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

FORM 10-K

FOR ANNUAL AND TRANSITIONAL REPORTS PURSUANT TO SECTIONS 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

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

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2000

OR

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

COMMISSION FILE NUMBER 0-27352

HYBRIDON, INC.

(EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CERTIFICATE OF INCORPORATION)

DELAWARE (STATE OR OTHER JURISDICTION OF INCORPORATION OR ORGANIZATION)

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04-3072298 (I.R.S. EMPLOYER IDENTIFICATION NO.)

02139

(ZIP CODE)

345 VASSAR STREET CAMBRIDGE, MASSACHUSETTS (ADDRESS OF PRINCIPAL EXECUTIVE OFFICES)

(617) 679-5500 (REGISTRANT'S TELEPHONE NUMBER, INCLUDING AREA CODE)

SECURITIES REGISTERED PURSUANT TO SECTION 12(b) OF THE ACT: NONE

SECURITIES REGISTERED PURSUANT TO SECTION 12(q) OF THE ACT:

COMMON STOCK, \$.001 PAR VALUE (TITLE OF CLASS)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to the filing requirements for the past 90 days. Yes [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 the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. []

The approximate aggregate market value of the voting stock held by non-affiliates of the registrant was \$8.8 million as of March 26, 2001.

For purposes of determining this number, 2,546,663 shares of common stock held by affiliates are excluded. As of March 26, 2001, the registrant had 18,693,259 shares of Common Stock outstanding. DOCUMENTS INCORPORATED BY REFERENCE Portions of the Registrant's Proxy Statement to be held on June 28, 2001...... Items 10, 11, 12 and 13 of Part III. _____ _____ 2 HYBRIDON, INC. FORM 10-K INDEX PAGE ____ PART I. Item 1. Business..... 1

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FORWARD-LOOKING STATEMENTS

The statements contained in this Annual Report on Form 10-K that are not historical are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, including statements regarding the expectations, beliefs, intentions or strategies regarding the future. Hybridon intends that all forward-looking statements be subject to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements reflect Hybridon's views as of the date they are made with respect to future events and financial performance, but are subject to many risks and uncertainties, which could cause actual results to differ materially from any future results expressed or implied by such forward-looking statements. Examples of such risks and uncertainties include the risks detailed in the Risk Factors section of this Annual Report on Form 10-K. Hybridon does not undertake to update any forward-looking statements.

PART I.

ITEM 1. BUSINESS

HYBRIDON

Hybridon, established in 1989, utilizes chemically-modified synthetic DNA for medical applications, including the discovery and development of genetically based drugs, which treat diseases by acting on a particular gene. The genetic drugs being developed by Hybridon are based on "antisense" technology, in that they use synthetic DNA material, also called oligonucleotides, with the aim of inhibiting or reducing the body's production of proteins that directly or indirectly cause or support a given disease. Hybridon has also developed a portfolio of chemically modified DNA compounds designed to stimulate responses of the immune system. Chemically-modified DNA is also being developed for use in the laboratory to determine the function of proteins produced by genes whose function has not yet been established. Hybridon has developed and owns certain medicinal chemistry innovations useful in the design of new synthetic DNA compounds. Hybridon also has rights to technology allowing the chemical modification of synthetic DNA.

Hybridon manufactured and sold synthetic DNA compounds on a large scale until September 21, 2000 when it sold its Hybridon Specialty Products or "HSP" business and assets in order to focus on its drug research and development activities and to provide working capital to fund these activities. For additional information about the HSP transaction, see "Management's Discussion and Analysis of Financial Condition and Results of Operations -- General."

RECENT DEVELOPMENTS

On March 30, 2001, Hybridon signed a binding agreement with unrelated institutional investors providing for the sale of 60% of Hybridon's holdings of shares of Class A and Class B stock of MethylGene, Inc. The agreement covers a total of 2,350,000 such shares and provides a purchase price of Canadian \$2.85 (approximately \$1.81 US Dollars as of March 30, 2001) per share or approximately US \$4.3 million in the aggregate. Closing of the transaction is subject to the satisfaction of various conditions, including waivers by MethylGene's shareholders of rights of first refusal which have now been executed by MethylGene's shareholders and received by the Company. Hybridon has given an option, exercisable at any time prior to April 30, 2001, to MethylGene and its shareholders to purchase the balance of Hybridon's holdings of MethylGene stock at Canadian \$2.85 per share. If all of these shares were purchased, Hybridon would receive an additional sum of US \$2.9 million.

Hybridon's holdings of MethylGene shares were subject to the security interest of the holders of its 8% Convertible notes due 2002 and its \$6.0 million notes due 2003. The following is a discussion of arrangements which Hybridon made with these noteholders to procure a release of their security interest.

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On March 5, 2001, Hybridon made an offer to the holders of its 8% Convertible notes due 2002 to exchange their notes for one share of a newly-designated class of Series B Convertible Preferred Stock (par value \$.01 per share) for each \$100 in principal amount of notes tendered. At the offer's expiration date of March 30, 2001, holders of \$6.9 million out of a total of \$7.5 million in principal amount of notes outstanding accepted the exchange offer which was then concluded. Shares of the Series B Convertible Preferred Stock have a face value of \$100 per share and are senior in right of payment with respect to liquidation, distributions and dividends to Hybridon's Series A Convertible Preferred Stock and common stock. Such shares will accrue dividends at the rate of 8% per annum which are payable in kind or in cash at Hybridon's option. Shares of Series B Convertible Preferred Stock are convertible into shares of common stock at an initial rate of one share of Series B Convertible Preferred Stock for 200 shares of common stock. If all shares of Series B Convertible Preferred Stock issued to the holders of 8% notes were converted to common stock at this time, Hybridon would be required to issue 15,209,200 shares of its common stock.

For interest calculation purposes, 8% notes submitted for exchange were deemed exchanged as of March 5, 2001. Under the offer, all accrued but unpaid interest on the exchanged notes will be paid through March 5, 2001 by issuing additional notes in an aggregate principal amount equal to the amount of accrued but unpaid interest. These additional notes were tendered for exchange by the noteholders participating in the offer. Any tender of notes involving denominations of less than \$100 in principal amount were exchanged for cash equal to such principal amount. Dividends on shares of Series B Convertible Preferred Stock will begin accruing on March 6, 2001.

As a result of the exchange offer, Hybridon has become entitled to the unrestricted use of \$5.0 million, which were proceeds from the sale of its HSP business. These proceeds had been pledged to secure Hybridon's obligations under

the 8% notes and the \$6.0 million notes.

On March 28, 2001, Hybridon entered into an agreement with the holders of its \$6.0 million notes whereby it would pay, out of the proceeds of the sale of its MethylGene shares, \$1.8 million to the holders in partial satisfaction of the notes. In addition, it agreed that it would deposit up to another \$1.2 million in a money market account for the purpose of securing payment of the balance of the outstanding notes and the sum of \$811,000 to secure the payment of the balance remaining on notes held by a particular lender group. This arrangement was made to encourage the holders of these notes to release their security interest in the MethylGene shares. If more than 60% of its holdings of MethylGene shares are sold, Hybridon will pay off additional notes up to a total of \$3,000,000 and the \$1,200,000 of money market funds securing the notes would decrease proportionately.

TECHNOLOGY OVERVIEW

Introduction

The heart, brain, liver and other organs in the human body function together to support life. Each microscopic cell within these organs produces proteins that affect how that cell functions within its organ, and ultimately how efficiently each organ functions within the body. Most human diseases are caused by abnormal production or performance of proteins within individual cells. In some instances, cell proteins act directly to cause or support a disease. In other instances, cell proteins interfere with other proteins that prevent or combat disease. Traditional drugs are designed to interact with protein molecules that cause or support diseases. Antisense drugs are designed to work at an earlier stage to stop the production of disease-causing or disease-supporting proteins.

The information that controls a cell's production of a specific protein is contained in the gene relating to that protein. Each gene is made up of two intertwined strands of DNA that form a structure called a "double helix." Each strand of DNA consists of a string of individual DNA building blocks, called nucleotides, arranged in a specific sequence. Each strand is made of linked molecules, known as the "backbone," and attached to the backbone are molecules known as "bases." It is the sequence of bases that contains genetic information. One of the paired strands contains the information that directs the composition of a specific protein, and is called the "coding" strand. The other strand, the "non-coding" strand, contains a different but complementary sequence of nucleotides.

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The full complement of human genes, known as the human "genome," contains the information required to produce all human proteins. A copy of the complete human genome is present in each cell, and each cell makes proteins based on its copy of the genome. Cells make proteins in a two-stage process. First, the cell creates a molecule of messenger RNA consisting of a string of nucleotides in a sequence that is the exact mirror image or complementary to the sequence of the coding strand of DNA. This is called the "sense" sequence. A sequence that is complementary to the sense sequence is called the "antisense" sequence. Then, the cell then produces proteins based on the information contained in the messenger RNA. The number of copies of messenger RNA the cell produces will affect how many copies of a given protein it produces.

A normal cell produces a given set of normal proteins in the right amount for the body to function properly. A diseased cell produces inappropriate or mutant proteins, or produces the wrong amount of normal proteins. A cell produces mutant proteins when its DNA changes, either through mutation, as in many types of cancer cells, or by infection with a virus.

Conventional Drugs

Most drugs are chemicals that stimulate or suppress the function of a

particular molecule, usually a protein, with tolerable side effects. Most drug side effects arise when a drug interacts with proteins in addition to the target protein. Generally, the fewer other proteins a drug interacts with, the fewer the side effects.

Conventional drugs generally aim to bind only two or three points of the target molecule. Frequently, however, sites on other non-target molecules resemble the target-binding site enough to permit the conventional drug to bind to some degree to those non-target molecules. This lack of selectivity can result in unwanted side effects, potentially leading to decreased effectiveness.

Another characteristic of conventional drugs is that developing them is a time-consuming and expensive process. For every compound that is found to be effective and have tolerable side effects, thousands may be investigated and rejected.

Antisense Drugs

A synthetic DNA with a sequence exactly complementary to that of the messenger RNA of a specific gene can bind to and inhibit the expression of the messenger RNA, thereby decreasing or eliminating the production of disease-causing or disease-supporting proteins. Antisense technology involves the design and synthesis of such synthetic DNA. Hybridon believes that drugs based on antisense technology may be more effective, cause fewer side effects, and have a greater range of applications than conventional drugs because antisense drugs are designed to intervene in a highly specific fashion in the production of proteins, rather than after the proteins are made.

Advances in mapping the human genome, including work conducted by academic institutions, biotechnology companies and pharmaceutical companies, have allowed many targets for antisense drugs to be identified. Once a gene associated with a disease-associated protein is identified, a synthetic DNA with an antisense mechanism can be designed, and the pharmaceutical effects of that synthetic DNA can be improved by chemical modification. Chemically-modified synthetic DNA can be composed of DNA, RNA, or a combination of the two.

Because the nucleotide sequence of a chemically-modified antisense synthetic DNA is complementary to its target sequence on the messenger RNA of a given gene, the antisense synthetic DNA forms a large number of bonds at the target site, typically between 40 and 60. This allows it to form a strong bond with the messenger RNA. A few identical messenger RNA molecules can cause the cell to produce many copies of a protein; similarly, a few identical molecules of chemically-modified antisense synthetic DNA can inhibit this process. This is due in part to an enzyme called RNase H that can destroy messenger RNA bound to synthetic DNA without destroying the synthetic DNA itself, thus freeing the synthetic DNA to bind with, and cause the destruction of, other messenger RNA molecules. This process is generally known as catalytic activity. All of Hybridon's drugs are designed to take advantage of this catalytic activity so that a relatively small number of antisense molecules can effectively inhibit production of disease-associated proteins.

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HYBRIDON ANTISENSE TECHNOLOGY

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Hybridon's antisense chemistry builds on the pioneering work in the antisense field begun in the 1970s by Dr. Paul C. Zamecnik, a founder, consultant, director and shareholder of Hybridon. Development of Hybridon's antisense chemistry has been directed by Dr. Sudhir Agrawal, Hybridon's Chief Scientific Officer, director, shareholder and now also President and Acting Chief Executive Officer. It has been based on Hybridon's "advanced chemistries," namely, its ability to alter the chemical makeup of the synthetic DNA backbone in a manner that makes synthetic DNA safer and more stable without adversely affecting its ability to promote the destruction of messenger RNA.

Medicinal Chemistries. Hybridon's first antisense drug, GEM(R)91, targeted

the messenger RNA that codes for an essential protein in Type 1 Human Immunodeficiency Virus, or "HIV-1." GEM(R)91 was based on first-generation chemistry, which altered the naturally-occurring, or native, form of DNA by replacing certain oxygen atoms in the backbone with sulfur atoms. GEM(R)91 was more stable than native DNA, but was still able to trigger the action of Rnase H, leading to catalytic activity. However, there were side effects caused by the administration of this modified DNA into the body. In particular, in the last clinical trial of GEM(R)91 treatment of three of the nine patients with advanced HIV disease was interrupted due to unacceptable decreases in platelet counts. As a result, Hybridon discontinued the GEM(R)91 program. Hybridon has, however, used the information gained from the human clinical trials of GEM(R)91 to design its second generation chemically-modified synthetic DNA chemistries.

On November 9, 2000, Hybridon announced the issuance of a U.S. patent that broadly claims second generation antisense compounds.

Hybridon has designed and made families of advanced synthetic DNA chemistries, including DNA/ RNA combinations, also called hybrid or mixed backbone chemistries. Hybridon believes that antisense compounds based on these advanced chemistries will show favorable pharmaceutical characteristics and significantly improve therapeutic value compared to earlier antisense drug candidates. These compounds are likely to have the following desirable characteristics:

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

Hybridon is actively exploring opportunities for licensing portions of its antisense technology platform towards the goal of generating substantial revenue from its antisense patent estate.

Drug Potentiation Technology. Hybridon has discovered that at times synthetic DNA is able to enhance the activity of irinotecan, a marketed anti-cancer drug, when the two are used together in animal models of cancer. The observed increase in activity is not solely due to an antisense mechanism. This discovery is being further studied to determine the mechanism of the effect and to possibly prepare for human clinical trials.

Functional Genomic Technology. With the advent of the human genome project, researchers have identified thousands of genes whose functions have not yet been established. A reliable, fast and economic way to study the function of any gene is through the use of synthetic DNA designed to target a specific messenger RNA. In order to reduce the possibility that a drug will be responsible for undesirable side effects, it is important to understand the role of each gene in normal and disease conditions before designing drugs for that specific target.

Hybridon has an established program in functional genomics in which synthetic DNA can be used for the study of the function of any newly discovered gene. Hybridon's synthetic DNA, designed as antisense molecules, are especially useful in these studies because of their enhanced ability to interact with very specific targets. In the design of synthetic DNA for functional genomics studies, Hybridon draws on its extensive experience in the antisense field to increase specific targeting and reduce non- antisense effects of the synthetic DNA employed in the functional genomics program. Hybridon's synthetic DNA chemistry program has also

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identified a novel antisense structure identified as a "cyclicon" that will further simplify the application of antisense to identify gene function. These modified DNA-like compounds present certain advantages over other available compounds for DNA chip or PCR-based gene expression techniques. Hybridon is actively seeking opportunities to license this technology to companies, which have identified specific genes and which are employing these genomics techniques for drug discovery and development.

Regulatory Know-How. Hybridon drug development personnel have extensive experience in working with the Food and Drug Administration and other drug regulatory agencies in an efficient and cost-effective manner. Hybridon has assisted its spin-off companies in preparing essential components of their submissions to the FDA.

SYNTHETIC DNA TECHNOLOGY FOR STIMULATING THE IMMUNE SYSTEM

Naturally occurring and synthetic DNA compounds containing certain sequences and arrangements of the building blocks that make up the DNA have been found to mobilize the body's immune response system. The most widely studied of these sequences involve the presence in the DNA of the base cytosine followed by the base guanosine, a sequence also known as a CpG-motif. The stimulation of the immune system by synthetic DNA can potentially be used in a beneficial manner to stimulate the immune defenses where they are deficient or as a cofactor to boost the responses to other agents. The latter use is illustrated by independently published reports which have shown that DNA compounds have therapeutic potential to enhance immunity following vaccines and as treatments for cancer, infectious and allergic diseases.

Hybridon has engaged in a systematic effort to make chemical modifications to synthetic DNA that contains CpG and related sequences. This has resulted in the creation of a portfolio of synthetic DNA and similar compounds that have immune stimulatory properties. Introducing modifications at specific locations in the DNA building blocks and their linkages causes substantial stimulation to the body's immune system. These discoveries have been used to synthesize proprietary chemically modified synthetic DNA that can be used alone or in association with other agents, including vaccines, to enhance the responsiveness of the immune system.

Hybridon has entered into materials transfer agreements with several companies whereby Hybridon supplies modified synthetic DNA to these companies which will evaluate their potential for stimulating the immune system.

DRUG DEVELOPMENT AND DISCOVERY

Drug Development and Approval Process

The process of taking a compound from the laboratory to human patients generally takes 10 to 15 years. This process is extremely expensive and is rigorously regulated by governmental agencies, including, in the U.S., the Food and Drug Administration, or the "FDA." Each drug must undergo a series of trials, both preclinical and clinical, before the FDA will consider approving it for commercial sale. The FDA or any company conducting drug trials can discontinue those trials at any time if it feels that patients are being exposed to an unacceptable health risk or if there is not enough evidence that the drug is effective. The FDA may also require a company to provide additional information or conduct additional tests before it will permit a drug to proceed from one phase of trials to the next.

The phases of preclinical and clinical trials are described below:

- Preclinical Studies. Preclinical trials involve the testing of a given compound in animals to provide data on the activity and safety of the compound before the compound is administered to humans.
- Investigational New Drug Application. If the data from research and preclinical trials are promising, Hybridon may file an Investigational New Drug Application, or "IND," with the FDA. The IND contains the results of the preclinical trials and the protocol for the first clinical trial. The IND becomes active in 30 days unless the FDA disapproves it or requires additional information. Once the IND becomes active, Hybridon

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- Phase I Clinical Trials. In Phase I trials, the drug is given to a small group of healthy individuals or patients with the disease. These trials are designed to produce data on the drug's safety, the maximum safe dose, and how the drug is absorbed, distributed, metabolized and excreted over time. In some cases, Phase I trials can give an early indication of a drug's effectiveness. A limited Phase I trial is sometimes called a Pilot Phase I trial.
- Phase I/II Clinical Trials. In Phase I/II trials, the drug is given to patients with the diseases to evaluate safety and to get an early indication of a drug's effectiveness. This type of trial is commonly used in the evaluation of oncology drugs.
- Phase II Clinical Trials. In Phase II trials, the drug is given to a larger group of patients with the disease for purposes of evaluating the drug's effectiveness and side effects at varying doses and schedules of administration and thereby determining the optimal dose and schedule for the larger Phase III trials that follow.
- Phase III Clinical Trials. These trials generally have a large number of patients. The primary purpose of a Phase III trial is to confirm the drug's effectiveness and produce additional information on side effects.
- New Drug Application. Once Phase III trials are complete, Hybridon will file a New Drug Application, or "NDA," with the FDA. The NDA contains all of the information gathered from the Phase I, I/II, II and III trials. Based on the FDA's review of the NDA, the FDA may approve the drug for commercial sale. The FDA may deny an NDA if the applicable regulatory requirements are not met. The FDA may also require additional tests before approving an NDA. Even after approval by the FDA, Hybridon must file additional reports about the drug with the FDA from time to time. The FDA may withdraw product approvals if a company fails to comply with ongoing regulatory standards or if problems occur after a company starts marketing a drug.
- Accelerated Approval. The FDA is authorized to grant accelerated review to NDAs for drugs that are intended to treat persons with debilitating and life-threatening illnesses, especially if no satisfactory alternatives are available. The more severe the disease, the more likely it is that the drug will qualify for accelerated review. If a new drug is approved after accelerated review, the FDA may require Hybridon to conduct specific post-marketing studies regarding the drug's safety, benefits and optimal use.

The regulatory process in other countries is generally similar to the U.S. regulatory process.

Drug Development and Discovery Programs

Hybridon is focusing its drug development and discovery efforts on developing synthetic DNA compounds with the potential to enhance immune responses, as well as antisense compounds for the treatment of diseases in three major therapeutic areas: cancer, viral infections and diseases of the eye. For example, in the treatment of cancer, compared to conventional anti-cancer drugs, antisense may provide more specific therapy and more rapid development of drugs targeting newly-discovered cancer-related proteins. It may also provide fewer toxic side effects, thereby allowing repeat and long-term therapy, either alone or in combination with other cancer therapies, such as radiation or chemotherapy. When used in combination therapy, it may provide therapeutic effects that complement the benefits of conventional drugs. Synthetic DNA-based compounds have been identified and studied in humans for their potential to treat viral infections (e.g., Human Immunodeficiency Virus, human cytomegalovirus). Other compounds, still in preclinical development, have been identified for hepatitis C. Diseases of the eye for which DNA-based therapies are in the research stage include conditions where new blood vessel formation is involved (e.g., macular degeneration, diabetic retinopathy).

CLINICAL PROGRAMS

Hybridon has conducted clinical trials with antisense drugs targeting cancer and HIV-1 AIDS. Hybridon is seeking partners for each of its compounds in clinical development.

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Cancer

Unlike normal human cells, cancer cells grow in an uncontrolled and harmful manner. The protein molecule protein kinase A, or "PKA," has been implicated in the formation and growth of various solid tumors, including colon, ovarian, breast, and lung tumors. There are two kinds of PKA. It is normal to find type I in developing fetuses, but abnormal to find it in adults. By contrast, PKA type II is found in, and is necessary to the health of, normal adults. Certain cancer cells produce PKA type I in adults. Hybridon is developing a cancer drug, GEM(R)231, that is designed to reduce the production of the harmful PKA type II. Most current drug candidates based on conventional mechanisms have unacceptable side effects.

Hybridon has conducted a Phase I clinical trial to evaluate the safety of GEM(R)231 at multiple doses, and has found that patients tolerate it well. This trial explored the maximum tolerated dose of GEM(R)231 for both single doses and multiple doses, and even high doses of GEM(R)231 did not show the side effects normally seen with current cancer treatments.

Hybridon is currently conducting additional Phase I/II studies with GEM(R)231 in patients with solid tumors that had not been cured by prior therapy. Hybridon has also begun Phase I/II trials treating patients with solid tumors with GEM(R)231 in combination with the anti-cancer therapies Taxol(R) and Taxotere(R).

HIV-1 and AIDS

Acquired Immune Deficiency Syndrome, "AIDS," is caused by infection with the HIV-1 virus and leads to severe, life-threatening impairment of the immune system. AIDS therapy using a combination of drugs has resulted in decreased rates of death and improvement in the quality of life for patients who are HIV-positive or have AIDS. There are, however, reports that this therapy may be failing to give sustained clinical benefit. Hybridon believes this underscores the need for new AIDS therapies.

Hybridon has completed a Pilot Phase I clinical study in Europe of GEM(R)92, Hybridon's advanced chemistry compound for the treatment of HIV-1 infection and AIDS. This study was designed to explore the safety of GEM(R)92 by injection and to provide information on its absorption after oral dosing and injection. The patients tolerated well all doses that they were given in the pilot study. Further, GEM(R)92 was detected in the blood after both oral dosing and injection, suggesting that it may be possible to develop GEM(R)92 as an oral drug. Hybridon believes this was the first study of the oral administration of an antisense molecule to humans. In laboratory studies, beneficial effects were observed when GEM(R)92 was used in combination with several marketed AIDS drugs. Importantly, both its medicinal approach and genetic target are unique, in that no antisense drug has been approved for the treatment of AIDS, and no other drug has the same target on the HIV-1 genome.

PRECLINICAL PROGRAMS

Hybridon has conducted preclinical studies and is seeking partners in the

| TARGET | PRIMARY THERAPEUTIC(S) |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| MDM2 a protein involved in programmed cell death VEGF (Vascular Endothelial Growth Factor) a protein that can cause abnormal formation of new blood | Cancer |
| vessels | Cancer Diseases of the eyes e.g. macular degeneration and diabetic retinopathy |
| Hepatitis C Virus | Hepatitis C can lead to liver cancer |

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HYBRIDON SPINOUTS

Hybridon has used multiple strategies to fund applications of its antisense technology that it cannot develop without external funding. Hybridon has used one such strategy: the establishment of spinout companies, to form MethylGene and OriGenix Technologies Inc. for the continued development of certain product candidates.

MethylGene, Inc.

In 1996, Hybridon and three Canadian institutional investors formed MethylGene. Hybridon owns 3,902,941 shares or approximately 22% of MethylGene. Hybridon has granted exclusive worldwide licenses and sublicenses to MethylGene to develop and market the following:

- antisense compounds for the treatment of any disease which act by inhibiting the production of DNA methyltransferase
- other methods of inhibiting DNA methyltransferase
- antisense compounds to inhibit up to two additional molecular targets

Current research by MethylGene has shown that DNA methyltransferase, a protein, is overproduced in some tumors, such as non-small-cell lung cancer, colon cancer, and breast cancer tumors. Research on MethylGene's first target, the DNA Methyltransferase enzyme, has yielded a unique anti-cancer drug presently in Phase I trials. MethylGene is researching several other targets for cancer as well as for infectious diseases.

See Item 1. Business -- Recent Developments for a description of an agreement whereby Hybridon has agreed to sell 60% of its holdings of MethylGene and offered an option to purchase the balance.

OriGenix Technologies Inc.

In January 1999, Hybridon and three Canadian institutional investors formed OriGenix to develop and market drugs for the treatment of infectious diseases, with an initial focus on viral diseases. Hybridon owns approximately 28% of OriGenix.

Hybridon has granted to OriGenix exclusive worldwide licenses and sublicenses to antisense technology developed by Hybridon for the treatment of human papillomavirus, or "HPV," and hepatitis B virus infections. HPV infection can cause a variety of warts, including benign genital warts. HPV infection can also lead to cervical cancer. Hepatitis B infections can lead to liver cirrhosis and cancer of the liver. OriGenix may in the future negotiate with Hybridon for licenses or sublicenses relating to additional targets.

OriGenix's first family of compounds targets HPV. The most advanced compound under development, ORI-1001, is a potent antiviral agent against HPV types 6 and 11 that are associated with genital warts. ORI-1001 recently has been formulated for topical delivery. An Investigational New Drug (IND) application is expected to be filed for this compound in 2001.

On September 21, 2000, Hybridon sold its HSP business. Prior to such sale, Hybridon had the exclusive right to manufacture and supply OriGenix and MethylGene with its synthetic DNA supply needs. In connection with the HSP sale, Avecia Biotechnology now supplies OriGenix and MethylGene with synthetic DNA. In addition, Hybridon permitted OriGenix and MethylGene through a worldwide, royalty free, paid-up license to manufacture its own compounds and amended the current license agreement between the parties accordingly. Hybridon receives a credit for orders placed by OriGenix and MethylGene with Avecia Biotechnology for its supply needs that count against Hybridon's minimum purchase requirement with Avecia Biotechnology. See "Management's Discussion and Analysis of Financial Condition and Results of Operations -- General."

CORPORATE COLLABORATION

An important part of Hybridon's business strategy is to enter into research and development collaborations, licensing agreements, or other strategic alliances, primarily with biotechnology and pharmaceutical corporations, to develop drug products. Subject to sufficient funds being available, Hybridon intends to

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proceed with Phase II clinical trials of its cancer drug GEM(R)231. For drugs other than GEM(R)231, Hybridon does not anticipate proceeding with any of its other clinical programs beyond their current stages of development without having a collaborative arrangement with a corporate partner.

G.D. Searle & Co.

From January 1996 to March 2000 Hybridon and Searle engaged in a research and development collaboration for the development of synthetic DNA antisense compounds. Most recently, Searle and Hybridon were investigating antisense inhibitors of MDM2, a protein involved in programmed cell death, or apoptosis. It is believed that MDM2 may play an important role in many types of cancer.

Through January 2000, Searle made annual research payments to Hybridon of \$600,000. In March 2000, however, Searle elected not to extend this research and development collaboration. Hybridon is seeking a new development partner for this program.

Consistent with its January 1996 agreement with Hybridon, Searle was required to return to Hybridon all licenses granted to Searle, including the recently issued U.S. patent 6,013,786, which covers specific synthetic DNA antisense inhibitors of human MDM2. Hybridon has the right to use any of Searle's patent rights relating to the work performed under the collaboration, including all synthetic DNA antisense rights relating to MDM2.

Hybridon will pay Searle a royalty if it successfully commercializes any antisense compounds discovered as a result of their collaboration.

Pursuant to their collaboration, Searle also purchased 200,000 shares of common stock in Hybridon's 1996 initial public offering.

Hybridon has entered into a number of collaborative research relationships with independent researchers and leading academic and research institutions and U.S. government agencies, including the National Institutes of Health, or "NIH." Such research relationships allow Hybridon to augment its internal research capabilities and obtain access to specialized knowledge or expertise.

In general, Hybridon's collaborative research agreements require Hybridon to pay various amounts to support the research. Hybridon usually procures the synthetic DNA, which the collaborator then tests. If in the course of conducting research under its agreement with Hybridon a collaborator, solely or jointly with Hybridon, creates any invention, Hybridon generally has an option to negotiate an exclusive, worldwide, royalty-bearing license to the invention. Inventions developed solely by Hybridon's scientists in connection with a collaborative relationship generally are owned exclusively by Hybridon. Most of these collaborative agreements are nonexclusive and can be cancelled on short notice.

Since July 1997, as part of its restructuring, Hybridon has allowed a number of its collaborative research agreements to expire and has terminated others, but has maintained those that it believes support its current drug discovery and development programs.

DRUG DEVELOPMENT SERVICES

Hybridon has experience in the design and conduct of preclinical and clinical trials and has prepared and submitted reports and other regulatory documents in connection with the three Hybridon advanced chemistry antisense compounds that have entered clinical studies. Pursuant to a contract with MethylGene that has now expired, Hybridon also used its expertise to help design and monitor the preclinical trials of MethylGene's antisense compound, MG98, that led to MethylGene's submission of IND applications in Canada and the U.S. MethylGene compensated Hybridon for these services.

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PATENTS, TRADE SECRETS, AND LICENSES

Hybridon's success will largely depend on its ability to:

- obtain U.S. and foreign patent protection for drug candidates and processes
- preserve trade secrets
- operate without infringing the proprietary rights of third parties.

Hybridon's policy is to file patent applications to protect technology, inventions and improvements that it considers important to the development of its business, and to obtain licenses to other patents that could help Hybridon maintain or enhance its competitive position. On November 9, 2000, Hybridon announced the issuance of a U.S. patent that broadly claims second generation antisense compounds. As of March 15, 2001, Hybridon owned or exclusively licensed 72 U.S. issued patents and allowed patent applications with corresponding foreign patents in the fields of antisense medicinal chemistries, antisense drug candidates for gene targets. Hybridon also has 52 pending U.S. patent applications with corresponding foreign applications in the areas of antisense medicinal chemistries, antisense drug candidates for gene targets, synthetic DNA technology for stimulating the immune system and drug potentiation technology. The foreign patent and patent application counts include Japan, Canada and Europe as a whole, as well as other non-European individual countries. These patents and applications cover various chemically modified synthetic DNA compounds, target sequences, synthetic DNA products, analytical methods, and methods for synthetic DNA antisense treatment of various diseases. The patents expire on dates ranging from 2006 to 2015.

Hybridon is the worldwide exclusive licensee under several U.S. issued

patents or allowed patent applications owned by University of Massachusetts Medical Center, or "UMMC," relating to synthetic DNA and hybrid or mixed backbone chemical modifications. Many of these patents and patent applications have corresponding patents issued by, or corresponding patent applications on file in other major industrial countries. One of the issued U.S. patents and one of the issued European patents cover antisense synthetic DNA as new compositions of matter for stopping the replication of HIV. Coverage of the other issued U.S. patents includes composition and use of synthetic DNA based on chemical modifications, composition of certain synthetic DNA molecules that are useful for diagnostic tests or assays, and methods of purifying synthetic DNA. The UMMC patents licensed to Hybridon expire at various dates starting in 2006.

Hybridon is the exclusive licensee under various other U.S. and foreign patents and patent applications, including two U.S. patent applications owned by McGill University relating to synthetic DNA and the protein DNA methyltransferase. Hybridon and Massachusetts General Hospital jointly own one issued U.S. patent applicable to Alzheimer's disease. Hybridon holds an exclusive license to Massachusetts General Hospital's interests under this patent.

The field of each of these licenses extends to a wide variety of genetic targets. Hybridon is also a nonexclusive licensee, along with other companies, of certain patents for which Genzyme has exclusively licensed, covering certain technology relating to MDM2.

The U.S. Patent and Trademark Office, or "PTO," has informed Hybridon that patent applications exclusively licensed by Hybridon from UMMC are allowable except that they may have interfering subject matter with several patents owned by the National Institutes of Health (NIH). A showing by Hybridon will be submitted to the Board of Patent Appeals and Interferences of the PTO to determine whether an interference should be declared with issued U.S. patents held by the NIH relating to specific chemical modifications of the DNA backbone. An interference proceeding is a proceeding to determine who was the first to invent, and thus who is entitled to a patent for, a claimed invention. While Hybridon is of the opinion that the UMMC patent application has a prima-facie case for priority against the NIH for an invention that includes a specific modification of the synthetic DNA backbone, there can be no assurance that the PTO will declare an interference, or if it does, what the outcome will be. If Hybridon were to win the interference, others making, using or selling the specific chemical modifications of the synthetic DNA backbone claimed in the NIH interference would be required to obtain a license from Hybridon. As part of the HSP sale, the

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Company granted Avecia Biotechnology an option to a license to use the patent applications that are the subject of the potential interference.

The PTO declared a four-way interference involving two other unrelated UMMC U.S. patents, for which Hybridon is the exclusive licensee, relating to a particular type of modified synthetic DNA. The other parties to this interference were Integrated DNA Technologies, Isis Pharmaceuticals, Inc. and Gilead Sciences, Inc. This interference was settled in early 1999. In connection with the settlement, Hybridon has obtained a nonexclusive license to certain patents and patent applications owned by IDT that broadly claim chemical modifications to synthetic DNA. Hybridon has also granted a nonexclusive license to certain certain of Hybridon's advanced chemistries.

Under its licenses, Hybridon is obligated to pay royalties on its net sales of products or processes covered by the licensed technology and, in some cases, to pay a percentage of sublicense income that it receives. These licenses impose various commercialization, sublicensing, insurance and other obligations on Hybridon. If Hybridon fails to comply with these requirements, the license could be terminated. Legal standards relating to the validity of patents covering pharmaceutical and biotechnological inventions and the scope of claims made under such patents are still developing. As a result, Hybridon's ability to obtain and enforce patents that protect its drugs is uncertain and involves complex legal and factual questions.

The fact that Hybridon owns or licenses pending or future patent applications does not mean that patents based on those applications will ultimately be issued. First, to obtain a patent on an invention, one must be the first to invent it in the U.S. or the first to file a patent application for it in the rest of the world. Patent applications in the U.S. are maintained in secrecy until patents are issued, and publication of any given discovery in the scientific or patent literature tends to lag behind the actual date of that discovery by several months. Consequently, Hybridon cannot be certain that the inventors of subject matter covered by patents and patent applications that it owns or licenses were the first to invent, or the first to file patent applications for, those inventions.

Others, including Hybridon's competitors, also hold issued patents and patent applications relating to antisense technology or particular genetic targets. Holders of any of these patents or patent applications may be able to require Hybridon to change or cease making or using some products or processes, or obtain an exclusive or nonexclusive license in return for licensing fees, which may be substantial. Hybridon may not be able to obtain any such licenses at a reasonable cost. Furthermore, such licenses may be made available to competitors of Hybridon on an exclusive or nonexclusive basis. Failure to obtain such licenses could have a material adverse effect on Hybridon.

Hybridon requires its employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements. These agreements provide that all confidential information developed or made known by Hybridon to the individual is to be kept confidential, subject to specific exceptions. In the case of employees, the agreements provide that all inventions conceived by the individual are the exclusive property of Hybridon. These agreements may not, however, provide meaningful protection for Hybridon's trade secrets or adequate remedies in the event of breach.

Consistent with pharmaceutical industry and academic standards, Hybridon's agreements with academic and research institutions and U.S. government agencies may provide that the results of a given collaboration, or any developments that derive from the collaboration, will be freely published, that information or materials supplied by Hybridon will not be treated as confidential, and that Hybridon must negotiate a license to developments and results in order to commercialize products incorporating them. There can be no assurance that Hybridon will be able to obtain successfully any such license at a reasonable cost or that such developments and results will not be made available to competitors of Hybridon on an exclusive or nonexclusive basis. See "Business -- Academic and Research Collaborations."

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GOVERNMENT REGULATION

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Hybridon's research and clinical development activities are regulated for safety, effectiveness and quality by numerous governmental authorities in the U.S. and other countries. Hybridon believes that it is in material compliance with all applicable federal, state and foreign legal and regulatory requirements.

In addition to regulations enforced by the FDA in connection with product approvals, Hybridon 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 Hybridon uses hazardous materials, chemicals, viruses, and various radioactive compounds, it must comply with U.S. Department of Transportation and Environmental Protection Agency regulations and other federal, state, and foreign laws and regulations regarding hazardous waste disposal, air emissions, and waste-water discharge. Although Hybridon believes that it complies with these laws and regulations, it cannot completely eliminate the risk of accidental contamination or injury from these materials.

COMPETITION

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 regulation of gene expression, including antisense drugs. One competitor of Hybridon received FDA approval to market an antisense therapeutic product for the treatment of CMV retinitis that was launched in November 1998.

Two privately held companies are developing synthetic DNA drugs designed to stimulate the responses of the immune system. These drug candidates are in clinical trials, either alone or in combination with vaccines to prevent or to treat various diseases. Hybridon believes that the interest in these technologies and products will increase. It is possible that Hybridon's competitors will succeed in developing products that are more effective than Hybridon's. Furthermore, Hybridon's proposed drugs will be competing with other kinds of drugs. Given the fundamental differences between antisense technology and other drug technologies, antisense drugs may be less effective at treating some diseases than other kinds of drugs.

Biotechnology and related pharmaceutical research programs have undergone and continue to be subject to rapid and significant change. Hybridon expects that the technologies associated with biotechnology research and development will continue to develop rapidly. Hybridon's future will depend in large part on its ability to compete with these technologies.

Hybridon has many competitors, including major pharmaceutical and chemical companies, biotechnology firms, and universities and other research institutions. Many of these competitors have substantially greater financial, technical, and human resources than Hybridon, and many have significantly greater experience than Hybridon in undertaking preclinical studies and clinical trials of new pharmaceutical products and obtaining FDA and other regulatory approvals. Accordingly, Hybridon's competitors may succeed in obtaining regulatory approvals for products more rapidly than Hybridon. Furthermore, if Hybridon receives approval to commence commercial sales of products, it will also be competing with respect to marketing capabilities, an area in which it has limited experience.

EMPLOYEES

As of March 27, 2001, Hybridon employed 14 individuals full-time, of whom 10 held advanced degrees. Eleven of these employees are engaged in research and development activities and three are employed in finance, corporate development, and legal and general administrative activities. Many of Hybridon's management and professional employees have had prior experience with pharmaceutical, biotechnology, or medical products companies. None of Hybridon's employees is covered by a collective bargaining agreement, and management considers relations with its employees to be good.

On February 15, 2000, Dr. Sudhir Agrawal, formerly Senior Vice President of Discovery, was elected President and Acting Chief Executive Officer. Also, James B. Wyngaarden was elected Chairman of the Board of Directors and Robert G. Andersen was elected Chief Financial Officer.

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ITEM 2. PROPERTIES

Hybridon leases approximately 26,000 square feet of laboratory and office space, including 6,000 square feet of specialized pre-clinical lab space, in Cambridge, Massachusetts under a lease that expires April 30, 2007. The annual

rent for this space is approximately \$650,000.

ITEM 3. LEGAL PROCEEDINGS

Hybridon is not a party to any litigation that it believes could damage Hybridon or its business.

