

HEMISPHERX BIOPHARMA INC  
Form S-3/A  
June 18, 2009

As filed with the Securities and Exchange Commission on June 18, 2008

Registration No. 333-159856

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SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

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AMENDMENT NO. 1 TO  
FORM S-3  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933

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

Delaware	2836	52-0845822
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

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1617 JFK Boulevard  
Philadelphia, Pennsylvania 19103  
(215) 988-0080  
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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William A. Carter, M.D., Chief Executive Officer  
Hemispherx Biopharma, Inc.  
1617 JFK Boulevard  
Philadelphia, Pennsylvania 19103  
(215) 988-0080  
(Name, address, including zip code, and telephone number, including area code, of agent for service)

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Approximate date of proposed sale to the public: From time to time or at one time after the effective date of this Registration Statement.

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If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. "

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 ("Securities Act"), other than securities offered only in connection with dividend or reinvestment plans, check the following box. x

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. "

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

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. "

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. "

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or a smaller reporting company. See definition of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer "	Accelerated filer x
Non-accelerated filer "	Smaller Reporting Company "

The Registrant hereby amends this registration statement on the date or dates as may be necessary to delay its effective date until the Registrant 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, as amended, or until the registration statement shall become effective on a date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

#### EXPLANATORY NOTE

This Amendment No. 1 to the Registration Statement on Form S-3 (File No. 333-159856) is being filed solely to incorporate by reference the Registrant's Current Report on Form 8-K filed with the Securities and Exchange Commission on June 17, 2009. No other changes have been made to the prospectus.

The information in this prospectus is not complete and may be amended. Neither we nor the selling stockholders may 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 it is not soliciting an offer to buy these securities in any state where an offer or sale is not permitted.

Subject to Completion  
Preliminary Prospectus Dated June 18, 2009  
\$150,000,000

HEMISPHERX BIOPHARMA, INC.

Common Stock  
Preferred Stock  
Warrants  
Debt Securities

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This prospectus relates to common stock, preferred stock, debt securities and warrants to purchase common stock, preferred stock or debt securities, either individually or in units, as well as common stock or preferred stock upon conversion of debt securities, common stock upon conversion of preferred stock, or common stock or preferred stock upon the exercise of warrants that we may sell from time to time in one or more offerings up to a total public offering price of \$150,000,000 on terms to be determined at the time of sale. We will provide specific terms of these securities in supplements to this prospectus. If there is any inconsistency between the information in this prospectus and a prospectus supplement, you should rely on the information in that prospectus supplement. You should read this prospectus and any supplement carefully before you invest.

This prospectus may not be used to offer and sell securities unless accompanied by a prospectus supplement for those securities.

See "Risk Factors" beginning on page 4 for a discussion of material risks that you should consider before you invest in our securities being sold with this prospectus.

Our common stock is traded on the NYSE Amex under the symbol "HEB." On June 8, 2009, the last reported sale price for our common stock on the NYSE Amex was \$3.05 per share.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is June \_\_, 2009.

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## PROSPECTUS SUMMARY

## Important Notice about the Information Presented in this Prospectus

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, utilizing a “shelf” registration process. Under this shelf process, we may from time to time sell any combination of securities described in this prospectus in one or more offerings. The aggregate amount of securities that we may offer under the registration statement is \$150,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of the securities being offered. That prospectus supplement may include a discussion of any risk factors or other special consideration that apply to those securities. The prospectus supplement may also add, update or change information contained in this prospectus. If there is any inconsistency between the information in this prospectus and a prospectus supplement, you should rely on the information in that prospectus supplement. You should read both this prospectus and any applicable prospectus supplement together with additional information described under the heading “Where You Can Find More Information.”

When acquiring any securities discussed in this prospectus, you should rely on the information provided in this prospectus and the prospectus supplement, including the information incorporated by reference. Neither we, nor any underwriters or agents, have authorized anyone to provide you with different information. We are not offering the securities in any state where such an offer is prohibited. You should not assume that the information in this prospectus, any prospectus supplement, or any document incorporated by reference, is truthful or complete at any date other than the date mentioned on the cover page of those documents. You should also carefully review the section entitled "Risk Factors," which highlights certain risks associated with an investment in our securities, to determine whether an investment in our securities is appropriate for you.

References in this prospectus to "Hemispherx," the "Company," "we," "us" and "our" are to Hemispherx Biopharma, Inc.

#### About Hemispherx

We are a specialty pharmaceutical company engaged in the clinical development, manufacture, marketing and distribution of new drug therapies based on natural immune system enhancing technologies for the treatment of viral and immune based chronic disorders. We were founded in the early 1970s doing contract research for the National Institutes of Health. Since that time, 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 certain chronic diseases.

Our current strategic focus is derived from four applications of our two core pharmaceutical technology platforms Ampligen® and Alferon N Injection®. The commercial focus for Ampligen includes application as a treatment for Chronic Fatigue Syndrome ("CFS") and as a vaccine enhancer (adjuvant) for both therapeutic and preventative vaccine development. Alferon N Injection® is an FDA approved product with an indication for refractory or recurring genital warts. Alferon LDO (Low Dose Oral) is an application currently under early stage development targeting influenza and viral diseases both as an adjuvant as well as a single entity anti-viral.

Ampligen® is an experimental drug currently undergoing clinical development for the treatment of CFS. In August 2004, we completed a Phase III clinical trial ("AMP 515") treating CFS patients with Ampligen® and we are presently in the registration process for a new drug application ("NDA") with the Food and Drug Administration ("FDA"). In July 2008, the FDA accepted for review our NDA for Ampligen® to treat CFS. On February 18, 2009, we were notified by the FDA that the originally scheduled Prescription Drug User Fee Act ("PDUFA") date of February 25, 2009 has been extended to May 25, 2009. On May 22, 2009, we were notified by the FDA that it may require up to one to two additional weeks to take action beyond the scheduled PDUFA action date of May 25, 2009.

We own and operate a 43,000 sq. ft. FDA approved facility in New Brunswick, New Jersey primarily designed to produce Alferon N Injection®. In 2006, we completed the installation of a polymer production line to produce Ampligen® raw materials on a more reliable and consistent basis.

Our principal executive offices are located at One Penn Center, 1617 JFK Boulevard, Philadelphia, Pennsylvania 19103, and our telephone number is 215-988-0080. We maintain a website at “<http://www.hemispherx.net>.” Information contained on our website is not considered to be a part of, nor incorporated by reference in, this prospectus.

## RISK FACTORS

The following cautionary statements identify important factors that could cause our actual results 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:

### Risks Associated With Our Business

No assurance of successful product development.

Ampligen® and related products. The development of Ampligen® and our other related products is subject to a number of significant risks. Ampligen® 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® 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. Please see the next risk factor.

Alferon N Injection®. Although Alferon N Injection® is approved for marketing in the United States for the intra-lesional 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.

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

All of our drugs and associated technologies, other than Alferon N Injection®, 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® is only approved for the intra-lesional treatment of refractory or recurring external genital warts in patients 18 years of age or older. Use of Alferon N Injection® for other indications will require regulatory approval.

Our products, including Ampligen®, 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® or any other proposed product and receive product revenues or royalties. We cannot assure you that Ampligen® will ultimately be demonstrated to be safe or efficacious. In addition, while Ampligen® is authorized for use in clinical trials including a cost recovery program in the United States and Europe, 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.

We filed an NDA with the FDA for treatment of CFS on October 10, 2007. On December 5, 2007 we received a Refusal to File letter from the FDA as our NDA filing was deemed “not substantially complete”. We responded to the FDA’s concerns by filing amendments to our NDA on April 25, 2008. These amendments should allow the FDA reviewers to better evaluate independently the statistical efficacy/safety conclusions of our NDA for the use of Ampligen® in treating CFS. On July 7, 2008, the FDA accepted our NDA filing for review. However, there are no assurances that upon review of the NDA that it will be approved by the FDA. On February 18, 2009, we were notified by the FDA that the originally scheduled PDUFA date of February 25, 2009 has been extended to May 25, 2009. On May 22, 2009, we were notified by the FDA that it may require up to one to two additional weeks to take action beyond the scheduled PDUFA action date of May 25, 2009.

If Ampligen® 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.

