HEMISPHERX BIOPHARMA INC
Form 424B3
April 27, 2009

Filed Pursuant to Rule 424(b)(3)
Registration No. 333-152727

HEMISPHERX BIOPHARMA, INC.

21,300,000 Shares of Common Stock

The Offering:

This Prospectus relates to the sale of up to 21,300,000 shares of our common stock by Fusion Capital Fund II, LLC. Fusion Capital is sometimes referred to in this Prospectus as the selling stockholder. The prices at which Fusion Capital may sell the shares will be determined by the prevailing market price for the shares or in negotiated transactions. We will not receive proceeds from the sale of our shares by Fusion Capital, but we will receive proceeds from sales of shares to Fusion Capital.

Our common stock is registered under Section 12(g) of the Securities Exchange Act of 1934 and quoted on the NYSE Amex (formerly, the American Stock Exchange) under the symbol "HEB." On April 23, 2009, the last reported sale price for our common stock as reported on the NYSE Amex was $0.48 per share.

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

Please see the risk factors beginning on page 6 to read about certain factors you should consider before buying shares of common stock.

The selling stockholder is an "underwriter" within the meaning of the Securities Act of 1933.

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

The date of this Prospectus is April 24, 2009

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WHERE YOU CAN FIND MORE INFORMATION

This Prospectus is part of a registration statement on Form S-1 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. Statements contained in this Prospectus as to the contents of any contract or other document are not necessarily complete and, in each instance, we refer you to the copy of that contract or document filed as an exhibit to the Registration Statement.

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 or through our website at 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.

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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 an important part of this Prospectus, and you should review that information in order to understand the nature of any investment by you in our common stock. Information contained in this Prospectus automatically updates and supersedes previously filed information. We are incorporating by reference the following

documents:

(a) Our annual report on Form 10-K for our fiscal year ended December 31, 2008, SEC File No. 1-13441.

(b) Our current report on Form 8-K, SEC File No. 1-13441 filed with the SEC on February 19, 2009.

(c) All of our filings pursuant to Sections 13(a) or 15(d) under the Securities Exchange Act of 1934, as amended, since the date of the filing of our Annual Report on Form 10-K for the fiscal year ended December 31, 2008 through the date of this Prospectus.

We will provide to each person, including any beneficial owner, to whom a Prospectus is delivered, a copy of any or all of the reports or documents that we have incorporated by reference in this Prospectus, at no cost. To obtain any such documents please write or telephone us at the following address: Hemispherx Biopharma, Inc., 1617 JFK Boulevard, Philadelphia, Pennsylvania 19103, telephone number 215-988-0080. In addition, these documents may be accessed at our website at www.hemispherx.net via a link to the SEC's website. Information contained on our website is not considered to be a part of, nor incorporated by reference in, this Prospectus.

You should rely only on the information incorporated by reference or provided in this Prospectus or any supplement. We have not authorized anyone else to provide you with different information. We and the selling stockholder 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 that the date on the front of those documents.

PROSPECTUS SUMMARY

This Prospectus provides you with a general description of the common stock being offered. You should read this Prospectus, including all documents incorporated herein by reference, together with additional information described under the heading "Where You Can Find More Information."

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

About Hemispherx

We are a biopharmaceutical company engaged in the clinical development, manufacture, marketing and distribution of new drug 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(R) and Alferon N

Injection(R). 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(R) 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(R) is an experimental drug currently undergoing clinical development for the treatment of CFS. In August 2004, we completed a Phase III clinical trial ("AMP 516") treating over 230 CFS patients with Ampligen(R) and are presently in the registration process for a new drug application ("NDA") with the Food and Drug Administration ("FDA"). Ampligen represents the first drug in the class of RNA (nucleic acid) molecules to apply for NDA review.

On July 7, 2008, the FDA accepted our NDA for review. On February 18, 2009, we were notified by the FDA that the originally scheduled Prescription Drug User Fee Act date of February 25, 2009 has been extended to May 25, 2009.

