	--	764,228	764,228
Net loss	--	(25,604,161)	--	(25,604,161)
BALANCE, DECEMBER 31, 1994	72,871,268	(67,794,499)	(324,174)	4,773,857
Issuance of Series G convertible preferred stock, net of cash issuance costs of $2,409,926	41,842,632	--	--	41,853,698
Issuance of common stock related to the exercise of stock options	41,494	--	--	41,500
Amortization of deferred compensation	--	--	324,174	324,174
Net loss	--	(34,546,676)	--	(34,546,676)
BALANCE, DECEMBER 31, 1995	114,755,394	(102,341,175)	--	12,446,553
Issuance of common stock related to initial public offering, net of issuance costs of $5,268,756	52,230,094	--	--	52,231,244
Conversion of convertible preferred stock to common stock	28,594	--	--	---
Issuance of common stock related to the exercise of stock options	1,089,618	--	--	1,089,676
Issuance of common stock related to the exercise of warrants	3,176,660	--	--	3,176,741
Deferred compensation related to grants of common stock options to nonemployees	1,967,116	--	(1,967,116)	--
Amortization of deferred compensation relating to grants of common stock options to nonemployees	--	--	763,190	763,190
Net loss	--	(46,852,600)	--	(46,852,600)
BALANCE, DECEMBER 31, 1996	173,247,476	(149,193,775)	(1,203,926)	22,854,804
Issuance of common stock related to the exercise of stock options	86,300	--	--	86,326
Issuance of common stock related to the exercise of warrants	9,075	--	--	9,075
Issuance of common stock for services rendered	146,869	--	--	146,874
Deferred compensation related to grants of common				

stock options to nonemployees	205,978	--	(205,978)	--
Amortization of deferred compensation relating to grants of common stock options to nonemployees	--	--	316,067	316,067
Net loss	--	(69,461,326)	--	(69,461,326)
BALANCE, DECEMBER 31, 1997	$ 173,695,698	$ (218,655,101)	$ (1,093,837)	$ (46,048,180)

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

HYBRIDON, INC. AND SUBSIDIARIES
(A DEVELOPMENT STAGE COMPANY)

CONSOLIDATED STATEMENTS OF CASH FLOWS

	YEARS ENDED DECEMBER 31			CUMULATIVE FROM INCEPTION (MAY 25, 1989) TO DECEMBER 31,
	1995	1996	1997	1997
CASH FLOWS FROM OPERATING ACTIVITIES:				
Net loss	$(34,546,676)	$(46,852,600)	$(69,461,326)	$(218,655,101)
Adjustments to reconcile net loss to net cash used in operating activities-				
Depreciation and amortization	2,023,553	2,393,751	4,488,719	11,186,454
Issuance of common stock for services rendered	--	--	146,874	146,874
Compensation on grant of stock options, warrants and restricted stock	324,174	763,190	316,067	8,123,798
Amortization of discount on convertible promissory notes payable	--	--	--	690,157
Amortization of deferred financing costs	--	--	479,737	696,469
Write-down of assets related to restructuring	--	--	600,000	600,000
Noncash interest on convertible promissory notes payable	--	--	--	260,799
Changes in assets and liabilities-				
Accounts receivable	--	(573,896)	44,194	(529,702)
Prepaid expenses and other current assets	(769,562)	(593,797)	539,499	(1,005,825)
Notes receivable from officers	8,446	(9,845)	70,728	(247,250)
Accounts payable and accrued expenses	483,585	2,747,122	11,713,930	19,969,116
Deferred revenue	--	--	(86,250)	--
Amounts payable to related parties	(80,351)	(12,500)	--	(200,000)
Net cash used in operating activities	(32,556,831)	(42,138,575)	(51,147,828)	(178,964,211)
CASH FLOWS FROM INVESTING ACTIVITIES:				
(Increase) decrease in short-term investments	--	(3,785,146)	3,785,146	--
Purchases of property and equipment	(4,889,624)	(8,902,989)	(7,509,755)	(29,312,465)
Investment in real estate partnership	(1,698,448)	(3,751,552)	--	(5,450,000)
Net cash used in investing activities	(6,588,072)	(16,439,687)	(3,724,609)	(34,762,465)
CASH FLOWS FROM FINANCING ACTIVITIES:				
Proceeds from issuance of convertible preferred stock	41,853,698	--	--	96,584,154
Proceeds from issuance of common stock related to stock options and restricted stock grants	41,500	1,089,676	86,326	1,260,928
Net proceeds from issuance of common stock	--	52,231,244	--	52,355,324
Repurchase of common stock	--	--	--	(263)
Proceeds from notes payable	--	7,500,000	--	9,450,000
Proceeds from issuance of convertible promissory notes payable	--	--	50,000,000	59,191,744
Proceeds from long-term debt	--	--	--	662,107
Proceeds from issuance of common stock related to stock warrants	--	3,176,741	9,075	3,185,816
Proceeds from sale/leaseback of fixed assets	--	1,722,333	1,205,502	4,001,018
Payments on long-term debt and capital leases	(537,977)	(446,163)	(1,564,268)	(3,365,880)
(Increase) decrease in restricted cash and other assets	(44,912)	401,990	(2,474,948)	(4,139,131)
(Increase) decrease in deferred financing costs	(278,927)	251,921	(2,820,790)	(3,256,939)
Net cash provided by financing activities	41,033,382	65,927,742	44,440,897	215,928,878
NET INCREASE (DECREASE) IN CASH AND CASH				

EQUIVALENTS	1,888,479	7,349,480	(10,431,540)	2,202,202
CASH AND CASH EQUIVALENTS, BEGINNING OF PERIOD	3,395,783	5,284,262	12,633,742	--
CASH AND CASH EQUIVALENTS, END OF PERIOD	$ 5,284,262	$ 12,633,742	$ 2,202,202	$ 2,202,202

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

HYBRIDON, INC. AND SUBSIDIARIES
(A DEVELOPMENT STAGE COMPANY)

NOTES TO 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 genetic medicines based primarily on antisense technology.

The Company is in the development stage. Since inception, the Company has devoted substantially all of its efforts toward product research and development and raising capital. Management anticipates that substantially all future revenues will be derived from the sale of proprietary biopharmaceutical products under development or to be developed in the future, and custom contract manufacturing of synthetic DNA products and reagent products (by the Hybridon Specialty Products Division (HSPD)), as well as from research and development revenues and fees and royalties derived from licensing of the Company's technology. Accordingly, although the Company has begun to generate revenues from its custom contract manufacturing business, the Company is dependent on the proceeds from possible future sales of equity securities, debt financings and research and development collaborations in order to fund future operations.

On December 3, 1997, the Company was delisted from the Nasdaq Stock Market, Inc. (NASDAQ) because the Company was not in compliance with the continued listing requirements of the NASDAQ National Market. The Company is currently trading on the NASDAQ OTC Bulletin Board.

As of December 31, 1997, the Company had a working capital deficit of $(24.1) million and a stockholders' deficit of $(46.0) million. Although the Company has raised approximately $4.8 million in gross proceeds from the 1998 Unit Financing, subsequent to December 31, 1997, the Company continues to have very limited cash resources and substantial obligations to lenders. The Company's ability to continue operations in 1998 depends on its success in raising new funds. There is substantial doubt concerning the Company's ability to continue as a going concern. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty. If the Company is unable to obtain a substantial amount of additional funding in April 1998, it will be required to terminate its operations or seek relief under applicable bankruptcy law by the end of April 1998. Management's plans to obtain additional financing are described below.

On January 22, 1998, the Company commenced a private placement (the 1998 Unit Financing) of units consisting of notes (the 1998 Unit Notes) and warrants to issue common stock. The 1998 Unit Financing is being offered through Pillar Investments Ltd., an entity with which two directors of the Company are affiliated and which is a significant shareholder of the Company (the placement agent), as the Company's placement agent, on a best effort basis. As consideration for these services, Pillar Investments Ltd., will receive fees consisting of 9% of the gross proceeds of the 1998 Unit Financing, a non-accountable expense allowance equal to 4% of the gross proceeds of the 1998 Unit Financing and warrants to purchase common stock. The 1998 Unit Notes bear interest at a rate of 14% per annum; provided that if the 1998 Unit Financing is terminated before the Mandatory Conversion Event (as defined below) has occurred, the interest rate shall increase to 18% per annum. The Company is required to make semi-annual interest payments on the outstanding

principal balance of the 1998 Unit Notes on April 1 and October 1 of each year during which such 1998 Unit Notes are outstanding, with the first such payment being due on April 1, 1998, which interest payment obligation may be satisfied through the issuance of additional 1998 Unit Notes valued at their principal amount. The Company plans to satisfy the interest payment due April 1, 1998 by issuing 1998 Unit Notes. The outstanding principal balance of the 1998 Unit Notes will become due on December 31, 2007. The 1998 Unit Notes are secured by substantially all of the Company's assets, subject to the lien on the Company's assets held by the Bank, are subordinate to the Company's existing indebtedness to the Bank, are senior to approximately 80% of the 9.0% Convertible Subordinated Notes (the 9% Notes, see Note 6(d)) to the extent provided in a subordination agreement executed by certain holders of the 9% Notes and, except as otherwise provided in this sentence, rank on a parity with the 9% Notes.

The 1998 Unit Notes are not convertible at the option of the holder, but will automatically convert into a new issue of Series B Convertible Preferred Stock of the Company if the aggregate net proceeds from the 1998 Unit Financing exceeds $20.0 million and the holders of at least 80% of the aggregate principal amount of the 9% Notes have exchanged such Notes for a new issue of Series A Convertible Preferred Stock of the Company pursuant to the exchange offer (the Exchange Offer) described in the following paragraph (such two conditions, the Mandatory Conversion Event). The Series B Convertible Preferred Stock underlying the 1998 Unit Notes would rank as to liquidation junior to the Series A Convertible Preferred Stock issuable in the Exchange Offer.

Each Unit includes warrants to purchase 15% (or, in certain circumstances, 20%) of the number of shares of common stock underlying the Series B Convertible Preferred Stock underlying the 1998 Unit Notes included in such Unit and may include additional warrants in certain circumstances described below. The Series B Convertible Preferred Stock, if issued, and warrants are convertible into, and exercisable for, common stock at a conversion or exercise price equal to the lowest of (i) 80% of the average closing bid price of the Company's common stock for the 30 consecutive trading days immediately preceding any closing in the 1998 Unit Financing or (ii) 80% of the average closing bid price of the Company's common stock for the five consecutive trading dates immediately preceding any closing in the 1998 Unit Financing; provided, however, that if on the termination date of the 1998 Unit Financing the Company has not received at least $20,000,000 in net proceeds from the 1998 Unit Financing or the holders of less than $40,000,000 in principal amount of the 9% Notes accept the Exchange Offer, holders of Units will be entitled to receive additional warrants to purchase, at an exercise price of $0.001 per share, a number of shares of common stock equal to 100% of the common stock then issuable upon conversion of the Series B Convertible Preferred Stock then issuable upon conversion of the 1998 Unit Notes purchased by such investors, in which case the 1998 Unit Notes will not be convertible into equity securities. If the market price of the common stock is less than 125% of the conversion price of the Series B Preferred Stock on the one-year anniversary of the final closing date of the 1998 Unit Financing, the conversion price of the Series B Convertible Preferred Stock will be further adjusted (the Series B Reset) to the greater of (a) the market price of the common stock at such time divided by 1.25 and (b) 50% of the conversion price of the Series B Convertible Preferred Stock at such time, and holders of the Series B Convertible Preferred Stock will also be entitled to receive additional warrants to purchase a number of shares of common stock equal to 50% of the additional number of shares of common stock issuable upon conversion of the Series B Convertible Preferred Stock following the Series B Reset. As of March 30, 1998, the Company has received $4.8 million of gross proceeds from the 1998 Unit Financing.

On February 6, 1998, the Company commenced an Exchange Offer to the holders of the 9% Notes to exchange the 9% Notes for a Series A Convertible Preferred Stock and certain warrants of the Company. In the Exchange Offer, each $1,000 of principal amount and accrued but unpaid interest on the 9% Notes may be exchanged, upon the terms and subject to the conditions set forth in the Exchange Offer documents, for 10 shares of Series A Convertible Preferred Stock, stated value $100 per share, and warrants to purchase such a number of shares of common stock of the Company equal to 15% of the number of shares of common stock into which such Series A Convertible Preferred Stock would be convertible at 212.5% of the initial conversion price of the Series B Convertible Preferred

Stock (the Stated Price). Such Series A Convertible Preferred Stock would have a liquidation preference of $100 per share plus accrued but unpaid dividends and would bear a dividend of the 6.5% per annum, payable on April 1 and October 1 of each year in cash or additional Series A Preferred Stock, at the option of the Company. The conversion price would be $35 per share of common stock through April 1, 2000 and the Stated Price thereafter, which conversion price would be reset upon the occurrence of any Series B Reset to 212.5% of the re-set Series B conversion price. Exchanging holders of the 9% Notes will be granted the right to designate the nominee to the Board of Directors of the Company (the Designated Director). As part of the Exchange Offer, approximately 82% of the 9% Note holders have consented as of March 30, 1998 to defer the interest payment due on April 1, 1998 to October 1, 1998. There can be no assurance that the Exchange Offer will be successful.

On March 30, 1998, the Company amended its Exchange Offer to provide that the terms of the Series A Convertible Preferred Stock and warrants issuable in the Exchange Offer would be revised as described below if the following conditions (the Equity Conditions) had been met no later than the date the Company accepts for exchange in the Exchange Offer at least $40 million principal amount of the 9% Notes: (i) the Company consummates an offering, the size of which is acceptable to the Designated Director, of units consisting of common stock priced (the Common Stock Offering Price) at the greater of $2.00 and 85% of the Market Price (as defined below) of the common stock and warrants to purchase a number of shares of common stock equal to 25% of such Common Stock sold at an exercise price equal to 120% of the Common Stock Offering Price (the 120% Exercise Price); (ii) the Company consummates an offering, with gross proceeds of at least $10 million, of Units consisting of shares of preferred stock having the same terms as the preferred stock issuable in the amended Exchange Offer, and warrants with the same 25% coverage as the warrants issuable in the amended Exchange Offer, as described in the following paragraph, but at the 120% Exercise Price (which shares are expected to be sold at a 30% discount from stated value); and (iii) all 1998 Note Units previously sold and accrued interest thereon are exchanged for common stock and warrants to purchase a number of shares of common stock equal to 30% of the common stock issued in such 1998 Note Unit exchange, such common stock and warrants to be valued, and to have the terms, described in clause (i) above. Market Price means the average reported closing bid price of the common stock for the five consecutive trading days immediately preceding the closing date.