Alferon® LDO is undergoing pre-clinical testing for possible prophylaxis against avian flu. Additional studies are anticipated for swine H1N1. While the studies to date have been encouraging. Preliminary testing in the laboratory and animals 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 Alferon® as a possible 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.



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 to get our experimental drug, Ampligen®, approved. As of March 31, 2009, our accumulated deficit was approximately \$200,496,000. 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 March 31, 2009, we had approximately \$5,541,000 in cash and cash equivalents and short-term investments. Since then, while we have continued to spend cash on operations, through June 8, 2009, we received approximately \$1,440,000 of equity funding from Fusion Capital Fund II, LLC during April and May 2009 and approximately \$28,250,000 from recent placements of shares and warrants and \$5,782,450, from the exercise of warrants issued in those placements. Given the harsh economic conditions, we have reviewed every aspect of our operations for cost and spending reductions to assure our long term survival while maintaining the resources necessary to achieve our primary objectives of commercializing Alferon N, obtaining NDA approval of Ampligen® and securing a strategic partner. Based on these actions and our recent financings, we do not anticipate that we will need additional financing in order to continue operations for the near future.

Aside from the sale of securities under this prospectus, we have in place one potential sources of financing - the Common Stock Purchase Agreement (the "Fusion Purchase Agreement") with Fusion Capital Fund II, LLC ("Fusion Capital") pursuant to which we have the right to sell shares of our Common Stock to Fusion Capital.

If we are unable to commercialize and sell Ampligen®, Alferon N Injection® or other products, we eventually will need to secure other sources of funding through additional equity or debt financing or from other sources in order to satisfy our working capital needs and to complete the necessary clinical trials and the regulatory approval processes including the commercializing of Ampligen® products. We anticipate, but cannot assure, that, should we need to raise additional funds, we will be able to do so from the sale of securities under this prospectus and/or the sale of shares under the Fusion Purchase Agreement. Pursuant to the Purchase Agreement, we only have the right to receive \$120,000 every two business days unless our stock price equals or exceeds \$0.80, in which case we can sell greater amounts to Fusion Capital as the price of our common stock increases. Fusion Capital does not have the right nor the obligation to purchase any shares of our common stock on any business day that the market price of our common stock is less than \$0.40.

In addition, as of June 8, 2009, we had approximately 42,000,000 shares authorized but unissued and unreserved. At our annual stockholders' meeting to be held in June 2009, we are seeking approval of an amendment to our Certificate of Incorporation to increase the number of authorized shares of Common Stock from 200,000,000 to 350,000,000. If that approval is not obtained, the amount of proceeds we may receive from the sale of our Common Stock will be limited.

We are unable to estimate the amount, timing or nature of future sales of outstanding common stock or instruments convertible into or exercisable for our common stock. Should we require additional financing and such financing is unavailable or prohibitively expensive, our ability to develop our products or continue our operations could be materially adversely affected.

Our Alferon N Injection® Commercial Sales have halted due to lack of finished goods inventory.

Our finished goods inventory of Alferon N Injection® reached its expiration date in March 2008. As a result, we have no product to sell at this time. The FDA declined to respond to our requests for an extension of the expiration date, therefore we consider the request to be denied. Since our testing of the product indicates that it is not impaired and could be safely utilized, the finished goods inventory of 2,745 Alferon N Injection® 5ml vials may be used to produce approximately 11,000,000 sachets of Low Dose Oral Alferon (LDO) for future clinical trials.

Production of Alferon N Injection® from our work-in-progress inventory, which has an approximate expiration date of 2012, has been put on hold at this time due to the resources needed to prepare our New Brunswick facility for the FDA preapproval inspection with respect to our Ampligen® NDA. Work on the Alferon N Injection® is expected to resume in mid-2009, which means that we may not have any Alferon N Injection® product commercially available until 2010. However, if there is a significant absence of the product from the market place, no assurance can be given that sales will return to prior levels.

Although preliminary in vitro testing indicates that Ampligen® 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® is currently being tested as a vaccine adjuvant for H5N1, a pathogenic avian influenza virus (“HPAIV”) in Japan, where the preclinical data has shown activity in preventing lethal challenge with the original virus used for vaccination as well as the other related, but not identical, isolates of H5N1 virus (i.e., cross-reactivity). The clinical testing phase of Ampligen® in Japan is expected to begin in late 2009 or early 2010. The results of laboratory testing with seasonal influenza virus vaccine in Australia for the effect of Ampligen® as an adjuvant is pending. No assurance can be given that similar results will be observed in clinical trials. Use of Ampligen® in the treatment of 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 above, obtaining regulatory approvals is a rigorous and lengthy process (see “Our drugs and related technologies are investigational and subject to regulatory approval. If we are unable to obtain regulatory approval, our operations will be significantly adversely affected” above).

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® for a particular disease in order to obtain exclusive rights for the commercial sale of Ampligen® for such disease. We obtained all rights to Alferon N Injection®, 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 experimental drug, Ampligen®, which is carried out according to standard operating procedure manuals. We also have been issued patents on the use of Ampligen® 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® in patients with Chronic Fatigue Syndrome. We have not yet been issued any patents in the United States for the use of Ampligen® as a sole treatment for any of the cancers, which we have sought to target. With regard to Alferon N Injection®, we have acquired from ISI its patents for natural alpha interferon produced from human peripheral blood leukocytes and its production process and we have filed a patent application for the use of Alferon® LDO in treating viral diseases including avian influenza. 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.

We have limited marketing and sales capability. If we are unable to obtain additional distributors and our current and future 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 in large part on the efforts of third parties, and there is no assurance that these efforts will be successful.

Our commercialization strategy for Ampligen®-CFS may include licensing/co-marketing agreements utilizing the resources and capacities of a strategic partner(s). We are currently seeking worldwide marketing partner(s), with the goal of having a relationship in place before approval is obtained. In parallel to partnering discussions, appropriate pre-marketing activities will be undertaken. We intend to control manufacturing of Ampligen on a world-wide basis.

We cannot assure that our U.S. or foreign marketing strategy will be successful 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. Our inability to establish viable marketing and sales capabilities would most likely 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® and/or Ampligen®.

A number of essential materials are used in the production of Alferon N Injection®, 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.

There are a limited number of manufacturers in the United States available to provide the polymers for use in manufacturing Ampligen®. At present, we do not have any agreements with third parties for the supply of any of these polymers. We have established relevant manufacturing operations within our New Brunswick, New Jersey facility for the production of Ampligen® polymers from raw materials in order to obtain polymers on a more consistent manufacturing basis.

If we are unable to obtain or manufacture the required polymers, 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® and the commercial production of Alferon N Injection® 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® 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.

Ampligen® has been produced to date only in limited quantities for use in our clinical trials and we are dependent upon a third party supplier for the manufacturing and bottling 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 large-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.

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

We have never produced Ampligen® 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® 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® 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®. 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 disease indications in which we plan to address include Gilead Pharmaceutical, Pfizer, Bristol-Myers, Abbott Labs, GlaxoSmithKline, 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® on the immune system, we cannot assure that we will be able to compete.

ALFERON N Injection®. Our 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® currently competes with Schering's injectable recombinant alpha interferon product (INTRON® A) for the treatment of genital warts. 3M Pharmaceuticals also offer competition from its immune-response modifier, Aldara®, a self-administered topical cream, for the treatment of external genital and perianal warts. In addition, Medigene has FDA approval for a self-administered ointment, Veregen™, which is indicated for the topical treatment of external genital and perianal warts. Alferon N Injection® 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®. If and when we obtain additional approvals of uses of this product, we expect to compete primarily on the basis of product performance. Our competitors have developed or may develop products (containing either alpha or beta interferon or other therapeutic compounds) or other treatment modalities for those uses. There can be no assurance that, if we are able to obtain regulatory approval of Alferon N Injection® 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®. Currently, our wholesale price on a per unit basis of Alferon N Injection® 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® or Alferon N Injection® could adversely affect potential revenues and physician/patient acceptability of our product.

Ampligen®. We believe that Ampligen® 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 15-20% 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 reducing the rate of infusion. 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® in certain clinical situations and therefore, could adversely affect potential revenues and physician/patient acceptability of our product.

Alferon N Injection®. At present, Alferon N Injection® is only approved for the intra-lesional (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®, 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® which could threaten or limit such product's usefulness.

