HEMISPHERX BIOPHARMA INC
Form 424B3
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HEMISPHERX BIOPHARMA, INC.

9,668,433 Shares of Common Stock

The Offering:

This prospectus relates to the resale of 9,668,433 shares of our common stock that may be offered and sold from time to time by selling shareholders and the persons to whom such selling stockholders may transfer their shares, consisting of: (1) 135% of 2,731,257 shares of common stock issuable upon the conversion, redemption or other payments relating to our Series A, B and C 7% Senior Convertible Debentures Due June 30, 2007 ("Debentures") and as payment of interest thereon and 135% of 3,615,512 shares of common stock issuable upon the exercise of related warrants ("Debenture Warrants"); (2) 948,333 shares of common stock issuable upon exercise of other warrants; and (3) 151,959 shares of common stock to be sold by certain of the selling stockholders. We are registering these shares of common stock pursuant to commitments to register the securities with the selling stockholders.

No securities are being offered or sold by us pursuant to this prospectus. The selling stockholders acquired the common stock and the warrants to purchase common stock directly from us in transactions exempt from the registration requirements of federal and state securities laws. We will not receive any of the proceeds from the sale of these shares by the selling stockholders, but we will receive proceeds from the cash exercise of warrants, if any.

Our common stock is listed on the American Stock Exchange under the symbol HEB. The reported last sale price on the American Stock Exchange on December 9, 2005 was $2.61.

The selling stockholders may sell their shares from time to time on the American Stock Exchange or otherwise, in one or more transactions at fixed prices, at prevailing market prices at the time of sale or at prices negotiated with purchasers. The selling stockholders will be responsible for any commissions or discounts due to brokers or dealers. We will pay substantially all expenses of registration of the shares covered by this prospectus.

Please see the risk factors beginning on page 5 to read about certain factors you should consider before buying shares of common stock.

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

The date of this prospectus is December 13, 2005

PROSPECTUS SUMMARY

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, utilizing a "shelf" registration statement. The selling stockholders may from time to time sell their shares of our common stock in one or more transactions. This prospectus provides you with a general description of the common stock being offered. You should read this prospectus, including all documents incorporated herein by reference, together with additional information described under the heading "Where You Can Find More Information."

The registration statement that contains this prospectus, including the exhibits to the registration statement, contains additional information about us and the securities being offered under this prospectus. You should read the registration statement and the accompanying exhibits for further information. The registration statement and exhibits can be read and are available to the public over the Internet at the SEC's website at http://www.sec.gov as described under the heading "Where You Can Find More Information."

About Hemispherx

We are a biopharmaceutical company engaged in the clinical development, manufacture, marketing and distribution of new drug entities based on natural immune system enhancing technologies for the treatment of viral and immune based chronic disorders. We were founded in the early 1970s, as a contract researcher for the National Institutes of Health. After almost 30 years, we have established a strong foundation of laboratory, pre-clinical, and clinical data with respect to the development of nucleic acids to enhance the natural antiviral defense system of the human body and to aid the development of therapeutic products for the treatment of chronic diseases. We own a U.S. Food and Drug Administration ("FDA") approved GMP (good manufacturing practice) manufacturing facility in New Jersey.

Our flagship products include Ampligen(R) and Alferon N Injection(R). Ampligen(R) is an experimental drug undergoing clinical development for the treatment of: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome ("ME/CFS" or "CFS"), and HIV. In August 2004, we completed a Phase III clinical trial ("AMP 516") treating over 230 ME/CFS patients with Ampligen(R) and are in the process of preparing a new drug application ("NDA") to be filed with the FDA. Over its developmental history, Ampligen(R) has received various designations, including Orphan Drug Product Certification (FDA), Emergency (compassionate) Cost Recovery Sales Authorization (FDA) and "promising" clinical outcome recognition based on the evaluation of certain summary clinical reports (AHRQ, Agency Health Research Quality). However to date, the FDA has determined it has yet to receive sufficient information to support the potential of Ampligen(R) to treat a serious or life threatening aspect of ME/CFS. The definition of the "seriousness of a condition", according to Guidance for Industry documents published in July, 2004 is "a matter of judgment, but generally based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one". The FDA has recently requested a "complete and audited report of the Amp 516 study to determine whether Ampligen(R) has a clinically meaningful benefit on a serious or life threatening aspect of ME/CFS in order to evaluate whether the Amp 516 study results do or do not support a "fast track designation". The FDA has also invited us to include a schedule for completion of all ME/CFS studies as well as a proposed schedule for our NDA submission. Because we believe our ME/CFS studies are complete, we intend to request a pre-NDA meeting to obtain advice on preparing and submitting our NDA. At the same time we will continue with our existing ongoing efforts to prepare a complete and audited report of

our various studies, including the well-controlled Amp 516 study. We are using our best efforts to complete the requisite reports including the hiring of new staff and various recognized expert medical/regulatory consultants, but can provide no assurance as to whether the outcome of this large data collection and filing process (approximately 750 patients, treated more than 45,000 times) will be favorable or unfavorable, specifically with respect to the FDA's perspective. Also, we can provide no guidance as to the tentative date at which the compilation and filing of such data will be complete, as significant factors are outside our control including, without limitation, the ability and willingness of the independent clinical investigators to complete the requisite reports at an acceptable regulatory standard, the ability to collect overseas generated data, and the ability of Hollister-Stier facilities to interface with our own New Brunswick staff/facilities to meet the manufacturing regulatory standards. In addition, Ampligen(R) is undergoing pre-clinical testing for possible treatment of avian influenza ("bird flu"). Alferon N Injection(R) is the registered trademark for our injectable formulation of natural alpha interferon, which is approved by the FDA for the treatment of genital warts. Alferon N Injection(R) is also in clinical development for treating Multiple Sclerosis and West Nile Virus ("WNV").

With the threat of an avian influenza pandemic rising and health officials warning that the virus could develop resistance to current flu treatments, the pursuit of a cost-effective and complementary treatment to existing antivirals and vaccines has become critical. This combination may permit the use of lower dosages and fewer injections of the antivirals and vaccines used to combat avian flu, thereby decreasing the cost of both immunization programs and treatment programs for the full-blown disease.

In antimicrobial (antibacterial) therapy, which is the best-studied clinical model, synergistic drug combinations may result in curative conditions/outcomes, often not observed when the single drugs are given alone. In the case of avian influenza where global drug supplies are presumptively in very limited supply relative to potential needs, therapeutic synergistic combinations could not only affect the disease outcome, but also the number of individuals able to access therapies.

We recently announced that true therapeutic synergy had been observed in the interaction between Ampligen(R) and Tamiflu in the inhibition of the avian influenza virus. Cell destruction was measured in vitro using different drug combinations. True therapeutic synergy is defined by mathematical equations which indicate that the therapeutic effect observed is in fact greater than the expected arithmetic sum of the two drugs working independently, and is referred to by pharmacologists as the "Chou/Talalay" equations developed at Johns Hopkins University.

In a recently reported study from a vaccine group in Japan, the incorporation of poly I: poly C (dsRNA) into a nasal administration of a killed influenza A preparation converted a poorly immunogenic response into a highly efficacious vaccine in protection of mice from lethal infection from human influenza A. Ampligen is a dsRNA which currently is undergoing testing in this animal model.

We have over 100 patents worldwide with 9 additional patents pending comprising our intellectual property. We continually review our patents rights to determine whether they have continuing value. Such review includes an analysis of the patent's ultimate revenue and profitability potential on an undiscounted cash basis to support the realizability of our respective capitalized cost. In addition, management's review addresses whether each patent continues to fit into our strategic business plans. We have a fully commercialized product (Alferon N Injection(R)), and a GMP certified manufacturing facility.

In March 2004, we completed the step-by-step acquisition from Interferon Sciences, Inc. ("ISI") of ISI's commercial assets, Alferon N Injection(R) inventory, a worldwide license for the production, manufacture, use, marketing and sale of Alferon N Injection(R). As well as, a 43,000 square foot manufacturing facility in New Jersey and the acquisition of all intellectual property related to Alferon Injection(R). Alferon N Injection(R) is a natural alpha interferon that has been approved by the FDA for commercial sale for the intra-lesional treatment of refractory or recurring external genital warts in patients 18 years of age or older. The acquisition was completed in Spring 2004 with the acquisition of all world wide commercial rights.

We outsource certain components of our research and development, manufacturing, marketing and distribution while maintaining control over the entire process through our quality assurance group and our clinical monitoring group.