The amended Exchange Offer provides that if the Equity Conditions are met, (a) the conversion terms of the Series A Convertible Preferred Stock will be revised as follows: (i) the conversion price will be 212.5% of the Common Stock Offering Price described above; (ii) such Series A Convertible Preferred Stock will not be convertible for one year following the closing; and (iii) such Series A Convertible Preferred Stock will have no conversion price reset mechanism and (b) the warrant coverage will increase from 15% to 25% of the number of shares of common stock underlying the Series A Convertible Preferred Stock (such warrants being exercisable at 212.5% of the Common Stock Offering Price) and will not have any conversion price reset provisions.

(2) SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

(a) Use of Estimates in the Preparation of Financial Statements

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and 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.

(b) Net Loss per Common Share

Effective December 31, the Company adopted Statement of Financial Accounting Standards (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 as the effects of the Company's potential common stock equivalents are antidilutive. The Company has applied the provisions of SFAS No. 128 retroactively to all periods presented. In accordance with staff Accounting Bulleting (SAB) No. 98, the Company has determined that there were no nominal issuances of capital in the period prior to the Company's initial public offering (IPO). Antidilutive securities which consist of stock options and warrants that are not included in diluted net loss per common share were 2,441,436, 2,595,496, and 2,404,561 for 1995, 1996, and 1997, respectively. The calculation of pro forma basic net loss per share assumes that all series of convertible preferred stock had been converted to common stock as of the original issuance date. Calculations of net loss per common share and potential common share are as follows:

	1995	1996	1997
Net loss	$(34,546,676)	$(46,852,600)	$(69,461,326)
Weighted average shares outstanding	364,810	4,575,555	5,049,840
Basic and diluted net loss per share	$ (94.70)	$ (10.24)	$ (13.76)
Weighted average shares outstanding	364,810	4,575,555	5,049,840
Convertible preferred stock	2,770,044	267,859	--
Pro forma weighted average shares outstanding	3,134,854	4,843,414	5,049,840
Pro forma basic and diluted net loss per share	$ (11.02)	$ (9.67)	$ (13.76)

(c) Principles of Consolidation

The accompanying consolidated financial statements include the results of the Company and its subsidiaries, Hybridon S.A. (Europe), a French corporation and Hybridon Canada, Inc. (an inactive majority-owned subsidiary). The consolidated financial statements also reflect the Company's 49% interest in MethylGene, Inc. (MethylGene), a Canadian corporation which is accounted for under the equity method (see Note 13). All material intercompany balances and transactions have been eliminated in consolidation.

(d) Cash Equivalents and Short-Term Investments

The Company applies SFAS No. 115, Accounting for Certain Investments in Debt and Equity Securities. Under SFAS No. 115, debt securities that the Company has the positive intent and ability to hold to maturity are reported at amortized cost and are

classified as held-to-maturity securities. These securities include cash equivalents, short term investments and restricted cash. At December 31, 1996 and 1997, the Company has classified all investments as held-to-maturity. The Company considers all highly liquid investments with maturities of three months or less when purchased to be cash equivalents. Short-term investments mature within one year of the balance sheet date. Cash and cash equivalents, short-term investments and restricted cash at December 31, 1996 and 1997 consisted of the following (at amortized cost, which approximates fair market value):

	DECEMBER 31, 1996	1997
Cash and Cash Equivalents-		
Cash and money market funds	$10,144,367	$1,702,272
Corporate bond	--	499,930
U.S. government securities	2,489,375	--
Total cash and cash equivalents	$12,633,742	$2,202,202
Short-Term Investments-		
U.S. government securities	$ 3,785,146	$ --
Restricted Cash (Note 5)-		
Certificates of deposit	$ 437,714	$2,016,364
Savings Account	--	1,034,618
	$ 437,714	$3,050,982

(e) 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	5 years
Equipment under capital lease	5 years
Office equipment	3-5 years
Furniture and fixtures	5 years

(f) Accrued Expenses

Accrued expenses on the accompanying consolidated balance sheets consist of the following:

	DECEMBER 31, 1996	1997
Restructuring	$ --	$ 8,316,148
Interest	--	1,125,000
Payroll and related costs	1,593,451	742,452
Outside research and clinical costs	1,381,124	1,231,818

Professional fees	390,440	150,000
Other	825,751	351,880
	$ 4,190,766	$11,917,298

(g) Revenue Recognition

The Company has recorded research and development revenue under the consulting and research agreements discussed in Notes 7 and 8. Revenue is recognized as earned on a straight-line basis over the term of the agreement, which approximates when work is performed and costs are incurred. Revenues from product sales are recognized when the products are shipped. Product revenue during 1996 and 1997 represents revenues from the sale of oligonucleoutides manufactured on a custom contract basis by HSPD.

(h) Research and Development Expenses

The Company charges research and development expenses to operations as incurred.

(i) Patent Costs

The Company charges patent expenses to operations as incurred.

(j) Reclassifications

Certain amounts in the prior periods consolidated financial statements have been reclassified to conform with the current periods presentation.

(k) New Accounting Standards

In June 1997, the Financial Accounting Standards Board (FASB) issued SFAS No. 130, Reporting Comprehensive Income. SFAS No. 130 requires disclosure of all components of comprehensive income on an annual basis and interim basis. Comprehensive income is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from nonowner sources. SFAS No. 130 is effective for fiscal years beginning after December 15, 1997. The Company does not expect this accounting pronouncement to materially effect its financial statements.

In July 1997, the FASB issued SFAS No. 131, Disclosures About Segments of an Enterprise and Related Information. SFAS No. 131 requires certain financial and supplementary information to be disclosed on an annual and interim basis for each reportable segment of an enterprise. SFAS No. 131 is effective for fiscal years beginning after December 15, 1997. Unless impracticable, companies would be required to restate prior period information upon adoption. The Company does not expect this accounting pronouncement to materially effect its financial statements.

(3) RESTRUCTURING

Beginning in July 1997, the Company implemented a restructuring plan to reduce expenditures on a phased basis over the balance of 1997 in an effort to conserve its cash resources. As part of this restructuring plan, in addition to terminating the clinical development of GEM 91, the

Company's first generation antisense drug for the treatment of AIDS and HIV infection, the Company reduced or suspended selected programs unrelated to its core advanced chemistry antisense drug development programs, including its ribozyme program. In connection with the reduction in programs, the Company has accrued termination fees related to research contracts and has incurred restructuring charges related to programs that have been suspended or canceled. As part of the restructuring, all outside testing, public relations, travel and entertainment and consulting arrangements were reviewed and where appropriate the terms were

renegotiated, contracts cancelled or the terms were significantly reduced. In addition, the Company terminated the employment of 84 employees at its Cambridge and Milford, Massachusetts facilities since July of 1997 and substantially reduced operations at its Paris, France office and terminated 10 employees at that location in August 1997.

In connection with the restructuring the Company entered into two different sub-leasing arrangements. The Company has sub-leased one facility in Cambridge, Massachusetts and a portion of its headquarters located at 620 Memorial Drive, Cambridge, Massachusetts. The Company incurred expenses relating to these sub-leases for broker fees and renovation expenses incurred in preparing the Memorial Drive space for the new tenant. In addition, the Company has accrued the estimated lease loss of subleasing 620 Memorial Drive. The Company has accrued the remaining lease costs of its Paris, France office prior to terminating the lease effective March 31, 1998.

The following are the significant components of the charge for restructuring:

Estimated loss on facility leases	$ 6,930,000
Employee severance, benefits and related costs	2,579,000
Writedown of assets to net realizable value	600,000
Termination costs of certain development programs	911,000
	$11,020,000

The total cash impact of the restructuring amounted to approximately $5,165,000. The total cash paid as of December 31, 1997 was approximately $1,453,000 and the remaining amount will be paid in 1998.

(4) NOTES RECEIVABLE FROM OFFICERS

At December 31, 1996 and 1997 the Company had notes receivable, including accrued interest, from officers of $317,978 and $247,250, respectively. As of December 31, 1997 one note remains outstanding with an interest rate of 6.0% per annum and matures in April 2001.

(5) RESTRICTED CASH

At December 31, 1996 and 1997, restricted cash was made up of the following:

	1996	1997
Capital lease obligations (Note 6(c))	$ 437,714	$ 257,822
Note payable to bank (Note 6(a))	--	1,758,542
Foreign bank account	--	1,034,618
	$ 437,714	$3,050,982

In November 1997, the Company was notified by Bank Fur Vermogensanlagen Und Handel AG (BVH) that the Federal Banking Supervisory Office (BAKred) in Germany had imposed a moratorium, effective as of August 19, 1997 on BVH and had closed BVH for business. Accordingly, the Company classified its deposit with BVH as restricted cash. The Company has contacted BVH and is actively pursuing the release of its deposit or sale of the deposit to a third party, including possibly an entity affiliated with a director of the Company. The Company expects to recover substantially all of its deposit in BVH through such means. However, the timing of the recovery may be over a period of up to one year. There can be no assurance that the Company will be able to recover all of its deposit or that the Company will not be required to write off a portion of the $1,034,618. Through March 18, 1998, the Company had recovered $250,000 of the BVH deposit.

(6) LONG-TERM DEBT AND CAPITAL LEASE OBLIGATIONS

(a) Note Payable to a Bank

In December 1996, the Company entered into a five year $7,500,000 note payable with a bank. The note contains certain financial covenants that require the Company to maintain minimum tangible net worth and minimum liquidity and prohibits the payment of dividends. On January 15, 1998 and March 30, 1998, the Company received waivers from the bank which included the following terms: (1) a waiver of any event of default that would otherwise arise as a result of the 1998 Unit Financing discussed in Note 1; (2) a requirement that the Company deposit at least 50% of its unencumbered cash with the bank, including proceeds raised from the 1998 Unit Financing discussed in Note 1; (3) in an event of default, a requirement that all net cash proceeds of any dispositions of assets of the Company permitted by the bank, as defined, shall be applied as a prepayment against the note (if the Company is not in default, only 50% of the net proceeds will be applied against the note); (4) a waiver of covenants of non-compliance through March 31, 1998 and; (5) an increase in the interest rate to the bank's prime rate plus 5%. Prior to the amendment the note bore interest at either the bank's prime rate plus 1% or LIBOR plus 3.5% (9.5% at December 31, 1997), at the Company's election. The Company has secured the obligations under the note with a lien on all of its assets, including intellectual property. The note is payable in 59 equal installments of $62,500 commencing on February 1, 1997 with a balloon payment of $3,812,500, due on January 1, 2002. Prior to the amendments discussed above, if at specified times, the Company's minimum liquidity is less than $15,000,000, $10,000,000, or $5,000,000, the Company is required to pledge cash collateral to the bank equal to 25%, 50% or 100%, respectively, of the then outstanding balance under the

note, pursuant to a cash pledge agreement. During 1997, the Company's minimum liquidity had fallen below $15,000,000 and the Company deposited $1,758,542 as collateral under the cash pledge agreement. The Company has classified the outstanding balance of $6,873,332 at December 31, 1997 as a current liability in the accompanying balance sheet as it does not currently have the financing to remain in compliance with the financial covenants. Also, in connection with the note, the Company issued 5 year warrants to purchase 13,000 shares of common stock at an exercise price of $34.49 per share. These warrants are fully exercisable at December 31, 1997.

(b) Note Payable to Landlord

In December 1994, the Company issued a $750,000 promissory note to its landlord to fund specific construction costs associated with the development of its manufacturing plant in Milford, Massachusetts. The promissory note bears interest at 13% per annum and is to be paid in equal monthly installments of principal and interest over the remainder of the 10-year lease term.

(c) Capital Lease Obligations

The Company has entered into various capital leases for equipment. In 1994, the Company received $1,073,000 as a part of a sale/leaseback transaction with a leasing company. These lease amounts are subject to interest at an effective rate of 4.29% and are being paid in equal installments of approximately $24,000 over 48-months through June 1998. In connection with this lease agreement, the Company is required to maintain a certain amount of cash in escrow as collateral. At December 31, 1997, the Company had $257,822 in escrow related to the agreement.

In December 1996, the Company sold certain laboratory equipment to a leasing company, at its original cost of $1,722,333. In connection with this transaction, the Company entered into a capital lease to lease the equipment from this leasing company for 48 monthly payments ranging from $36,000 to $50,000. The sale of the equipment resulted in a gain of $291,960 which has been offset against the cost of the asset in the accompanying consolidated balance sheet and is being amortized over the life of the lease. In June 1997, the Company sold additional laboratory equipment to the leasing company, at its original cost of $1,205,502. In connection with this transaction, the Company entered into a capital lease to lease the equipment from this leasing company for 24 monthly payments ranging from $24,000 to $34,000. The sale of the equipment resulted in a gain of $127,378, which has been offset against the cost of the asset in the accompanying consolidated balance sheet and is being amortized over the life of the lease.

In January 1997, the Company entered into a five year $1,169,000 lease with a leasing company to finance certain furniture and fixtures in the Cambridge facility. The lease bears interest at a

rate of 13.7% and is payable in 60 equal monthly installments of approximately $26,000 through February 2002.

Future minimum payments due under various notes payable and capital lease obligations, excluding the 9% Notes due April 1, 2004, are as follows at December 31, 1997:

CALENDAR YEAR	AMOUNT
1998	$ 8,206,684
1999	1,404,777
2000	1,324,184
2001	601,038
2002	136,000
Thereafter	195,881
Total long-term debt and capital lease obligations	11,868,564
Less--Amount representing interest	717,967
Principal obligations	11,150,597
Less--Current portion	7,868,474
	$ 3,282,123

(d) 9.0% Convertible Subordinated Notes

On April 2, 1997, the Company issued $50,000,000 of 9.0% convertible subordinated notes (the 9% Notes). Under the terms of the 9% Notes, the Company must make semiannual interest payments on the outstanding principal balance through the maturity date of April 1, 2004. If the 9% Notes are converted prior to April 1, 2000, the Noteholders are entitled to receive accrued interest from the date of the most recent interest payment through the conversion date. 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, subject to adjustment under certain circumstances, as defined.

