HYBRIDON INC
Form S-3/A
December 05, 2003

Table of Contents

As filed with the Securities and Exchange Commission on December 5, 2003

Registration No. 333-109630

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

Amendment No. 1 to

FORM S-2
on
FORM S-3

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

HYBRIDON, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**04-3072298**
(State or other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)

345 Vassar Street
Cambridge, Massachusetts 02139
(617) 679-5500
(Address, Including Zip Code, and Telephone Number,
Including Area Code, of Registrant s Principal Executive Offices)

Stephen R. Seiler
Chief Executive Officer
345 Vassar Street
Cambridge, Massachusetts 02139
(617) 679-5500
(Name, Address, Including Zip Code, And Telephone Number,
Including Area Code, of Agent For Service)

Copies to:
David E. Redlick, Esq.
Hale and Dorr LLP
60 State Street

Boston, Massachusetts 02109
(617) 526-6000

Approximate date of commencement of proposed sale to the public: As soon as practicable after this registration statement becomes effective.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. x

If the registrant elects to deliver its latest annual report to security holders, or a complete and legible facsimile thereof, pursuant to Item 11(a)(1) of this form, check the following box. o

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o _____

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o _____

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o _____

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. o

Table of Contents

_____

The Company hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Company shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), shall determine.

Table of Contents

The information in this prospectus is not complete and may be changed. The selling stockholders named in this prospectus may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and neither we nor the selling stockholders named in this prospectus are soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated December 5, 2003

PROSPECTUS

HYBRIDON, INC.

29,852,703 SHARES OF COMMON STOCK

This prospectus relates to the resale from time to time of up to 29,852,703 shares of common stock of Hybridon, Inc. by the selling stockholders identified in this prospectus. We will not receive any proceeds from the sale of shares of our common stock offered by this prospectus.

The selling stockholders identified in this prospectus, or their pledgees, donees, transferees or other successors-in-interest, may offer the shares offered by this prospectus from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices.

Our common stock is traded on the American Stock Exchange under the symbol HBY. Prior to December 5, 2003, our common stock was traded on the OTC Bulletin Board. On December 1, 2003, the closing sale price of our common stock on the OTC Bulletin Board was $1.40 per share. You are urged to obtain current market quotations for our common stock.

Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page 3.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is _____ __, 2003.

TABLE OF CONTENTS

Table of Contents

Table Of Contents

We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. The selling stockholders are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of common stock.

Table of Contents

PROSPECTUS SUMMARY

This summary highlights important features of this offering and information included or incorporated in this prospectus. This summary may not contain all of the information that is important to you. You should read the entire prospectus carefully, including Risk Factors beginning on page 3, before deciding to invest in our common stock.

Hybridon, Inc.

We are engaged in the discovery and development of novel therapeutics using synthetic DNA. Our activities are primarily based on two technology platforms:

Our immunomodulatory oligonucleotide, or IMO, technology uses synthetic DNA that contains specific sequences that mimic bacterial DNA to modulate responses of the immune system; and

Our antisense technology uses synthetic DNA to block the production of disease causing proteins at the cellular level.

We are currently conducting clinical trials of two drug candidates. We are conducting phase 1 clinical trials of HYB2055, our lead 2nd generation IMO compound, in oncology patients and in healthy volunteers, and a phase 1/2 clinical trial of GEM231, our lead 2nd generation antisense compound, for the treatment of cancer. In addition, we have licensed HYB2055 for use as an adjuvant in the development of a potential therapeutic and prophylactic vaccine for HIV infection. We also have collaborations for the development of other 2nd generation antisense oligonucleotides for the treatment of cancer and viral infections.

Corporate Information

Our executive offices are located at 345 Vassar Street, Cambridge, MA 02139, our telephone number is (617) 679-5500 and our Internet address is www.hybridon.com. The information on our Internet website is not incorporated by reference in this prospectus and should not be considered to be part of this prospectus. Our website address is included in this prospectus as an inactive technical reference only. Unless the context otherwise requires, references in this prospectus to Hybridon, we, us, and our refer to Hybridon, Inc.

Hybridon® and GEM® are our registered trademarks. Amplivax , Cyclicon , IMOxine and IMO are also our trademarks. All other trademarks and service marks referenced in this prospectus are the property of their respective owners.

Table of Contents

The Offering

Common stock offered by the selling stockholders	29,852,703 shares, including 9,799,681 shares issuable upon the exercise of warrants held by the selling stockholders.
Use of proceeds	We will not receive any proceeds from the sale of shares in this offering.
American Stock Exchange symbol	HBY

Table of Contents

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below in addition to the other information included or incorporated by reference in this prospectus before purchasing our common stock. If any of the following risks actually occurs, our business, financial condition or results of operations would likely suffer, possibly materially. In that case, the trading price of our common stock could fall, and you may lose all or part of the money you paid to buy our common stock.

Risks Relating to Our Business, Strategy and Industry

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

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

In order to obtain regulatory approvals for the commercial sale of our products, we will be required to complete extensive clinical trials in humans to demonstrate the safety and efficacy of our drug candidates. In 2003, we commenced phase 1 clinical trials of HYB2055, our lead 2nd generation IMO compound, in oncology patients and in healthy volunteers, and we are currently conducting a phase 1/2 clinical trial of GEM231, our lead 2nd generation antisense compound, for the treatment of cancer. We may not be able to obtain authority from the FDA or other equivalent foreign regulatory agencies to complete these trials or commence and complete any other clinical trials.

The results from preclinical testing of a drug candidate that is under development may not be predictive of results that will be obtained in human clinical trials. In addition, the results of early human clinical trials may not be predictive of results that will be obtained in larger scale, advanced stage clinical trials. Furthermore, we, one of our collaborators, or a regulatory agency with jurisdiction over the trials, may suspend clinical trials at any time if the subjects or patients participating in such trials are being exposed to unacceptable health risks, or for other reasons. As an example, in 1997, after reviewing the results from the clinical trial of GEM91, our lead 1st generation antisense compound at the time, we determined not to continue the development of GEM91 and suspended clinical trials of this product candidate.

The rate of completion of clinical trials is dependent in part upon the rate of enrollment of patients. Patient accrual is a function of many factors, including:

- the size of the patient population,
- the proximity of patients to clinical sites,
- the eligibility criteria for the study,

Table of Contents

the nature of the study,

the existence of competitive clinical trials, and

the availability of alternative treatments.

Delays in planned patient enrollment may result in increased costs and prolonged clinical development.

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

The biotechnology industry is highly competitive and characterized by rapid and significant technological change. We face, and will continue to face, intense competition from organizations such as pharmaceutical and biotechnology companies, as well as academic and research institutions and government agencies. Some of these organizations are pursuing products based on technologies similar to our technologies. Other of these organizations have developed and are marketing products, or are pursuing other technological approaches designed to produce products, that are competitive with our product candidates in the therapeutic effect these competitive products have on diseases targeted by our product candidates. Our competitors may discover, develop or commercialize products or other novel technologies that are more effective, safer or less costly than any that we are developing. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours.

Many of our competitors are substantially larger than we are and have greater capital resources, research and development staffs and facilities than we have. In addition, many of our competitors are more experienced than we are in drug discovery, development and commercialization, obtaining regulatory approvals and drug manufacturing and marketing.

We anticipate that the competition with our products and technologies will be based on a number of factors including:

product efficacy,

safety,

reliability,

availability,

price and

patent position.

The timing of market introduction of our products and competitive products will also affect competition among products. We also expect the relative speed with which we can develop products, complete the clinical trials and approval processes and supply commercial quantities of

Table of Contents

the products to the market to be an important competitive factor. Our competitive position will also depend upon our ability to attract and retain qualified personnel, to obtain patent protection or otherwise develop proprietary products or processes and to secure sufficient capital resources for the period between technological conception and commercial sales.

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

The commercial success of any of our products for which we may obtain marketing approval from the FDA or other regulatory authorities will depend upon their acceptance by the medical community and third party payors as clinically useful, cost-effective and safe. Many of the products that we are developing are based upon technologies or therapeutic approaches that are relatively new and unproven. The FDA has not granted marketing approval to any products based on antisense technology or IMO-like technology and no such products are currently being marketed, except for one antisense product that is currently being marketed for the treatment of cytomegalovirus retinitis, an infectious disease, in patients with AIDs. As a result, it may be more difficult for us to achieve market acceptance of our products. Our efforts to educate the medical community on these potentially unique approaches may require greater resources than would be typically required for products based on conventional technologies or therapeutic approaches. The safety, efficacy, convenience and cost-effectiveness of our products as compared to competitive products will also affect market acceptance.

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

Our success is highly dependent on the retention of principal members of our technical and management staff, including Stephen Seiler and Sudhir Agrawal. Mr. Seiler, our Chief Executive Officer, has extensive experience in the pharmaceutical industry and as an investment banker and provides strategic leadership for us. The loss of Mr. Seiler s services would be detrimental to the execution of our strategic plan. Dr. Agrawal serves as our President and Chief Scientific Officer. Dr. Agrawal has made significant contributions to the field of nucleic acid chemistry and is named as an inventor on over 200 U.S. patents and patent applications. Dr. Agrawal provides the scientific leadership for our research and development activities and directly supervises our research staff. The loss of Dr. Agrawal s services would be detrimental to our ongoing scientific progress.

We are a party to employment agreements with each of Mr. Seiler and Dr. Agrawal, but each of these agreements may be terminated by us or the employee for any reason or no reason at any time upon notice to the other party. We do not carry key man life insurance for Mr. Seiler or Dr. Agrawal.

Furthermore, our future growth will require hiring a significant number of qualified technical and management personnel. Accordingly, recruiting and retaining such personnel in the future will be critical to our success. There is intense competition from other companies and research and academic institutions for qualified personnel in the areas of our activities. If we are

Table of Contents

not able to continue to attract and retain, on acceptable terms, the qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or grow.

Regulatory Risks

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

All of the products that we are developing or may develop in the future will require additional research and development, extensive preclinical studies and/or clinical trials and regulatory approval prior to any commercial sales. This process is lengthy, often taking a number of years, and is expensive. Since our inception, we have conducted clinical trials of five compounds. In 1997, we determined not to continue clinical development of GEM91. The other four compounds are still in development. Currently, we are conducting clinical trials of two of these compounds, GEM231 and HYB2055.

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

We are subject to comprehensive regulatory requirements, which are costly and time consuming to comply with; if we fail to comply with these requirements, we could be subject to adverse consequences and penalties.

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

In general, submission of materials requesting permission to conduct clinical trials may not result in authorization by the FDA or any equivalent foreign regulatory agency to commence clinical trials. In addition, submission of an application for marketing approval to the relevant regulatory agency following completion of clinical trials may not result in the regulatory agency approving the application if applicable regulatory criteria are not satisfied, and may result in the regulatory agency requiring additional testing or information.

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

Both before and after approval is obtained, violations of regulatory requirements may result in:

Table of Contents

the regulatory agency s delay in approving, or refusal to approve, a product;

restrictions on such products or the manufacturing of such products;

withdrawal of the products from the market;

voluntary or mandatory recall;

fines;

suspension of regulatory approvals;

product seizure;

injunctions or the imposition of civil penalties; and

criminal penalties.

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

We have only limited experience in filing and prosecuting the applications necessary to gain regulatory approvals. Moreover, the products that result from our research and development programs will likely be based on new technologies and new therapeutic approaches that have not been extensively tested in humans. The regulatory requirements governing these types of products may be more rigorous than for conventional drugs. As a result, we may experience a longer regulatory process in connection with obtaining regulatory approvals of any product that we develop.

Risks Relating to Our Financial Results and Need for Financing

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

We have incurred losses in every year since our inception, except for 2002 when our recognition of revenues under a license and collaboration agreement resulted in us reporting net income for the year. As of September 30, 2003, we had incurred operating losses of approximately $277.5 million. We expect to continue to incur substantial operating losses in future periods. We have received no revenues from the sale of drugs. To date, almost all of our revenues have been from collaborative and license agreements, interest income and the sale of manufactured synthetic DNA and reagent products by the Hybridon Specialty Products Division prior to our selling that division in September 2000. We cannot be certain whether or when we will become profitable because of the significant uncertainties with respect to our ability to generate revenues from the sale of products and from any potential strategic alliances.

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

Table of Contents

We will require substantial funds to conduct research and development, including preclinical testing and clinical trials of our drugs. We will also require substantial funds to conduct regulatory activities and to establish commercial manufacturing, marketing and sales capabilities. We believe that, based on our current operating plan, our existing cash and cash equivalents and short term investments, including the net proceeds from the private placement of securities that we consummated with the selling stockholders in August 2003, will be sufficient to fund our cash requirements at least through December 2004. However, we will need to raise additional funds to operate our business beyond such time.