Since the completion of our AMP 516 ME/CFS Phase III clinical trial for use of Ampligen(R) in the treatment of ME/CFS we have received inquiries from and, under confidentiality agreements, are having dialogue with other companies regarding marketing opportunities. No proposals or agreements have resulted from the dialogue, nor can we be assured that any proposals or agreements will result from these inquiries.

Our principal executive offices are located at One Penn Center, 1617 JFK Boulevard, Philadelphia, Pennsylvania 19103, and its telephone number is 215-988-0080.

Securities Offered

Common stock to be offered by the selling stockholders	9,668,433 Shares
Common stock outstanding prior to this offerng	54,940,700 Shares
Use of Proceeds	We will not receive any of the proceeds from the sale of the shares of common stock because they are being offered by the selling stockholders and we are not offering any shares for sale under this prospectus, but we may receive proceeds from the exercise of warrants held by certain of the selling stockholders. We will apply such proceeds, if any, toward funding our research and development efforts, capital improvements and working capital. See "Use of Proceeds."
American Stock Exchange symbol	HEB

The 9,668,433 shares of our common stock offered consist of:

- 135% of 2,731,257 shares of common stock issuable upon the conversion, redemption or other payments relating to our Series A, B and C 7% Senior Convertible Debentures Due June 30, 2007 (collectively, the "Debentures" and individually, "Series A Debentures," Series B Debentures" and "Series C Debentures") and as payment of interest thereon;

- 135% of 3,615,512 shares of common stock issuable upon the exercise of related warrants ("Debenture Warrants");

- 948,333 shares of common stock issuable upon exercise of other warrants; and

- 151,959 shares of common stock owned by certain of the selling stockholders.

RISK FACTORS

Special Note Regarding Forward-Looking Statements

Certain statements in this prospectus constitute "forwarding-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities and Exchange Act of 1995 (collectively, the "Reform Act"). Certain, but not necessarily all, of such forward-looking statements can be identified by the use of forward-looking terminology such as "believes," "expects," "may," "will," "should," or "anticipates" or the negative thereof or other variations thereon or comparable terminology, or by discussions of strategy that involve risks and uncertainties. All statements other than statements of historical fact, included in this prospectus regarding our financial position, business strategy and plans or objectives for future operations are forward-looking statements. Without limiting the broader description of forward-looking statements above, we specifically note that statements regarding potential drugs, their potential therapeutic effect, the possibility of obtaining regulatory approval, our ability to manufacture and sell any products, market acceptance or our ability to earn a profit from sales or licenses of any drugs or our ability to discover new drugs in the future are all forward-looking in nature.

Such forward-looking statements involve known and unknown risks, uncertainties and other factors, including but not limited to, the risk factors discussed below, which may cause the actual results, performance or achievements of Hemispherx and its subsidiaries to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements and other factors referenced in this prospectus. We do not undertake and specifically decline any obligation to publicly release the results of any revisions which may be made to any forward-looking statement to reflect events or circumstances after the date of such statements or to reflect the occurrence of anticipated or unanticipated events.

The following cautionary statements identify important factors that could cause our actual result to differ materially from those projected in the forward-looking statements made in this prospectus. Among the key factors that have a direct bearing on our results of operations are:

No assurance of successful product development

Ampligen(R) and related products. The development of Ampligen(R) and our other related products is subject to a number of significant risks. Ampligen(R) may be found to be ineffective or to have adverse side effects, fail to receive necessary regulatory clearances, be difficult to manufacture on a commercial scale, be uneconomical to market or be precluded from commercialization by proprietary right of third parties. Our products are in various stages of clinical and pre-clinical development and, require further clinical studies and appropriate regulatory approval processes before any such products can be marketed. We do not know when, if ever, Ampligen(R) or our other products will be generally available for commercial sale for any indication. Generally, only a small percentage of potential therapeutic products are eventually approved by the FDA for commercial sale.

The clinical development of the experimental therapeutic, Ampligen(R) for CFS was initiated approximately 16 years ago. To date federal health agencies have yet to reach a consensus regarding various aspects of ME/CFS, including parameters of "promising therapies" for ME/CFS and which aspects of ME/CFS are anticipated to be "serious or life-threatening".

Over its developmental history, Ampligen(R) has received various designations, including Orphan Drug Product Certification (FDA), Emergency (compassionate) Cost Recovery Sales Authorization (FDA) and "promising" clinical outcome recognition based on the evaluation of certain summary clinical reports (AHRQ, Agency Health Research Quality). However to date, the FDA has determined it has yet to receive sufficient information to support the potential of Ampligen(R) to treat a serious or life threatening aspect of ME/CFS. The definition of the "seriousness of a condition", according to Guidance for Industry documents published in July, 2004 is "a matter of judgment, but generally based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one". The FDA has recently requested a "complete and audited report of the Amp 516 study to determine whether Ampligen(R) has a clinically meaningful benefit on a serious or life threatening aspect of ME/CFS in order to evaluate whether the Amp 516 study results do or do not support a "fast track designation". The FDA has also invited us to include a schedule for completion of all ME/CFS studies as well as a proposed schedule for our NDA submission. Because we believe our ME/CFS studies are complete, we intend to request a pre-NDA meeting to obtain advice on preparing and submitting our NDA. At the same time we will continue with our existing ongoing efforts to prepare a complete and audited report of our various studies, including the well-controlled Amp 516 study. We are using our best efforts to complete the requisite reports including the hiring of new staff and various recognized expert medical/regulatory consultants, but can provide no assurance as to whether the outcome of this large data collection and filing process (approximately 750 patients, treated more than 45,000 times) will be favorable or unfavorable, specifically with respect to the FDA's perspective. Also, we can provide no guidance as to the tentative date at which the compilation and filing of such data will be complete, as significant factors are outside our control including, without limitation, the ability and willingness of the independent clinical investigators to complete the requisite reports at an acceptable regulatory standard, the ability to collect overseas generated data, and the ability of Hollister-Stier facilities to interface with our own New Brunswick staff/facilities to meet the manufacturing regulatory standards.

ALFERON N Injection(R). Although ALFERON N Injection(R) is approved for marketing in the United States for the intralesional treatment of refractory or recurring external genital warts in patients 18 years of age or older; to date it has not been approved for other indications. We face many of the risks discussed above, with regard to developing this product for use to treat other ailments such as multiple sclerosis and cancer.

Our drug and related technologies are investigational and subject to regulatory approval. If we are unable to obtain regulatory approval, our operations will be significantly affected.

All of our drugs and associated technologies, other than ALFERON N Injection(R), are investigational and must receive prior regulatory approval by appropriate regulatory authorities for general use and are currently legally available only through clinical trials with specified disorders. At present, ALFERON N Injection(R) is only approved for the intralesional treatment of refractory or recurring external genital warts in patients 18 years of age or older. Use of ALFERON N Injection(R) for other indications will require regulatory approval. In this regard, ISI, the company from which we obtained our rights to ALFERON N Injection(R), conducted clinical trials related to use of

ALFERON N Injection(R) for treatment of HIV and Hepatitis C. In both instances, the FDA determined that additional studies were necessary in order to fully evaluate the efficacy of ALFERON N Injection(R) in the treatment of HIV and Hepatitis C diseases. We have no immediate plans to conduct these additional studies at this time.

Our products, including Ampligen(R), are subject to extensive regulation by numerous governmental authorities in the U.S. and other countries, including, but not limited to, the FDA in the U.S., the Health Protection Branch ("HPB") of Canada, and the Agency for the Evaluation of Medicinal Products ("EMEA") in Europe. Obtaining regulatory approvals is a rigorous and lengthy process and requires the expenditure of substantial resources. In order to obtain final regulatory approval of a new drug, we must demonstrate to the satisfaction of the regulatory agency that the product is safe and effective for its intended uses and that we are capable of manufacturing the product to the applicable regulatory standards. We require regulatory approval in order to market Ampligen(R) or any other proposed product and receive product revenues or royalties. We cannot assure you that Ampligen(R) will ultimately be demonstrated to be safe or efficacious. In addition, while Ampligen(R) is authorized for use in clinical trials in the United States, we cannot assure you that additional clinical trial approvals will be authorized in the United States or in other countries, in a timely fashion or at all, or that we will complete these clinical trials. If Ampligen(R) or one of our other products does not receive regulatory approval in the U.S. or elsewhere, our operations most likely will be materially adversely affected.

Although preliminary in vitro testing indicates that Ampligen(R) enhances the effectiveness of different drug combinations on avian influenza, preliminary testing in the laboratory is not necessarily predictive of successful results in clinical testing or human treatment.