Beginning April 1, 2000, the Company may redeem the 9% Notes at its option for a 4.5% premium over the original issuance price provided that from April 1, 2000 to March 31, 2001, the 9% Notes may not be redeemed unless the closing price of the common stock equals or exceeds 150% of the conversion price for a period of at least 20 out of 30 consecutive trading days and the 9% Notes are redeemed within 60 days after such trading period. The premium decreases by 1.5% each year through March 31, 2003. 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 issuance price.

(7) G.D. SEARLE & CO. AGREEMENT

In January 1996, the Company and G.D. Searle & Co. (Searle) entered into a collaboration relating to research and development of therapeutic antisense compounds directed at up to eight molecular targets in the field of inflammation/immunomodulation (the Searle Field).

Pursuant to the collaboration, the parties are conducting research and development relating to a compound directed at a molecular target in the Searle Field designated by Searle. In this project, Searle is funding certain research and development efforts by the Company, and each of Searle and the Company have committed certain of its own personnel to the collaboration. The initial phase of research and development activities relating to the initial target will be conducted through the earlier of (i) the achievement of certain product candidate milestones or (ii) 36 months after commencement of the collaboration, subject to early termination by Searle (although in any event Searle is required to

pay 18 months of research and development funding). The parties may extend the initial collaboration by mutual agreement, including agreement as to additional research funding by Searle.

In addition, Searle has the right, at its option, to designate up to six additional molecular targets in the Searle Field (the Additional Targets) for collaborative research and development with the Company on terms substantially consistent with the terms of the collaboration applicable to the initial molecular target. This right is exercisable by Searle with respect to each of the Additional Targets upon the payment by Searle of certain research payments (beyond the project-specific payments relating to the particular Additional Target) and the purchase of additional common stock from the Company by Searle (at the then fair market value). The aggregate amount to be paid by Searle for such research payments and equity investment in order to designate each of the Additional Targets is $10,000,000 per Additional Target. In the event that Searle designates all of the Additional Targets, the aggregate amount to be paid by Searle for research payments will be $24,000,000, and the aggregate amount to be paid by Searle in equity investment will be $36,000,000. If Searle has not designated all of the Additional Targets by the time it advances the product candidate for the initial molecular target to certain stages of preclinical development, Searle will be required to purchase an additional $10,000,000 of common stock (at the then fair market value) on specified dates in order to maintain its right to designate any of the Additional Targets that it has not yet designated. The payment for any such common stock will be creditable against the equity investment portion of the payments to be made by Searle with respect to the designation of any of the Additional Targets that Searle has not yet designated.

Searle also has the right, at its option, to designate a molecular target in the Searle Field to develop a therapeutic agent for cancer that acts through immunomodulation (the Searle Cancer Target) for collaborative research and development with the Company on terms substantially consistent with the terms of the collaboration applicable to the initial molecular target. At the time of such designation, Searle will be required to make certain research payments to the Company and purchase additional common stock from the Company (at the then fair market value). The aggregate amount to be paid by Searle for such research payments and equity investment will range from $12,000,000 (composed of $5,000,000 in research payments and $7,000,000 in equity investment) if the Searle Cancer Target is designated in 1997 to $26,000,000 (composed of $21,000,000 in research payments and $5,000,000 in equity investment) if the Searle Cancer Target is designated in 2000.

Searle has exclusive rights to commercialize any products resulting from the collaboration. If Searle determines, in its sole discretion, to commercialize a product, Searle will fund and perform preclinical tests and clinical trials of the product candidate and will be responsible for regulatory approvals for and marketing of the product. In certain

instances and for specified periods of time, the Company has agreed to perform research and development work in the Searle Field exclusively with Searle. In addition, as to each product candidate, the Company will be entitled to milestone payments from Searle totaling up to an aggregate of $10,000,000 upon the achievement of certain development benchmarks. The Company also will be entitled to royalties from net sales of products resulting from

the collaboration. Subject to satisfying certain conditions relating to its manufacturing capacities and capabilities, the Company will retain manufacturing rights, and Searle will be required to purchase its requirements of products from the Company on an exclusive basis at specified transfer prices. Upon a change in control of the Company, Searle would have the right to terminate the Company's manufacturing rights, although the royalty payable would be increased in such event.

Under the collaboration, in the event that Searle designates (and makes the required payments and equity investments for) all of the Additional Targets or in certain other instances relating to Hybridon's failure to satisfy certain requirements relating to its manufacturing capacities and capabilities, Searle will have the right, exercisable in its sole discretion, to require Hybridon to form a joint venture with Searle for the development of products in the Searle Field (other than products relating to molecular targets that have already been designated by Searle) to which each party will contribute $50,000,000 in cash, although the Company's cash contribution would be reduced by the value of the technology and other rights contributed by the Company to the joint venture. The Company and Searle would each own 50% of the joint venture, although Searle's ownership interest in the joint venture would increase based upon a formula to up to a maximum of 75% if the joint venture is established in certain instances relating to the Company's failure to satisfy certain requirements relating to its manufacturing capacities and capabilities.

During 1996 and 1997, the Company earned $400,000 and $600,000, respectively, in research and development revenues from Searle. Under the collaboration, Searle also purchased 200,000 shares of common stock in the Company's initial public offering of common stock at the initial public offering price as discussed in Note 14(b).

(8) F. HOFFMANN-LA ROCHE LTD. COLLABORATION

In December 1992, the Company and Roche entered into a collaboration involving the application of Hybridon's antisense oligonucleotide chemistry to the development of compounds for the treatment of hepatitis B, hepatitis C and human papilloma virus.

Under this collaboration, Roche funded research and development efforts relating to the collaboration and committed personnel of its own to the collaboration. In 1995, Roche notified the Company that it had selected an antisense oligonucleotide directed at hepatitis C as a lead compound for further development and made a milestone payment to the Company in connection with such designation. In the third quarter of 1996, Roche notified the Company that it had selected an antisense oligonucleotide directed at human papilloma virus as a lead compound for further development, and in the fourth quarter of 1996, made a milestone payment to the Company in connection with such designation. At such time, Roche also notified the Company that Roche had elected not to continue the hepatitis B program under the research and development collaboration. In addition, Roche notified the Company that Roche

was exercising its option to terminate the entire research and development phase of the collaboration as of March 31, 1997. On September 3, 1997, Roche notified the Company that it had decided not to pursue further collaboration with the Company and was terminating the collaboration effective February 28, 1998.

The Company has recorded $1,186,124, $1,019,389 and $345,000 of research and development revenue related to this collaboration in 1995, 1996 and 1997, respectively.

In conjunction with the Roche Collaboration, Roche purchased 163,678 shares of common stock for $6,000,000. Roche was also issued five-year warrants for the purchase of 110,345 shares of common stock at an initial price of $57.50 per share, such exercise price increases commencing on August 12, 1995 on an annual basis at a compound rate of 25%. At December 31, 1997, the exercise price of these warrants are $112.30 per share. The warrants expired on February 12, 1998.

(9) MEDTRONIC, INC. COLLABORATIVE STUDY AGREEMENT

In May 1994, the Company and Medtronic, Inc. (Medtronic) entered into a collaborative study agreement (the Medtronic Agreement) involving the development of antisense compounds for the treatment of Alzheimer's disease and a drug delivery system to deliver such compounds into the central nervous system. The Company will be responsible for the development of, and hold all rights to, any drug developed pursuant to this collaboration, and Medtronic will be responsible for the development of, and hold all rights to, any delivery system developed pursuant to this collaboration. The parties may extend this collaboration by mutual agreement to other neurodegenerative disease targets. The research and development to be conducted is determined and supervised by a committee comprised of an equal number of designees of the Company and Medtronic. As part of the Medtronic Agreement, Medtronic purchased 131,667 shares of common stock for $5,000,000.

(10) LICENSING AGREEMENT

The Company has entered into a licensing agreement with the Worcester Foundation for Biomedical Research, Inc., which merged in 1997 into the University of Massachusetts Medical Center (the Foundation License), under which the Company has received exclusive licenses to technology in certain 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.

(11) PHARMACIA BIOTECH, INC. AGREEMENT

In December 1994, the Company and Pharmacia Biotech, Inc. (Pharmacia) entered into a collaboration involving the design and development of a large-scale oligonucleotide synthesis machine. Following completion of the machine, the collaboration expired in December 1996, and Pharmacia retained the right to sell the machine to third parties, subject to an obligation to pay the Company royalties on such third party sales. During 1996 and 1997, the Company has received $62,321 and $48,000, respectively, of royalty income related to such third party sales.

(12) PERKIN-ELMER CORPORATION SUPPLY AGREEMENT

In September 1996 the Company and the Applied Biosystems Division of Perkin-Elmer signed a four year sales and supply agreement under which Perkin-Elmer agreed to refer potential customers to HSPD for the manufacture of custom oligonucleotides and the Company agreed that amidites for the manufacture of these oligonucleotides would be purchased from Perkin-Elmer and a percentage of the sales price would be paid to Perkin-Elmer. In addition, Perkin-Elmer licensed to the Company its oligonucleotide synthesis patents.

(13) INVESTMENT IN METHYLGENE, INC.

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

The Company has granted to MethylGene exclusive worldwide licenses and sublicenses in respect of certain technology relating to the methylgene fields. These fields are defined as (i) antisense compounds to inhibit DNA methyltransferase for the treatment of cancers, (ii) other methods of inhibiting DNA methyltransferase for the treatment of any indications, and (iii) antisense compounds to inhibit a second molecular target other than DNA methyltransferase for the treatment of cancers, to be agreed upon by the Company and MethylGene. In December 1997, the Company and MethylGene expanded the methylgene fields to include (a) antisense compounds to inhibit DNA methyltransferase for any indication and (b) antisense compounds to inhibit a second and third molecular target for any indications, as may be selected by MethylGene, so long as such molecular targets are not already targeted by the Company. In addition, the Company and MethylGene have entered into a supply agreement pursuant to which MethylGene is obligated to purchase from the Company all required formulated bulk oligonucleotides at specified transfer prices.

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 (the Institution Investors). The Institutional Investors have the right to exchange (the MethylGene Exchange) all (but not less than all) of their shares of stock in MethylGene for an aggregate of 100,000 shares of Hybridon common stock (subject to adjustment for

stock splits, stock dividends and the like). This option is exercisable only during a 90-day period commencing on the earlier of the date five years after the closing of the Institutional Investors' investment in MethylGene or the date on which MethylGene ceases operations. This option terminates sooner if MethylGene raises certain additional amounts of equity or debt financing or if MethylGene enters into a corporate collaboration that meets certain requirements. Subsequent to December 31, 1997, MethylGene raised additional proceeds from outside investors that decreased the Company's interest to 30%, which did not terminate the

MethyGene Exchange available to the Institutional Investors. The Company is accounting for its investment in MethylGene under the equity method and, due to the existence of the investors exchange rights, the Company has recorded, up to its original investment, 100% of MethylGene's losses in the accompanying consolidated statement of operations.

(14) STOCKHOLDERS' EQUITY (DEFICIT)

(a) Common Stock

The Company has 100,000,000 authorized shares of common stock, $.001 par value, of which 5,059,650 shares were issued and outstanding at December 31, 1997.

(b) Initial Public Offering

On February 2, 1996, the Company completed its initial public offering of 1,150,000 shares of common stock at $50.00 per share. The sale of common stock resulted in net proceeds to the Company of approximately $52,231,000 after deducting expenses related to the offering.

(c) Reverse Stock Split

On December 10, 1997, the Board of Directors declared a one-for-five reverse split of its common stock. Share quantities and related per share amounts have been retroactively restated to reflect the stock split.

(d) Warrants

The Company has the following exercisable warrants outstanding for the purchase of common stock at December 31, 1997:

EXPIRATION DATE	SHARES	EXERCISE PRICE PER SHARE
February 12, 1998	110,345	$112.30
March 31, 1998-October 25, 2000	953,936	50.00
February 28, 2000	20,000	37.50
December 31, 2001	13,000	34.49
April 2, 2002	71,301	35.06
	1,168,582	
Average per share exercise price		$ 54.59

As a component of the sale of preferred stock in 1994 and 1995, the Company issued to the investors in such offering warrants for the purchase of 585,425 shares of common stock at $40.00 to $50.00 per share. Warrants to purchase 331,382 shares of common stock at an exercise price of $50.00 per share expire on March 31, 1998, and the remaining warrants for the purchase of 254,043 shares of common stock at an exercise price of $40.00 per share expired on October 25, 1997.

Five-year warrants to purchase 368,620 shares of common stock at

$50.00 per share were issued in 1994 and 1995 as a component of the compensation for services of several placement agents of the Company's convertible preferred stock. Of these warrants, 304,335 were issued to a company that is controlled by two directors of the Company (see Note 15(a)). The remaining 64,285 warrants were issued to various other companies that acted as placement agents.

(e) Stock Options

In 1990 and 1995, the Company established the 1990 Stock Option Plan (the 1990 Option Plan) and the 1995 Stock Option Plan (the 1995 Option Plan), respectively, which provide for the grant of incentive stock options and nonqualified stock options. Options granted under these plans vest over various periods and expire no later than 10 years from the date of grant. However, under the 1990 Option Plan in the event of a change in control (as defined in the 1990 Plan), 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, 1997, options to purchase a total of 604,863 shares of common stock remained outstanding under the 1990 Option Plan.

A total of 700,000 shares of common stock may be issued upon the exercise of options granted under the 1995 Option 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% (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 option (which, in the case of incentive stock options, may not exceed 10 years). As of December 31, 1997, options to purchase a total of 534,914 shares of common stock remained outstanding under the 1995 Option Plan.

In October 1995, the Company adopted the 1995 Director Stock Option Plan (the Director Plan). A total of 50,000 shares of common stock may be issued upon the exercise of options granted under the Director Plan. Under the terms of the Director Plan, options to purchase 1,000 shares of common stock were granted to eligible directors upon the closing of the Company's initial public offering at the fair market value of the common stock on the date of the closing. Thereafter, options to purchase 1,000 shares of common stock will be granted to each eligible director on May 1 of each year commencing in 1997. All options will 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, 1997, options to purchase a total of 14,000 shares of common stock remained outstanding under the Director Plan.