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

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

Our former independent public accountant, Arthur Andersen LLP, has been found guilty of a federal obstruction of justice charge. Arthur Andersen LLP has not consented to the inclusion of its audit report with respect to our consolidated financial statements in this prospectus, and you may be unable to exercise effective remedies against it in any legal action.

Our former independent public accountant, Arthur Andersen LLP, provided us with auditing services for prior fiscal periods through December 31, 2001, including issuing an audit report with respect to our audited consolidated financial statements as of and for the years ended December 31, 2000 and 2001, which report was included in our Annual Report on Form 10-K for the year ended December 31, 2002 and is incorporated by reference in this prospectus. On June 15, 2002, a jury in Houston, Texas found Arthur Andersen LLP guilty of a federal obstruction of justice charge arising from the federal government s investigation of Enron Corp. On August 31, 2002, Arthur Andersen LLP ceased practicing before the Securities and Exchange Commission, or SEC.

We were unable to obtain Arthur Andersen LLP s consent to include its report with respect to our audited consolidated financial statements as of and for the years ended December 31, 2000 and 2001 in our Annual Report on Form l0-K for the year ended December 31, 2002, in this prospectus or in any other filing that we may make with the SEC. As a result, you may not have an effective remedy against Arthur Andersen LLP in connection with a material misstatement or omission with respect to our audited consolidated financial statements that are included in our Annual Report on Form 10-K and incorporated by reference in this prospectus or any other filing that we may make with the SEC. In addition, even if you were able to assert such a claim, as a result of its conviction and other lawsuits, Arthur Andersen LLP

Table of Contents

may fail or otherwise have insufficient assets to satisfy claims made by investors or by us that might arise under federal securities laws or otherwise relating to any alleged material misstatement or omission with respect to our audited consolidated financial statements.

Risks Relating to Collaborators

We need to establish collaborative relationships in order to succeed.

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

The success of collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Our collaborators will have significant discretion in determining the efforts and resources that they will apply to these collaborations. The risks that we face in connection with these collaborations include the following:

disputes may arise in the future with respect to the ownership of rights to technology developed with collaborators;

disagreements with collaborators could delay or terminate the research, development or commercialization of products, or result in litigation or arbitration;

we may have difficulty enforcing the contracts if one of our collaborators fails to perform;

our collaborators may terminate their collaborations with us, which could make it difficult for us to attract new collaborators or adversely affect the perception of us in the business or financial communities;

collaborators have considerable discretion in electing whether to pursue the development of any additional drugs and may pursue technologies or products either on their own or in collaboration with our competitors that are similar to or competitive with our technologies or products that are the subject of the collaboration with us; and

our collaborators may change the focus of their development and commercialization efforts. Pharmaceutical and biotechnology companies historically have re-evaluated their priorities following mergers and consolidations, which have been common in recent years in these industries. The ability of our products to reach their potential could be limited if our collaborators decrease or fail to increase spending relating to such products.

Table of Contents

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

Risks Relating to Intellectual Property

If we are unable to obtain patent protection for our discoveries, the value of our technology and products will be adversely affected.

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

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

obtain patents;

obtain licenses to the proprietary rights of others on commercially reasonable terms;

operate without infringing upon the proprietary rights of others;

prevent others from infringing on our proprietary rights; and

protect trade secrets.

We do not know whether any of our patent applications or those patent applications which we license will result in the issuance of any patents. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, invalidated or circumvented, and the rights granted thereunder may not provide us proprietary protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies or duplicate any technology developed by us. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our products can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thus reducing any advantage of the patent.

Because patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, or in some cases not at all, and because publications of discoveries in the scientific literature often lag behind actual discoveries, neither we nor our licensors can be certain that we or they were the first to make the inventions claimed in issued patents or pending patent applications, or that we or they were the first to file for protection of the inventions set forth in these patent applications.

Table of Contents

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

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

We may lose our rights to patents, patent applications or technologies of third parties if our licenses from these third parties are terminated. In such event, we might not be able to develop or commercialize products covered by the licenses.

We are party to eleven royalty-bearing license agreements under which we have acquired rights to patents, patent applications and technology of third parties. Under these licenses we are obligated to pay royalties on net sales by us of products or processes covered by a valid claim of a patent or patent application licensed to us. We also are required in some cases to pay a specified percentage of any sublicense income that we may receive. These licenses impose various commercialization, sublicensing, insurance and other obligations on us. Our failure to comply with these requirements could result in termination of the licenses. These licenses generally will otherwise remain in effect until the expiration of all valid claims of the patents covered by such licenses or upon earlier termination by the parties. The issued patents covered by these licenses expire at various dates ranging from 2006 to 2021. If one or more of these licenses is terminated, we may be delayed in our efforts, or be unable, to develop and market the products that are covered by the applicable license or licenses.

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

There has been substantial litigation and other proceedings regarding patent and other intellectual property rights in the biotechnology industry. We may become a party to various types of patent litigation or other proceedings regarding intellectual property rights from time to time. For instance, in the fourth quarter of 2002, we became involved in an interference declared by the United States Patent and Trademark Office involving a patent application exclusively licensed by us from University of Massachusetts Medical Center, or UMMC, and three patents issued to the National Institutes of Health, and in the third quarter of 2003, we became involved in an interference declared by the United States Patent and Trademark Office involving another patent exclusively licensed to us from UMMC and a patent application assigned jointly to the University of Montreal and The Massachusetts Institute of Technology. We are not practicing nor do we intend to practice any of the intellectual property involved in either interference.

Table of Contents

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

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

Risks Relating to Product Manufacturing, Marketing and Sales

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

If we receive regulatory approval to commence commercial sales of any of our products, we will face competition with respect to commercial sales, marketing and distribution. These are areas in which we have no experience. To market any of our products directly, we would need to develop a marketing and sales force with technical expertise and with supporting distribution capability. In particular, we would need to recruit a large number of experienced marketing and sales personnel. Alternatively, we could engage a pharmaceutical or other healthcare company with an existing distribution system and direct sales force to assist us. However, to the extent we entered into such arrangements, we would be dependent on the efforts of third parties. If we are unable to establish sales and distribution capabilities, whether internally or in reliance on third parties, our business would suffer materially.

Because we have limited manufacturing experience, we are dependent on third-party manufacturers to manufacture products for us. If we can not rely on third party manufacturers, we will be required to incur significant costs and devote significant efforts to establish our own manufacturing facilities and capabilities.

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

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

There are a limited number of manufacturers that operate under the FDA s good manufacturing practices regulations capable of manufacturing our products. As a result, we may have difficulty finding manufacturers for our products with adequate capacity for our needs. If we are unable to arrange for third party manufacturing of our products on a timely basis, or to do

Table of Contents

so on commercially reasonable terms, we may not be able to complete development of our products or market them.

Reliance on third party manufacturers entails risks to which we would not be subject if we manufactured products ourselves, including:

- reliance on the third party for regulatory compliance and quality assurance,
- the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control,
- the possibility of termination or nonrenewal of the agreement by the third party, based on its own business priorities, at a time that is costly or inconvenient for us,
- the potential that third party manufacturers will develop know-how owned by such third party in connection with the production of our products that is necessary for the manufacture of our products, and
- reliance upon third party manufacturers to assist us in preventing inadvertent disclosure or theft of our proprietary knowledge.

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

The availability and levels of reimbursement by governmental and other third party payors such as health maintenance organizations, Medicaid, medical insurance companies, medical plan administrators, pharmacy benefit managers, physician and hospital alliances and other physician organizations affect the market for healthcare products. These third party payors continually attempt to contain or reduce the costs of healthcare by challenging the prices charged for medical products and services. If reimbursement for our products is unavailable or limited in scope or amount, our business could be materially harmed.

In both the United States and some foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the healthcare system and further proposals are likely. In the United States, for example, both the House of Representatives and Senate have passed bills that in different ways would reduce Medicare payments for drugs. The potential for adoption of these proposals affects or will affect our ability to raise capital, obtain collaborators and market our products.

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

Table of Contents

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

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

Risks Relating to an Investment in Our Common Stock

Our corporate governance structure, including provisions in our certificate of incorporation and by-laws, our stockholder rights plan and Delaware law, may prevent a change in control or management that stockholders may consider desirable.

Section 203 of the Delaware General Corporation Law and our certificate of incorporation, by-laws and stockholder rights plan contain provisions that might enable our management to resist a takeover of our company or discourage a third party from attempting to take over our company These provisions include:

a classified board of directors,

limitations on the removal of directors,

limitations on stockholder proposals at meetings of stockholders,

the inability of stockholders to act by written consent or to call special meetings, and

the ability of our board of directors to designate the terms of and issue new series of preferred stock without stockholder approval.

These provisions could have the effect of delaying, deferring, or preventing a change in control of us or a change in our management that stockholders may consider favorable or beneficial. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors and take other corporate actions. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock.

Table of Contents

Our stock price could be extremely volatile, and you may not be able to resell your shares at or above the price you paid for such shares. You may lose all or a significant portion of your investment.

The stock market has experienced significant price and volume fluctuations, and the market prices of biotechnology companies have been highly volatile. In addition, broad market and industry fluctuations that are not within our control may adversely affect the trading price of our common stock. During the period from January 1, 2002 to December 1, 2003, the closing sale price of our common stock ranged from a high of $1.85 per share to a low of $0.60 per share. As a result, you may not be able to resell your shares at or above the price you paid for such shares. You must be willing to bear the risk of fluctuations in the price of our common stock and the risk that the value of your investment in our stock could decline.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents we incorporate by reference contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. All statements, other than statements of historical facts, included or incorporated in this prospectus regarding our strategy, future operations, financial position, future revenues, projected costs, prospects, plans and objectives of management are forward-looking statements. The words anticipates, believes, estimates, expects, intends, may, plans, projects, will, would and similar expressions are intended to identify forward-looking statements, although not all forward-looki statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus, particularly under the heading Risk Factors, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. In addition, any forward-looking statements represent our estimates only as of the date this prospectus is filed with the SEC and should not be relied upon as representing our estimates as of any subsequent date. We do not assume any obligation to update any forward-looking statements.

Table of Contents

THE COMPANY

Overview

We are engaged in the discovery and development of novel therapeutics using synthetic DNA. Our activities are primarily based on two technology platforms:

Our immunomodulatory oligonucleotide, or IMO, technology uses synthetic DNA that contains specific sequences that mimic bacterial DNA to modulate responses of the immune system. We have designed a class of IMO compounds, which we refer to as 2nd generation IMO compounds, that we believe may offer potential advantages over earlier immunostimulatory oligonucleotides. These earlier immunostimulatory oligonucleotides are generally referred to in the industry as CpG oligos because they contain a segment of DNA consisting of a cytosine (C) molecule and a guanine (G) molecule linked by a phosphorothioate bond (p). We are designing our IMO compounds to be used as monotherapies in the treatment of conditions such as cancer, infectious diseases and allergies/asthma, as well as in combination therapies with chemotherapeutics, vaccines and antibodies; and

Our antisense technology uses synthetic DNA to block the production of disease causing proteins at the cellular level. We have developed advanced antisense chemistries that serve as the basis for our 2nd generation antisense drug candidates. We believe that these 2nd generation antisense drug candidates may offer potential advantages over earlier antisense drug candidates and are potentially applicable to a wide variety of therapeutic indications. We are currently focusing our internal antisense efforts on cancer and infectious diseases. In addition, we are collaborating with other companies to develop antisense therapeutics in the areas of cancer and viral infections.

We have also developed two other technology platforms:

Our cancer therapy potentiation technology uses synthetic DNA to enhance the antitumor activity of some marketed anticancer drugs and increase their effectiveness. This technology is based on our discovery in preclinical studies that when oligonucleotides are administered in combination with specific marketed anticancer drugs, such as irinotecan which is marketed in the United States under the name Camptosar®, the activity of the co-administered anticancer drug is greatly improved; and

Our Cyclicon technology uses novel synthetic DNA structures for identifying gene function in drug target validation and drug discovery.

Drug Development Strategy

In the near term, we are focusing our internal drug development efforts on developing the two lead drug candidates in our pipeline, HYB2055 and GEM231.

Table of Contents

HYB2055. HYB2055 is the lead clinical drug candidate in our IMO program.