We may be subject to product liability claims from the use of Ampligen®, Alferon N Injection®, or other of our products which could negatively affect our future operations. We have temporarily discontinued product liability insurance.

We face an inherent business risk of exposure to product liability claims in the event that the use of Ampligen® 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.

On November 28, 2008, we suspended product liability insurance for Alferon® N and Ampligen® until we receive regulatory clearance for Ampligen®. We now require third parties to indemnify us in conjunction with all overseas emergency sales of Ampligen® and Alferon® LDO. We concluded that years of successfully addressing the limited number of product liability claims filed against Ampligen® and Alferon® LDO, combined with the mandatory patient waivers completed as an element of clinical trials and lack of any commercial sales since April 2008, that temporarily discontinuing the liability insurance was an acceptable risk given our financial condition and need to conserve cash.

Currently, without product liability coverage for Ampligen® and Alferon® LDO, a claim against the products could have a materially adverse effect on our business and financial condition.

The loss of services of key personnel including Dr. William A. Carter could hurt our chances for success.

Our success is dependent on the continued efforts of our staff, especially certain doctors and researchers along with 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®, and his knowledge of our overall activities, including patents and clinical trials. The loss of the services of personnel key to our operations or Dr. Carter could have a material adverse effect on our operations and chances for success. As a cash conservation measure, we have elected to discontinue the Key Man life insurance in the amount of \$2,000,000 on the life of Dr. Carter until we receive regulatory clearance for Ampligen®. An employment agreement continues to exist with Dr. Carter that, as amended, runs until December 31, 2010. 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 an 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. This is especially true given the current significant instability in the financial markets. 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;
    - overall investment market fluctuation; and
  - occurrence of any of the risks described in these "Risk Factors."

Our common stock is listed for quotation on the NYSE Amex. For the 12-month period ended April 30, 2009, the closing price of our common stock has ranged from \$0.25 to \$1.20 per share. As of June 8, 2009, the last reported sale price for our common stock on the NYSE Amex was \$3.05 per share. We expect the price of our common stock to remain volatile. The average daily trading volume of our common stock varies significantly.

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 are sold in the public market.

We have registered \$150,000,000 of securities for public sale pursuant to this prospectus. In May 2009 we issued an aggregate of 25,543,339 shares and warrants to purchase an additional 14,708,687 shares under a prior universal shelf registration statement. In connection with entering into the Purchase Agreement with Fusion Capital, we registered 21,300,000 shares in the aggregate, consisting of 20,000,000 shares which we may sell to Fusion Capital and 1,300,000 shares we have issued or may issue to Fusion Capital as a commitment fee. As of June 8, 2009, 2009, we have sold an aggregate of 6,642,632 shares to Fusion Capital under the Purchase Agreement, leaving 14,657,368 shares. The sale of a substantial number of shares of our common stock under this prospectus or by Fusion Capital, 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. However, we have the right to control the timing and amount of any sales of our shares to Fusion Capital and the agreement may be terminated by us at any time at our discretion without any cost to us.

We also previously registered 35% of 3,615,514 shares issuable upon exercise of warrants related to our former convertible debentures and 14,442,294 shares issuable upon exercise of certain other warrants. To the extent the exercise price of our outstanding 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 exercise price of certain of these warrants are adjusted pursuant to anti-dilution protection, the warrants could be exercisable or convertible for even more shares of common stock. We also may issue shares pursuant to this prospectus or otherwise 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 or instruments convertible into or exercisable for our common stock.

Sales of substantial amounts of our common stock in the public market, including our sale of securities under this Prospectus or pursuant to the Purchase Agreement with Fusion Capital, 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.

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 6.05% 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® 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 revenue.

### SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Certain statements in this prospectus constitute “forward-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 above, 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.

### RATIO OF EARNINGS TO FIXED CHARGES

We have incurred \$10.4 million in fixed charges in the past five years. Fixed charges mainly represent interest expensed as well as amortized discounts related to indebtedness. We have incurred losses totaling \$20.9 million, \$12.4 million, \$19.4 million, \$18.1 million and \$12.2 million for the years ended December 31, 2004, 2005, 2006, 2007 and 2008, respectively. Until we achieve profitability, we will not be able to cover our fixed charges from earnings.

### USE OF PROCEEDS

Except as otherwise provided in the applicable prospectus supplement, we intend to use the net proceeds from the sale of the securities offered by this prospectus to fund commercialization of Alferon® and Ampligen® along with general corporate purposes, which may include working capital, capital expenditures, research and development expenditures, regulatory affairs expenditures, clinical trial expenditures, acquisitions of new technologies and investments, and the repayment, refinancing, redemption or repurchase of future indebtedness or capital stock. Additional information on the use of net proceeds from the sale of securities offered by this prospectus may be set forth in the prospectus supplement relating to that offering.

## DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock currently consists of 200,000,000 shares of common stock, par value \$0.001 per share, and 5,000,000 shares of preferred stock, \$0.01 par value per share. At our annual stockholders' meeting to be held in June 2009, we are seeking approval of an amendment to our Certificate of Incorporation to increase the number of authorized shares of Common Stock from 200,000,000 to 350,000,000. No assurance can be given that stockholders will approve the increase.

The following summary of certain provisions of our common and preferred stock does not purport to be complete. You should refer to our Amended and Restated Certificate of Incorporation, amendments thereto, and our By laws, as amended, all of which are filed with the SEC. The summary below is also qualified by provisions of applicable law.

### Common Stock

Holders of common stock are entitled to one vote per share on matters on which our stockholders vote. There are no cumulative voting rights. Holders of common stock are entitled to receive dividends, if declared by our board of directors, out of funds that we may legally use to pay dividends. If we liquidate or dissolve, holders of common stock are entitled to share ratably in our assets once our debts and any liquidation preference owed to any then-outstanding preferred stockholders are paid. All shares of common stock that are outstanding as of the date of this prospectus are fully-paid and non-assessable.

### Preferred Stock

We are currently authorized to issue 5,000,000 shares of preferred stock, none of which are currently outstanding.

Our board of directors has the authority to designate any or all shares of preferred stock in one or more series and to fix the rights of each series. Prior to issuance of shares of each series, our Board of Directors will adopt resolutions and file a certificate of designation fixing for each series the designations, powers, preferences, conversion and other rights, voting powers, qualifications, limitations as to dividends, restrictions and terms and conditions of redemption. The preferred stock will, when issued, be fully paid and nonassessable and will not have, or be subject to, any preemptive or similar rights.

If we sell preferred stock, the prospectus supplement relating to the series of preferred stock offered by that supplement will describe the specific terms of those securities, including:

1. the title and stated value of that preferred stock;
2. the number of shares of that preferred stock offered, the liquidation preference per share and the offering price of that preferred stock;
3. the dividend rate(s), period(s) and/or payment date(s) or method(s) of calculation thereof applicable to that preferred stock;
4. whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends on that preferred stock will accumulate;
5. the voting rights applicable to that preferred stock;
6. the procedures for any auction and remarketing, if any, for that preferred stock;
7. the provisions for a sinking fund, if any, for that preferred stock;
8. the provisions for redemption, if applicable, of that preferred stock;
9. any listing of that preferred stock on any securities exchange;
10. the terms and conditions, if applicable, upon which that preferred stock will be convertible into shares of the Common Stock, including the conversion price (or manner of calculation of the conversion price) and conversion period;
11. a discussion of federal income tax considerations applicable to that preferred stock;
12. any limitations on issuance of any series of preferred stock ranking senior to or on a parity with that series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of our affairs; and
13. any other specific terms, preferences, rights, limitations or restrictions of that preferred stock.

We believe the power to issue preferred stock will provide our board of directors with flexibility in connection with certain possible corporate transactions. The issuance of preferred stock, however, could adversely affect the voting power of holders of our common stock, restrict their rights to receive payment upon liquidation, and have the effect of delaying, deferring, or preventing a change in control.



## Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Continental Stock Transfer & Trust Company.

## DESCRIPTION OF WARRANTS

The following description of our warrants for the purchase of our common stock, preferred stock and/or debt securities in this prospectus contains the general terms and provisions of the warrants. The particular terms of any offering of warrants will be described in a prospectus supplement relating to such offering. The statements below describing the warrants are subject to and qualified by the applicable provisions of our certificate of incorporation, bylaws and the relevant provisions of the laws of the State of Delaware.