In May 1997, the Company adopted the 1997 Stock Option Plan (the 1997 Option Plan), which provides for the grant of incentive and non-qualified stock options. A total of 600,000 shares of common

stock may be issued upon the exercise of options granted to any employee under the 1997 Option Plan. The maximum number of shares with respect to which options may be granted to any employee under the 1997 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% (110% in the case of incentive stock) 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 ten years). As of December 31, 1997, options to purchase a total of 36,720 shares of common stock remained outstanding under the 1997 Option Plan.

All stock option activity since inception is summarized as follows:

	NUMBER OF SHARES	EXERCISE PRICE PER SHARE	WEIGHTED AVERAGE PRICE PER SHARE
Options granted	66,940	$ .01	$ .01
Options exercised	(33,460)	.01	.01
Outstanding, December 31, 1990	33,480	.01	.01
Options granted	1,700	.01	.01
Options terminated	(540)	.01	.01
Outstanding, December 31, 1991	34,640	.01	.01
Options granted	192,540	1.25 - 25.00	9.90
Options exercised	(34,615)	.01 - 5.00	.10
Options terminated	(4,865)	2.50 - 5.00	2.80
Outstanding, December 31, 1992	187,700	.01 - 25.00	10.05
Options granted	288,108	17.50 - 62.50	41.90
Options exercised	(8,725)	.01 - 5.00	3.05
Options terminated	(25,275)	.01 - 50.00	3.95
Outstanding, December 31, 1993	441,808	.01 - 62.50	31.30
Options granted	134,500	25.00 - 35.00	26.65
Options exercised	(4,800)	.01 - 5.00	2.80
Options terminated	(15,000)	.01 - 25.00	19.15
Outstanding, December 31, 1994	556,508	.01 - 62.50	30.50
Options granted	407,108	37.50 - 50.00	37.75
Options exercised	(5,880)	2.50 - 25.00	7.05
Options terminated	(219,528)	2.50 - 62.50	49.10
Outstanding, December 31, 1995	738,208	.01 - 50.00	29.15
Options granted	476,020	25.00 - 65.60	49.55
Options exercised	(57,740)	.01 - 37.50	18.85
Options terminated	(20,100)	25.00 - 57.85	40.20
Outstanding, December 31, 1996	1,136,388	1.25 - 65.60	38.05
Options granted	315,675	27.50 - 32.50	30.75
Options exercised	(25,005)	1.25 - 40.00	12.60
Options terminated	(236,561)	2.50 - 65.60	40.35
Outstanding, December 31, 1997	1,190,497	$ .01 - $ 65.60	$ 36.18
Exercisable, December 31, 1997	740,780	$ .01 - $ 65.60	$ 34.40

In October 1995, the FASB issued SFAS No. 123, Accounting for Stock-Based Compensation. SFAS No. 123 requires the measurement of the fair value of stock options or warrants 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 Accounting Principles Board Opinion No. 25 and elect the disclosure-only alternative under SFAS No. 123. In 1996 and 1997, the Company recorded $1,967,116 and $205,978 of deferred compensation related to grants to nonemployees which will be amortized over the vesting period of the options. The Company has recorded compensation expense of $763,190 and $316,067 in 1996 and 1997, respectively.

The Company has computed the pro forma disclosures require by SFAS No. 123 for all stock options and warrants granted after January 1, 1995 using the Black-Scholes option pricing model. The assumptions used are as follows:

	DECEMBER 31,		
	1995	1996	1997
Risk free interest rate	6.41%	6.14%	6.22%
Expected dividend yield	--	--	--
Expected lives	6 years	6 years	6 years
Expected volatility	60%	60%	60%

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 effect of applying SFAS No. 123 would be as follows:

	DECEMBER 31,		
	1995	1996	1997
Net Loss, as reported:	$ (34,546,676)	$ (46,852,600)	$ (69,461,326)
Pro forma Net Loss:	$ (41,447,381)	$ (52,890,455)	$ (73,402,170)
Basic and Diluted net loss, as reported			
Basic and Diluted	$ (94.70)	$ (10.24)	$ (13.76)
Pro forma	$ (11.02)	$ (9.67)	$ --
Basic and Diluted net loss, pro forma			
Basic and Diluted	$ (113.61)	$ (11.56)	$ (14.54)
Pro forma	$ (13.22)	$ (10.92)	$ --

(f) Employee Stock Purchase Plan

In October 1995, the Company adopted the 1995 Employee Stock Purchase Plan (the Purchase Plan), under which up to 100,000 shares of common stock may be issued to participating employees of the Company or its subsidiaries. All full-time employees of the Company, except those who would immediately after the grant own 5% or more of the total combined voting power or value of the stock of the Company or any subsidiary, are eligible to participate.

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 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 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 which 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.

(g) Preferred Stock

The Certificate of Incorporation of the Company permits its Board of Directors to issue up to 5,000,000 shares of preferred stock, par value $.01 per share (the Preferred Stock), 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. No shares of Preferred Stock are currently outstanding.

(15) COMMITMENTS

The Company has entered into a lease for a production plant in Milford, Massachusetts. The lease has a 10-year term, which commenced on July 1, 1994, with certain extension options.

On February 4, 1994, the Company entered into a lease for an approximately 91,500 square-foot building in Cambridge, Massachusetts (the Cambridge Lease). The Cambridge Lease is with a partnership that is affiliated with three directors of the Company. The Cambridge Lease has a term of 15 years, commencing February 1, 1997, and may be extended for three additional five-year terms at the option of the Company. The Cambridge Lease provides for annual rent of $37.79 per year per

square foot for the first five years, $42.73 per year per square foot for the second five years and $47.00 per year per square foot for the third five years. As compensation for arranging this lease, the Company issued Pillar Limited (see Note 15(a)) five-year warrants for the purchase of 100,000 shares of the Company's common stock at an exercise price of $50.00 per share. These warrants are exercisable through February 4, 1999.

Under the terms of the Cambridge Lease, the Company elected to treat $5,450,000 of its payments for a portion of the costs of the construction of the leased premises (primarily relating to tenant improvements) as contributions to the capital of the Cambridge landlord in exchange for a limited partnership interest in the Cambridge landlord (the Partnership Interest). The Company's Partnership Interest represents a 32.15% interest in the Cambridge Landlord. The Company's right to receive distributions of cash generated from operations or from any sale or refinancing of the property would be subordinate to the distribution to certain other limited partners of priority amounts currently totaling approximately $6,500,000 (approximately $3,500,000 of which is subject to annual increase at a rate of between 12% and 15% as a result of a cumulative return to one of the limited partners of the Cambridge Landlord). In the case of a sale or refinancing of the property, after payment of the priorities described in the preceding sentence, the Company would be entitled to a return of its capital contribution and, thereafter, to its pro rata share of the remaining funds available for distribution. The Company has the right, at any time prior to February 2000 to sell the Partnership Interest back to certain limited partners of the Cambridge Landlord for a price equal to the greater of (i) the total paid for the Partnership Interest ($5,450,000) or (ii) the fair market

value of the Partnership Interest at the time. The assets of these limited partners are limited to their investment in the Cambridge Landlord.

Future approximate minimum rent payments as of December 31, 1997, under the lease agreements through 2012 discussed above, net of sublease agreements are as follows:

CALENDAR YEAR	AMOUNT
1998	$ 2,275,000
1999	2,831,000
2000	4,248,000
2001	4,677,000
2002	4,991,000
Thereafter	40,586,000
	$59,608,000

During 1995, 1996 and 1997, facility rent expense, net of sublease revenue, was approximately $2,142,000, $2,352,000 and $4,613,000, respectively.

(a) Consulting 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 two shareholders and directors of the Company. The terms of the agreements with the affiliated companies, S.A. Pillar Investment N.V. (Pillar Investment), Pillar S.A. (formerly Commerce Consult S.A.) and Pillar Investment Limited (formerly Ash Properties Limited) (Pillar Limited), are described below.

In March 1994, the Company entered into a consulting agreement with Pillar S.A., which was amended in March 1995 (the 1994 Pillar Consulting Agreement). Under the 1994 Pillar Consulting Agreement, the Company agreed to pay to Pillar S.A. cash compensation for financial advisory and managerial services in connection with the Company's overseas operations, including support services in connection with contracts, agreements and arrangements with the Agence Nationale de Recherches sur le SIDA (ANRS), and for overhead costs and reimbursement of certain authorized out-of-pocket expenditures. The Company is committed to pay Pillar S.A. a monthly fee of approximately $96,000 with respect to this agreement. The agreement expires on February 28, 1998, as amended. During 1995, 1996 and 1997, the Company had expensed $1,226,000, $1,106,000 and $998,000 under this consulting agreement, respectively.

In connection with the 1994 Pillar Consulting Agreement, the Company issued to Pillar S.A. two, five-year warrants to purchase up to 40,000 shares of the Company's common stock. The first warrant was issued on March 1, 1994 at an exercise price of $50.00 per share and will expire on February 28, 1999 and is fully exercisable as of December 31, 1997. The second warrant was issued on March 1, 1995 at an exercise price of $37.50 per share and will expire on February 28, 2000 and is fully exercisable as of December 31, 1997.

All of the warrants issued to Pillar S.A. under the 1994 Pillar Consulting Agreements and certain other warrants previously issued to Pillar S.A. provide that within 15 days after the date of any exercise, in full or in part, Pillar S.A. will pay to the Company an amount in cash equal to the lesser of (i) 50% of all amounts paid to Pillar S.A. as compensation under the various Pillar S.A. consulting agreements and (ii) the positive difference, if any, between the aggregate fair market value of the shares of common stock purchased upon such exercise and the aggregate exercise price for such shares.

On September 9, 1994, the Company entered into modifications to its arrangements with Pillar S.A. and its affiliates, including: (i) a reduction in the exercise price of certain warrants previously issued to $50.00 per share; (ii) an amendment to the terms of each of the warrants issued to Pillar S.A. and its affiliates described above to provide for cashless exercise in connection with a sale or change in control of the Company; (iii) a grant of additional five-year warrants (the Additional Pillar Warrants) to purchase 22,800 shares of Common Stock at an

exercise price of $50.00 per share; and a right of first negotiation for Pillar S.A. to provide seed financing for any spin-offs by the Company which do not involve or relate to antisense therapeutic compounds.

On July 8, 1995, the Company entered into an agreement (the Pillar Europe Agreement) with Pillar S.A. pursuant to which Pillar S.A. agreed to provide to the Company certain consulting, advisory and related services and serve as the Company's exclusive agent in connection with potential corporate partnerships in Europe and as a nonexclusive placement agent of the Company in connection with future private placements of securities of the Company for a period of two years. As discussed below, the Pillar Europe Agreement was significantly amended on November 1, 1995.

The Company and Pillar S.A. agreed to modify the Pillar Europe Agreement to provide that (i) Pillar would cease to serve as the Company's exclusive agent in connection with potential corporate partnerships in Europe but would continue to serve as a nonexclusive agent in such respect; (ii) Pillar would receive a retainer of $26,470 per month for the balance of the term of the Pillar Europe Agreement; (iii) certain fees to be received by Pillar in connection with European license or collaboration agreements would only be payable to Pillar in connection with potential collaborations with five specified French pharmaceutical companies; and (iv) any compensation payable to Pillar S.A. in connection with its services with respect to other corporate collaborations or any placements of securities would be negotiated on a case-by-case basis and would be subject to the approval of the independent members of the Board of Directors of the Company. In consideration of such modification, the Company paid Pillar in 1995 a fee totaling $300,000.

Pillar Limited acted as a placement agent for the Company for certain sales of convertible preferred stock outside the United States and, in addition, provided the Company with certain financial advisory services with respect to the sale of such preferred stock outside the United States. In connection with such services, Pillar earned fees of $492,604 and $2,020,751 during 1994 and 1995, respectively. Pillar received payment for such fees

through $2,435,883 of cash payments and through the issuance of five-year warrants for the purchase of 438,267 shares of common stock at $50.00 per share, expiring on various dates beginning on July 14, 1998 through October 25, 2000.

(b) Other Research and Development Agreements

The Company has entered into consulting and research agreements with the universities, research and testing organizations and individuals, under which consulting and research support is provided to the Company. These agreements are for varying terms through

and provide for certain minimum annual or per diem fees plus reimbursable expenses to be paid during the contract periods. Future minimum fees payable under these contracts as of December 31, 1997 are approximately as follows:

CALENDAR YEAR	AMOUNT
1998	$ 253,000
1999	129,000
	$ 382,000

Total fees and expenses under these contracts were approximately $5,470,000, $7,171,000 and $9,372,000 during 1995, 1996 and 1997, respectively.

(c) Employment Agreements

The Company has entered into employment agreements with certain of its executive officers which 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.

(16) INCOME TAXES

The Company applies SFAS No. 109, Accounting for Income Taxes. At December 31, 1997, the Company had net operating loss and tax credit carryforwards for income tax purposes of approximately $205,997,000 and $3,436,000, respectively, available to reduce federal taxable income and federal income taxes, respectively. The Tax Reform Act of 1986 (the Act), enacted in October 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 Act, which, as of December 31, 1997, have resulted in ownership changes in excess of 50%, as defined under the Act. Ownership changes in future periods may limit 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,		
2005	$ 666,000	$ 15,000
2006	3,040,000	88,000
2007	7,897,000	278,000
2008	18,300,000	627,000
2009	25,670,000	689,000
2010	36,134,000	496,000
2011	44,947,000	493,000
2012	69,343,000	750,000
	$ 205,997,000	$ 3,436,000

The components of the deferred tax amounts, carryforwards and the valuation allowance are approximately as follows:

	DECEMBER 31, 1996	1997
Operating loss carryforwards	$ 54,661,000	$ 82,399,000
Temporary differences	1,325,000	5,243,000
Tax credit carryforwards	2,686,000	3,436,000
	58,672,000	91,078,000
Valuation allowance	(58,672,000)	(91,078,000)
	$ --	$ --

A valuation allowance has been provided, as it is uncertain if the Company will realize the deferred tax asset. The net change in the total valuation allowance during 1997 was an increase of approximately $32,406,000.