We filed an Investigational New Drug Application, or IND, for HYB2055 with the FDA, which became effective March 6, 2003. We are developing HYB2055 for oncology applications under the name IMOxine. In May 2003, we commenced a phase 1 clinical trial of IMOxine in the United States in patients with refractory malignant tumors. This trial is being conducted at the Lombardi Comprehensive Cancer Center at Georgetown University Medical Center. We plan to complete enrollment in this trial in the first quarter of 2004. Preliminary results indicate that IMOxine has been well tolerated by the first 14 patients enrolled in this trial, and that in five of the first eight patients evaluated for disease status at eight weeks and one of the first three patients evaluated for disease status at 16 weeks, the disease has been stable. Assuming that this trial is successful and is completed when anticipated, we plan to commence a phase 2 clinical trial of IMOxine in the first half of 2004. The phase 2 clinical trial of IMOxine and any future trials of IMOxine may involve the evaluation of IMOxine as a monotherapy for the treatment of cancer and/or in combination with other anticancer agents, including chemotherapeutics, antibodies, and vaccines/antigens.

We are also developing HYB2055 for use as an adjuvant for vaccines and monoclonal antibodies. We are developing HYB2055 under the name Amplivax for these applications. We have licensed Amplivax to another company for use in their development of a potential therapeutic and prophylactic vaccine for HIV infection. We anticipate that our collaborative partner will initiate a clinical trial of this vaccine during the first half of 2004.

In the third quarter of 2003, we completed the database for a phase 1 clinical trial of HYB2055 that was conducted in the United Kingdom in 28 healthy volunteers. The goal of this trial was to study the safety and immunological activity of HYB2055 over a broad range of dosing levels. In the trial, HYB2055 was well tolerated by the volunteers, who did not experience any significant treatment-related adverse effects. In addition, HYB2055 demonstrated biological activity in the volunteers, including transient activation of lymph nodes and effects on immune cells in the blood.

GEM231. GEM231 is a 2nd generation antisense compound for treating solid tumor cancers. GEM231 is designed to inhibit Protein Kinase A, or PKA, a protein which has been shown to be present at increased levels in the cells of many human cancers. We are currently conducting a phase 1/2 clinical trial of GEM231 as a combination therapy with Camptosar. This trial is being conducted at Vanderbilt University s Vanderbilt Ingram Cancer Center. In this trial, we are evaluating the safety of GEM231 and Camptosar in combination and measuring the presence of extra-cellular PKA, or ECPKA, in blood as a potential biomarker for GEM231 antisense activity on PKA. A biomarker is a biological parameter monitored as a possible indicator of drug activity. In July 2003, we presented data from early patients in the trial indicating that ECPKA levels had been reduced in a statistically significant manner. We expect to complete enrollment of this combination treatment trial in the first quarter of 2004. Following analysis of the pharmacokinetic data and depending on these and other findings from the phase 1/2 clinical trial, we would plan to commence a phase 2 clinical trial using this drug combination in the first half of 2004.

Product Pipeline

The table below summarizes the principal products we are developing independently or in collaboration with third parties and the therapeutic use and development status of these products.

Table of Contents

Product Description	Therapeutic Use	Development Status
IMO		
IMOxine 2nd generation IMO (HYB2055)	Cancer	phase 1
Amplivax 2nd generation IMO (HYB2055) being used as an adjuvant in combination with REMUNE®, an immune-based HIV therapeutic vaccine, in the development of a vaccine candidate[1]	HIV	preclinical candidate
Antisense		
GEM231 2nd generation antisense drug candidate targeted to PKA	Cancer	phase 1/2
GEM92 2nd generation antisense drug candidate targeted to a specific region of HIV-1	HIV	phase 1
MBI 1121 2nd generation antisense drug candidate targeted to human papillomavirus[2], an infectious disease	Human Papillomavirus	phase 1
GEM220 2nd generation antisense drug candidate targeted to Vascular Endothelial Growth Factor, a growth factor that contributes to the growth of new blood vessels	Cancer	preclinical candidate
GEM240 2nd generation antisense drug candidate targeted to Mdm2, a protein found in increased levels in many human cancers	Cancer	preclinical candidate
GEM640 (AEG35156) 2nd generation antisense drug candidate targeted to the XIAP gene,[3] a gene which has been implicated in the resistance of cancer cells to chemotherapy	Cancer	preclinical candidate
Cancer Therapy Potentiation		
GEM231 2nd generation antisense drug candidate used to potentiate the antitumor activity of Camptosar	Cancer	phase 1/2

[1] Being developed by The Immune Response Corporation in collaboration with us.

[2] Being developed by Micrologix Biotech, Inc. in collaboration with us.

[3] Being developed by Aegera Therapeutics, Inc. in collaboration with us.

Table of Contents

USE OF PROCEEDS

We will not receive any proceeds from the sale of the shares offered pursuant to this prospectus. The selling stockholders will receive all of the proceeds from the sale of the shares of common stock offered by this prospectus. For information about the selling stockholders, see Selling Stockholders.

The selling stockholders will pay any underwriting discounts and commissions and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in disposing of the shares. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including all registration and filing fees and fees and expenses of our counsel and our accountants.

Table of Contents

SELLING STOCKHOLDERS

The shares of common stock covered by this prospectus include:

- 20,053,022 shares of common stock that we issued to the selling stockholders in a private placement in August 2003;
- 6,015,934 shares of common stock issuable upon exercise of warrants to purchase common stock which we issued to the selling stockholders in connection with their purchase of shares of common stock in the private placement, which we refer to as the investor warrants; and
- 3,783,747 shares of common stock issuable upon exercise of warrants to purchase common stock which we issued to the selected dealer and the placement agent for our private placement which we refer to as the dealer warrants.

The table below sets forth, to our knowledge, information about the selling stockholders as of September 1, 2003.

We do not know when or in what amounts a selling stockholder may offer shares for sale. The selling stockholders may not sell any or all of the shares offered by this prospectus. Because the selling stockholders may offer all or some of the shares pursuant to this offering, and because there are currently no agreements, arrangements or understandings with respect to the sale of any of the shares, we cannot estimate the number of shares that will be held by the selling stockholders after completion of this offering. For purposes of this table, however, we have assumed that, after completion of this offering, none of the shares covered by this prospectus will be held by the selling stockholders.

Beneficial ownership is determined in accordance with the rules of the SEC, and includes voting or investment power with respect to shares. Shares of common stock issuable upon exercise of warrants or stock options that are exercisable within 60 days after September 1, 2003 are deemed outstanding for computing the percentage ownership of the person holding the warrants or options but are not deemed outstanding for computing the percentage ownership of any other person. Unless otherwise indicated below, to our knowledge, all persons named in the table have sole voting and investment power with respect to the shares of common stock beneficially owned by them, except to the extent authority is shared by spouses under applicable law. The inclusion of any shares in this table does not constitute an admission of beneficial ownership for the person named below.

Table of Contents

Name of Selling Stockholder(1)	Shares of Common Stock Beneficially Owned Prior to Offering(2)		Number of Shares of Common Stock Being Offered(2)	Shares of Common Stock to be Beneficially Owned After Offering	
	Number	Percentage		Number	Percentage
Clarence A. Abramson	22,260	*	22,260		
Lincoln Adair & Sally Adair TIC	71,232	*	71,232		
Bruce Alexander	14,382(3)	*	14,382(3)		
Marcos Anszelowicz	44,520	*	44,520		
Charles Aquilina	2,877(3)	*	2,877(3)		
Arnel Aquino	4,794(3)	*	4,794(3)		
Dr. Jan Arnett	133,561	*	133,561		
Sharon Aviles	4,448(3)	*	4,448(3)		
Helen Bachthaler	1,918(3)	*	1,918(3)		
DCG&T C/F Jack T. Badgett IRA R/O	22,260	*	22,260		
Joel Barth	17,807	*	17,807		
Donna Baselice	14,382(3)	*	14,382(3)		
Glen Basinger	26,711	*	26,711		
Roger Baumberger	23,969(3)	*	23,969(3)		
Robert S. Beadle	44,520	*	44,520		
Joe N. & Jamie Behrendt Revocable Trust 10/20/96	44,520	*	44,520		
Bel Air Associates, LLC	89,041	*	89,041		
Lon Bell	89,041	*	89,041		
James Benedict	28,764(3)	*	28,764(3)		
Robert Bennie	44,520	*	44,520		
Stephanie C. Berg	17,807	*	17,807		
Better Home Plastics Corp.	445,205	*	445,205		
Fred B. Bialek	89,041	*	89,041		
Ronni & Paul Bianco JTWROS	8,904	*	8,904		
Blue & Gold Enterprises LLC	222,602	*	222,602		
Delaware Charter G&T Co. FBO Elizabeth H. Bone SEP IRA	41,848	*	41,848		
James Bonvissuto	89,041	*	89,041		
Mark Boyce	44,520	*	44,520		
John W. Boyd	35,616	*	35,616		
Gordon Bruce	44,520	*	44,520		
Laura Cabo	5,127(3)	*	5,127(3)		
Deanna Caffarone	2,989(3)	*	2,989(3)		

Table of Contents

Name of Selling Stockholder(1)	Shares of Common Stock Beneficially Owned Prior to Offering(2)		Number of Shares of Common Stock Being Offered(2)	Shares of Common Stock to be Beneficially Owned After Offering	
	Number	Percentage		Number	Percentage
William J. Callahan	178,082	*	178,082		
Capital Growth Equity Fund I, LLC	445,205	*	445,205		
Scott Cardone	8,794(3)	*	8,794(3)		
Jack Cardwell & Evonne Cardwell JTWROS	178,082	*	178,082		
Jodi Castoro & Vincent Castoro TIC	13,355	*	13,355		
Troy Cates	4,794(3)	*	4,794(3)		
CGF Securities, LLC	53,425(3)	*	53,425(3)		
Daniel Chestler	53,424	*	53,424		
Clariden Bank	267,123	*	267,123		
Morgan Stanley FBO Charles C. Clark IRA	89,041	*	89,041		
John Clarke	12,221(3)	*	12,221(3)		
John A. Cleary	35,616	*	35,616		
Joseph L. Codi	44,520	*	44,520		
Kevin P. Conroy	178,082	*	178,082		
Geoff Coy	89,041	*	89,041		
Rosa Cubeiro-Iglesias	2,877(3)	*	2,877(3)		
Dr. Malcolm R. Currie	44,520	*	44,520		
Ernst de Flines	89,041	*	89,041		
Arnaud de Vienne	2,672(3)	*	2,672(3)		
DCG&T C/F Dennis Deloach IRA RO	22,260	*	22,260		
Dennis R. Deloach, Jr.	22,260	*	22,260		
Nicholas & Barbara DeLuca JTWROS	44,520	*	44,520		
Steven H. Deutsch & Wilma K. Deutsch JTWROS	48,120	*	44,520	3,600	*
David DiGiacinto	28,764(3)	*	28,764(3)		
William Dioguardi	54,163(3)	*	54,163(3)		
Dr. Richard Dold	26,711	*	26,711		
Cindy Dolgin	44,520	*	44,520		
Carl J. Domino	178,082	*	178,082		
Heather Donahue	35,043(3)	*	35,043(3)		
Jules H. Dreyfuss	44,520	*	44,520		
Torben Duer	311,644	*	311,644		
Andrew M. Dyer	178,082	*	178,082		

Table of Contents

Name of Selling Stockholder(1)	Shares of Common Stock Beneficially Owned Prior to Offering(2)		Number of Shares of Common Stock Being Offered(2)	Shares of Common Stock to be Beneficially Owned After Offering	
	Number	Percentage		Number	Percentage
Matthew Ehrlich	22,260	*	22,260		
Seymour J. Eisenberg	89,041	*	89,041		
Ronald Eller	44,520	*	44,520		
DiAnn Ellis	7,493(3)	*	7,493(3)		
U. Bertram Ellis, Jr.	89,041	*	89,041		
Jacob M. Engel	89,041	*	89,041		
Theresa M. Fabiani	44,520	*	44,520		
Donald Farley	33,557(3)	*	33,557(3)		
Donald Farley Inter-Vivos Trust, U/A/D 7/31/98	44,520	*	44,520		
Harold Finelt	44,520	*	44,520		
Pershing LLC as Custodian IRA FBO Carol J. Fiol	44,520	*	44,520		
DCG&T C/F Baruch Fischhoff IRA	22,260	*	22,260		
Gary Fischoff	44,520	*	44,520		
Jonathan Fleisig	178,082	*	178,082		
Richard J. Forsyth	44,520	*	44,520		
James B. Gallinatti, Jr. & Ellen T. Gallinatti JTWROS	89,041	*	89,041		
Walter G. Gans	44,520	*	44,520		
Garfield Associates LLC	89,041	*	89,041		
Joseph Gatti, Jr.	4,794(3)	*	4,794(3)		
Harold S. Gault	178,082	*	178,082		
Pershing LLC as Custodian IRA FBO Phyllis Gelles	89,041	*	89,041		
Alfred A. Gilbert	22,260	*	22,260		
Richard Gill	44,520	*	44,520		
David M. Gilson	53,424	*	53,424		
Jerome Z. Ginsburg	44,520	*	44,520		
Samuel Goekjian	44,520	*	44,520		
Janine Goldblatt	2,877(3)	*	2,877(3)		
William M. Goldstein	89,041	*	89,041		
Peter C. Gould	44,520	*	44,520		
Maurice & Stacy Gozlan TIE	89,041	*	89,041		