### General

We may issue warrants for the purchase of our common stock, preferred stock and/or debt securities. We may issue warrants independently or together with any of our securities, and warrants also may be attached to our securities or independent of them. We may issue series of warrants under a separate warrant agreement between us and a specified warrant agent described in the prospectus supplement. The warrant agent will act solely as our agent in connection with the warrants and will not assume any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants.

### Terms

A prospectus supplement will describe the specific terms of any warrants that we issue or offer, including:

- the title of the warrants;
- the aggregate number of warrants;
- the price or prices at which the warrants will be issued;
- the currencies in which the price or prices of the warrants may be payable;
- the designation, amount and terms of our capital stock or debt securities purchasable upon exercise of the warrants;
- the designation and terms of our other securities, if any, that may be issued in connection with the warrants, and the number of warrants issued with each corresponding security;
- if applicable, the date that the warrants and the securities purchasable upon exercise of the warrants will be separately transferable;

- the prices and currencies for which the securities purchasable upon exercise of the warrants may be purchased;
  - the date that the warrants may first be exercised;
  - the date that the warrants expire;
- the minimum or maximum amount of warrants that may be exercised at any one time;
  - information with respect to book-entry procedures, if any;
  - a discussion of certain federal income tax considerations; and
- any other material terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

#### Exercise of Warrants

Each warrant will entitle the holder to purchase for cash the principal amount of debt securities or shares of preferred stock or common stock at the applicable exercise price set forth in, or determined as described in, the applicable prospectus supplement. Warrants may be exercised at any time up to the close of business on the expiration date set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Warrants may be exercised by delivering to the corporation trust office of the warrant agent or any other officer indicated in the applicable prospectus supplement (a) the warrant certificate properly completed and duly executed and (b) payment of the amount due upon exercise. As soon as practicable following exercise, we will forward the debt securities or shares of preferred stock or common stock purchasable upon exercise. If less than all of the warrants represented by a warrant certificate are exercised, a new warrant certificate will be issued for the remaining warrants.

#### DESCRIPTION OF DEBT SECURITIES

We anticipate that any debt securities which we offer by this prospectus will be issued under an indenture between us and a trustee to be identified in the prospectus supplement. If a proposed debt transaction is not exempt under the Trust Indenture Act of 1939, as amended (the "Trust Indenture Act"), the terms of the debt securities will include those stated in the indenture and those made part of the indenture by reference to the Trust Indenture Act, as in effect on the date of the indenture. If a proposed transaction is exempt under the Trust Indenture Act, we may not use an indenture (and, thus a trustee) or, if we use an indenture, it may not fully comply with the requirements of the Trust Indenture Act. The following description summarizes only the material provisions of the indenture. Accordingly, you should read the form of indenture, a copy of which has been filed as an exhibit to the registration statement of which this prospectus forms a part, because it, and not this description, defines your rights as holders of our debt securities. The following description also provides general information that will be contained in any debt instrument we may use if we do not use an indenture. You should also read the applicable prospectus supplement for additional information and the specific terms of the debt securities.

General

We may, at our option, issue debt securities in one or more series from time to time. “Debt securities” may include senior debt, senior subordinated debt or subordinated debt. The particular terms of the debt securities offered by any prospectus supplement, and the extent, if any, to which such general provisions do not apply to the debt securities will be described in the prospectus supplement relating to such debt securities. The following summaries set forth certain general terms and provisions of the indenture and the debt securities. The prospectus supplement relating to a series of debt securities being offered will contain the following terms, if applicable:

- the title and ranking;
- the aggregate principal amount and any limit on such amount;
- the price at which such debt securities will be issued;
- the date on which the debt securities mature;
- the fixed or variable rate at which the debt securities will bear interest, or the method by which such rate shall be determined;
- the timing, place and manner of making principal, interest and any premium payments on the debt securities, and, if applicable, where such debt securities may be surrendered for registration of transfer or exchange;
- the date or dates, if any, after which the debt securities may be converted or exchanged into or for shares of our common stock, preferred stock or another company’s securities or properties or cash and the terms of any such conversion or exchange;
  - any redemption or early repayment provisions;
  - any sinking fund or similar provisions;
  - the authorized denominations;
  - any applicable subordination provisions;
  - any guarantees of such securities by our subsidiaries or others;
- the currency in which we will pay the principal, interest and any premium payments on such debt securities;
- whether the amount of payments of principal of (and premium, if any) or interest, if any, on the debt securities may be determined with reference to an index, formula or other method and the manner in which such amounts shall be determined;
- the time period within which, the manner in which and the terms and conditions upon which the purchaser of the securities can select the payment currency;

- the provisions, if any, granting special rights to the holders of debt securities upon certain events;
- any additions to or changes in the events of default or covenants of Hemispherx with respect to the debt securities and any change in the right of the trustee or the holders to declare the principal, premium and interest with respect to such securities to be due and payable;
- whether and under what circumstances we will pay any additional amounts on such debt securities for any tax, assessment or governmental charge and, if so, whether we will have the option to redeem such debt securities instead of paying such amounts;
- the form (registered and/or bearer securities), any restrictions applicable to the offer, sale or delivery of bearer securities and the terms, if any, upon which bearer securities may be exchanged for registered securities and vice versa;
- the date of any bearer securities or any global security, if other than the date of original issuance of the first security of the series to be issued;
  - the person to whom and manner in which any interest shall be payable;
  - whether such securities will be issued in whole or in part in the form of one or more global securities;
    - the identity of the depository for global securities;
- whether a temporary security is to be issued with respect to such series and whether any interest payable prior to the issuance of definitive securities of the series will be credited to the account of the persons entitled thereto;
- the terms upon which beneficial interests in a temporary global security may be exchanged in whole or in part for beneficial interests in a definitive global security or for individual definitive securities and the terms upon which such exchanges may be made;
  - the securities exchange(s), if any, on which the securities will be listed;
  - whether any underwriter(s) will act as market maker(s) for the securities;
    - the form (certificated or book-entry);
- the form and/or terms of certificates, documents or conditions which may be necessary, if any, for the debt securities to be issuable in final form; and
  - additional terms not inconsistent with the provisions of the indenture.

One or more series of debt securities may be sold at a substantial discount below their stated principal amount bearing no interest or interest at a rate below the market rate at the time of issuance. One or more series of debt securities may be variable rate debt securities that may be exchanged for fixed rate debt securities. In such cases, all material United States federal income tax and other considerations applicable to any such series will be described in the applicable prospectus supplement. You should consult with your own tax advisor before making a decision to purchase any debt security.

We will comply with Section 14(e) under the Exchange Act, to the extent applicable, and any other tender offer rules under the Exchange Act, which may then be applicable, in connection with any obligation of Hemispherx to purchase debt securities at the option of the holders thereof. Any such obligation applicable to a series of debt securities will be described in the applicable prospectus supplement.

#### Exchange, Registration, Transfer and Payment

We expect payment of principal, premium, if any, and any interest on the debt securities to be payable, and the exchange and the transfer of debt securities will be registrable, at the office of the trustee or at any other office or agency we maintain for such purpose. We expect to issue debt securities in denominations of U.S. \$1,000 or integral multiples thereof. No service charge will be made for any registration of transfer or exchange of the debt securities, but we may require a payment to cover any tax or other governmental charges payable in connection therewith.

#### Global Debt Securities

Unless we indicate otherwise in the applicable prospectus supplement, the following provisions will apply to all debt securities.

The debt securities of a series may be issued in whole or in part in the form of one or more global securities that will be deposited with a depository that we will identify in a prospectus supplement. Each global security will be deposited with the depository and will bear a legend regarding any related restrictions or other matters as may be provided for pursuant to the applicable indenture.

Unless a prospectus supplement states otherwise, no global security may be transferred to, or registered or exchanged for debt securities registered in the name of, any person or entity other than the depository, unless:

- the depository has notified us that it is unwilling or unable or is no longer qualified to continue as depository;
  - we order the trustee that such global security shall be so transferable, registrable and exchangeable, and such transfers shall be registrable; or
  - other circumstances, if any, as may be described in the applicable prospectus supplement.