(17) EMPLOYEE BENEFIT PLAN

On October 10, 1991, the Company adopted 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 matching 50% of employee contributions to the plan, up to 6% of the employee's annual base salary, and charged to operations approximately $125,000, $224,000 and $253,000 during 1995, 1996 and 1997, respectively.

HYBRIDON, INC. AND SUBSIDIARIES
(A DEVELOPMENT STAGE COMPANY)

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

(Continued)

(18) SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION

The accompanying consolidated financial statements include the following cash flow information:

	DECEMBER 31			CUMULATIVE FROM INCEPTION (MAY 25, 1989) TO DECEMBER 31,
	1995	1996	1997	1997
SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION:				
Cash paid during the period for interest	$ 172,757	$ 124,052	$3,264,596	$3,630,450
SUPPLEMENTAL DISCLOSURE OF NONCASH INVESTING ACTIVITIES:				
Purchase of property and equipment under capital leases	$ 90,562	$1,722,333	$2,374,502	$5,604,370
SUPPLEMENTAL DISCLOSURE OF NONCASH FINANCING ACTIVITIES:				
Issuance of Series C convertible preferred stock in exchange for convertible promissory notes	$ --	$ --	$ --	$1,700,000
Issuance of Series D convertible preferred stock in exchange for convertible promissory notes and accrued interest	--	--	--	9,382,384
Issuance of Series E convertible preferred stock in exchange for subscriptions receivable	--	--	--	555,117
Issuance of Series F convertible preferred stock in exchange for subscriptions receivable	--	--	--	2,535,000
Issuance of Series G convertible preferred stock in exchange for subscriptions receivable	--	--	--	2,535,000
Issuance of convertible promissory notes in exchange for subscriptions receivable	--	--	--	906,016
Issuance of stock warrants in exchange for deferred financing costs	--	--	--	937,000
Cancellation of warrants and reduction of deferred financing costs	--		--	238,000
Conversion of preferred stock into common stock	--	--	--	68,000
Issuance of common stock for services rendered	--	159,822	--	159,822
Deferred compensation related to restricted stock awards and grant of stock options	--	--	146,874	146,874
	--	1,967,116	205,978	6,751,286

EXHIBIT INDEX

Exhibit No.	Description
3.1	Restated Certificate of Incorporation of the Registrant, as amended.
3.2*	Amended and Restated By-Laws of the Registrant.

3.3###	Form of Certificate of Designation of Series A Preferred Stock.
3.4###	Form of Certificate of Designation of Series B Preferred Stock.
4.1*	Specimen Certificate for shares of Common Stock, $.001 par value, of the Registrant.
4.2#	Indenture dated as of March 26, 1997 between Forum Capital Markets L.P. and the Registrant.
+10.1*	License Agreement dated February 21, 1990 and restated as of September 8, 1993 between the Registrant and the Worcester Foundation for Biomedical Research, Inc., as amended.
+10.2*	Patent License Agreement dated September 21, 1995 between the Registrant and National Institutes of Health.
+10.3*	License Agreement effective as of October 13, 1994 between the Registrant and McGill University.
+10.4*	License Agreement effective as of October 25, 1995 between the Registrant and The General Hospital Corporation.
+10.5*	License Agreement dated as of October 30, 1995 between the Registrant and Yoon S. Cho-Chung.
+10.6*	Collaborative Study Agreement effective as of December 30, 1992 between the Registrant and Medtronic, Inc.
+10.7*	System Design and Procurement Agreement dated as of December 16, 1994 between the Registrant and Pharmacia Biotech, Inc.
10.8*	Lease dated March 10, 1994 between the Registrant and Laborer's Pension/Milford Investment Corporation for space located at 155

	Fortune Boulevard, Milford, Massachusetts, including Note in the original principal amount of $750,000.
10.9*	Lease dated February 4, 1994 between the Registrant and Charles River Building Limited Partnership for space located at 620 Memorial Drive, Cambridge, Massachusetts.
10.10*	Series G Convertible Preferred Stock and Warrant Purchase Agreement dated as of September 9, 1994 among the Registrant and certain Purchasers, as amended (the "Series G Agreement").
10.11*	Registration Rights Agreement dated as of February 21, 1990 between the Registrant, the Worcester Foundation for Biomedical Research, Inc. and Paul C. Zamecnik.
10.12*	Registration Rights Agreement dated as of June 25, 1990 between the Registrant and Nigel L. Webb.
10.13*	Registration Rights Agreement dated as of February 6, 1992 between the Registrant and E. Andrews Grinstead, III.
10.14*	Registration Rights Agreement dated as of February 6, 1992 between the Registrant and Anthony J. Payne.
++10.15*	1990 Stock Option Plan, as amended.
++10.16*	1995 Stock Option Plan.
++10.17*	1995 Director Stock Plan.

++10.18*	1995 Employee Stock Purchase Plan.
10.19*	Form of Warrant to purchase shares of Series C Convertible Preferred Stock originally issued to Pillar Investment Limited (formerly known as Ash Properties Limited), as amended.
10.20*	Form of Warrant to purchase shares of Common Stock issued in connection with the issuance of the Registrant's series of notes known as its 10% Convertible Subordinated Notes due September 16, 1993 and the Registrant's 10% Convertible Subordinated Note Due March 19, 1993, as amended.
10.21*	Warrant issued to Pillar S.A. to purchase up to 175,000 shares of Common Stock dated as of December 1, 1992, as amended.

10.22*	Form of Warrant originally issued to Pillar Investment Limited to purchase 427,126 shares of Common Stock dated as of February 15, 1993, as amended.
10.23*	Form of Warrant originally issued to Pillar Investment Limited to purchase 350,000 shares of Common Stock dated as of February 15, 1993, as amended.
10.24*	Warrant issued to Pillar Investment Limited to purchase 500,000 shares of Common Stock dated as of February 4, 1994, as amended.
10.25*	Form of Warrant issued to Pillar Investment Limited to purchase shares of Common Stock issued as placement commissions in connection with the sale of shares of Series F Convertible Preferred Stock and in consideration of financial advisory services, as amended.
10.26*	Warrant issued to Pillar S.A. to purchase 100,000 shares of Common Stock dated as of March 1, 1994, as amended.
10.27*	Form of Warrant to purchase shares of Common Stock issued as part of the Units (as defined in the Series G Agreement) issued and sold to investors pursuant to the Series G Agreement on or prior to March 31, 1995, as amended.
10.28*	Form of Warrant to purchase shares of Common Stock issued as part of the Units issued and sold to investors pursuant to the Series G; Agreement after March 31, 1995.
10.29*	Warrant issued to Pillar S.A. to purchase 100,000 shares of Common Stock dated as of March 1, 1995.
10.30*	Form of Warrant issued to Pillar Investment Limited to purchase shares of Common Stock issued as placement commissions in connection with the sale of Units pursuant to the Series G Agreement.
++10.31***	Employment Agreement dated as of March 1, 1997 between the Registrant and E. Andrews Grinstead, III.
10.32*	Indemnification Agreement dated as of February 6, 1992 between the Registrant and E. Andrews Grinstead, III.
++10.33**	Employment Agreement dated March 1, 1997 between the Registrant and Dr. Sudhir Agrawal.

++10.34*	Consulting Agreement dated as of February 21, 1990 between the Registrant and Dr. Paul C. Zamecnik.
10.35*	Consulting Agreement dated as of March 1, 1994 between the Registrant and Pillar S.A.
10.36*	Consulting Agreement dated as of July 8, 1995 between the Registrant and Pillar S.A., as amended.
10.37*	Master Lease Agreement dated as of March 1, 1994 between the Registrant and General Electric Capital Corporation.
10.38*	First Amendment to Lease dated as of November 30, 1995 between the Registrant and Charles River Building Limited Partnership for space located at 620 Memorial Drive, Cambridge, Massachusetts.
+10.39**	Research, Development and License Agreement dated as of January 24, 1996 between the Registrant and G.D. Searle & Co.
+10.40**	Manufacturing and Supply Agreement dated as of January 24, 1996 between the Registrant and G.D. Searle & Co.
10.41**	Registration Rights Agreement dated as of January 24, 1996 between the Registrant and G.D. Sear1e & Co.
10.42**	Second Amendment to Lease dated as of February 23, 1996 between the Registrant and Charles River Building Limited Partnership for space located at 620 Memorial Drive, Cambridge, Massachusetts.
10.43**	Third Amendment to Lease dated as of February 28, 1996 between the Registrant and Charles River Building Limited Partnership for space located at 620 Memorial Drive, Cambridge, Massachusetts.
10.44***	Fourth Amendment to Lease dated as of July 25, 1996 between the Registrant and Charles River Building Limited Partnership for space located at 620 Memorial Drive, Cambridge, Massachusetts.
10.45***	Fifth Amendment to Lease dated as of March 14, 1997 between the Registrant and Charles River Building Limited Partnership for space located at 620 Memorial Drive, Cambridge, Massachusetts.
10.46***	Loan and Security Agreement dated as of December 31, 1996 between the Registrant and Silicon Valley Bank (the "Silicon Agreement").

10.47***	Warrant issued to Silicon Valley Bank to purchase 65,000 shares of Common Stock dated as of December 31, 1996.
10.48***	Registration Rights Agreement dated as of December 31, 1996 between the Registrant and Silicon Valley Bank.
10.49***	Master Equipment Lease Agreement dated as of October 25, 1996 between the Registrant and Finova Technology Finance, Inc.
+++10.50***	Supply and Sales Agreement dated as of September 1, 1996 between the Registrant and P.E. Applied Biosystems.
10.51#	Registration Rights Agreement dated as of March 26, 1997 between Forum Capital Markets L.P. and the Registrant.

10.52#	Warrant Agreement dated as of March 26, 1997 between Forum Capital Markets L.P. and the Registrant.
+++10.53##	Amendment No. 1 to License Agreement, dated as February 21, 1990 and restated as of September 8, 1993, by and between the Worcester Foundation for Biomedical Research, Inc. and the Registrant, dated as of November 26, 1996.
10.54##	Letter Agreement dated May 12, 1997 between the Registrant and Pillar S.A. amending the Consulting Agreement dated as of March 1, 1994 between the Registrant and Pillar S.A.
10.55##	Amendment dated July 15, 1997 to the Series G Convertible Preferred Stock and Warrant Purchase Agreement dated as of September 9, 1994 among the Registrant and certain purchasers, as amended.
10.56##	Sixth Amendment to Lease dated April 1997 between the Registrant and Charles River Building Limited Partnership for space located at 620 Memorial Drive, Cambridge, Massachusetts.
10.57	Consent Agreement dated January 15, 1998 between Silicon Valley Bank and the Registrant relating to the Silicon Agreement.
10.58###	Form of Unit Purchase Agreement (the "Unit Purchase Agreement") in connection with the sale of Notes due 2007 by and among the Registrant and certain purchasers.
10.59###	Form of Notes due 2007 of the Registrant issued to or issuable pursuant to the Unit Purchase Agreement.

10.60###	Form of Warrants of the Registrant issued or issuable purusant to the Unit Purchase Agreement.
21.*	Subsidiaries of the Registrant.
23.1	Consent of Arthur Andersen LLP.
23.2	Consent of McDonnell Boehnen Hulbert & Berghoff.
27.1	Financial Data Schedule [EDGAR] - Year Ended December 31, 1997
27.2	Financial Data Schedule [EDGAR] - Year Ended December 31, 1996

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

** Incorporated by reference to Exhibits to the Registrant's Annual Report on Form 10-K for the year ended December 31, 1995.

*** Incorporated by reference to Exhibits to the Registrant's Annual Report on Form 10-K for the year ended December 31, 1996.

Incorporated by reference to Exhibits to the Registrant's Current Report on Form 8-K dated April 2, 1997.

Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended June 30, 1997.

Incorporated by reference to Exhibit 9(a)(1) to the Registrant's

Schedule 13E-4 dated February 6, 1998.

+ 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 this Annual Report on Form 10-K.

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

Exhibit 3.1

RESTATED

CERTIFICATE OF INCORPORATION

OF

HYBRIDON, INC.

Hybridon, Inc., a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware, does hereby certify as follows:

1. The Corporation filed its original Certificate of Incorporation with the Secretary of State of Delaware on May 25, 1989, which Certificate of Incorporation was amended by a Certificate of Amendment of Certificate of Incorporation filed on February 21, 1990, and amended and restated by a Restated Certificate of Incorporation filed on June 5, 1990. A Restated Certificate of Incorporation was filed with the Secretary of State of the State of Delaware on November 20, 1990, which Restated Certificate of Incorporation was amended by a Certificate of Amendment of Restated Certificate of Incorporation filed on October 16, 1991, a Certificate of Amendment of Restated Certificate of Incorporation filed on March 3, 1992, a Certificate of Amendment of Restated Certificate of Incorporation filed on March 23, 1992, a Certificate of Amendment of Restated Certificate of Incorporation filed on October 23, 1992, a Certificate of Amendment of Restated Certificate of Incorporation

filed on February 12, 1993, a Certificate of Amendment of Restated Certificate of Incorporation filed on June 17, 1993, a Certificate of Amendment of Restated Certificate of Incorporation filed on July 13, 1993, a Certificate of Amendment of Restated Certificate of Incorporation filed on September 9, 1994, a Certificate of Amendment of Restated Certificate of Incorporation filed on July 7, 1995, a Certificate of Amendment of Restated Certificate of Incorporation filed on December 19, 1995, and a Certificate of Retirement of Stock filed on even date herewith.

2. At a meeting of the Board of Directors of the Corporation, a resolution was duly adopted, pursuant to Sections 141(f) and 245 of the General Corporation Law of the State of Delaware, setting forth a Restated Certificate of Incorporation of the Corporation and declaring said Restated Certificate of Incorporation advisable. The resolution setting forth the Restated Certificate of Incorporation is as follows:

RESOLVED: That the Restated Certificate of Incorporation of the Corporation, as amended, be and hereby is amended and restated in its entirety so that the same shall read as follows:

FIRST. The name of the Corporation is:

Hybridon, Inc.