Table of Contents

Name of Selling Stockholder(1)	Shares of Common Stock Beneficially Owned Prior to Offering(2)		Number of Shares of Common Stock Being Offered(2)	Shares of Common Stock to be Beneficially Owned After Offering	
	Number	Percentage		Number	Percentage
Irwin Gruverman	44,520	*	44,520		
Ronald Haboush	445,205	*	445,205		
Anita C. Haffey Revocable Trust	44,520	*	44,520		
Joseph W. Halligan Trust DTD Dec. 20, 2001	44,520	*	44,520		
Robert Hammer	17,807	*	17,807		
Tara Hanley	11,185(3)	*	11,185(3)		
Todd Harrigan	59,431(3)	*	59,431(3)		
Harold A. Havekotte Inc. Pension Plan 11/28/80	44,520	*	44,520		
Headwaters Holdings LLC	178,082	*	178,082		
John Heidenreich	15,768(3)	*	15,768(3)		
DCG&T C/F Robert G. Heidenreich IRA	71,232	*	71,232		
William Henner	44,520	*	44,520		
Tim Herrmann	34,480(3)	*	34,480(3)		
Kenneth J. Heuer	11,185(3)	*	11,185(3)		
John Hewins	14,382(3)	*	14,382(3)		
John Higgins	43,144(3)	*	43,144(3)		
Lee O. Hill	17,807	*	17,807		
DCG&T C/F Lee O. Hill IRA R/O	44,520	*	44,520		
David Hochman	179,754(3)	*	179,754(3)		
Susan Hoffmann	4,506(3)	*	4,506(3)		
Timothy Holland	44,520	*	44,520		
Byron C. & Julie L. Hughey Tenants by the Entirety	17,807	*	17,807		
Ronald Hutchison & Lisa Hutchison JTWROS	22,260	*	22,260		
Thomas Hutzel	28,764(3)	*	28,764(3)		
Immunoclin Limited	6,500(3)	*	6,500(3)		
Roland Isaacson	89,041	*	89,041		
Andre Iseli	44,520	*	44,520		
Alec Jaret	22,260	*	22,260		

Table of Contents

Name of Selling Stockholder(1)	Shares of Common Stock Beneficially Owned Prior to Offering(2)		Number of Shares of Common Stock Being Offered(2)	Shares of Common Stock to be Beneficially Owned After Offering	
	Number	Percentage		Number	Percentage
DCG&T C/F Chatri Jhunjhnuwala SEP IRA	89,041	*	89,041		
W. Kahle Johnson, Jr.	22,260	*	22,260		
JSP Holdings ApS	291,327	*	178,082	113,245	*
K&R Negotiation Associates LLC	44,520	*	44,520		
Pershing LLC as Custodian SEP FBO Robert Kalman	44,520	*	44,520		
Arun Kapur & Meera Kapur TIC	44,520	*	44,520		
Valerie Lee Karraker	22,260	*	22,260		
John J. Kealy Revocable Trust dtd 8/15/96 John J. Kealy TTEE	22,260	*	22,260		
Steven & Marilyn Keenan JTWROS	222,602	*	222,602		
DCG&T C/F John H. Keller	35,616	*	35,616		
The Shirley Keys Family Trust UAD 4/22/99 Shirley Keys TTEE	22,260	*	22,260		
Delaware Charter G&T Co. FBO Benjamin King IRA	26,711	*	26,711		
Everett P. Kirch & Linda R. Kirch JTWROS	22,260	*	22,260		
Robert Klein	106,848	*	106,848		
Charles D. Kleinow	89,041	*	89,041		
William P. Klingenstein	89,041	*	89,041		
John Kokales	44,520	*	44,520		
Michael A. Kolber & Terri L. Meinking JTWROS	17,807	*	17,807		
Christian Kolster	89,041	*	89,041		
Patricia Koo	23,969(3)	*	23,969(3)		
Kenneth J. Kostal	44,520	*	44,520		
Athanasios Koukoulis	22,260	*	22,260		

Table of Contents

Name of Selling Stockholder(1)	Shares of Common Stock Beneficially Owned Prior to Offering(2)		Number of Shares of Common Stock Being Offered(2)	Shares of Common Stock to be Beneficially Owned After Offering	
	Number	Percentage		Number	Percentage
Kredietbank (Suisse) SA Acting for Customers A/C	89,041	*	89,041		
John C. Kroening	44,520	*	44,520		
Thaddeus B. Kubis & Maria G. Kubis JTWROS	26,711	*	26,711		
J. Allen Lamb	44,520	*	44,520		
David Landskowsky	86,003(3)	*	86,003(3)		
Bruce Larson	178,082	*	178,082		
Paul Latchford	33,557(3)	*	33,557(3)		
William Lederer	11,185(3)	*	11,185(3)		
Aaron Lehmann	17,807	*	17,807		
Moseh Lehrfield & Jennifer Lehrfield JT TEN	17,807	*	17,807		
Scott Leishman	23,969(3)	*	23,969(3)		
DCG&T C/F Scott Leishman IRA Rollover	22,260	*	22,260		
Bruno Lerer	33,557(3)	*	33,557(3)		
Lee A. Levine	89,041	*	89,041		
Robert Levy, Jr.	89,041	*	89,041		
Lincoln Associates LLC	53,424	*	53,424		
Charles Loegering	44,520	*	44,520		
Kirk Loury	748(3)	*	748(3)		
Ronald Luken	28,764(3)	*	28,764(3)		
U/W/O Edward C. Mack 1973 Trust	44,520	*	44,520		
Delaware Charter G&T Co. FBO Todd Maibach IRA	22,260	*	22,260		
Brian J. Malecek	44,520	*	44,520		
Richard Mandell & Audrey R. Lee Mandell JTWROS	44,520	*	44,520		
Robert F. Mann Revocable Trust U/A/D 1/29/91	22,260	*	22,260		
Robert Manning	11,185(3)	*	11,185(3)		
Joseph O. Manzi	44,520	*	44,520		
Erika McCarthy	2,877(3)	*	2,877(3)		

Table of Contents

Name of Selling Stockholder(1)	Shares of Common Stock Beneficially Owned Prior to Offering(2)		Number of Shares of Common Stock Being Offered(2)	Shares of Common Stock to be Beneficially Owned After Offering	
	Number	Percentage		Number	Percentage
Patrick McGovern	43,144(3)	*	43,144(3)		
Kathleen S. McHugh	22,260	*	22,260		
Meadowbrook Capital Corp. Profit Sharing Plan	178,082	*	178,082		
Rosemarie Melnichuk	2,877(3)	*	2,877(3)		
Daniel Michael	44,520	*	44,520		
Lawrence W. Milne, MD PC, Profit Sharing Plan	178,082	*	178,082		
Richard J. Mish	68,387(4)	*	68,387(4)		
Delaware Charter Guarantee and Trust Co. FBO Richard Mish IRA	22,260	*	22,260		
E.A. Moos & Co. LP	178,082	*	178,082		
Leonard Moskowitz	44,520	*	44,520		
Mouton Family Living Trust	22,260	*	22,260		
Franz Muster	44,520	*	44,520		
Howard Nathel	89,041	*	89,041		
Steve Nicholson	6,360(3)	*	6,360(3)		
Gus & Karen Nicolopoulos	17,807	*	17,807		
O.T. Finance, SA	44,520	*	44,520		
Gerard O Brien	22,260	*	22,260		
Edward J. O Connell	89,041	*	89,041		
Edwin O Connor	17,807	*	17,807		
Mel Okeon M.D. Med. Corp. Profit Sharing Trust	178,082	*	178,082		
Bernard Oleyar	22,260	*	22,260		
James Oliphant	44,520	*	44,520		
Elizabeth Olsen	14,382(3)	*	14,382(3)		
Gilbert S. Omenn	89,041	*	89,041		
Dr. Peter Oppenheimer & Sandi Oppenheimer JTWROS	22,260	*	22,260		
Optima Life Sciences Limited	7,150,495(5)	11.0%	7,150,495(5)		
Reed S. Oslan	35,616	*	35,616		

Table of Contents

Name of Selling Stockholder(1)	Shares of Common Stock Beneficially Owned Prior to Offering(2)		Number of Shares of Common Stock Being Offered(2)	Shares of Common Stock to be Beneficially Owned After Offering	
	Number	Percentage		Number	Percentage
OTAPE Investments LLC	178,082	*	178,082		
Larry Pallini	44,520	*	44,520		
PAM Investments I	89,041	*	89,041		
Suresh Patel	44,520	*	44,520		
Bruce H. Paul	89,041	*	89,041		
Eric Paul	58,902(4)	*	58,902(4)		
Tanya Peress	2,877(3)	*	2,877(3)		
Performance Capital Group, LLC	89,041	*	89,041		
Sheldon Perl & Ruth Perl TIC	89,041	*	89,041		
Kenneth J. Peterson	89,041	*	89,041		
Lisa Peterson & Mark Smith JTWROS	26,711	*	26,711		
The Paul F. Petrus Rev. Trust of 1988 UAD 4-15-88	44,520	*	44,520		
Jessica Phillips	14,382(3)	*	14,382(3)		
Pillar Investment Limited	587,709(6)	*	587,709(6)		
James Pizzo	26,711	*	26,711		
Plum Glen Partners LP/Jerry Mendelson General Partner	44,520	*	44,520		
Joseph Porfeli	33,557(3)	*	33,557(3)		
Alida Provence	2,877(3)	*	2,877(3)		
K.V. Rajagopalan	35,616	*	35,616		
Dr. V.J. L.K. Raju & Dr. Govind S. Raju JTWROS	22,260	*	22,260		
Richard Ramlall	28,764(3)	*	28,764(3)		
Susan Read	2,877(3)	*	2,877(3)		
Joanne Reda	2,877(3)	*	2,877(3)		
Delaware Charter G&T Co. FBO Gary Reich IRA	22,260	*	22,260		
Donald S. Rice	26,711	*	26,711		
George E. Robb, Jr.	89,041	*	89,041		
Elisha Rothman	89,041	*	89,041		
Eric Rubenstein	245,823(3)	*	245,823(3)		

Table of Contents

Name of Selling Stockholder(1)	Shares of Common Stock Beneficially Owned Prior to Offering(2)		Number of Shares of Common Stock Being Offered(2)	Shares of Common Stock to be Beneficially Owned After Offering	
	Number	Percentage		Number	Percentage
Alan Rubin	178,082	*	178,082		
Neil Rubin	90,638(3)	*	90,638(3)		
Stanley M. Rubin	44,520	*	44,520		
Richard Russey	22,260	*	22,260		
Bernard D. Sadow	89,041	*	89,041		
Richard Sakakeeny	17,807	*	17,807		
Wayne Saker	89,041	*	89,041		
Albert L. Salvatico	89,041	*	89,041		
Antonio Santos	1,918(3)	*	1,918(3)		
Stephen Schloss	89,041	*	89,041		
Scott Schulte	5,244(3)	*	5,244(3)		
Susan Schwartz-Giblin	22,260	*	22,260		
Aaron Segal	17,016(3)	*	17,016(3)		
Allen Sessoms	35,616	*	35,616		
Barry Shemaria	44,520	*	44,520		
Ship Commodities International Inc.	53,424	*	53,424		
J. Edward Shrawder	44,520	*	44,520		
Dr. Alan M. Shuman	44,520	*	44,520		
Michael Siek	107,478(3)	*	107,478(3)		
Laurie K. Silverman	8,904	*	8,904		
Michael Silverman	6,423(3)	*	6,423(3)		
Silverman Family Limited Partnership	53,424	*	53,424		
Allen Snelling	14,581(3)	*	14,581(3)		
Elliot Sokolow	44,520	*	44,520		
Lydia Soler	11,185(3)	*	11,185(3)		
James Soyak and Deborah Soyak JT/WROS	178,082	*	178,082		
Spencer Trask & Co.	1,154,434(3)	1.8%	1,154,434(3)		
Spencer Trask Illumination Fund LLC	178,082	*	178,082		
Spencer Trask Investment Partners, LLC	1,780,822	2.8%	1,780,822		
Spencer Trask Private Equity Accredited Fund III, LLC	445,205	*	445,205		
Spencer Trask Private Equity Fund I LP	712,329	1.1%	712,329		

