HYBRIDON INC
Form S-2
October 10, 2003

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As filed with the Securities and Exchange Commission on October 10, 2003

Registration No. 333-

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

FORM S-2

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

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CALCULATION OF REGISTRATION FEE

Title of Shares to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price Per Share(2)	Proposed Maximum Aggregate Offering Price(2)	Amount of Registration Fee
Common Stock, $0.001 par value per share	29,852,703	$1.12	$33,435,027	$2,705

(1) Consists of (a) 20,053,022 shares of common stock and 9,799,681 shares of common stock issuable upon the exercise of common stock purchase warrants and (b) additional shares, of a currently indeterminable amount, as may from time to time become issuable by reason of stock splits, stock dividends and other similar transactions, which shares are registered hereunder pursuant to Rule 416 under the Securities Act.

(2) Estimated solely for purposes of calculating the registration fee pursuant to Rule 457(c) under the Securities Act and based upon the average of the high and low prices on the OTC Bulletin Board on October 8, 2003.

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.

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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 October 10, 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 OTC Bulletin Board under the symbol HYBN.OB. On October 9, 2003, the closing sale price of our common stock on the OTC Bulletin Board was $1.14 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.

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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.

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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 and diagnostics using synthetic DNA. Our activities are based on four technologies:

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

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

Our cancer therapy potentiation technology uses synthetic DNA to enhance the antitumor activity of some marketed anticancer drugs and increase their effectiveness.

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

We are currently conducting clinical trials of two drug candidates. We are conducting two phase 1 clinical trials of HYB2055, our lead 2nd generation IMO compound, for the treatment of solid tumor cancers, and a phase 1/2 clinical trial of GEM 231, our lead 2nd generation antisense compound, for the treatment of cancer.

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. Cyclicon and IMO are also our trademarks. All other trademarks and service marks are the property of their respective owners.

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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.
OTC Bulletin Board symbol	HYBN.OB

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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 two phase 1 clinical trials of HYB2055, our lead 2nd generation IMO compound, for the treatment of solid tumor cancers, 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,

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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

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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

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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:

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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 June 30, 2003, we had incurred operating losses of approximately $272.7 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.

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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 resources, 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

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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.

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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.

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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.

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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

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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.

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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.

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

The SEC has adopted regulations which generally define penny stock to be an equity security that has a market price of less than $5.00 per share or an exercise price of less than $5.00 per share, subject to specific exemptions. Presently, the market price of our common stock is substantially less than $5.00 per share and therefore is designated as a penny stock according to SEC rules. SEC rules require any broker or dealer selling such securities to

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obtain a written agreement to the transaction from the purchaser setting forth the identity and quantity of securities to be purchased, to determine that the securities are suitable for the purchaser and that the purchaser has sufficient knowledge and experience in financial matters to be capable of evaluating the risk of investment in such securities, to provide to the purchaser a written statement setting forth the basis upon which the broker has determined the investment to be suitable, and to obtain a written acknowledgement from the purchaser of the substance of the basis for the determination. These rules may restrict the ability of brokers or dealers to sell our common stock and may affect the ability of investors to sell their shares. In addition, since our common stock is only traded on the OTC Bulletin Board, investors may find it difficult to obtain accurate quotations of our common stock.

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 September 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.

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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.

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THE COMPANY

Overview

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

- 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;

- 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, infectious diseases and pulmonary disease;

- 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.

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HYB2055. HYB2055 is the lead clinical drug candidate in our IMO program. We are evaluating HYB2055 for the treatment of solid tumor cancers. The Investigational New Drug Application, or IND, we submitted to the FDA, covering HYB2055 became effective on March 6, 2003. In March 2003, we commenced a phase 1 clinical trial of HYB2055 in the United Kingdom in healthy volunteers. The goal of this trial is to study the safety and immunological activity of HYB2055 in healthy volunteers. We are evaluating the drug candidate over a broad range of dosing levels. We completed this trial during the third quarter of 2003 and expect to report the results of this trial in the fourth quarter of 2003.

In May 2003, we commenced a phase 1 clinical trial of HYB2055 in the United States in patients with refractory malignant tumors. This trial is being conducted at Georgetown University s Vince Lombardi Cancer Center. We plan to complete this trial in late 2003 or early 2004. Thereafter, we anticipate conducting future clinical trials of HYB2055 as a monotherapy for the treatment of cancer or in combination with other anticancer agents, including chemotherapeutics and antibodies.

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 levels of which have been shown to be increased 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. We recently 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 fourth quarter of 2003. 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.

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Product Description	Therapeutic Use	Development Status
IMO		
HYB2055 2nd generation IMO	Cancer	phase 1
HYB2055 2nd generation IMO 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.

Private Placement and Related Matters

In August 2003, we raised approximately $14.6 million in gross proceeds from a private placement to institutional and accredited investors. In the private placement, we sold 20,053,022 shares of our common stock and warrants to purchase 6,015,934 shares of our common stock. The warrants to purchase common stock have an exercise price of $1.00 per share and will expire if not exercised by August 28, 2008. The warrants may be exercised with cash or by

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using the cashless exercise feature in the warrants. We may redeem the warrants at a price of $.05 per share of common stock issuable upon exercise of the warrants if the average closing price of our common stock for a ten consecutive trading day period is greater than or equal to $2.00 per share. The net proceeds to us, excluding the proceeds of any exercise of the warrants, are expected to total approximately $13.1 million.

In connection with the private placement, we also issued warrants to selected dealers and placement agents which assisted us with the private placement. These include warrants to purchase 2,458,405 shares of our common stock at an exercise price of $0.73 per share and warrants to purchase 1,325,342 shares of our common stock at an exercise price of $1.00 per share. These warrants will expire if not exercised by August 28, 2008. These warrants may be exercised with cash or by using the cashless exercise feature in the warrants. We may not redeem these warrants.

In conjunction with the private placement, we have entered into voting agreements with the holders of 59.3% of the outstanding shares of our series A convertible preferred stock. Under these voting agreements, these holders have agreed to vote to approve amendments to our certificate of incorporation providing for:

- a reduction in the liquidation preference of the series A convertible preferred stock from $100 per share to $1 per share;
- a reduction in the dividend on the series A convertible preferred stock from 6.5% per annum to 1.0% per annum; and
- an increase in the number of shares of common stock issuable upon conversion of our series A convertible preferred stock by 25% over the number of shares of common stock that would otherwise be issuable upon conversion of our series A convertible preferred stock, for a 30-day period following the filing of the certificate of amendment to certificate of incorporation effecting the amendments to our certificate of incorporation.

In addition, in these voting agreements, these holders of series A convertible preferred stock agreed to convert a number of shares of series A convertible preferred stock held by them, representing 46.3% of the outstanding shares of our series A convertible preferred stock into common stock during the 30-day period following the filing of the certificate of amendment. We expect that additional shares of series A convertible preferred stock will be converted into common stock during the 30-day period.

We have agreed to call a special meeting of stockholders to vote on the amendments to our certificate of incorporation. The amendments require the approval of the holders of a majority of the outstanding shares of series A convertible preferred stock entitled to vote at the meeting and the approval of the holders of a majority of the outstanding shares of common stock entitled to vote at the meeting, with each class voting separately. The description of the amendments and the special meeting of stockholders in this prospectus should not be deemed, and is not intended as, a solicitation of the approval of the amendments. We will only solicit

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approval of the amendments pursuant to a proxy statement filed with the SEC and complying with the Exchange Act.

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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.

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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.

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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		