SECOND. The address of its registered office in the State of Delaware is Corporation Trust Center, 1209 Orange Street, in the City of Wilmington, County of New Castle. The name of its registered agent at such address is The Corporation Trust Company.

THIRD. The nature of the business or purposes to be conducted or promoted by the Corporation is as follows:

To engage in any lawful act or activity for which corporations may be organized under the General Corporation Law of Delaware.

FOURTH. The total number of shares of all classes of stock which the Corporation shall have authority to issues is One Hundred Million (100,000,000) shares of Common Stock, $.001 par value per share ("Common Stock"), and (ii) Five Million ($5,000,000)shares of Preferred Stock, $.01 par value per share ("Preferred Stock"), which may be issued from time to time in one or more series as set forth in Part B of this Articles FOURTH.

The following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation.

A. COMMON STOCK.

1. GENERAL. The voting, dividend and liquidation rights of the holders of the Common Stock are subject to and qualified by the rights of the holders of the Preferred Stock of any series as may be designated by the Board of Directors upon any issuance of the Preferred Stock of any series.

2. VOTING. The holders of the Common Stock are entitled to one vote for each share held at all meetings of stockholders (and written actions in lieu of meetings). There shall be no cumulative voting.

The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of a majority of the stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of Delaware.

3. DIVIDENDS. Dividends may be declared and paid on the Common Stock from funds lawfully available therefor as and when determined by the Board of Directors and subject to any preferential dividend rights of any then outstanding Preferred Stock.

4. LIQUIDATION. Upon the dissolution or liquidation of the Corporation, whether voluntary or involuntary, holders of Common Stock will be entitled to receive all assets of the Corporation available for distribution to its stockholders,

subject to any preferential rights of any then outstanding Preferred Stock.

B. PREFERRED STOCK.

Preferred Stock may be issued from time to time in one or more series, each of such series to have such terms as stated or expressed herein and in the resolution or resolutions providing for the issue of such series adopted by the Board of Directors of the Corporation as hereinafter provided. Any shares of Preferred Stock which may be redeemed, purchased or acquired by the Corporation may be reissued except as otherwise provided by law. Different series of Preferred Stock shall not be construed to constitute different classes of shares for the purposes of voting by classes unless expressly provided.

Authority is hereby expressly granted to the Board of Direc tors from time to time to issue the Preferred Stock in one or more series, and in connection with the creation of any such series, by resolution or resolutions providing for the issue of the shares thereof, to determine and fix such voting powers, full or limited, or no voting powers, and such designations, preferences and relative participating, optional or other special rights, and qualifications, limitations or restrictions thereof, including without limitation thereof, dividend rights, conversion rights, redemption privileges and liquidation preferences, as shall be stated and expressed in such resolutions, all to the full extent now or

hereafter permitted by the General Corporation Law of Delaware. Without limiting the generality of the foregoing, the resolutions providing for issuance of any series of Preferred Stock may provide that such series shall be superior or rank equally or be junior to the Preferred Stock of any other series to the extent permitted by law. Except as otherwise specifically provided in this Certificate of Incorporation, no vote of the holders of the Preferred Stock or Common Stock shall be a prerequisite to the issuance of any shares of any series of the Preferred Stock authorized by and complying with the conditions of the Certificate of Incorporation, the right to have such vote being expressly waived by all present and future holders of the capital stock of the Corporation.

FIFTH. The name and mailing address of the sole incorporator are as follows:

NAME	MAILING ADDRESS
David P. Johst	60 State Street Boston, MA 02109

SIXTH. In furtherance of and not in limitation of powers conferred by statute, it is further provided:

1. Election of directors need not be by written ballot.

2. The Board of Directors is expressly authorized to adopt, amend or repeal the By-Laws of the Corporation.

SEVENTH. Whenever a compromise or arrangement is proposed between this corporation and its creditors or any class of them and/or between this corporation and its stockholders or any class of them, any court of equitable jurisdiction within the State of Delaware may, on the application in a summary way of this corporation or of any creditor or stockholder thereof, or on the application of any receiver or receivers appointed for this corporation under the provisions of section 291 of Title 8 of the Delaware Code or on the application of trustees in dissolution or of any receiver or receivers appointed for this corporation under the provisions of section 279 of Title 8 of the Delaware Code order a meeting of the creditors or class of creditors, and/or of the stockholders or class of stockholders of this corporation, as the case may be, to be summoned in such manner as the said court directs. If a majority in number representing three-fourths in value of the creditors or class of creditors, and/or of the stockholders or class of stockholders of this corporation, as the case may be, agree to any compromise or arrangement and to any promise or arrangement, the said compromise or arrangement and the said reorganization shall, if sanctioned by the court to which the said application has been made, be binding on all the creditors or class of creditors, and/or on all the stockholders or class of stockholders, of this corporation, as the case may be, and also on this corporation.

EIGHTH. Except to the extent that the General Corporation Law of the State of Delaware prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty, no director of the Corporation shall be personally liable to the Corporation or its stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability. No amendment to or repeal of this provision shall apply to or have any effect on the liability or alleged liability of any director of the Corporation for or with respect to any acts or omissions of such director occurring prior to such amendment.

NINTH. 1. ACTION, SUITS AND PROCEEDINGS OTHER THAN BY

OR IN THE RIGHT OF THE CORPORATION. The Corporation shall indemnify each person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the Corporation), by reason of the fact that he is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) (all such persons being referred to hereafter as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) judgment, fines and amounts paid in settlement actually and reasonably incurred by him or on his behalf in connection with such action, suit or proceeding and any appeal therefrom, if he acted in good faith and in a manner he reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction or upon a plea of NOLO CONTENDERE or its equivalent, shall not, of itself, create a presumption that the person did not act in good faith and in a manner which he reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that his conduct was unlawful. Notwithstanding anything to the contrary in this Article, except as set forth in Section 6 below, the Corporation shall not indemnify an Indemnitee seeking indemnification in connection with a proceeding (or part thereof) initiated by the Indemnitee unless the initiation thereof was approved by the Board of Directors of the Corporation.

2. ACTIONS OR SUITS BY OR IN THE RIGHT OF THE CORPORATION. The Corporation shall indemnify any Indemnitee who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the Corporation to procure a judgment in its favor by reason of the fact that he is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and

amounts paid in settlement actually and reasonably incurred by him or on his behalf in connection with such action, suit or proceeding and any appeal therefrom, if he acted in good faith and in a manner he reasonably believed to be in, or not opposed to, the best interests of the Corporation, except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the Corporation unless and only to the extent that the Court of Chancery of Delaware or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of such liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses (including attorneys' fees) which the Court of Chancery of Delaware or such other court shall deem proper.

3. INDEMNIFICATION FOR EXPENSES OF SUCCESSFUL PARTY. Notwithstanding the other provisions of this Article, to the extent that an Indemnitee has been successful, on the merits or otherwise, in defense of any action, suit or proceeding referred to in Sections 1 and 2 of this Article, or in defense of any claim, issue or matter therein, or on appeal from any such action, suit or proceeding, he shall be indemnified against all expenses (including attorneys' fees) actually and reasonably incurred by him or on his behalf in connection therewith. Without limiting the foregoing, if any action, suit or proceeding is disposed of, on the merits or otherwise (including a disposition without prejudice), without (i) the disposition being adverse to the Indemnitee, (ii) an adjudication that the Indemnitee was liable to the Corporation, (iii) a plea of guilty or NOLO CONTENDERE by the Indemnitee, (iv) an adjudication that the

Indemnitee did not act in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Corporation, and (v) with respect to any criminal proceeding, an adjudication that the Indemnitee had reasonable cause to believe his conduct was unlawful, the Indemnitee shall be considered for the purposes hereof to have been wholly successful with respect thereto.

4. NOTIFICATION AND DEFENSE OF CLAIM. As a condition precedent to his right to be indemnified, the Indemnitee must notify the Corporation in writing as soon as practicable of any action, suit, proceeding or investigation involving him for which indemnity will or could be sought. With respect to any action, suit, proceeding or investigation of which the Corporation is so notified, the Corporation will be entitled to participate therein at its own expense and/or to assume the defense thereof at its

own expense, with legal counsel reasonably acceptable to the Indemnitee. After notice from the Corporation to the Indemnitee of its election so to assume such defense, the Corporation shall not be liable to the Indemnitee for any legal or other expenses subsequently incurred by the Indemnitee in connection with such claim, other than as provided below in this Section 4. The Indemnitee shall have the right to employ his own counsel in connection with such claim, but the fees and expenses of such counsel incurred after notice from the Corporation of its assumption of the defense thereof shall be at the expense of the Indemnitee unless (i) the employment of counsel by the Indemnitee has been authorized by the Corporation, (ii) counsel to the Indemnitee shall have reasonably concluded that there may be a conflict of interest or position on any significant issue between the Corporation and the Indemnitee in the conduct of the defense of such action or (iii) the Corporation shall not in fact have employed counsel to assume the defense of such action, in each of which cases the fees and expenses of counsel for the Indemnitee shall be at the expense of the Corporation, except as otherwise expressly provided by this Article. The Corporation shall not be entitled, without the consent of the Indemnitee, to assume the defense of any claim brought by or in the right of the Corporation or as to which counsel for the Indemnitee shall have reasonably made the conclusion provided for in clause (ii) above.

5. ADVANCE OF EXPENSES. Subject to the provisions of Section 6 below, in the event that the Corporation does not assume the defense pursuant to Section 4 of this Article of any action, suit, proceeding or investigation of which the Corporation receives notice under this Article, any expenses (including attorneys' fees) incurred by an Indemnitee in defending a civil or criminal action, suit, proceeding or investigation or any appeal therefrom shall be paid by the Corporation in advance of the final disposition of such matter, PROVIDED, HOWEVER, that the payment of such expense incurred by an Indemnitee in advance of the final disposition of such matter shall be made only upon receipt of an undertaking by or on behalf of the Indemnitee to repay all amounts so advanced in the event that it shall ultimately be determined that the Indemnitee is not entitled to be indemnified by the Corporation as authorized in this Article. Such undertaking may be accepted without reference to the financial ability of such person to make such repayment.

6. PROCEDURE FOR INDEMNIFICATION. In order to obtain indemnification or advancement of expenses pursuant to Section 1, 2, 3 or 5 of this Article, the Indemnitee shall submit to the Corporation a written request, including in such request such documentation and information as is reasonably available to the Indemnitee and is reasonably necessary to determine whether and

to what extent the Indemnitee is entitled to indemnification or advancement of expenses. Any such indemnification or advancement of expenses shall be made

promptly, and in any event within 60 days after receipt by the Corporation of the written request of the Indemnitee, unless with respect to requests under Section 1, 2 or 5 the Corporation determines, by clear and convincing evidence, within such 60-day period that the Indemnitee did not meet the applicable standard of conduct set forth in Section 1 or 2, as the case may be. Such determination shall be made in each instance by (a) a majority vote of a quorum of the directors of the Corporation consisting of persons who are not at that time parties to the action, suit or proceeding in question ("disinterested directors'), (b) if no such quorum is obtainable, a majority vote of a committee of two or more disinterested directors, (c) a majority vote of a quorum of the outstanding shares of stock of all classes entitled to vote for directors, voting as a single class, which quorum shall consist of stockholders who are not at that time parties to the action, suit or proceeding in question, (d) independent legal counsel (who may be regular legal counsel to the Corporation), or (e) a court of competent jurisdiction.

7. REMEDIES. The right to indemnification or advances as granted by this Article shall be enforceable by the Indemnitee in any court of competent jurisdiction if the Corporation denies such request, in whole or in part, or if no disposition thereof is made within the 60-day period referred to above in Section 6. Unless otherwise provided by law, the burden of proving that the Indemnitee is not entitled to indemnification or advanced of expenses under this Article shall be on the Corporation. Neither the failure of the Corporation to have made a determination prior to the commencement of such action that indemnification is proper in the circumstances because the Indemnitee has met the applicable standard of conduct, nor an actual determination by the Corporation pursuant to Section 6 that the Indemnitee has not met such applicable standard of conduct, shall be a defense to the action or create a presumption that the Indemnitee has not met the applicable standard of conduct. The Indemnitee's expenses (including attorneys' fees) incurred in connection with successfully establishing his right to indemnification, in whole or in part, in any such proceeding shall also be indemnified by the Corporation.

8. SUBSEQUENT AMENDMENT. No amendment, termination or repeal of this Article or of the relevant provisions of the General Corporation Law of Delaware or any other applicable laws shall affect or diminish in any way the rights of any Indemnitee

to indemnification under the provisions hereof with respect to any action, suit, proceeding or investigation arising out of or relating to any actions, transactions or facts occurring prior to the final adoption of such amendment, termination or repeal.

9. OTHER RIGHTS. The indemnification and advancement of expenses provided by this Article shall not be deemed exclusive of any other rights to which an Indemnitee seeking indemnification or advancement of expenses may be entitled under any law (common or statutory), agreement or vote of stockholders or disinterested directors or otherwise, both as to action in his official capacity and as to action in any other capacity while holding office for the Corporation, and shall continue as to an Indemnitee who has ceased to be a director or officer, and shall inure to the benefit of the estate, heirs, executors and administrators of the Indemnitee. Nothing contained in this Article shall be deemed to prohibit, and the Corporation is specifically authorized to enter into, agreements with officers and directors providing indemnification rights and procedures different from those set forth in this Article. In addition, the Corporation may, to the extent authorized from time to time by its Board of Directors, grant indemnification rights to other employees or agents of the Corporation or other persons serving the Corporation and such rights may be equivalent to, or greater or less than, those set forth in this Article.

10. PARTIAL INDEMNIFICATION. If an Indemnitee is entitled under any provision of this Article to indemnification by the Corporation for some or a portion of the expenses (including attorneys' fees), judgments, fines or amounts paid in settlement actually and reasonably incurred by him or on his behalf in connection with any action, suit, proceeding or investigation and any appeal, therefrom but not, however, for the total amount thereof, the Corporation shall nevertheless indemnify the Indemnitee for the portion of such expenses

(including attorneys' fees), judgments, fines or amounts paid in settlement to which the Indemnitee is entitled.