Table of Contents

Name of Selling Stockholder(1)	Shares of Common Stock Beneficially Owned Prior to Offering(2)		Number of Shares of Common Stock Being Offered(2)	Shares of Common Stock to be Beneficially Owned After Offering	
	Number	Percentage		Number	Percentage
Spencer Trask Private Equity Fund II LP	356,164	*	356,164		
Richard M. Spitalny	44,520	*	44,520		
Donald Spongberg	2,885(3)	*	2,885(3)		
Statler Family Trust	35,616	*	35,616		
Arthur Steinberg	44,520	*	44,520		
Adam K. Stern	165,266(4)	*	165,266(4)		
William C. Wetzel TTEE for the Livingston, Barger, Brandt & Schroeder Self Employment Ret. Plan DTD 9/30/94 FBO Richard Stites	89,041	*	89,041		
David & Susan Stollwerk JTWROS	44,520	*	44,520		
Lawrence Storch	44,520	*	44,520		
Joanna Struett	89,041	*	89,041		
Sunflower Trading Fund	178,082	*	178,082		
Jack Swartz	67,620	*	44,520	23,100	*
Sweetland L.L.C	44,520	*	44,520		
Pershing LLC as Custodian IRA Rollover FBO Robert Swift	208,082	*	178,082	30,000	*
Tan/DeMattei Family Trust of 1999	44,520	*	44,520		
Christopher Terzini	14,382(3)	*	14,382(3)		
William Thacker & Susan Thacker JTWROS	44,520	*	44,520		
Matthew Thomas	23,881(3)	*	23,881(3)		
Frederick Tramutola	44,520	*	44,520		
Jed Trosper	33,557(3)	*	33,557(3)		
Charles Tully & Kathleen Tully JTWROS	44,520	*	44,520		
Sam V. Vail	30,878(3)	*	30,878(3)		

Table of Contents

Name of Selling Stockholder(1)	Shares of Common Stock Beneficially Owned Prior to Offering(2)		Number of Shares of Common Stock Being Offered(2)	Shares of Common Stock to be Beneficially Owned After Offering	
	Number	Percentage		Number	Percentage
CGM IRA Rollover Custodian FBO Sam V. Vail	44,520	*	44,520		
John V. Wagner	44,520	*	44,520		
DCG&T C/F Ross Graham Walker III IRA R/O	71,232	*	71,232		
Joan K. Warnke	22,260	*	22,260		
Rachel Waters	2,877(3)	*	2,877(3)		
Jerold Weinger & Lilli Weinger JTWROS	178,082	*	178,082		
Paul J. Weir	44,520	*	44,520		
Kevin Weisbeck	44,520	*	44,520		
Weiskopf, Silver & Co., LP	133,561	*	133,561		
DIYR Plans, Inc. Money Purchase Plan and Trust as Adopted by Don Wheeler Enterprises, Inc.	178,082	*	178,082		
Ralph C. Wintrode Trust dtd May 9, 2001	44,520	*	44,520		
Josh Wisotsky	11,474(3)	*	11,474(3)		
William Woodfield	23,969(3)	*	23,969(3)		
Woodlands Construction LLC	44,520	*	44,520		
James B. Wyngaarden	714,443(7)	1.1%	44,520	669,923	1.0%
Wayne P. Yetter	44,520	*	44,520		
Don & Sheri Yohe JTWROS	89,041	*	89,041		
Paul C. Zamecnik	921,030(8)	1.4%	89,041	831,989	1.3%
Carol Zervoulei	18,869(3)	*	18,869(3)		
Michael Zimmerman	17,807	*	17,807		

* Less than one percent.

(1) The term selling stockholders includes donees, pledgees, transferees or other successors-in-interest selling shares received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other non-sale related transfer.

Table of Contents

(2) Unless otherwise noted in these footnotes, includes shares of common stock issuable upon exercise of the investor warrants.

(3) Consists of shares of common stock issuable upon exercise of the dealer warrants.

(4) Includes shares of common stock issuable upon exercise of both the dealer warrants and the investor warrants.

(5) Includes 1,650,114 shares of common stock issuable upon the exercise of warrants held by Optima.

(6) Consists of shares of common stock issuable upon the exercise of warrants held by Pillar.

(7) Includes 530,000 shares subject to outstanding stock options that are exercisable within 60 days after September 1, 2003 and 10,274 shares of common stock issuable upon the exercise of warrants.

(8) Includes 201,200 shares subject to outstanding stock options that are exercisable within 60 days after September 1, 2003 and 20,548 shares of common stock issuable upon the exercise of warrants.

Relationships with Selling Stockholders

Except for the selling stockholders listed below, no selling stockholder has had any position, office or other material relationship with us or our affiliates within the past three years.

Optima Life Sciences Limited and Pillar Investment Limited

One of our directors, Youssef El-Zein, is a director of Optima Life Sciences Limited and Pillar Investment Limited. Pillar Investment Limited is the manager and investment advisor of Optima.

Pillar Investment Limited acted as a placement agent for us in connection with our August 2003 private placement under the terms of an engagement letter dated April 18, 2003 to which we are a party with Pillar Investment Limited and PrimeCorp Finance S.A. Under the terms of the engagement letter, we paid Pillar Investment Limited $300,319 in cash and issued Pillar Investment Limited warrants to purchase 587,709 shares of common stock at an exercise price of $1.00 per share as fees in connection with the participation of non-U.S. investors in our August 2003 private placement.

During the past three years, Pillar S.A., an affiliate of Pillar Investment Limited and Mr. El-Zein, has provided consulting services to us relating to international investor relations, employment contracts with our management team and various transactions in which we have engaged including our sale of shares of Methylgene Inc. in 2001, our license and collaboration with Isis Pharmaceuticals, Inc. in 2001, the conversion of our 8% convertible notes into our series B convertible preferred stock in 2001, our early exercise program in 2001 in which we exchanged common stock for our series B convertible preferred stock, several classes of our warrants and our 8% convertible notes and our repurchase of common stock in 2003. For these services, we have paid Pillar a total of $568,500 in cash and issued to Pillar 178,571 shares of common stock.

Mr. El-Zein converted 8% convertible notes in the principal amount of $30,968 and accrued interest of $1,057 into 317 shares of our series B convertible preferred stock in 2001 and exchanged 3,851 shares of our series B convertible preferred stock and warrants to purchase 748,248 shares of common stock for a total of 1,437,054 shares of common stock in our early exercise program in 2001.

Spencer Trask Entities

Spencer Trask Ventures, Inc., an affiliate of Spencer Trask & Co., Inc., Spencer Trask Illumination Fund LLC, Spencer Trask Investment Partners LLC, Spencer Trask Private Equity Accredited Fund III LLC, Spencer Trask Private Equity Fund I LP and Spencer Trask Private Equity Fund II LP, acted as a selected dealer for us in connection with our August 2003 private placement under the terms of a selected dealer agreement dated July 22, 2003. Under the terms of the selected dealer agreement, we paid Spencer Trask Ventures, Inc. $1,064,310 in cash and issued warrants to purchase 2,458,405 shares of our common stock at an exercise price of $0.73 per share and warrants to purchase 737,633 shares of our common stock at an exercise price of $1.00 per share as fees in connection with our August 2003 private placement.

James B. Wyngaarden

James B. Wyngaarden has served as the Chairman of our Board of Directors since February 2000 and as one of our directors since 1990. In 2001, Dr. Wyngaarden acquired 27,737 shares of common stock upon the exercise of warrants in our early exercise program for an aggregate

exercise price of $10,817.

Paul C. Zamecnik

Paul C. Zamecnik has served as a director on our Board of Directors since 1990. Dr. Zamecnik also provides consulting services to us for which we pay Dr. Zamecnik a fee of $20,000 per year. Since October 1, 2000, we have paid Dr. Zamecnik a total of $60,000 in consulting fees.

Dr. Zamecnik converted 8% convertible notes in the principal amount of $27,695 and accrued interest of $954 into 286 shares of our series B convertible preferred stock in 2001. Dr. Zamecnik also participated in our early exercise program in 2001, exchanging 1,066 shares of our series B convertible preferred stock for 266,500 shares of common stock and acquiring 230,793 shares of common stock upon the exercise of warrants for an aggregate exercise price of $91,018.

Table of Contents

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock summarizes the material terms and provisions of the indicated securities. For the complete terms of our common stock, preferred stock and preferred stock purchase rights, please refer to our certificate of incorporation, by-laws and stockholder rights plan that we have filed with the SEC. The terms of these securities may also be affected by the General Corporation Law of the State of Delaware.

We are authorized to issue 150,000,000 shares of common stock and 5,000,000 shares of preferred stock, $0.01 par value per share, of which 1,500,000 are designated series A convertible preferred stock and 150,000 shares are designated series C junior participating preferred stock. As of September 1, 2003, there were 63,578,377 shares of common stock outstanding, 699,980 shares of series A convertible preferred stock outstanding, no shares of series C junior participating preferred stock outstanding and no other shares of preferred stock issued and outstanding.

Common Stock

Voting. For all matters submitted to a vote of stockholders, each holder of common stock is entitled to one vote for each share registered in that stockholder s name on our books. Our common stock does not have cumulative voting rights. As a result, subject to the voting rights, of which there currently are none, of any outstanding preferred stock, persons who hold more than 50% of the outstanding common stock entitled to elect members of our board of directors can elect all of the directors who are up for election in a particular year.

Dividends. If our board of directors declares a dividend, holders of common stock will receive payments from our funds that are legally available to pay dividends. However, this dividend right is subject to any preferential dividend rights that we have granted or may grant to the persons who hold preferred stock.

Liquidation and Dissolution. If we are liquidated or dissolved, the holders of our common stock will be entitled to share ratably in all the assets that remain after we pay our liabilities, including without limitation liabilities under the unit purchase agreement described below, and any amounts we may owe to the persons who hold preferred stock, if any is outstanding.

Other Rights and Restrictions. The outstanding shares of our common stock are validly issued, fully paid and nonassessable. Holders of our common stock do not have preemptive rights, and they have no right to convert their common stock into any other securities. Our common stock is not subject to redemption by us. The rights, preferences and privileges of common stockholders are subject to the rights of the stockholders of any series of preferred stock that are issued and outstanding or that we may issue in the future. Our certificate of incorporation and by-laws do not restrict the ability of a holder of common stock to transfer his or her shares of common stock.

Transfer Agent and Registrar. The transfer agent and registrar for our common stock is Mellon Investor Services LLC.

Table of Contents

Put Right. Pursuant to the terms of a unit purchase agreement dated as of May 5, 1998, we issued and sold a total of 9,597,476 shares of common stock, which we refer to as the put shares, at a price of $2.00 per share. Under the terms of the unit purchase agreement, the initial purchasers, which we refer to as the put holders, of the put shares have the right, which we refer to as the put right, to require us to repurchase the put shares. The put right may not be exercised by any put holder unless all of the following occur:

- we liquidate, dissolve or wind up our affairs pursuant to applicable bankruptcy law, whether voluntarily or involuntarily,
- all of our indebtedness and obligations, including without limitation the indebtedness under our outstanding notes, has been paid in full, and
- all rights of the holders of any series or class of capital stock ranking prior and senior to the common stock with respect to liquidation, including without limitation the series A convertible preferred stock, have been satisfied in full.

We may terminate the put right upon written notice to the put holders if the closing sales price of our common stock exceeds $4.00 per share for the 20 consecutive trading days prior to the date of notice of termination. Because the put right is not transferable, in the event that a put holder has transferred put shares since May 5, 1998, the put right with respect to those shares has terminated. As a consequence of the put right, in the event we are liquidated, holders of shares of common stock that do not have put rights with respect to such shares may receive smaller distributions per share upon our liquidation than if there were no put rights outstanding.

As of December 31, 2002, 5,467,686 of the put shares continued to be held in the name of the put holders. On February 14, 2003, we repurchased 2,415,880 of these put shares. We cannot determine at this time whether the put rights with respect to the balance of the put shares have terminated.