All debt securities issued in exchange for a global security or any portion thereof will be registered in such names as the depository may direct. The specific terms of the depository arrangement with respect to any portion of a series of debt securities to be represented by a global security will be described in the applicable prospectus supplement.

Debt securities which are to be represented by a global security to be deposited with or on behalf of a depository will be represented by a global security registered in the name of such depository or its nominee. Upon the issuance of such global security, and the deposit of such global security with the depository, the depository will credit, on its book-entry registration and transfer system, the respective principal amounts of the debt securities represented by such global security to the accounts of institutions that have accounts with such depository or its nominee (the "Participants"). The accounts to be credited will be designated by the underwriters or agents of such debt securities or by us, if such debt securities are offered and sold directly by us.

Ownership of beneficial interests in such global security will be limited to Participants or persons that may hold interests through Participants. Ownership of beneficial interests in such global security will be shown on, and the transfer of that ownership interest will be effected only through, records maintained by the depository or its nominee for such global security or by Participants or persons that hold through Participants.

The laws of some jurisdictions require that certain purchasers of securities take physical delivery of such securities in certificated form. The foregoing limitations and such laws may impair the ability to transfer beneficial interests in such global securities.

So long as the depository, or its nominee, is the registered owner of such global security, such depository or such nominee, as the case may be, will be considered the sole owner or holder of the debt securities represented by such global security for all purposes under the indenture. Payment of principal of, and premium and interest, if any, on debt securities will be made to the depository or its nominee as the registered owner or bearer as the case may be of the global security representing such debt securities. Each person owning a beneficial interest in such global security must rely on the procedures of the depository and, if such person is not a Participant, on the procedures of the Participant through which such person owns its interest, to exercise any rights of a holder under the indenture. If we request any action of holders or if an owner of a beneficial interest in such global security desires to give any notice or take any action a holder is entitled to give or take under the indenture, the depository will authorize the Participants to give such notice or take such action, and Participants would authorize beneficial owners owning through such Participants to give such notice or take such action or would otherwise act upon the instructions of beneficial owners owning through them.

The rights of any holder of a debt security to receive payment of principal and premium of, if any, and interest on such debt security, on or after the respective due dates expressed or provided for in such debt security, or to institute suit for the enforcement of any such payment on or after such respective dates, shall not be impaired or affected without the consent of the holders.

Neither we, the trustee, any paying agent nor the security registrar for such debt securities will have any responsibility or liability for any aspect of the records relating to or payments made on account of beneficial ownership interests of the global security for such debt securities or for maintaining, supervising or receiving any records relating to such beneficial ownership interests.

We expect that the depositary or its nominee, upon receipt of any payment of principal, premium or interest, will credit immediately Participants' accounts with payments in amounts proportionate to their respective beneficial interests in the principal amount of the global security for such debt securities as shown on the records of such depositary or its nominee. We also expect that payments by Participants to owners of beneficial interests in such global security held through such Participants will be governed by standing instructions and customary practices, as is now the case with securities held for the accounts of customers in bearer form or registered in "street name," and will be the responsibility of such Participants.

If the depositary for a global security representing debt securities of a particular series is at any time unwilling or unable to continue as depositary and we do not appoint a successor depositary within 90 days, we will issue debt securities of such series in definitive form in exchange for such global security. In addition, we may at any time and in our sole discretion determine not to have the debt securities of a particular series represented by one or more global securities and, in such event, will issue debt securities of such series in definitive form in exchange for all of the global securities representing debt securities of such series.

#### Covenants

Except as permitted under "Consolidation, Merger and Sale of Assets," the indenture will require us to do or cause to be done all things necessary to preserve and keep in full force and effect our existence and rights (declaration and statutory); provided, however, that we shall not be required to preserve any right if we determine that the preservation thereof is no longer desirable in the conduct of our business and that the loss thereof is not disadvantageous in any material respect to the holders of the debt securities.

The indenture will require us to pay or discharge or cause to be paid or discharged, before the same shall become delinquent, all taxes, assessments and governmental charges levied or imposed upon us except any tax, assessment, charge or claim whose amount or applicability is being contested in good faith.

Reference is made to the indenture and applicable prospectus supplement for information with respect to any additional covenants specific to a particular series of debt securities.

### Consolidation, Merger and Sale of Assets

Except as set forth in the applicable prospectus supplement, the indenture will provide that we shall not consolidate with, or sell, assign, transfer, lease or convey all or substantially all of our assets, or merge into, to any person unless:

- we are the surviving entity or, in the event that we are not the surviving entity, the entity formed by the transaction (in a consolidation) or the entity which received the transfer of assets is a corporation organized under the laws of any state of the United States or the District of Columbia;
  - such entity assumes all of our obligations under the debt securities and the indenture; and
- immediately after giving effect to the transaction, no event of default, as defined in the indenture, shall have occurred and be continuing.

Notwithstanding the foregoing, we may merge with another person or acquire by purchase or otherwise all or any part of the property or assets of any other corporation or person in a transaction in which we are the surviving entity.

### Events of Default

Unless otherwise specified in the applicable prospectus supplement, the following are events of default with respect to any series of debt securities issued under the indenture:

- failure to pay principal of any debt security of that series when due and payable at maturity, upon acceleration, redemption or otherwise;
- failure to pay any interest on any debt security of that series when due, and the default continues for 30 days;
- failure to comply with any covenant or warranty contained in the indenture, other than covenants or warranties contained in the indenture solely for the benefit of other series of debt securities, and the default continues for 30 days after notice from the trustee or the holders of at least 25% in principal amount of the then outstanding debt securities of that series;
  - certain events of bankruptcy, insolvency or reorganization; and
  - any other event of default provided with respect to that particular series of debt securities.

If an event of default occurs and continues, then upon written notice to us the trustee or the holders of at least 25% in principal amount of the outstanding debt securities of that series may declare the unpaid principal amount of, and any accrued and unpaid interest on, all debt securities of that series to be due and payable immediately. However, at any time after a declaration of acceleration with respect to debt securities of any series has been made, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul such acceleration:



- if all events of default other than the nonpayment of principal of or interest on the debt securities of that series which have become due solely because of the acceleration have been waived or cured; and
- the rescission would not conflict with any judgment or decree of a court of competent jurisdiction. For information as to waiver of defaults, see “Amendment, Supplement and Waiver” below.

The indenture will provide that, subject to the duty of the trustee during an event of default to act with the required standard of care, the trustee will be under no obligation to exercise any of its rights or powers under the indenture at the request or direction of any of the holders, unless such holders shall have offered to the trustee reasonable security or indemnity. Subject to certain provisions, including those requiring security or indemnification of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series.

We will be required to furnish to the trustee under the indenture annually a statement as to the performance by us of our obligations under that indenture and as to any default in such performance.

#### Discharge of Indenture and Defeasance

Except as otherwise set forth in the applicable prospectus supplement, we may terminate our obligations under the debt securities of any series, and the corresponding obligations under the indenture when:

- we have paid or deposited with the trustee funds or United States government obligations in an amount sufficient to pay at maturity all outstanding debt securities of such series, including interest other than destroyed, lost or stolen debt securities of such series which have not been replaced or paid;
- all outstanding debt securities of such series have been delivered (other than destroyed, lost or stolen debt securities of such series which have not been replaced or paid) to the trustee for cancellation; or
  - all outstanding debt securities of any series have become due and payable; and
  - we have paid all other sums payable under the indenture.

In addition, we may terminate substantially all our obligations under the debt securities of any series and the corresponding obligations under the indenture if:

- we have paid or deposited with the trustee, in trust an amount of cash or United States government obligations sufficient to pay all outstanding principal of and interest on the then outstanding debt securities of such series at maturity or upon their redemption, as the case may be;
  - such deposit will not result in a breach of, or constitute a default under, the indenture;
- no default or event of default shall have occurred and continue on the date of deposit and no event of default as a result of a bankruptcy or event which with the giving of notice or the lapse of time would become a bankruptcy event of default shall have occurred and be continuing on the 91st day after such date;
- we deliver to the trustee a legal opinion that we have received from, or there has been published by, the United States Internal Revenue Service a ruling, or there has been a change in tax law, in either case to the effect that the holders of the debt securities of such series will not recognize income, gain or loss for Federal income tax purposes as a result of our exercise of such option and shall be subject to Federal income tax on the same amounts and in the same manner and at the same times as would have been the case if such option had not been exercised; and
  - certain other conditions are met.