Ampligen(R) is undergoing pre-clinical testing for possible treatment of avian flu. Although preliminary in vitro testing indicates that Ampligen(R) enhances the effectiveness of different drug combinations on avian flu, preliminary testing in the laboratory is not necessarily predictive of successful results in clinical testing or human treatment. No assurance can be given that similar results will be observed in clinical trials. Use of Ampligen(R) in the treatment of avian flu requires prior regulatory approval. Only the FDA can determine whether a drug is safe, effective or promising for treating a specific application. As discussed in the prior risk factor, obtaining regulatory approvals is a rigorous and lengthy process.

In addition, Ampligen(R) is being tested on one strain of avian flu. There are a number of strains and strains mutate. No assurance can be given that a Ampligen(R) will be effective on any strains that might infect humans.

We may continue to incur substantial losses and our future profitability is uncertain.

We began operations in 1966 and last reported net profit from 1985 through 1987. Since 1987, we have incurred substantial operating losses, as we pursued our clinical trial effort and expanded our efforts in Europe. As of September 30, 2005 our accumulated deficit was approximately $147,741,000. We have not yet generated significant revenues from our products and may incur substantial and increased losses in the future. We cannot assure that we will ever achieve significant revenues from product sales or become profitable. We require, and will continue to require, the commitment of substantial resources to develop our products. We cannot assure that our product development efforts will be successfully completed or that required regulatory approvals will be obtained or that any products will be manufactured and marketed successfully, or be profitable.

We may require additional financing which may not be available.

The development of our products will require the commitment of substantial resources to conduct the time-consuming research, preclinical development, and clinical trials that are necessary to bring pharmaceutical products to market. As of September 30, 2005, we had approximately $11,632,000 in cash and cash equivalents and short-term investments. These funds should be sufficient to meet our operating cash requirements, including debt service, for the near term. However, we may need to raise additional funds through additional equity or debt financing or from other sources in order to complete the necessary clinical trials and the regulatory approval processes including the commercializing of Ampligen(R) products. There can be no assurances that we will raise adequate funds which may have a material adverse effect on our ability to develop our products. Also, we have the ability to curtail discretionary spending, including some research and development activities, if required to conserve cash.

Under the common stock purchase agreement signed with Fusion Capital on July 8, 2005, we only have the right to receive $40,000 per trading day unless our stock price equals or exceeds $2.00, in which case the daily amount may be increased under certain conditions as the price of our common stock increases (For a more detailed description of the terms of this agreement, see the agreement filed as an exhibit to our Current Report on Form 8-K filed with the SEC on July 11, 2005). Fusion Capital shall not have the right nor the obligation to purchase any shares of our common stock on any trading days that the market price of our common stock is less than $1.00. Since we initially registered 10,000,000 shares purchasable by Fusion Capital pursuant to the common stock purchase agreement, the selling price of our common stock to Fusion Capital will have to average at least $2.00 per share for us to receive the maximum proceeds of $20.0 million without registering additional shares of common stock. As of November 28, 2005, we need an average selling price of $2.04 per share for the remainder of the agreement to realize the $20,000,000 in proceeds. The closing price of our stock was $2.26 on November 28, 2005. Subject to approval by our board of directors, we have the right, but not the obligation, to issue more than 10,000,000 shares to Fusion Capital. In the event we elect to issue more than 10,000,000 shares, we will be required to file a new registration statement and have it declared effective by the Securities and Exchange Commission. In the event that we decide to issue more than 10,113,278 (19.99% of our outstanding shares of common stock as of the date of our agreement), we would first be required to seek stockholder approval in order to be in compliance with the American Stock Exchange Market rules.

The extent to which we rely on Fusion Capital as a source of funding will depend on a number of factors including, the prevailing market price of our common stock and the extent to which we are able to secure working capital from other sources. Specifically, Fusion Capital shall not have the right nor the obligation to purchase any shares of our common stock on any trading days that the market price of our common stock is less than $1.00. If obtaining sufficient financing from Fusion Capital were to prove unavailable or prohibitively dilutive and if we are unable to commercialize and sell Ampligen(R) and/or increase sales of ALFERON N Injection(R) or our other products, we will need to secure another source of funding in order to satisfy our working capital needs. Even if we are able to access the full $20.0 million under the common stock purchase agreement with Fusion Capital, we may still need additional capital to fully implement our business, operating and development plans. Should the financing we require to sustain our working capital needs be unavailable or prohibitively expensive when we require it, the consequences would materially adversely affect our business, operating results, financial condition and prospects.

We may not be profitable unless we can protect our patents and/or receive approval for additional pending patents.

We need to preserve and acquire enforceable patents covering the use of Ampligen(R) for a particular disease in order to obtain exclusive rights for the commercial sale of Ampligen(R) for such disease. We obtained all rights to ALFERON N Injection(R), and we plan to preserve and acquire enforceable patents covering its use for existing and potentially new diseases. Our success depends, in large part, on our ability to preserve and obtain patent protection for our products and to obtain and preserve our trade secrets and expertise. Certain of our know-how and technology is not patentable, particularly the procedures for the manufacture of our drug product which are carried out according to standard operating procedure manuals. We have been issued certain patents including those on the use of Ampligen(R) and Ampligen(R) in combination with certain other drugs for the treatment of HIV. We also have been issued patents on the use of Ampligen(R) in combination with certain other drugs for the treatment of chronic Hepatitis B virus, chronic Hepatitis C virus, and a patent which affords protection on the use of Ampligen(R) in patients with Chronic Fatigue Syndrome. We have not yet been issued any patents in the United States for the use of Ampligen(R) as a sole treatment for any of the cancers, which we have sought to target. With regard to ALFERON N Injection(R), we have acquired from ISI its patents for natural alpha interferon produced from human peripheral blood leukocytes and its production process. We cannot assure that our competitors will not seek and obtain patents regarding the use of similar products in combination with various other agents, for a particular target indication prior to our doing such. If we cannot protect our patents covering the use of our products for a particular disease, or obtain additional patents, we may not be able to successfully market our products.

The patent position of biotechnology and pharmaceutical firms is highly uncertain and involves complex legal and factual questions.

To date, no consistent policy has emerged regarding the breadth of protection afforded by pharmaceutical and biotechnology patents. There can be no assurance that new patent applications relating to our products or technology will result in patents being issued or that, if issued, such patents will afford meaningful protection against competitors with similar technology. It is generally anticipated that there may be significant litigation in the industry regarding patent and intellectual property rights. Such litigation could require substantial resources from us and we may not have the financial resources necessary to enforce the patent rights that we hold. No assurance can be made that our patents will provide competitive advantages for our products or will not be successfully challenged by competitors. No assurance can be given that patents do not exist or could not be filed which would have a materially adverse effect on our ability to develop or market our products or to obtain or maintain any competitive position that we may achieve with respect to our products. Our patents also may not prevent others from developing competitive products using related technology.

There can be no assurance that we will be able to obtain necessary licenses if we cannot enforce patent rights we may hold. In addition, the failure of third parties from whom we currently license certain proprietary information or from whom we may be required to obtain such licenses in the future, to adequately enforce their rights to such proprietary information, could adversely affect the value of such licenses to us.

If we cannot enforce the patent rights we currently hold we may be required to obtain licenses from others to develop, manufacture or market our products. There can be no assurance that we would be able to obtain any such licenses on commercially reasonable terms, if at all. We currently license certain proprietary information from third parties, some of which may have been developed with government grants under circumstances where the government maintained certain rights with respect to the proprietary information developed. No assurances can be given that such third parties will adequately enforce any

rights they may have or that the rights, if any, retained by the government will not adversely affect the value of our license.

There is no guarantee that our trade secrets will not be disclosed or known by our competitors.

To protect our rights, we require certain employees and consultants to enter into confidentiality agreements with us. There can be no assurance that these agreements will not be breached, that we would have adequate and enforceable remedies for any breach, or that any trade secrets of ours will not otherwise become known or be independently developed by competitors.

If our distributors do not market our products successfully, we may not generate significant revenues or become profitable.

We have limited marketing and sales capability. We are dependent upon existing and, possibly future, marketing agreements and third party distribution agreements for our products in order to generate significant revenues and become profitable. As a result, any revenues received by us will be dependent on the efforts of third parties, and there is no assurance that these efforts will be successful. Our agreement with Accredo offers the potential to provide some marketing and distribution capacity in the United States while agreements with Bioclones (Proprietary), Ltd ("Bioclones"), Biovail Corporation and Laboratorios Del Dr. Esteve S.A. may provide a sales force in South America, Africa, United Kingdom, Australia and New Zealand, Canada, Spain and Portugal. On December 27, 2004, we initiated a lawsuit in Federal Court identifying a conspiratorial group seeking to illegally manipulate our stock for purposes of bringing about the hostile takeover of Hemispherx. This conspiratorial group includes Bioclones and the potential legal action may adversely effect our agreement with Bioclones and the potential for marketing and distribution capacity in South America, Africa, United Kingdom, Australia and New Zealand.