Warrants

We have the following warrants outstanding and exercisable for the purchase of common stock as of September 1, 2003:

- a warrant to purchase 173,333 shares of common stock at an exercise price of $3.00 per share, which expires on November 30, 2003;
- a warrant to purchase 500,000 shares of common stock at an exercise price of $0.50 per share, which expires on March 31, 2006;
- a warrant to purchase 100,000 shares of common stock at an exercise price of $1.65 per share, which expires on January 1, 2007;
- warrants to purchase an aggregate of 7,341,276 shares of common stock at an exercise price of $1.00 per share, which expire on August 28, 2008; and

Table of Contents

warrants to purchase an aggregate of 2,458,405 shares of common stock at an exercise price of $0.73 per share, which expire on August 28, 2008.

Preferred Stock

Our board of directors is authorized, subject to any limitations prescribed by law, without further stockholder approval, to issue from time to time up to 5,000,000 shares of preferred stock, in one or more series. Each series of preferred stock shall have the number of shares, designations, preferences, voting powers, qualifications and special or relative rights or privileges as shall be determined by our board of directors, which may include, among others, dividend rights, voting rights, redemption and sinking fund provisions, liquidation preferences, conversion rights and preemptive rights.

Our stockholders have granted the board of directors authority to issue the preferred stock and to determine its rights and preferences in order to eliminate delays associated with a stockholder vote on specific issuances. The rights of the holders of common stock will be subject to, and may be adversely affected by, the rights of holders of any preferred stock that may be issued in the future. The issuance of preferred stock, while providing desirable flexibility in connection with possible acquisitions and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from attempting to acquire, a majority of our outstanding voting stock.

Series A Convertible Preferred Stock

Dividends. Each share of series A convertible preferred stock is entitled to receive cumulative semi-annual dividends payable, at our option, in cash or additional shares of series A convertible preferred stock, at the rate of 1.0% per annum plus accrued but unpaid dividends. Prior to an amendment to the terms of the series A convertible preferred stock effected on December 4, 2003 following approval of the amendment by our stockholders, dividends were payable at a rate of 6.5% per annum plus accrued but unpaid dividends. Dividends accrue from the date of issuance and are 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 business day. Dividends are paid, at our election, either in cash or additional 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 is valued at $100 per share, subject to appropriate adjustment to reflect any stock split, combination, reclassification or reorganization of the series A convertible preferred stock.

Liquidation Preference. In the event of one of the following liquidation events:

our liquidation, dissolution or winding up, whether voluntary or involuntary,

a sale or other disposition of all or substantially all of our assets, or

any consolidation, merger, combination, reorganization or other transaction in which we are not the surviving entity or if stock constituting more than 50% of our voting power is exchanged for or changed into stock or securities of another entity, cash, or any other property,

after payment of our debts and other liabilities, the holders of shares of series A convertible preferred stock will be entitled to be paid out of our available assets, before any payment to

Table of Contents

holders of shares ranking junior to the series A convertible preferred stock, an amount equal to $1 per share plus accrued but unpaid dividends. Prior to the amendment effected on December 4, 2003, holders of series A convertible preferred stock were entitled to a liquidation preference of $100 per share plus accrued but unpaid dividends. In the case of a transaction listed in the third bullet above, however, this payment may be made in cash, property or securities of the entity surviving the transaction. If upon any liquidation event, whether voluntary or involuntary, the assets to be distributed to the holders of the series A convertible preferred stock are insufficient to permit the payment to such shareholders of the full amount owed, then all of our available assets will be distributed ratably to the holders of the series A convertible preferred stock.

All shares of series A convertible preferred stock rank, as to payment upon the occurrence of any liquidation event, senior to the common stock and senior to all other series of preferred stock, unless the terms of any series provides otherwise.

Right of Conversion. Shares of series A convertible preferred stock are convertible, at the option of the holder, into shares of common stock or other securities and property. The conversion price per share of common stock is $4.25, and is subject to adjustment as described below. The conversion rate at which each share of series A convertible preferred stock is convertible at any time into common stock will be determined by dividing the then existing conversion price into the dividend base amount for a share of series A convertible preferred stock. The dividend base amount equals $100 plus accrued but unpaid dividends, subject to adjustment to reflect any stock split, combination, reclassification or reorganization. As of September 1, 2003, each share of series A convertible preferred stock was convertible into approximately 23.53 shares of common stock. Following the amendment to the terms of the series A convertible preferred stock effected on December 4, 2003, during the period commencing on December 4, 2003 and ending on February 2, 2004, each share of series A convertible preferred stock will be convertible into a number of shares of common stock that is 25% greater than the number of shares of common stock that would otherwise be issuable upon conversion of a share of series A convertible preferred stock. As a result, during this conversion period, each share of series A convertible preferred stock will be convertible into approximately 29.41 shares of common stock.

Adjustment of Conversion Rate and Conversion Price. In order to preserve the economic value of shares of series A convertible preferred stock, the conversion rate and the conversion price will be adjusted if we do the following;

pay a dividend or make a distribution on any class of capital stock in shares of common stock;

subdivide our outstanding common stock into a greater number of shares;

combine our outstanding common stock into a smaller number of shares;

issue shares of common stock or preferred stock generally to the holders of our common stock or preferred stock rights to acquire shares of common stock or preferred stock at a price per share less than the market price;

pay or distribute to the holders of common stock or preferred stock assets, properties or rights to acquire our capital stock at a price per share less than the market price; or

make a distribution consisting solely of cash to the holders of any class of capital stock where, during a specified 12-month period, the cash distribution exceeds 10% of the product of the market price of the common stock multiplied by the total number of shares of outstanding common stock.

Table of Contents

Exceptions to Adjustments. No adjustment will, however, be made to either the conversion rate or the conversion price for issuances of common stock or preferred stock, or cash paid to holders of shares of convertible preferred stock as payment for accrued dividends or as a mandatory conversion or mandatory redemption payment.

Other Changes in Conversion Rate. We 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, we will notify registered holders.

We may also increase the conversion rate 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.

The conversion price may not be adjusted to an amount less than $0.001 per share, the current par value of the common stock into which the series A convertible preferred stock is convertible.

Mandatory Conversion. Upon giving notice to the holders of the convertible preferred stock, we may, at our option, cause the series A convertible preferred stock to be converted in whole or in part, on a pro rata basis, into shares of common stock using a conversion price equal to $4.00 if the closing bid price of the common stock equals or exceeds 250% of the then current conversion price for at least 20 trading days in any period of 30 consecutive trading days.

Redemption. We may, at our option, redeem the series A convertible preferred stock for cash equal to the dividend base amount.

Class Voting Rights. We may not, without the affirmative vote or consent of the holders of at least 50% of all outstanding shares of series A convertible preferred stock, voting separately as a class:

amend, alter or repeal any provision of our certificate of incorporation or by-laws so as adversely to affect the rights of the series A convertible preferred stock, except that the issuance of securities ranking prior to, or pari passu with, the series A convertible preferred stock upon a liquidation event or with respect to the payment of dividends or distributions will not be considered to affect adversely the relative rights of the series A convertible preferred stock; or

authorize or issue, or increase the authorized amount of, the convertible preferred stock, other than the series A convertible preferred stock issuable as dividends on the series A convertible preferred stock.

Preemptive Rights. The series A convertible preferred stock is not entitled to any preemptive or subscription rights in respect of any of our securities.

Restrictions on Change of Control. So long as any 9% convertible subordinated notes issued by us under an indenture dated as of March 26, 1997 remain outstanding, no holder of any

Table of Contents

shares of series A convertible preferred stock may, without our prior written consent, have voting rights under our certificate of incorporation, be entitled to receive any of our voting securities under our certificate of incorporation, or be entitled to exercise any conversion rights with respect to the series A convertible preferred stock to the extent that such voting rights, receipt of voting securities or exercise of conversion rights could, in our reasonable judgment, either alone or in conjunction with other issuances or holdings of our capital stock, warrants or convertible securities, result in a change of control as defined in the indenture. As of September 1, 2003, the outstanding principal amount of our 9% notes was $1,306,000. Our 9% notes mature on April 1, 2004.

Series C Junior Participating Preferred Stock

Voting. Each share of series C junior participating preferred stock is entitled to 1,000 votes, subject to adjustment if we effect a stock split or issue a stock dividend. Except as provided below, each share of series C junior participating preferred stock votes together with the holders of common stock and all of our other capital stock on all matters voted on by stockholders.

Dividends. The holders of shares of series C junior participating preferred stock are entitled to quarterly cash dividends equal to the greater of $10 or 1,000 times the dividend declared per share of common stock, if any, other than dividends payable in common stock or by a subdivision of the outstanding common stock.

Liquidation and Dissolution. If we are liquidated or dissolve or wind up, then we must pay the holders of outstanding shares of series C junior participating preferred stock, before we make any payment to the holders of shares of stock ranking junior to the series C junior participating preferred stock, an amount equal to $1,000 per share, plus all accrued and unpaid dividends and an amount equal to 1,000 times the amount to be paid to holders of common stock. For purposes of this liquidation preference, neither the consolidation, merger or other business combination of us with another entity nor the sale of all or any of our property, assets or business will be treated as a liquidation, dissolution or winding up of our company.

Merger, Consolidation, etc. If we are a party to any merger, consolidation or similar transaction in which shares of our common stock are exchanged or changed into stock or securities of another entity, cash or property of another entity, then the series C junior participating preferred stock will be exchanged or changed into an amount per share equal to 1,000 times the amount of consideration into which or for which each share of common stock is changed or exchanged in the merger, consolidation or similar transaction.

Adjustments for Stock Splits and Other Events. If we declare a dividend on our common stock that is payable in common stock or if we effect a subdivision, combination or consolidation of the outstanding shares of our common stock into a greater or lesser number of shares, then the

Table of Contents

dividend, liquidation and merger or consolidation amounts payable to holders of series C junior participating preferred stock will be increased or reduced in proportion to the resulting increase or decrease in the total number of shares of common stock outstanding.

Redemption. We may not redeem the series C junior participating preferred stock.

Stockholder Rights Plan

On December 10, 2001, our board of directors adopted a stockholder rights plan. Under the plan, each holder of our common stock at the close of business on January 7, 2002 received a dividend of one preferred stock purchase right, or a right, for each outstanding share of common stock that the stockholder owned. In addition, each share of our common stock issued after January 7, 2002 receives one right. The rights trade automatically with our shares of common stock and become exercisable only under the circumstances described below. The rights will expire on the close of business on December 10, 2011, subject to earlier expiration or termination as described in the rights plan.

The purpose of the rights is to encourage potential acquirors to negotiate with our board of directors before attempting a takeover bid and to provide our board of directors with leverage in negotiating on behalf of our stockholders the terms of any proposed takeover. The rights may have antitakeover effects. They should not, however, interfere with any merger or other business combination approved by our board of directors.

The following description is a summary of the material terms of our stockholder rights plan. It does not restate all of the terms of the plan. The stockholder rights plan, and not this description, defines the terms and provisions of the plan.

Exercise of Rights. Until a right is exercised, the holder of a right will not have any rights as a stockholder. Currently, the rights are not exercisable. When the rights become exercisable, if ever, holders of the rights will be able to purchase from us a unit equal to 1/1000th of a share of our series C junior participating preferred stock at a purchase price of $13.00 per unit.

In general, the rights will become exercisable upon the earlier of:

ten business days following a public announcement that a person or group, other than an exempted person, has acquired beneficial ownership of 15% or more of the outstanding shares of our common stock; or

ten business days after the beginning of a tender offer or exchange offer that would result in a person or group, other than an exempted person, beneficially owning 15% or more of our common stock.

Pillar Investment Limited, together with its affiliates and associates, are exempted persons under our stockholder rights plan. Pillar and its affiliates and associates will remain exempted persons until they beneficially own more than 11,000,000 shares of our common stock, subject to adjustment, or less than 14% of the outstanding shares of our common stock.

Table of Contents

Flip-In Event. If a person or group, other than an exempted person, becomes the beneficial owner of 15% or more of our common stock, then each right, other than those rights held by the person or group that exceeded the 15% threshold, will then entitle its holder to receive, upon exercise, a number of shares of our common stock which is equal to the exercise price of the right divided by one-half of the market price of our common stock on the date of the occurrence of the flip-in event. However, the rights are not exercisable following such an event until such time as the rights are no longer redeemable by us, as described below.

Flip-Over Event. If at any time after a person or group, other than an exempted person, becomes the beneficial owner of 15% or more of our common stock,

we are acquired in a merger or other transaction in which we do not survive or in which our common stock is changed or exchanged; or

50% or more of our assets or earning power is sold or transferred,

then each holder of a right, other than the person or group that exceeded the 15% threshold, will be entitled to receive, upon exercise, a number of shares of common stock of the acquiring company in the transaction equal to the exercise price of the right divided by one-half of the market price of the acquiring company s common stock on the date of the occurrence of the flip-over event.