We own and operate a 43,000 sq. ft. FDA approved facility in New Brunswick, NJ primarily designed to produce Alferon N Injection(R). In 2006, we completed the installation of a polymer production line to produce Ampligen(R) 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.

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Fusion Capital Transaction

On July 2, 2008, we entered into a Common Stock Purchase Agreement with Fusion Capital Fund II, LLC, an Illinois limited liability company. Under the Purchase Agreement, Fusion Capital is obligated, under certain conditions, to purchase shares from us in an aggregate amount of up to $30 million from time to time over a 25 month period from August 21, 2008. Under the terms of the Purchase Agreement, Fusion Capital has received a commitment fee consisting of 650,000 shares of our common stock. Also, we will issue to Fusion Capital up to an additional 650,000 shares as a commitment fee pro rata as we receive the $30 million of future funding. We originally registered herein 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 April 23, 2009 we have sold an aggregate of 4,377,515 shares to Fusion Capital (exclusive of any shares issued as a commitment fee) under the Purchase Agreement for gross proceeds of approximately $1,860,000.

Our common stock is quoted on the NYSE Amex (formerly, the American Stock Exchange) under the symbol "HEB." In connection with this transaction, under the rules of the NYSE Amex, we may not issue more than 14,823,651 shares (19.99% of our outstanding shares as of July 2, 2008, the date of the Purchase Agreement) without first obtaining the approval of our stockholders. Under the Purchase Agreement and a Registration Rights Agreement with Fusion Capital we are required to register and have included in the offering pursuant to this Prospectus (1) 650,000 shares which have already been issued, (2) an additional 650,000 shares which we may issue in the future as a commitment fee pro rata as

we receive up to the $30 million of future funding and (3) at least 13,523,651 shares which we may sell to Fusion Capital after this registration statement is declared effective. In the aggregate, this is 14,823,651 or 19.99% of our outstanding shares on July 2, 2008, the date of the Purchase Agreement.

Under the Purchase Agreement, we have the right but not the obligation to sell more than the 20,000,000 shares to Fusion Capital (excluding the 1,300,000 shares we have issued or may issue to Fusion Capital as a commitment fee). This 21,300,000 shares is greater than 19.99% of our outstanding shares of common stock as of the date of the Purchase Agreement. On November 11, 2008, at our Annual Meeting of Stockholders, we received stockholder approval of the Purchase Agreement in order to be in compliance with the NYSE Amex rules permitting us to sell more than 14,823,651 or 19.99% of our outstanding shares on July 2, 2008, the date of the Purchase Agreement.

As of the date of this Prospectus, we do not have any plans or intent to sell to Fusion Capital any shares beyond the 20,000,000 shares offered hereby (excluding the 1,300,000 shares we have issued or may issue to Fusion Capital as a commitment fee). However, if we elect to sell more than the 20,000,000 shares, which we have the right but not the obligation to do, we must first register under the Securities Act any additional shares we may elect to sell to Fusion Capital before we can sell such additional shares, which could cause substantial dilution to our stockholders.

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Generally, we have the right but not the obligation from time to time to sell our shares to Fusion Capital in amounts between $120,000 and $1.0 million depending on certain conditions. We have the right to control the timing and amount of any sales of our shares to Fusion Capital. The purchase price of the shares will be determined based upon the market price of our shares without any fixed discount at the time of each sale. Fusion Capital does not have the right nor the obligation to purchase any shares of our common stock on any business day that the price of our common stock is below $0.40. There are no negative covenants, restrictions on future fundings, penalties or liquidated damages in the Purchase Agreement or the Registration Rights Agreement. The Purchase Agreement may be terminated by us at any time at our discretion without any cost to us.

The number of shares ultimately offered for sale by Fusion Capital is dependent upon the number of shares purchased by Fusion Capital under the Purchase Agreement.

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

products will be generally available for commercial sale for any indication. Generally, only a small percentage of potential therapeutic products are eventually approved by the FDA for commercial sale. Please see the next risk factor.

Alferon N Injection(R). Although Alferon N Injection(R) 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.