We shall be released from our obligations with respect to the covenants to deliver reports required to be filed with the SEC and an annual compliance certificate, and to make timely payments of taxes (including covenants described in a prospectus supplement) and any event of default occurring because of a default with respect to such covenants as they related to any series of debt securities if:

- we deposit or cause to be deposited with the trustee in trust an amount of cash or United States government obligations sufficient to pay and discharge when due the entire unpaid principal of and interest on all outstanding debt securities of any series;
  - such deposit will not result in a breach of, or constitute a default under, the indenture;
- no default or event of default shall have occurred and be continuing on the date of deposit and no event of default as a result of a bankruptcy or event which with the giving of notice or the lapse of time would become a bankruptcy event of default shall have occurred and be continuing on the 91st day after such date;
  - we deliver to the trustee a legal opinion that the holders of the debt securities of such series will not recognize income, gain or loss for Federal income tax purposes as a result of our exercise of such option and shall be subject to Federal income tax on the same amounts and in the same manner and at the same times as would have been the case if such option had not been exercised; and
    - certain other conditions are met.

Upon satisfaction of such conditions, our obligations under the indenture with respect to the debt securities of such series, other than with respect to the covenants and events of default referred to above, shall remain in full force and effect.

Notwithstanding the foregoing, no discharge or defeasance described above shall affect the following obligations to or rights of the holders of any series of debt securities:

- rights of registration of transfer and exchange of debt securities of such series;
- rights of substitution of mutilated, defaced, destroyed, lost or stolen debt securities of such series;
- rights of holders of debt securities of such series to receive payments of principal thereof and premium, if any, and interest thereon when due;
- rights, obligations, duties and immunities of the trustee;
- rights of holders of debt securities of such series as beneficiaries with respect to property deposited with the trustee and payable to all or any of them; and
- our obligations to maintain an office or agency in respect of the debt securities of such series.

#### Transfer and Exchange

A holder of debt securities may transfer or exchange such debt securities in accordance with the indenture. The registrar for the debt securities may require a holder, among other things, to furnish appropriate endorsements and transfer documents, and to pay any taxes and fees required by law or permitted by the indenture. The registrar is not required to transfer or exchange any debt security selected for redemption or any debt security for a period of 15 days before a selection of debt security to be redeemed.

The registered holder of a debt security may be treated as the owner of such security for all purposes.

#### Amendment, Supplement and Waiver

Subject to certain exceptions, the terms of the indenture or the debt securities may be amended or supplemented by us and the trustee with the written consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the amendment with each series voting as a separate class. Without the consent of any holder of the debt securities, we and the trustee may amend the terms of the indenture or the debt securities to:

- cure any ambiguity, defect or inconsistency;
- provide for the assumption of our obligations to holders of the debt securities by a successor corporation;
- provide for uncertificated debt securities in addition to certificated debt securities;

- make any change that does not adversely affect the rights of any holder of the debt securities in any material respect;
- add to, change or eliminate any other provisions of the indenture in respect of one or more series of debt securities if such change would not (i) apply to any security of any series created prior to the execution of a supplemental indenture and entitled to the benefit of such provision and (ii) modify the rights of the holder of any such security with respect to such provision or become effective only when there is no outstanding security of any series created prior to the execution of such supplemental indenture and entitled to such benefits;
  - establish any additional series of debt securities; or
- comply with any requirement of the SEC in connection with the qualification of the indenture under the Trust Indenture Act.

However, holders of each series of debt securities affected by a modification must consent to modifications that have the following effect:

- reduce the principal amount of debt securities the holders of which must consent to an amendment, supplement or waiver of any provision of the indenture;
  - reduce the rate or change the time for payment of interest on any debt security;
  - reduce the principal of or change the fixed maturity of any debt securities;
- change the date on which any debt security may be subject to redemption or repurchase, or reduce the redemption or repurchase price therefor;
  - make any debt security payable in currency other than that stated in the debt security;
  - waive any existing default or event of default and the consequences with respect to that series;
- modify the right of any holder to receive payment of principal or interest on any debt security on or after the respective due dates expressed or provided for in the debt security;
- impair the right of any holder to institute suit for the enforcement of any payment in or with respect to any such debt security; or
  - make any change in the foregoing amendment provisions which require each holder's consent.

Any existing default may be waived with the consent of the holders of at least a majority in principal amount of the then outstanding debt securities of the series affected thereby.

The consent of the holders of debt securities is not necessary to approve the particular form of any proposed amendment to any indenture. It is sufficient if any consent approves the substance of the proposed amendment.

### Replacement Securities

Any mutilated certificate representing a debt security or a certificate representing a debt security with a mutilated coupon will be replaced by us at the expense of the holder upon surrender of such certificate to the trustee. Certificates representing debt securities or coupons that become destroyed, stolen or lost will be replaced by us at the expense of the holder upon delivery to us and the trustee of evidence of any destruction, loss or theft satisfactory to us and the trustee, provided that neither we nor the trustee has been notified that such certificate or coupon has been acquired by a bona fide purchaser. In the case of any coupon which becomes destroyed, stolen or lost, such coupon will be replaced by issuance of a new certificate representing the debt security in exchange for the certificate representing the debt security to which such coupon appertains. In the case of a destroyed, lost or stolen certificate representing the debt security or coupon, an indemnity bond satisfactory to the trustee and us may be required at the expense of the holder of such debt security before a replacement certificate will be issued.

### Regarding the Trustee

We will identify in the prospectus supplement relating to any series of debt securities the trustee with respect to such series. The indenture and provisions of the Trust Indenture Act incorporated by reference therein contain certain limitations on the rights of the trustee, should it become a creditor of Hemispherx, to obtain payment of claims in certain cases, or to realize on certain property received in respect of any such claim, as security or otherwise. The trustee and its affiliates may engage in, and will be permitted to continue to engage in, other transactions with us and our affiliates; provided, however, that if it acquires any conflicting interest, as defined in the Trust Indenture Act, it must eliminate such conflict or resign.

The holders of a majority in principal amount of the then outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for exercising any remedy available to the trustee. The Trust Indenture Act and the indenture provide that in case an event of default shall occur, and be continuing, the trustee will be required, in the exercise of its rights and powers, to use the degree of care and skill of a prudent man in the conduct of his own affairs. Subject to such provision, the trustee will be under no obligation to exercise any of its rights or powers under the indenture at the request of any of the holders of the debt securities issued thereunder, unless they have offered to the trustee indemnity satisfactory to it.

### Governing Law

The debt securities will be governed by and construed in accordance with the laws of the State of New York.

## PLAN OF DISTRIBUTION

We may sell the securities registered under this prospectus:

- through underwriting syndicates represented by one or more managing underwriters;
  - to or through underwriters or dealers;
  - through agents;
  - directly to one or more purchasers;
- through a block trade in which the broker or dealer engaged to handle the block trade will attempt to sell the securities as agent, but may position and resell a portion of the block as principal to facilitate the transaction; or
  - through a combination of any of these methods of sale.

We may, from time to time, authorize underwriters acting as our agents to offer and sell the securities upon the terms and conditions as are set forth in the applicable prospectus supplement. We will describe the name or names of any underwriters and the purchase price of the securities in a prospectus supplement relating to the securities. Any underwritten offering may be on a best efforts or a firm commitment basis. The obligations, if any, of the underwriter to purchase any securities will be subject to certain conditions.

If a dealer is used in an offering of securities, we may sell the securities to the dealer as principal. We will describe the name or names of any dealers and the purchase price of the securities in a prospectus supplement relating to the securities. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of sale. Any public offering price and any discounts or concessions allowed, re-allowed, or paid to dealers may be changed from time to time and will be described in a prospectus supplement relating to the securities.

We, or any underwriter, dealer or agent, may distribute the securities from time to time in one or more transactions at:

- a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to prevailing market prices; or
- at negotiated prices.

Any of these prices may represent a discount from the prevailing market prices.