We cannot assure that our domestic or foreign marketing partners will be able to successfully distribute our products, or that we will be able to establish future marketing or third party distribution agreements on terms acceptable to us, or that the cost of establishing these arrangements will not exceed any product revenues. The failure to continue these arrangements or to achieve other such arrangements on satisfactory terms could have a materially adverse effect on us.

There are no long-term agreements with suppliers of required materials. If we are unable to obtain the required raw materials, we may be required to scale back our operations or stop manufacturing ALFERON N Injection(R) and/or Ampligen(R).

A number of essential materials are used in the production of ALFERON N Injection(R), including human white blood cells. We do not have long-term agreements for the supply of any of such materials. There can be no assurance we can enter into long-term supply agreements covering essential materials on commercially reasonable terms, if at all.

At present, we do not have any agreements with third parties for the supply of any polymers for use in manufacturing Ampligen(R). We are establishing relevant manufacturing operations within our New Brunswick, New Jersey facility for the production of Ampligen(R) raw materials in order to obtain polymers on a more consistent manufacturing basis. The establishment of an Ampligen(R) raw materials production line within our own facilities, while having obvious advantages with respect to regulatory compliance (other parts of the 43,000 sq. ft. wholly owned facility are already in compliance for Alferon N Injection(R) manufacture), may delay certain steps in the commercialization process, specifically a targeted NDA filing.

If we are unable to obtain or manufacture the required raw materials, we may be required to scale back our operations or stop manufacturing. The costs and availability of products and materials we need for the production of Ampligen(R) and the commercial production of ALFERON N Injection(R) and other products which we may commercially produce are subject to fluctuation depending on a variety of factors beyond our control, including competitive factors, changes in technology, and FDA and other governmental regulations and there can be no assurance that we will be able to obtain such products and materials on terms acceptable to us or at all.

There is no assurance that successful manufacture of a drug on a limited scale basis for investigational use will lead to a successful transition to commercial, large-scale production.

Small changes in methods of manufacturing, including commercial scale-up, may affect the chemical structure of Ampligen(R) and other RNA drugs, as well as their safety and efficacy, and can, among other things, require new clinical studies and affect orphan drug status, particularly, market exclusivity rights, if any, under the Orphan Drug Act. The transition from limited production of pre-clinical and clinical research quantities to production of commercial quantities of our products will involve distinct management and technical challenges and will require additional management and technical personnel and capital to the extent such manufacturing is not handled by third parties. There can be no assurance that our manufacturing will be successful or that any given product will be determined to be safe and effective, capable of being manufactured economically in commercial quantities or successfully marketed.

We have limited manufacturing experience and capacity.

Ampligen(R) has been only produced in limited quantities for use in our clinical trials and we are dependent upon third party suppliers for key components of our products and for substantially all of the production process. The failure to continue these arrangements or to achieve other such arrangements on satisfactory terms could have a material adverse affect on us. Also, to be successful, our products must be manufactured in commercial quantities in compliance with regulatory requirements and at acceptable costs. To the extent we are involved in the production process, our current facilities are not adequate for the production of our proposed products for large-scale commercialization, and we currently do not have adequate personnel to conduct commercial-scale manufacturing. We intend to utilize third-party facilities if and when the need arises or, if we are unable to do so, to build or acquire commercial-scale manufacturing facilities. We will need to comply with regulatory requirements for such facilities, including those of the FDA pertaining to current Good Manufacturing Practices ("cGMP") regulations. There can be no assurance that such facilities can be used, built, or acquired on commercially acceptable terms, or that such facilities, if used, built, or acquired, will be adequate for our long-term needs.

In connection with settling various manufacturing infractions previously noted by the FDA, Schering-Plough ("Schering") entered into a "Consent Decree" with the FDA whereby, among other things, it agreed to discontinue various contract (third party) manufacturing activities at various facilities including its San Juan, Puerto Rico, plant. Ampligen(R) (which was not involved in any of the cited infractions) was produced at this Puerto Rico plant from year 2000-2004. Operating under instructions from the Consent Decree, Schering has advised us that it would no longer manufacture Ampligen(R) in this facility beyond 2004 and would assist us in an orderly transfer of said activities to other non Schering facilities.

On September 9, 2005, we signed a Letter of Intent ("LOI") with Hollister-Stier Laboratories LLC of Spokane, Washington ("Hollister-Stier"), for

the contract manufacturing of Ampligen(R). In November 2005, we paid $100,000 upon executing the LOI in order to initiate the manufacturing project. The LOI shall remain in full force and effect for 90 calendar days or until a definitive agreement is reached. The achievement of the initial objectives described in the LOI, in combination with our polymer production facility under construction in New Brunswick, N.J., may enable us to manufacture the raw materials for approximately 10,000 doses of Ampligen(R) per week. Based on the LOI, Hollister-Stier has agreed to formulate and bottle Ampligen(R) using raw materials received from us. We have an executed confidentiality agreement in place and; therefore, have commenced the preliminary transfer of our manufacturing technology to Hollister-Stier. Our decision to transfer relevant manufacturing technology absent of an executed agreement, was done in part to expedite the eventual manufacture of Ampligen(R) by Hollister-Stier. On November 30, 2005 we completed our negotiations and executed a Supply Agreement with Hollister-Stier for the production of Ampligen(R) for a five year term. We have agreed to pay a one time start up fee and will provide funds to acquire certain equipment dedicated to Ampligen production.

We have identified two other capable cGMP facilities in the US for the manufacture of Ampligen(R) and obtained proposals from both. If either of these two facilities are acceptable, we would be able to maintain a minimum of two independent production sites. We are in the process of reviewing these other proposals.

The purified drug concentrate utilized in the formulation of ALFERON N Injection(R) is manufactured in our New Brunswick, New Jersey facility and ALFERON N Injection(R) was formulated and packaged at a production facility formerly owned and operated by Abbott Laboratories located in Kansas. Abbott Laboratories has sold the facility to Hospira. Hospira recently completed the production of 12,000 vials. Hospira is ceasing the labeling and packaging of Alferon N Injection(R) as they are seeking larger production runs for cost efficiency purposes. We have identified five new potential contract manufacturers, obtained proposals from all five, and have audited two, concerning the future formulation and packaging of Alferon N Injection(R). If we are unable to secure a new facility within a reasonable period of time to formulate and package ALFERON N Injection(R) at an acceptable cost, our ability to sell ALFERON N Injection(R) and to generate profits therefrom will be adversely affected.

We may not be profitable unless we can produce Ampligen(R) or other products in commercial quantities at costs acceptable to us.

We have never produced Ampligen(R) or any other products in large commercial quantities. We must manufacture our products in compliance with regulatory requirements in large commercial quantities and at acceptable costs in order for us to be profitable. We intend to utilize third-party manufacturers and/or facilities if and when the need arises or, if we are unable to do so, to build or acquire commercial-scale manufacturing facilities. If we cannot manufacture commercial quantities of Ampligen(R) or enter into third party agreements for its manufacture at costs acceptable to us, our operations will be significantly affected. Also, each production lot of Alferon N Injection(R) is subject to FDA review and approval prior to releasing the lots to be sold. This review and approval process could take considerable time, which would delay our having product in inventory to sell.

Rapid technological change may render our products obsolete or non-competitive.

The pharmaceutical and biotechnology industries are subject to rapid and substantial technological change. Technological competition from pharmaceutical and biotechnology companies, universities, governmental entities and others diversifying into the field is intense and is expected to increase. Most of these entities have significantly greater research and development

capabilities than us, as well as substantial marketing, financial and managerial resources, and represent significant competition for us. There can be no assurance that developments by others will not render our products or technologies obsolete or noncompetitive or that we will be able to keep pace with technological developments.

Our products may be subject to substantial competition.