11. INSURANCE. The Corporation may purchase and maintain insurance, at its expense, to protect itself and any director, officer, employee or agent of the Corporation or another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) against any expense, liability or loss incurred by him in any such capacity, or arising out of his status as such, whether or not the Corporation would have the power to indemnify such person against such expense, liability or loss under the General Corporation law of Delaware.

12. MERGER OR CONSOLIDATION. If the Corporation is merged into or consolidated with another corporation and the Corporation is not the surviving corporation, the surviving corporation shall assume the obligations of the Corporation under this Article with respect to any action, suit, proceeding or investigation arising out of or relating to any actions, transactions or facts occurring prior to the date of such merger or consolidation.

13. SAVINGS CLAUSE. If this Article or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the Corporation shall nevertheless indemnify each Indemnitee as to any expenses (including attorneys' fees) judgments, fines and amounts paid in settlement in connection with any action, suit, proceeding or investigation, whether civil, criminal or administrative, including an action by or in the right of the Corporation, to the fullest extent permitted by any applicable portion of this Article that shall not have been invalidated and to the fullest extent permitted by applicable law.

14. DEFINITIONS. Terms used herein and defined in Section 145(h) and Section 145(i) of the General Corporation Law of Delaware shall have the respective meanings assigned to such terms in such Section 145(h) and Section 145(i).

15. SUBSEQUENT LEGISLATION. If the General Corporation Law of Delaware is amended after adoption of this Article to expand further the indemnification permitted to Indemnitees, then the Corporation shall indemnify such persons to the fullest extent permitted by the General Corporation Law of Delaware, as so amended.

TENTH. The Corporation reserves the right to amend, alter, change or repeal any provision contained in this Restated Certificate of Incorporation, in the manner now or hereafter prescribed by statute and this Restated Certificate of Incorporation, and all rights conferred upon stockholders herein are granted subject to this reservation.

ELEVENTH. This Article is inserted for the management of the business and for the conduct of the affairs of the Corporation and shall not become effective until the closing of the sale of shares of Common Stock in an underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, resulting in at least $10,000,000 of gross proceeds to the Corporation (a "Public Offering").

1. NUMBER OF DIRECTORS. The number of directors of the Corporation shall not be less than three. The exact number of directors within the limitations specified in the preceding sentence shall be fixed from time to time by, or in the manner provided in, the Corporation's By-Laws.

2. CLASSES OF DIRECTORS. The Board of Directors shall be and is divided

into three classes: Class I, Class II and Class III. No one class shall have more than one director more than any other class. If a fraction is contained in the quotient arrived at by dividing the designated number of directors by three, then, if such fraction is one-third, the extra director shall be a member of Class II, and if such fraction is two-thirds, one of the extra directors shall be a member of Class I and one of the extra directors shall be a member of Class II, unless otherwise provided from time to time by resolution adopted by the Board of Directors.

3. ELECTION OF DIRECTORS. Elections of directors need not be by written ballot except as and to the extent provided in the By-Laws of the Corporation.

4. TERMS OF OFFICE. Each director shall serve for a term ending on the date of the third annual meeting following the annual meeting at which such director was elected; PROVIDED, that each initial director in Class I shall serve for a term ending on the date of the annual meeting in 1996; each initial director in Class II shall serve for a term ending on the date of the annual meeting in 1997; and each initial director in Class III shall serve for a term ending on the date of the annual meeting in 1998; and PROVIDED FURTHER, that the term of each director shall be subject to the election and qualification of his successor and to his earlier death, resignation or removal.

5. ALLOCATION OF DIRECTORS AMONG CLASSES IN THE EVENT OF INCREASES OR DECREASES IN THE NUMBER OF DIRECTORS. In the event of any increase or decrease in the authorized number of directors, (i) each director then serving as such shall nevertheless continue as a director of the class of which he is a member and (ii) the newly created or eliminated directorships resulting from such increase or decrease shall be apportioned by the Board of Directors among the three classes of directors so as to ensure that no one class has more than one director more than any other class. To the extent possible, consistent with the foregoing rule, any newly created directorships shall be added to those classes whose terms of office are to expire at the latest dates following such allocation, and any newly eliminated

directorships shall be subtracted from those classes whose terms of offices are to expire at the earliest dates following such allocation, unless otherwise provided from time to time by resolution adopted by the Board of Directors.

6. QUORUM; ACTION AT MEETING. A majority of the directors at any time in office shall constitute a quorum for the transaction of business. In the event one or more of the directors shall be disqualified to vote at any meeting, then the required quorum shall be reduced by one for each director so disqualified, provided that in no case shall less than one-third of the number of directors fixed pursuant to Section 1 above constitute a quorum. If at any meeting of the Board of Directors there shall be less than such a quorum, a majority of those present may adjourn the meeting from time to time. Every act or decision done or made by a majority of the directors present at a meeting duly held at which a quorum is present shall be regarded as the act of the Board of Directors unless a greater number is required by law, by the By-Laws of the Corporation or by this Restated Certificate of Incorporation.

7. REMOVAL. Directors of the Corporation may be removed only for cause by the affirmative vote of the holders of at least two-thirds of the shares of the capital stock of the Corporation issued and outstanding and entitled to vote.

8. VACANCIES. Any vacancy in the Board of Directors, however occurring, including a vacancy resulting from an enlargement of the board, shall be filled only by a vote of a majority of the directors then in office, although less than a quorum, or by a sole remaining director. A director elected to fill a vacancy shall be elected to hold office until the next election of the class for which such director shall have been chosen, subject to the election and qualification of his successor and to his earlier death, resignation or removal.

9. STOCKHOLDER NOMINATIONS AND INTRODUCTION OF BUSINESS, ETC. Advance notice of stockholder nominations for election of directors and other business

to be brought by stockholders before a meeting of stockholders shall be given in the manner provided by the By-Laws of the Corporation.

10. AMENDMENTS TO ARTICLE. Notwithstanding any other provisions of law, this Restated Certificate of Incorporation or the By-Laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote

of the holders of at least seventy-five percent (75%) of the shares of capital stock of the Corporation issued and outstanding and entitled to vote shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article ELEVENTH.

TWELFTH. Until the closing of a Public Offering, any action which is required to be taken or which may be taken at any annual or special meeting of stockholders of the Corporation may be taken without a meeting, without prior notice and without a vote, if a consent in writing, setting forth the action so taken, is signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares entitled to vote on such action were present and voted. Effective upon the closing of a Public Offering, stockholders of the Corporation may not take any action by written consent in lieu of a meeting. Notwithstanding any other provisions of law, the Restated Certificate of Incorporation or the By-Laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the shares of capital stock of the Corporation issued and outstanding and entitled to vote shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article TWELFTH.

THIRTEENTH. Effective upon the closing of a Public Offering, special meetings of stockholders may be called at any time by only the Chief Executive Officer (or if there is no Chief Executive Officer, the President) or the Board of Directors. Business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting. Notwithstanding any other provision of law, this Restated Certificate of Incorporation or the By-Laws of the Corporation, as amended, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the shares of capital stock of the Corporation issued and outstanding and entitled to vote shall be required to amend or repeal, or to adopt any provision inconsistent with this Article THIRTEENTH.

IN WITNESS WHEREOF, the Corporation has caused its corporate seal to be affixed hereto and this Restated Certificate of Incorporation to be signed by its Chairman this 28TH March, 1996.

HYBRIDON, INC.

By: /s/ E. Andrews Grinstead, III

Chairman

[Corporate Seal]

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CERTIFICATE OF AMENDMENT
OF
RESTATED
CERTIFICATE OF INCORPORATION
OF HYBRIDON, INC.

Pursuant to Section 242 of the General
Corporation Law of the State of Delaware

HYBRIDON, INC. (the "Corporation"), organized and existing under and by virtue of the General Corporation Law of the State of Delaware, does hereby certify as follows:

By written action of the Board of Directors of the Corporation, dated October 20, 1997, the Board of Directors duly adopted resolutions pursuant to Sections 141(f) and 242 of the General Corporation Law of the State of Delaware setting forth an amendment to the Restated Certificate of Incorporation of the Corporation, as amended, and declaring said amendment to be advisable. The stockholders of the Corporation duly approved, pursuant to said Section 242, said proposed amendment at a Special Meeting of Stockholders held on November 18, 1997. The resolution setting forth the amendment to the Restated Certificate of Incorporation is as follows:

RESOLVED: That, subject to stockholder approval, the following paragraph be inserted prior to the first paragraph of Article FOURTH of the Certificate of Incorporation:

"That upon the filing date of the Certificate of Amendment of Restated Certificate of Incorporation of the Corporation (the "Effective Date"), a one-for-five reverse split of the Corporation's Common Stock (as defined below) shall become effective, such that each five shares of Common Stock outstanding and held of record by each stockholder of the Corporation (including treasury shares)

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immediately prior to the Effective Date shall represent one share of Common Stock from and after the Effective Date."

IN WITNESS WHEREOF, the Corporation has caused this Certificate of Amendment to be executed by its Chairman of the Board of Directors, President and Chief Executive Officer this 10th day of December, 1997.

HYBRIDON, INC.

By: /s/ E. Andrews Grinstead, III

E. Andrews Grinstead, III
Chairman of the Board of Directors,
President and Chief Executive Officer

EXHIBIT 10.57

January 15, 1998

Hybridon, Inc.
620 Memorial Drive
Cambridge, Massachusetts
Attention: E. Andrews Grinstead

Re: Consent to Issuance of Notes due 2007 in the principal amount of up to $68,750,000 and Waiver of Covenants and Defaults under Loan Agreement

Dear Sir/Madam:

Reference is hereby made to that certain Loan and Security Agreement by and between HYBRIDON, INC. (the "BORROWER") and SILICON VALLEY BANK (the "BANK"), originally dated December 31, 1996 (the "LOAN AGREEMENT"). You have indicated that the Borrower contemplates entering into and performing its obligations under a UNIT PURCHASE AGREEMENT (as defined below) pursuant to which the Borrower intends to commence an offering (the "OFFERING") of units (the "UNITS") consisting of Notes due 2007 (the "NOTES") and warrants to purchase common stock (the "WARRANTS") as more particularly described in the Restructuring Proposal Term Sheet attached hereto as EXHIBIT A (the "TERM SHEET"). The Notes and Warrants shall be issued on substantially the terms and conditions set forth in the form of Unit Purchase Agreement by and among the Borrower and each Purchaser of Units party thereto (the "UNIT PURCHASE AGREEMENT") attached hereto as EXHIBIT B, and the form of Note and of Certificate of Designation for the Series B Preferred Stock of the Borrower attached hereto as EXHIBIT C, (collectively, the "NOTE DOCUMENTS"). Upon the satisfaction of certain conditions more particularly set forth in the Notes, the Notes and any accrued but unpaid interest thereon will convert into preferred stock of the Borrower (the "CONVERSION SECURITIES") having substantially the terms set forth in Certificate of Designation for the Series B Preferred Stock hereto. The placement agents for the Offering, or their designees, shall also receive placement and advisory warrants (the "PLACEMENT AND ADVISORY WARRANTS") to purchase Units equal, in the aggregate up to 25% of the Units issued to purchasers in the Offering. As contemplated by the Term Sheet, the Borrower may also issue the Exchange Preferred Stock and Exchange Warrants referenced therein and may, in certain instances, issue the Conversion Securities directly.

You have also indicated that the Borrower has had discussions with representatives of certain holders of its 9% Convertible Subordinated Notes due 2004 (the "CONVERTIBLE NOTES") contemplating the exchange (the "EXCHANGE") of Convertible Notes and accrued interest

thereonfor shares of Series A Preferred Stock of the Borrower having substantially the terms set forth on EXHIBIT D annexed hereto (the "EXCHANGE PREFERRED") and warrants to purchase common stock as set forth on the Term Sheet and contemplating waivers of certain provisions of the Indenture pursuant to which the Convertible Notes were issued, as described on EXHIBIT E annexed hereto (the "INDENTURE WAIVERS"). You have requested that the Bank amend or waive certain provisions of the Loan Agreement, the Negative Pledge Agreement entered into in connection with the Loan Agreement (the "Negative Pledge Agreement") consent to the issuance of, and performance by the Borrower of its obligations under, the Unit Purchase Agreement, the Notes, the Conversion Securities and the Exchange Preferred and other related transactions.

1. The Bank hereby consents to the issuance of the Notes, the Conversion Securities and the Exchange Preferred and to the performance by the Borrower of its obligations thereunder, including without limitation the payment of interest and dividends thereunder, and to the Exchange, and such consent constitutes the prior written consent required by Sections 7.4 and 7.6 of the Loan Agreement. The Bank further agrees that the Notes constitute "Subordinated Debt" as that term is defined in Section 1.1 of the Loan Agreement, and consents to the Indenture Waivers. This consent and agreement is conditioned upon the

execution among the Bank and the Secured Party referenced in the Unit Purchase Agreement of an intercreditor agreement limiting the Bank's contractual right of offset contained in the Loan Documents in certain instances until the earliest of: i) the date on which at least $35,000,000 in net proceeds has been received in the Offering, ii) the Termination Date, as defined in the Unit Purchase Agreement, or iii) the termination of the Offering by the Borrower or Pillar Investments, Ltd..

2. The Bank's consent to the issuance of the Notes is expressly subject to the provisions of Section 7.10 of the Loan Agreement which prohibits any amendment of the Notes without the Bank's express written consent.

3. The Bank hereby waives compliance by the Borrower with the Minimum Liquidity covenant contained in Section 6.9 of the Loan Agreement for the months ended November 30, 1997, December 31, 1997, January 31, 1998 and February 28, 1998 (ie. the first possible date on which the Borrower would be required to pledge amounts pursuant to Section 6.9 would be April 15, 1998). The Bank will require compliance with all of the financial covenants contained in the Loan Agreement commencing March 1, 1998, and first tested as of March 31, 1998 based upon a compliance certificate to be provided to the Bank on or before April 15, 1998. In addition, the Borrower will provide the Bank with a projected Compliance Certificate for March 31, 1998, as set forth in paragraph 9 hereof. The Loan Agreement is hereby modified to provide that the Compliance Certificate required to be provided pursuant to Section 6.3 of the Loan Agreement will be provided by the fifteenth of each month for the period ended on the last business day of the previous month; provided, however, that the due date of the

pledge referred to in Section 6.9 shall be the last business day of such month with respect to any Minimum Liquidity compliance level for which Borrower is no more than $250,000 short of achieving compliance with such Minimum Liquidity level, and on the next business day in the event that the Borrower is more than $250,000 short of achieving compliance of such Minimum Liquidity level. The Bank requires as a condition to the waivers contained in this paragraph that at least fifty (50%) of the net proceeds of the Offering will be deposited in the Borrower's demand deposit or other deposit accounts with the Bank, and that at least fifty (50%) of the Borrower's present unencumbered cash will be maintained with the Bank, all such funds to be used in the Borrower's discretion subject to the covenants in the Loan Agreement. The Bank will continue to hold all of the cash presently pledged to it as of the date of this letter as security for the Borrower's obligations to the Bank under the Loan Documents.