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

No matters were submitted to a vote of security holders in the quarter ended December 31, 2000.

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EXECUTIVE OFFICERS OF HYBRIDON

The executive officers and significant employees of Hybridon as of March 29, 2001 are as follows:

| NAME | AGE | POSITION |
|---------------------------------------------|-----|----------------------------------------------------------------------------------------------------------|
| | | |
| Sudhir Agrawal, D.Phil | 47 | President and Acting Chief Executive Officer, Chief Scientific Officer, and Director |
| Robert G. Andersen | 50 | Vice President of Operations and Planning, Chief Financial Officer, Treasurer and Assistant Secretary |
| R. Russell Martin, M.D Jinyan Tang, Ph.D | | Senior Vice President of Drug Development Vice President of Chemistry |

Dr. Sudhir Agrawal joined Hybridon 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, Senior Vice President of Discovery in March 1994, and President and Acting Chief Executive Officer in February 2000. He has served on the board of directors since March 1993. Prior to joining Hybridon, Dr. Agrawal served as a Foundation Scholar at the Worcester Foundation from 1987 through 1991. Dr. Agrawal served as a Research Associate at Research Council Laboratory of Molecular Biology in Cambridge, England from 1985 to 1986, studying synthetic oligonucleotides. Dr. Agrawal received a 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.

Robert G. Andersen joined Hybridon in November 1996 and served as Vice President of Systems Engineering and Management Information Systems prior to being appointed Vice President of Operations and Planning in 1997, Treasurer in March 1998, and Chief Financial Officer of Hybridon in February 2000. Mr. Andersen also serves as a director of OriGenix, Inc., a Hybridon spin-off company based in Montreal, Canada. Prior to joining Hybridon, 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 Business Unit. 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 for Otis Elevator Company's European Operations. Mr. Andersen received his B.E.E. in Electrical Engineering from The City College of New York in 1972 and an M.S. in Management from Northeastern University in 1978. He is also a graduate of the United Technologies Advanced Studies Program.

Dr. R. Russell Martin joined Hybridon and was appointed Vice President of Clinical Research in 1994. He became Vice President of Drug Development during 1996 and Senior Vice President of Drug Development in 1998. Dr. Martin is also a member of the Board of Directors of MethylGene, Inc., one of Hybridon's spin-offs. Prior to joining Hybridon, Dr. Martin served in a variety of positions at Bristol-Myers Squibb, most recently as Vice President of Infectious Diseases Clinical Research. Dr. Martin received an A.B. degree from Yale University in 1956 and a M.D. degree from the Medical College of Georgia in 1960. From 1971 to 1983, he was on the faculty of Baylor College of Medicine, most recently as Professor of Medicine, Microbiology and Immunology.

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

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PART II.

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

(a) MARKET INFORMATION

From January 24, 1996 until December 2, 1997, Hybridon'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 Hybridon's common stock.

On December 2, 1997, Hybridon's common stock was removed from the Nasdaq National Market and began being quoted on the NASD OTC Bulletin Board. Quotes on the NASD OTC Bulletin Board may reflect inter-dealer prices, without retail markups, markdowns or commissions and do not necessarily represent actual transactions.

On December 10, 1997 Hybridon 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 payments for any fractional shares.

The following table sets forth for the periods indicate the high and low sales prices per share of the common stock during each of the quarters set forth below as reported on the NASD OTC Bulletin Board since January 1, 1999:

| | HIGH | LOW |
|----------------|---------|---------|
| | | |
| 1999 | | |
| First Quarter | \$1.969 | \$1.000 |
| Second Quarter | 1.500 | 0.250 |
| Third Quarter | 1.500 | 0.344 |
| Fourth Quarter | 2.000 | 0.375 |
| 2000 | | |
| First Quarter | \$6.875 | \$0.844 |
| Second Quarter | 3.438 | 0.750 |
| Third Quarter | 1.313 | 0.500 |
| Fourth Quarter | 1.016 | 0.281 |

The reported closing sales price of the common stock on the NASD OTC Bulletin Board on March 30, 2001 was 0.55 per share.

(b) HOLDERS

The number of common stockholders of record on March 30, 2001 was 303.

(c) DIVIDENDS

Hybridon's Series A convertible preferred stock pays dividends at 6.5% per year, payable semi-annually in arrears. These dividends may be paid either in cash or in additional shares of convertible preferred stock, at the discretion of Hybridon.

On March 6, 2001, Hybridon's board authorized the creation of a Series B preferred stock which, when issued, will pay dividends at 8% per year, payable semi-annually in arrears. These dividends will be payable either in cash or in additional shares of convertible preferred stock, at the discretion of Hybridon.

Hybridon has never declared or paid cash dividends on its capital stock, and Hybridon does not expect to pay any dividends on its common stock or any cash dividends on the convertible preferred stock in the foreseeable future. The indenture under which Hybridon issued 9% convertible subordinated notes on April 2, 1997, limits Hybridon's ability to pay dividends or make other distributions on its common stock or to pay cash dividends on the convertible preferred stock. As of March 30, 2001, \$1,306,000 in total principal amount of the 9% notes remained outstanding.

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In addition, Hybridon is currently prohibited from paying cash dividends under the loan held by the Lender. See "Management's Discussion and Analysis of Financial Condition and Results of Operation -- 1998 Financing Activities -- \$6.0 Million Loan."

(d) RECENT SALES OF UNREGISTERED SECURITIES

Sales by Hybridon during the quarterly period ended December 31, 2000, of securities that were not registered under the Securities Act of 1933, as amended were as follows:

On May 30, 2000, the Board of Directors of Hybridon approved a Line of Credit Agreement with certain lenders who provided Hybridon with a \$2,000,000 credit facility in a private placement transaction. This 8% convertible loan was used to provide working capital pending the closing of the sale of Hybridon's Hybridon Specialty Products (HSP) manufacturing operation. On September 30, 2000, two of the lenders, Dr. Paul Zamecnik and Dr. James Wyngaarden, elected to convert their portion of the loan, including accrued interest, into shares of Common Stock. Dr. Zamecnik converted \$202,956 into 187,922 shares of Common Stock. Dr. Wyngaarden converted \$28,211 into 26,121 shares of Common Stock. The portion of the loan owned by other lenders was repaid with interest.

Hybridon agreed to issue to the \$2,000,000 credit facility lenders warrants to purchase 1,000,000 shares of Common Stock at a price of \$1.08 per share. Hybridon also agreed to issue warrants to purchase up to 500,000 shares of Common Stock at a price of \$1.08 per share to the representatives of the lenders. The convertible loans made under the \$2,000,000 credit facility and the related warrants were offered and sold to "accredited investors" in reliance upon the exemption from registration under Section 4(2) of the Securities Act relating to sales by an issuer not involving any public offering.

On March 30, 2001, Hybridon completed an exchange offer to the holders of its 8% Convertible Notes due 2001 whereby it will issue a total of 76,046 shares of a newly designated class of Series B Convertible Preferred Stock in exchange for the cancellation of \$7.6 million of principal amount of 8% Notes and accrued interest. The selected financial data presented below have been derived from Hybridon's consolidated financial statements, as adjusted to reflect the disposition of Hybridon's HSP business as discontinued operations, which have been audited by Arthur Andersen LLP, independent public accountants. The financial data should be read along with, and are qualified by reference to, "Management's Discussion and Analysis of Financial Condition and Results of Operations," Hybridon's consolidated financial statements and notes thereto and the Report of Independent Public Accountants included elsewhere in this Annual Report on Form 10-K.

HYBRIDON, INC.

| | YEAR ENDED DECEMBER 31, | | | | | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|----------------------------------------------------------------|------------------------------------------------------------------|-----------------------------------------------------------------------------|--------------------------------------------------------------------------------------|--|
| | | | 1997 1998 1999 | | 2000 | |
| | | (IN THOUSANDS | , EXCEPT PER | SHARE DATA) | | |
| STATEMENT OF OPERATIONS DATA: | | | | | | |
| Revenues: Service revenue Research and development Royalty and other income Interest income | \$ 1,419 62 1,447 | \$ 945 1,079 | \$ 375 1,100 148 | \$ 365 600 123 92 | \$ 82 179 229 83 | |
| Total revenues | 2,928 | 2,024 | 1,623 | 1,180 | 573 | |
| Operating Expenses: Research and development General and administrative Interest Restructuring | 33,150 11,347 34 | 35,326 11,027 4,278 10,345 | 14,183 6,573 2,820 | 5,783 3,664 683 | 3,620 3,184 2,154 | |
| Total operating expenses | 44,531 | 60,976 | 23,576 | 10,130 | 8,958 | |
| Loss from continuing operations Income (loss) from discontinued operations | (41,603) (5,250) | (58,952) (10,509) | (21,953) (4,028) | (8,950) (1,553) | (8,385) 5,462 | |
| Loss before extraordinary gain Extraordinary item: Gain on conversion of 9% convertible Subordinated notes payable | (46,853) | (69,461) | (25,981) | (10,503) | (2,923) | |
| Net lossAccretion of preferred stock dividend | (46,853) | (69,461) | (17,104) (2,689) | (10,503) (4,232) | (2,923) (4,087) | |
| Net loss applicable to common stockholders | | \$ (69,461) | \$ (19,793) | \$ (14,735) | \$ (7,010) | |
| Basic and diluted net loss per common share from: Continuing operations Discontinued operations Extraordinary gain | \$ (9.09) (1.15) | \$ (11.67) (2.08) | \$ (1.85) (0.34) 0.75 | \$ (0.57) (0.10) | \$ (0.48) 0.31 | |
| Net loss per share Accretion of preferred stock dividends | (10.24) | (13.76) | (1.44) (0.23) | (0.66) (0.27) | (0.17) (0.23) | |
| Net loss per share applicable to common stockholders | \$ (10.24) | \$ (13.76) | \$ (1.67) | \$ (0.93) | \$ (0.40) | |
| Shares Used in Computing Basic and diluted Net Loss per common share(1) | 4,576 | 5,050 | 11,859 | 15,811 | 17,418 | |
| <pre>BALANCE SHEET DATA: Cash, cash equivalents and short-term investments(2) Working capital (deficit) Total assets Restricted cash. Long-term debt and capital lease obligations, net of current portion</pre> | \$ 16,419 9,483 38,295 438 6,959 (149,194) 22,855 | \$ 2,202 (21,992) 30,480 3,051 1,328 50,000 | \$ 5,608 (5,306) 15,092 1,306 (238,448) 2,249 | \$ 2,552 (6,534) 10,717 1,306 6,100 (253,183) (6,072) | \$ 3,532 (4,238) 10,001 5,000 1,306 8,046 (260,193) (7,530) | |

(1) Computed on the basis described in Note 2(k) of Notes to consolidated financial statements appearing elsewhere in this document.

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

QUARTERLY OPERATING RESULTS (UNAUDITED)

The following table presents our unaudited statement of operations data for each of the eight quarters in the period ended December 31, 2000. The information for each of these quarters is unaudited, but has been prepared on the same basis as the audited financial statements appearing elsewhere in this document. In our opinion, all necessary adjustments, consisting only of normal recurring adjustments, have been made to present fairly the unaudited quarterly results when read in conjunction with our audited financial statements and the notes thereto appearing elsewhere in this document. These operating results are not necessarily indicative of the results of operations that may be expected for any future period.

| | THREE MONTHS ENDED | | | | | | | |
|-------------------------------------------------------------------------------------|--------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| | MAR. 31 1999 | JUN. 30 1999 | SEP. 30 1999 | DEC. 31 1999 | MAR. 31 2000 | JUN. 30 2000 | SEP. 30 2000 | DEC. 31 2000 |
| | | | | | PT PER SHAR | | | |
| STATEMENT OF OPERATIONS DATA: Revenues: | | | | | | | | |
| Service revenue | \$ 110 | \$ 73 | \$ 113 | \$ 70 | \$ 45 | \$ | \$ 25 | \$ 13 |
| Research and development | 150 | 150 | 150 | 150 | | | | 179 |
| Royalty and other income | 40 | 15 | 52 | 16 | 32 | 25 | 19 | 6 |
| Interest income | 53 | 16 | 13 | 10 | 35 | 16 | 16 | 163 |
| Total revenues | 353 | 254 | 327 | 246 | 112 | 41 | 60 | 361 |
| Operating Expenses: | | | | | | | | |
| | | 1,019 | 2,108 | 1,258 | 1,173 | 860 | 761 | 826 |
| General and administrative | 1,121 153 | 941 150 | 884 208 | 717 172 | 903 346 | 875 559 | 562 952 | 844 297 |
| Interest Restructuring | | | 208 | | | | 952 | |
| Total operating | | | | | | | | |
| expenses | 2,672 | 2,110 | 3,200 | 2,147 | 2,422 | 2,294 | 2,275 | 1,968 |
| Loss from continuing operations Income (loss) from | (2,319) | (1,856) | (2,873) | (1,901) | (2,310) | (2,253) | (2,215) | (1,607) |
| discontinued operations | (647) | (778) | 141 | (269) | (394) | (182) | 5,868 | 170 |
| Loss before extraordinary | | | | | | | | |
| gain Extraordinary item: Gain on conversion of 9% convertible Subordinated | (2,966) | (2,634) | (2,732) | (2,171) | (2,704) | (2,435) | 3,653 | (1,437) |
| notes payable | | | | | | | | |
| Net (loss) income | (2,966) | (2,634) | (2,732) | (2,171) | (2,704) | (2,435) | 3,653 | (1,437) |
| Accretion of preferred stock dividend | (1,042) | (1,076) | (1,076) | (1,038) | (1,071) | (1,021) | (1,021) | (975) |
| Net (loss) income applicable to | | | | | | | | |
| common stockholders | \$(4,008) | \$(3,710) | \$(3,808) | \$(3,209) | \$(3,775) | \$(3,455) | \$ 2,632 | \$(2,412) |
| Basic and diluted net (loss) | | | | | | | | |
| income per common share from: Continuing operations | \$ (0.15) | \$ (0.12) | \$ (0.18) | \$ (0.12) | \$ (0.14) | \$ (0.13) | \$ (0.12) | \$ (0.09) |
| Discontinued operations | (0.04) | (0.05) | 0.01 | (0.02) | (0.02) | (0.01) | 0.33 | 0.01 |
| Extraordinary gain | | | | | | | | |
| Net (loss) income per | | | | | | | | |
| share | (0.19) | (0.17) | (0.17) | (0.13) | (0.17) | (0.14) | 0.20 | (0.08) |
| Accretion of preferred stock dividends | 0.07 | 0.07 | 0.07 | 0.06 | 0.07 | 0.06 | 0.06 | 0.05 |
| Net (loss) income per share | | | | | | | | |
| applicable to common | | | | | | | | |
| stockholders | \$ (0.26) | \$ (0.24) | \$ (0.24) | \$ (0.20) | \$ (0.23) | \$ (0.20) | \$ 0.15 | \$ (0.13) |
| Shares Used in Computing Basic and diluted Net (Loss) per common | | | | | | | | |
| share(1) | 15,305 | 15,661 | 15,984 | 16,261 | 16,261 | 17,243 | 17,923 | 18,380 |
| | | | | | | | | |

 Computed on the basis described in Note 2(k) of Notes to consolidated financial statements appearing elsewhere in this document.

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GENERAL

Hybridon, established in 1989, utilizes chemically-modified synthetic DNA for medical applications, including the discovery and development of genetically based drugs, which treat diseases by acting on a particular gene. The genetic drugs being developed by Hybridon are based on "antisense" technology, in that they use synthetic DNA material, also called oligonucleotides, with the aim of inhibiting or reducing the body's production of proteins that directly or indirectly cause or support a given disease. Chemically-modified DNA is also being developed for use in the laboratory to determine the function of proteins produced by genes whose function has not yet been established. Hybridon has also developed a portfolio of chemically-modified DNA compounds designed to stimulate responses of the immune system.

Hybridon has developed and owns certain innovations in areas of medicinal chemistry, which concern the design of new synthetic DNA compounds. Hybridon also has rights to technology allowing the chemical modifications of synthetic DNA.

Hybridon began operations in February 1990 and since that time has been involved primarily in research and development efforts, developing its manufacturing capabilities, and raising capital. In order to commercialize its therapeutic products, Hybridon will need to address a number of technological challenges and comply with comprehensive regulatory requirements. Revenues received by Hybridon to date have been from collaborative agreements, interest on invested funds and revenues from the custom contract manufacturing of synthetic DNA and reagent products by its manufacturing business, Hybridon Specialty Products or "HSP" prior to the disposal thereof in September 2000.

Hybridon has incurred total losses of approximately \$260.0 million through December 31, 2000. Hybridon expects that its research and development and general and administrative expenses will be significant in 2001 and future years as it pursues its core drug development programs and expects to continue to incur operating losses and significant capital needs.

On September 21, 2000, Hybridon completed the sale of its HSP business to Avecia Biotechnology, a subsidiary of one of Europe's leading specialty chemicals companies. Avecia Biotechnology acquired the HSP business and intellectual property useful in DNA manufacturing for US\$15.0 million, of which approximately \$12.0 million was paid at closing, and the remaining \$3.0 million is payable on September 21, 2001, subject to certain offset rights. As part of this transaction, Hybridon entered into an agreement whereby it may have an obligation to purchase synthetic DNA products from Avecia Biotechnology. To the extent that Avecia Biotechnology's third party sales of HSP product exceed certain goals, Hybridon does not have any such purchase commitment. If Avecia Biotechnology's third party sales do not meet such goals, Hybridon must make purchases sufficient to cover the shortfall, subject to an agreed upon formula. Hybridon's commitment is on a "take-or-pay" basis for the fourth quarter of 2000 and each quarter of 2001. Purchases by OriGenix and MethylGene are applied against Hybridon's commitment. Any unpaid amounts under this agreement will reduce the \$3.0 million contingent payment to be received in September 2001. The balance of the term of this agreement (through March 31, 2003) does not require minimum purchases. In December 2000, Hybridon accrued approximately \$337,000 for its purchasing shortfall.

In connection with the sale of the HSP business, Avecia Biotechnology agreed to take over Hybridon's obligations to supply MethylGene, Inc. and OriGenix with quantities of synthetic DNA. Avecia gives Hybridon credit under its minimum purchase requirements for any orders for synthetic DNA, which Avecia receives, from MethylGene or OriGenix.

On May 30, 2000, Hybridon entered into a Line of Credit Agreement pursuant to which the lenders agreed to provide Hybridon with an 8%, \$2.0 million credit facility. The \$2.0 million credit facility was intended to provide Hybridon with working capital any time prior to the earlier of September 30, 2000, and the date the HSP sale was consummated. On July 10, 2000 and August 10, 2000, Hybridon drew down approximately \$0.5 million on each of these dates under the \$2.0 million credit facility, representing a total draw down of \$1.0 million. On September 28, 2000 Hybridon paid back approximately \$0.8 million and

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converted the remaining \$0.2 million to common stock in October 2000. Hybridon has no additional borrowing capacity under this credit facility.

As of March 27, 2001, Hybridon had 14 full-time employees.

The financial statements of Hybridon have been restated to reflect the financial results of the HSP business as a discontinued operation for the years ended December 31, 2000, 1999, and 1998.

RESULTS OF OPERATIONS

YEARS ENDED DECEMBER 31, 1998, 1999 AND 2000

Revenues

Hybridon had total revenues from continuing operations of \$1.6 million in 1998, \$1.2 million in 1999, and \$0.6 million in 2000. During 1998, 1999 and 2000, Hybridon received revenues from research and development collaborations of \$1.1 million, \$0.6 million and \$0.2 million, respectively. Research and development collaboration revenues decreased during this period, primarily due to a reduction in revenues recorded under its license agreement with MethylGene and the termination of the Searle collaboration agreement in early 2000.

Service revenues were \$0.4 million in 1998, \$0.4 million in 1999 and \$0.1 million in 2000. The decrease in revenues in 2000 from those in 1999 was primarily due to a decrease in support services provided to MethylGene, and OriGenix Technologies, Inc., entities in which Hybridon has a minority interest. Service revenues include drug development, clinical research, bio-analytical work and information services, which include access to research, pre-clinical and clinical information and data from Hybridon. As of December 31, 2000, Hybridon had no collaborations under which it will be receiving research funding.

Revenues from royalty and other income were zero in 1998, \$0.1 million in 1999 and \$0.1 million in 2000. The 1999 and 2000 revenue consisted primarily of a NIH grant and an equipment lease between Hybridon and OriGenix.

Revenues from interest income were \$0.1 million in 1998, \$0.1 million in 1999 and \$0.2 million in 2000. The increase in interest income in 2000 over 1999 was the result of higher cash balances available for investment, resulting from the HSP sale in 2000.

Research and Development Expenses

During 1998, 1999 and 2000, Hybridon expended \$14.2 million, \$5.8 million and \$3.6 million, respectively, on research and development activities.

The decreases in research and development expenses reflect more focused R&D activities in order to conserve cash by minimizing operating expenses such as salaries and related costs, clinical and outside testing, consulting, materials and lab expenses.

In addition, research and development facilities expenses decreased significantly during this period due to the consolidation of corporate offices and laboratory space and the disposition of one of Hybridon's Cambridge, Massachusetts facilities in July, 1998 and the disposition of the Milford, Massachusetts facility in September, 2000.

Hybridon's patent expenses remained at approximately the same level in 1999 as 1998 and decreased slightly in 2000 with the sale of its HSP business.

Hybridon incurred general and administrative expenses of \$6.6 million in 1998, \$3.7 million in 1999 and \$3.2 million in 2000. The decreases reflect the facilities consolidation mentioned above, as well as reductions in business development, public relations, legal fees and accounting expenses during 1999.

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Interest Expense

Interest expense was \$2.8 million in 1998, \$0.7 million in 1999 and \$2.2 million in 2000. The decrease in 1999 from 1998 is attributable to the exchange of approximately \$48.7 million of the 9% convertible subordinated notes issued in the second quarter of 1997 for Series A preferred stock on May 5, 1998. In addition, the outstanding balance of loans needed to finance the purchase of property and equipment was reduced in May 1998, resulting in a subsequent reduction in interest expense. Due to the issuance of the 8% convertible subordinated notes in December 1999 and the draw down on the \$2.0 million credit facility in 2000, Hybridon's interest expense increased in 2000 over that of 1999.

Loss from Continuing Operations

As a result of the above factors, Hybridon incurred losses from continuing operations of 22.0 million in 1998, 9.0 million in 1999 and 8.4 million in 2000.

Loss from Discontinued Operations

Hybridon incurred losses from discontinued operations of \$4.0 million in 1998, \$1.6 million in 1999 and realized a gain of \$5.5 million in 2000. The income from discontinued operations, as presented on the consolidated statement of operations for 2000, includes the gain on sale of HSP of \$6.3 million net of the operating loss from the discontinued HSP operations, totaling \$0.8 million. For all other years presented, the net loss relates solely to the operating results of HSP. Hybridon has not allocated interest expense to discontinued operations.

Net Loss

Hybridon incurred losses from operations before extraordinary items of \$26.0 million in 1998, \$10.5 million in 1999 and \$2.9 million in 2000. Hybridon had extraordinary income of \$8.9 million in 1998 resulting from the conversion of \$48.7 million principal amount of its 9% notes to Series A preferred stock in the second quarter of 1998. In accordance with Statement of Financial Accounting Standards No. 15, Accounting by Debtors and Creditors for Troubled Debt Restructurings, Hybridon recorded an extraordinary gain of approximately \$8.9 million related to the exchange. The extraordinary gain represents the difference between the carrying value of the 9% notes offered for exchange and the fair value of the Series A preferred stock issued upon the exchange, as determined by the per share sales price of such stock sold in May 1998 in the private offering described below. As a result of this extraordinary gain, Hybridon's net loss was reduced to \$17.1 million for 1998.

Preferred stock dividends on the Series A convertible preferred stock amounted to \$2.7 million, \$4.2 million and \$4.1 million in 1998, 1999 and 2000, respectively, resulting in a net loss applicable to common stockholders of \$19.8 million, \$14.7 million and \$7.0 million for 1998, 1999 and 2000, respectively.

LIQUIDITY AND CAPITAL RESOURCES

General

Since inception, Hybridon has incurred significant losses, which it has

funded through the issuance of equity securities, debt issuances, product sales by HSP, the sale of HSP during 2000 and through research and development collaborations and licensing arrangements.

During the year ended December 31, 2000, Hybridon utilized approximately \$7.6 million to fund continuing operating activities and approximately \$36,000 for capital expenditures. The primary use of cash for operating activities was to fund Hybridon's \$8.4 million loss from continuing operations.

Cash Resources

Hybridon had cash and cash equivalents of \$8.5 million at December 31, 2000, of which \$5.0 million is classified as restricted cash. This restricted cash had been pledged as collateral, to secure Hybridon's

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obligation to, among others, the holders of the 8% Convertible Notes. The pledge provided for a release of the restricted cash upon payment of the 8% Convertible Notes. The exchange of such notes effective March 5, 2001 has resulted in a release of those funds to Hybridon for discretionary purposes.

On March 30, 2001, Hybridon's obligations included \$1.3 million principal amount of 9% notes, a \$6.0 million loan from Founders Financial Group LP, formerly Forum Capital Markets, LLC and other lenders, approximately \$0.6 million in 8% Convertible Notes and accrued interest as described below, and approximately \$0.8 million of accounts payable. The loan agreement covering the \$6.0 million loan from the lenders, contains financial covenants that require Hybridon to maintain minimum tangible net worth and minimum liquidity requirements. Compliance with these covenants has been waived through September 30, 2001 by the noteholders.

Hybridon received approximately \$12.0 million of the \$15.0 million from the sale of HSP to Avecia. The remaining \$3.0 million is payable on September 21, 2001, subject to offset rights under the agreement to purchase HSP. As part of this transaction, Hybridon entered into a supply agreement whereby it may have an obligation to purchase products from Avecia Biotechnology. To the extent that Avecia Biotechnology's third-party sales of HSP product exceed certain goals, Hybridon does not have any such purchase commitment. If Avecia Biotechnology's third party sales do not meet such goals, Hybridon must make purchases sufficient to cover the shortfall, subject to an agreed upon formula. Hybridon's commitment is on a "take-or-pay" basis for the fourth quarter of 2000 and each quarter of 2001. Purchases by OriGenix and MethylGene are applied against Hybridon's commitment. Any unpaid amounts under this agreement will reduce the \$3.0 million contingent payment to be received in September 2001. The balance of the term of this agreement (through March 31, 2003) does not require minimum purchases. In December 2000, Hybridon accrued approximately \$337,000 for its purchasing shortfall. See Note 14 of the footnotes to the financial statements.

To facilitate the sale of the HSP's business and assets, the holders of the 8% Convertible Notes due 2002 and the \$6.0 million notes due 2003 amended the terms of a Subordination and Intercreditor Agreement, to release their lien on that portion of Hybridon's assets being conveyed to Avecia. In return for this partial release, Hybridon set aside, from the proceeds of the HSP sale, the sum of \$5.0 million, which it classifies as restricted cash on its balance sheet and pledged the same as collateral to secure its obligation to the 8% Convertible Noteholders and the lenders of the \$6.0 million loan. The amendment provided that the restrictions on the \$5.0 million would be released upon substantial payment of the 8% notes. The exchange of the Notes into Series B shares, being a discharge of Hybridon's obligation under the notes, has resulted in a release of the \$5.0 million to Hybridon's use.

On May 30, 2000, Hybridon entered into a Line of Credit Agreement pursuant to which the lenders under this agreement agreed to provide Hybridon with an 8%, \$2.0 million credit facility. The \$2.0 million credit facility was intended to provide Hybridon with working capital until the HSP sale was consummated. Hybridon drew down approximately \$0.5 million on July 10, 2000 and approximately \$0.5 million on August 10, 2000, representing a total draw down of approximately \$1.0 million under the \$2.0 million credit facility. On September 28, 2000, following the close of the HSP sale, Hybridon repaid approximately \$0.8 million of principal and interest in cash. In October 2000, Hybridon converted the remaining \$0.2 million of principal and interest into equivalent shares of common stock at \$1.08 per share, 214,043 shares, pursuant to the terms of the agreement. Hybridon has no additional borrowing capacity under this \$2.0 million credit facility.

In connection with the \$2.0 million credit facility, Hybridon has (a) issued to the representatives of the lenders of the \$2.0 million credit facility warrants to purchase up to 500,000 shares of Hybridon's common stock at an exercise price of \$1.08 per share and (b) issued to the lenders of the \$2.0 million credit facility, proportionate to their respective interests in the \$2.0 million credit facility, warrants to purchase 1,000,000 shares of Hybridon's common stock at an exercise price of \$1.08 per share.

Hybridon believes that its existing cash resources and the additional funds to be received upon consummation of the transactions discussed below will be sufficient to fund operations through December 31, 2001. Hybridon will be required to raise substantial additional funds from external sources to support its operations in 2002 and beyond.

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On March 30, 2001 Hybridon signed a binding agreement with unrelated institutional investors, providing for the sale of 60% of Hybridon's holdings of shares of Class A and Class B stock of MethylGene. The agreement covers a total of 2,350,000 such shares and provides for a purchase price of Canadian \$2.85 per share or a total of approximately Canadian \$6.7 million or US \$1.81 per share (as of March 30, 2001) or approximately US \$4.3 million in the aggregate. For additional information about this transaction, see "Business -- Hybridon."

Effective March 5, 2001, Hybridon completed an exchange whereby \$6.9 million of its \$7.5 million in principal, of 8% Notes due 2002 have been exchanged for shares of a newly-designated Series B Convertible Preferred Stock. The exchange ratio was one such share for each \$100 in principal amount of notes exchanged. For additional information about this exchange, see "Business -- Recent Developments."

Additionally, Hybridon has reached agreements with the holders of its \$6.0 million notes due 2003 providing for a partial payment on the outstanding balance of such notes from the proceeds of the sale of the MethylGene shares and the deposit of additional sums to secure the payment of a portion of the balance of such notes, which remain outstanding. For additional information about this transaction, see "Business -- Recent Developments."

During the second quarter of 2001, Hybridon expects to emerge from a period of restructuring with its core scientific and management team intact, with very little debt outstanding and with a substantial portfolio of patents and patent applications in place. Hybridon has established a strong proprietary position in the immune stimulation and antisense fields and expects to be able to continue its research and development efforts in immune stimulation and antisense. As our compounds are developed in the clinic and in the research pipeline, Hybridon will seek opportunities to license the antisense technology base in chemistry and delivery for use with other company's proprietary genes.

1999 Financing Activities -- 8% Convertible Notes Due 2002

The following is a description of Hybridon's 8% Convertible Notes due 2002. At March 30, 2001, \$7.5 million of principal amount was outstanding. All but \$0.6 million of this amount was exchanged on that day for shares of newly designated Series B Preferred Stock.

Hybridon sold an aggregate of \$1.5 million principal amount of promissory notes to E. Andrews Grinstead, III, Hybridon's then Chief Executive Officer, at

face value during September and November of 1999. These notes accrued interest at 12% per annum and in December 1999 were converted into 8% Convertible Notes due 2002. Hybridon also sold an aggregate of approximately \$0.5 million of debt to purchasers in a private placement transaction in October and November 1999; as of December 13, 1999, this debt automatically converted into Hybridon's 8% Convertible Notes due 2002.

On December 13, 1999, Hybridon sold an aggregate of an additional \$4.1 million principal amount of 8% Convertible Notes due 2002 to purchasers in a private placement transaction. At December 31, 1999, including the 8% Convertible Notes issued upon conversion of the debt issued to Mr. Grinstead and other purchasers, the principal amount of 8% notes outstanding was \$6.1 million. After the financing was completed in the first quarter of 2000, the principal amount of 8% Convertible Notes outstanding, including financing costs and accrued interest, was approximately \$7.7 million.

Under the terms of the 8% Convertible Notes, Hybridon must make semiannual interest payments on the outstanding principal balance through the maturity date of November 30, 2002. Hybridon has been electing to make these interest payments by issuing additional 8% Convertible Notes in lieu of cash payments. The 8% Convertible Notes are convertible at any time prior to the maturity date at a conversion price equal to \$0.60 per share of common stock, the "Conversion Ratio", subject to adjustment under certain circumstances, as defined. If the 8% Convertible Notes are prepaid before the maturity date, all noteholders are entitled to receive warrants to purchase the number of shares of common stock equal to the number of shares of common stock that would be issued using the Conversion Ratio, with an exercise price of \$0.60 per share of common stock.

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In connection with the 8% Convertible Notes, Hybridon must comply with certain covenants. These covenants include, without limitation, the requirement that Hybridon make all payments of interest when due and maintain consolidated cash balances of at least \$1.5 million as of the last day of any calendar month. At September 30, 2000, Hybridon is in compliance with the covenant regarding consolidated cash balances. If an event of default occurs, the noteholders may declare the unpaid principal and interest due and payable immediately. If Hybridon defaults with respect to payment of interest, Hybridon will be required to pay interest at a default rate equal to 12%.

In connection with the issuance of the 8% Convertible Notes, the lenders of the \$6.0 million loan received a warrant to purchase 2,750,000 shares of common stock at \$.60 per share. The warrant was granted as consideration to the lenders of the \$6.0 million loan for subordinating to holders of the 8% Convertible Notes their security interest in Hybridon's assets. Hybridon computed the value of the warrant to be \$547,328, using the Black-Scholes option-pricing model. Hybridon has recorded this amount as a deferred financing cost, which will be amortized to interest expense over the term of the 8% Convertible Notes.

1998 Financing Activities -- 9% Notes and Stock Issuances

On February 6, 1998, Hybridon commenced an offer to the holders of 9% notes issued in 1997 to exchange the 9% notes for Series A preferred stock and certain warrants of Hybridon. On May 5, 1998, noteholders holding \$48.7 million of principal and \$2.4 million of interest tendered such principal and accrued interest to Hybridon for 510,505 shares of Series A preferred stock and warrants to purchase 3,002,958 shares of common stock with an exercise price of \$4.25 per share.

On May 5, 1998, Hybridon completed a private offering of equity securities raising total gross proceeds of approximately \$26.7 million from the issuance of 9,597,476 shares of common stock, 114,285 shares of Series A preferred stock and warrants to purchase 3,329,486 shares of common stock at \$2.40 per share. The gross proceeds include the conversion of approximately \$5.9 million of accounts payable, capital lease obligations and other obligations into common stock. Hybridon issued 597,699 shares of common stock and warrants to purchase

1,720,825 shares of common stock at \$2.40 per share to the placement agents. In addition, Hybridon was obligated to issue an additional 300,000 shares in connection with this transaction. For more information about this transaction, see note 9(b) of the notes to consolidated statements.

Hybridon may redeem the 9% notes, of which \$1.3 million was outstanding at March 30, 2001, 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 Hybridon, as defined, Hybridon will be required to offer to repurchase the 9% notes at 150% of the original issuance price.

Facility Leases

As of December 31, 2000, Hybridon had future operating lease commitments of approximately \$3.9 million through 2007 for its existing leases.

Net Operating Loss Carryforwards

As of December 31, 2000, Hybridon had approximately \$235.6 million and \$4.2 million of net operating loss and tax credit carryforwards, respectively. The Tax Reform Act of 1986 contains certain provisions that may limit Hybridon'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. Hybridon has completed several financings since the effective date of the Tax Act, which, as of December 31, 1999, have resulted in ownership changes in excess of 50%, as defined under the Tax Act and which will limit Hybridon's ability to utilize its net operating loss carryforwards.

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RISK FACTORS

OUR FINANCIAL CONDITION AND NEED FOR SUBSTANTIAL ADDITIONAL FUNDING

Your Investment Could Be Substantially Diluted if We Issue Shares to Obtain Financing We Need.

Our business is the discovery and development of genetic drugs, which act on genes either to increase the production of proteins that combat disease or suppress the production of proteins which cause or support diseases. Since our founding in 1989, we have not produced any commercially viable drugs and we have operated at a loss. In the past, we have financed our operations largely from the sale of shares of common or preferred stock and the sale of debt or other securities convertible into common stock.

In order to obtain the funds to continue our operations, we will need to issue shares of common stock or debt or securities convertible into shares of common stock. We will probably need to issue a significant number of shares in order to raise sufficient funds to pay our creditors, meet covenants of our credit facility and continue our operations. This could result in substantial dilution to the book value of our shares.

We Are Not in Compliance With One of the Covenants in Our Loan Agreement. If Our Lenders Foreclose, We Will Have Few, or No, Assets to Distribute to Our Shareholders.

We owe \$6.0 million under a 1996 loan and we owe \$0.6 million under our 8% notes, both of which are secured by substantially all of our assets. The loan and the 8% notes are owned in part by our affiliates. The loan agreement for the \$6.0 million loan requires us to maintain liquidity of \$2.0 million and a net worth of \$6.0 million. The 8% notes require us to maintain liquidity of \$1.5

million. See Note 15(c) of the footnotes to the financial statements. On numerous occasions in the past, our lenders have waived our compliance with these requirements and have done so through September 30, 2001, although they may not be willing to do so in the future. If our lenders and noteholders ever decline to give us waivers, we will be in default and they will have the right to accelerate the repayment date on the loan and the 8% notes and foreclose on our assets. Foreclosure will likely force us to cease doing business or file for bankruptcy. If this should happen, and we are liquidated, there will be few or no tangible assets available for distribution to our shareholders. Since the debt is owned in part by our affiliates, the court may treat the loan as a capital contribution in which case there may be assets available for distribution to our shareholders, along with the lenders.

We Expect Our Operating Losses to Continue into the Future.

As of December 31, 2000, we have incurred operating losses of approximately \$260 million. We expect to continue incurring operating losses until revenues from the sale of any drugs that we succeed in developing exceed our research and development and administrative costs. We will need to spend substantial additional amounts on research and development, including preclinical studies and clinical trials, in order to obtain the necessary regulatory approvals. If we obtain regulatory approval, we will then need to spend substantial amounts on sales and marketing efforts.

OUR OPERATIONS

We May Not Succeed in Developing a Commercially Viable Drug.

We do not currently have any drugs on the market and the drug candidates we are working on are still in development. Before a drug is approved for sale by the regulatory authorities, the drug, which has undergone pre-clinical trials with animals to test activity and safety, must then pass several clinical trials with humans. The development of a new drug generally requires three phases of clinical trials. Phase I testing is conducted on a small group of healthy individuals for safety and dosage. Phase I/II testing is on patients with targeted diseases to test safety and, to a degree, effectiveness. Phase III is on a large patient group to confirm effectiveness. Our drug closest to commercialization, GEM(R)231, is still in Phase II clinical trials. Another drug, GEM(R)92, has been administered to the volunteers in a pilot Phase I study. All of our other drugs that are under consideration for development are in pre-clinical trials and have not been tested on humans.

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Drug candidates, in general, have a low overall probability of being commercialized, but that probability increases as the drug advances through the various development stages. A drug may, for instance, be ineffective, have undesirable side effects, or demonstrate other therapeutic characteristics that prevent or limit its commercial use, or may prove too costly to produce in commercial quantities. If our drug candidates cannot be successfully developed, or if we are unable to obtain the necessary regulatory approval, we will not be able to generate the revenues from the sale of drugs that we would need in order to be profitable.

We Sold Substantially All of Our Revenue-Generating Operations.

Throughout our history we have engaged primarily in the research and development of genetic drugs. However, in 1996 we formed Hybridon Specialty Products to manufacture synthetic DNA compounds for Hybridon's internal use, for use by our collaborators and for sale to third parties. We sold the business and assets of Hybridon Specialty Products on September 21, 2000, for approximately \$15,000,000. We are now dependent for revenue solely upon the ultimate success of our drug research and development activities for our long-term viability.

We Have Many Competitors, and May Not Be Able to Compete Successfully Against Them.

Several companies, in particular Isis Pharmaceuticals, Inc. and Genta Incorporated, are also in the business of developing synthetic DNA drugs. Isis, which has received the approval of the U.S. Food and Drug Administration, or "FDA," for Vitravene(R), and is currently marketing this drug for the treatment of CMV retinitis. Isis has several other drugs in clinical testing for the possible treatment of cancer, including ISIS 3521 and 2503. Genta is testing Genasense (G3139) in humans, also for the treatment of cancer. These potential new drugs are further along in clinical testing than Hybridon's cancer drug GEM(R)231. Other companies also have synthetic DNA drugs in preclinical and clinical development.