Ampligen(R). Competitors may be developing technologies that are, or in the future may be, the basis for competitive products. Some of these potential products may have an entirely different approach or means of accomplishing similar therapeutic effects to products being developed by us. These competing products may be more effective and less costly than our products. In addition, conventional drug therapy, surgery and other more familiar treatments may offer competition to our products. Furthermore, many of our competitors have significantly greater experience than us in pre-clinical testing and human clinical trials of pharmaceutical products and in obtaining FDA, HPB and other regulatory approvals of products. Accordingly, our competitors may succeed in obtaining FDA, HPB or other regulatory product approvals more rapidly than us. There are no drugs approved for commercial sale with respect to treating ME/CFS in the United States. The dominant competitors with drugs to treat HIV diseases include Gilead Pharmaceutical, Pfizer, Bristol-Myers, Abbott Labs, Glaxo Smithkline, Merck and Schering-Plough Corp. These potential competitors are among the largest pharmaceutical companies in the world, are well known to the public and the medical community, and have substantially greater financial resources, product development, and manufacturing and marketing capabilities than we have. Although we believe our principal advantage is the unique mechanism of action of Ampligen(R) on the immune system, we cannot assure that we will be able to compete.

ALFERON N Injection(R). Many potential competitors are among the largest pharmaceutical companies in the world, are well known to the public and the medical community, and have substantially greater financial resources, product development, and manufacturing and marketing capabilities than we have. ALFERON N Injection(R) currently competes with Schering's injectable recombinant alpha interferon product (INTRON(R) A) for the treatment of genital warts. 3M Pharmaceuticals also received FDA approval for its immune-response modifier, Aldara(R), a self-administered topical cream, for the treatment of external genital and perianal warts. ALFERON N Injection(R) also competes with surgical, chemical, and other methods of treating genital warts. We cannot assess the impact products developed by our competitors, or advances in other methods of the treatment of genital warts, will have on the commercial viability of ALFERON N Injection(R). If and when we obtain additional approvals of uses of this product, we expect to compete primarily on the basis of product performance. Our potential competitors have developed or may develop products (containing either alpha or beta interferon or other therapeutic compounds) or other treatment modalities for those uses. In the United States, three recombinant forms of beta interferon have been approved for the treatment of relapsing-remitting multiple sclerosis. There can be no assurance that, if we are able to obtain regulatory approval of ALFERON N Injection(R) for the treatment of new indications, we will be able to achieve any significant penetration into those markets. In addition, because certain competitive products are not dependent on a source of human blood cells, such products may be able to be produced in greater volume and at a lower cost than ALFERON N Injection(R). Currently, our wholesale price on a per unit basis of ALFERON N Injection(R) is higher than that of the competitive recombinant alpha and beta interferon products.

General. Other companies may succeed in developing products earlier than we do, obtaining approvals for such products from the FDA more rapidly than we do, or developing products that are more effective than those we may develop. While we will attempt to expand our technological capabilities in order to

remain competitive, there can be no assurance that research and development by others or other medical advances will not render our technology or products obsolete or non-competitive or result in treatments or cures superior to any therapy we develop.

Possible side effects from the use of Ampligen(R) or ALFERON N Injection(R) could adversely affect potential revenues and physician/patient acceptability of our product.

Ampligen(R). We believe that Ampligen(R) has been generally well tolerated with a low incidence of clinical toxicity, particularly given the severely debilitating or life threatening diseases that have been treated. A mild flushing reaction has been observed in approximately 15% of patients treated in our various studies. This reaction is occasionally accompanied by a rapid heart beat, a tightness of the chest, urticaria (swelling of the skin), anxiety, shortness of breath, subjective reports of "feeling hot," sweating and nausea. The reaction is usually infusion-rate related and can generally be controlled by slowing the infusion rate. Other adverse side effects include liver enzyme level elevations, diarrhea, itching, asthma, low blood pressure, photophobia, rash, transient visual disturbances, slow or irregular heart rate, decreases in platelets and white blood cell counts, anemia, dizziness, confusion, elevation of kidney function tests, occasional temporary hair loss and various flu-like symptoms, including fever, chills, fatigue, muscular aches, joint pains, headaches, nausea and vomiting. These flu-like side effects typically subside within several months. One or more of the potential side effects might deter usage of Ampligen(R) in certain clinical situations and therefore, could adversely affect potential revenues and physician/patient acceptability of our product.

ALFERON N Injection(R). At present, ALFERON N Injection(R) is only approved for the intralesional (within the lesion) treatment of refractory or recurring external genital warts in adults. In clinical trials conducted for the treatment of genital warts with ALFERON N Injection(R), patients did not experience serious side effects; however, there can be no assurance that unexpected or unacceptable side effects will not be found in the future for this use or other potential uses of ALFERON N Injection(R) which could threaten or limit such product's usefulness.

We may be subject to product liability claims from the use of Ampligen(R), Alferon N Injection(R), or other of our products which could negatively affect our future operations.

We face an inherent business risk of exposure to product liability claims in the event that the use of Ampligen(R) or other of our products results in adverse effects. This liability might result from claims made directly by patients, hospitals, clinics or other consumers, or by pharmaceutical companies or others manufacturing these products on our behalf. Our future operations may be negatively affected from the litigation costs, settlement expenses and lost product sales inherent to these claims. While we will continue to attempt to take appropriate precautions, we cannot assure that we will avoid significant product liability exposure. Although we currently maintain product liability insurance coverage, there can be no assurance that this insurance will provide adequate coverage against Ampligen(R) and/or Alferon N Injection(R) product liability claims. A successful product liability claim against us in excess of Ampligen(R)'s $1,000,000 in insurance coverage; $3,000,000 in aggregate, or in excess of Alferon N Injection(R)'s $5,000,000 in insurance coverage; $5,000,000 in aggregate; or for which coverage is not provided could have a negative effect on our business and financial condition.

The loss of Dr. William A. Carter's services could hurt our chances for success.

Our success is dependent on the continued efforts of Dr. William A.

Carter because of his position as a pioneer in the field of nucleic acid drugs, his being the co-inventor of Ampligen(R), and his knowledge of our overall activities, including patents and clinical trials. The loss of Dr. Carter's services could have a material adverse effect on our operations and chances for success. We have secured key man life insurance in the amount of $2,000,000 on the life of Dr. Carter and we have an employment agreement with Dr. Carter that, as amended, runs until May 8, 2008. However, Dr. Carter has the right to terminate his employment upon not less than 30 days prior written notice. The loss of Dr. Carter or other personnel, or the failure to recruit additional personnel as needed could have a materially adverse effect on our ability to achieve our objectives.

Uncertainty of health care reimbursement for our products.

Our ability to successfully commercialize our products will depend, in part, on the extent to which reimbursement for the cost of such products and related treatment will be available from government health administration authorities, private health coverage insurers and other organizations. Significant uncertainty exists as to the reimbursement status of newly approved health care products, and from time to time legislation is proposed, which, if adopted, could further restrict the prices charged by and/or amounts reimbursable to manufacturers of pharmaceutical products. We cannot predict what, if any, legislation will ultimately be adopted or the impact of such legislation on us. There can be no assurance that third party insurance companies will allow us to charge and receive payments for products sufficient to realize an appropriate return on our investment in product development.

There are risks of liabilities associated with handling and disposing of hazardous materials.

Our business involves the controlled use of hazardous materials, carcinogenic chemicals, flammable solvents and various radioactive compounds. Although we believe that our safety procedures for handling and disposing of such materials comply in all material respects with the standards prescribed by applicable regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of such an accident or the failure to comply with applicable regulations, we could be held liable for any damages that result, and any such liability could be significant. We do not maintain insurance coverage against such liabilities.

Risks Associated With and Investment in Our Common Stock

The market price of our stock may be adversely affected by market volatility.

The market price of our common stock has been and is likely to be volatile. In addition to general economic, political and market conditions, the price and trading volume of our stock could fluctuate widely in response to many factors, including:

- announcements of the results of clinical trials by us or our competitors;
- adverse reactions to products;
- governmental approvals, delays in expected governmental approvals or withdrawals of any prior governmental approvals or public or regulatory agency concerns regarding the safety or effectiveness of our products;
- changes in U.S. or foreign regulatory policy during the period of product development;

- developments in patent or other proprietary rights, including any third party challenges of our intellectual property rights;
- announcements of technological innovations by us or our competitors;
- announcements of new products or new contracts by us or our competitors;
- actual or anticipated variations in our operating results due to the level of development expenses and other factors;
- changes in financial estimates by securities analysts and whether our earnings meet or exceed the estimates;
- conditions and trends in the pharmaceutical and other industries; new accounting standards; and
- the occurrence of any of the risks described in these "Risk Factors."

Our common stock is listed for quotation on the American Stock Exchange. For the 12-month period ended September 30, 2005, the price of our common stock has ranged from $1.25 to $2.50 per share. We expect the price of our common stock to remain volatile. The average daily trading volume of our common stock varies significantly. Our relatively low average volume and low average number of transactions per day may affect the ability of our stockholders to sell their shares in the public market at prevailing prices and a more active market may never develop.