Exchange of Rights. At any time after a flip-in event, our board of directors may exchange the rights, other than those rights held by the person or group that exceeded the 15% threshold, in whole or in part, at an exchange ratio of one share of our common stock or one one-thousandth of a share of our series C junior participating preferred stock for each right.

Redemption of Rights. At any time prior to the tenth business day after the occurrence of a flip-in event, we may redeem the rights in whole, but not in part, at a price of $0.001 per right.

Certain Effects of Authorized but Unissued Stock

We have shares of common stock and preferred stock available for future issuance without stockholder approval. We may use these additional shares for a variety of corporate purposes, including future public offerings to raise additional capital, facilitating corporate acquisitions or paying a dividend on our capital stock.

The existence of unissued and unreserved shares of common stock and preferred stock may enable our board of directors to issue shares to persons friendly to current management or to issue preferred stock with terms that could render more difficult or discourage a third party s attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise, thereby protecting the continuity of our management. In addition, our issuance of preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation.

Delaware Law and Specified Certificate of Incorporation and By-Law Provisions

Table of Contents

Staggered Board. Our certificate of incorporation and by-laws provide for the division of our board of directors into three classes as nearly equal in size as possible with staggered three-year terms. In addition, our certificate of incorporation and by-laws provide that directors may be removed only for cause by the affirmative vote of the holders of two-thirds of the shares of our capital stock entitled to vote. Under our certificate of incorporation and by-laws, any vacancy on the board of directors, however occurring, including a vacancy resulting from an enlargement of the board, may only be filled by vote of a majority of the directors then in office. The classification of the board of directors and the limitations on the removal of directors and filling of vacancies could have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from acquiring, control of us.

Stockholder Action; Special Meeting of Stockholders. Our certificate of incorporation and by-laws provide that stockholders may take action only at a duly called annual or special meeting of stockholders and may not take action by written consent. Our certificate of incorporation and by-laws further provide that special meetings of our stockholders may be called only by a majority of the board of directors or by our chief executive officer or, if the office of chief executive officer is vacant, our president, and in no event may the stockholders call a special meeting.

Advance Notice Requirements for Stockholder Proposals and Director Nominations. Our by-laws provide that stockholders seeking to bring business before an annual meeting of stockholders, or to nominate candidates for election as directors at an annual meeting of stockholders, must meet specified procedural requirements. The by-laws also include a similar requirement for making nominations for directors. These provisions may preclude stockholders from bringing matters before an annual meeting of stockholders or from making nominations for directors at an annual or special meeting of stockholders.

Supermajority Votes Required. The General Corporation Law of Delaware provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation s certificate of incorporation or by-laws, unless a corporation s certificate of incorporation or by-laws, as the case may be, requires a greater percentage. Our certificate of incorporation and by-laws require the affirmative vote of the holders of at least 75% of the shares of our capital stock issued and outstanding and entitled to vote to amend or repeal any of the provisions described in the prior three paragraphs.

Limitation of Liability; Indemnification. Our certificate of incorporation contains provisions permitted under the General Corporation Law of Delaware relating to the liability of directors. The provisions eliminate a director s liability for monetary damages for a breach of fiduciary duty, except in circumstances involving wrongful acts, such as the breach of a director s duty of loyalty or acts or omissions that involve intentional misconduct or a knowing violation of law. This limitation of liability does not alter the liability of our directors and officers under federal securities laws. Furthermore, our certificate of incorporation contains provisions to indemnify our directors and officers to the fullest extent permitted by the General Corporation Law of Delaware. These provisions do not limit or eliminate our right or the right of any of our stockholders to seek non-monetary relief, such as an injunction or rescission in the event of a breach by a director or an officer of his or her duty of care. We believe that these provisions will assist us in attracting and retaining qualified individuals to serve as directors.

Table of Contents

Business Combinations. We are subject to the provisions of section 203 of the General Corporation Law of Delaware. Section 203 prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. A business combination includes mergers, asset sales and other transactions resulting in a financial benefit to the interested stockholder. Subject to specified exceptions, an interested stockholder is a person who, together with affiliates and associates, owns, or within three years did own, 15% or more of the corporation s voting stock.

Table of Contents

PLAN OF DISTRIBUTION

The selling shareholders may offer and sell the shares covered by this prospectus from time to time. The term selling stockholders includes donees, pledgees, transferees or other successors-in-interest selling shares received after the date of this prospectus from the selling stockholders as a gift, pledge, partnership distribution or other transfer. The selling stockholders will act independently of us in making decisions with respect to the timing, manner and size of each sale. Such sales may be made on one or more exchanges or in the over-the-counter market or otherwise, at prices and under terms then prevailing or at prices related to the then current market price or in negotiated transactions. The selling stockholders may sell their shares by one or more of, or a combination of, the following methods:

purchases by a broker-dealer as principal and resale by such broker-dealer for its own account pursuant to this prospectus;

ordinary brokerage transactions and transactions in which the broker solicits purchasers;

block trades in which the broker-dealer so engaged will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;

an over-the-counter distribution;

in privately negotiated transactions; and

in options transactions.

In addition, the selling stockholders may sell any shares that qualify for sale pursuant to Rule 144 under Rule 144 rather than pursuant to this prospectus.

In connection with distributions of the shares or otherwise, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions. In connection with such transactions, broker-dealers or other financial institutions may engage in short sales of the common stock in the course of hedging the positions they assume with selling stockholders. The selling stockholders may also sell the common stock short and redeliver the shares to close out such short positions. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus, as supplemented or amended to reflect such transaction. The selling stockholders may also pledge shares to a broker-dealer or other financial institution, and, upon a default, such broker-dealer or other financial institution, may effect sales of the pledged shares pursuant to this prospectus, as supplemented or amended to reflect such transaction.

In effecting sales, broker-dealers or agents engaged by the selling stockholders may arrange for other broker-dealers to participate. Broker-dealers or agents may receive

Table of Contents

commissions, discounts or concessions from the selling stockholders in amounts to be negotiated immediately prior to the sale.

In offering the shares covered by this prospectus, the selling stockholders and any broker-dealers who execute sales for the selling stockholders may be deemed to be underwriters within the meaning of the Securities Act in connection with such sales. Any profits realized by the selling stockholders and the compensation of any broker-dealer may be deemed to be underwriting discounts and commissions.

In order to comply with the securities laws of some states, if applicable, the shares must be sold in those states only through registered or licensed brokers or dealers. In addition, some states may restrict the selling stockholders from selling their shares unless the shares have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

We have advised the selling stockholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the selling stockholders and its affiliates. In addition, we will make copies of this prospectus available to the selling stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against some liabilities, including liabilities arising under the Securities Act.

At the time a particular offer of shares is made, if required, we will distribute a prospectus supplement that will set forth the number of shares being offered and the terms of this offering, including the name of any underwriter, dealer or agent, the purchase price paid by any underwriter, any discount, commission and other item constituting compensation, any discount, commission or concession allowed or reallowed or paid to any dealer, and the proposed selling price to the public. In addition, we may amend or supplement this prospectus from time to time to describe a specific plan of distribution.

We have agreed to indemnify the selling stockholders against some liabilities, including some liabilities under the Securities Act.

We have agreed with the selling stockholders to use our best efforts to cause the registration statement of which this prospectus constitutes a part to remain effective until the earliest of:

August 28, 2005;

such time as all of the shares covered by this prospectus and held by the selling stockholders are eligible to be sold under Rule 144 of the Securities Act without restriction by the volume limitations of Rule 144(e) of the Securities Act; and

such time as all of the shares covered by this prospectus have been sold pursuant to the registration statement of which this prospectus constitutes a part, to or through a broker or dealer or underwriter in a public securities transaction or in a

Table of Contents

transaction exempt from the registration and prospectus delivery requirements of the Securities Act such that all transfer restrictions and restrictive legends, if any, are removed upon the consummation of such sale.

LEGAL MATTERS

The validity of the common stock offered hereby will be passed upon for us by Hale and Dorr LLP, Boston, Massachusetts.

EXPERTS

Ernst & Young LLP, independent auditors, have audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2002, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements as of and for the year ended December 31, 2002 are incorporated by reference in reliance on Ernst & Young LLP s report, given on their authority as experts in accounting and auditing.

Our consolidated financial statements as of December 31, 2001 and 2000, and for each of the years then ended appearing in our Annual Report on Form 10-K have been audited by Arthur Andersen LLP, independent accountants. On August 31, 2002, Arthur Andersen LLP ceased practicing before the SEC. Therefore, Arthur Andersen LLP did not participate in the preparation of the Annual Report on Form 10-K, did not re-issue its audit report with respect to these financial statements and did not consent to the inclusion of its report in the Annual Report on Form 10-K or this prospectus. For more information, see Risk Factors Our former independent public accountant, Arthur Andersen LLP, has been found guilty of a federal obstruction of justice charge. Arthur Andersen LLP has not consented to the inclusion of its audit report with respect to our consolidated financial statements in this prospectus, and you may be unable to exercise effective remedies against it in any legal action.

WHERE YOU CAN FIND MORE INFORMATION

We file reports, proxy statements and other documents with the SEC. You may read and copy any document we file at the SEC s public reference room at Judiciary Plaza Building, 450 Fifth Street, N.W., Room 1024, Washington, D.C. 20549. You should call 1-800-SEC-0330 for more information on the public reference room. Our SEC filings are also available to you on the SEC s Internet site at http://www.sec.gov.

This prospectus is part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus regarding us and our common stock, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC s internet site.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC requires us to incorporate into this prospectus information that we file with the SEC in other documents. This means that we can disclose important information to you by referring to other documents that contain that information. The information incorporated by reference is considered to be part of this prospectus. Information contained in this prospectus and information that we file with the SEC in the future and incorporate by reference in this prospectus automatically updates and supersedes previously filed information. We incorporate by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, prior to the sale of all the shares covered by this prospectus.

Table of Contents

The following documents filed by us with the SEC are incorporated herein by reference:

(1) Our Annual Report on Form 10-K for the year ended December 31, 2002, as filed with the SEC on March 31, 2003.

(2) Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2003, as filed with the SEC on May 15, 2003.

(3) Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2003, as filed with the SEC on August 14, 2003.

(4) Our Quarterly Report on Form 10-Q for the quarter ended September 30, 2003, as filed with the SEC on November 14, 2003.

(5) Our Current Report on Form 8-K, as filed with the SEC on February 14, 2003.

(6) Our Current Report on Form 8-K, as filed with the SEC on April 8, 2003.

(7) Our Current Report on Form 8-K, as filed with the SEC on August 29, 2003.

(8) Our Current Report on Form 8-K, as filed with the SEC on September 2, 2003.
(9) Our Current Report on Form 8-K, as filed with the SEC on November 26, 2003.
(10) Our Current Report on Form 8-K, as filed with the SEC on December 5, 2003.
(11) The description of our capital stock contained in our Registration Statement on Form 8-A dated December 4, 2003.
(12) All of our filings pursuant to the Exchange Act after the date of filing the initial registration statement and prior to effectiveness of the registration statement.

You may request copies of the documents incorporated by reference, at no cost, by writing to or telephoning us at the address and telephone number below. We will provide copies of the exhibits to these filings only if they are specifically incorporated by reference in these filings.

Hybridon, Inc.
345 Vassar Street
Cambridge, Massachusetts 02139
Attention: Investor Relations
(617) 679-5500

Table of Contents

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses Of Issuance And Distribution

The following table sets forth the various expenses to be incurred in connection with the sale and distribution of the securities being registered hereby (except any underwriting discounts and commissions), all of which will be borne by Hybridon. All amounts shown are estimates except the SEC registration fee.

Filing Fee Securities and Exchange Commission	US$	2,705
Legal fees and expenses	US$	30,000
Accounting fees and expenses	US$	17,500
Printing fees	US$	20,000
Miscellaneous expenses	US$	29,795
Total expenses	US$	100,000

Item 15. Indemnification Of Directors And Officers

Article EIGHTH of the Registrant s Restated Certificate of Incorporation provides that no director of the Registrant shall be personally liable for any monetary damages for any breach of fiduciary duty as a director, except to the extent that the Delaware General Corporation Law prohibits the elimination or limitation of liability of directors for breach of fiduciary duty.