In general, the human health care products industry is extremely competitive. Many drugs are currently marketed for the treatment of cancer, such as Taxol(R), Carboplatin, Taxotere(R) and Camptosar(R). While it is unlikely that GEM(R)231 will compete against these drugs, it may be used in combination with them. GEM(R)231 and other Hybridon synthetic DNA drugs may not, however, be able to capture sufficient market share to be profitable.

To our knowledge two privately held companies are developing synthetic DNA drugs specially designed to stimulate the responses of the immune system. These potential new drugs are in clinical trials, either alone or in combination with vaccines to prevent or to treat various diseases.

Furthermore, biotechnology and related pharmaceutical technologies have undergone rapid and significant change and we expect that the technologies associated with biotechnology research and development will continue to develop rapidly. Our prospects depend in large part on our ability to compete with these technologies. Any compounds, drugs or processes that we develop may become obsolete before we recover the expenses incurred in developing them.

Our Ability to Compete Will Suffer if We Are Unable to Protect Our Patent Rights and Trade Secrets or if We Infringe the Proprietary Rights of Third Parties.

Our success will depend to a large extent on our ability to obtain U.S. and foreign patent protection for drug candidates and processes, preserve trade secrets and operate without infringing the proprietary rights of third parties.

To obtain a patent on an invention, the inventor must be the first to invent it or the first to file a patent application for it. We cannot be sure that the inventors of subject matter covered by patents and patent applications that we own or license were the first to invent, or the first to file patent applications for, those inventions. Furthermore, patents we own or license may be challenged, infringed upon, invalidated, found to be unenforceable, or circumvented by others, and our rights under any issued patents may not provide sufficient protection against competing drugs or otherwise cover commercially valuable drugs or processes. See "Business -- Patents, Trade Secrets, and Licenses."

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We seek to protect trade secrets and other unpatented proprietary information, in part by means of confidentiality agreements with our collaborators, employees, and consultants. If any of these agreements is breached, we may be without adequate remedies. Also, our trade secrets may become known or be independently developed by competitors.

OUR SECURITIES

Because "Penny Stock" Rules Apply to Trading in Our Common Stock, You May Find It Difficult to Sell these Shares.

Our common stock is a "penny stock," as it is not listed on a national securities exchange and trades at less than \$5.00 a share. Broker-dealers who sell penny stocks must provide purchasers of these stocks with a standardized risk-disclosure document. It provides information about penny stocks and the

nature and level of risks involved in investing in the penny-stock market. A broker must also give a purchaser, orally or in writing, bid and offer quotations and information regarding broker and salesperson compensation, make a written determination that the penny stock is a suitable investment for the purchaser, and obtain the purchaser's written agreement to the purchase. The penny stock rules may make it difficult for you to sell your shares of our stock. Because of the rules, there is less trading in penny stocks. Also, many brokers choose not to participate in penny stock transactions.

Certain Existing Stockholders Hold a Substantial Portion of Our Stock, and Consequently Could Control Most Matters Requiring Approval by Stockholders.

Our officers, directors and principal stockholders own or control more than 55% of our common stock on a fully-diluted basis. As a result, these stockholders, acting together, have the ability to control most matters requiring approval by the stockholders. This concentration of ownership may have the effect of delaying or preventing a change in control of Hybridon.

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that do not reflect historical facts, but instead reflect Hybridon's current expectations, estimates and projections regarding its business. Forward-looking statements can be found in the material set forth under "Risk Factors," "Business," and "Management's Discussion and Analysis of Financial Condition and Results of Operations," and are characterized by use of words such as "believes," "plans," "expects," and "anticipates." Forward-looking statements are not guarantees of future performance, and necessarily involve risks and uncertainties, and Hybridon's results could differ materially from those anticipated in the forward-looking statements contained in this prospectus.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Historically, Hybridon's primary exposures have been related to nondollar-denominated operating expenses in Europe. As of December 31, 2000, Hybridon's assets and liabilities related to nondollar-denominated currencies were not material.

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.

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PART III.

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF HYBRIDON

The response to this item is contained in part under the caption "Executive Officers of Hybridon" in Hybridon's Proxy Statement for the Annual Meeting of Stockholders to be held on June 14, 2001 (the "2001 Proxy Statement"), under the caption "Election of Directors," which section is incorporated herein by this reference. The 2001 Proxy Statement will be filed with the Securities and Exchange Commission (the "Commission") not later than 120 days after the fiscal year covered by this Annual Report on Form 10-K.

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

ITEM 11. COMPENSATION OF EXECUTIVE OFFICERS

The response to this item is contained in the 2001 Proxy Statement under the caption "Election of Directors," which section is incorporated herein by this reference. The 2001 Proxy Statement will be filed with the Commission not later than 120 days after the fiscal year covered by this Annual Report on Form 10-K.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The response to this item is contained in the 2001 Proxy Statement under the caption "Stock Ownership of Certain Beneficial Owners and Management," which section is incorporated herein by this reference. The 2001 Proxy Statement will be filed with the Commission not later than 120 days after the fiscal year covered by this Annual Report on Form 10-K.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

The response to this item is contained in the 2001 Proxy Statement under the caption "Certain Relationships and Related Transactions," which section is incorporated herein by this reference. The 2001 Proxy Statement will be filed with the Commission not later than 120 days after the fiscal year covered by this Annual Report on Form 10-K.

PART IV.

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

- (a) (1) Financial Statements. Reference is made to the Index to Consolidated Financial Statements under Item 8 of this Annual Report on Form 10-K.
 - (2) Hybridon 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.
 - (3) The list of Exhibits filed as a part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately preceding such Exhibits, and is incorporated herein by this reference.
- (b)Reports on Form 8-K. During the fourth quarter of 2000, Hybridon did not file any reports on Forms 8-K.

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(c) Exhibits required by Item 601 of Regulation S-K with each management contract, compensatory plan or arrangement required to be filed identified.

EXHIBIT NO.

DESCRIPTION

3.1(1) Restated Certificate of Incorporation of the Registrant, as amended.
3.2(2) Amended and Restated Bylaws of the Registrant.
3.3(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(2) Specimen Certificate for shares of Common Stock, \$.001 par value, of the Registrant.

4.2(4) Indenture dated as of March 26, 1997 between Forum Capital

| | Markets LLC and the Registrant. |
|------------|---------------------------------------------------------------|
| 4.3(7) | Certificate of Designation of Series A Preferred Stock, par |
| | value \$.01 per share, dated May 5, 1998. |
| 4.4(7) | Class A Warrant Agreement dated May 5, 1998. |
| 4.5(7) | Class B Warrant Agreement dated May 5, 1998. |
| 4.6(7) | Class C Warrant Agreement dated May 5, 1998. |
| 4.7(7) | Class D Warrant Agreement dated May 5, 1998. |
| 4.8 | Specimen Certificate for shares of Series B Preferred Stock, |
| | \$.01 par value, of the Registrant. |
| +10.1(2) | 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(2) | Patent License Agreement dated September 21, 1995 between |
| | the Registrant and National Institutes of Health. |
| +10.3(2) | Patent License Agreement effective as of October 13, 1994 |
| | between the Registrant and McGill University. |
| +10.4(2) | License Agreement effective as of October 25, 1995 between |
| | the Registrant and the General Hospital Corporation. |
| +10.5(2) | License Agreement dated as of October 30, 1995 between the |
| | Registrant and Yoon S. Cho-Chung. |
| +10.6(2) | Collaborative Study Agreement effective as of December 30, |
| | 1992 between the Registrant and Medtronic, Inc. |
| +10.7(2) | System Design and Procurement Agreement dated as of December |
| | 16, 1994 between the Registrant and Pharmacia Biotech, Inc. |
| 10.8(2) | 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(2) | Registration Rights Agreement dated as of February 21, 1990 |
| | between the Registrant, the Worcester Foundation for |
| | Biomedical Research, Inc. and Paul C. Zamecnik. |
| 10.10(2) | Registration Rights Agreement dated as of June 25, 1990 |
| | between the Registrant and Nigel L. Webb. |
| 10.11(2) | Registration Rights Agreement dated as of February 6, 1992 |
| | between the Registrant and E. Andrews Grinstead, III. |
| 10.12(2) | Registration Rights Agreement dated as of February 6, 1992 |
| | between the Registrant and Anthony J. Payne. |
| ++10.13(2) | 1990 Stock Option Plan, as amended. |
| ++10.14(2) | 1995 Stock Option Plan. |

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| EXHIBIT NO. | DESCRIPTION |
|------------------------|-----------------------------------------------------------------------------------------------------------------|
| ++10.15(2) | |
| ++10.16(2) 10.17(2) | 1995 Employee Stock Purchase Plan. Form of Warrant originally issued to Pillar Investment |
| 10.17(2) | 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 service, as amended. |
| 10.18(2) | Warrant issued to Pillar S.A. to purchase 100,000 shares of Common Stock dated as of March 1, 1994, as amended. |
| 10.19(2) | Warrant issued to Pillar S.A. to purchase 100,000 shares of Common Stock dated as of March 1, 1995. |
| 10.20(2) | 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. |
| ++10.21(5) | Employment Agreement dated as of March 1, 1997 between the |
| | Registrant and E. Andrews Grinstead, III. |

| 10.22(2) | Indemnification Agreement dated as of February 6, 1992 |
|------------|-------------------------------------------------------------------------------------------------|
| | between the Registrant and E. Andrews Grinstead, III. |
| ++10.23(6) | Employment Agreement dated March 1, 1997 between the |
| | Registrant and Dr. Sudhir Agrawal. |
| ++10.24(2) | Consulting Agreement dated as of February 21, 1990 between |
| | the Registrant and Dr. Paul C. Zamecnik. |
| 10.25(2) | Master Lease Agreement dated as of March 1, 1994 between the |
| | Registrant and General Electric Capital Corporation. |
| +10.26(6) | Research, Development and License Agreement dated as of |
| | January 24, 1996 between the Registrant and G.D. Searle & |
| | Co. |
| +10.27(6) | Manufacturing and Supply Agreement dated as of January 24, |
| | 1996 between the Registrant and G.D. Searle & Co. |
| 10.28(6) | Registration Rights Agreement dated as of January 24, 1996 |
| | between the Registrant and G.D. Searle & Co. |
| 10.29(5) | Loan and Security Agreement dated as of December 31, 1996 |
| | between the Registrant and Silicon Valley Bank. |
| 10.30(7) | First Amendment to Loan and Security Agreement dated March |
| | 30, 1998 between Hybridon, Inc. and Silicon Valley Bank. |
| 10.31(8) | Second Amendment to Loan and Security Agreement dated May |
| | 19, 1998, effective as of April 30, 1998, between Hybridon, |
| 1.0 | Inc. and Silicon Valley Bank. |
| 10.32(9) | Third Amendment to Loan and Security Agreement dated |
| | September 18, 1998 between Hybridon, Inc. and Silicon Valley |
| 10 22 (0) | Bank. |
| 10.33(9) | Fourth Amendment to Loan and Security Agreement dated |
| | October 30, 1998, effective as of September 29, 1998 between |
| 10.34(12) | Hybridon, Inc. and Silicon Valley Bank. Fifth Amendment to Loan and Security Agreement dated |
| 10.34(12) | December 4, 1998 between Hybridon, Inc. and Silicon Valley |
| | Bank. |
| 10.35(5) | Warrant issued to Silicon Valley Bank to purchase 65,000 |
| TO.33(3) | shares of Common Stock dated as of December 31, 1996. |
| | Shares of common stock dated as of becember 51, 1990. |

10.36(5) Registration Rights Agreement dated as of December 31, 1996 between the Registrant and Silicon Valley Bank.

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EXHIBIT NO. DESCRIPTION _____ _____ +10.37(5)Supply and Sales Agreement dated as of September 1, 1996 between the Registrant and P.E. Applied Biosystems. Registration Rights Agreement dated as of March 26, 1997 10.38(2)between Forum Capital Markets LLC and the Registrant. 10.39(2) Warrant Agreement dated as of March 26, 1997 between Forum Capital Markets LLC and the Registrant. Amendment No. 1 to License Agreement, dated as of February +10.40(6)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. 10.41(10)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. Amendment dated July 15, 1997 to the Series G Convertible 10.42(10)Preferred Stock and Warrant Purchase Agreement dated as of September 9, 1994 among the Registrant and certain purchasers, as amended. Consent Agreement dated January 15, 1998 between Silicon 10.43(1)Valley Bank and the Registrant relating to the Silicon Agreement.

10.44(11) Letter Agreement between the Registrant and Forum Capital

| | Markets LLC and Pecks Management Partners Ltd. for the purchase of the Loan and Security Agreement with Silicon Valley Bank. |
|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 10.45(7) | Financial Advisory Agreement between Registrant and Pillar Investments Ltd. dated May 5, 1998. |
| 10.46(7) | Placement Agency Agreement between Registrant and Pillar Investments Ltd. dated as of January 15, 1998. |
| +++10.47(12) | Licensing Agreement dated March 12, 1999 by and between Hybridon, Inc. and Integrated DNA Technologies, Inc. |
| +++10.48(13) | Licensing Agreement dated September 7, 1999 by and between Hybridon, Inc. and Genzyme Corporation. |
| 10.49(13) | Form of loan agreement relating to a loan in the amount of \$454,901 made to Hybridon, Inc. in October 1999 by various parties. |
| 10.50(13) | Form of promissory note relating to a loan in the amount of \$454,901 made to Hybridon, Inc. in October 1999 by various parties. |
| 10.51(13) | Loan Agreement dated as of September 1, 1999, between Hybridon, Inc. and E. Andrews Grinstead, III. |
| 10.52(13) | Term promissory note in the amount of \$500,000 dated September 1, 1999, by Hybridon, Inc. in favor of E. Andrews Grinstead, III. |
| 10.53(13) | Term promissory note in the amount of \$500,000 dated September 27, 1999, by Hybridon, Inc. in favor of E. Andrews Grinstead, III. |
| 10.54(11) | Subordination and Intercreditor Agreement by and among Hybridon, the holders of Notes due 2002, Forum and entities advised by Pecks, dated as of December 7, 1999. |
| 10.55(11) | Letter Agreement between Hybridon and Pillar Investments dated December 10, 1999. |
| 10.56(11) | Form of Subscription Agreements dated as of December 13, 1999, by and among Hybridon and the purchasers of Notes due 2002. |
| 10.57(11) | First Amended and Restated Subordination and Intercreditor Agreement by and among Hybridon, the holders of Notes due 2002, Forum and entities advised by Pecks. |
| 10 50(11) | |

10.58(11) License Agreement dated September 20, 2000 by and between Hybridon and Boston Biosystems, Inc.

| EXHIBIT NO. | DESCRIPTION |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| | |
| 10.59(11) | Assignment of Coexclusive License dated September 20, 2000 by and between Hybridon and the Public Health Service. |
| 10.60(11) | Oligonucleotide Purification Patent License Agreement dated September 20, 2000 by and between Hybridon and Boston Biosystems, Inc. |
| 10.61(14) | Asset Purchase Agreement dated June 29, 2000 by and between Hybridon and Boston Biosystems, Inc. |
| +++10.62(11) | Assignment of Patent Rights dated September 20, 2000 by and between Hybridon and Boston Biosystems, Inc. |
| +++10.63(11) | PNT Monomer Patent License and Option Agreement dated September 20, 2000 by and between Hybridon and Boston Biosystems, Inc. |
| +++10.64(11) | Agreement Relating to Patents Forming Part of Acquired Assets but to be Licensed Back to Hybridon for the Purposes of OriGenix Agreements dated September 20, 2000 by and between Hybridon and Boston Biosystems, Inc. |
| ++10.65 10.66 | E. Andrews Grinstead Settlement Letter. Agreement dated March 28, 2001 by and between Hybridon, |

| | Founders Financial Group, Pecks Management Partners L.T.D. |
|----------|--------------------------------------------------------------|
| | and General Motors Investment Management Corporation, in its |
| | capacity as Trustee for the General Motors Employees Global |
| | Trust Group. |
| 10.67 | Stock Purchase Agreement by and between Paul Capital |
| | Partners L.P. and PCP Associates and Hybridon dated March |
| | 30, 2001. |
| 10.68 | Agreement and Mutual Release between Hybridon and |
| | MethylGene, Inc. dated March 21, 2001. |
| 10.69 | Offer to Exchange Series B Preferred Stock of Hybridon dated |
| | March 5, 2001. |
| 21.1(2) | Subsidiaries of the Registrant. |
| 23.1 | Consent of Arthur Andersen LLP. |
| 23.2(11) | Consent of McDonnell Boehnen Hulbert & Berghoff. |
| | |

- Incorporated by reference to Exhibits to the Registrant's Annual Report on Form 10-K for the year ended December 31, 1997.
- (2) Incorporated by reference to Exhibits to the Registrant's Registration Statement on Form S-1 (File No. 33-99024).
- (3) Incorporated by reference to Exhibit 9(a)(1) to the Registrant's Schedule 13E-4 dated February 6, 1998.
- (4) Incorporated by reference to Exhibits to the Registrant's Current Report on Form 8-K dated April 2, 1997.
- (5) Incorporated by reference to Exhibits to the Registrant's Annual Report on Form 10-K for the year ended December 31, 1996.
- (6) Incorporated by reference to Exhibits to the Registrant's Annual Report on Form 10-K for the year ended December 31, 1995.
- (7) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended March 31, 1998.
- (8) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended June 30, 1998.
- (9) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended September 30, 1998.

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- (10) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended June 30, 1997.
- (11) Incorporated by reference to Exhibits to the Registrant's Registration Statement on Form S-1 (File No. 333-69649).
- (12) Incorporated by reference to Exhibits to the Registrant's Annual Report on Form 10-K for the year ended December 31, 1998.
- (13) Incorporated by reference to Exhibits to the Registrant's Quarterly Report on Form 10-Q for the period ended September 30, 1999.
- (14) Incorporated by reference to the Registrant's Proxy Statement dated August 8, 2000.
- + Confidential treatment granted as to certain portions, which portions are omitted and filed separately with the Commission.
- ++ Management contract or compensatory plan or arrangement required to be filed as an Exhibit to the Annual Report on Form 10-K.

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

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, on this 12th day of April 2001.

Hybridon, Inc.

By: /s/ SUDHIR AGRAWAL Sudhir Agrawal, D. Phil. President and Acting Chief Executive Officer

POWER OF ATTORNEY AND SIGNATURES

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

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

| SIGNATURE | TITLE | DATE |
|------------------------------------------------------|-----------------------------------------------------------------------------------------------|----------------|
| /s/ SUDHIR AGRAWAL Sudhir Agrawal, D. Phil. | President, Acting Chief Executive Officer (Principal Executive Officer) and Director | April 12, 2001 |
| /s/ JAMES B. WYNGAARDEN James B. Wyngaarden, M.D. | Chairman of the Board of Directors | April 12, 2001 |
| /s/ ROBERT G. ANDERSEN Robert G. Andersen | Chief Financial Officer and Vice President of Operations and Planning | April 12, 2001 |
| /s/ NASSER MENHALL Nasser Menhall | Director | April 12, 2001 |
| /s/ PAUL C. ZAMECNIK | Director | April 12, 2001 |
| Paul C. Zamecnik, M.D. /s/ YOUSSEF EL-ZEIN | Director | April 12, 2001 |
| Youssef El-Zein /s/ ARTHUR W. BERRY | Director | April 12, 2001 |
| Arthur W. Berry | | |

| SIGNATURE | TITLE | DATE |
|----------------------|----------|----------------|
| /s/ C. KEITH HARTLEY | Director | April 12, 2001 |
| C. Keith Hartley | | |
| /s/ CAMILLE CHEBEIR | Director | April 12, 2001 |
| Camille Chebeir | | |

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HYBRIDON, INC. AND SUBSIDIARIES

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS DECEMBER 31, 2000

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| Consolidated Statements of Operations | F-4 |
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| Consolidated Statements of Cash Flows | F-6 |
| Notes to Consolidated Financial Statements | F-7 |

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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) and subsidiaries as of December 31, 1999 and 2000, and the related consolidated statements of operations, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2000. These financial statements are the responsibility of Hybridon, Inc. and subsidiaries' management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Hybridon, Inc. and subsidiaries as of December 31, 1999 and 2000, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2000, in conformity with accounting principles generally accepted Boston, Massachusetts April 12, 2001

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HYBRIDON, INC. AND SUBSIDIARIES

CONSOLIDATED BALANCE SHEETS

ASSETS

| | DECEMB | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|--------------------------------|
| | | 2000 |
| Current Assets: Cash and cash equivalents Short-term investments Receivables Prepaid expenses and other current assets | \$ 2,551,671 | 2,000,000 337,403 71,616 |
| Total current assets | | 3,941,174 |
| Property and equipment, at cost: Leasehold improvements Laboratory equipment and other | 150,342 5,249,621 | 150,342 5,236,299 |
| Less Accumulated depreciation and amortization | | 5,386,641 5,295,963 |
| | 170,449 | 90,678 |
| Other assets: Deferred financing costs and other assets Restricted cash Note receivable from officer | 1,325,149 270,050 | 969,631 5,000,000 |
| | 1,595,199 | 5,969,631 |
| Net assets from discontinued operations | 6,101,518 | |
| | | \$ 10,001,483 |
| LIABILITIES AND STOCKHOLDERS' DEFI | CIT | |
| Current liabilities: Current portion of long-term debt Accounts payable Accrued expenses | \$ 6,000,000 1,263,943 2,119,864 | 1.094.735 |
| Total current liabilities | | 8,179,065 |
| 9% CONVERTIBLE SUBORDINATED NOTES PAYABLE | 1,306,000 | 1,306,000 |
| 8% CONVERTIBLE NOTES PAYABLE | | 8,046,420 |
| Commitments and Contingencies (Notes 7, 10 and 14) Stockholders' equity (deficit): Preferred stock, \$0.01 par value Authorized 5,000,000 shares Series A convertible preferred stock Designated 1,500,000 shares Issued and outstanding 661,856 and 626,170 shares at December 31, 1999 and 2000, respectively (liquidation preference of \$63,592,143 at December 31, 2000) | 6,618 | |
| | | |

| Common stock, \$0.001 par value Authorized 100,000,000 shares Issued and outstanding 16,260,722 and 18,382,237 | | |
|----------------------------------------------------------------------------------------------------------------------|---------------|---------------|
| shares at December 31, 1999 and 2000, respectively | 16,261 | 18,382 |
| Additional paid-in capital | 247,813,331 | 252,645,636 |
| Accumulated deficit | (253,183,130) | (260,193,046) |
| Deferred compensation | (725,383) | (7,236) |
| Total stockholders' deficit | (6,072,303) | (7,530,002) |
| | \$ 10,717,279 | \$ 10,001,483 |

The accompanying notes are an integral part of these consolidated financial statements. $$\rm F\mathcal{F-3}$

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HYBRIDON, INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF OPERATIONS

| 1998 | 1999 | 2000 |
|----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|
| \$ 375,000 1,099,915 148,067 | \$ 365,000 600,000 122,544 92,202 | \$ 82,500 179,277 82,826 228,695 |
| 1,622,982 | 1,179,746 | |
| 14,182,952 6,572,502 2,819,659 | 5,783,092 3,663,811 683,134 | 3,620,203 3,184,017 2,153,831 |
| | | 8,958,051 |
| (4,028,242) | (1,552,751) | (8,384,753) 5,462,154 |
| | | (2,922,599) |
| 8,876,685 | | |
| | (4,232,251) | (2,922,599) (4,087,317) |
| \$(19,792,736) | | |
| \$ (1.85) (0.34) 0.75 | \$ (0.57) (0.10) | \$ (0.48) 0.31 |
| (1.44) | (0.66) | (0.17) (0.23) |
| \$ (1.67) | \$ (0.93) | \$ (0.40) |
| | 15,810,664 | 17,418,233 |
| | 1998 375,000 1,099,915 148,067 1,622,982 14,182,952 6,572,502 2,819,659 23,575,113 (21,952,131) (4,028,242) (25,980,373) 8,876,685 (17,103,688) (2,689,048) (2,689,048) (2,689,048) (1,85) (0,34) 0.75 (1.44) (0.23) \$ (1.67) | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ |

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

HYBRIDON, INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)

| | CONVE PREFERB | ES A RTIBLE ED STOCK | COMMON | | | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|----------------------------|------------------------------------|-------------------|----------------------------------|------------------------|
| | | \$0.01 PAR VALUE | NUMBER OF SHARES | | ADDITIONAL PAID-IN CAPITAL | ACCUMULATED DEFICIT |
| BALANCE, DECEMBER 31, 1997 Issuance of Series A convertible preferred stock and attached warrants in exchange for conversion of 9% convertible subordinated | | | 5,059,650 | \$ 5 , 060 | \$173,695,698 | \$(218,655,101) |
| notes payable and accrued interest, net of issuance costs of \$1,195,398 Issuance of common stock and attached warrants in exchange for conversion of | 510,504 | \$5,105 | | | 38,729,489 | |
| accounts payable and other obligations Issuance of Series A convertible preferred | | | 3,217,154 | 3,217 | 5,931,341 | |
| stock Issuance of common stock to placement | 114,285 | 1,143 | | | 7,998,817 | |
| agent Issuance of common stock and attached warrants in exchange for conversion of convertible notes payable, net of issuance | | | 597,699 | 598 | 1,194,800 | |
| <pre>cost of \$566,167 Issuance of common stock and attached warrants, net of issuance costs of</pre> | | | | 3,157 | | |
| \$1,069,970 Issuance of common stock for services | | | | 3,223 | 6,873,453 | |
| rendered Deferred compensation related to grants of stock options to nonemployees, net of | | | 50,000 | 50 | 93,700 | |
| terminations Issuance of warrants in connection with | | | | | 109,734 | |
| notes payable Accretion and issuance of Series A | | | | | 85,433 | |
| convertible preferred stock dividends Amortization of deferred compensation | | 165 | | | 2,688,883 | (2,689,048) |
| Net loss | | | | | | (17,103,688) |
| BALANCE, DECEMBER 31, 1998 Issuance of common stock to placement | | | 15,304,825 | | | (238,447,837) |
| agents Conversion of Series A convertible preferred | | | 460,000 | 460 | 999,540 | |
| stock into common stock Issuance of warrants in connection with | | (211) | 495,897 | 496 | (285) | |
| notes payable Accretion and issuance of Series A | | | | | 547,328 | |
| convertible preferred stock dividends Fair value of stock options to | 41,673 | 416 | | | 4,231,835 | (4,232,251) |
| nonemployees Amortization of deferred compensation | | | | | 402,889 | |
| Net loss | | | | | | (10,503,042) |
| BALANCE, DECEMBER 31, 1999 Exercise of common stock options Retirement of common stock | | 6,618 | 16,260,722 335,240 (250,000) | 16,261 336 | 247,813,331 167,287 | (253,183,130) |
| Cancellation of stock options Revaluation of stock options issued to non- | | | (230,000) | | (50,781) | |
| employees Accretion and issuance of Series A | | | | | (449,665) | |
| convertible preferred stock dividends Issuance of stock options to | 41,363 | 414 | | | 4,086,903 | (4,087,317) |
| non-employees Issuance of warrants in connection with line | | | | | 117,523 | |
| of credit Conversion of line of credit into common | | | | | 731,136 | |
| stock Conversion of Series A convertible preferred | | | 214,043 | | 230,953 | |
| stock into common stock Amortization of deferred compensation | (77,049) | | 1,822,232 | 1,821 | (1,051) | |
| Net loss | | | | | | (2,922,599) |
| BALANCE, DECEMBER 31, 2000 | 626,170 ====== | \$6,262 ===== | 18,382,237 | \$18,382 | \$252,645,636 ====== | \$(260,193,046) |

| | DEFERRED COMPENSATION | TOTAL STOCKHOLDERS EQUITY (DEFICIT) |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|----------------------------------------------|
| BALANCE, DECEMBER 31, 1997 Issuance of Series A convertible preferred stock and attached warrants in exchange for conversion of 9% convertible subordinated notes payable and accrued interest, net of | \$(1,093,837) | \$(46,048,180) |
| issuance costs of \$1,195,398 Issuance of common stock and attached warrants in exchange for conversion of | | 38,734,594 |
| accounts payable and other obligations Issuance of Series A convertible preferred | | 5,934,558 |
| stock | | 7,999,960 |

| Issuance of common stock to placement agent Issuance of common stock and attached | | 1,195,398 | | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------|------------------------------------------------|--------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|
| warrants in exchange for conversion of convertible notes payable, net of issuance cost of \$566,167 Issuance of common stock and attached | | 4,233,833 | | |
| warrants, net of issuance costs of \$1,069,970 Issuance of common stock for services | | 6,876,676 | | |
| rendered Deferred compensation related to grants of | | 93,750 | | |
| stock options to nonemployees, net of terminations Issuance of warrants in connection with | (109,734) | | | |
| notes payable | | 85,433 | | |
| convertible preferred stock dividends Amortization of deferred compensation Net loss | 246,444 | 246,444 (17,103,688) | | |
| BALANCE, DECEMBER 31, 1998 | (957,127) | 2,248,778 | | |
| Issuance of common stock to placement agents Conversion of Series A convertible preferred stock into common stock | | 1,000,000 | | |
| stock into common stock Issuance of warrants in connection with | | | | |
| notes payable | | 547,328 | | |
| | | | | |
| Accretion and issuance of Series A convertible preferred stock divide | ends | | | |
| Fair value of stock options to | | | | |
| nonemployees | | • | | 402,889 |
| Amortization of deferred component | | 221 | 711 | 221 744 |
| Amortization of deferred compensat. Net loss | ion | | 744 | 231,744 (10,503,042) |
| Net loss | ion | · | | (10,503,042) |
| Net loss BALANCE, DECEMBER 31, 1999 | ion | . (725, | 383) | (10,503,042) (6,072,303) |
| Net loss BALANCE, DECEMBER 31, 1999 Exercise of common stock options | ion | . (725, | 383) | (10,503,042) |
| Net loss BALANCE, DECEMBER 31, 1999 Exercise of common stock options Retirement of common stock Cancellation of stock options | ion | . (725, | 383) | (10,503,042) (6,072,303) 167,623 |
| Net loss BALANCE, DECEMBER 31, 1999 Exercise of common stock options Retirement of common stock | ion | . (725, | 383) 781 | (10,503,042) (6,072,303) 167,623 (250) |
| Net loss BALANCE, DECEMBER 31, 1999 Exercise of common stock options Retirement of common stock Cancellation of stock options Revaluation of stock options issued | ion d to non- | . (725, | 383) 781 | (10,503,042) (6,072,303) 167,623 (250) |
| Net loss BALANCE, DECEMBER 31, 1999 Exercise of common stock options Retirement of common stock Cancellation of stock options Revaluation of stock options issue employees Accretion and issuance of Series A convertible preferred stock divide | ion | . (725, . 50, . 449, | 383) 781 | (10,503,042) (6,072,303) 167,623 (250) |
| Net loss BALANCE, DECEMBER 31, 1999 Exercise of common stock options Retirement of common stock Cancellation of stock options Revaluation of stock options issue employees Accretion and issuance of Series A | ion d to non- ends | . (725, . 50, . 50, | 383) 781 | (10,503,042) (6,072,303) 167,623 (250) |
| Net loss BALANCE, DECEMBER 31, 1999 Exercise of common stock options Retirement of common stock Cancellation of stock options issue employees Accretion and issuance of Series A convertible preferred stock divide Issuance of stock options to non-employees Issuance of warrants in connection | ion d to non- ends with line | . (725, . 50, . 50, . 449, | 383) 781 | (10,503,042) (6,072,303) 167,623 (250) 117,523 |
| Net loss BALANCE, DECEMBER 31, 1999 Exercise of common stock options Retirement of common stock Cancellation of stock options issue employees Accretion and issuance of Series A convertible preferred stock divide Issuance of stock options to non-employees | ion d to non- ends with line | . (725, . 50, . 50, . 449, | 383) 781 | (10,503,042) (6,072,303) 167,623 (250) |
| Net loss BALANCE, DECEMBER 31, 1999 Exercise of common stock options Retirement of common stock Cancellation of stock options issue employees Accretion and issuance of Series A convertible preferred stock divide Issuance of stock options to non-employees Issuance of warrants in connection of credit Conversion of line of credit into a | ion d to non- ends with line common | . (725, . 50, . 50, . 449, | 383) 781 | (10,503,042) (6,072,303) 167,623 (250) 117,523 |
| Net loss BALANCE, DECEMBER 31, 1999 Exercise of common stock options Retirement of common stock Cancellation of stock options issue employees Accretion and issuance of Series A convertible preferred stock divide Issuance of stock options to non-employees Issuance of warrants in connection of credit Conversion of line of credit into stock Convertible Series A convertible | ion d to non- ends with line common preferree | . (725, . 50, . 50, . 449, | 383) 781 | (10,503,042) (6,072,303) 167,623 (250) 117,523 731,136 |
| Net loss BALANCE, DECEMBER 31, 1999 Exercise of common stock options Retirement of common stock Cancellation of stock options issue employees Accretion and issuance of Series A convertible preferred stock divide Issuance of stock options to non-employees Issuance of warrants in connection of credit Conversion of line of credit into a | ion d to non- ends with line common preferree | . (725, . 50, . 50, . 449, | 383) 781 665 | (10,503,042) (6,072,303) 167,623 (250) 117,523 731,136 231,167 |
| Net loss BALANCE, DECEMBER 31, 1999 Exercise of common stock options Retirement of common stock Cancellation of stock options issue employees Accretion and issuance of Series A convertible preferred stock divide Issuance of stock options to non-employees Issuance of warrants in connection of credit Conversion of line of credit into stock Conversion of Series A convertible stock into common stock | ionion | . (725, . 50, . 449, . 449, . 217, | 383) 781 665 701 | (10,503,042) (6,072,303) 167,623 (250) 117,523 731,136 231,167 217,701 (2,922,599) |
| Net loss BALANCE, DECEMBER 31, 1999 Exercise of common stock options Retirement of common stock Cancellation of stock options issue employees Accretion and issuance of Series A convertible preferred stock divide Issuance of stock options to non-employees Issuance of warrants in connection of credit Conversion of line of credit into stock Conversion of Series A convertible stock into common stock Amortization of deferred compensat | ion | . (725, . 50, . 449, . 449, . 217, | 383) 781 665 701 701 236) | (10,503,042) (6,072,303) 167,623 (250) 117,523 731,136 231,167 217,701 (2,922,599) |

The accompanying notes are an integral part of these consolidated financial statements. $$\rm F{-}5$$

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HYBRIDON, INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF CASH FLOWS

| | YEARS ENDED DECEMBER 31, | | |
|--------------------------------------------------------|--------------------------|------|------|
| | 1998 | 1999 | 2000 |
| CASH FLOWS FROM OPERATING ACTIVITIES: | | | |
| Net loss Income (loss) from discontinued operations | | | |

| Loss from continuing operations Adjustments to reconcile net loss to net cash used in | | | |
|-----------------------------------------------------------------------------------------------|------------------------|--------------------|--------------|
| operating activities | | | |
| Extraordinary gain on exchange of 9% convertible | | | |
| subordinated notes payable | (8,876,685) | 394,381 | 115 403 |
| Depreciation and amortization Compensation expense related to the issuance of stock | 2,120,212 | 394,301 | 115,403 |
| options | | | 117,523 |
| Amortization of deferred compensation | 246,444 | | 217,701 |
| Amortization of deferred financing costs | 160,813 | 123,140 | 456,919 |
| Interest expense related to the issuance of common stock | | | |
| warrants | | | 731,136 |
| Non cash interest expense | | 65,485 | |
| Issuance of common stock for services rendered Changes in operating assets and liabilities | 93,750 | | |
| Receivables | (511,652) | 114,694 209,341 | (140,875) |
| Prepaid expenses and other current assets | 894,998 | 209,341 | 30,298 |
| Note receivable from officer | (11,400) | (11, 400) | |
| Accounts payable and accrued expenses | (276,463) | (1,153,013) | (935,000) |
| Net cash used in continuing operating activities | | (8,573,030) | (7,640,571) |
| Net cash provided by (used in) discontinued | | | |
| operations | (4,090,858) | (130,581) | (162,472) |
| CASH FLOWS FROM INVESTING ACTIVITIES: | | | |
| Increase in other assets | | | (101,401) |
| Purchases of short-term investments | | | (2,000,000) |
| Proceeds from sale of discontinued operations | | (8,303) | 11,726,144 |
| Purchases of property and equipment | 114,576 | (8,303) | (35,572) |
| Proceeds from sale of property and equipment | 714,400 5,450,000 | | |
| Proceeds from sale of real estate partnership | 5,450,000 | | |
| Net cash (used in) provided by investing | | | |
| activities | 6,278,976 | (8,303) | 9,589,171 |
| | | | |
| CASH FLOWS FROM FINANCING ACTIVITIES: | | | |
| Net proceeds from issuance of Series A convertible preferred stock | 7,999,960 | | |
| Net proceeds from issuance of common stock | 6 876 676 | | |
| Net borrowings under line of credit | | | 231,167 |
| Proceeds from notes payable | 6,000,000 | | |
| Proceeds from issuance of convertible notes payable and | | | |
| warrants | 4,233,833 | 4,534,290 | 1,795,566 |
| Proceeds from related party notes payable | | 1,500,000 | |
| Payments on long-term debt | (7,234,300) | (378,587) | |
| Increase in deferred financing costs | (400,000) | (378,587) | |
| (Increase) decrease in restricted cash and other assets | 2,976,822 | | (5,000,000) |
| Net cash provided by (used in) financing | | | |
| activities | | 5,655,703 | (2,805,644) |
| | | | |
| Net (decrease) increase in cash and cash equivalents | 3,405,680 2,202,202 | (3,056,211) | (1,019,516) |
| Cash and cash equivalents, beginning of period | 2,202,202 | 5,607,882 | 2,551,671 |
| Cash and cash equivalents, end of period | | \$ 2,551,671 | \$ 1,532,155 |
| | = | = | |

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

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS DECEMBER 31, 2000

(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.

Since inception, the Company has been primarily engaged in research and development efforts, development of its manufacturing capabilities and organizational efforts, including recruiting 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 based on the antisense mechanism. 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 collaboration and licensing agreements, interest on investment funds and revenues from the custom contract manufacturing of synthetic DNA and reagent products by the Company's Hybridon Specialty Products business prior to the disposal thereof.

On September 21, 2000, the Company completed the sale (see Note 14) of its Hybridon Specialty Products business to a subsidiary of Avecia, Inc. (Avecia) of Manchester, United Kingdom, for up to \$15.0 million, referred to as the HSP sale.

The Company believes that its existing cash resources and the additional funds to be received upon consummation of the transactions discussed in Note 15 will be sufficient to fund operations through December 31, 2001. The Company will be required to raise substantial additional funds from external sources to support its operations in 2002 and beyond.

(2) SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

(a) Use of Estimates

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.

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

(b) Principles of Consolidation

The accompanying consolidated financial statements include the results of the Company and its subsidiary Hybridon S.A., an inactive French corporation. The consolidated financial statements also reflect the Company's approximately 22% interest in MethylGene, Inc., and the Company's approximately 28% interest in OriGenix Technologies Inc., both Canadian corporations that are accounted for under the equity method (see Notes 7 and 8, respectively). All material intercompany balances and transactions have been eliminated in consolidation.

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HYBRIDON, INC. AND SUBSIDIARIES

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

(c) Cash Equivalents and Short-Term Investments

The Company considers all highly liquid investments with maturities of 90 days or less when purchased to be cash equivalents. Cash and cash equivalents at December 31, 1999 and 2000 consist of the following (at amortized cost, which approximates fair market value):

| | DECEMBER 31 | | |
|-----------------------------------------------------------------------------|-------------------------|------------------------|--|
| | 1999 | 2000 | |
| Cash and cash equivalents* Cash and money market funds Corporate bond | \$ 505,794 2,045,877 | \$238,327 1,293,828 | |
| Total cash and cash equivalents | \$2,551,671 | \$1,532,155 ====== | |

The Company follows the provisions of Statement of Financial Accounting Standards (SFAS) No. 115, Accounting for Certain Investments in Debt and Equity Securities. The Company's short-term investments are classified as held-to-maturity and are recorded at amortized cost. At December 31, 2000 the Company's short-term investments consisted of corporate bonds, which mature in January 2001.