4. The Bank's consent to the issuance of the Notes and waiver of the covenant breaches and defaults referenced in this letter is expressly subject to the Borrower's agreement to execute and deliver to the Bank i) an Intellectual Property Security Agreement in form attached hereto and ii) a pledge agreement in the form attached hereto respecting all stock of all subsidiaries of the Borrower and all of the Borrower's ownership interests in any limited partnerships or other business entities. Such executed agreements shall be provided to the Bank in recordable form acceptable to the Bank within two business days of delivery of this letter. The Borrower will provide the Bank with a quarterly update of all intellectual property owned by the Borrower and will cooperate with the Bank in amending the Intellectual Property Security Agreement to include any new patents, pending applications and amendments thereto owned by the Borrower. The Borrower will cooperate with the Bank in executing and delivering such other documents, instruments and agreements and taking such other actions as may be necessary to perfect the Bank's security interests granted in the Intellectual Property Security Agreement and the pledge agreement. The Bank agrees to

release its security interest in the Borrower's interest in Charles River Limited Partnership ("CRLP") to permit a sale of CRLP in accordance with paragraph 10.

5. The Borrower agrees, in consideration of the Bank's consents herein that the effective rate of interest on the Borrower's obligations to the Bank under the Loan Agreement, will increase effective January 15, 1998 to the Prime Rate plus three (3%) percent per annum. If the Borrower does not receive net proceeds from the Offering of at least $5,000,000 on or before February 16, 1998, the effective interest rate on the Borrower's obligations to the Bank under the Loan Agreement shall be increased, effective January 15, 1998 to the Prime Rate plus five (5%) percent per annum.

6. The Bank's consent to the issuance of the Notes and waiver of the covenant breaches and defaults referenced in this letter is expressly subject to, and not effective until, payment by the Borrower to the Bank of a "Consent and Waiver Fee" in the amount of Thirty-Five Thousand ($35,000) Dollars. If the Borrower does not receive net proceeds from the Offering of at least $5,000,000 on or before February 16, 1998, the Borrower shall pay to the Bank an additional "Consent and Waiver Fee" of Fifteen Thousand ($15,000) Dollars on February 17, 1998. If the Borrower does not receive net proceeds from the Offering of at least $12,500,000 on or before March 16, 1998, the Borrower shall pay to the Bank, in addition to the amounts previously referenced in this paragraph, the sum of Five Thousand ($5,000) Dollars on March 17, 1998 and a like sum on the fifteenth day of each month thereafter until the Borrower has received aggregate net proceeds from the Offering of at least $35,000,000.

7. The Borrower and the Bank hereby also agree that the Loan Agreement is hereby modified to delete any references to Anthony Payne contained therein, to waive any existing default in respect of his departure from the Borrower and to incorporate the understanding of the parties that the term "unencumbered cash on hand" contained in the definition of Minimum Liquidity in Section 6.9 of the Loan Agreement includes all cash of the Borrower, including cash which is subject to an unperfected security interest in favor of the purchasers of the Notes and the Secured Party, except as provided in paragraphs 9 and 10 hereof.

8. The Bank hereby waives any breach of any covenant set forth in the Loan Agreement (including, without limitation, Sections 7.4, 7.6, 7.7, 7.9 and 7.10) or the Negative Pledge Agreement which would otherwise be breached solely on account of any of the transactions described above, including, without limitation, the compensation payable to Pillar Investments, Ltd., as placement agent, in connection with the issuance of the Notes. The Bank waives any Event of Default under Section 8.3 which may presently exist as a result of the delisting of the Borrower's stock, and agrees that the granting of a security interest in favor of the purchasers of the Notes junior to the security interest in favor of the Bank on the conditions set forth in the Unit Purchase Agreement and herein, the Intercreditor Agreement and the execution and delivery of the Negative Pledge Agreement shall not constitute a "material impairment of the value or priority of the Bank's security interest in the Collateral" under Section 8.3 of the Loan Agreement. The Bank further acknowledges that the Unit Purchase Agreement and Intercreditor Agreement and attached form of Note are a "subordination agreement entered into with the Bank" for purposes of Section 8.8 of the Loan Agreement, and that the Exchange is not an Event of Default under the Loan Agreement.

9. Provided that the Borrower would have Minimum Liquidity of at

least $10,000,000, both before and after the payment (or escrowing) of such interest payment and that the Borrower is otherwise in compliance with the provisions of this letter, the Bank also hereby consents to the deferral by the Borrower of interest payments due April 1, 1998 (the "Deferred Payments") on the Convertible Notes until October 1, 1998, at which time the Deferred Payments may be paid in cash on Convertible Notes which are then outstanding, notwithstanding the provisions of Article 11 of the Indenture governing the Notes. For purposes of determining compliance with the Minimum Liquidity covenant, the Borrower shall provide the Bank on or before March 25, 1998 with a statement and evidence of cash balances as of such date, together with projected cash disbursements through March 31, 1998, less the scheduled amount of the April 1, 1998 interest payment on the Convertible Notes; such projected Minimum Liquidity must be at least $10,000,000 as of March 31, 1998 for the Borrower to be deemed in compliance with such covenant. The Bank shall exclude the amount of the Deferred Payments from unencumbered cash on hand in calculating Minimum Liquidity from and after April 1, 1998, provided that no exclusion shall be required with respect to Deferred Payments in respect of Convertible Notes which are no longer outstanding.

10. The Borrower and the Bank agree that Fifty (50%) percent of the net cash proceeds (excluding customary and reasonable selling expenses and estimated taxes accrued or payable on such sales) of all sales of assets of the Borrower permitted by the Bank (other than sales of inventory in the ordinary course of business and licensing of intellectual property in the ordinary course of business and sales of assets with net cash proceeds less than $5,000 per asset), shall be paid to the Bank as a prepayment of the principal of the Borrower's obligations to the Bank under the Loan Agreement, to be applied against payments due in the inverse order of maturity of such payments. The Borrower shall not sell or otherwise alienate any of its properties or assets (other than sales of inventory and licensing of technology in the ordinary course of its business) in an aggregate amount of more than $10,000 in any thirty day period without the written consent of the Bank. The Bank and the Borrower agree that Fifty (50%) of the net proceeds of the expected sale by the Borrower of its interest in CRLP (expected to be in the aggregate $3.4 Million and expressly excluded from the limitation set forth above) shall be made available to the Borrower for payment against outstanding accounts payable of the Borrower and that the balance of such net sales proceeds (the "CRLP Withold") shall be pledged to the Bank unless or until net proceeds of at least $10,000,000 have been received by the Borrower in the Offering (which must be, in all events prior to the Termination Date). The CRLP Withold shall not be considered unencumbered cash for purposes of calculating compliance with the Minimum Liquidity covenant. If the Borrower has raised net proceeds of at least $10,000,000 by such date, the CRLP Withold shall be

promptly released to the Borrower. If the Borrower has not raised net proceeds of at least $10,000,000 by such date, the CRLP Withold shall be applied by the Bank against the outstanding obligations of the Borrower to the Bank under the Loan Agreement, in the inverse order of maturity. Upon the maturity of the certificate of deposit pledged to the Bank pursuant to Section 6.9 of the Loan Agreement, the Bank will apply such funds (the "Applied Funds") against the obligations of the Borrower to the Bank under the Loan Agreement, in inverse order of maturity. In computing compliance with the Minimum Liquidity covenant after the date of application of the Applied Funds, the outstanding loan balance on which the cash pledge under Section 6.9 is calculated shall be the outstanding loan balance at the time of calculation of the required pledge plus the Applied Funds, and in computing the required pledge amount, the Borrower shall only be required to pledge the required pledge amount (calculated as provided in this sentence) minus the Applied Funds.

11. The Borrower shall not sublease, or otherwise alienate, all or any portion of the Milford property leased by the Borrower without the written consent of the Bank. The Borrower shall, as a condition to the consents and waivers contained herein, provide the Bank with evidence of current payment of amounts due under the Milford lease and the note related thereto.

12. The Borrower agrees, in consideration of the foregoing, that the Borrower shall not pay any cash interest payment on the Notes at any time that there is an Event of Default under the Loan Agreement.

13. The Borrower shall as a condition to this consent and waiver have delivered to the Bank complete and up to date agings of its accounts payable and accounts receivable, in form acceptable to the Bank, and shall provide the Bank with evidence of the payment status of the lease and related note with respect to the Milford property. The Borrower shall also provide the Bank with a complete listing of all of its leasehold interests in real and personal property, the outstanding remaining payment obligations on such leases, the amount and frequency of the periodic payments under each lease, next payment due date for each lease and description of the property subject to each lease on or before January 22, 1998.

14. The Borrower hereby ratifies and affirms all of the representations and warranties made by it in the Loan Agreement as of the date of this letter, except as expressly disclosed to the Bank.

15. The Borrower shall pay to the Bank, in addition to all other amounts due under the Loan Agreement and hereunder, all of the Bank's reasonable costs and expenses in connection with the negotiation, documentation and implementation

of this letter and the documents, instruments and agreements contemplated hereby and by the Unit Purchase Agreement, including without limitation travel and other expenses reasonably incurred by the Bank.

16. The Borrower acknowledges and confirms that to the extent that the Borrower may have any claims, offsets, counterclaims, or defenses, asserted or unasserted, the Borrower, for itself, and on behalf of its successors, assigns, parents, subsidiaries, agents, affiliates, predecessors, employees, officers, directors, executors and heirs, as applicable (collectively, the "Borrower Affiliates") releases and forever discharges the Bank, its subsidiaries, affiliates, employees, officers, directors, agents, successors and assigns, both present and former (collectively, the "Bank Affiliates") of and from any and all manner of claims, offsets, counterclaims, defenses, action and actions, cause and causes of action, suits, debts, controversies, damages, judgments, executions, and demands whatsoever, asserted or unasserted, in law or in equity, which against the Bank and/or the Bank Affiliates, they or the Borrower Affiliates ever had to and including the date hereof, upon or by reason of any matter, cause, causes or thing whatsoever, in connection with the Loan Agreement, the Note, this letter, the Intellectual Property Security Agreement, Pledge Agreement, Intercreditor Agreement and any other document, instrument or agreement given in connection with the Loan Agreement or the transactions related to this letter except for the obligations of the Bank in such documents, instruments and agreements to be performed after the date of this letter. The Borrower shall indemnify, defend and hold the Bank harmless of and from any claim brought or threatened against the Bank by the Borrower or any other person (as well as from attorneys' fees and expenses in connection therewith) on account of the Loan Agreement, the Note, this letter, the Intellectual Property Security Agreement, Pledge Agreement, Intercreditor Agreement and any other document, instrument or agreement given

in connection with the Loan Agreement or the transactions related to this letter (each of which may be defended, compromised, settled or pursued by the Bank with counsel of the Bank's election reasonably acceptable to the Borrower, but at the expense of the Borrower), except in the case of the Bank's failure to comply with its obligations hereunder or thereunder, its gross negligence or willful misconduct.

The foregoing consents and waivers are given by the Bank as of this 15th day of January, 1998, for the express purpose of facilitating the transactions described above, and are conditioned upon the undertakings of the Borrower set forth herein. Except as expressly provided herein, this consent and waiver letter shall not create a course of dealing or imply or create any course of conduct or obligation upon the Bank to consent to any future like or unlike transaction(s). The Bank expressly reserves all of its rights and remedies except to the limited extent affected hereby, and the Borrower acknowledges and agrees with the foregoing limited consent and waiver and hereby ratifies and confirms the terms and provisions of the Loan Agreement and

ancillary documents, instruments and agreements between the Bank and the Borrower, except as expressly modified hereby.

This letter, when executed by the Borrower and the Bank shall constitute a contract under seal within the Commonwealth of Massachusetts, and shall be construed and enforced in accordance with the laws of the Commonwealth of Massachusetts.

SILICON VALLEY BANK

By: /s/ Phillip S. Ernst

Name: Phillip S. Ernst, Vice President

AGREED AND ACKNOWLEDGED:
HYBRIDON, INC.

By: /s/ E. Andrews Grinstead III

Name: E. Andrews Grinstead III
Chairman, Chief Executive Officer
and President

Exhibit 23.1

CONSENT OF INDEPENDENT PUBLIC ACCOUNTANTS

As independent public accountants, we hereby consent to the use of our report dated March 18, 1998 (except with respect to the matters discussed in Note 1 and Note 6(a), as to which the date is March 30, 1998) included in this Form 10-K into the Company's previously filed Registration Statement File No's 33-3896, 33-3898, 33-3900 and 33-3902.

/s/ Arthur Andersen LLP

ARTHUR ANDERSEN LLP

Boston, Massachusetts
March 30, 1998

EXHIBIT 23.2

[Letterhead of McDonnell, Boehnen, Hulbert & Berghoff Appears Here]

March 30, 1998

Hybridon, Inc.
629 Memorial Drive
Cambridge, Massachusetts 02139

Re: Hybridon, Inc. -- Annual Report on Form 10-K

Dear Sirs:

McDonnell, Boehnen, Hulbert & Berghoff hereby consents to the reference to our firm under the section "Business -- Patents, Trade Secrets and Licenses" in the Hybridon, Inc. Annual Report on Form 10-K for the year ended December 31, 1997.

Yours very truly,

/s/ Paul H. Berghoff

Paul H. Berghoff

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<FN>
<F1>Basic and diluted EPS information has been prepared in accordance with SFAS No. 128, and basic and diluted EPS have been entered in place of primary and diluted EPS, respectively.
</FN>