To the extent permitted by and in accordance with Regulation M under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), in connection with an offering an underwriter may engage in over-allotments, stabilizing transactions, short covering transactions and penalty bids. Over-allotments involve sales in excess of the offering size, which creates a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would be otherwise. If commenced, the underwriters may discontinue any of these activities at any time. We will describe any of these activities in the prospectus supplement.

We may authorize underwriters, dealers or agents to solicit offers by certain institutions to purchase our securities at the public offering price under delayed delivery contracts. If we use delayed delivery contracts, we will disclose that we are using them in the prospectus supplement and will tell you when we will demand payment and delivery of the securities under the delayed delivery contracts. These delayed delivery contracts will be subject only to the conditions that we set forth in the prospectus supplement. We will indicate in our prospectus supplement the commission that underwriters and agents soliciting purchases of our securities under delayed delivery contracts will be entitled to receive.

In connection with the sale of the securities and as further set forth in an applicable prospectus supplement, underwriters may receive compensation from us or from purchasers of the securities for whom they may act as agents, in the form of discounts, concessions or commissions. Underwriters may sell the securities to or through dealers, and these dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for whom they may act as agents. Underwriters, dealers and agents that participate in the distribution of the securities may be deemed to be underwriters, and any discounts or commissions they receive from us, and any profit on the resale of the securities they realize, may be deemed to be underwriting discounts and commissions under the Securities Act of 1933, as amended (the “Securities Act”). The prospectus supplement will identify any underwriter or agent and will describe any compensation they receive from us.

Unless otherwise specified in the prospectus supplement, each series of the securities will be a new issue with no established trading market, other than our common stock, which is currently listed on the NYSE Amex. We will apply to the NYSE Amex to list any additional shares of common stock that we offer and sell pursuant to a prospectus supplement. To the extent permitted by and in accordance with Regulation M under the Exchange Act, any underwriters who are qualified market makers on the NYSE Amex may engage in passive market making transactions in the securities on the NYSE Amex during the business day prior to the pricing of an offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker’s bid, however, the passive market maker’s bid must then be lowered when certain purchase limits are exceeded. It is possible that one or more underwriters may make a market in our securities, but underwriters will not be obligated to do so and may discontinue any market making at any time without notice. Therefore, we can give no assurance about the liquidity of our securities that may be sold pursuant to this prospectus.

Under agreements we may enter into, we may indemnify underwriters, dealers and agents who participate in the distribution of the securities against certain liabilities, including liabilities under the Securities Act.

Certain of the underwriters, dealers and agents and their affiliates may be customers of, engage in transactions with, and perform services for us and our subsidiaries from time to time in the ordinary course of business. Any such relationships will be disclosed in an applicable prospectus supplement.

If indicated in the prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by institutions to purchase securities from us pursuant to contracts providing for payment and delivery on a future date. Institutions with which we may make these contracts include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and others. The obligations of any purchaser under any such contract will be subject to the condition that the purchase of the securities shall not at the time of delivery be prohibited under the laws of the jurisdiction to which the purchaser is subject. The underwriters and other agents will not have any responsibility with regard to the validity or performance of these contracts.

#### LEGAL MATTERS

The validity of the securities offered in this prospectus will be passed upon for us by Silverman Sclar Shin & Byrne PLLC, New York, New York.

#### EXPERTS

The financial statements, the related financial statement schedule, and the effectiveness of internal control over financial reporting incorporated by reference in this Prospectus and Registration Statement have been audited by McGladrey & Pullen, LLP, an independent registered public accounting firm, as stated in their report incorporated herein by reference, and are incorporated in reliance upon such report and upon the authority of such firm as experts in accounting and auditing.



#### WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement on Form S-3 that we filed with the SEC. This prospectus does not contain all of the information included in the registration statement. For further information about us and our securities, you should refer to the registration statement and the exhibits filed with the registration statement.

We are subject to the information requirements of the Securities Exchange Act of 1934 and file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at [www.sec.gov](http://www.sec.gov) or through our website at [www.hemispherx.net](http://www.hemispherx.net). Information contained on our website is not considered to be a part of, nor incorporated by reference in, this prospectus. You may also read and copy any document we file with the SEC at its Public Reference Room at 100 F Street, NE, Washington, D.C. 20549.

You may also obtain copies of the documents at prescribed rates by writing to the Public Reference Room of the SEC at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

#### INFORMATION INCORPORATED BY REFERENCE

The SEC 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 an important part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the following documents and any future filing made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 prior to the termination of the offering:

- (a) Our annual report on Form 10-K for our fiscal year ended December 31, 2008, SEC File No. 1-13441.
- (b) Our quarterly report on Form 10-Q for the period ended March 31, 2009, SEC File No. 1-13441.
- (c) Our current reports on Form 8-K, SEC File No. 1-13441 filed with the SEC on June 17, 2009, May 27, 2009, May 26, 2009, May 19, 2009 and February 19, 2009.

(d) Our proxy statement on schedule 14A for our 2009 annual meeting, SEC File No. 1-13441.

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 will not make offers to sell 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 than the date on the front of those documents.

HEMISPHERX BIOPHARMA, INC.

\$150,000,000

Common Stock  
Preferred Stock  
Warrants  
Debt Securities

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PROSPECTUS

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June \_\_, 2009

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## PART II

## INFORMATION NOT REQUIRED IN PROSPECTUS

## ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION.

The following table sets forth the costs and expenses payable by us in connection with the preparation and filing of this registration statement. All amounts are estimates subject to future contingencies except the SEC registration statement filing fee.

SEC Filing Fees	\$ 8,370
NYSE Amex Listing Fee	\$ 60,000
Printing and Engraving Expenses	\$ 2,000
Accounting Fees and Expenses	\$ 15,000
Legal Fees and Expenses	\$ 15,000
Transfer Agent and Registrar Fees	\$ 2,000
Miscellaneous	\$ 3,000
Total Expenses	\$ 105,370

## ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS.

The Registrant's Amended and Restated Certificate of Incorporation provides that the Registrant shall indemnify to the extent permitted by Delaware law any person whom it may indemnify thereunder, including directors, officers, employees and agents of the Registrant. Such indemnification (other than an order by a court) shall be made by the Registrant only upon a determination that indemnification is proper in the circumstances because the individual met the applicable standard of conduct. Advances for such indemnification may be made pending such determination. In addition, the Registrant's Amended and Restated Certificate of Incorporation eliminates, to the extent permitted by Delaware law, personal liability of directors to the Registrant and its stockholders for monetary damages for breach of fiduciary duty as directors.

The Registrant's authority to indemnify its directors and officers is governed by the provisions of Section 145 of the Delaware General Corporation Law, as follows:

- (a) A corporation shall have the power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than action by or in the right of the corporation) by reason of the fact that he is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction, or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that the person did not act in good faith and in a manner which he reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that the person's conduct was unlawful.

- (b) A corporation shall have the power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that he is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against expenses (including attorneys' fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation and except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.
- (c) To the extent that a present or former director or officer of a corporation has been successful on the merits or otherwise in defense of any action, suit or proceeding referred to in subsections (a) and (b) of this section, or in defense of any claim, issue or matter therein, such person shall be indemnified against expenses (including attorneys' fees) actually and reasonably incurred by such person in connection therewith.
- (d) Any indemnification under subsections (a) and (b) of this section (unless ordered by a court) shall be made by the corporation only as authorized in the specific case upon a determination that indemnification of the present or former director, officer, employee or agent is proper in the circumstances because he has met the applicable standard of conduct set forth in subsections (a) and (b) of this section. Such determination shall be made, with respect to a person who is a director or officer at the time of such determination (1) by a majority vote of the directors who are not parties to such action, suit or proceeding, even though less than a quorum, or (2) by a committee of such directors designated by majority vote of such directors, even though less than a quorum, or (3) if there are no such directors, or if such directors so direct, by independent legal counsel in a written opinion, or (4) by the stockholders.
- (e) Expenses (including attorneys' fees) incurred by an officer or director in defending a civil or criminal action, suit or proceeding may be paid by the corporation in advance of the final disposition of such action, suit or proceeding upon receipt of an undertaking by or on behalf of such director or officer to repay such amount if it shall ultimately be determined that such person is not entitled to be indemnified by the corporation as authorized in this section. Such expenses incurred by former directors and officers and other employees and agents may be so paid upon such terms and conditions, if any, as the corporation deems appropriate.
- (f) The indemnification and advancement of expenses provided by, or granted pursuant to, the other subsections of this section shall not be deemed exclusive of any other rights to which those seeking indemnification or advancement of expenses may be entitled under any by, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in such person's official capacity and as to action in another capacity while holding such office.