- * Does not include restricted cash of 5,000,000 at December 31, 2000 (see Note 4(f)).
 - (d) Depreciation and Amortization

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

| | ESTIMATED |
|--------------------------------|-------------|
| ASSET CLASSIFICATION | USEFUL LIFE |
| | |
| Teecheld improvements | |
| Leasehold improvements | |
| Laboratory equipment and other | 3 - 5 years |

- (e) Accrued Expenses
 - At December 31, 1999 and 2000, accrued expenses consist of the following:

| | DECEMBER 31 | | |
|------------------------------------|-------------|-----------------------|--|
| | 1999 | 2000 | |
| Payroll and related costs Other | | \$ 127,856 966,879 | |
| | \$2,119,864 | \$1,094,735 | |

(f) Reclassifications

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

(g) Revenue Recognition

The Company has recorded revenue under the consulting and research agreements discussed in Notes 7 and 8. Revenue is recognized as earned on the straight-line basis over the term of the agreement, which approximates when work is performed and costs are incurred. Revenues from service sales are recognized when the services are performed. Service revenues include drug development, clinical research, bio-analytical

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

work and information services, which include access to research, pre-clinical and clinical information and data from the Company.

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

(h) Financial Instruments

Statement of Financial Accounting Standards SFAS No. 107, Disclosures About Fair Value of Financial Instruments, requires disclosure of an estimate of the fair value of certain financial instruments. The Company's financial instruments consist of cash and cash equivalents, accounts receivable and debt obligations. The estimated fair value of these financial instruments approximates their carrying value at December 31, 2000 and 1999, respectively. The estimated fair values have been determined through information obtained from market sources and management estimates, The Company does not have any material derivative or any other financial instruments as defined by SFAS No. 119, Disclosure about Derivative Financial Instruments and Fair Value of Financial Instruments.

(i) Concentration of Credit Risk and Significant Customers

SFAS No. 105, Disclosure of Information About Financial Instruments with Off-Balance-Sheet Risk and Financial Instruments with Concentrations of Credit Risk, requires disclosure of any significant off-balance-sheet and credit risk concentrations. Financial instruments that subject the Company to the potential for credit risk consist primarily of accounts receivable. As of December 31, 2000, accounts receivable consists of approximately \$337,000 relating to Avecia's minimum purchase requirement (see Note 14).

(j) Comprehensive Loss

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

(k) Net Loss per Common Share

The Company applies SFAS No 128, Earnings per Share. Under SFAS No. 128, basic net loss per common share is computed using the weighted average number of shares of common stock outstanding during the period. Diluted net loss per common share is the same as basic net loss per common share as the effects of the Company's potential common stock equivalents are antidilutive. Antidilutive securities, which consist of stock options, warrants and convertible preferred stock and convertible debt instruments (on an as-converted basis) that are not included in diluted net loss per common share were 30,312,133, 45,557,695 and 49,098,529 for 1998, 1999 and 2000, respectively.

(1) Segment Reporting

The Company applies SFAS No. 131, Disclosures About Segments of an Enterprise and Related Information. SFAS No. 131 establishes standards for

reporting information regarding operating segments in annual financial statements and requires selected information for those segments to be presented in interim financial reports issued to stockholders. SFAS No. 131 also establishes standards for related disclosures about products and services and geographic areas. To date, the Company has viewed its operations and manages its

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

business as principally one operating segment. As a result, the financial information disclosed herein represents all of the material financial information related to the Company's principal operating segment. All of the Company's revenues are generated in the United States and substantially all assets are located in the United States.

(m) New Accounting Pronouncement

In June 1998, the Financial Accounting Standards Board (FASB) issued SFAS No. 133, Accounting for Derivative Instruments and Hedging Activities. This statement establishes accounting and reporting standards for derivative instruments, including derivative instruments embedded in other contracts and for hedging activities. SFAS No. 133, as amended by SFAS Nos. 137 and 138, is effective for all fiscal quarters of fiscal years beginning after June 15, 2000. In addition, the Emerging Issues Task Force (EITF) has issued a number of derivative-related tentative and final consensuses. The Company does not expect the adoption of any of these new standards to have a material impact on its consolidated financial statements or results of operation.

In March 2000, the FASB issued Interpretation No. 44 (FIN 44), Accounting for Certain Transactions Involving Stock Compensation -- an Interpretation of APB Opinion No. 25. This interpretation clarifies the application of Accounting Principles Board (APB) Opinion No. 25, Accounting for Stock Issued to Employees in certain situations, as defined. The interpretation was effective July 1, 2000, but covers certain events occurring during the period after December 15, 1998 but before the effective date. To the extent that events covered by this interpretation occur during the period after December 31, 1998 but before the effective date, the effects of applying this interpretation would be recognized on a prospective basis from the effective date. Accordingly, upon initial application of the final interpretation, (i) no adjustments would be made to the consolidated financial statements before the effective date and (ii) no expense would be recognized for any additional compensation cost measured that is attributable to periods before the effective date. The adoption of this interpretation did not have any effect on the Company's consolidated financial statements or results of operations. The adoption of FIN 44 will affect the accounting for stock options repriced during fiscal year 1999 (see Note 9(f)).

(3) NOTE RECEIVABLE FROM OFFICER

At December 31, 1999, the Company had a note receivable and accrued interest from an officer of \$270,050, with an interest rate of 6.0% per annum. The Company forgave the note in 2000 and charged this amount to general and administrative expense.

(4) LONG-TERM DEBT

(a) Note Payable

During November 1998, the Company entered into a \$6,000,000 note payable with Forum Capital Markets, LLC, which is now Founders Financial Group, L.P. (Founders), and certain investors associated with Pecks Management Partners Ltd. (Pecks). The terms of the note payable are as follows: (i) the maturity is November 30, 2003; (ii) the interest rate is 8%; (iii) interest is payable monthly in arrears, with the principal due in full at maturity of the loan; (iv) the note payable is convertible, at Pecks' and Founders' option, in whole or in part, into shares of common stock at a conversion price equal to \$2.40 per share, a premium to fair value at date of issuance, and (v) the note requires minimum liquidity, as defined, of \$2,000,000. The Company has classified the outstanding balance of \$6,000,000 at December 31, 1999 and 2000 as a current liability in the accompanying consolidated balance sheets as it does not currently have the financing to remain in compliance with the financial covenants. In connection with the issuance of the note payable, Forum received a fee of \$400,000, which was reinvested by Founders to purchase 160,000 shares of

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

common stock with 40,000 attached warrants at an exercise price of \$3.00 per share. The Company has recorded the \$400,000 as a deferred financing cost, which will be amortized to interest expense over the term of the note. As an additional fee, Forum received warrants to purchase 133,333 shares of common stock of the Company at \$3.00 per share. The Company computed the value of the warrants to be \$85,433, by using the Black-Scholes option pricing model. The Company has recorded this \$85,433 as a deferred financing cost, which will be amortized to interest expense over the term of the note. See Note 15 for subsequent events.

(b) Capital Lease Obligations

The Company had entered into various capital leases for equipment. During 1998, the Company settled its capital lease obligations in full through the issuance of common stock and warrants (see Note 9(b)).

(c) 9% Convertible Subordinated Notes Payable

On April 2, 1997, the Company issued \$50,000,000 of 9% convertible subordinated notes Payable (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 per share, a premium to fair value at the date of issuance, 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.

On May 5, 1998, holders of \$48,694,000 of principal and \$2,361,850 of accrued interest tendered such principal and accrued interest on the 9% Notes to the Company for 510,505 shares of Series A convertible preferred stock and warrants to purchase 3,002,958 shares of common stock with an exercise price of \$4.25 per share. In accordance with SFAS No. 15, Accounting by Debtors and Creditors for Troubled Debt Restructurings, the Company recorded an extraordinary gain of \$8,876,685 related to the exchange. The extraordinary gain represents the difference between the carrying value of the 9% Notes plus accrued interest, less \$2,249,173 of deferred financing costs written off, and the fair value of the Series A convertible preferred stock, as determined by the

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per share sales price of Series A convertible preferred stock sold in the 1998 Unit Financing (see Note 9(b)), and warrants to purchase common stock issued by the Company. As of December 31, 2000, \$1,306,000 of 9% Notes are outstanding.

(d) 8% Convertible Notes Payable

In December 1999, the Company completed an offering of the 8% Convertible Notes Payable (8% Notes). As of December 31, 1999, the Company had received approximately \$5.7 million in principal with respect to the 8% Notes. Subsequent to December 31, 1999, the Company received approximately an additional \$1.2 million in principal of 8% Notes. In connection with the closing of the 8% Notes in December, the Company converted the outstanding balance of the promissory notes payable to the Company's chief executive officer into 8% Notes (see Note 4(e)). Under the terms of the 8% Notes, the Company must make semiannual interest payments on the outstanding principal balance through the maturity date of November 30,

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

2002. The 8% Notes are convertible at any time prior to the maturity date at a conversion price equal to \$0.60 per share of common stock, fair value at the commitment date, the "Conversion Ratio," subject to adjustment under certain circumstances, as defined. If the 8% Notes are prepaid before the maturity date, all noteholders are entitled to receive a warrant to purchase the number of shares of common stock equal to the number of shares of common stock that would be issued using the Conversion Ratio. As of December 31, 2000, \$8,046,420 of 8% Notes are outstanding.

In connection with the 8% Notes, the Company must comply with certain covenants, including making all payments of interest when due and maintaining consolidated cash balances of at least \$1.5 million as of the last day of any calendar month. At December 31, 2000 the Company is in compliance with the covenant regarding consolidated cash balances. If an event of default occurs, as defined, the noteholders may declare the unpaid principal and interest due and payable immediately. If the Company defaults with respect to payment of interest, the Company will be required to pay interest at a default rate equal to 12%. On July 10, 2000, the holders of the 8% notes entered into an amendment (See Note 4(f)) to the Subordination and Intercreditor Agreement.

In addition, in connection with the issuance of the 8% Notes, the holders of the note payable to Pecks and Founders (see Note 4(a)) received a warrant to purchase 2,750,000 shares of the Company's common stock at \$0.60 per share. The warrant was granted as consideration to Pecks and Founders for relinquishing their seniority upon liquidation of the Company to the holders of the 8% Notes. The Company computed the value of the warrants to be \$547,328, by using the Black-Scholes option pricing model. The Company has recorded the \$547,328 as a deferred financing cost, which will be amortized to interest expense over the term of the 8% Notes.

See Note 15 for subsequent events.

(e) Related Party Notes Payable

During September 1999, the Company entered into two \$500,000 promissory notes payable to the Company's chief executive officer. During November 1999, the Company entered into an additional \$500,000 promissory note payable to its chief executive officer. In connection with the issuance of the 8% Notes (see Note 4(d)), the Company converted the principal balance of \$1,500,000, and the accrued but unpaid interest of \$46,502 into 8% Notes.

(f) \$2.0 Million Line of Credit

On May 30, 2000, the Company entered into a line of credit agreement

pursuant to which the \$2.0 million line of credit lenders agreed to provide the Company with a line of credit (see Note 1). The \$2.0 million line of credit was intended to provide the Company with working capital pending the closing of the HSP sale. On July 10, 2000 and August 10, 2000, the Company drew down approximately \$0.5 million each of these dates under the \$2.0 million line of credit, representing a total draw down of \$1.0 million.

On September 28, 2000, following the close of the sale of HSP, the Company received a Notice of Repayment from the \$2.0 million line of credit lenders and repaid approximately \$0.8 million of principal and interest in cash and \$0.2 million of principal and interest in equivalent shares of common stock (214,043 shares) at \$1.08 per share, a premium to fair value at the date of the line of credit agreement, in October 2000, pursuant to the terms of the original agreement. The Company has no additional borrowing capacity under this \$2.0 million line of credit.

The \$2.0 million line of credit lenders, the holders of the 8% Convertible Notes (Note 4(d)), and the Lender (Note 4(a)) on July 10, 2000 entered into an amendment to the Subordination and Intercreditor Agreement. In the Subordination and Intercreditor Agreement, as amended all parties agreed to release their F-12

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

lien on the portion of the collateral that includes assets to be conveyed in the HSP sale (Note 14). In return for this partial release, the Company undertook in the Subordination and Intercreditor Agreement, as amended, that upon consummation of the HSP sale it would set aside from the proceeds thereof the sum of \$5.0 million with which it will purchase a money market instrument and pledge the same as collateral to secure its obligation to the holders of the 8% Convertible Notes and the \$2.0 million line of credit lenders. The amount of the pledge will be reduced as the Company's obligations are converted to equity or repaid. The Company is entitled to collect and keep interest income generated by the money market account. The lenders that are party to the Subordination and Intercreditor Agreement, as amended, will continue to have a lien on substantially all of the Company's assets remaining after the HSP sale.

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

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

In January 1996, the Company and G.D. Searle & Co. entered into a collaboration relating to research and development of therapeutic antisense compounds. The Company and Searle were investigating antisense inhibitors of MDM2, a protein involved in programmed cell death, or apoptosis. In March 2000, the Company announced that Searle had elected not to extend its collaboration agreement with the Company.

During 1998 and 1999, the Company earned \$600,000 each year, in research and development revenues from Searle. Under the collaboration, Searle also purchased 200,000 shares of common stock in the Company at the offering price of \$50.00 per share.

(6) LICENSING AGREEMENT

The Company has entered into a licensing agreement with the Worcester

Foundation for Biomedical Research, Inc., which has merged with the University of Massachusetts Medical Center, under which the Company has received exclusive licenses to technology in 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.

(7) INVESTMENT IN METHYLGENE, INC.

In January 1996, the Company and institutional investors formed a Quebec company, MethylGene, Inc. 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 technology relating to the MethylGene fields. These fields are defined as (i) antisense compounds for the treatment of any disease which act by inhibiting the production of DNA methyltransferase; (ii) other methods of inhibiting DNA methyltransferase and (iii) antisense compounds to inhibit up to two additional molecular targets, to be agreed upon by the Company and MethylGene.

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

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

In May 1998, this agreement was amended to grant MethylGene a nonexclusive right to use any and all antisense chemistries discovered by the Company or any of its affiliates for a period commencing on May 5, 1998 and ending on the earlier of (i) the effective date of termination by MethylGene of its contract for development services to be provided by the Company; (ii) May 5, 1999, unless MethylGene exercises its option to continue contracting for development services provided by the Company or (iii) May 5, 2000. As additional consideration for this nonexclusive right, MethylGene is required to pay the Company milestone amounts, as defined, and transfer 300,000 shares of MethylGene's Class B shares to the Company. The Company has placed no value on these shares. During 1998, 1999 and 2000, the Company recognized \$875,000, \$285,000 and \$72,500, respectively, of revenue related to this agreement.

On September 21, 2000, the Company sold its HSP business (Note 14). Prior to such sale, the Company supplied MethylGene with its synthetic DNA supply needs. During 1998, 1999 and 2000, the Company recognized \$810,932, \$1,641,889 and \$25,695, respectively, of product revenue from sales to MethylGene in discontinued operations. In connection with the HSP sale, the purchaser now supplies MethylGene with synthetic DNA. Also, the Company sold MethylGene a worldwide, royalty free, paid-up license to manufacture their compounds. The Company recognized approximately \$179,000 of revenue in 2000, related to this license sale. The Company's supply agreement to MethylGene was directly part of in its original license agreement to MethylGene. MethylGene has created a separate license agreement, whereby the Company receives a credit for orders placed by MethylGene with Avecia Biotechnology for its supply needs, as discussed in Note 14.

See Note 15 for subsequent events.

(8) ORIGENIX TECHNOLOGIES, INC.

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

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

On September 21, 2000, the Company sold its HSP business (Note 14). Prior to such sale, the Company supplied OriGenix with its synthetic DNA supply needs. During 1999 and 2000, the Company recognized \$16,290 and \$89,869, respectively, of product revenue from sales to OriGenix in discontinued operations. In connection with the sale of its synthetic DNA manufacturing assets, or HSP sale, the purchaser now supplies OriGenix with synthetic DNA. Also, the Company sold OriGenix a worldwide, royalty free, paid-up license to manufacture their compounds and amended its license agreement. The Company receives a credit for orders placed by OriGenix with Avecia, Inc. for its supply needs as discussed in Note 14.

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

(9) STOCKHOLDERS' EQUITY (DEFICIT)

(a) Common Stock

The Company has 100,000,000 authorized shares of common stock, \$.001 par value, of which 18,382,237 shares were issued and outstanding at December 31, 2000.

(b) 1998 Unit Financing

On May 5, 1998, the Company completed a private offering of equity securities raising total gross proceeds of \$26,681,164 from the issuance of 9,597,476 shares of common stock, 114,285 shares of Series A convertible preferred stock and warrants to purchase 3,329,486 shares of common stock at \$2.40 per share. The gross proceeds include the conversion of \$5,934,558 of accounts payable, capital lease obligations and other obligations into common stock. The Company incurred \$1,636,137 of cash expenses related to the private offering and issued 597,699 shares of common stock and warrants to purchase 1,720,825 shares of common stock at \$2.40 per share to the placement agents. The compensation received by Pillar Investment Limited (Pillar), a company affiliated with certain directors of the Company, with respect to the offshore component of the private offering consisted of (i) 9% of gross proceeds of such offshore offerings and (ii) a nonaccountable expense allowance equal to 4% of gross proceeds of such offshore offering. Pillar received \$1,636,137 and warrants to purchase 1,111,630 shares of common stock at \$2.40 per share.

In addition, Pillar was entitled to 300,000 shares of common stock, in connection with its efforts in assisting the Company in restructuring its balance sheet. The Company has recorded \$600,000 of general and administrative expense in the accompanying consolidated statement of operations during 1998, which represents the value of the common stock on May 5, 1998, with an offsetting amount to accrued expenses for the shares to be issued. These shares were issued in 1999.

(c) Units Issued to Primedica Corporation

In connection with the unit financing (see Note 9(b)), the Company issued 250,000 shares of common stock and 62,500 warrants to purchase common stock to Primedica Corporation for future services to be provided. The services shall commence upon the Company's request after (i) the Company securities are listed on a nationally recognized exchange and (ii) the average closing price of the Company's common stock is at least \$2.00 per share for the 20 day trading period preceding the contract commencement date. In the event that the Company does not use these services as a result of the failure to meet the contract conditions, Primedica shall forfeit to the Company recorded these shares as issued and outstanding during 1998 at par value. The Company reacquired and retired these shares and cancelled the associated warrants during 2000, since the Company did not use Primedica's services.

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

(d) Warrants

The Company has the following warrants outstanding and exercisable for the purchase of common stock at December 31, 2000:

| EXPIRATION DATE | OUTSTANDING AND EXERCISABLE | EXERCISE PRICE PER SHARE |
|--------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------|-------------------------------------------------|
| December 31, 2001 April 2, 2002 December 31, 2002 May 4, 2003 September 20, 2003 November 30, 2003. | 13,000 588,235 2,750,000 7,990,766 1,500,000 173,333 | \$34.49 4.25 0.60 3.10 1.08 3.00 |
| Weighted average exercise price per share | 13,015,334 ====== | \$ 2.42 |

Substantially all of such warrants were issued in connection with various equity and debt financings described herein. Pursuant to EITF Issue 00-19, Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock, the Company believes that equity classification is appropriate for all outstanding warrants.

(e) Stock Options

In 1990 and 1995, the Company established the 1990 Stock Option Plan and the 1995 Stock 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, 2000, options to purchase a total of 344,880 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% and 110% in the case of incentive stock options granted to a stockholder owning in excess of 10% of the Company's common stock, of the fair market value of the common stock as of the date of grant and (iv) the duration of the options which in the case of incentive stock options may not exceed 10 years. As of December 31, 2000, options to purchase a total of 608,515 shares of common stock remained outstanding under the 1995 Option Plan.

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

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

April 30 of each year with respect to options granted in the previous year. As of December 31, 2000, options to purchase a total of 120,000 shares of common stock remained outstanding under the Director Plan.

In May 1997, the Company adopted the 1997 Stock Option Plan and has reserved and may issue up to 8,500,000 shares for the grant of incentive and nonqualified stock options. 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 10 years. As of December 31, 2000, options to purchase a total of 4,328,438 shares of common stock remained outstanding under the 1997 Option Plan.

As of December 31, 2000, 4,223,807 options remain available for grant under the 1995 Option Plan, the Director Plan and the 1997 Option Plan.

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

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

| | NUMBER OF SHARES | WEIGHTED EXERCISE PRICE PER SHARE | |
|----------------------------------------------------------------------|----------------------------------------------------|------------------------------------------------------|------------------------------|
| Outstanding, December 31, 1997 Granted Terminated | 1,190,497 2,513,000 | \$1.25 - \$65.60 2.00 - 3.13 2.50 - 57.85 | \$36.18 2.00 |
| Outstanding, December 31, 1998 Granted Terminated | 3,460,732 | 1.25 - 65.60 | 11.25 0.85 7.53 |
| Outstanding, December 31, 1999 Granted Exercised Terminated | 5,389,550 1,351,026 (335,240) (1,003,503) | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 0.50 1.18 0.50 0.82 |
| Outstanding, December 31, 2000 | 5,401,833 | \$0.50 - \$ 2.00 | \$ 0.67 ===== |
| Exercisable, December 31, 1998 | 1,650,021 | \$1.25 - \$65.60 ======= | \$17.13 |
| Exercisable, December 31, 1999 | 2,772,099 | \$0.50 - \$ 2.00 ======= | \$ 0.50 ===== |
| Exercisable, December 31, 2000 | 3,980,476 | \$0.50 - \$ 1.25 ======= | \$ 0.60 ===== |

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

| | (| OPTIONS OUTSTANDING | | OPTIONS E | XERCISABLE |
|----------------------------------------|---------------------------------------------------------------------|-----------------------------------------------------------------|-------------------------------------------------------|--------------------------------------------------|-------------------------------------------------------|
| EXERCISE PRICES | NUMBER | WEIGHTED AVERAGE REMAINING CONTRACTUAL LIFE (YEARS) | WEIGHTED AVERAGE EXERCISE PRICE PER SHARE | NUMBER | WEIGHTED AVERAGE EXERCISE PRICE PER SHARE |
| | | | | | |
| 0\$.50 1.06 1.25 1.75 2.00 | 4,111,833 500,000 750,000 5,000 35,000 5,401,833 | 7.25 9.00 9.45 9.36 9.33 7.74 | \$0.50 1.06 1.25 1.75 2.00 \$0.67 | 3,340,080 434,715 205,681 3,980,476 | \$0.50 1.06 1.25 \$0.60 ===== |

In accordance with EITF No. 96-18, Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling Goods or Services, the Company will measure the fair value of nonemployee options as they vest using the Black-Scholes option pricing model. The Company has recorded compensation expense of \$246,444, \$231,744 and \$217,701 in 1998, 1999 and 2000, respectively, related to grants to nonemployees.

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

| | 1998 | 1999 | 2000 |
|--------------------------------------------------------------------------------------------|----------------|----------------|----------------|
| | | | |
| Average risk free interest rate Expected dividend yield | 5.15% | 6.12% | 6.39% |
| Expected lives Expected volatility Weighted Average Grant Date fair value of options | 6 years 60% | 6 years 60% | 6 years 90% |
| granted during the period (per share) | \$ 0.93 | \$ 0.37 | \$ 0.98 |

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

The pro forma effect of applying SFAS No. 123 for the three years ended December 31, 2000 would be as follows:

| | 1 | 998 | | 1999 | 2 | 2000 |
|-----------------------------------------------------------------------------------------------------------------|-----------------|--------------------|-----------------|--------------------|---------------|----------|
| Net loss applicable to common stockholders, as reported | \$(19, ===== | 792,736) ====== | \$(14) ===== | ,735 , 293) | \$(7, ==== | 009,916) |
| Pro forma net loss applicable to common stockholders, as adjusted for the effect of applying SFAS No. 123 | \$(23, ===== | 131,304) ====== | | ,647,864) | \$(8, ==== | 389,005) |
| Basic and Diluted net loss per common shares As reported | \$ | (1.67) | \$ | (0.93) | \$ | (0.40) |
| Pro forma | \$ ===== | (1.95) | \$ ===== | (1.18) | \$ ==== | (0.48) |

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

(f) Repricing

In September 1999, the Company's Board of Directors authorized the repricing of options to purchase 5,251,827 shares of common stock to \$0.50 per share, which represented the market value on the date of the repricing. These options will be subject to variable plan accounting (see Note 2(m)), as defined in FIN 44. The repriced options have been reflected as grants and cancellations in the stock option activity for the year ended December 31, 1999. FIN 44 became effective on July 1, 2000. The Company is following the provisions of FIN 44 and will remeasure the intrinsic value of the repriced options, through the earlier of the date of exercise, cancellation or expiration, at each reporting date. As of December 31, 2000, the Company has not recognized any compensation expense to date related to the repriced options, as the fair market value of the repriced option.

(g) Employee Stock Purchase Plan

In October 1995, the Company adopted the 1995 Employee Stock Purchase Plan,

under which up to 100,000 shares of common stock may be issued to participating employees of the Company, as defined, or its subsidiaries.

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

(h) Preferred Stock

The restated Certificate of Incorporation of the Company permits its Board of Directors to issue up to 5,000,000 shares of preferred stock, par value \$0.01 per share, in one or more series, to designate the number of shares constituting such series, and fix by resolution, the powers, privileges, preferences and relative, optional or special rights thereof, including liquidation preferences and dividends, and conversion and redemption rights of each such series. During 1998, the Company designated 1,500,000 shares as Series A convertible preferred stock.

(i) Series A Convertible Preferred Stock

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

Dividends

The holders of the Series A convertible preferred stock, as of March 15 or September 15, are entitled to receive dividends payable at the rate of 6.5% per annum, payable semi-annually in arrears. Such dividends shall accrue from the date of issuance of such share and shall be paid semi-annually on April 1 and October 1 of each year. Such dividends shall be paid, at the election of the Company, either in cash or additional duly

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

authorized, fully paid and non assessable shares of Series A convertible preferred stock. In calculating the number of shares of Series A convertible preferred stock to be paid with respect to each dividend, the Series A convertible preferred stock shall be valued at \$100.00 per share. During 2000, the Company recorded a total accretion of \$4,087,317 for the dividend on Series A preferred stock and issued 41,363 shares of Series A convertible preferred stock as a dividend.

Liquidation

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

Conversion

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

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

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

Mandatory Conversion

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

At any time after April 1, 2000, the Company, at its option, may redeem the Series A convertible preferred stock for cash equal to \$100.00 per share plus all accrued and unpaid dividends at such time, if the Market Trigger has occurred in the period ending three days prior to the date of notice of redemption.

(10) COMMITMENTS AND CONTINGENCIES

(a) Facilities

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

The Company vacated its Milford, Massachusetts's facility in September 2000, following the HSP Sale (see Note 14) and moved its corporate facilities to the Vassar Street facility.

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

Future approximate minimum rent payments as of December 31, 2000, under existing lease agreements through 2007, are as follows:

| 2001. 2002. 2003. 2004. 2005. Thereafter. | 620,000 611,000 611,000 611,000 |
|----------------------------------------------------------|------------------------------------------|
| | |

During 1998, 1999 and 2000, facility rent expense for continuing operations net of sublease revenue was approximately \$1,363,000, \$67,000 and \$246,000, respectively.

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

The Company has entered into consulting agreements, stock placement agreements and an advisory agreement with several companies that are controlled by two shareholders and directors of the Company including Forum, S.A. Pillar Investment N.V., Pillar S.A., formerly Commerce Consult S.A., and Pillar Investment Limited, formerly Ash Properties Limited. During 1998, 1999 and 2000, the Company recorded expenses of \$1,300,000, \$336,000 and \$74,000, respectively, under these agreements with related parties.

(c) Employment Agreements

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

(d) Contingencies

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

(11) INCOME TAXES

The Company applies SFAS No. 109, Accounting for Income Taxes. Accordingly, a deferred tax asset or liability is determined based on the difference between the financial statement and tax basis of assets and liabilities, as measured by the enacted tax rates expected to be in effect when these differences reverse. At December 31, 2000, the Company had net operating loss and tax credit carryforwards for federal income tax purposes of approximately \$235,569,000 and \$4,236,000, respectively, available to reduce federal taxable income and federal income taxes, respectively. The Tax Reform Act of 1986, 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 Tax Reform Act of 1986, which as of December 31, 2000, have resulted in ownership changes in excess of 50%, as defined under the Act and which will limit the Company's ability to utilize its net operating loss carryforwards. Ownership changes in future

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000 periods may place additional limits on the Company's ability to utilize net operating loss and tax credit carry forwards.

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 | 60,087,000 | 750,000 |
| 2018 | 21,366,000 | 500,000 |
| 2019 | 10,637,000 | 250,000 |
| 2020 | 6,825,000 | 50,000 |
| | | |
| | \$235,569,000 | \$4,236,000 |
| | | |

As of December 31, 1999 and 2000, the components of the deferred tax assets are approximately as follows:

| | 1999 | 2000 |
|------------------------------|---------------|---------------|
| | | |
| Operating loss carryforwards | \$ 91,498,000 | \$ 94,177,000 |
| Temporary differences | 3,378,000 | 1,085,000 |
| Tax credit carryforwards | 4,186,000 | 4,186,000 |
| | | |
| | 99,062,000 | 99,448,000 |
| Valuation allowance | (99,062,000) | (99,448,000) |
| | | |
| | \$ | \$ |
| | ============ | |

(12) 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 continuing operations approximately \$166,000, \$54,000 and \$47,000 during 1998, 1999 and 2000, respectively.

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HYBRIDON, INC. AND SUBSIDIARIES

(13) SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION

Supplemental disclosure of cash flow information for the following periods presented are as follows:

| | | DECEMBER 31, | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|--------------|-------------|
| | 1998 | 1999 | 2000 |
| Cash paid during the period for interest | \$ 1,666,127 | | \$ 641,132 |
| Conversion of preferred stock into common stock | | \$ 496 | \$ 1,821 |
| Conversion of line of credit into common stock | \$ | \$ | \$ 231,167 |
| Deferred compensation related to grants of stock options to nonemployees, net of terminations | \$ 109,734 | \$ | \$ (50,781) |
| Forgiveness of note receivable | \$ | \$ | \$ 270,050 |
| Issuance of Series A convertible preferred stock and attached warrants in exchange for conversion of 9% convertible subordinated notes payable and accrued interest | \$51,055,850 | \$ | \$ |
| Accretion of Series A convertible preferred stock dividends | | \$4,232,251 | |
| Issuance of common stock and attached warrants in exchange for conversion of convertible promissory notes payable | \$ 4,800,000 ======= | \$ | \$ |
| Issuance of common stock and attached warrants in exchange for conversion of accounts payable and other obligations | \$ 5,934,558 | ş | ş |
| Issuance of common stock in lieu of services | ========= \$ | \$1,000,000 | |

(14) HSP SALE

On September 21, 2000, the Company completed the sale of its Hybridon Specialty Products business, which manufactures, markets and sells oligonucleotides, to a subsidiary of Avecia, Inc. of Manchester, United Kingdom, Avecia Biotechnology, for up to \$15.0 million. The Company recorded a gain of approximately \$6.3 million on the HSP sale, comprised of net proceeds of approximately \$12.0 million less transaction and other costs of approximately \$1.2 million and the book value of the net assets sold. The remaining \$3.0 million is subject to performance under the supply agreement described below and will be recorded as a gain, net of payments for minimum purchases of product, when earned and received. The transaction costs consist principally of legal and accounting fees, severance arrangements with certain employees, and other estimated costs associated with consummating the sale. As a condition of the HSP sale requested by Avecia, the Company held a special meeting of shareholders on September 12, 2000, and obtained the approval of the HSP sale by the common and preferred stock and the debt holders.

The gain on the Asset Sale is computed as follows:

| Proceeds | | \$12,000,000 |
|--------------------------------------------|-------------|--------------|
| Property and equipment sold, net | \$4,894,887 | |
| Security deposit | 90,000 | |
| | | |
| Net book value of assets sold | 4,984,887 | |
| Current liabilities assumed by the buyer | (88,969) | |
| Long term liabilities assumed by the buyer | (324,555) | |

| Net assets sold | (4,571,363) |
|-----------------------------|--------------|
| Transaction and other costs | (1,157,578) |
| | |
| Gain on sale | \$ 6,271,059 |
| | ========== |

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

The consolidated financial statements of the Company have been restated to reflect the financial results of the Hybridon Specialty Products business as a discontinued operation for the years ended December 31, 1998, 1999, and 2000. Reported revenues, expenses and cash flows exclude the operating results of the discontinued operations. Revenues from discontinued operations for the years ended December 31, 1998, 1999 and 2000 are approximately \$1,623,000, \$5,821,000 and \$2,950,000, respectively. The net income from discontinued operations, as presented on the consolidated statement of operations for the year ended December 31, 2000, includes the gain on sale as calculated above of \$6.3 million as well as the operating loss from discontinued operations for the year ended December 31, 2000, totaling \$0.8 million. For all other years presented, the net loss relates solely to the operating results of the Hybridon Specialty Products business.

As part of this transaction, the Company entered into a supply agreement whereby it may have an obligation to purchase products from Avecia Biotechnology. To the extent that Avecia Biotechnology's third-party sales of HSP product exceed certain goals, the Company does not have any such purchase commitment. If Avecia Biotechnology's third party sales do not meet such goals, the Company must make purchases sufficient to cover the shortfall, subject to an agreed upon formula. The Company's commitment is on a "take-or-pay" basis for the fourth quarter of 2000 and each quarter of 2001. Purchases by OriGenix and MethylGene are applied against the Company's commitment. Any unpaid amounts under this agreement will reduce the \$3.0 million contingent payment to be received in September 2001. The balance of the term of this agreement (through March 31, 2003) does not require minimum purchases.

To the extent that the Company purchases products under this agreement for use in the normal course of business, the Company will record in a manner consistent with its accounting treatment for research materials (expense as incurred). To the extent that the Company makes payments for a purchasing shortfall where it has no use for the related products, the Company will record such amount as an offset against the gain to be recorded in September 2001 upon receipt of the additional \$3.0 million payment. In December 2000, the Company accrued approximately \$337,000 for its purchasing shortfall. This amount is included in receivables and accounts payable on the accompanying balance sheet.

(15) SUBSEQUENT EVENTS

(a) Investment in MethylGene, Inc.

On March 30, 2001, the Company signed a binding agreement with unrelated institutional investors, providing for the sale of 60% of the Company's holdings of shares of Class A and Class B stock of MethylGene. The agreement covers a total of 2,350,000 such shares and provides a purchase price of Canadian \$2.85 (approximately \$1.81 US Dollars as of March 30, 2001) per share or approximately US \$4.3 million in the aggregate. Closing of the transaction is subject to the satisfaction of various conditions, including waivers by MethylGene's shareholders of rights of first refusal which have now been executed by MethyGene's shareholders and received by the Company. The Company has given an option, exercisable at any time prior to April 30, 2001, to MethylGene and its shareholders to purchase the balance of its holdings of MethylGene stock at Canadian \$2.85 per share. If all of these shares were purchased, the Company would receive an additional sum of approximately US \$2.9 million.

The Company's holdings of MethylGene shares were subject to the security interest of its 8% Convertible Notes due 2002 and its \$6.0 million Notes due 2003. (See Note 15(b) and (c))

(b) 8% Convertible Notes Payable

On March 5, 2001, the Company made an offer to the holders of its 8% Convertible Notes due 2002 to exchange their notes for one share of a newly-designated class of Series B Convertible Preferred Stock (par value \$.01 per share) for each \$100 in principal amount of notes tendered. At the offer's expiration date of

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HYBRIDON, INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED) DECEMBER 31, 2000

March 30, 2001, holders of \$6.9 million out of a total of \$7.5 million in principal amount of notes outstanding accepted the exchange offer which has been declared effective. Shares of the Series B Convertible Preferred Stock have a face value of \$100 per share and are senior in right of payment in regards to liquidation distributions and dividends to the Company's Series A Convertible Preferred Stock and common stock. Such shares will accrue dividends at the rate of 8% per annum which are payable in kind or in cash at the Company's option. Shares of Series B Convertible Preferred Stock are convertible into shares of common stock at an initial rate of one share of Series B Convertible Preferred Stock for 200 shares of common stock.

For interest calculation purposes, 8% notes submitted for exchange were deemed exchanged as of March 5, 2001. Under the offer, all accrued but unpaid interest on the exchanged notes will be paid through March 5, 2001 by issuing additional notes in an aggregate principal amount equal to the amount of accrued but unpaid interest. These additional notes were tendered for exchange by the noteholders participating in the offer. Dividends on shares of Series B Convertible Preferred Stock will begin to accrue on March 6, 2001.

As a result of the exchange offer, the Company has become entitled to the unrestricted use of \$5.0 million, which were proceeds from the sale of its HSP business. These proceeds had been pledged to secure the Company's obligations under the 8% notes and the \$6.0 million notes.

(c) Note Payable

On March 28, 2001, the Company entered into an agreement with the holders of its \$6.0 million of notes due 2003 whereby it would pay, out of the proceeds of the sale of its MethylGene shares, (Note 15(a)) \$1.8 million to the holders in partial satisfaction of the notes. In addition, the Company agreed that it would deposit up to another \$1.2 million in a money market account for the purpose of securing payment of the balance of the outstanding notes and the sum of \$811,000 to secure the payment of the balance remaining on notes held by a particular lender group. This arrangement was made to encourage the holders of these notes to release their security interest in the MethylGene shares. If more than 60% of its holdings of MethylGene shares are sold, Hybridon will pay off additional notes up to a total of \$3,000,000 and the \$1,200,000 of money market funds securing the notes would decrease proportionately.

Exhibit No. 3.4

CERTIFICATE OF DESIGNATION for SERIES B CONVERTIBLE PREFERRED STOCK of HYBRIDON, INC.

Pursuant to Section 151 of the General Corporation Law of the State of Delaware

HYBRIDON, INC., a corporation organized and existing under the laws of the State of Delaware (the "Corporation"), does hereby certify that pursuant to the authority conferred on the board of directors of the Corporation (the "Board of Directors") by the Restated Certificate of Incorporation, as amended (the "Certificate of Incorporation") of the Corporation and in accordance with Section 151 of the General Corporation Law of the State of Delaware, the Board of Directors adopted the following resolution establishing a series of 85,000 shares of preferred stock of the Corporation designated as "Series B Convertible Preferred Stock":

RESOLVED, that pursuant to the authority conferred on the Board of Directors by the Certificate of Incorporation, a series of preferred stock, par value \$.01 per share, of the Corporation is hereby established and created, and that the designation and number of shares thereof and the voting and other powers, preferences and relative participating, optional or other special rights of, the shares of such series and the qualifications, limitations and restrictions thereof are as follows:

Series B Convertible Preferred Stock

1. Designation and Amount and Definitions. (a) There shall be a series of Preferred Stock designated as "Series B Convertible Preferred Stock" and the number of shares constituting such series shall be 85,000. Such series is referred to herein as the "Series B Preferred Stock". Notwithstanding any other provision in this Certificate of Designation of the Series B Preferred Stock (the "Certificate of Designation") to the contrary, such series shall be senior to the common stock, par value \$.001 per share of the Corporation (the "Common Stock"), and the Series A Convertible Preferred Stock, \$.01 par value per share, of the Corporation (the "Series A Preferred Stock"), with respect to dividends and the distribution of assets upon liquidation, dissolution or winding up. Such number of shares may be increased or decreased by resolution of the Board of Directors, subject to the provisions of Section 7 hereof; provided, however, that no decrease shall reduce the number of shares of Series B Preferred Stock to fewer than the number of shares then issued and outstanding.