In the past, following periods of volatility in the market price of the securities of companies in our industry, securities class action litigation has often been instituted against companies in our industry. If we face securities litigation in the future, even if without merit or unsuccessful, it would result in substantial costs and a diversion of management attention and resources, which would negatively impact our business.

Our stock price may be adversely affected if a significant amount of shares, primarily those registered herein and in prior registration statements, are sold in the public market.

As of November 28, 2005, approximately 1,132,457 shares of our common stock, constituted "restricted securities" as defined in Rule 144 under the Securities Act of 1933, 402,798 of which are registered for public sale. Also, we have registered 21,106,907 shares issuable (i) to Fusion Capital pursuant to the common stock purchase agreement with Fusion Capital; (11) upon conversion of approximately 135% of Debentures that we issued in 2003 and 2004; (iii) as payment of 135% of the interest on all of the Debentures; (iv) upon exercise of 135% of the certain Warrants; and (v) upon exercise of certain other warrants. In addition we will be registering an aggregate of 1,224,983 shares representing 135% of shares issuable upon exercise of the October 2009 Warrants and as additional interest shares (resulting from the amendment to the Debentures. Registration of the shares permits the sale of the shares in the open market or in privately negotiated transactions without compliance with the requirements of Rule 144. To the extent the exercise price of the warrants is less than the market price of the common stock, the holders of the warrants are likely to exercise them and sell the underlying shares of common stock and to the extent

that the conversion price and exercise price of these securities are adjusted pursuant to anti-dilution protection, the securities could be exercisable or convertible for even more shares of common stock. We also may issue shares to be used to meet our capital requirements or use shares to compensate employees, consultants and/or directors. We are unable to estimate the amount, timing or nature of future sales of outstanding common stock. Sales of substantial amounts of our common stock in the public market could cause the market price for our common stock to decrease. Furthermore, a decline in the price of our common stock would likely impede our ability to raise capital through the issuance of additional shares of common stock or other equity securities.

The sale of our common stock to Fusion Capital may cause dilution and the sale of the shares of common stock acquired by Fusion Capital and other shares by Selling Stockholders listed in this prospectus and another prospectus could cause the price of our common stock to decline.

The sale by Fusion Capital and other selling stockholders listed in this prospectus and another prospectus of our common stock will increase the number of our publicly traded shares, which could depress the market price of our common stock. Moreover, the mere prospect of resales by Fusion Capital and other selling stockholders could depress the market price for our common stock. The issuance of shares to Fusion Capital under the common stock purchase agreement dated July 8, 2005, will dilute the equity interest of existing stockholders and could have an adverse effect on the market price of our common stock.

The purchase price for the common stock to be sold to Fusion Capital pursuant to the common stock purchase agreement will fluctuate based on the price of our common stock. All shares sold to Fusion Capital are freely tradable. Fusion Capital may sell none, some or all of the shares of common stock purchased from us at any time. We expect that the shares will be sold over a period of in excess of 25 months from August 3, 2005. Depending upon market liquidity at the time, a sale of shares under this offering at any given time could cause the trading price of our common stock to decline. The sale of a substantial number of shares of our common stock to Fusion Capital pursuant to the purchase agreement, or anticipation of such sales, could make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise wish to effect sales.

Provisions of our Certificate of Incorporation and Delaware law could defer a change of our management which could discourage or delay offers to acquire us.

Provisions of our Certificate of Incorporation and Delaware law may make it more difficult for someone to acquire control of us or for our stockholders to remove existing management, and might discourage a third party from offering to acquire us, even if a change in control or in management would be beneficial to our stockholders. For example, our Certificate of Incorporation allows us to issue shares of preferred stock without any vote or further action by our stockholders. Our Board of Directors has the authority to fix and determine the relative rights and preferences of preferred stock. Our Board of Directors also has the authority to issue preferred stock without further stockholder approval. As a result, our Board of Directors could authorize the issuance of a series of preferred stock that would grant to holders the preferred right to our assets upon liquidation, the right to receive dividend payments before dividends are distributed to the holders of common stock and the right to the redemption of the shares, together with a premium, prior to the redemption of our common stock. In this regard, in November 2002, we adopted a stockholder rights plan and, under the Plan, our Board of Directors declared a dividend distribution of one Right for each outstanding share of Common Stock to stockholders of record at the close of business on November 29, 2002. Each Right initially entitles holders to buy one unit of preferred stock for $30.00. The Rights generally are not transferable apart from the common stock and will not

be exercisable unless and until a person or group acquires or commences a tender or exchange offer to acquire, beneficial ownership of 15% or more of our common stock. However, for Dr. Carter, our chief executive officer, who already beneficially owns 10.3% of our common stock, the Plan's threshold will be 20%, instead of 15%. The Rights will expire on November 19, 2012, and may be redeemed prior thereto at $.01 per Right under certain circumstances.

Because the risk factors referred to above could cause actual results or outcomes to differ materially from those expressed in any forward-looking statements made by us, you should not place undue reliance on any such forward-looking statements. Further, any forward-looking statement speaks only as of the date on which it is made and we undertake no obligation to update any forward-looking statement or statements to reflect events or circumstances after the date on which such statement is made or reflect the occurrence of unanticipated events. New factors emerge from time to time, and it is not possible for us to predict which will arise. In addition, we cannot assess the impact of each factor on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. Our research in clinical efforts may continue for the next several years and we may continue to incur losses due to clinical costs incurred in the development of Ampligen(R) for commercial application. Possible losses may fluctuate from quarter to quarter as a result of differences in the timing of significant expenses incurred and receipt of licensing fees and/or cost recovery treatment revenues in Europe, Canada and in the United States.

SELLING STOCKHOLDERS

We have registered all 9,668,433 shares of common stock covered by this prospectus on behalf of the selling stockholders named in the table below. We issued the shares, the Debentures convertible into shares, and the warrants exercisable for shares to the selling stockholders in private transactions. We have registered the shares to permit the selling stockholders and their respective transferees, assignees or other successors-in-interest that receive their shares from a selling stockholder to resell the shares, from time to time, when they deem appropriate.

The table below identifies the selling stockholders who will be offering shares and other information regarding the beneficial ownership of the common stock held by each of the selling stockholders. For the Debenture holders (the first two stockholders listed below), the second column lists the number of shares of common stock beneficially owned by each selling stockholder as of November 28, 2005, based on each selling stockholder's ownership of shares of common stock, Debentures and Debenture Warrants, and assumes the conversion of all the Debentures, the payment of all interest in stock and the exercise of all Debenture Warrants. Because the conversion price of the Debentures and the exercise price of the warrants are subject to adjustment for anti-dilution protection, the interest on the Debentures may be paid in cash or common stock, and the value attributed to any shares issued to the investors as interest (the "Interest Shares") depends on the average closing price of the common stock during the five consecutive business days ending on the third business day immediately preceding the applicable interest payment date, the numbers listed in the second column may change. For the other selling stockholders, the second column lists the number of shares of common stock beneficially owned by the selling stockholder as of the above date, based on each selling stockholder's ownership of shares of common stock, and, except as set forth in the relevant footnotes, does not assume the conversion of any of the Debentures, the exercise

of any warrants or the payment of any interest on the Debentures in the form of common stock rather than cash.

The third column lists each selling stockholder's portion, based on agreements with us, of the 9,668,433 shares of common stock being offered by this prospectus. With regard to the first two selling stockholders, the number of shares being offered by this prospectus was determined in accordance with the terms of the registration rights agreements with them, in which we agreed to register the resale of 135% of (w) the number of shares of common stock issuable upon conversion of the Debentures, plus (x) the number of shares of common stock issuable upon exercise of the Debenture Warrants, plus (y) an estimate of the number of Interest Shares that may be issued to the selling stockholders as interest payments on the Debentures and assuming interest is paid exclusively in Interest Shares over the full term of the Debentures, rather than in cash. As we stated above, the number of shares that will actually be issued may be more or less than the 9,668,433 shares being offered by this prospectus.

Under the terms of the Debentures and the Debenture Warrants, no selling stockholder who owns any of these securities may convert any of their Debentures or exercise any of the foregoing Warrants to the extent that the conversion or exercise would cause the selling stockholder, together with its affiliates, to beneficially own more than 4.99% of the shares of our then outstanding common stock following such conversion or exercise. For purposes of making this determination, shares of common stock issuable upon conversion of those Debentures which have not been converted and upon exercise of the Warrants which have not been exercised are excluded. The number of shares in the second and third columns does not reflect this limitation.