Article NINTH of the Registrant s Restated Certificate of Incorporation provides that a director or officer of the Registrant (a) shall be indemnified by the Registrant against all expenses (including attorneys fees), judgments, fines and amounts paid in settlement incurred in connection with any litigation or other legal proceeding (other than an action by or in the right of the Registrant) brought against him by virtue of his position as a director or officer of the Registrant if he acted in good faith and in a manner he reasonably believed to be in, or not opposed to, the best interests of the Registrant, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful and (b) shall be indemnified by the Registrant against all expense (including attorneys fees) and amounts paid in settlement incurred in connection with any action by or in the right of the Registrant brought against him by virtue of his position as a director or officer of the Registrant if he acted in good faith and in a manner he reasonably believed to be in, or not opposed to, the best interests of the Registrant, except that no indemnification shall be made with respect to any matter as to which such person shall have been adjudged to be liable to the Registrant, unless a court determines that, despite such adjudication but in view of all of the circumstances, he is entitled to indemnification of such expenses. Notwithstanding the foregoing, to the extent that a director or officer has been successful, on the merits or otherwise, including, without limitation, the

Table of Contents

dismissal of an action without prejudice, he is required to be indemnified by the Registrant against all expenses (including attorneys fees) incurred in connection therewith. Expenses shall be advanced to a director or officer at his request, provided that he undertakes to repay the amount advanced if it is ultimately determined that he is not entitled to indemnification for such expenses.

Indemnification is required to be made unless the Registrant determines that the applicable standard of conduct required for indemnification has not been met. In the event of a determination by the Registrant that the director or officer did not meet the applicable standard of conduct required for indemnification, or if the Registrant fails to make an indemnification payment within 60 days after such payment is claimed by such person, such person is permitted to petition the court to make an independent determination as to whether such person is entitled to indemnification. As a condition precedent to the right of indemnification, the director or officer must give the Registrant notice of the action for which indemnity is sought and the Registrant has the right to participate in such action or assume the defense thereof.

Article NINTH of the Registrant s Restated Certificate of Incorporation further provides that the indemnification provided therein is not exclusive, and provides that in the event that the Delaware General Corporation Law is amended to expand the indemnification permitted to directors or officers the Registrant must indemnify those persons to the full extent permitted by such law as so amended.

Section 145 of the Delaware General Corporation law provides that a corporation has the power to indemnify a director, officer, employee or agent of the corporation and certain other persons serving at the requires of the corporation in related capacities against amounts paid and expense incurred in connection with an action or proceeding to which he is or is threatened to be made a party by reason of such position, if such person shall have acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal proceeding, if such person had no reasonable cause to believe his conduct was unlawful; provided that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the adjudicating court determines that such indemnification is proper under the circumstances.

Hybridon has obtained directors and officers insurance for the benefit of its directors and its officers.

Item 16. Exhibits

The exhibits listed in the Exhibit Index immediately preceding the exhibits are filed as part of this Registration Statement on Form S-2.

Item 17. Undertakings

The undersigned Registrant hereby undertakes:

Table of Contents

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act;

(ii) To reflect in the prospectus any facts or events arising after the effective date of this Registration Statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in this Registration Statement. Notwithstanding the foregoing, any increase or decrease in the volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective Registration Statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in this Registration Statement or any material change to such information in this Registration Statement.

(2) That, for the purposes of determining any liability under the Securities Act each post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at the time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

provided, however, that paragraphs (1)(i) and (1)(ii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the Commission by the Registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended, that are incorporated by reference in this Registration Statement.

(2) That, for the purposes of determining any liability under the Securities Act, each post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at the time shall be deemed to be the initial *bona fide* offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

The Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant s annual report pursuant to Section 13(a) or 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan s annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in this Registration Statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the indemnification provisions described herein, or otherwise, the Registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

Table of Contents

SIGNATURE

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on December 5, 2003.

Hybridon, Inc.

By: /s/ Stephen R. Seiler

Stephen R. Seiler
Chief Executive Officer

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated:

Signature	Title	Date
*	Chairman of the Board of Directors	December 5, 2003
James B. Wyngaarden, M.D.		
/s/ Stephen R. Seiler	Chief Executive Officer and Director (Principal Executive Officer)	December 5, 2003
Stephen R. Seiler		

Table of Contents

Signature	Title	Date
/s/ Sudhir Agrawal Sudhir Agrawal, D. Phil	President, Chief Scientific Officer and Director	December 5, 2003
/s/ Robert G. Andersen Robert G. Andersen	Chief Financial Officer, Vice President of Operations, Treasurer and Secretary (Principal Financial and Accounting Officer)	December 5, 2003
* Youssef El-Zein	Director	December 5, 2003
* C. Keith Hartley	Director	December 5, 2003
* Anthony Georges Marcel, M.D., Ph.D.	Director	December 5, 2003
* William S. Reardon, C.P.A	Director	December 5, 2003
* Paul C. Zamecnik, M.D.	Director	December 5, 2003

*By: /s/ Stephen R. Seiler
Stephen R. Seiler
Attorney-in-Fact

Table of Contents

EXHIBIT INDEX

Exhibit No.	Description
3.1(17)	Restated Certificate of Incorporation of the Registrant, as amended.
3.2(2)	Amended and Restated By-laws of the Registrant.
4.1(2)	Specimen Certificate for shares of Common Stock, $.001 par value, of the Registrant.
4.2(3)	Indenture dated as of March 26, 1997 between Forum Capital Markets LLC and the Registrant.
4.3*	Rights Agreement dated December 10, 2001 by and between the Registrant and Mellon Investor Services LLC, as rights agent, as amended.
5.1*	Opinion of Hale and Dorr LLP.
10.1(2)	License Agreement dated February 21, 1990 and restated as of September 8, 1993 between the Registrant and University of Massachusetts Medical Center.
10.2(2)	Patent License Agreement effective as of October 13, 1994 between the Registrant and McGill University.
10.3(2)	License Agreement effective as of October 25, 1995 between the Registrant and the General Hospital Corporation.
10.4(2)	License Agreement dated as of October 30, 1995 between the Registrant and Yoon S. Cho-Chung.
10.5(2)	System Design and Procurement Agreement dated as of December 16, 1994 between the Registrant and Pharmacia Biotech, Inc.
10.6(2)	Registration Rights Agreement dated as of February 21, 1990 between the Registrant, the Worcester Foundation for Biomedical Research, Inc. and Paul C. Zamecnik.
10.7(2)	1990 Stock Option Plan, as amended.
10.8(2)	1995 Stock Option Plan.
10.9(2)	1995 Director Stock Plan.
10.10(2)	1995 Employee Stock Purchase Plan.
10.11(14)	Employment Agreement dated April 1, 2002 between the Registrant and Dr. Sudhir Agrawal.
10.12(15)	Consulting Agreement dated as of March 1, 2003 between the Registrant and Dr. Paul C. Zamecnik.
10.13(4)	Amendment No. 1 to License Agreement, dated as of February 21, 1990 and restated as of September 8, 1993, by and between University of Massachusetts Medical Center and the Registrant, dated as of November 26, 1996.
10.14(5)	Licensing Agreement dated March 12, 1999 by and between the Registrant and Integrated DNA Technologies, Inc.
10.15(6)	Licensing Agreement dated September 7, 1999 by and between the Registrant and Genzyme Corporation.
10.16(7)	License Agreement dated September 20, 2000 by and

Table of Contents

Exhibit No.	Description
	between the Registrant and Boston Biosystems, Inc.
10.17(7)	Assignment of Coexclusive License dated September 20, 2000 by and between the Registrant and the Public Health Service.
10.18(7)	Oligonucleotide Purification Patent License Agreement dated September 20, 2000 by and between the Registrant and Boston Biosystems, Inc.
10.19(8)	Asset Purchase Agreement dated June 29, 2000 by and between the Registrant and Boston Biosystems, Inc.
10.20(7)	Assignment of Patent Rights dated September 20, 2000 by and between the Registrant and Boston Biosystems, Inc.
10.21(7)	PNT Monomer Patent License and Option Agreement dated September 20, 2000 by and between the Registrant and Boston Biosystems, Inc.
10.22(7)	Agreement Relating to Patents Forming Part of Acquired Assets but to be Licensed Back to the Registrant for the Purposes of OriGenix Agreements dated September 20, 2000 by and between the Registrant and Boston Biosystems, Inc.
10.23(9)	Agreement dated March 28, 2001 by and between the Registrant, 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.
10.24(9)	Stock Purchase Agreement by and between Paul Capital Partners L.P. and PCP Associates and the Registrant dated March 30, 2001.
10.25(9)	Agreement and Mutual Release between the Registrant and MethylGene, Inc. dated March 21, 2001.
10.26(10)	Amended and Restated 1997 Stock Incentive Plan.
10.27(11)	Collaboration and License Agreement by and between Isis Pharmaceuticals, Inc., and the Registrant, dated May 24, 2001.
10.28(11)	Master Agreement relating to the Cross License of Certain Intellectual Property and Collaboration by and between Isis Pharmaceuticals, Inc. and the Registrant, dated May 24, 2001.
10.29(11)	Share Purchase Agreement between Hybridon, Inc. and Royal Bank Ventures, Inc., Fonds De Solidarite Des Travailleurs Du Quebec (F.T.Q.), and Ontario Teacher s Pension Plan Board, dated May 11, 2001.
10.30(12)	Employment Agreement by and between Stephen R. Seiler and the Registrant effective as of July 25, 2001.
10.31(13)	Unit Purchase Agreement by and among the Registrant and certain persons and entities listed therein, dated April 1, 1998.
10.32(13)	Offer to Exchange Hybridon Warrants and Shares of Series B Convertible Preferred Stock, dated July 29, 2001.
10.33(14)	Employment Agreement dated April 1, 2002 between the Registrant and Robert G. Andersen.
10.34(1)	Executive Stock Option Agreement for 3,150,000 Options effective as of July 25, 2001 between the Registrant and Stephen R. Seiler.
10.35(1)	Executive Stock Option Agreement for 490,000 Options effective as of July 25, 2001 between the Registrant and Stephen R. Seiler.
10.36(16)	Executive Stock Option Agreement for 1,260,000 Options effective as of July 25, 2001 between the Registrant and Dr. Sudhir Agrawal.
10.37(16)	Executive Stock Option Agreement for 550,000 Options effective as of July 25, 2001 between the Registrant and Dr. Sudhir Agrawal.
10.38(16)	Executive Stock Option Agreement for 500,000 Options effective as of July 25, 2001 between the Registrant and Dr. Sudhir Agrawal.
10.39(16)	Consulting Agreement effective as of October 1, 2002 between the Registrant and Pillar, S.A.
10.40(15)	Amendment No. 1 to the Collaboration and License Agreement, dated as of May 24, 2001, by and between Isis Pharmaceuticals, Inc. and the Registrant, dated as of August 14, 2002.

Table of Contents

Exhibit No.	Description
10.41(15)	License Agreement by and between Louisiana State University and the Registrant, dated July 1, 1998.
10.42*	Engagement Letter, dated as of April 18, 2003, by and among Hybridon, Inc., Pillar Investment Limited and PrimeCorp Finance S.A.
10.43*	Registration Rights Agreement, dated as of August 28, 2003, by and among the Registrant, the Purchasers and the Agents.
10.44*	Form of Common Stock Purchase Warrant issued to purchasers of units in a private placement on August 28, 2003 and August 29, 2003.
10.45*	Form of Common Stock Purchase Warrant issued to selected dealers and placement agents on August 28, 2003 in connection with a private placement.
23.1*	Consent of Hale and Dorr LLP, included in Exhibit 5.1.
23.2**	Consent of Ernst & Young LLP.
24.1*	Power of Attorney.

* Previously filed in this Registration Statement on Form S-2 (File No. 333-109630).
** Filed herewith.

(1) Incorporated by reference to Exhibits to the Registrant s Quarterly Report on Form 10-Q for the period ended June 30, 2002. (File No. 0-27352)

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

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

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

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

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

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

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

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

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

Table of Contents

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

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

(13) Incorporated by reference to Exhibits to the Registrant s Annual Report on Form 10-K for the year ended December 31, 2001. (File No. 0-27352)

(14) Incorporated by reference to Exhibits to the Registrant s Quarterly Report on Form 10-Q for the period ended March 31, 2002. (File No. 0-27352)

(15) Incorporated by reference to Exhibits to the Registrant s Annual Report on Form 10-K for the year ended December 31, 2002. (File No. 0-27352)

(16) Incorporated by reference to Exhibits to the Registrant s Quarterly Report on Form 10-Q for the period ended September 30, 2002. (File No. 0-27352)

(17) Incorporated by reference to Exhibits to the Registrant s Registration Statement on Form 8-A dated December 4, 2003.

Table of Contents

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.