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(b) As used in this Certificate of Designation, except as otherwise provided in Subsection 4(c), the following terms shall have the following meanings:

(i) "Closing Bid Price" for any security for each trading day shall be the reported per share closing bid price of such security regular way on the Stock Market on such trading day, or, if there were no transactions on such trading day, the average of the reported closing bid and asked prices, regular way, of such security on the relevant Stock Market on such trading day.

(ii) "Fair Market Value" of any asset (including any security) means the fair market value thereof as mutually determined by the Corporation and the holders of a majority of the Series B Preferred Stock then outstanding. If the Corporation and the holders of a majority of the Series B Preferred Stock then outstanding are unable to reach agreement on any valuation matter, such valuation shall be submitted to and determined by a nationally recognized independent investment bank selected by the Board of Directors and the holders of a majority of the Series B Preferred Stock then outstanding (or, if such selection cannot be agreed upon promptly, or in any event within ten (10) days, then such valuation shall be made by a nationally recognized independent investment banking firm selected by the American Arbitration Association in New York City in accordance with its rules), the costs of which valuation shall be paid for by the Corporation.

(iii) "Market Price" shall mean the average Closing Bid Price for twenty (20) consecutive trading days, ending with the trading day prior to the date as of which the Market Price is being determined (with appropriate adjustments for subdivisions or combinations of shares effected during such period), provided that if the prices referred to in the definition of Closing Bid Price cannot be determined on any trading day, the Closing Bid Price for such trading day will be deemed to equal Fair Market Value of such security on such trading day.

 $({\rm iv})$ "Registered Holders" shall mean, at any time, the holders of record of the Series B Preferred Stock.

(v) "Stock Market" shall mean, with respect to any security, the principal national securities exchange on which such security is listed or admitted to trading or, if such security is not listed or admitted to trading on any national securities exchange, shall mean The Nasdaq National Market System ("NNM") or The Nasdaq SmallCap Market ("SCM" and, together with NNM, "Nasdaq") or, if

such security is not quoted on Nasdaq, shall mean the OTC Bulletin Board or, if such security is not quoted on the OTC Bulletin Board, shall mean the over-the-counter market as furnished by any NASD member firm selected from time to time by the Corporation for that purpose.

(vi) "Trading Day" shall mean a day on which the relevant Stock Market is open for the transaction of business.

2. Dividends and Distributions. (a) The holders, as of the Dividend Record Date (as defined below), of the Series B Preferred Stock shall be entitled to receive semi-annual dividends on their respective shares of Series B Preferred Stock (aggregating, for this purpose, all shares of Series B Preferred Stock held of record or, to the Corporation's knowledge, beneficially by such holder), payable, at the option of the Corporation, in cash or additional shares of Series B Preferred Stock, at the rate of 8% per annum (computed on the basis of a 360-day year of twelve 30 day months) of the Dividend Base Amount (as defined below), payable semi-annually in arrears; provided that, to the extent the declaration or payment of such dividend is prohibited by applicable law, such dividend need not be paid but shall nevertheless accrue and shall be paid promptly when applicable law permits. Such dividends shall accrue (i) from March 6, 2001 for shares of Series B Preferred Stock issued within thirty days of the date of the filing of this Certificate of Designation, or (ii) from the date of issuance for shares of Series B Preferred Stock issued after thirty days from the date of filing of this Certificate of Designation, and shall be paid semi-annually on April 1 and October 1 of each year or, if any such day is not a business day, on the next succeeding business day. Such dividends shall be paid, at the election of the Corporation, either in cash or additional duly authorized, fully paid and non assessable shares of Series B Preferred Stock. In calculating the number of shares of Series B Preferred Stock to be paid with respect to each dividend, the Series B Preferred

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Stock shall be valued at \$100.00 per share (subject to appropriate adjustment to reflect any stock split, combination, reclassification or reorganization of the Series B Preferred Stock). Notwithstanding the foregoing, the Corporation shall not be required to issue fractional shares of Series B Preferred Stock; the Corporation may elect, in its sole discretion, independently for each holder, whether such number of shares (on an aggregated basis) will be rounded to the nearest whole share (with .5 of a share rounded upward) or whether such holder will be given cash in lieu of any fractional shares. The "Dividend Base Amount" of a share of Series B Preferred Stock shall be \$100.00 plus all accrued but unpaid dividends (subject to appropriate adjustment to reflect any stock split, combination, reclassification or reorganization of the Series B Preferred Stock). The "Dividend Record Date" shall mean, for each semi-annual dividend, the March 15 or September 15, as the case may be, immediately preceding the dividend payment date.

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(b) In addition to the foregoing, subject to the rights of the holders of any shares of any series or class of capital stock ranking prior, and superior to, or pari passu with, the shares of Series B Preferred Stock with respect to dividends, and prior to the rights of the holders of Common Stock, Series A Preferred Stock and any other series or class of capital stock, the holders of shares of Series B Preferred Stock shall be entitled to receive, as, when and if declared by the Board of Directors, out of assets legally available for that purpose, dividends or distributions in cash, stock or otherwise.

(c) The Corporation shall not declare or pay any dividend or distribution on any Junior Stock (as defined below) of the Corporation unless all dividends required by Section 2(a) have been or contemporaneously are declared and paid, or declared and a sum sufficient for the payment thereof set apart for such payment, on the Series B Preferred Stock.

(d) [Reserved]

(e) All dividends or distributions declared upon the Series B Preferred Stock shall be declared pro rata per share.

(f) Any reference to "distribution" contained in this Section 2 shall not be deemed to include any distribution made in connection with or in lieu of any Liquidation Event (as defined below).

(g) No interest, or sum of money in lieu of interest, shall be payable in respect of any dividend payment or payments on the Series B Preferred Stock which may be in arrears (it being understood that this provision does not alter the Corporation's obligations under Section 2(a)).

(h) So long as any shares of the Series B Preferred Stock are outstanding, no dividends, except as described in the next succeeding sentence, shall be declared or paid or set apart for payment on any class or series of stock of the Corporation ranking, as to dividends, on a parity with the Series B Preferred Stock, for any period unless all dividends have been or contemporaneously are declared and paid, or declared and a sum sufficient for the payment thereof set apart for such payment, on the Series B Preferred Stock. When dividends are not paid in full or a sum sufficient for such payment is not set apart, as aforesaid, upon the shares of the Series B Preferred Stock and any other class or series of stock ranking on a parity as to dividends with the Series B Preferred Stock, all dividends declared upon such other stock shall be declared pro rata so that the amounts of dividends per share declared on the Series B Preferred Stock and such other stock shall in all cases bear to each other the same ratio that accrued dividends per share

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on the shares of the Series $\ensuremath{\mathsf{B}}$ Preferred Stock and on such other stock bear to each other.

(i) So long as any shares of the Series B Preferred Stock are outstanding, no other stock of the Corporation ranking on a parity with the Series B Preferred Stock as to dividends or upon liquidation, dissolution or winding up shall be redeemed, purchased or otherwise acquired for any consideration (or any moneys be paid to or made available for a sinking fund or otherwise for the purchase or redemption of any shares of any such stock) by the Corporation unless the dividends, if any, accrued on all outstanding shares of the Series B Preferred Stock shall have been paid or set apart for payment.

(j) "Junior Stock" shall mean the Common Stock, Series A Preferred Stock, and any shares of preferred stock of any series or class of the Corporation, whether presently outstanding or hereafter issued, which are junior to the shares of Series B Preferred Stock with respect to (i) the distribution of assets on any voluntary or involuntary liquidation, dissolution or winding up of the Corporation, (ii) dividends or (iii) voting.

3. Liquidation Preference. (a) In the event of a (i) liquidation, dissolution or winding up of the Corporation, whether voluntary or involuntary, (ii) a sale or other disposition of all or substantially all of the assets of the Corporation or (iii) any consolidation, merger, combination, reorganization or other transaction in which the Corporation is not the surviving entity or shares of Common Stock constituting in excess of 50% of the voting power of the Corporation are exchanged for or changed into stock or securities of another entity, cash and/or any other property (a "Merger Transaction") (items (i), (ii) and (iii) of this sentence being collectively referred to as a "Liquidation Event"), after payment or provision for payment of debts and other liabilities of the Corporation, the holders of the Series B Preferred Stock then outstanding shall be entitled to be paid out of the assets of the Corporation available for distribution to its stockholders, whether such assets are capital, surplus, or earnings, before any payment or declaration and setting apart for payment of any amount shall be made in respect of any Junior Stock of the Corporation, an amount equal to the Dividend Base Amount at such time; provided, however, in the case of a Merger Transaction, such payment may be made in cash, property (valued as provided in Subsection 3(b)) and/or securities (valued as provided in Subsection 3(b)) of the entity surviving such Merger Transaction. In the case of property or in the event that any such securities are subject to an investment letter or other similar restriction on transferability, the value of such property or securities shall be determined by agreement between the Corporation and the holders of a majority of the Series B Preferred Stock then outstanding. If upon any Liquidation Event, whether voluntary or involuntary, the assets to be distributed to the holders of the Series B Preferred Stock shall be insufficient to

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permit the payment to such shareholders of the full preferential amounts aforesaid, then all of the assets of the Corporation to be distributed shall be so distributed ratably to the holders of the Series B Preferred Stock on the basis of the number of shares of Series B Preferred Stock held. Notwithstanding item (iii) of the first sentence of this Subsection $\Im(a)$, any consolidation, merger, combination, reorganization or other transaction in which the Corporation is not the surviving entity but the stockholders of the Corporation immediately prior to such transaction own in excess of 50% of the voting power of the corporation surviving such transaction and own amongst themselves such interest in substantially the same proportions as prior to such transaction, shall not be considered a Liquidation Event provided that the surviving corporation shall make appropriate provisions to ensure that the terms of this Certificate of Designation survive any such transaction. All shares of Series B Preferred Stock shall rank as to payment upon the occurrence of any Liquidation Event senior to the Common Stock, the Series A Preferred Stock, and, unless the terms of such series shall provide otherwise, senior to all other series of the Corporation's preferred stock.

(b) Any securities or other property to be delivered to the holders of the Series B Preferred Stock pursuant to Subsection 3(a) hereof shall be valued as follows:

(i) Securities not subject to an investment letter or other similar restriction on free marketability:

(A) If actively traded on a Stock Market, the per share value shall be deemed to be the Market Price of such securities as of the third day prior to the date of

valuation.

(B) If not actively traded on a Stock Market, the value shall be the Fair Market Value of such securities.

(ii) For securities for which there is an active public market but which are subject to an investment letter or other restrictions on free marketability, the value shall be the Fair Market Value thereof, determined by discounting appropriately the per share Market Price thereof.

(iii) For all other securities, the value shall be the Fair Market Value thereof.

4. Conversion.

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(a) Right of Conversion. The shares of Series B Preferred Stock are convertible, in whole or in part, at the option of the holder thereof and upon notice to the Corporation as set forth in Subsection 4(b), into fully paid and nonassessable shares of Common Stock and such other securities and property as hereinafter provided. The initial conversion price per share of Common Stock (the "Conversion Price"), shall be \$.50, subject to adjustment as provided herein. The rate at which each share of Series B Preferred Stock is convertible at any time into Common Stock (the "Conversion Rate") shall be determined by dividing the then existing Conversion Price (determined in accordance with this Section 4, including the last paragraph hereof) into the Dividend Base Amount.

(b) Conversion Procedures. Any holder of shares of Series B Preferred Stock desiring to convert such shares into Common Stock shall surrender the certificate or certificates evidencing such shares of Series B Preferred Stock at the office of the transfer agent for the Series B Preferred Stock, which certificate or certificates, if the Corporation shall so require, shall be duly endorsed to the Corporation or in blank, or accompanied by proper instruments of transfer to the Corporation or in blank, accompanied by irrevocable written notice to the Corporation that the holder elects so to convert such shares of Series B Preferred Stock and specifying the name or names (with address) in which a certificate or certificates evidencing shares of Common Stock are to be issued. The Corporation need not deem a notice of conversion to be received unless the holder complies with all the provisions hereof. The Corporation will instruct the transfer agent (which may be the Corporation) to make a notation of the date that a notice of conversion is received, which date of receipt shall be deemed to be the date of receipt for purposes hereof.

The Corporation shall, as soon as practicable after such deposit of certificates evidencing shares of Series B Preferred Stock accompanied by the written notice and compliance with any other conditions herein contained, deliver at such office of such transfer agent to the person for whose account such shares of Series B Preferred Stock were so surrendered, or to the nominee or nominees of such person, certificates evidencing the number of full shares of Common Stock to which such person shall be entitled as aforesaid, subject to Section 4(d). Subject to the following provisions of this paragraph, such conversion shall be deemed to have been made as of the date of such surrender of the shares of Series B Preferred Stock to be converted, and the person or persons entitled to receive the Common Stock deliverable upon conversion of such Series B Preferred Stock shall be treated for all purposes as the record holder or holders of such Common Stock on such date; provided, however, that the Corporation shall not be required to convert any shares of Series B Preferred Stock while the stock transfer books of the Corporation are closed for any purpose, but the surrender of Series B Preferred Stock for conversion during any period while such books are so closed shall become effective for

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conversion immediately upon the reopening of such books as if the surrender had

been made on the date of such reopening, and the conversion shall be at the conversion rate in effect on such date. No adjustments in respect of any dividends on shares surrendered for conversion or any dividend on the Common Stock issued upon conversion shall be made upon the conversion of any shares of Series B Preferred Stock.

The Corporation shall at all times, reserve and keep available out of its authorized but unissued shares of Common Stock, solely for the purpose of effecting the conversion of the shares of Series B Preferred Stock, such number of shares of Common Stock as shall from time to time be sufficient to effect the conversion of all outstanding shares of the Series B Preferred Stock.

All notices of conversion shall be irrevocable; provided, however, that if the Corporation has sent notice of an event pursuant to Subsection 4(g) hereof, a holder of Series B Preferred Stock may, at its election, provide in its notice of conversion that the conversion of its shares of Series B Preferred Stock shall be contingent upon the occurrence of the record date or effectiveness of such event (as specified by such holder), provided that such notice of conversion is received by the Corporation prior to such record date or effective date, as the case may be.

(c) Adjustment of Conversion Rate and Conversion Price.

(i) As used in this Subsection 4(c), the following terms shall have the following meanings:

"Capital Stock" of any Person means the Common Stock or Preferred Stock of such Person. Unless otherwise stated herein or the context otherwise requires, "Capital Stock" means Capital Stock of the Corporation; "Common Stock" of any Person other than the Corporation means the common equity (however designated), including, without limitation, common stock or partnership or membership interests of, or participation or interests in such Person (or equivalents thereof).

"Common Stock" of the Corporation means the Common Stock, par value \$.001 per share, of the Corporation, any successor class or classes of common equity (however designated) of the Corporation into or for which such Common Stock may hereafter be converted, exchanged or reclassified and any class or classes of common equity (however designated) of the Corporation which may be distributed or issued with respect to such Common Stock or successor class of classes to holders thereof generally. Unless otherwise stated herein or the

context requires otherwise, "Common Stock" means Common Stock of the Corporation;

"Current Market Price" means, when used with respect to any security as of any date, the last sale price, regular way, or, in case no such sale takes place on such date, the average of the closing bid and asked prices, regular way, of such security in either case as reported for consolidated transactions on the New York Stock Exchange or, if such security is not listed or admitted to trading on the New York Stock Exchange, as reported for consolidated transactions with respect to securities listed on the principal national securities exchange on which such security is listed or admitted to trading or, if such security is not listed or admitted to trading on any national securities exchange, as reported on the Nasdaq National Market, or, if such security is not listed or admitted to trading on the Nasdaq National Market, as reported on the Nasdaq SmallCap Market, or if such security is not listed or admitted to trading on any national

securities exchange or the Nasdaq National Market or the Nasdaq SmallCap Market, the average of the high bid and low asked prices of such security in the over-the-counter market, as reported by the National Association of Securities Dealers, Inc. Automated Quotations System or such other system then in use or, if such security is not quoted by any such organization, the average of the closing bid and asked prices of such security furnished by an NASD member firm selected by the Corporation. If such security is not quoted by any such organization and no such NASD member firm is able to provide such prices, the Current Market Price of such security shall be the Fair Market Value thereof;

"Fair Market Value" means, at any date as to any asset, Property or right (including without limitation, Capital Stock of any Person, evidence of indebtedness or other securities, but excluding cash), the fair market value of such item as determined in good faith by the Board of Directors, whose determination shall be conclusive; provided, however, that such determination is described in an Officers' Certificate filed with the transfer agent and that, if there is a Current Market Price for such item on such date, "Fair Market Value" means such Current Market Price (without giving effect to the last sentence of the definition thereof);

"GAAP" means, as of any date, generally accepted accounting principles in the United States and does not include any $% \left({\left[{{{\rm{AP}}} \right]_{\rm{AP}}} \right)$

interpretations or regulations that have been proposed but that have not become effective;

"Officer" means, with respect to any Person, the Chairman of the Board, the Chief Executive Officer, the President, the Chief Operating Officer, the Chief Financial Officer, the Treasurer, any Assistant Treasurer, the Controller, the Secretary, any Assistant Secretary or any Vice President of such Person;

"Officers' Certificate" means a certificate signed on behalf of the Corporation by two Officers, one of whom must be the Chairman of the Board, the President, the Treasurer or a Vice-President of the Corporation;

"Person" means any individual, corporation, partnership, association, trust or any other entity or organization, including a government or political subdivision or any agency or instrumentality thereof;

"Preferred Stock" of any Person means the class or classes of equity, ownership or participation interests (however designated) in such Person, including, without limitation, stock, share, partnership and membership interests, which are preferred as to the payment of dividends or distributions by, or as to the distribution of assets upon any voluntary or involuntary liquidation or dissolution of, such Person (or equivalent thereof) over interests of any other class of interests of such Person. Unless otherwise stated herein or the context otherwise requires, "Preferred Stock" means Preferred Stock of the Corporation;

"Property" of any Person means any and all types of real, personal, tangible, intangible or mixed property owned by such Person whether or not included on the most recent consolidated balance sheet of such Person in accordance with GAAP; "Subsidiary" of a Person on any date means any other Person of whom such Person owns, directly or indirectly through a Subsidiary or Subsidiaries of such Person, Capital Stock with voting power, acting independently and under ordinary circumstances, entitling such person to elect a majority of the board of directors or other governing body of such other Person. Unless otherwise stated herein or the context otherwise requires, "Subsidiary" means a Subsidiary of the Corporation.

(ii) If the Corporation shall (i) pay a dividend or other distribution, in Common Stock, on any class of Capital Stock of the Corporation, (ii) subdivide the outstanding Common Stock into a greater number of shares by any means or (iii) combine the outstanding Common Stock into a smaller number of shares by any means including, without limitation, a reverse stock split), then in each such case the Conversion Price in effect immediately prior thereto shall be adjusted so that the Registered Holder of any shares of Series B Preferred Stock thereafter surrendered for conversion shall be entitled to receive the number of shares of Common Stock that such Registered Holder would have owned or have been entitled to receive upon the happening of such event had such Series B Preferred Stock been converted immediately prior to the relevant record date or, if there is no such record date, the effective date of such event. An adjustment made pursuant to this Paragraph 4(c)(ii) shall become effective immediately after the record date for the determination of stockholders entitled to receive such dividend or distribution and shall become effective immediately after the effective date of such subdivision or combination, as the case may be.

(iii) If the Corporation shall (i) issue or distribute (at a price per share less than the Current Market Price per share of such Capital Stock on the date of such issuance or distribution) Capital Stock generally to holders of Common Stock or to holders of any class or series of Capital Stock which is convertible into or exchangeable or exercisable for Common Stock (excluding an issuance or distribution of Common Stock described in Paragraph 4(c)(ii)) or (ii) issue or distribute generally to such holders rights, warrants, options or convertible or exchangeable securities entitling the holder thereof to subscribe for, purchase, convert into or exchange for Capital Stock at a price per share less than the Current Market Price per share of such Capital Stock on the date of issuance or distribution, then, in each such case, at the earliest of (A) the date the Corporation enters into a firm contract for such issuance or distribution, (B) the record date for the determination of stockholders entitled to receive any such Capital Stock or any such rights, warrants, options or convertible or exchangeable securities or (C) the date of actual issuance or distribution of any such Capital Stock or any such rights, warrants, options or convertible or exchangeable securities, the Conversion Price shall be reduced by multiplying the Conversion Price in effect immediately prior to such earliest date by:

> (A) if such Capital Stock is Common Stock, a fraction the numerator of which is the number of shares of Common Stock outstanding, on such earliest date plus the number of shares of Common Stock which could be purchased at the Current Market Price per share of Common Stock on the date of such issuance or distribution with the aggregate consideration (based on the Fair Market Value thereof) received or

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receivable by the Corporation either (A) in connection with such issuance or distribution or (B) upon the conversion, exchange, purchase or subscription of all such rights, warrants, options or convertible or exchangeable securities (the "Aggregate Consideration"), and the denominator of which is the number of shares of Common Stock outstanding on such earliest date plus the number of shares of Common Stock to be so issued or distributed or to be issued upon the conversion, exchange, purchase or subscription of all such rights, warrants, options or convertible or exchangeable securities; or

(B) if such Capital Stock is other than Common Stock, a fraction the numerator of which is the Current Market Price per share of Common Stock on such earliest date minus an amount equal to (A) the difference between (1) the Current Market Price per share of such Capital Stock multiplied by the number of shares of such Capital Stock to be so issued and (2) the Aggregate Consideration, divided by (B) the number of shares of Common Stock outstanding on such date, and the denominator of which is the Current Market Price per share of Common Stock on such earliest date.

Such adjustment shall be made successively whenever any such Capital Stock, rights, warrants, options or convertible or exchangeable securities are so issued or distributed. In determining whether any rights, warrants, options or convertible or exchangeable securities entitle the holders thereof to subscribe for, purchase, convert into or exchange for shares of such Capital Stock at less than such Current Market Price, there shall be taken into account the Fair Market Value of any consideration received or receivable by the Corporation for such rights, warrants, options or convertible or exchangeable securities. If any right, warrant, option or convertible or exchangeable security, the issuance of which resulted in an adjustment in the Conversion Price pursuant to this Paragraph 4(c)(iii), shall expire and shall not have been exercised, the Conversion Price shall immediately upon such expiration be recomputed to the Conversion Price which would have

been in effect if such right, warrant, option or convertible or exchangeable securities had never been distributed or issued. Notwithstanding anything contained in this paragraph to the contrary, (i) the issuance of Capital Stock upon the exercise of such rights, warrants or options or the conversion or exchange of such convertible or exchangeable securities will not cause an adjustment in the Conversion Price if no such adjustment would have been required at the time such right, warrant, option or convertible or exchangeable security was issued or distributed; provided, however, that, if the consideration payable upon such exercise, conversion or exchange and/or the Capital Stock receivable thereupon are changed after the time of the issuance or distribution of such right, warrant, option or convertible or exchangeable security then such change shall be deemed to be the expiration thereof without having been exercised and the issuance or distribution of new options, rights, warrants or convertible or exchangeable securities and (ii) the issuance of convertible preferred stock of the Corporation as a dividend on convertible preferred stock of the Corporation will not cause an adjustment in the Conversion Price if no such adjustment would have been required at the time such underlying

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convertible preferred stock was issued (or as a result of any subsequent modification to the terms thereof) and the conversion provisions of such convertible stock so issued as a dividend are the same as in such underlying convertible preferred stock.

Notwithstanding any contained in this Certificate of Designation to the contrary, options, rights or warrants issued or distributed by the Corporation, including options, rights or warrants distributed prior to the date of filing of this Certificate of Designation, to holders of Common Stock generally which, until the occurrence of a specified event or events (a "Trigger Event"), (i) are deemed to be transferred with Common Stock, (ii) are not exercisable and (iii) are also issued on a pro rata basis with respect to future issuances of Common Stock, shall be deemed not to have been issued or distributed for purposes of this Subsection 4(c) (and no adjustment to the Conversion Price under this Subsection 4(c) will be required) until the occurrence of the earliest Trigger Event. Upon the occurrence of a Trigger Event, such options, rights or warrants shall continue to be deemed not to have been issued or distributed for purposes of this Subsection 4(c) (and no adjustment to the Conversion Price under this Subsection 4(c) will be required) if and for so long as each Registered Holder who thereafter converts such Registered Holder's Series B Preferred Stock shall be entitled to receive upon such conversion, in addition to the shares of Common Stock issuable upon such conversion,

a number of such options, rights or warrants, as the case may be, equal to the number of options, rights or warrants to which a holder of the number of shares of Common Stock equal to the number of shares of Common Stock issuable upon conversion of such Registered Holder's Series B Preferred Stock is entitled to receive at the time of such conversion in accordance with the terms and provisions of, and applicable to, such options, rights or warrants. Upon the expiration of any such options, rights or warrants or at such time, if any, as a Registered Holder is not entitled to receive such options, rights or warrants upon conversion of such Registered Holder's Series B Preferred Stock, an adjustment (if any is required) to the Conversion Price shall be made in accordance with this Paragraph 4(c)(iii) with respect to the issuance of all such options, rights and warrants as of the date of issuance thereof, but subject to the provisions of the preceding paragraph, if any such option, right or warrant, including any such options right or warrants distributed prior to the date of filing of this Certificate of Designation, are subject to events, upon the occurrence of which such options, rights or warrants become exercisable to purchase different securities, evidence of indebtedness, cash, Properties or other assets or different amounts thereof, then, subject to the preceding provision of this paragraph, the date of the occurrence of any and each such event shall be deemed to be the date of distribution and record date with respect to new options, right or warrants with such new purchase rights (and a termination or expiration of the existing options, rights or warrants without exercise thereof). In addition, in the event of any distribution (or deemed distribution) of options, rights or warrants, or any Trigger Event or other event of the type described in the preceding sentence, that required (or would have required but for the provisions of Paragraph 4(c)(vi) or this paragraph) an adjustment to the Conversion Price under this Subsection 4(c) and such options, rights or warrants shall thereafter have been redeemed or repurchased without having been exercised, then the Conversion Price shall be adjusted upon such redemption or repurchase to give effect

to such distribution, Trigger Event or other event, as the case may, as though it had instead been a cash distribution, equal on a per share basis to the result of the aggregate redemption or repurchase price received by holders of such options, rights or warrants divided by the number of shares of Common Stock outstanding as of the date of such repurchase or redemption, made to holders of Common Stock generally as of the date of such redemption or repurchase.

(iv) If the Corporation shall pay or distribute, as a dividend or otherwise, generally to holders of Common Stock or any class or series of Capital Stock which is convertible into or exercisable or exchangeable for Common Stock any assets, Properties or rights (including, without limitation, evidences of indebtedness of the Corporation, any Subsidiary or any other Person, cash or Capital Stock or other securities of the Corporation, any Subsidiary or any other Person, but excluding payments and distributions as described in Paragraphs 4(c)(ii) or (iii), dividends and distributions in connection with a Liquidation Event and distributions consisting solely of cash described in Paragraph 4(c)(v), then in each such case the Conversion Price shall be reduced by multiplying the Conversion Price in effect immediately prior to the date of such payment or distribution by a fraction, the numerator of which is the Current Market Price per share of Common Stock on the record date for the determination of stockholders entitled to receive such payment or distribution less the Fair Market Value per share of Common Stock on such record date of the assets, Properties or rights so paid or distributed, and the denominator of which is the Current Market Price per share of Common Stock on such record date. Such adjustment shall become effective immediately after such record date. For purposes of this Paragraph 4(c)(iv), such Fair Market Value per share shall equal the aggregate Fair Market Value on such record date of the assets, Properties or rights so paid or distributed divided by the number of shares of Common Stock outstanding on such record date. For all purposes of this Certificate of Designation, adjustments to any security's conversion or exercise price pursuant to such security's original terms shall not be deemed a distribution or dividend to holders thereof.

(v) If the Corporation shall, by dividend or otherwise, make a distribution (other than in connection with the liquidation, dissolution or winding up of the Corporation in its entirety), generally to holders of Common Stock or any class or series of Capital Stock which is convertible into or exercisable or exchangeable for Common Stock, consisting solely of cash where (x) the sum of (i) the aggregate amount for such cash plus (ii) the aggregate amount of all cash so distributed (by dividend or otherwise) to such holders within the 12-month period ending on the record date for determining stockholder entitled to receive such distribution with respect to which no adjustment has been made to the Conversion Price pursuant to this Paragraph 4(c)(v) exceeds (y) 10% of the result of the multiplication of (1) the Current Market Price per share of Common Stock on such record date times (2)

the number of shares of Common Stock outstanding on such record date, then the Conversion Price shall be reduced, effective immediately prior to the opening of business on the day following such record date, by multiplying the Conversion Price in effect immediately prior to the close of business on the day prior to such record date by a fraction, the numerator of which is the Current Market Price per share of Common Stock on such record date less the aggregate amount of cash per

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share so distributed and the denominator of which is such Current Market Price; provided, however, that, if the aggregate amount of cash per share is equal to or greater than such Current Market Price, then, in lieu of the foregoing adjustment, adequate provisions shall be made so that each Registered Holder shall have the right to receive upon conversion (with respect to each share of Common Stock issued upon such conversion and in addition to the Common Stock issuable upon conversion) the aggregate amount of cash per share such Registered Holder would have received had such Registered Holder's Series B Preferred Stock been converted immediately prior to such record date. In no event shall the Conversion Price be increased pursuant to this Paragraph 4(c)(v); provided, however, that if such distribution is not so made, the Conversion Price shall be adjusted to be the Conversion Price which would have been in effect if such distribution had not been declared. For purposes of this Paragraph 4(c)(v), such aggregate amount of cash per share shall equal such sum divided by the number of shares of Common Stock outstanding on such record date.

(vi) The provisions of this Subsection 4(c) shall similarly apply to all successive events of the type described in this Subsection 4(c). Notwithstanding anything contained herein to the contrary, no adjustment in the Conversion Price shall be required unless such adjustment would require an increase or decrease of at least 1% in the Conversion Price then in effect; provided, however, that any adjustments which by reason of this Paragraph 4(c)(vi) are not required to be made shall be carried forward and taken into account in any subsequent adjustment. All calculations under this Section 4 shall be made by the Corporation and shall be made to the nearest cent or to the nearest one hundredth of a share, as the case may be, and the transfer agent shall be entitled to rely conclusively thereon. Except as provided in this Section 4, no adjustment in the Conversion Price will be made for the issuance of Common Stock or any securities convertible into or exchangeable for Common Stock or carrying the right to purchase Common Stock or any securities so convertible or exchangeable.

(vii) Whenever the Conversion Price is adjusted as provided herein, the Corporation shall promptly file with the transfer agent an Officers' Certificate setting forth the Conversion Price in effect after such adjustment and setting forth a brief statement of the facts requiring such adjustment. Promptly after delivery of such Officers' Certificate, the Corporation shall give or cause to be given to each Registered Holder a notice of such adjustment of the Conversion Price setting forth the adjusted Conversion Price and the date on which such adjustment becomes effective.

(viii) Notwithstanding anything contained herein to the contrary, in any case in which this Subsection 4(c) provides that an adjustment in the Conversion Price shall become effective immediately after a record date for an event, the Corporation may defer until the occurrence of such event (i) issuing to the Registered Holder of any Series B Preferred Stock converted after such record date and before the occurrence of such event the additional shares of Common Stock issuable upon such conversion by reason of the adjustment required by such event over and above the number of shares of Common Stock issuable upon such conversion before giving effect to such adjustment and (ii) paying to such Registered Holder any amount in cash in lieu of any fractional share of Common Stock pursuant to Subsection 4(d). (ix) Notwithstanding any other provision hereof, no adjustment to the Conversion Price shall be made upon the issuance or exercise or conversion of (1) any Capital Stock issued or cash paid as dividends on the Series B Preferred Stock, or (2) any Capital Stock issued or cash paid upon the mandatory conversion or redemption of any Series B Preferred Stock in accordance with Section 5 of this Certificate of Designation.

(d) No Fractional Shares. No fractional shares or scrip representing fractional shares of Common Stock shall be issued upon conversion of Series B Preferred Stock. If more than one certificate evidencing shares of Series B Preferred Stock shall be surrendered for conversion at one time by the same holder, the number of full shares issuable upon conversion thereof shall be computed on the basis of the aggregate number of shares of Series B Preferred Stock so surrendered. Instead of any fractional share of Common Stock which would otherwise be issuable upon conversion of such aggregate number of shares of Series B Preferred Stock, the Corporation may elect, in its sole discretion, independently for each holder, whether such number of shares of Common Stock will be rounded to the nearest whole share (with a .5 of a share rounded upward) or whether such holder will be given cash, in

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lieu of any fractional share, in an amount equal to the same fraction of the Market Price of the Common Stock as of the close of business on the day of conversion.

(e) [Reserved]

(f) Reservation of Shares; Transfer Taxes, Etc. The Corporation shall at all times reserve and keep available, out of its authorized and unissued shares of Common Stock, solely for the purpose of effecting the conversion of the Series B Preferred Stock, such number of shares of its Common Stock free of preemptive rights as shall be sufficient to effect the conversion of all shares of Series B Preferred Stock from time to time outstanding. The Corporation shall use its best efforts from time to time, in accordance with the laws of the State of Delaware to increase the authorized number of shares of Common Stock if at any time the number of shares of authorized, unissued and unreserved Common Stock shall not be sufficient to permit the conversion of all the then-outstanding shares of Series B Preferred Stock.

The Corporation shall pay any and all issue or other taxes (excluding any income taxes) that may be payable in respect of any issue or delivery of shares of Common Stock on conversion of the Series B Preferred Stock. The Corporation shall not, however, be required to pay any tax which may be payable in respect of any transfer involved in the issue or delivery of Common Stock (or other securities or assets) in a name other than that in which the shares of Series B Preferred Stock so converted were registered, and no such issue or delivery shall be made unless and until the person requesting such issue has paid to the Corporation the amount of such tax or has established, to the satisfaction of the Corporation, that such tax has been paid or need not be paid.

(g) Prior Notice of Certain Events. In case:

(i) the Corporation shall declare any dividend (or any other distribution); or

(ii) the Corporation shall authorize the granting to the holders of Common Stock or the Series A Preferred Stock of rights or warrants to subscribe for or purchase any shares of stock of any class or of any other rights or warrants; or

(iii) of any reclassification of Common Stock (other than a subdivision or combination of the outstanding Common Stock, or a change in par value, or from par value to no par value, or from no par value to par value); or (iv) of any consolidation or merger to which the Corporation is a party and for which approval of any stockholders of the Corporation shall be required, or of the sale or transfer of all or substantially all of the assets of the Corporation or of any compulsory share exchange whereby the Common Stock is converted into other securities, cash or other property; or

(v) of any Liquidation Event;

then the Corporation shall cause to be filed with the transfer agent for the Series B Preferred Stock, and shall cause to be mailed to the Registered Holders, at their last addresses as they shall appear upon the stock transfer books of the Corporation, at least twenty (20) days prior to the applicable record date hereinafter specified, a notice stating (x) the date on which a record (if any) is to be taken for the purpose of such dividend, distribution or granting of rights or warrants or, if a record is not to be taken, the date as of which the holders of Common Stock or Series A Preferred Stock of record to be entitled to such dividend, distribution, rights or warrants are to be determined and a description of the cash, securities or other property to be received by such holders upon such dividend, distribution or granting of rights or warrants or (y) the date on which such reclassification, consolidation, merger, sale, transfer, share exchange or Liquidation Event is expected to become effective, the date as of which it is expected that holders of Common Stock of record shall be entitled to exchange their shares of Common Stock for securities or other property deliverable upon such exchange or Liquidation Event and the consideration, including securities or other property, to be received by such holders upon such exchange; provided, however, that no failure to mail such notice or any defect therein or in the mailing thereof shall affect the validity of the corporate action required to be specified in such notice.

(h) Other Changes in Conversion Rate. The Corporation from time to time may increase the Conversion Rate by any amount for any period of time if the period is at least 20 days and if the increase is irrevocable during the period. Whenever the Conversion Rate is so increased, the Corporation shall mail to the Registered Holders a notice of the increase at least 15 days before the date the increased Conversion Rate takes effect, and such notice shall state the increased Conversion Rate and the period it will be in effect.

The Corporation may make such increases in the Conversion Rate, in addition to those required or allowed by this Section 4, as shall be determined by it, as evidenced by a resolution of the Board of Directors, to be advisable in order to avoid or diminish any income tax to holders of Common Stock resulting from any dividend or distribution of stock or issuance of rights or warrants to purchase or subscribe for stock or from any event treated as such for income tax purposes.

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Notwithstanding anything to the contrary herein, in no case shall the Conversion Price be adjusted to an amount less than \$.001 per share, the current par value of the Common Stock into which the Series B Preferred Stock is convertible.

(i) Ambiguities/Errors. The Board of Directors of the Corporation shall have the power to resolve any ambiguity or correct any error in the provisions relating to the convertibility of the Series B Preferred Stock, and its actions in so doing shall be final and conclusive.

5. Mandatory Conversion and Redemption. (a) In the event the Corporation causes the Series A Preferred Stock to be converted in whole or in part, into fully paid and nonassessable shares of Common Stock, then the Corporation shall also convert the Series B Preferred Stock, in whole or in part, on a pro rata basis among holders of the Series B Preferred Stock, into fully paid and nonassessable shares of Common Stock using a conversion price of \$.50. Any shares of Series B Preferred Stock so converted shall be treated as having been surrendered by the holder thereof for conversion pursuant to Section 4 on the date of such mandatory conversion (unless previously converted at the option of the holder).

(b) If, at any time, the Corporation redeems the Series A Preferred Stock, the Corporation may, at its option, redeem the Series B Preferred Stock, in whole or in part, on a pro rata basis among holders of the Series B Preferred Stock.

(c) No greater than 60 nor fewer than 20 days prior to the date of any such mandatory conversion or redemption, notice by first class mail, postage prepaid, shall be given to the holders of record of the Series B Preferred Stock to be converted or redeemed, addressed to such holders at their last addresses as shown on the stock transfer books of the Corporation. Each such notice shall specify the date fixed for conversion or redemption, the place or places for surrender of shares of Series B Preferred Stock and the then effective Conversion Rate pursuant to Section 4.

Any notice which is mailed as herein provided shall be conclusively presumed to have been duly given by the Corporation on the date deposited in the mail, whether or not the holder of the Series B Preferred Stock receives such notice; and failure properly to give such notice by mail, or any defect in such notice, to the holders of the shares to be converted or redeemed shall not affect the validity of the proceedings for the conversion or redemption of any other shares of Series B Preferred Stock. On or after the date fixed for conversion or redemption (the "Take-Out Date") as stated in such notice, each holder of shares called to be converted or

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redeemed shall surrender the certificate evidencing such shares to the Corporation at the place designated in such notice for conversion or redemption. After the mailing of such notice, but before the Take-Out Date as stated therein, all rights whatsoever with respect to the shares so called for conversion or redemption (except the right of the holders to convert such shares pursuant to Section 4 and to have such shares converted or redeemed, as the case may be, upon surrender of their certificates therefor, pursuant to this Section 5) shall terminate. On or after the Take-Out Date, notwithstanding that the certificates evidencing any shares properly called for conversion or redemption shall not have been surrendered, such shares shall no longer be deemed outstanding and all rights whatsoever with respect to the shares so called for conversion or redemption (except the right of the holders to have such shares converted or redeemed, as the case may be, upon surrender of their certificates therefor, pursuant to this Section 5) shall terminate.

6. Outstanding Shares. For purposes of this Certificate of Designation, a share of Series B Preferred Stock, when issued, shall be deemed outstanding except (i) from the date, or the deemed date, of surrender of certificates evidencing shares of Series B Preferred Stock, all shares of Series B Preferred Stock converted into Common Stock or redeemed pursuant to Section 5 and (ii) from the date of registration of transfer, all shares of Series B Preferred Stock held of record by the Corporation or any subsidiary of the Corporation.