Any selling stockholder may sell all, some or none of its respective shares in this offering. See "How The Shares May Be Distributed" below.

Effective October 6, 2005, we amended our outstanding debentures due to mature on October 31, 2005 and January 31, 2006 to extend the maturity dates to June 30, 2007 and increase the interest rates from 6% per annum to 7% per annum. These debentures, as so amended, are referred to as the Series A, B and C 7% Senior Secured Convertible Debenture due June 30, 2007. In addition we issue to the debenture holders common stock purchase warrants to purchase, in the aggregate, 225,000 shares of our common stock for a period of four years at an exercise price of $2.50 per share. Pursuant to our agreement with the holders, we have registered on their behalf 135% of the shares issuable upon (i) payment of additional interest on the debentures resulting from the above mentioned revisions to the debentures and (ii) exercise of the warrants. These shares are included in the table below.

Selling Stockholder	Common Stock Owned Prior To Offering	No. of Shares Being Offered
Portside Growth & Opportunity Fund	3,207,477 (1)	3,940,
Leonardo L.P.	3,427,756 (2)	4,
Cardinal Securities LLC	156,666 (3)	
Windward Capital Advisors, LLC	186,667 (4)	

HefCap Holdings, LLC	186,667 (5)	
Baxter Capital Advisors, Inc.	30,000 (6)	
CEOCast, Inc.	20,000 (7)	
Christopher Chipman	30,000 (8)	
Fried Epstein & Rettig LLP	5,000 (9)	
Business Asia Consultants, Inc.	17,959 (10)	
JMBL, LTD	75,000 (11)	
The Investor Relations Group	84,000 (12)	
William Mason	131,066 (13)	41,
W. Barry McDonald	131,067 (13)	41,
Wayne Pambianchi	131,067 (13)	41,
Gordon Ramseier	131,066 (13)	41,
Daniel Tripodi	131,067 (13)	41,
Michael Burrows	690,000 (14)	

(1) Includes (i) up to 1,116,654 shares of common stock issuable upon conversion of the Debentures, (ii) up to 107,104 shares of common stock issuable upon exercise of the Debenture Warrants; (iii) up to 650,000 shares of common stock issuable upon exercise of Warrants that expire in May 2009, (iv) up to 650,000 shares of common stock issuable upon exercise of Warrants that expire in June 2009 and (v) up to 395,257 shares of common stock issuable upon exercise of Warrants that expire in July 2009. Common Stock owned prior to the offering also includes an additional 288,462 shares issuable upon exercise of warrants issued in the August 5, 2004 Private Placement, which shares have been registered in another registration statements and are eligible for resale pursuant to a separate prospectus. Ramius Capital Group, LLC ("Ramius Capital") is the investment adviser of Portside Growth & Opportunity Fund ("Portside") and consequently has voting control and investment discretion over securities held by Portside. Ramius Capital disclaims beneficial ownership of the shares held by Portside. Peter A. Cohen, Morgan B. Stark, Thomas W. Strauss and Jeffrey M. Solomon are the sole managing members of C4S& Co., LLC, the sole managing member of Ramius Capital. As a result, Messrs. Cohen, Stark, Strauss and Solomon may be

considered beneficial owners of any shares deemed to be beneficially owned by Ramius Capital. Messrs. Cohen, Stark, Strauss and Solomon disclaim beneficial ownership of these shares.

(2) Represents (i) up to 1,614,603 shares of common stock issuable upon conversion of the Debentures, (ii) up to 117,896 shares of common stock issuable upon exercise of the Debenture Warrants; (iii) up to 1,300,000 shares of common stock issuable upon exercise of Warrants that expire in May 2009, and (iv) up to 395,257 shares of common stock issuable upon exercise of Warrants that expire in July 2009. Angelo, Gordon & Co., L.P. ("Angelo, Gordon") is the sole director of the general partner of Leonardo, L.P. ("Leonardo") and consequently has voting control and investment discretion over securities held by Leonardo. Angelo, Gordon disclaims beneficial ownership of the shares held by Leonardo. Mr. John M. Angelo, the Chief Executive Officer of Angelo, Gordon, and Mr. Michael L. Gordon, the Chief Operating Officer of Angelo, Gordon, are the sole general partners of AG Partners, L.P., the sole general partner of Angelo, Gordon. As a result, Messrs. Angelo and Gordon may be considered beneficial owners of any shares deemed to be beneficially owned by Angelo, Gordon. Messrs. Angelo and Gordon disclaim beneficial ownership of these shares.

(3) Represents up to 156,666 shares of common stock issuable upon exercise of warrants owned by Cardinal of which (i) 33,750 are exercisable at a price of $2.57 per share, (ii) 66,666 are exercisable at a price of $2.50 per share, (iii) 26,250 are exercisable at a price if $2.42 per share, and (iv) 30,000 are exercisable at a price of $3.04 per share. The members of Cardinal, who share voting control and investment discretion, are H. David Coherd and Robert Rosenstein. Does not include shares beneficially owned by Messrs. Coherd and Rosenstein through, respectively, Windward Capital Advisors, LLC and HefCap Holdings, LLC.

(4) H. David Coherd is the sole member of Windward Capital Advisors, LLC. Mr. Coherd is one of the members of Cardinal Securities LLC. Accordingly, the shares beneficially owned by Cardinal are deemed to be beneficially owned by this selling stockholder. In addition, shares owned and offered include up to 186,667 shares of common stock issuable upon exercise of warrants of which (i) 33,750 are exercisable at a price of $2.57 per share, (ii) 91,667 are exercisable at a price of $2.50 per share, (iii) 6,250 are exercisable at a price if $2.42 per share, and (iv) 30,000 are exercisable at a price of $3.04 per share, and (v) 25,000 are exercisable at a price of $4.07 per share.

(5) Robert Rosenstein is the sole member of Hefcap Holdings, LLC. Mr. Rosenstein is one of the members of Cardinal Securities LLC. Accordingly, the shares beneficially owned by Cardinal are deemed to be beneficially owned by this selling stockholder. In addition, shares owned and offered include up to 186,667 shares of common stock issuable upon exercise of warrants of which (i) 33,750 are exercisable at a price of $2.57 per share, (ii) 91,667 are exercisable at a price of $2.50 per share, (iii) 6,250 are exercisable at a price if $2.42 per share, (iv) 30,000 are exercisable at a price of $3.04 per share, and (v) 25,000 are exercisable at a price of $4.07 per share.

(6) Peter Baxter is the president of Baxter Capital Advisors, Inc. Shares owned and offered include up to 30,000 shares of common stock issuable upon exercise of warrants of which (i) 11,250 are exercisable at a price of $2.57 per share, (ii) 8,750 are exercisable at a price if $2.42 per share, and (iii) 10,000 are exercisable at a price of $3.04 per share.

(7) Messrs. Ken Sgro and Rachel Glicksman share voting control and investment discretion over the shares. CEOCast provides investor relations consulting services to us.

(8) Represents (i) 5,000 shares issuable upon exercise of warrants exercisable at $3.91 per shares expiring on February 28, 2009, (ii) 5,000 shares issuable upon exercise of warrants exercisable at $4.25 per shares expiring on January 31, 2009, (iii) 5,000 shares issuable upon the exercise of warrants at $3.51 per share expiring March 31, 2009. (iv) 5,000 shares issuable upon the exercise of warrants at $1.50 expiring March 31, 2010, (v) 5,000 shares issuable upon the exercise of warrants at $1.87 expiring June 30, 2010 and (vi) 5,000 shares issuable upon the exercise of warrants at $1.70 expiring September 30, 2010. Mr. Chipman provides us with financial and accounting consulting services.

(9) Represents shares issued to Fried Epstein & Rettig LLP, a law firm, for legal services provided to us. The three named partners share voting control and investment discretion over the shares.

(10) Business Asia Consultants, Inc. provides consulting services related to obtaining distribution channels in China. It is owned by Lawrence Kronick.

(11) Jeffrey M. Busch, the principal of JMBL LLC, is deemed to be the beneficial owner of all shares of common stock owned by JMBL LLC. Mr. Busch has voting and investment power over the JMBL LLC shares being offered under this prospectus. Common Stock owned prior to the offering also includes 50,000 shares, which shares have been registered in another registration statements and are eligible for resale pursuant to a separate prospectus.

(12) Dian Griesel is the owner of the Investor Relations Group and is deemed to be the beneficial owner of all common stock owned by the Investors Relations Group.