- (g) A corporation shall have power to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against such person and incurred by such person in any such capacity, or arising out of his status as such, whether or not the corporation would have the power to indemnify such person against such liability under this section.
- (h) For purposes of this section, references to the "corporation" shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had the power and authority to indemnify its directors, officers, and employees or agents, so that any person who is or was a director, officer, employee or agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, shall stand in the same position under this section with respect to the resulting or surviving corporation as such person would have with respect to such constituent corporation if its separate existence had continued.
- (i) For purposes of this section, references to "other enterprises" shall include employee benefit plans, references to "fines" shall include any excise taxes assessed on a person with respect to any employee benefit plan, and references to "serving at the request of the corporation" shall include any service as a director, officer, employee, or agent with respect to any employee benefit plan, its participants or beneficiaries, and a person who acted in good faith and in a manner such person reasonably believed to be in the interest of the participants and beneficiaries of any employee benefit plan shall be deemed to have acted in a manner "not opposed to the best interests of the corporation" as referred to in this section.
- (j) The indemnification and advancement of expenses provided by, or granted pursuant to, this section shall, unless otherwise provided when authorized or ratified, continue as to a person who has ceased to be a director, officer, employee or agent and shall inure to the benefit of the heirs, executors and administrators of such a person.
- (k) The Court of Chancery is hereby vested with exclusive jurisdiction to hear and determine all actions for advancement of expenses or indemnification brought under this section, or under any bylaw, agreement, vote of stockholders or disinterested directors, or otherwise. The Court of Chancery may summarily determine a corporation's obligation to advance expenses (including attorneys' fees).

#### ITEM 16. EXHIBITS.

Exhibit No.	Description
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- |     |  |
|-----|--|
| 1.1 | Form of Underwriting Agreement. (1)                    |
| 4.1 | Specimen certificate representing our Common Stock.(2) |
| 4.2 | Form of Warrant. (1)                                   |
| 4.3 | Form of Indenture.                                     |

- 4.4 Rights Agreement, dated as of November 19, 2002, between the Company and Continental Stock Transfer & Trust Company. The Right Agreement includes the Form of Certificate of Designation, Preferences and Rights of the Series A Junior Participating Preferred Stock, the Form of Rights Certificate and the Summary of the Right to Purchase Preferred Stock.(3)
- 5.1 Opinion of Silverman Sclar Shin & Byrne PLLC, legal counsel.
- 23.1 Consent of McGladrey & Pullen, LLP
- 23.2 Consent of Silverman Sclar Shin & Byrne PLLC, legal counsel (included in Exhibit 5.1).
- 24.1 Powers of Attorney (included on Signature Pages to this Registration Statement).
- 25.1 Statement of Eligibility of Trustee on Form T-1. (1)

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(1) To be filed either by amendment or incorporated herein by reference in connection with the offering of specific securities.

(2) Filed with the Securities and Exchange Commission as an exhibit to the Company's Registration Statement on Form S-1 (Registration No. 33-93314) declared effective by the Securities and Exchange Commission on November 2, 1995.

(3) Filed with the Securities and Exchange Commission on November 20, 2002 as an exhibit to the Company's Registration Statement on Form 8-A (No. 0-27072) and is hereby incorporated by reference.

## ITEM 17. UNDERTAKINGS

(a) The undersigned registrant hereby undertakes:

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

i. To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

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

iii. To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement.

Provided however, that Paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) of this section do not apply if the registration statement is on Form S-3 or Form F-3 and the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

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

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

i. If the registrant is relying on Rule 430B:

(A) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date; or



ii. If the registrant is subject to Rule 430C, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities: The undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

- i. Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
- ii. Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
- iii. The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
- iv. Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(6) To file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act in accordance with the rules and regulations prescribed by the SEC under Section 305(b)(2) of the Trust Indenture Act.

(b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirement of the Securities Act of 1933, this Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Amendment No. 1 to its registration statement to be signed on its behalf by the undersigned, thereunto duly authorized in the City of Philadelphia, Commonwealth of Pennsylvania, on the 18th day of June, 2009.

HEMISPHERX  
 BIOPHARMA, INC.  
 (Registrant)

By: s/ William A.  
 Carter  
 William A.  
 Carter, M.D.,  
 Chief Executive  
 Officer

Pursuant to the requirements of the Securities Act of 1933, this Amendment No. 1 to the registration statement on Form S-3 has been signed by the following persons in the capacities indicated on the dates indicated.

Signature	Title	Date
s/ William A. Carter William A. Carter, M.D.	Chairman of the Board, Chief Executive Officer (Principal Executive) and Director	June 18, 2009
* Richard C. Piani	Director	June 18, 2009
* Charles T. Bernhardt, CPA	Chief Financial Officer and Chief Accounting Officer	June 18, 2009
* Thomas K. Equels	Secretary and Director	June 18, 2009
* William M. Mitchell, M.D., Ph.D.	Director	June 18, 2009
* Iraj Eqhbal Kiani, Ph.D.	Director	June 18, 2009

\* s/ William A.  
 By: Carter  
 William A.  
 Carter, M.D.,  
 Attorney-in-Fact

Hemispherx Biopharma, Inc.  
Form S-3  
Index to Exhibits

Exhibit No. Description

23.1 Consent of McGladrey & Pullen, LLP, independent registered public accounting firm.

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SILVERMAN SCLAR SHIN & BYRNE PLLC  
381 Park Avenue South  
Suite 1601  
New York, New York 10016  
212.779.8600

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Facsimile: 212.779.8858

June 18, 2009

Jeffrey Riedler  
Assistant Director  
Division of Corporation Finance  
Securities and Exchange Commission  
100 F Street, NE  
Washington, DC 20549

Re: Hemispherx Biopharma, Inc.  
Registration Statement on Form S-3  
Filed June 9, 2009  
File No. 333-159856

Dear Mr. Riedler:

On behalf of Hemispherx Biopharma, Inc. (the "Company"), we file herewith Amendment No. 1 to the above-mentioned registration statement.

Amendment No. 1 is being filed solely to incorporate by reference the Company's Current Report on Form 8-K filed with the Commission on June 17, 2009.

By separate letter filed with the Commission today, the Company is requesting that the effective date of its Form S-3 Registration Statement be accelerated so that it is declared effective at 5:00 p.m. on June 22, 2009 or as soon thereafter as practicable.

Very truly yours,

s/Richard Feiner  
Richard Feiner

cc: Hemispherx Biopharma, Inc.

HEMISPHERX BIOPHARMA, INC.  
1617 JFK Boulevard  
Philadelphia, Pennsylvania 19103

June 18, 2009

Jeffrey P. Riedler, Esq.  
Assistant Director  
Division of Corporation Finance  
Securities and Exchange Commission  
100 F Street, NE  
Washington, DC 20002

Re: Hemispherx Biopharma, Inc.  
Registration Statement  
on Form S-3 (SEC filing No. 333-159856)

Dear Mr. Riedler:

Hemispherx Biopharma, Inc. (“Hemispherx”) hereby requests, pursuant to Rule 461 of Regulation C, that the effective date of its Registration Statement on Form S-3, as amended, be accelerated so that it is declared effective at 5:00 p.m. on June 22, 2009 or as soon thereafter as practicable.

Hemispherx acknowledges that the disclosure in the filing is the responsibility of Hemispherx.

Hemispherx also represents to the Commission that should the Commission or the staff acting pursuant to delegated authority, declare the filing effective, it does not foreclose the Commission from taking any action with respect to the filing and Hemispherx represents that it will not assert this action as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

Hemispherx further acknowledges, that the action of the Commission or the staff, acting pursuant to delegated authority, in declaring the filing effective does not relieve Hemispherx from its full responsibility for the adequacy and accuracy of the disclosures in the filing.

Very truly yours,

HEMISPHERX  
BIOPHARMA, INC.

By: /s/ William A. Carter  
William A. Carter, MD  
Chief Executive Officer