7. Class Voting Rights. The Corporation shall not, without the affirmative vote or consent of the holders of at least 50% of all outstanding Series B Preferred Stock, voting separately as a class, (i) amend, alter or repeal any provision of the Certificate of Incorporation or the Bylaws of the Corporation so as to adversely affect the relative rights, preferences, qualifications, limitations or restrictions of the Series B Preferred Stock; (ii) authorize or issue, or increase the authorized amount of, Series B Preferred Stock, other than Series B Preferred Stock issuable in exchange for 8% Notes or accrued interest thereon or issuable as dividends on Series B Preferred Stock; or (iii) issue securities ranking prior to, or pari passu with the Series B Preferred Stock.

8. Status of Acquired Shares. Shares of Series B Preferred Stock received upon conversion or redemption pursuant to Section 4 or Section 5 or otherwise acquired by the Corporation will be restored to the status of authorized but unissued shares of Preferred Stock, without designation as to class, and may thereafter be issued, but not as shares of Series B Preferred Stock.

9. Preemptive Rights. The Series B Preferred Stock is not entitled to any preemptive or subscription rights in respect of any securities of the Corporation.

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10. Severability of Provisions. Whenever possible, each provision hereof shall be interpreted in a manner as to be effective and valid under applicable law, but if any provision hereof is held to be prohibited by or invalid under applicable law, such provision shall be ineffective only to the extent of such prohibition or invalidity, without invalidating or otherwise adversely affecting the remaining provisions hereof. If a court of competent jurisdiction should determine that a provision hereof would be valid or enforceable if a period of time were extended or shortened or a particular percentage were increased or decreased, then such court may make such changes as shall be necessary to render the provision in question effective and valid under applicable law.

IN WITNESS WHEREOF, Sudhir Agrawal, President and Acting Chief Executive Officer of the Corporation, acting for and on behalf of the Corporation, has hereunto subscribed his name this day of March, 2001.

HYBRIDON, INC.

By:

Name: Sudhir Agrawal Title: President and Acting Chief Executive Officer

Exhibit 4.8

SHARES

[Hybridon LOGO]

ΗP

SERIES A CONVERTIBLE PREFERRED STOCK

----- NUMBER

SEE REVERSE FOR CERTAIN DEFINITIONS

HYBRIDON, INC. INCORPORATION UNDER THE LAWS OF THE STATE OF DELAWARE

CUSIP 44860M 88 4

THIS CERTIFIES THAT

IS THE OWNER OF

FULLY PAID AND NON-ASSESSABLE SHARES \$.01 PAR VALUE, OF THE SERIES A CONVERTIBLE PREFERRED STOCK OF

transferable on the books of the Corporation in person or by attorney upon surrender of this certificate duly endorsed or assigned. This certificate and the shares represented hereby are issued under and subject to the laws of the State of Delaware and the provisions of the Restated Certificate of Incorporation and By-laws of the Corporation, as from time to time amended. This certificate is not valid until countersigned and registered by the Transfer Agent and Registrar.

IN WITNESS WHEREOF, the facsimile seal of the Corporation and the facsimile signatures of its duly authorized officers.

Dated:

ΒY

[HYBRIDON, INC. SEAL 1989 DELAWARE]

> /s/ Suhdir Agrawal PRESIDENT

COUNTERSIGNED AND REGISTERED MELLON INVESTOR SERVICES LLC

> TRANSFER AGENT AND REGISTRAR

AND REGISTRAR

AUTHORIZED SIGNATURE

/s/ Robert Andersen TREASURER

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| HYBRIDON, | INC. |
|-----------|------|
|-----------|------|

The following abbreviations, when used in the inscription on the face of this Certificate, shall be construed as though they were written out in full according to applicable laws or regulations:

UNIF GIFT MIN ACT - Custodian (Cust) (Minor)

> under Uniform Gifts to Minors Act (State)

Additional abbreviations may also be used though not in the above list.

For value received, hereby sell, assign and transfer unto

PLEASE INSERT SOCIAL SECURITY OR OTHER IDENTIFYING NUMBER OF ASSIGNEE

(PLEASE PRINT OR TYPEWRITE NAME AND ADDRESS, INCLUDING ZIP CODE, OF ASSIGNEE)

Shares

of the common stock represented by the within Certificate, and do hereby irrevocably constitute and appoint

Attorney

to transfer the said stock on the books of the within named Company with full power of substitution in the premises.

Dated _____

NOTICE: THE SIGNATURE TO THIS ASSIGNMENT MUST CORRESPOND WITH THE NAME AS WRITTEN UPON THE FACE OF THE CERTIFICATE IN EVERY PARTICULAR, WITHOUT ALTERATION OR ENLARGEMENT OR ANY CHANGE WHATEVER. AN ELIGIBLE GUARANTOR INSTITUTION (BANKS STOCKBROKERS, SAVINGS AND LOAN ASSOCIATIONS AND CREDIT UNIONS WITH MEMBERSHIP IN AN APPROVED SIGNATURE GUARANTEE MEDALLION PROGRAM), PURSUANT TO S.E.C. RULE 17Ad-15.

Pursuant to Section 151 of the Delaware General Corporation Law, Hybridon, Inc. (the "Company") will furnish without charge to each stockholder who so requests the powers, designations, preferences and relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

Mr. E. Andrews Grinstead 33 Edgehill Road Brookline, MA 02446

Dear Andy:

This letter sets forth the terms we have agreed upon with respect to your termination of employment from Hybridon, Inc. ("Hybridon" or the "Company"). This letter agreement ("Agreement") is effective seven (7) days after it has been signed by each of us (the "Effective Date"). We agree as follows:

1. Your employment with the Company shall be deemed to have terminated as of April 30, 2000 (the "Termination Date"), and you shall accrue service time for all purposes with the Company through the Termination Date, including vesting of options.

2. Your termination shall be deemed to be a termination because of a disability and you shall be entitled to all rights and benefits accruing to you as a result of such termination under your 1997 Employment Agreement and under all other agreements related to your employment.

3. Because your termination is a result of a disability, in accordance with your 1997 Employment Agreement, you shall have until two years after the Termination Date to exercise all Hybridon stock options that are fully vested as of the Termination Date.

4. As of the Termination Date, you had an outstanding note with Hybridon totaling \$273,850 (the "Note"). As of the Termination Date, the note will be forgiven and no further payments of either principal or interest shall be due thereunder.

5. You shall be eligible for distribution of retirement benefits in accordance with the terms of the Hybridon plan and you shall receive all benefits that are provided to you under the various Hybridon employee benefit plans, in accordance with their respective terms except as modified by the 1997 Employment Agreement. Hybridon shall pay the cost of the monthly premium for you and your family for the duration of the group health insurance COBRA continuation coverage period. You are eligible for payment of benefits under the Hybridon long-term disability insurance plan. The Company will assist you by using its best reasonable efforts to ensure that the long-term disability benefit is paid to you in accordance with its terms.

6. Hybridon shall pay your reasonable attorney's fees with respect to advice and counsel you have received to your termination of employment, up to \$10,000.

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7. By signing below, you acknowledge and agree that the consideration contained herein and in Paragraphs 4, 5 and 6 in particular, represents full and complete consideration for your release of claims pursuant to Paragraph 8 below.

8. Pursuant to this Agreement you shall be deemed to have resigned as an officer and Director of the Company as of the close of business on the Effective Date.

9. (a) You, on behalf of yourself, and your heirs, family members, executors, administrators and assigns, hereby fully and forever release the Company and its members, managers, officers, employees, directors, successors,

and assigns (the "Releasees"), from any claim, duty, obligation or cause of action relating to your employment by the Company, whether presently known or unknown, suspected or unsuspected, that you may possess arising from any omission, acts or facts that have occurred up until and including the Effective Date including, without limitation:

- any and all claims relating to your employment relationship with the Company and the termination of that relationship;
- any and all claims for wrongful discharge of employment, breach of contract, both express and implied; breach of a covenant of good faith and fair dealing, both express and implied, negligent or intentional infliction of emotional distress; negligent or intentional misrepresentation; negligent or intentional interference with contract or prospective economic advantage; defamation; negligence; personal injury; assault, battery; invasion of privacy; false imprisonment, and conversation; and
- any and all claims for violation of any federal, state or municipal statute, including, but not limited to, Title VII of the Civil Rights Act of 1964, the Civil Rights Act of 1991, the Age Discrimination in Employment Act of 1967, the Americans with Disabilities Act of 1990, the Family and Medical Leave Act, the Fair Labor Standards Act, M.G.L. c .151B, and The Massachusetts Fair Employment Practices Act, M.G.L. c 151B.

You agree that the release set forth in this Paragraph shall be and remain in effect in all respects as a complete general release as to the matters released. This release does not extend to any obligations incurred under this Agreement, nor does it extend to any claims you may have as a shareholder, option holder or holder of a note or other form of security of the Company, whether such claims relate to an event or omission occurring before or after the Effective Dated.

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(b) The Releases hereby irrevocably and unconditionally release, acquit and forever discharges you, your spouse, heirs and successors from any claim, duty, obligation or cause of action relating to your employment by the Company, whether presently known or unknown, suspected or unsuspected, that they or each of them may possess arising from any omissions, acts or facts that have occurred up until and including the Effective Date including, without limitation, all charges, complaints, claims, liabilities, obligations, promises, agreements, controversies, damages, actions, causes of actions, suits, rights, demands, costs, losses, damages and expenses (including attorney's fees and costs actually incurred) of any nature whatsoever known or unknown, suspected or unsuspected.

10. You acknowledge that you are waiving and releasing any rights you may have against the Company, including claims under the Age Discrimination in Employment Act ("ADEA"), as of the Effective Date. You acknowledge that the consideration given for this waiver and release Agreement is in addition to anything of value to which you are already entitled. You further acknowledge that you have been advised by this writing and understand and agree that:

- you have been advised to consult with an attorney prior to executing this Agreement;
- you have carefully read and fully understand this Agreement;
- you are, through this Agreement, releasing the Company and the Releasees referenced in 9(a) above, from any and all claims you may have against it and them, as described herein;
- you knowingly and voluntarily agree to all of the terms set forth in this Agreement;

- you have had at least twenty-one (21) days within which to consider this Agreement;
- you have seven (7) days following the execution of this Agreement by the Parties to revoke the Agreement; and
- this Agreement shall not be effective until the revocation period has expired.

By your signature below, you acknowledge that you have read and understood the terms of this Agreement, and that you are signing it voluntarily and without coercion. You and the Company further acknowledge that the

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mutual release waivers contained in this Agreement are knowing, conscious and made with full appreciation that each is forever foreclosed from pursuing any of the rights so waived. The undersigned represents and warrants that he has authority from the Company to enter into this Agreement.

ACKNOWLEDGED AND AGREED:

| Dated: | 1 | 2000 | | | | | |
|--------|---|------|---|----|---------|------------|-----|
| | | | | | | | |
| | | | 1 | Е. | Andrews | Grinstead, | III |

HYBRIDON, INC.

Dated: , 2000

By:_____

Exhibit No. 10.66

AGREEMENT

THIS AGREEMENT (the "Agreement") is entered into as of the __ day of March, 2001 by and between Hybridon, Inc., a Delaware corporation ("Hybridon") and the Lenders (as defined in the Fifth Amendment to the Loan and Security Agreement entered into as of December 4, 1998 between Hybridon and the Lenders thereunder).

WHEREAS, Hybridon desires to sell shares of the capital stock of Methylgene Inc., a company organized under the laws of Quebec (the "Methylgene Shares") to Paul Capital Partners (the "Transaction");

WHEREAS, the Methylgene Shares are subject to a security interest granted to the Lenders pursuant to that Loan and Security Agreement between Hybridon and Silicon Valley Bank, dated December 31, 1996, as amended, and purchased by the Lenders on November 20, 1998 (the "Loan Agreement");

WHEREAS, a portion of the holders (the "Noteholders") of 8% Notes due 2002 of Hybridon (the "Notes") have agreed to convert their Notes into shares of Hybridon's Series B Preferred Stock (the "Series B"), pending the sale of the MethylGene Shares;

WHEREAS, the Lenders desire that the Loan (as defined in the Loan Agreement), or a portion thereto, be prepaid by the Company by September 30, 2001.

NOW, THEREFORE, in consideration of the foregoing and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Hybridon and the Lenders agree as follows:

1. Release and Waiver. Upon the execution of this Agreement, the Lenders shall execute and deliver to Hybridon the Release and Waiver (the "Release") attached hereto as Exhibit A, thereby releasing their entire interest in the MethylGene Shares, and waiving certain rights granted to them in the Loan Agreement pertaining to Hybridon's disposal of property.

2. Waiver of Defaults. The Lenders hereby waive any existing defaults in the Minimum Liquidity and Tangible Net Worth Covenants (as such terms are defined in the Loan Agreement), and waive compliance by Hybridon with the Minimum Liquidity and Tangible Net Worth Covenants at least until September 30, 2001.

3. Repayment.

(a) Upon the closing of the Transaction, Hybridon shall repay \$1,800,000 of the outstanding principal Loan amount in the event 60% of Hybridon's holding of MethylGene Shares is sold. In the event Hybridon's entire holding of MethylGene Shares is sold in the Transaction, \$3,000,000 of the outstanding principal Loan amount shall be repaid by Hybridon. In the event that an amount greater than 60% of Hybridon's holding of MethylGene Shares is sold, Hybridon's repayment amount shall increase at a rate of \$30,000 per each percentage point over 60%. In no event shall Hybridon repay more than \$3,000,000 of the outstanding principal Loan amount. Any repayment amount made by Hybridon hereunder shall be made proportionately among the Lenders based on the Lenders' respective interests in the Loan.

(b) In the event Hybridon pays the Lenders less than \$3,000,000 from the proceeds of the Transaction, it shall invest an amount equal to the difference between \$3,000,000 and the amount so paid (the "Differential Amount") in a segregated, interest-bearing instrument (the "Lenders' Money Market Instrument"), on a pro rata basis proportionate to each Lenders' interest in the Loan, and Hybridon shall deliver and pledge the Lenders' Money Market Instrument to the Lenders as Collateral under the Loan Agreement. The Lenders' Money Market Instrument shall be subject to and governed by the terms and conditions of this Agreement, the Loan Agreement, and the First Amended and Restated Subordination and Intercreditor Agreement, dated as of June 24, 2000, by and among Hybridon, the Lenders, and certain of Hybridon's other creditors (the "Intercreditor Agreement"). Upon the closing of any transaction or combination of transactions resulting in \$10,000,000 or more of net proceeds to Hybridon, Hybridon shall pay the Lenders the Differential Amount, and (i) the pledge of the Lenders' Money Market Instrument shall be released, (ii) Hybridon shall be entitled to use the released funds as it sees fit, and (iii) the Lenders shall execute and deliver such instruments as may be necessary to effectuate the release.

(c) In addition, upon the closing of the Transaction, and separately from Section 3(b) above, Hybridon shall invest \$811,000 in a segregated, interest-bearing instrument (the "Pecks Money Market Instrument"), and Hybridon shall deliver and pledge the Pecks Money Market Instrument to Pecks Management Partners ("Pecks") only, as Collateral under the Loan Agreement securing Hybridon's repayment of Pecks' interest in the remaining principal balance of the Loan. The Pecks Money Market Instrument shall be subject to and governed by the terms and conditions of this Agreement, the Loan Agreement, and the Intercreditor Agreement. Upon Hybridon's repayment in full of Pecks' interest in the Loan, (i) the pledge of the Pecks Money Market Instrument shall be released, (ii) Hybridon shall be entitled to use the released funds as it sees fit, and (iii) Pecks shall execute and deliver such instruments as may be necessary to effectuate the release.

(d) The parties agree to amend the Intercreditor Agreement as necessary to reflect the transactions contemplated by Sections 3(b) and 3(c) above $% \left(\left(1+1\right) \right) =0$

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(the "Amendment"). In the event the Intercreditor Agreement is terminated by Hybridon's payment in full of its Senior Obligations (as that term is defined in the Intercreditor Agreement) prior to the Amendment, this Agreement shall remain in full force and effect, and parties' rights and obligations vis-a-vis each other shall be subject to and governed by this Agreement and the Loan Agreement.

(e) Hybridon's right to repay the balance of the Loan at any time, as granted under the Loan Agreement, shall continue after the date hereof.

4. Conversion Price Adjustment. Upon closing of the Transaction, Hybridon agrees to execute an amendment to the Loan Agreement, lowering the conversion price on the remaining principal Loan balance from \$2.40 to \$1.50 per share, effective through September 30, 2001.

5. Hybridon Option. In the event the remaining principal Loan balance is not repaid by Hybridon on or before September 30, 2001, Hybridon shall either (i) repay the outstanding Loan balance in full, or (ii) execute an amendment to the Loan Agreement further lowering the conversion price on the remaining principal Loan balance from \$1.50 to \$.50 for the remaining life of the Loan.

6. Representations and Warranties. Each of Hybridon and the Lenders severally represent and warrant solely as to themselves that, except as provided in the Loan Agreement:

(a) It has the full right, power and authority to enter into this Agreement and to consummate the transactions contemplated hereby.

(b) This Agreement constitutes the legal, valid and binding obligation of the parties, enforceable against the parties in accordance with its terms; and

(c) It is not a party to, subject to or bound by any agreement or any judgment, order, writ, prohibition, injunction or decree of any court or other governmental body which would prevent the execution or delivery of this Agreement by such party or the consummation of the transactions contemplated hereby.

Each Lender also jointly represents and warrants to Hybridon that, except as provided in the Loan Agreement, it has good and marketable title to the portion of the principal of the Loan held by it, free and clear of any and all covenants, conditions, restrictions, voting trust arrangements, liens, charges, encumbrances, options and adverse claims or rights whatsoever.

7. Conditions. The parties' obligations hereunder are subject to those Noteholders who do not convert their Notes into Series B agreeing and acknowledging in writing that any security interest they may have in and to the

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Lenders' Money Market Instrument and the Pecks' Money Market Instrument shall be subordinate to the security interests of the Lenders therein.

8. Miscellaneous.

(a) Entire Agreement. This Agreement constitutes the entire agreement between the parties and supersedes all prior agreements and understandings, whether written or oral, relating to the subject matter of this Agreement.

(b) Amendment. This Agreement may be amended or modified only by a written instrument executed by Hybridon and the Lenders.

(c) Governing Law. This Agreement shall be construed, interpreted and enforced in accordance with the laws of the Commonwealth of Massachusetts.

(d) Successors and Assigns. This Agreement shall be binding upon, and inure to the benefit of, the parties and their respective successors and assigns; provided, however, that no party shall assign this Agreement without the prior written consent of the other party.

(e) Captions. The captions of the sections of this Agreement are for convenience of reference only and in no way define, limit or affect the scope or substance of any section of this Agreement.

| | EXECUTED | in | counterparts | as | of | the | date | set | forth | in | the | first | |
|-----------|-----------|----|--------------|----|----|-----|------|-----|-------|----|-----|-------|--|
| paragraph | n hereof. | | | | | | | | | | | | |

| HYBRIDON, | INC. | | |
|------------|-----------|-------|--|
| By: | | | |
| Name: | | | |
| Title: | | | |
| LENDERS: | | | |
| FOUNDERS H | FINANCIAL | GROUP | |
| By: | | | |
| Name: | | | |
| Title: | | | |
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DELAWARE STATE EMPLOYEES RETIREMENT FUND; DECLARATION OF TRUST FOR THE DEFINED BENEFIT PLANS OF ICI AMERICAN HOLDINGS, INC.; DECLARATION OF TRUST FOR THE DEFINED BENEFIT PLANS OF ZENECA HOLDINGS INC.; THE J.W. MCCONNELL FAMILY FOUNDATION. By: PECKS MANAGEMENT PARTNERS LTD. By: -----Name: -----Title: _____ GENERAL MOTORS INVESTMENT MANAGEMENT CORPORATION, SOLELY IN ITS CAPACITY AS TRUSTEE FOR THE GENERAL MOTORS EMPLOYEES GLOBAL TRUST GROUP (AS DIRECTED BY GENERAL MOTORS INVESTMENT MANAGEMENT CORPORATION) AND NOT IN ITS INDIVIDUAL CAPACITY. By: -----Name: -----Title: _____ 5

EXHIBIT A

5

RELEASE AND WAIVER

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Exhibit No. 10.67

STOCK PURCHASE AGREEMENT

FOR THE PURCHASE OF

COMMON SHARES OF METHYLGENE INC.

FROM

HYBRIDON, INC.

THE SELLER

BY

PAUL CAPITAL PARTNERS VI, L.P. AND PCP ASSOCIATES, L.P.

THE PURCHASERS

MARCH 30, 2001

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STOCK PURCHASE AGREEMENT

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STOCK PURCHASE AGREEMENT

This Stock Purchase Agreement is made and entered into as of March 30, 2001 (the "Agreement") by PAUL CAPITAL PARTNERS VI, L.P. and PCP ASSOCIATES, L.P. (collectively, the "Purchaser" or the "Purchasers"), and HYBRIDON, INC. (the "Seller").

WITNESSETH

WHEREAS, the Seller is the owner of the Shares (as hereinafter

defined); and

WHEREAS, the Seller is a party to the Shareholders' Agreement (as hereinafter defined) governing disposition of the Shares and granting certain rights with respect to the Shares;

WHEREAS, the Purchasers desire to purchase from the Seller, and the Seller desires to sell to the Purchasers, the Shares upon the terms and subject to the conditions set forth in this Agreement;

WHEREAS, the purchase of the Shares is conditional upon the Purchasers becoming parties to the Shareholders' Agreement as same is to be amended as set forth hereinafter;

NOW, THEREFORE, in consideration of the premises and the mutual agreements, covenants, representations, warranties and indemnities contained in this Agreement, the Purchasers and the Seller hereby agree as follows:

ARTICLE I

PURCHASE AND SALE OF SHARES

1.1 CERTAIN DEFINITIONS. For purposes of this Agreement, the following terms shall have the meanings set forth below:

(a) "Ancillary Agreements" shall mean the Shareholders' Agreement Amendment.

(b) "C\$" shall mean Canadian dollars.

(c) "Closing" shall have the meaning assigned to it in Section 5.1 hereof.

(d) "Closing Date" shall have the meaning assigned to it in Section 5.1 hereof.

(e) "Company" shall mean MethylGene Inc., a corporation organized under the laws of Quebec.

(f) "Contractual Rights" shall mean all of the contractual rights of the Seller relating to the Shares or the Company, including, without limitation, all rights of first refusal,

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STOCK PURCHASE AGREEMENT

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first offer and co-sale among shareholders or partners of the Company; and all rights to receive financial and other information from the Company as is currently held by the Company's shareholders.

(g) "Encumbrance" shall mean any Lien pertaining to the sale, assignment, disposition, transfer or the voting rights of, on or pertaining to the Shares (including, without limitation, any consents or approvals of transfers, options, rights of first refusal and co-sale rights).

(h) "Lien", shall mean any lien, pledge, claim, security interest, encumbrance, charge, restriction or limitation of any kind, whether arising by agreement, operation of law or otherwise other than Permitted Encumbrances.

(i) "Material Adverse Change" shall have the meaning set forth in Section 1.6 hereof.

(j) "Permitted Encumbrances" shall mean those Encumbrances arising under the Shareholders' Agreement to the extent they do not relate or apply to the transactions contemplated by this Agreement.

(k) "Portfolio Company Certificates" shall mean certificates provided by the Company to the Purchaser substantially in the form of Exhibit A and Exhibit B attached hereto pursuant to which the Company represents and warrants to the Purchasers as follows:

(i) In Exhibit A, with respect to the Company, the representations and warranties of the Seller set forth in Section 2.5 are true and correct as to the number of authorized and outstanding shares of capital stock and Share Equivalents of the Company and the number of securities held by the Seller;

(ii) In Exhibit B, the Certificate of Transfer, that with respect to the Company, the transfer of the Shares to the Purchaser will upon Closing be made by the Company's transfer agent and the Purchasers shall become the holders of record of the Shares;

(1) "Realizations" shall mean all pre-tax and pre-withholding

payments, interest, dividends, and other distributions declared, paid or made to and received by or on behalf of the Seller with respect to or in connection with the ownership of, and any proceeds from the sale, assignment, transfer, conversion, exchange, redemption, exercise, repayment, waiver, release, compromise, settlement or satisfaction of, any Shares held by the Seller after the Record Date and prior to the Closing.

(m) "Record Date" shall mean December 31, 2000.

(n) "Securities" shall have the meaning ascribed to that term in the Securities Act of 1933, as amended.

(o) "Share Equivalents" shall have the meaning assigned to it in Section 2.5;

STOCK PURCHASE AGREEMENT

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(p) "Shareholders' Agreement" shall mean, collectively (i) that certain Shareholders' Agreement, dated as of January 4, 1996, among Fonds de solidarite des travailleurs du Quebec (F.T.Q.) ("Fonds"), Fonds d'Investissement en Biotechnologie BioCapital II, societe en commandite ("Biocapital"), Societe Innovatech du Grand Montreal ("Innovatech"), Seller and the Company, as amended by that certain Amendment to Shareholders' Agreement, dated as of February 27, 1998, Amendment to Shareholders' Agreement, dated as of July 14, 2000, and Amendment to Shareholders' Agreement, dated as of January 4, 1996, among Fonds, Biocapital, Innovatech, Seller and the Company, as amended by that certain Amendment to Unanimous Shareholders' Agreement, dated as of January 27, 1998.

(q) "Shares" shall mean 2,350,000 Common shares of the Company to be acquired by the Purchasers at the Closing created by the conversion of the Company's Class A shares and Class B shares into Common shares which is contemplated by this Agreement. The number of such Shares will be appropriately adjusted for any stock splits or dividends which are declared and paid after the Record Date and prior to the Closing.

1.2 PURCHASE AND SALE OF SHARES. Upon the terms and subject to the conditions set forth in this Agreement, at the Closing the Seller shall sell, assign, transfer and deliver to the Purchasers at the Closing and the Purchasers shall purchase and acquire from the Seller at the Closing, all right, title and interest in and to that number of the Shares as set forth opposite each such Purchaser's name on Schedule 1.2 hereto, free and clear of all Liens (other than the Encumbrances to the extent they do not apply to the transactions contemplated by this Agreement).

1.3 PURCHASE PRICE. The purchase price due and payable at Closing (the "Payment") for the Shares to be sold pursuant to this Agreement shall be C\$6,697,500 (less the value of any Realizations after the Record Date and the value of the Withholding, if any) and shall be paid to the Seller, by wire transfer of federal funds or other immediately available funds, to the account designated by the Seller.

1.4 REALIZATIONS. Realizations shall be retained by the Seller and shall reduce the Purchase Price as provided in Section 1.3. Within five (5) business days after receipt by the Seller of any Realizations or any notice of an entitlement to receive any Realizations but in no event later than the Closing Date, the Seller shall notify the Purchaser of the receipt of such Realizations or such notice, as the case may be, and the amount, nature and time of receipt or anticipated receipt, as the case may be, of the Realizations received or to be received by the Seller.

1.5 FINANCIAL STATEMENTS. The Seller will cooperate with the Purchaser in its efforts to have the Company make financial statements available to the Purchaser.

1.6 MATERIAL ADVERSE CHANGE. From the Record Date until the Closing Date, in the event of a material adverse change in the Company, the value of the Shares or the Contractual Rights ("Material Adverse Change"), the Purchaser, in its sole discretion, upon written notice to the Seller, may terminate this Agreement with respect to its obligations hereunder.

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STOCK PURCHASE AGREEMENT

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1.7 NONASSIGNABLE SHARES OR CONTRACTUAL RIGHTS. To the extent that the assignment of the Shares or Contractual Rights shall require the consent of any other party thereto, or shall be subject to any option in any other person by virtue of a request for permission to sell, assign or transfer or by reason of or pursuant to any sale, assignment or transfer to the Purchaser, this Agreement shall not constitute a contract to assign the same to the extent that an attempted assignment would (i) constitute a breach thereof, (ii) create rights in others not desired by the Purchaser or (iii) create rights in third parties against the Seller. The Seller shall cooperate with the Purchaser in any reasonable arrangement not in violation of the Shareholders' Agreement requested by the Purchaser designed to provide for the Purchaser the economic benefits, rights, privileges and entitlements of the Shares, provided, that the Seller shall not be required to pay any monetary compensation to any third party as a part of such arrangements.

ARTICLE II

REPRESENTATIONS AND WARRANTIES OF THE SELLER

The Seller hereby represents and warrants to the Purchaser as follows:

2.1 ORGANIZATION. The Seller is duly formed, validly existing and in good standing under the laws of the jurisdiction in which it is organized.

2.2 AUTHORIZATION. The Seller has all necessary power and authority to enter into, execute and deliver this Agreement and the Ancillary Agreements and to perform all of the obligations to be performed by it hereunder and thereunder. Each of this Agreement and the Ancillary Agreements has been duly authorized, executed and delivered by the Seller and constitutes its valid and binding obligation, enforceable against the Seller in accordance with its terms.

2.3 VALIDITY. Neither the execution and delivery of this Agreement or the Ancillary Agreements nor the performance or consummation of the transactions contemplated hereby or thereby will conflict with, result in a breach or violation of, constitute a default under, or accelerate the performance provided by the terms of: (i) any law, any rule or regulation of any government or any agency of any government, or any judgment, order, writ, decree, permit or license of any court or other agency of any government to which the Seller may be subject; (ii) the articles or the by-laws of this Company; or (iii) subject to obtaining appropriate waivers of rights of first refusal and co-sale rights, the Shareholders' Agreement or any other contract, agreement, commitment or instrument to which the Seller is a party or by which it or any of its assets is bound or committed. Neither the execution and delivery of this Agreement or the Ancillary Agreements nor the performance or consummation of the transactions contemplated hereby or thereby will constitute an event which, with the lapse of time or action by a third party, could result in the default under any of the foregoing or result in the creation of any Lien upon the Shares. Other than the registrations, filings, consents and approvals that have been made or obtained and the filings required to be made by Seller pursuant for Section 4.2 below, and the execution and delivery of this Agreement and the Ancillary Agreements and the performance and consummation of the transactions contemplated hereby and thereby will not require any registration, filing, consent or approval under any such law, rule, regulation, judgment, order,

STOCK PURCHASE AGREEMENT

writ, decree, permit or license, or consent or approval of, any third party, including, without limitation, any governmental or regulatory authority or any party to any of the Shareholders' Agreement or other contract, agreement, commitment or instrument.

2.4 OWNERSHIP OF THE SHARES. Except as set forth on Schedule 2.4, the Seller owns, or immediately prior to the Closing will own, all right, title and interest (legal and beneficial) in and to the Shares identified as being owned by the Seller free and clear of all Liens. All of the Encumbrances potentially applicable to the transaction contemplated by this Agreement will have been duly waived or satisfied on or before the Closing Date, or, in the case of any rights of first refusal, first offer, or co-sale will have been duly waived or all applicable notice periods will have expired without such rights having been exercised on or before the Closing Date, by all interested parties. Upon delivery of the Shares identified as being owned by the Seller to the Purchaser and payment therefor in accordance with this Agreement, the Purchaser will acquire such Shares free and clear of all Liens. The Shares have been validly subscribed and issued and are outstanding as fully paid and non-assessable.

2.5 CAPITALIZATION OF THE COMPANY. To the best of the Seller's knowledge, after due inquiry; (i) set forth on Schedule 2.5 attached hereto is a complete and accurate list of all of the Company's Securities for each class and series of Securities issued by the Company, the aggregate number of such Security authorized and the aggregate number of each such Security outstanding, all of which are fully paid and nonassessable and (ii) except as set forth on Schedule 2.5, there are no (A) equity securities of any class or series of the Company, or (B) any security exchangeable into or exercisable for such equity securities, issued, reserved for issuance or outstanding, and there are no options, warrants, equity securities, calls, rights, commitments or agreements of any character to which the Company is a party or by which the Company is bound obligating the Company to issue, deliver or sell, or cause to be issued, delivered or sold additional shares of capital stock of the Company (collectively, "Share Equivalents").

2.6 REALIZATIONS. The Seller has not, since the Record Date, received, or been notified that it is entitled to receive, any Realizations. The Seller has no obligations pursuant to any letter of credit, guarantee, pledge, hypothecation, borrowing or other similar arrangement in connection with the acquisition of any of the Shares or any transaction with the Company.

2.7 CERTAIN CONDUCT. Since the Record Date, the Seller has not, except with the prior acknowledgment and approval by the Purchaser, (i) sold, assigned, transferred, delivered or otherwise disposed of any of the Shares, (ii) converted, exchanged or redeemed any of the Shares, (iii) forgiven, released, compromised or demanded payment of any indebtedness owed to it by the Company other than upon full payment thereof, (iv) amended, canceled or terminated the Shareholders' Agreement or entered into any new Shareholders' Agreement, (v) waived, amended, cancelled, terminated, exercised or failed to exercise any of the material Contractual Rights, (vi) created or permitted to exist any Lien on any of the Shares other than the Encumbrances, or (vii) agreed to do any of the foregoing.

2.8 COMPLETENESS OF DOCUMENTS. The Seller or the Company has furnished the Purchaser with, or has made available to the Purchaser, accurate and complete copies of all instruments, agreements and other documents representing, relating to or constituting the Shares or any part thereof and all material correspondence and other written communications sent or

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STOCK PURCHASE AGREEMENT

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received by or on behalf of the Seller in its capacity as a shareholder of the Company or by virtue of its representation on the Board of Directors of the Company (including any written internal compilations, analyses or reports derived therefrom), which would reasonably be expected to influence the Purchaser's decision to complete the transactions contemplated by this Agreement.

2.9 SHAREHOLDERS' AGREEMENT. Attached hereto as Schedule 2.9 are accurate and complete copies of the Shareholders' Agreement, including all amendments and interventions thereto up to and including the date hereof. Neither the Seller, nor to the best knowledge of the Seller, any other party is in breach or violation of, or in default under, the Shareholders' Agreement. The documents attached hereto as Schedule 2.9 constitute the only agreements among the shareholders of the Company regarding the subject matter thereof or the Shares.

2.10 LITIGATION. There is no (i) action, suit, claim, proceeding or investigation pending or threatened against the Seller, at law or in equity, or before or by any federal, provincial state, municipal or other governmental department, commission, board, bureau, agency court, or instrumentality, domestic or foreign, (ii) arbitration proceeding relating to the Seller pending, or (iii) governmental inquiry pending or threatened against the Seller, which, if adversely determined, would question the validity of, or prevent the consummation of, the transactions contemplated by this Agreement. There is no action or suit by the Seller pending or threatened against others relating to the Shares.

2.11 FINDERS. The Seller has not directly or indirectly dealt with anyone acting in the capacity of a finder or broker or incurred any obligation for any finder's or broker's fee or commission in connection with the transactions contemplated by this Agreement. The Seller agrees to indemnify and hold harmless the Purchaser from any liability for any commission or compensation in the nature of a finders' fee (and the costs and expenses of defending against such liability or asserted liability) for which the Seller is responsible.

2.12 FULL DISCLOSURE; ACCURACY OF INFORMATION. The Seller has fully provided the Purchaser with all the information that the Purchaser has requested for deciding whether to purchase the Shares and all agreements to which the Seller is a party and all information relating to the Shares and the Company that the Seller possesses or has received in its capacity as a shareholder of the Company or by virtue of its representation on the Board of Directors of the Company (including any written internal compilations, analyses or reports derived therefrom), which would reasonably be expected to influence the Purchaser's decision to complete the transactions contemplated by this Agreement. Neither this Agreement nor the Schedules or Exhibits thereto or any certificate to be delivered at the Closing by the Seller to the Purchaser in connection with this Agreement or any of the transactions contemplated hereby contains an untrue statement of a material fact or omits to state a material fact necessary to make the statements made, in the light of the circumstances under which they are made, not misleading, or contains a material statement which is misleading. Except as set forth in this Agreement, the Schedules and Exhibits attached hereto and any certificate to be delivered at the Closing, there is no fact that the Seller has not disclosed to the Purchaser in writing and of which it has become aware in its capacity as a shareholder of the Company or by virtue of its representation on the Board of Directors of the Company (including any written internal compilations, analyses or reports derived therefrom) and that has had or would reasonably be expected to have a material adverse effect upon the financial condition, operating results, assets, customer or supplier

STOCK PURCHASE AGREEMENT

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relations, employee relations or business prospects of the Company or on the value of the Shares or the Contractual Rights. The statements contained in any certificate to be delivered at the Closing by the Seller to the Purchaser in connection with this Agreement or any of the transactions contemplated hereby shall be deemed to constitute representations and warranties under this Agreement to the same extent as if set forth in this Agreement in full.

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2.13 COMPLIANCE WITH SECURITIES LAWS. Neither the Seller nor anyone acting on Seller's behalf has offered to sell the Shares by means of any general solicitation or any advertising.

ARTICLE III

REPRESENTATIONS AND WARRANTIES OF THE PURCHASER

The Purchaser hereby represents and warrants to the Seller as follows:

3.1 ORGANIZATION. The Purchaser is duly formed, validly existing and in good standing under the laws of the jurisdiction in which it is organized.

3.2 AUTHORIZATION. The Purchaser has all necessary power and authority to enter into, execute and deliver this Agreement and the Ancillary Agreements and to perform all of the obligations to be performed by it hereunder and thereunder. Each of this Agreement and the Ancillary Agreements has been duly authorized, executed and delivered by the Purchaser and constitutes its valid and binding obligation, enforceable against the Purchaser in accordance with its terms.

3.3 VALIDITY. Neither the execution and delivery of this Agreement or the Ancillary Agreements nor the performance or consummation of the transactions contemplated hereby or thereby will conflict with, result in a breach or violation of, constitute a default under, or accelerate the performance provided by the terms of: (i) any law, any rule or regulation of any government or any agency of any government, or any judgment, order, writ, decree, permit or license of any court or other agency of any government to which the Purchaser may be subject; (ii) any contract, agreement, commitment or instrument to which the Purchaser is a party or by which the Purchaser or any of its assets are bound or committed; or (iii) the Purchaser's constituent charter documents or other governing instruments.

3.4 PURCHASE FOR INVESTMENT. The Shares to be purchased by the Purchaser pursuant to this Agreement are being purchased for the Purchaser's own account, for investment and not with a view to the distribution or resale thereof, except in compliance with the Securities Act of 1933, as amended (the "Act") and applicable Canadian legislation.

3.5 ACCREDITED INVESTOR. The Purchaser is an Accredited Investor within the meaning of Rule 501 of Regulation D of the Act.

3.6 RESTRICTED SECURITIES. The Purchaser understands that the Shares it is purchasing are characterized as "restricted securities" under U.S. federal securities laws inasmuch as they are being acquired in a transaction not involving a public offering and that under such laws and

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applicable regulations such Shares may be resold without registration under the Act only in certain limited circumstances. In the absence of an effective registration statement covering the Shares or an available exemption from registration under the Act, the Shares must be held indefinitely. In this connection, the Purchaser represents that it is familiar with SEC Rule 144, as presently in effect, and understands the resale limitations imposed thereby and by the Act.

3.7 FINDERS. The Purchaser has not directly or indirectly dealt with anyone acting in the capacity of a finder or broker and has not incurred any obligations for any finders' or broker's fee or commission in connection with the transactions contemplated by this Agreement.

ARTICLE IV

COVENANTS

4.1 COOPERATION. The parties hereto shall cooperate fully with each other in furnishing any information or performing any action reasonably requested by each to the other party, which information or action is necessary to the prompt and successful consummation of the transactions contemplated by this Agreement. Subject to its further rights under this Agreement, each party hereto shall cause the Closing to occur by the Closing Date or as soon thereafter as practicable.

4.2 FILINGS BY SELLER. The Seller shall, at its own expense, make in a timely manner, all appropriate filings required to be made with the Quebec Securities Commission or any other Canadian regulatory agency in connection with the sale of the Shares pursuant to this Agreement, including the filing required to be made pursuant to Section 51 of the Quebec Securities Act.

4.3 TRANSFER TAXES, FEES AND EXPENSES. Each party shall bear responsibility for its own expenses associated with the sale, purchase and transfer of the Shares. Any expenses incurred in connection with the transfer of the Shares and requested to be paid by the Company shall be paid by the Seller.