(13) Both columns include shares issuable upon the exercise of outstanding options exercisable at $1.55 per share expiring February 14, 2015. The first column also includes 89,400 shares owned by The Sage Group. The principals of The Sage Group are Wayne Pambianchi, Daniel Tripodi, W. Barry McDonald, Gordon Ramseier and R. Douglas Hulse. The foregoing securities were issued to The Sage Group and its principals for services provided to us. Mr. Hulse is our President.

(14) Consists of shares issuable upon exercise of 150,000 options issued in 2005 to purchase common stock at $2.00 per share expiring September 23, 2015. Mr. Burrows is a former member of the Board of Directors ad serves as an advisor to the Company from time to time. Also includes 540,000 shares of common stock of which Mr. Burrows is the beneficial owner.

The selling stockholders have not been employed by, held office in, or had any other material relationship with us or any of our affiliates within the past three years except as described in the footnotes above.

HOW THE SHARES MAY BE DISTRIBUTED

The shares to be sold in this offering have been or are in the process of being listed on the American Stock Exchange, subject to official notice of issuance. The selling stockholders may sell their shares of common stock from time to time in various ways and at various prices. The shares may be sold in one or more transactions at fixed prices, at prevailing market prices at the

time of the sale, at varying prices determined at the time of sale, or at negotiated prices. These sales may be effected in transactions that may involve crosses or block transactions. Some of the methods by which the selling stockholders may sell the shares include:

o on any national securities exchange or quotation service on which the shares may be listed or quoted at the time of sale;

o in the over-the-counter market;

o in transactions otherwise than on these exchanges or systems or in the over-the-counter market;

o through the writing of options, whether such options are listed on an options exchange or otherwise;

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

o privately negotiated transactions;

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

o purchases by a broker or dealer as principal and resale by that broker or dealer for the selling stockholder's account under this prospectus;

o sales under Rule 144 rather than by using this prospectus;

o through the settlement of short sales;

o a combination of any of these methods of sale; or

o any other legally permitted method.

In connection with sales of the shares or otherwise, the selling stockholders may enter into hedging transactions with broker-dealers, which may in turn engage in short sales of the shares in the course of hedging in positions they assume. The selling stockholders may also sell shares short and deliver shares to close out short positions, provided that the selling stockholders may not close out short positions entered into prior to the effective date of the registration statement of which this prospectus is a part with any shares included in this prospectus. The selling stockholders may also pledge their shares as collateral for a margin loan under their customer agreements with their brokers. If there is a default by the selling stockholders, the brokers may offer and sell the pledged shares from time to time under this prospectus or an amendment to this prospectus under Rule 424(b)(3) or other applicable provisions of the Securities Act amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

Brokers or dealers may receive commissions or discounts from the selling stockholders (or, if the broker-dealer acts as agent for the purchaser of the shares, from that purchaser) in amounts to be negotiated. These commissions may exceed those customary in the types of transactions involved.

We cannot estimate at the present time the amount of commissions or discounts, if any, that will be paid by the selling stockholders in connection with sales of the shares.

The selling stockholders and any broker-dealers or agents that

participate with the selling stockholders in sales of the shares may be deemed to be "underwriters" within the meaning of the Securities Act in connection with such sales. In that event, any commissions received by the broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. The selling stockholders have advised us that they have not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of the shares. There is no underwriter or coordinating broker acting in connection with the proposed sale of shares by the selling stockholders. In addition, each of the selling stockholders who is a registered broker-dealer or is affiliated with a registered broker-dealer has advised us that:

o it purchased the shares in the ordinary course of business; and

o at the time of the purchase of the shares to be resold, it had no agreements or understandings, directly or indirectly, with any person to distribute the shares.

Under the securities laws of certain states, the shares may be sold in those states only through registered or licensed broker-dealers. In addition, the shares may not be sold unless they have been registered or qualified for sale in the relevant state or unless they qualify for an exemption from registration or qualification.

We do not know whether any selling stockholder will sell any or all of the shares registered by the shelf registration statement of which this prospectus forms a part.

We have agreed to pay all fees and expenses incident to the registration of the shares, including certain fees and disbursements of counsel to certain of the selling stockholders. We have agreed to indemnify the selling stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

Certain of the selling stockholders have also agreed to indemnify us, our directors, officers, agents and representatives against certain liabilities, including certain liabilities under the Securities Act.

The selling stockholders and other persons participating in the distribution of the shares offered under this prospectus are subject to the applicable requirements of Regulation M promulgated under the Exchange Act in connection with sales of the shares.

We have agreed with the selling stockholders to keep the registration statement of which this prospectus is a part effective until all the shares registered under the registration statement have been resold.

USE OF PROCEEDS

We will not receive any proceeds from the sale of the shares of common stock offered by the selling stockholders. Proceeds from the exercising of the Warrants, if any, will be used for funding our research and development efforts, capital improvements and working capital.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the Securities and Exchange Commission. You may read and copy any document we file at the Securities and Exchange Commission's public

reference rooms at 450 Fifth Street, N.W., Washington, D.C. 20549. Please call the Securities and Exchange Commission at 1-800-SEC-0330 for further information on the public reference rooms. Many of our Securities and Exchange Commission filings are also available to the public from the Securities and Exchange Commission's Website at "http://www.sec.gov."

We have filed with the Securities and Exchange Commission a registration statement (which contains this prospectus) as amended on Form S-3 under the Securities Act of 1933. The registration statement relates to the securities offered by the selling stockholders. This prospectus does not contain all of the information set forth in the registration statement and the exhibits and schedules to the registration statement. Please refer to the registration statement and its exhibits and schedules for further information with respect to us, the common stock and the Warrants. Statements contained in this prospectus as to the contents of any contract or other document are not necessarily complete and, in each instance, we refer you to the copy of that contract or document filed as an exhibit to the Registration Statement. You may read and obtain a copy of the registration statement and its exhibits and schedules from the SEC, as described in the preceding paragraph.

INFORMATION INCORPORATED BY REFERENCE

The Commission allows us to "incorporate by reference" the information that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and later information that we file with the Commission will automatically update and supercede this information. We incorporate by reference the following documents and any future filing made with the Commission under Sections 13(a), 14 or 15(d) of the Securities Exchange Act of 1934 until we and the selling stockholders sell all the securities included in this prospectus:

(a) Our annual report on Form 10-K for our fiscal year ended December 31, 2004, SEC File No. 1-13441.

(b) Our quarterly report on Form 10-Q for the quarterly period ended March 31, 2005, SEC File No. 1-13441.

(c) Our proxy statement on schedule 14A for our 2005 annual meeting, SEC File No. 1-13441.

(d) Our quarterly report on Form 10-Q for the quarterly period ended June 30, 2005, SEC File No. 1-13441.

(e) Our current report on Form 8-K filed on October 20, 2005, SEC File No. 1-13441.

(f) Our current report on Form 8-K/A filed on October 28, 2005, SEC File No. 1-13441.

(g) Our quarterly report on Form 10-Q for the quarterly period ended September 30, 2005, SEC File No. 1-13441

(h) A description of our common stock contained in our registration statement on Form S-1, SEC File No. 33-93314, and any amendment or report filed for the purpose of updating this description filed subsequent to the date of this prospectus and prior to the termination of this offering.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address: Hemispherx Biopharma, Inc., 1617 JFK Boulevard, Philadelphia, Pennsylvania 19103, telephone number 215-988-0080.

You should rely only on the information incorporated by reference or provided in this prospectus or any supplement. We have not authorized anyone else to provide you with different information. We and the selling stockholders will not make offers to these shares in any state where the offer is not permitted. You should not assume that the information in this prospectus or any supplement is accurate as of any date other that the date on the front of those documents.

LEGAL MATTERS

The validity of the common stock offered in this prospectus has been passed upon for us by Silverman Sclar Shin & Byrne PLLC, 381 Park Avenue South, Suite 1601, New York, New York 10016.

EXPERTS

The financial statements incorporated by reference in this Prospectus have been audited by BDO Seidman, LLP, an independent registered public accounting firm, to the extent and for the periods set forth in their reports incorporated herein by reference, and are incorporated herein in reliance upon such reports given upon the authority of said firm as experts in auditing and accounting.

No dealer, salesman or any other person is authorized to give any information or to represent anything not contained in this prospectus. You must not rely on any unauthorized information or representations. This prospectus is an offer to sell these securities and it is not a solicitation of an offer to buy these securities in any state where the offer or sale is not permitted. The information contained in this Prospectus is current only as of this date.

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9,668,433 SHARES OF
COMMON STOCK

HEMISPHERX BIOPHARMA, INC.

PROSPECTUS

December 13, 2005