4.4 CONSENTS AND WAIVERS. The Seller shall use its best efforts to obtain the Portfolio Company Certificates, and, to the extent necessary, appropriate or desirable, consents in writing to the transactions contemplated by this Agreement and/or such amendments, assignments, waivers or modifications of such documents or instruments as may be required so that the transactions contemplated by this Agreement may be consummated and shall not result in any default or breach of any of the articles or bylaws of the Company, the Shareholders' Agreement or other contract, agreement, commitment or instrument to which the Seller is a party or by which the Seller or any of the Seller's assets are bound or committed, including waivers of all rights of first refusal, first offer or co-sale rights potentially applicable to the sale, assignment or transfer of the Shares and consents to, or approvals of, the sale, assignment and transfer to the Purchaser of all of the Contractual Rights.

4.5 ACCESS. The Seller shall permit the Purchaser and its partners, advisors, attorneys, accountants and other representatives full access after reasonable notice during normal business hours to the Shares, the Shareholders' Agreement and all other instruments, agreements and

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documents representing or constituting the Shares or any part thereof or relating to the capital stock of the Company that are in the Seller's possession on the date hereof.

4.6 CERTAIN CONDUCT. Without the prior written consent of the Purchaser, prior to the Closing Date the Seller shall not (i) sell, assign, transfer, deliver or otherwise dispose of the Shares, (ii) forgive, release, compromise or demand payment of any indebtedness owed to it by the Company other than upon full payment thereof, (iii) amend, cancel or terminate the Shareholders' Agreement, (iv) waive, amend, cancel, terminate, exercise or fail to exercise any of the Contractual Rights, (v) create or permit to exist any Lien on the Shares or (vi) agree to do any of the foregoing.

4.7 CONFIDENTIALITY. All information furnished by the Purchaser to the Seller or by the Seller to the Purchaser in connection with this Agreement and the transactions contemplated hereby, as well as the terms, conditions and provisions of this Agreement and the Ancillary Agreements, including the amount and form of the Payment, shall be kept strictly confidential by the Seller and the Purchaser and shall be used by the Seller and the Purchaser only in connection with this Agreement and the transactions contemplated hereby, except to the extent that such information (i) is already known by the party to whom the information is disclosed or in the public domain at the time the information is disclosed, other than by reason of breach of this provision, (ii) thereafter becomes lawfully obtainable from other sources other than by breach of the confidentiality obligations of such party, (iii) is required to be disclosed in

any document to be filed with any federal, state, provincial, municipal or other governmental department, commission, board, court, bureau, agency or instrumentality, domestic or foreign or (iv) is required under securities laws or regulations applicable to the Seller or Purchaser (including notice of the transactions contemplated hereby given pursuant to rules and regulations of the Securities and Exchange Commission and applicable Canadian securities legislation); provided, however, in the cases of subsections (iii) and (iv) of this sentence, any party required to make any such disclosure shall only do so, to the extent feasible, after notice to, and consultation with the other parties hereto. No party hereto shall issue any press release or make any public announcement relating to the subject matter of this Agreement without the prior written approval, not to be unreasonably withheld, of the other parties hereto except as may be required by law (and then, to the extent feasible, only after notice to, and consultation with the other party). Notwithstanding the foregoing, the Seller and the Purchaser may disclose such information to their partners, directors, officers, employees, investors, advisors, trustees and representatives on a need-to-know basis in connection with the transactions contemplated hereby (disclosure by Purchaser of asset price information to its investors shall qualify under the need-to-know-basis), provided that such persons shall be informed of the confidential nature of such information and shall be contractually obligated to keep such information confidential pursuant to the terms of this Section 4.7.

4.8 OTHER NEGOTIATIONS. The Seller shall not, and shall not authorize or permit any of its agents or other representatives to, directly or indirectly, initiate, facilitate, solicit, encourage or participate in discussions with, provide information to, or approve or enter into a transaction, agreement or contract with, any corporation, partnership, person or other entity or group concerning any sale, assignment, transfer or other disposition of any of the Shares (all such transactions being referred to herein as "Disposition Transactions"). The Seller shall promptly communicate to the Purchaser the terms of any proposal which it may receive in respect of a

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Disposition Transaction and any request by or indication of interest on the part of any third party with respect to initiation of any Disposition Transaction or discussions with respect thereto.

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ARTICLE V

CLOSING MATTERS

5.1 THE CLOSING. Subject to satisfaction or waiver of all conditions precedent set forth in Article VI, the closing with respect to the transfer of the Shares (the "Closing") shall be held at the offices of Brobeck, Phleger & Harrison LLP, San Francisco, CA 94105, at 3:00 pm on April 30, 2001, or on such other date as the Purchaser and the Seller may agree (the "Closing Date"). If any condition in Article VI is not satisfied in any respect (or is not duly waived) at the Closing, the party or parties whose obligations are subject to such condition may extend the date of the Closing (during which extension each of the other parties shall use all reasonable efforts to cause all such conditions to be satisfied in all respects). If all conditions are determined to be satisfied (or are duly waived) at the Closing (whether or not delayed), the Closing shall be consummated.

5.2 DELIVERY OF SHARES AND ASSIGNMENTS. At the Closing, the Seller shall deliver, to the extent not previously delivered, or cause to be delivered to the Purchaser (i) all of the instruments and other documents that represent or constitute the Shares to be transferred at the Closing, together with all transfer forms duly signed necessary to register the transfer of the Shares to the Purchaser in the books of the Company, (ii) such releases, approvals, consents, waivers and other supporting documents as may in the reasonable opinion of the Purchaser be necessary to permit the Purchaser to acquire the Shares free and clear of all Liens (other than the Encumbrances to the extent they do not apply to the transactions contemplated by this Agreement), and (iii) the Shareholders' Agreement Amendment, and (iv) the other documents and agreements referenced in Section 6.1.

5.3 DOCUMENTS AND CERTIFICATES. The Purchaser and the Seller shall use all reasonable efforts, on or prior to the Closing, to execute and deliver all such instruments, documents or certificates as may be necessary, appropriate or desirable, on the advice of counsel, for the consummation at the Closing of the transactions contemplated by this Agreement.

ARTICLE VI

CONDITIONS OF CLOSING

6.1 CONDITIONS APPLICABLE TO THE PURCHASER. The obligations of the Purchaser under this Agreement to consummate the transactions contemplated by this Agreement at the Closing are, at its option, subject to the following conditions:

(a) PERFORMANCE OF THIS AGREEMENT. All the terms, covenants and conditions of this Agreement to be complied with and performed by the Seller at or before the Closing shall have been fully complied with and performed in all material respects.

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(b) ACCURACY OF REPRESENTATIONS AND WARRANTIES. The representations and warranties of the Seller set forth in this Agreement shall be true and correct in all material respects both on the date of this Agreement and as of the Closing Date (with the same force and effect as if such representations and warranties were made anew at and as of the Closing Date, except (i) to the extent that such representations and warranties are by their express provisions made as of the date of this Agreement or another specified date and (ii) for the effect of any activities or transactions which may have taken place after the date of this Agreement which are contemplated by this Agreement).

(c) LITIGATION. No action, suit, litigation, proceeding or investigation shall (i) have been formally instituted and be pending with regard to the transactions contemplated by this Agreement or (ii) be threatened with regard to the transactions contemplated by this Agreement. On the Closing Date, there shall not be in force any injunction, order or decree restricting or enjoining consummation of the transactions contemplated by this Agreement.

(d) REQUIRED CONSENTS, WAIVERS AND NOTICES. The Seller shall have obtained all required consents in writing to the transactions contemplated by this Agreement and such amendments, assignments, waivers or modifications of such documents or instruments as may be required so that the transactions contemplated by this Agreement may be consummated and shall not result in any default or breach of the Shareholders' Agreement or any other agreement, contract, commitment or instrument to which the Seller are parties or by which the Seller or any of their assets are bound or committed, including waivers of all rights of first refusal, first offer or co-sale rights potentially applicable to the sale, assignment or transfer of the Shares and consents to, or approvals of, the sale, assignment and transfer to the Purchaser of all of the Contractual Rights. The Seller shall have timely given notice to all parties that may be required in order to effect the transfer of the Shares and all rights relating thereto. All such consents, waivers and approvals referred to in this Section 6.1(d) shall be in a form and substance which is satisfactory to the Purchaser, in its sole discretion.

(e) CERTIFICATE CONCERNING THIS AGREEMENT. The Seller shall furnish to the Purchaser a certificate dated the Closing Date, signed by it to the effect that the conditions set forth in subsections (a) through (d) of this Section 6.1 have been satisfied.

(f) MATERIAL ADVERSE CHANGE, INACCURACY OR BREACH. No fact or

circumstance shall have come to the attention of the Purchaser which in the judgment of the Purchaser constitutes or would constitute a Material Adverse Change, or constitute a material breach of any covenant of the Seller hereunder or constitute or reflect any material inaccuracy in or breach of any representation and warranty made or to be made by the Seller in connection with this Agreement.

(g) PROCEEDINGS. All proceedings to be taken by the Seller in connection with the transactions contemplated by this Agreement and all documents incident thereto shall be reasonably satisfactory in form and substance to the Purchaser, and the Purchaser shall have received copies of all such documents and other evidence as it may reasonably request to establish the consummation of such transactions and the taking of all proceedings in connection therewith.

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(h) PORTFOLIO COMPANY CERTIFICATES. The Purchaser shall have received the Portfolio Company Certificates from the Company.

(i) LEGAL OPINION. The Purchaser shall have received from Holland & Knight a legal opinion, addressed to the Purchaser and dated the Closing Date, substantially in the form of Exhibit 6.1(i) hereto.

(j) TAX CLEARANCE CERTIFICATES. The Seller shall have received tax clearance certificates from each of the Canada Customs and Revenue Agency and the Minister of Revenue for Quebec with respect to the sale of the Shares, in each case fixing a certificate limit or an estimated or actual amount of proceeds of disposition which, in the aggregate, shall not be less than C\$6,697,500 (the "Certificate Limit"), and the Purchaser shall have received copies of each such certificate (the "Clearance Certificates").

The Purchaser may waive the preceding condition if the Seller has not received and delivered the Clearance Certificates at the Closing in which case the Purchaser will withhold thirty seven percent (37%) of the Payment (the "Withholding"). If the Seller delivers to the Purchaser the Clearance Certificates before the last business day that is not more than twenty seven (27) days after the last day of the month in which the Closing occurred (the "Remittance Date"), the Purchaser shall remit to the Seller forthwith upon the delivery of such Clearance Certificates the amount of the Withholding. If the Clearance Certificates are not delivered to the Purchaser on or before the Remittance Date, the Purchaser shall remit the amount of the Withholding to the Receiver General of Canada and the Minister of Revenue for Quebec in accordance with the Income Tax Act (Canada) and the Taxation Act (Quebec). The Seller shall have no recourse against the Purchaser for having withheld and remitted any amount in compliance with this paragraph and the Income Tax Act (Canada) and the Taxation Act (Quebec).

(k) SHAREHOLDERS' AGREEMENT. The Seller, the Company and all other parties to the Shareholders' Agreement shall have entered into an amendment to the Shareholders' Agreement in a form and substance satisfactory to the Purchaser in its sole discretion (the "Shareholders' Agreement Amendment").

(1) AMENDMENT TO ARTICLES OF INCORPORATION. The Articles of Incorporation of the Company shall have been amended to convert the Company's Class A shares and Class B shares into Common shares of the Company in a form and substance satisfactory to the Purchaser in its sole discretion.

(m) NOTE HOLDER RELEASE. The Purchaser shall have received evidence, in a form and substance satisfactory to the Purchaser in its sole discretion, that the holders of the Seller's 8% notes due 2002 and the holders of the Seller's \$6,000,000 notes due 2003, have released their security interest in the Shares.

6.2 CONDITIONS APPLICABLE TO THE SELLER. The obligations of the Seller under this Agreement to consummate the transactions contemplated by this

Agreement at the Closing are, at their option, subject to the following conditions:

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(a) PERFORMANCE OF THIS AGREEMENT. All terms, covenants and conditions of this Agreement to be complied with and performed by the Purchaser at or before the Closing shall have been fully complied with and performed in all material respects.

(b) ACCURACY OF REPRESENTATIONS AND WARRANTIES. The representations and warranties of the Purchaser set forth in this Agreement shall have been true and correct in all material respects both on the date of this Agreement and as of the Closing Date (with the same force and effect as if such representations and warranties were made anew at and as of the Closing Date, except (i) to the extent that such representations and warranties are by their express provisions made as of the date of this Agreement or another specified date and (ii) for the effect of any activities or transactions which may have taken place after the date of this Agreement which are contemplated by this Agreement).

(c) LITIGATION. No action, suit, litigation, arbitration, proceeding or investigation shall (i) have been formally instituted and be pending with regard to the transactions contemplated by this Agreement or (ii) be threatened by any governmental authority of the United States or any State thereof with regard to the transactions contemplated by this Agreement. On the Closing Date, there shall not be in force any injunction, order or decree restraining or enjoining consummation of the transactions contemplated by this Agreement.

(d) REQUIRED CONSENTS AND WAIVERS. The Seller shall have obtained all required consents in writing to the transactions contemplated by this Agreement and such amendments, assignments, waivers or modifications of such documents or instruments as may be required so that the transactions contemplated by the Agreement may be consummated and shall not result in any default or breach of the Shareholders' Agreement, or any other agreement, contract, commitment or instrument to which the Seller is a party or by which the Seller or any of its assets are bound or committed, including waivers of all rights of first refusal and rights of co-sale potentially applicable to the sale, assignment or transfer of the Shares and consents to, or approvals of, the sale, assignment and transfer to the Purchaser of all of the Contractual Rights.

(e) SHAREHOLDERS' AGREEMENT. The Purchaser, the Company and all other parties to the Shareholders' Agreement shall have entered into the Shareholders' Agreement Amendment.

(f) PROCEEDINGS. All proceedings to be taken by the Purchaser in connection with the transactions contemplated by this Agreement and all documents incident thereto shall be reasonably satisfactory in form and substance to the Seller, and the Seller shall have received copies of all such documents and other evidence as the Seller may reasonably request to establish the consummation of such transactions and the taking of all proceedings in connection therewith.

ARTICLE VII

TERMINATION

7.1 BY MUTUAL CONSENT. This Agreement may be terminated and the transactions contemplated by this Agreement abandoned before the Closing pursuant to the mutual written consent of the Purchaser and the Seller at any time prior to the Closing for any reason.

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7.2 BY PURCHASER. This Agreement may be terminated at any time by the Purchasers (i) in accordance with Section 1.6; or (ii) if any event occurs or condition exists which would render impossible the satisfaction of one or more conditions to the obligations of the Purchasers to consummate the transactions contemplated by this Agreement as set forth in Section 6.1; provided, however, that the right to terminate this Agreement under this Section 7.2 shall not be available if Purchaser's failure to fulfill any obligation under this Agreement shall have been the cause of, or shall have resulted in, the failure to satisfy such conditions.

7.3 BY SELLER. This Agreement may be terminated at any time by the Seller if any event occurs or condition exists which would render impossible the satisfaction of one or more conditions to the obligations of the Seller to consummate the transactions contemplated by this Agreement as set forth in Section 6.2; provided, however, that the right to terminate this Agreement under this Section 7.3 shall not be available if Seller's failure to fulfill any obligation under this Agreement shall have been the cause of, or shall have resulted in, the failure to satisfy such conditions.

7.4 BY EITHER PARTY. This Agreement may be terminated by either the Purchasers or the Seller if the Closing shall not have occurred by April 30, 2001, which date may be extended by mutual agreement of the parties pursuant to Section 5.1; provided, however, that the right to terminate this Agreement under this Section 7.4 shall not be available to any party whose failure to fulfill any obligation under this Agreement shall have been the cause of, or shall have resulted in, the failure of the Closing to occur on or prior to such date.

7.5 SURVIVAL UPON TERMINATION. If this Agreement is terminated, the agreements of the Seller and the Purchaser contained in Sections 4.7, 7.5, 7.6 and 9.1 and Article VIII shall survive such termination.

7.6 EXPENSES. In the event of termination of this Agreement under Section 7.1, each party hereto will pay all of its own fees and expenses and there will be no further liability hereunder on the part of any party hereto, except for liability for a willful breach by a party of its covenants or representations and warranties hereunder.

ARTICLE VIII

INDEMNIFICATION

8.1 INDEMNIFICATION. The Seller hereby agrees to defend, indemnify and hold harmless the Purchaser from and against any damage, liability, loss, cost or expense (including reasonable attorneys' fees) occasioned or caused by, resulting from or arising out of (i) any failure by the Seller to perform any of its covenants or obligations as set forth in this Agreement or in any certificate or instrument delivered pursuant to this Agreement; (ii) any inaccuracy in or breach of any of the representations or warranties of the Seller set forth in this Agreement; and (iii) any and all actions, suits, litigations, arbitrations, proceedings, investigations or claims arising out of any of the foregoing or out of facts relating to the foregoing that have occurred on or prior to the Closing Date even though such proceeding or claim may not be filed or come to light until after the Closing Date (the "Purchaser's Damages").

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The maximum aggregate amount for which the Seller shall be liable for under the indemnification obligations set forth in this Section 8.1 is an amount equal to the Payment. In no event whether in contract or tort (including breach of warranty, negligence and strict liability in tort), shall either party be liable to the other party for indirect or consequential damages, even if such party has been advised of the possibility of such damages in advance. 8.2 INDEMNIFICATION BY PURCHASER. The Purchaser hereby agrees to defend, indemnify and hold harmless the Seller from and against any damage, liability, loss, cost or expense (including reasonable attorneys' fees) occasioned or caused by, resulting from or arising out of (i) any failure by the Purchaser to perform any of its covenants or obligations as set forth in this Agreement or in any certificate or instrument delivered pursuant to this Agreement; (ii) any inaccuracy in or breach of any of the representations or warranties of the Purchaser set forth in this Agreement; and (iii) any and all actions, suits, litigations, arbitrations, proceedings, investigations or claims arising out of any of the foregoing or out of facts relating to the foregoing that have occurred on or prior to the Closing Date even though such proceeding or claim may not be filed or come to light until after the Closing Date (the "Seller's Damages").

The maximum aggregate amount for which the Purchaser shall be liable for under the indemnification obligations set forth in this Section 8.2 is an amount equal to the Payment. In no event whether in contract or tort (including breach of warranty, negligence and strict liability in tort), shall either party be liable to the other party for indirect or consequential damages, even if such party has been advised of the possibility of such damages in advance.

8.3 INDEMNIFICATION PROCEDURE. As used in this Section 8.3, the term "Indemnified Party" shall mean either the Seller or the Purchaser, as the case may be, that is asserting a claim for indemnity under this Article VIII and the term "Indemnifying Party" shall mean the party against whom the Indemnified Party is seeking indemnification. The Indemnified Party agrees to give the Indemnifying Party prompt notice of any event, or any written claim by a third party, of which it obtains knowledge, which could give rise to any damage, liability, loss, cost or expense as to which it may request indemnification under this Agreement, and, in the case of such third party claims or assertions, the Indemnified Party, at the expense of the Indemnifying Party, will cooperate with the Indemnifying Party in determining the validity of any such claim or assertion. In connection with any such third party claim if the Indemnifying Party shall have acknowledged in writing its obligation to indemnify in respect of such claim which might give rise to a claim for indemnity hereunder, the Indemnifying Party may select counsel to direct the defense of such third party claim, which counsel shall be reasonably satisfactory to the indemnified party. The Indemnifying Party shall arrange for such counsel to inform the Indemnified Party on a regular basis of the status of such case. The Indemnified Party may, at its election and expense, participate in the defense of such third party claim. The Indemnifying Party shall not settle any such claim without the consent of the Indemnified Party if any relief, other than the payment of money damages, would be granted by such settlement or if the Indemnified Party would be liable to the third party for the amount of such settlement.

8.4 NO WAIVER; OTHER INDEMNIFICATION PROVISIONS. In no event will the any party hereto be deemed to waive any breach by the other parties of any representation, warranty, covenant or agreement by reason of such party's completing the Closing with knowledge thereof. Except as provided in Section 8.1, the indemnification provisions of this Article VIII are in

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addition to, and not in derogation of, any statutory or common law remedy any party may have for breach of representation, warranty, or covenant.

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ARTICLE IX

MISCELLANEOUS

9.1 SURVIVAL OF REPRESENTATION AND WARRANTIES. All representations and warranties of the parties to this Agreement shall survive for twenty-four (24) months following the execution and delivery of this Agreement except that Seller's representations and warranties pursuant to Sections 2.4 shall survive in perpetuity; provided, however, that the representations and warranties of the

parties to this Agreement shall not survive the termination of this Agreement pursuant to Sections 7.1, 7.2 or 7.3, and, upon such termination, there shall be no liability on the part of either party hereto except (i) as set forth in Section 7.5, and (ii) that nothing herein shall relieve either party from liability for any willful and intentional breach of this Agreement. Any investigation or other examination that may have been made or may be made at any time by or on behalf of the party to whom representations and warranties are made shall not limit, diminish or in any way affect the representations and warranties in this Agreement, and the parties may rely on the representations and warranties in this Agreement irrespective of any information obtained by them by any investigation, examination or otherwise.

9.2 ADDITIONAL DOCUMENTS AND ACTS. After the Closing, each of the parties hereto shall execute and deliver such additional documents, certificates and instruments, and perform such additional acts, as may be reasonably requested and necessary or appropriate to carry out all of the provisions of this Agreement and to consummate all of the transactions contemplated by this Agreement.

9.3 SPECIFIC PERFORMANCE. Each of the parties hereto acknowledges that the other party will have no adequate remedy at law if it fails to perform any of its obligations under this Agreement. In such event, each of the parties agrees that the other party shall have the right, in addition to any other rights it may have (whether at law or in equity), to specific performance of this Agreement.

9.4 NOTICES. All notices, consents, waivers and other communications hereunder shall be in writing and shall be deemed to have been duly given when delivered in person, sent by facsimile transmission or posted by registered or certified mail, return receipt requested, with postage prepaid, addressed as follows:

if to any Purchaser:

c/o Paul Capital Partners 50 California Street, Suite 3000 San Francisco, CA 94111 Attention: Jeffrey Moelis

with a copy (not constituting notice) to: STOCK PURCHASE AGREEMENT

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Brobeck, Phleger & Harrison LLP One Market Spear Street Tower San Francisco, CA 94105 Attention: Ronald B. Moskovitz, Esq.

if to the Seller:

Hybridon, Inc. 345 Vassar Street Cambridge, MA 02139 Attention: Robert Andersen

with a copy (not constituting notice) to:

Holland & Knight LLP One Beacon Street Boston, MA 02108 Attention: James Pollock, Esq.

or to such other address or addresses as the Purchasers or the Seller may from time to time designate by notice as provided herein, except that notices of changes of address shall be effective only upon receipt. 9.5 ASSIGNMENT. Neither party hereto may assign or delegate this Agreement or any rights or obligations hereunder to any person without the prior written consent of the other.

9.6 WAIVER. Either party hereto may, by express written notice to the other, (i) extend the time for the performance of any of the obligations or other actions of the other party under this Agreement; (ii) waive any inaccuracies in the representations or warranties of the other party contained in this Agreement or in any document delivered pursuant to this Agreement; (iii) waive compliance with any of the conditions or covenants of the other party contained in this Agreement; or (iv) waive or modify performance of any of the obligations of the other party under this Agreement. Except as provided in the preceding sentence, no action taken pursuant to this Agreement, including, without limitation, any investigation by or on behalf of any party, shall be deemed to constitute a waiver by the party taking such action of compliance by the other party with any of the representations, warranties, covenants, conditions, agreements or indemnities contained in this Agreement. The waiver by any party of a breach of any provision of this Agreement shall not operate or be construed as a waiver of any subsequent breach.

9.7 ENTIRE AGREEMENT. This Agreement and the Ancillary Agreements, together with the Schedules and Exhibits to this Agreement (which are incorporated herein by reference) and certificates to be delivered at Closing pursuant to this Agreement, supersedes any other agreement, whether written or oral, that may have been made or entered into by the parties hereto relating to the matters contemplated hereby, and constitutes the entire agreement of the parties hereto with respect to the subject matter hereof.

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9.8 AMENDMENTS, SUPPLEMENTS, ETC. This Agreement may be amended or supplemented only by additional written agreements, articles or certificates signed by the Purchaser and the Seller, as may be determined by the parties hereto to be necessary, appropriate or desirable to further the purposes of this Agreement, to clarify the intention of the parties, or to add to or to modify the covenants, terms or conditions hereof.

9.9 INTERPRETATION. When a reference is made in this Agreement to Articles, Sections, Schedules, Exhibits or certificates such reference shall be to an Article, Section, Schedule, Exhibit or certificate to this Agreement unless otherwise indicated. The words "include," "includes" and "including" when used herein shall be deemed in each case to be followed by the words "without limitation." Neither party hereto shall be or be deemed to be the drafter of this Agreement for the purposes of construing this Agreement against one party or the other.

9.10 HEADINGS AND CAPTIONS. The headings and captions in this Agreement are for convenience and reference purposes only and shall not be considered a part of or affect the construction or interpretation of any provision of this Agreement.

9.11 COUNTERPARTS. This Agreement may be executed in two or more counterparts, each of which shall be an original, but all of which together shall constitute one and the same instrument.

9.12 SUCCESSORS AND ASSIGNS. This Agreement shall be binding upon, inure to the benefit of and may be enforced by, each of the parties hereto and their respective permitted successors and assigns.

9.13 ATTORNEYS' FEES. In the event of any legal action or proceeding respecting this Agreement, the prevailing party shall be entitled to recover its costs and expenses (including, without limitation, reasonable attorneys' fees) incurred in such action or proceeding.

9.14 SEVERABILITY. If any provision of this Agreement is held to be

9.15 GOVERNING LAW. This Agreement shall be governed by and construed, interpreted and enforced in accordance with the laws of the State of California, without giving effect to the principles of conflicts of law thereof. [REMAINDER OF PAGE INTENTIONALLY LEFT BLANK] STOCK PURCHASE AGREEMENT 18 IN WITNESS WHEREOF, the Purchasers and the Seller have caused this Stock Purchase Agreement to be duly executed and delivered as of the date first above written. PURCHASERS: HYBRIDON, INC. PAUL CAPITAL PARTNERS VI HOLDINGS Bv: PAUL CAPITAL MANAGEMENT, LLC Its General Partner _____ Name: Robert Andersen Its: Vice President and Chief Financial Officer By: ------Jeffrey Moelis, Manager Member 50 California Street Suite 3000 San Francisco, CA 94111 PCP ASSOCIATES, L.P. PAUL CAPITAL MANAGEMENT, LLC By: Its General Partner Bv: ------Jeffrey Moelis, Manager Member 50 California Street Suite 3000 San Francisco, CA 94111 SIGNATURE PAGE TO

invalid or unenforceable, the remaining provision shall nevertheless be given

STOCK PURCHASE AGREEMENT FOR PURCHASE OF METHYLGENE INC. SHARES FROM HYBRIDON, INC.

19.

STOCK PURCHASE AGREEMENT

23

full force and effect.

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SELLER:

By:

EXHIBIT A CERTIFICATE OF CAPITALIZATION

The undersigned hereby certifies to the Purchaser, its affiliated entities and its investors that he or she is the duly elected President, Chief Financial Officer or Secretary of MethylGene Inc., a corporation formed under the laws of Quebec (the "Company"), and that as such he or she is authorized to execute this certificate for and on behalf of the Company, and further certifies for and on behalf of the Company that set forth on Annex A attached hereto is a complete and accurate list of the authorized and outstanding shares of capital stock of the Company, including all shares and securities which are issuable upon the exercise, exchange or conversion of any rights, options or warrants to purchase shares of the capital stock of the Company, issued by the Company as of the date first written below, and the number of shares of such stock and/or securities and rights, options or warrants to purchase such shares or securities of the Company held by Hybridon, Inc. Further, there has been no issuance of common

stock equivalents issued since the date of the capitalization table set forth on Annex A.

IN WITNESS HEREOF, this Certificate of Capitalization is hereby executed as of , 2001.

METHLYGENE Inc.

By: -----

------ (Print Name)

(IIIIC Nam

(Title)

Annex A

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EXHIBIT B

CERTIFICATE OF TRANSFER

The undersigned hereby certifies to the Purchaser (the "Transferee") that he or she is the duly elected President, Chief Financial Officer or Secretary of MethylGene Inc., a corporation formed under the laws of Quebec (the "Company"), and that as such he or she is authorized to execute this certificate for and on behalf of the Company, and further certifies for and on behalf of the Company that the proposed transfer of 2,350,000 Common shares of the Company (the "Shares") owned by Hybridon, Inc. (the "Transferor"), will upon delivery of the share certificates duly endorsed or accompanied with a transfer form duly signed for transfer of the Shares for the Transferee be duly recorded in the corporate records of the Company and that the Transferee will be the holder of record of the Shares and as such will have all attendant rights pertaining to the shares granted under the articles of the Company.

IN WITNESS HEREOF, this Certificate of Transfer is hereby executed as of , 2001.

METHYLGENE INC.

By:

(Print Name)

(Title)

Attachment A

SCHEDULE 1.2 PURCHASER DETAILS

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| Purchaser Name | Number of Common Shares being Purchased |
|--------------------------------|-----------------------------------------|
| | |
| Paul Capital Partners VI, L.P. | 2,009,964 |
| PCP Associates, L.P. | 340,036 |

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SCHEDULE 2.4

THE METHYLGENE INC. SHARES OWNED BY SELLER ARE THE SUBJECT OF A SECURITY INTEREST FOR THE BENEFIT OF THE HOLDERS OF SELLER'S 8% NOTES DUE 2002 AND SELLER'S \$6,000,000 NOTES DUE 2003. SUCH HOLDERS HAVE SIGNED AN INSTRUMENT WAIVING THEIR RIGHTS WITH RESPECT TO DISPOSITIONS OF THE METHYLGENE INC. AND RELEASING THEIR SECURITY INTEREST THEREIN FOR THE PURPOSE OF PERMITTING SUCH SHARES TO BE SOLD BY SELLER TO PURCHASER.

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SCHEDULE 2.5 COMPANY CAPITALIZATION

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SCHEDULE 2.9 SHAREHOLDERS' AGREEMENT

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EXHIBIT 6.1(i) FORM OF OPINION OF SELLER'S COUNSEL

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April , 2001

PAUL CAPITAL PARTNERS VI, L.P. and PCP ASSOCIATES, L.P. c/o Paul Capital Partners 50 California Street, Suite 3000 San Francisco, CA 94111

Attention: Jeffrey Moelis

Re: Hybridon, Inc. Sale of Stock of Methylgene, Inc. Under Stock Purchase Agreement dated as of March 30, 2001

Ladies and Gentlemen:

We have acted as special counsel for Hybridon, Inc., a Delaware corporation (the "COMPANY"), in connection with the preparation, execution and delivery of, and sale of stock under, the Stock Purchase Agreement, dated as of March __, 2001, between you and the Company (the "AGREEMENT"). This letter is delivered to you pursuant to Section 6.1(i) of the Agreement. Capitalized terms not defined in this letter have the meanings ascribed to them in the Agreement.

For purposes of our opinions, we have reviewed such documents and made such other investigation as we have deemed appropriate. As to matters of fact, we have relied on the representations and warranties made by the parties in the Agreement and on certificates of public officials and officers of the Company. We have made no independent investigation of the accuracy or completeness of such matters of fact. In rendering the following opinions, we have relied, without independent investigation, upon the following assumptions:

(a) Each party to the Agreement (other than the Company) is duly organized and is validly existing and in good standing in its jurisdiction of organization;

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(b) Each party to the Agreement (other than the Company) has full power and authority to execute, deliver and perform its obligations under the Agreement, and the Agreement has been duly authorized by all necessary action on its part and has been duly executed and duly delivered by it;

(c) The Agreement constitutes the valid and binding obligation of each party to the Agreement (other than the Company), enforceable against such party in accordance with its terms;

(d) Each natural person executing the Agreement or any document referred to herein is legally competent to do so;

(e) Each party to the Agreement (other than the Company) has complied with all legal requirements pertaining to its status as such status relates to its rights to enforce the Agreement against the Company (including, but not limited to, qualifying to do business, if required, in the Commonwealth of Massachusetts;

(f) Each document submitted to us for review is accurate and complete, each such document that is an original is authentic, each such document that is a copy conforms to an authentic original, and all signatures on each such document are genuine;

(g) There has not been any mutual mistake of fact or misunderstanding, fraud, duress or undue influence;

(h) The Agreement will be enforced in circumstances and in a manner in which it is commercially reasonable to do so and the conduct of the parties complies with any requirement of good faith and fair dealing;

(i) There are no agreements or understandings among the parties, written or oral, and there is no usage of trade or course of prior dealing among the parties that would, in either case, define, supplement or qualify the terms of the Agreement; and

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(j) Each person who has taken any action relevant to any of our opinions in the capacity of director or officer was duly elected to that director or officer position and held that position when such action was taken.

For purposes of this opinion letter, the terms "to our knowledge", "we are not aware" or similar terms means the conscious awareness of facts or other information, at the time of delivery of this opinion letter, by the lawyers in our firm who have had involvement in the negotiation and preparation of the Agreement. Except to the extent expressly set forth herein, we have not undertaken any independent investigation to determine the existence or absence of any facts or other information, and no inference as to our knowledge or the existence or absence of any such facts or other information should be drawn from the fact of our representation of the Company as special counsel.

Notwithstanding our opinions expressed herein, we express no opinion with respect to any of the following provisions in the Agreement:

(a) Choice-of-law provisions;

(b) Covenants not to compete, including covenants not to interfere with business or employee relations, covenants not to solicit customers, and covenants not to solicit or hire employees;

(c) Indemnification of a party for its own gross negligence, willful misconduct, recklessness or other wrongful conduct;

(d) Provisions mandating contribution towards judgments or settlements among various parties;

(e) Waivers of (i) legal or equitable defenses, (ii) rights to damages, (iii) rights to counter claim or set off, (iv) statutes of limitations, (v) rights to notice, (vi) the benefits of statutory, regulatory, or constitutional rights, unless and to the extent the statute, regulation, or constitution explicitly allows waiver, and (vii) other benefits to the extent they cannot be waived under applicable law;

(f) Provisions providing for forfeitures or the recovery of amounts deemed to constitute penalties or for liquidated damages;

(g) Provisions that provide a time limitation after which a remedy may not be enforced;

(h) Agreements to submit to the jurisdiction of any particular court or other governmental authority; provisions restricting access to courts; waiver of service of process requirements which would otherwise be applicable; and provisions otherwise purporting to affect the jurisdiction and venue of courts;

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(i) Provisions that attempt to change or waive rules of evidence or fix the method or quantum of proof to be applied in litigation or similar proceedings;

(j) Any Federal, state or local law relating to taxation, zoning, land use, the environment, antitrust, banking, securities or ERISA; and

(k) Provisions regarding arbitration.

Based on and subject to the foregoing and subject to the exceptions, qualifications and limitations hereinafter set forth, we express the following opinions.

1. The Company is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware, and the Company has the requisite corporate power and authority to own its properties and to conduct its business as, to our knowledge, it is presently conducted.

- The Company has the requisite corporate power and authority to execute, deliver and perform the Agreement. The Agreement has been duly and validly authorized by the Company, has been duly executed and delivered by an authorized officer of the Company and constitutes a legal, valid and binding obligation of the Company, enforceable by you against the Company in accordance with its terms.
- Neither the execution or delivery by the Company of the Agreement nor the consummation by the Company at the Closing of the transactions contemplated thereby will (i) violate any provision of the Articles of Incorporation or Bylaws of the Company, (ii) violate or be in conflict with any federal or Massachusetts laws which to our knowledge are applicable to the Company, (iii) to our knowledge, violate or contravene any judgment, decree, injunction or order of any federal or Massachusetts court, or any arbitrator or governmental agency or authority, having jurisdiction over

the Company or its properties or by which the Company may be bound or (iv) constitute a material breach of, or result in a material default under, any term or provision of any material contracts of which we have knowledge.

2. No consents, approvals or authorizations of or filings with any governmental authority of the Commonwealth of Massachusetts, State of Delaware or the United States are required or necessary on the part of the Company in connection with the execution, delivery and performance at the Closing by the Company of the Agreement, except for (i) such consents, approvals, authorizations or filings which have been obtained, waived or made prior to the date hereof, and (ii) the consents, approvals, authorizations and filings listed in Section 2.1 of the Disclosure Schedule to the Purchase Agreement.

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3. We are not aware that there is any action, proceeding or governmental investigation pending, or threatened in writing, against the Company which questions the validity or enforceability of the Agreement or the right of the Company to enter into the Agreement.

The offer and sale of the Shares pursuant to the Agreement are exempt from the registration requirements of the Securities Act of 1933, as amended, and from the registration requirements of the applicable securities laws of the Commonwealth of Massachusetts.

Our opinions are subject to bankruptcy, insolvency, fraudulent conveyance, reorganization, moratorium and other laws affecting the rights and remedies of creditors generally and to general principles of equity, regardless of whether considered in a proceeding in equity or at law.

Our opinions are also subject to the effect of rules of law that:

(a) limit or affect the enforcement of provisions of a contract that purport to waive, or to require waiver of, the obligations of good faith, fair dealing, diligence and reasonableness;

(b) provide that forum selection clauses in contracts are not necessarily binding on the court(s) in the forum selected;

(c) limit the availability of a remedy under certain circumstances where another remedy has been elected;

(d) provide a time limitation after which a remedy may not be enforced;

(e) limit the right of a creditor to use force or cause a breach of the peace in enforcing rights;

(f) relate to the sale or disposition of collateral or the requirements of a commercially reasonable sale;

(g) limit the enforceability of provisions releasing, exculpating or exempting a party from, or requiring indemnification of a party for, liability for its own action or inaction, to the extent the action or inaction involves gross negligence, recklessness, willful misconduct, unlawful conduct, violation of law or public policy or litigation against another party determined adversely to such party;

(h) may, if less than all of a contract is unenforceable, limit the enforceability of the remainder of the contract to circumstances in which the unenforceable portion is not an essential part of the agreed exchange;

(i) govern and afford judicial discretion regarding the determination of damages and entitlement to attorneys' fees and other costs;

(j) permit a party that has materially failed to render or offer performance required by the contract to cure that failure unless (i) permitting a cure would unreasonably hinder the aggrieved party from making substitute arrangements for performance, or (ii) it was important in the circumstances to the aggrieved party that performance occur by the date stated in the contract; and

(k) in the absence of a waiver or consent, discharge a guarantor to the extent that (i) action by a creditor impairs the value of collateral securing guaranteed debt to the detriment of the guarantor, or (ii) guaranteed debt is materially modified.

This opinion letter is based as to matters of law solely on (i) the General Corporation Law of the State of Delaware, and (ii) such internal law of the Commonwealth of Massachusetts (but not including any statutes, ordinances, administrative decisions, rules or regulations of any political subdivision of the Commonwealth of Massachusetts), and such Federal law that, in each case in our experience, is normally applicable to a transaction of the type contemplated by the Agreement and to the parties thereto.

Our advice on each legal issue addressed herein represents our opinion concerning how that issue would be resolved were it to be considered by the highest court of the jurisdiction upon whose law our opinion on that issue is based. The manner in which any particular issue would be treated in any actual court case would depend in part on facts and circumstances peculiar to the case, and our opinions are not a guaranty of an outcome of any legal dispute which may arise with regard to the Agreement.

This letter speaks as of the date hereof. We disclaim any obligation to provide you with any subsequent opinion or advice by reason of any future changes or events which may affect or alter any opinion rendered herein.

This letter is being delivered to you in connection with the Agreement and may not be relied upon by you for any other purpose. This letter may not be relied upon by, furnished to, referred to, quoted, in whole or part, by, or filed with, any other Person without our prior written consent.

Very truly yours,

HOLLAND & KNIGHT LLP

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AND:

AGREEMENT AND MUTUAL RELEASE AND DISCHARGE dated as of the day of , 2001.

BY AND BETWEEN: METHYLGENE INC. (hereinafter referred to as the "METHYLGENE")

HYBRIDON, INC.

(hereinafter referred to as "HYBRIDON")

WHEREAS Hybridon is currently a shareholder of Methylgene;

WHEREAS Hybridon wishes to sell shares it owns in the share capital of Methylgene pursuant to an offer (the "OFFER") dated February 12, 2001 from Paul Capital Partners (Paul Capital Partners and any affiliates thereof hereinafter referred to as "PAUL CAPITAL") and accepted by Hybridon on February 14, 2001;

WHEREAS Hybridon may sell other shares it owns in the share capital of Methylgene to certain existing shareholders or to others; and

WHEREAS Methylgene has agreed to cooperate and assist Hybridon in effecting these transactions;

THEREFORE, FOR GOOD AND VALUABLE CONSIDERATION RECEIVED, THE PARTIES HERETO AGREE AS FOLLOWS:

- 1. COMPLIANCE METHYLGENE
 - 1.1 Methylgene hereby certifies that it is and, to its knowledge, Hybridon is in compliance with and not in default of any and all agreements between Hybridon and Methylgene existing as at the date hereof including, for greater certainty but not limited to, the agreements listed in Schedule A attached hereto;

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2. COMPLIANCE - HYBRIDON

2.1 Hybridon hereby certifies that it is and, to its knowledge, Methylgene is in compliance with and not in default of any and all agreements between Hybridon and Methylgene existing as at the date hereof including, for greater certainty but not limited to, the agreements listed in Schedule A attached hereto;

3. NON-COMPETITION

- 3.1 The introductory paragraph of Section 13.1 of the Shareholders Agreement (as defined in Schedule A) is amended by deleting same and replacing it with the following:
 - "13.1 Hybridon undertakes in favour of Methylgene, whether directly or indirectly, alone or in partnership, association, joint venture or other collaboration with any other person, company, partnership, business or entity, as a principal, agent, shareholder, employee, partner, consultant, subcontractor, unless for the benefit of Methylgene, at the request of Methylgene or with the consent of Methylgene, not to:"
- 3.2 Section 13.1.1 of the Shareholders Agreement is amended by deleting same and replacing it with the following:
 - "13.1(A) from the date of the Agreement and Mutual Release and Discharge entered into between Methylgene and Hybridon until the expiry of a thirty (30) month period starting the later of (a) May 31, 2001, (b) the closing of the transaction contemplated by the Offer and (c) Hybridon no longer having a nominee on Methylgene's Board of Directors (the "COMMENCEMENT DATE"), research, develop or market anywhere in the world (i) any antisense compounds to inhibit DNA Methyltransferases ("DNA METASES"), or (ii) any method of inhibiting DNA MeTases for the treatment of any indication;
 - 13.1(B) from the date of the Agreement and Mutual Release and Discharge entered into between Methylgene and Hybridon until the expiry of an eighteen (18) month period starting on the Commencement Date (the "RESTRICTIVE TERM"), not to engage in research or development or marketing anywhere in the world relating to the fields of histone deacetylases and beta-lactamases. If prior to the expiration of the Restrictive Term, Methylgene gives Hybridon written notice designating a target gene or genes within either histone deacetylases or beta-lactamases or both, as the case may be, as the Second Molecular Target and Third Molecular Target, respectively, under the License Agreement dated January 4, 1996 as amended and restated

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between the parties as of September 21, 2000 (the "LICENSE AGREEMENT"), then Hybridon, for an additional period of 18 months from the expiration of the Restrictive Term, shall refrain from research or development or marketing anywhere in the world relating to either histone deacetylases or beta lactamases, or both, depending upon which is the location of the target gene or genes so designated by Methylgene, and the designation of such target gene

or genes shall be deemed to have exhausted Methylgene's rights under the License Agreement, to specify a Second Molecular Target, if one designation is made and a Third Molecular Target if two designations are made;"

- 3.3 Sections 13.1.3 and 13.1.4 of the Shareholders Agreement are amended by deleting same and replacing them with the following:
 - "13.1.3 from the date of the Agreement and Mutual Release and Discharge entered into between Methylgene and Hybridon until the expiry of a two (2) year period starting on the Commencement Date, solicit entities which are customers or suppliers of Methylgene on the relevant date with respect to compounds or methods of the type described in 13.1(A) and 13.1(B); or
 - 13.1.4 from the date of the Agreement and Mutual Release and Discharge entered into between Methylgene and Hybridon until the expiry of a two (2) year period starting on the Commencement Date, encourage any person employed by Methylgene to leave Methylgene or solicit for employment any person who is at the time of solicitation employed by Methylgene."
- 3.4 Section 13.1 of the Shareholders Agreement is amended by adding the following:
 - "13.1.5 Nothing in the foregoing shall restrict the right of Hybridon to own up to 5% of the outstanding capital stock of companies whose shares are traded on a recognized stock exchange."
- 3.5 In the event of a merger or acquisition involving Hybridon and a non-affiliate third party (as the term "affiliate" is defined in the License Agreement), the provisions of Section 13 of the Shareholders' Agreement (until their expiration pursuant to the provisions of such Section 13), as hereinabove amended, and the provisions of Section 4 below shall continue to apply to the surviving entity but shall not be construed in any way which would prejudice and shall not prejudice the right and ability of the surviving entity to continue to do any research and development activities which the non-affiliate third party was undertaking prior to the time of the merger.
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Page 4

3.6 All other provisions of Section 13 of the Shareholders Agreement shall continue to apply mutatis mutandis. To the extent Hybridon is still a party to the Shareholders Agreement at the time of the initial public offering of the shares of Methylgene (the "IPO"), Hybridon undertakes that, pursuant to such IPO, it will agree to the termination of the Shareholders Agreement, save and except for the provisions of its Section 13, as amended hereby, which shall continue to apply for the relevant period.

4. CONFIDENTIALITY

4.1 Hybridon agrees, as long as such information or knowledge is not part of the public domain or required to be disclosed in accordance with applicable law, not to disclose, publish or

reveal in any manner whatsoever and to whomever, any information or knowledge of a confidential nature concerning the business operated by Methylgene, including, without limiting the generality of the foregoing, trade secrets, biological targets, chemical structures, inventions, software, computer programs, patents, licences, manufacturing processes, know-how, customer lists or contracts of Methylgene, whether acquired by it in its capacity as a shareholder or through any nominee on the Board of Directors, its representatives on the scientific advisory board of Methylgene or from any other means, Hybridon hereby expressly acknowledging that such trade secrets, biological targets, chemical structures, inventions, software, computer programs, patents, licences, manufacturing processes, know-how, customer lists or contract and all other information of a confidential nature concerning the business operated by Methylgene has been disclosed to it at any time on a confidential basis.

5. UNDERTAKING - LOCK-UP AGREEMENT

5.1 Hybridon shall, if it is a shareholder of Methylgene, at the request of the underwriters engaged by Methylgene in connection with its IPO, sign a lock-up agreement in their favour in customary form under which Hybridon shall agree not to sell or otherwise dispose of in any way any of its shares in the share capital of Methylgene for the period applicable to other significant shareholders of Methylgene following the IPO, the whole as required by the underwriters. Furthermore, Hybridon recognizes that it may be subject to certain escrow requirements imposed by regulators in connection with an IPO and agrees to comply therewith.

6. RELEASE AND DISCHARGE - HYBRIDON

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- 6.1 Except for obligations of the parties set forth in any agreement between them which are intended to survive the execution of this agreement, Hybridon hereby releases and discharges Methylgene from any claims, liabilities, actions or demands of any kind which Hybridon now has or hereafter can, shall or may
 - Page 5

have against Methylgene for or by reason of or in any way arising out of any cause, matter or thing whatsoever existing up to the present time.

7. RELEASE AND DISCHARGE - METHYLGENE

7.1 Except for obligations of the parties set forth in any agreement between them which are intended to survive the execution of this agreement, Methylgene hereby releases and discharges Hybridon from any claims, liabilities, actions or demands of any kind which Methylgene now has or hereafter can, shall or may have against Hybridon for or by reason of or in any way arising out of any cause, matter or thing whatsoever existing up to the present time. 8.1 Notwithstanding any provision of the Shareholders' Agreement, Hybridon agrees that, in the event it should own less than 350,000 shares in the share capital of Methylgene, Hybridon shall no longer be entitled to appoint or elect a nominee on Methylgene's Board of Directors and shall cause its nominee at that time to resign and execute a full release and discharge in customary form upon written notice by Methylgene to Hybridon.

9. EXPENSES

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9.1 Hybridon hereby agrees to pay any and all out-of-pocket expenses (including, without limitation, the fees and disbursements of Methylgene's legal and patents counsel) incurred by Methylgene in connection with the proposed sale by Hybridon of its shares in the share capital of Methylgene to Paul Capital, to any other shareholder of Methylgene or to any other person.

10. OBLIGATIONS OF METHYLGENE

- 10.1 Methylgene agrees to use its commercially reasonable efforts to approve such measures as are necessary to combine its presently outstanding class A and class B common shares into a single class so as to eliminate any preference between them in the distribution of assets as dividends or distributions upon liquidation and in furtherance of this Methylgene shall recommend that the holders of its class A and class B common shares approve and agree to any action required of them to implement the combination of the two classes of stock. Upon such approval, Methylgene will see to the implementation of these actions.
- 10.2 Methylgene agrees to use its commercially reasonable efforts to obtain the approval and consent of the other shareholders of Methylgene to the amendment to the Shareholders Agreement contemplated by Section 3 herein.

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Notwithstanding the foregoing however, Hybridon undertakes and agrees to abide by the provisions of Section 3 of this agreement, whether or not the other shareholders of Methylgene give their approval and consent to the amendments to the Shareholders Agreement contemplated thereby.

10.3 Methylgene shall and shall cause its counsel promptly to review and comment upon the forms of waiver and waiver request letter proposed by Hybridon for the purpose of Hybridon soliciting the waiver by the holders of shares of Methylgene capital stock of rights in the nature of preemption or first refusal which are a precondition of Hybridon's selling its shares to Paul Capital and to recommend such waivers to its shareholders. Furthermore, and subject to compliance with the terms of the Shareholders Agreement, Hybridon agrees, if one or more offers are made to it prior to the later of May 31, 2001 and the closing of the transaction contemplated by the Offer, to sell any other shares it owns in the capital of Methylgene to the other shareholders, to Methylgene or to a third party arranged by Methylgene at the same price and on substantially the same commercial terms as set forth in the Offer.

- 11. This agreement shall terminate on April 30, 2001 if the transaction contemplated in the Offer does not close on or prior to April 30, 2001 and, save and except for Section 9, no provision of this agreement shall survive such termination,.
- 12. This mutual release and discharge may be executed in one or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. The agreements herein are in addition to any other agreements or understandings between the parties, which other agreements and understandings are not terminated hereby and continue to apply.
- 13. The mutual release and discharge is governed by the laws of the Province of Quebec.
- 14. The present release and discharge is being drafted in English language at the request of the parties hereto. La presente quittance a ete redigee en langue anglaise a la demande des parties aux presentes.

METHYLGENE INC.

Per:

HYBRIDON, INC.

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Page 7

Per:

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SCHEDULE A

- Unanimous Shareholders' Agreement dated January 4, 1996, as amended from time to time;
- Shareholders Agreement dated January 4, 1996, as amended from time to time as restated on September 21, 2000 (the "SHAREHOLDERS' AGREEMENT");
- License Agreement dated January 4, 1996, as amended from time to time;
- License Agreement dated March 12, 1999 between Hybridon and Integrated DNA Technologies Inc. ("IDT"), and the letter agreement dated July 26, 1999 between Methylgene and IDT;

- License Agreement dated October 13, 1994 between McGill University and Hybridon, as amended from time to time;
- License Agreement dated December 15, 1995 between McGill University and Hybridon;
- License Agreement dated February 1, 1990 between the Worcester Foundation for Experimental Biology Inc. and Hybridon and restated September 8, 1993;
- Letter Agreement dated February 27, 1998 between Methylgene and McGill University;
- Letter Agreement dated July 1, 1999 between Methylgene and the University of Massachussetts (UMASS); and
- All licensed and sublicensed patents.
- Letter Agreement dated December 18, 1995 among Hybridon and Worcester Foundation for Biomedical Research, Inc. and into which Methylgene intervened.
- Various confidentiality agreements executed from time to time between Methylgene and Hybridon.

OFFER TO EXCHANGE SERIES B PREFERRED STOCK OF HYBRIDON, INC. ("HYBRIDON") FOR ANY AND ALL OUTSTANDING PRINCIPAL AMOUNT OF 8% NOTES DUE 2002 OF HYBRIDON

DATED MARCH 5, 2001

THIS OFFER TO EXCHANGE WILL EXPIRE AT 12:00 MIDNIGHT, BOSTON TIME, ON MARCH 16, 2001, UNLESS THE OFFER IS EXTENDED.

Hybridon, Inc., a Delaware corporation ("Hybridon"), invites the holders of its 8% Notes due 2002 (the "Notes") to tender their Notes in exchange (the "Exchange") for 1 share of Series B Preferred Stock, par value \$.01 per share, of Hybridon ("Series B Preferred Stock"), for each \$100 in principal amount of the Notes tendered, upon the terms of this Offer to Exchange. This Offer to Exchange constitutes the "Offer."

Hybridon will pay all accrued but unpaid interest on the Notes due through the date of the Exchange by issuing additional Notes in an aggregate principal amount equal to the amount of accrued but unpaid interest. Notes which will be paid in respect of accrued interest will be deemed tendered for exchange by a Noteholder participating in the Offer to Exchange, unless said Noteholder indicates otherwise in Box One below. The Offer is open to all holders of Notes. The shares of Hybridon's Common Stock (the "Common Stock") into which the Notes are convertible have been registered by Hybridon in its Registration Statement on Form S-1 (No. 333-69649) (the "Registration Statement"), which became effective under the Securities Act of 1933, as amended, on February 8, 2001. Upon an amendment to the Registration Statement, the shares of Common Stock into which shares of the Series B Preferred Stock are convertible will be registered. As part of the Exchange, the registration rights granted to the holders of the Notes in Section 12 of the Subscription Agreement between Hybridon and the holders of the Notes, dated as of December 13, 1999 (the "Subscription Agreement"), shall survive, and shall be applied in full force and effect to the shares of Common Stock issuable upon conversion of the Series B Preferred Stock. The definition of "Registrable Securities" in Section 12.1(f) of the Subscription Agreement, as it will apply to the shares of Common Stock issuable upon conversion of the Series B Preferred Stock, will substitute "shares of Series B Preferred Stock" for "Notes."

DELIVERY OF THE OFFER TO EXCHANGE TO AN ADDRESS OTHER THAN THAT OF THE DEPOSITARY AS SET FORTH HEREIN WILL NOT CONSTITUTE A VALID DELIVERY.

PLEASE READ THIS ENTIRE OFFER TO EXCHANGE CAREFULLY. QUESTIONS AND REQUESTS FOR ASSISTANCE SHOULD BE DIRECTED TO

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THE DEPOSITARY AT THE ADDRESS AND TELEPHONE NUMBER SET FORTH HEREIN. REQUESTS FOR ADDITIONAL COPIES OF THE OFFER TO EXCHANGE SHOULD BE DIRECTED TO THE DEPOSITARY AT THE ADDRESS AND PHONE NUMBER LISTED HEREIN.

ANY TENDER OF NOTES WHICH INVOLVES DENOMINATIONS OF LESS THAN \$100 IN PRINCIPAL AMOUNT THEREOF WILL BE EXCHANGED BY PAYMENT IN CASH OF AN AMOUNT EQUAL TO SAID DENOMINATION.

Any holder of Notes (a "Noteholder") desiring to tender all or any portion of the principal amount of such Notes should (i) sign this Offer to Exchange or a facsimile thereof, and (ii) mail or deliver the signed Offer to Exchange to the Depositary specified herein, along with either (A) the original Notes to the Depositary, or, (B) for any Noteholder whose original Notes have been mutilated, lost, stolen or destroyed, an affidavit of lost note, in substantially the same form as Exhibit A attached hereto (the "Affidavit of Lost Note"), in lieu of such Notes so mutilated, lost, stolen or destroyed, by the Expiration Date. THIS TRANSACTION HAS NOT BEEN APPROVED OR DISAPPROVED BY THE SECURITIES AND EXCHANGE COMMISSION OR ANY STATE SECURITIES COMMISSION NOR HAS THE COMMISSION OR ANY STATE SECURITIES COMMISSION PASSED UPON THE FAIRNESS OR MERITS OF THIS TRANSACTION NOR UPON THE ACCURACY OR ADEQUACY OF THE INFORMATION CONTAINED IN THIS DOCUMENT. ANY REPRESENTATION TO THE CONTRARY IS UNLAWFUL.

INFORMATION REGARDING HYBRIDON

Current information regarding Hybridon can be obtained by reference to its prospectus (the "Prospectus") contained within the Registration Statement. Please note that the Prospectus contains financial information about Hybridon not later than September 30, 2000. Audited financial statements for the year ended December 31, 2000 are not yet available. A copy of the prospectus can be obtained from Robert Andersen, Chief Financial Officer of Hybridon, or by accessing EDGAR.

SUMMARY

This general summary is provided solely for the convenience of the Noteholders and is qualified in its entirety by reference to the full text and more specific details contained in this Offer to Exchange, and any amendments hereto.

| Hybridon | Hybridon, Inc., a Delaware corporation. |
|------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| The Notes | 8% Notes due 2002 of Hybridon. |
| Amount of Notes Sought | All of the outstanding Notes. |
| Consideration | The consideration being offered per \$100 in principal amount of the Notes tendered consists of 1 share of Series B Preferred Stock of Hybridon. |
| Conditions of Offer | The Offer is not conditioned upon any minimum of the principal amount of the Notes being tendered. |
| Expiration Date | March 16, 2001, at 12:00 Midnight, Boston time, unless extended. |
| How to Tender Notes | See "Procedure for Tendering Notes." For further information, call the Depositary. |
| Purpose of Offer | The Offer is part of the restructuring of Hybridon's capital structure to reduce Hybridon's debt service obligations. |
| Exchange Date | As soon as practicable after the Expiration Date, which is expected to be no later than four business days after the Expiration Date. |
| Further Information | Additional copies of this Offer to Exchange may be obtained by contacting the Depositary at the address and telephone number shown herein. |
| Effect of Exchange on Rights | Although shares of the Series B Preferred of Shareholders are prior in liquidation to shares of Common Stock and Hybridon's Series A Preferred Stock, those Noteholders who exchange their Notes will be surrendering the security interest in Hybridon's assets securing the payment of their Notes. Under Hybridon's First Amended and Restated Subordination and |

Intercreditor Agreement dated June 29, 2000 (the "Intercreditor Agreement"), to the extent that Noteholders accept this Offer to Exchange, the benefit of said security interest will inure largely to the lenders of a \$6,000,000 loan which was otherwise junior.

TERMS OF THE OFFER

Upon the terms described herein, Hybridon will exchange all Notes that are validly tendered on or prior to the Expiration Date (as defined below) at the rate of 1 share of Series B Preferred Stock for each \$100 in principal amount of the Notes tendered. Any tender of Notes which involves denominations of less than \$100 in principal amount thereof will be exchanged by payment in cash of an amount equal to said denomination.

Hybridon will pay all accrued but unpaid interest on the Notes due through the date of the Exchange by issuing additional Notes in an aggregate principal amount equal to the amount of accrued but unpaid interest. Notes which will be paid in respect of accrued interest will be deemed tendered for exchange by a Noteholder participating in the Offer to Exchange, unless said Noteholder indicates otherwise in Box One below.

CONSIDERATION BEING OFFERED

SERIES B PREFERRED STOCK

For a summary of the terms of the Series B Preferred Stock, and a comparison of those terms with the terms of Hybridon's presently outstanding shares of Series A Preferred Stock, see the summary attached hereto as Exhibit B. For a full statement of the rights, preferences and privileges of the Series B Preferred Stock, see Hybridon's Certificate of Designation for the Series B Preferred Stock (the "Certificate") attached hereto as Exhibit C, which Hybridon will file with the Delaware Secretary of State for purposes of amending its Certificate of Incorporation and authorizing the issuance of the Series B Preferred Stock.

PROCEDURE FOR TENDERING NOTES

To validly tender the Notes pursuant to the Offer, the tendering Noteholder must (i) sign this Offer to Exchange or a facsimile thereof, and (ii) mail or deliver the signed Offer to Exchange to the Depositary (at its address set forth herein), along with either (A) the original Notes to the Depositary, or (B) for any Noteholder whose certificates for the Notes have been mutilated, lost, stolen or destroyed, an Affidavit of Lost Note, in lieu of such Notes so mutilated, lost, stolen or destroyed, on or prior to the Expiration Date.

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All questions as to the form of documents and the validity, eligibility (including time of receipt) and acceptance for payment of any tender of Notes will be determined by Hybridon, in its sole discretion, and its determination shall be final and binding. Hybridon reserves the absolute right to reject any or all tenders of Notes that (i) it determines are not in proper form, or (ii) the acceptance for payments of or payment for which may, in the opinion of Hybridon's counsel, be unlawful. Hybridon also reserves the absolute right to waive any defect or irregularity in any tender of Notes. None of Hybridon, the Depositary or any other person will be under any duty to give notice of any defect or irregularity in tenders, nor shall any of them incur any liability for failure to give any such notice.

ACCEPTANCE FOR EXCHANGE OF NOTES

Upon the terms of the Offer and as promptly as practicable after the Expiration Date (which is expected to be within four (4) business days after the Expiration Date), Hybridon will accept for exchange and exchange the Notes validly tendered. Thereafter, exchange for all Notes validly tendered on or prior to the Expiration Date and accepted for exchange pursuant to the Offer will be made by the Depositary as promptly as practicable. In all cases, exchange pursuant to

the Offer will be made only after timely receipt by the Depositary of the original Notes or an Affidavit of Lost Note, and a properly completed and duly executed Offer to Exchange, or facsimile thereof. Notes not accepted for exchange by Hybridon, or a replacement Note for the portion of the Notes not tendered by the Noteholder or not accepted for exchange by Hybridon, will be returned as promptly as practicable, without expense to the tendering Noteholder.

EXTENSION

Prior to the Expiration Date, Hybridon may extend the period of time during which the Offer is open or otherwise amend or modify the Offer and may terminate the Offer for any reason. There can be no assurance, however, that Hybridon will extend the Offer. During any such extension, all Notes previously tendered will remain subject to the Offer.

REPRESENTATIONS AND WARRANTIES OF HYBRIDON

In connection with this Offer and the Exchange, Hybridon represents and warrants as follows:

ORGANIZATION

Hybridon is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware and has all requisite power and authority

6 to own and lease its property and to carry on its business as presently conducted. Hybridon is duly qualified to do business as a corporation in all jurisdictions in which the failure to be so qualified would have an adverse affect on the financial or any other business condition of Hybridon.

AUTHORIZATION OF SERIES B PREFERRED STOCK

The issuance of shares of Series B Preferred Stock in accordance with the Offer has been, or will be on or prior to the Exchange Date, duly authorized by all necessary corporate action on the part of Hybridon, and all such shares of Series B Preferred Stock have been duly reserved for issuance.

AUTHORIZATION OF OFFER

The execution, delivery and performance by Hybridon of this Offer and of the transactions contemplated hereby have been duly authorized by all requisite action on the part of Hybridon. This Offer has been duly executed and delivered by the Company and constitutes a valid and binding obligation of Hybridon, enforceable in accordance with its respective terms.

CONSENTS AND APPROVALS

No authorization, consent, approval or other order of, or declaration to or filing with, any governmental agency or body (other than filings required to be made under applicable federal and state securities laws) is required for the valid authorization, execution, delivery and performance by Hybridon of this Offer or the issuance of the shares of Series B Preferred Stock.

SECURITIES LAWS

Based on the representations of the holders of the Notes set forth below, the offer and issuance of the shares of Series B Preferred Stock will not be in violation of the Securities Act of 1933, as amended (The "Securities Act").

REPRESENTATIONS AND WARRANTIES OF THE HOLDERS OF THE NOTES

In connection with this Offer and the Exchange, as to himself, herself or itself, the holders of the Notes represent and warrant as follows:

INVESTMENT INTENT

Each Note holder recognizes that the Exchange involves a high degree of risk including, but not limited to, the following: (i) Hybridon remains a development stage business with limited operating history and requires substantial funds in addition to any proceeds derived from the Exchange; (ii) an investment in Hybridon is highly speculative, and only investors who can afford the loss of their entire investment should consider investing in Hybridon, or the shares of Series B Preferred Stock, or shares of Series B Preferred Stock-Underlying Common Stock, (iii) such Note holder may not be able to liquidate his investment; (iv) transferability of the Series B Preferred Stock is extremely limited; and (v) in the event of a disposition of the Series B Preferred Stock and the Series B Preferred Stock-Underlying Common Stock, such Note holder could sustain the loss of his entire investment.

LACK OF LIQUIDITY

Each Note holder confirms that he or it is able (i) to bear the economic risk of this investment, (ii) to hold the Series B Preferred Stock and any shares of Series B Preferred Stock-Underlying Common Stock for an indefinite period of time, and (iii) presently to afford a complete loss of his or its investment; and represents that he or it has sufficient liquid assets so that the illiquidity associated with this investment will not cause any undue financial difficulties or affect such Note holder's ability to provide for his or its current needs and possible financial contingencies, and that his or its commitment to all speculative investments is reasonable in relation to his or its net worth and annual income. Furthermore, each Note holder acknowledges that the Series B Preferred Stock contains certain restrictions, as more particularly set forth in the Certificate of Designation for the Series B Preferred Stock attached hereto as Exhibit C.

KNOWLEDGE AND EXPERIENCE

Each Note holder hereby acknowledges and represents that such Note holder has prior investment experience, including investment in securities that are non-listed, unregistered and are not traded on the Nasdaq National or SmallCap Market, nor on the National Association of Securities Dealers, Inc.'s (the "NASD") automated quotation system, or such Note holder has employed at its own expense the services of an investment advisor, attorney and/or accountant to request documents from Hybridon and to read all of the documents furnished or made available by Hybridon to such Note holder and to evaluate the investment, tax and legal merits and the consequences and risks of such a transaction on such Note holder's behalf, that such Note holder or such professional advisor has such knowledge and experience in financial and business matters and that such Note holder or such professional

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advisor is capable of evaluating the merits and risks of the prospective investment and, if applicable, satisfies the conditions set out in Rule 501(h) under the Securities Act.

NOTE HOLDER CAPACITY

Each Note holder hereby represents that such Note holder either by reason of such Note holder's business or financial experience, or the business or financial experience of such Note holder's professional advisors (who are unaffiliated with, and who are not compensated by, Hybridon or any affiliate or selling agent of Hybridon, directly or indirectly), has the capacity to protect such Note holder's own interests in connection with the transaction contemplated hereby.

REGISTRATION

Each Note holder hereby acknowledges that the Offer has not been reviewed by the Securities and Exchange Commission or any state regulatory authority. No Note holder shall sell or otherwise transfer the Series B Preferred Stock or any Series B Preferred Stock-Underlying Common Stock unless such securities are registered under the Securities Act or unless an exemption from such registration is available.

LEGEND

Each Note holder consents to the placement of the legend set forth below on any certificate or other document evidencing the shares of the Series B Preferred Stock: THESE SECURITIES HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT"), OR APPLICABLE STATE SECURITIES LAWS. THESE SECURITIES HAVE BEEN ACQUIRED FOR INVESTMENT AND NOT WITH A VIEW TO THEIR DISTRIBUTION OR RESALE, AND MAY NOT BE SOLD, PLEDGED, OR OTHERWISE TRANSFERRED WITHOUT AN EFFECTIVE REGISTRATION STATEMENT FOR SUCH SECURITIES UNDER THE SECURITIES ACT AND APPLICABLE STATE SECURITIES LAWS, OR AN OPINION OF COUNSEL SATISFACTORY TO THE COMPANY TO THE EFFECT THAT SUCH REGISTRATION IS NOT REQUIRED.

POWER AND AUTHORITY

Each Note holder represents that such Note holder has full power and authority (corporate, statutory and otherwise) to execute and deliver this Offer and to exchange their Notes for shares of Series B Preferred Stock and any shares of Series B Preferred Stock-Underlying Common Stock. This Agreement constitutes the legal,

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valid and binding obligation of each Note holder, enforceable against such Note holder in accordance with its terms.

ACCREDITED INVESTOR

Each Note holder represents that it is an "accredited investor" as such term is defined in Rule 501 of Regulation D.

DEPOSITARY

The Depositary for this Offer to Exchange is:

Holland & Knight LLP Attn: Sean B. Leonard, Esq. 10 St. James Avenue Boston, MA 02116 Telephone: (617) 523-2700 Facsimile: (617) 523-6850

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SIGNATURE(S) MUST BE PROVIDED IN BOX TWO BELOW

| [_] | CHECK | HERE | ΙF | ICATE | OF | LOST | NOTE | IS | ENCLOSED | HEREWITH. | |
|-----|-------|------|----|-----------|-----|------|------|----|----------|-----------|--|
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LIST BELOW THE NOTES TO WHICH THIS OFFER TO EXCHANGE RELATE. IF THE SPACE PROVIDED BELOW IS INADEQUATE, THE NOTE NUMBERS AND PRINCIPAL AMOUNTS SHOULD BE LISTED ON A SEPARATE SIGNED SCHEDULE AFFIXED HERETO. NOTEHOLDERS WHO WISH TO TENDER THEIR NOTES MUST COMPLETE THE TABLE BELOW AND COMPLETE AND SIGN IN BOX TWO.

HYBRIDON WILL PAY ALL ACCRUED BUT UNPAID INTEREST ON THE NOTES DUE BY ISSUING ADDITIONAL NOTES IN AN AGGREGATE PRINCIPAL AMOUNT EQUAL TO THE AMOUNT OF ACCRUED BUT UNPAID INTEREST. NOTES WHICH WILL BE PAID IN RESPECT OF ACCRUED INTEREST SHALL BE DEEMED TENDERED FOR EXCHANGE, UNLESS SPECIFIED TO THE CONTRARY BY CHECKING THE BOX BELOW. CHECK THE BOX BELOW IF YOU DO NOT WANT NOTES WHICH WILL BE PAID IN RESPECT OF ACCRUED INTEREST DEEMED TENDERED FOR EXCHANGE.

[] CHECK HERE IF YOU DO NOT WANT NOTES WHICH WILL BE PAID IN RESPECT OF

ACCRUED INTEREST DEEMED TENDERED FOR EXCHANGE. _____ DESCRIPTION OF NOTES _____ 1 2 3 4 NOTE NUMBER(S) NAME(S) AND AGGREGATE PRINCIPAL ADDRESS(ES) OF (ATTACH LIST IF PRINCIPAL AMOUNT REGISTERED HOLDER(S) NECESSARY) * AMOUNT (S) TENDERED** _____ _____ _____ _____ * NEED NOT BE COMPLETED BY NOTEHOLDERS TENDERING BY AFFIDAVIT OF LOST NOTE IF NOTE NUMBER NOT AVAILABLE. ** UNLESS OTHERWISE INDICATED, THE NOTEHOLDER WILL BE DEEMED TO HAVE TENDERED THE ENTIRE PRINCIPAL AMOUNT OF NOTES REPRESENTED BY TENDERED NOTES 11 _____ BOX TWO _____ ACCEPTANCE OF OFFER TO EXCHANGE PLEASE SIGN HERE TO BE COMPLETED BY ALL HOLDERS TENDERING NOTES (WHETHER OR NOT NOTES ARE BEING PHYSICALLY TENDERED OR BEING TENDERED BY AFFIDAVIT OF LOST NOTE) I have read this Offer to Exchange, and hereby accept such Offer to Exchange, and further agree to be bound by the foregoing. _____ Signature(s) of Registered Noteholder(s) or Authorized Signatory Type or Print Name , 2001 Dated: _____ Area Code and Telephone No(s): _____ Must be signed by the registered Noteholder(s) exactly as the name(s) appear(s) on the certificate and by person(s) authorized to become registered

Noteholder(s) as evidenced by endorsements and documents.

EXHIBIT A

AFFIDAVIT OF LOST NOTE

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AFFIDAVIT OF LOST NOTE

The undersigned (the "Noteholder"), a Noteholder of Hybridon, Inc. (the "Company"), does hereby certify:

1. The Noteholder is the beneficial owner of that certain 8% Note due 2002 Number ____ of the Company (the "Note") dated December 13, 1999, and registered in the name of the Noteholder, in the principal amount of \$_____, and is entitled to the full and exclusive possession of the Note;

2. The Noteholder has made an extensive search to locate the Note but it appears to have been mutilated, lost, stolen or destroyed so that it cannot be found or produced for exchange for shares of the Company's Series B Preferred Stock;

3. Neither the Note nor the rights of the Noteholder, therein, have in whole or in part been assigned, transferred, pledged or otherwise hypothecated by the Noteholder;

4. The Note was not endorsed;

5. The Noteholder hereby requests and this Affidavit of Lost Note is made for the purpose of inducing the Company and its transfer agent (i) to refuse to recognize any person other than the Noteholder as the owner of the Note, (ii) to refuse to make any payment, transfer, registration, delivery or exchange in connection with the Note to any other person other than the Noteholder, and (iii) to refuse to take any other action pursuant to the request or demand of any person other than the Noteholder with respect to the Note;

6. In consideration for the Company's acceptance of this Affidavit of Lost Note, the Noteholder agrees to indemnify and hold the Company harmless against any person, firm or entity now or hereafter acting as the Company's transfer agent, or any successors and assigns of such person, firm, entity in such capacity, from and against any and all claims, demands, liabilities, losses, damages and expenses, including attorney's fees and costs of suits, incurred in connection with or arising out of their compliance with this Affidavit of Lost Note, as set forth therein;

7. If the original Note comes into the possession of the Noteholder, it will promptly be delivered to the Company for cancellation.

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| 14 | | | | | |
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| Dated | this | day of | | , | 2001. |
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Note Number:

Principal Amount of Note:

15

EXHIBIT B

SUMMARY OF SERIES B PREFERRED STOCK

16

SERIES B CONVERTIBLE PREFERRED STOCK

ISSUED IN CONNECTION WITH THE EXCHANGE OF 8% NOTES DUE 2002

Set forth below is a summary of the principal terms of a Series B Convertible Preferred Stock (the "Preferred B") of Hybridon, Inc. (the "Company"), to be offered in exchange for the 8% Notes of the Company due 2002. The terms of the Company's Series A Convertible Preferred Stock (the "Preferred A") are set forth for comparison. Differences between the Preferred A and Preferred B are highlighted in the Preferred B column. This general summary is provided solely for the convenience of the Noteholders and is qualified in its entirety by reference to the full text and more specific details contained in the Certificate of Designation for the Preferred B.

| Rights, Preferences, Privileges | Preferred A | Preferred B |
|---------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| (1) Dividend Provisions | dividends on semi-annual basis at rate of 6.5% of Dividend Base Amount (\$100 plus accrued but unpaid dividends) | dividends on semi-annual basis at rate of 8% of Dividend Base Amount (\$100 plus accrued but unpaid dividends) |
| 17 | payable in cash, or at Company's option, PIK in preference to dividends paid on Common Preferred A valued at \$100.00/share for calculating PIK payable if declared by Board | payable in cash, or at Company's option, PIK in preference to dividends paid on Common AND PREFERRED A Preferred B valued at \$100.00/share for calculating PIK payable if declared by Board NO DIVIDEND OR DISTRIBUTION PAID TO COMMON OR PREFERRED A UNLESS PAID TO PREFERRED B FIRST |
| | | |
| (2) Liquidation Preference | upon (i) liquidation, dissolution, or winding up, (ii) sale of all or substantially all assets, or (iii) any merger transaction, entitled to receive Dividend Base Amount prior to any distribution to Common | upon (i) liquidation, dissolution, or winding up, (ii) sale of all or substantially all assets, or (iii) any merger transaction, entitled to receive Dividend Base Amount prior to any distribution to Common OR PREFERRED A |
| (3) Conversion | - "Conversion Price" is \$4.25, subject to adjustment in Section 4 | - "Conversion Price" is \$.50, subject to adjustment in Section 4 |

| | - "Conversion Rate" determined by dividing then-existing Conversion Price into Dividend Base Amount | "Conversion Rate" determined by dividing then-existing Conversion Price into Dividend Base Amount |
|--------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| (4) Antidilution | Conversion Price subject to proportional adjustment if Company: | Conversion Price subject to proportional adjustment if Company: |
| | pays dividend or makes distribution on any class of capital stock in shares of Common; | pays dividend or makes distribution on any class of capital stock in shares of Common; |
| | subdivides outstanding Common into greater number of shares; | subdivides outstanding Common into greater number of shares; |
| 18 | | |
| | combines outstanding Common into smaller number of shares; | combines outstanding Common into smaller number of shares; |
| | issues shares of a series or class of capital stock to any holder of Common, Preferred A or Preferred B or rights to acquire shares of a series or class of capital stock at price per share less than market price; | issues shares of a series or class of capital stock to any holder of Common, Preferred A or Preferred B or rights to acquire shares of a series or class of capital stock at price per share less than market price; |
| | pays or distributes to the holders of a series or class of capital stock assets, properties, or rights to acquire Company's capital stock at price per share less than market price; | pays or distributes to the holders of a series or class of capital stock assets, properties, or rights to acquire Company's capital stock at price per share less than market price; |
| | or makes distribution consisting solely of cash to holders of any class of capital stock where, during specified 12 month period, cash distribution exceeds 10% of product of market price of Common multiplied by total outstanding shares of Common | or makes distribution consisting solely of cash to holders of any class of capital stock where, during specified 12 month period, cash distribution exceeds 10% of product of market price of Common multiplied by total outstanding shares of Common |
| 19 | | |
| (5) Mandatory Conversion | converted into shares of Common using Conversion Price of \$4.00 if closing bid price of Common equals or exceeds 250% of Conversion Price for at least 20 trading days in any period of 30 consecutive trading days | - CONVERTED INTO SHARES OF COMMON IF ALL OF PREFERRED A IS CONVERTED, USING A CONVERSION PRICE OF \$.50 |
| (6) Redemption | at Company's option, redeemable for cash equal to the Dividend Base Amount if closing bid price of Common equals or exceeds 250% of Conversion Price of Preferred A for at least 20 trading days in any period of 30 consecutive | at Company's option, redeemable for cash equal to the Dividend Base Amount if closing bid price of Common equals or exceeds 250% of Conversion Price of Preferred A for at least 20 trading days in any period of 30 consecutive |

| | trading days | trading days |
|-------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| (7) Voting Rights | Company needs 50% vote of all outstanding Preferred A to: | Company needs 50% vote of all outstanding PREFERRED B to: |
| | amend, alter or repeal any provision of Certificate of Incorporation or Bylaws adversely affecting relative rights, preferences, qualifications, limitations or | amend, alter or repeal any provision of Certificate of Incorporation or Bylaws adversely affecting relative rights, preferences, qualifications, limitations or |
| 20 | | |
| | restrictions of Preferred A (issuance of securities ranking prior to, or pari passu with Preferred A upon Liquidation Event or with respect to payment of dividends does not adversely affect such); or authorize or issue, or increase authorized amount of, Preferred A, other than Preferred A issuable as dividends on Preferred A or in exchange for 9% Notes | restrictions of PREFERRED B; ISSUE SECURITIES RANKING PRIOR TO, OR PARI PASSU WITH PREFERRED B UPON LIQUIDATION EVENT OR WITH RESPECT TO PAYMENT OF DIVIDENDS; OR authorize or issue, or increase authorized amount of, PREFERRED B, other than PREFERRED B, other than PREFERRED B ISSUABLE AS DIVIDENDS ON PREFERRED B OR IN EXCHANGE FOR 8% NOTES |

EXHIBIT C

CERTIFICATE OF DESIGNATION FOR SERIES B PREFERRED STOCK OF HYBRIDON

CONSENT OF INDEPENDENT PUBLIC ACCOUNTANTS

As independent public accountants, we hereby consent to the use of our report dated April 12, 2001 included in this Form 10-K into the Hybridon, Inc.'s previously filed Registration Statement File No.'s 33-3896, 33-3898, 33-3900, 33-3902 and 333-34008.

/s/ Arthur Andersen LLP

Boston, Massachusetts April 12, 2001