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

All of our drugs and associated technologies, other than Alferon N Injection(R), are investigational and must receive prior regulatory approval by appropriate regulatory authorities for general use and are currently legally available only through clinical trials with specified disorders. At present, Alferon N Injection(R) is only approved for the intra-lesional treatment of refractory or recurring external genital warts in patients 18 years of age or older. Use of Alferon N Injection(R) for other indications will require regulatory approval.

Our products, including Ampligen(R), are subject to extensive regulation by numerous governmental authorities in the U.S. and other countries, including, but not limited to, the FDA in the U.S., the Health Protection Branch ("HPB") of Canada, and the Agency for the Evaluation of Medicinal Products ("EMEA") in Europe. Obtaining regulatory approvals is a rigorous and lengthy process and requires the expenditure of substantial resources. In order to obtain final regulatory approval of a new drug, we must demonstrate to the satisfaction of the regulatory agency that the product is safe and effective for its intended uses and that we are capable of manufacturing the product to the applicable regulatory standards. We require regulatory approval in order to market Ampligen(R) or any other proposed product and receive product revenues or royalties. We cannot assure you that Ampligen(R) will ultimately be demonstrated to be safe or efficacious. In addition, while Ampligen(R) is authorized for use in clinical trials 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 an RTF 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(R) 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 Prescription Drug User Fee Act date of February 25, 2009 has been extended to May 25, 2009.

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If Ampligen(R) or one of our other products does not receive regulatory

approval in the U.S. or elsewhere, our operations most likely will be materially adversely affected.

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(R), approved. As of December 31, 2008, our accumulated deficit was approximately $197,409,000. 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 December 31, 2008, we had approximately $6,119,000 in cash and cash equivalents and short-term investments. Given the harsh economic conditions, we have reviewed every aspect of our operations for cost and spending reductions to assure the long term survival of our Company while maintaining the resources necessary to achieve our primary objectives of obtaining NDA approval of Ampligen(R) and securing a strategic partner. Based on these actions, we anticipate, but cannot assure, that these funds will be sufficient to meet our operating cash requirements for the next 16 months.

We have in place two potential sources of financing: 1) the Common Stock Purchase Agreement (the "Purchase Agreement") with Fusion Capital Fund II, LLC ("Fusion") pursuant to which we have the right to sell shares of our Common Stock to Fusion; and 2) a Standby Financing Agreement with certain of our executives, directors and strategic consultants.

We anticipate, but cannot assure, that we will be able to raise additional capital from the sale of shares to Fusion Capital under the 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. As of April 23, 2009, we have sold an aggregate of 4,377,515 shares to Fusion Capital (exclusive of any shares issued as a commitment fee) under the Purchase Agreement for gross proceeds of approximately $1,860,000. Since we registered an aggregate of 20,000,000 shares for sale to Fusion Capital pursuant to this Prospectus (exclusive of the 1,300,000 shares issued or to be issued as a commitment fee), the selling price of the remaining 15,622,485 shares we can sell to Fusion Capital will have to average at least $1.80 per share for us to receive the maximum proceeds of $30 million. Assuming a purchase price of $0.48 per share (the closing sale price of the common stock on April 23, 2009) and the purchase by Fusion Capital of the full 15,622,485 shares remaining under the Purchase Agreement, proceeds to us would only be $7,498,793. Subject to approval by our board of directors, we have the right but not the obligation to issue more than 20,000,000 shares to Fusion Capital. In the event we elect to issue more than 20,000,000 shares offered hereby, we will be required to file a new registration statement and have it declared effective by the Securities and Exchange

Commission.

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The extent we rely on Fusion Capital as a source of funding will depend on a number of factors including, the prevailing market price of our common stock and the extent to which we are able to secure working capital from other sources. Specifically, Fusion Capital does not have the right nor the obligation to purchase any shares of our common stock on any business days that the market price of our common stock is less than $0.40. While the current market price is in excess of $0.40 per share, during the past few months, the price of our common stock often has been below $0.40.

In February 2009, we entered into a Standby Financing Agreement pursuant to which certain individuals ("Individuals"), consisting of Dr. Carter and Thomas Equels, agreed to loan us up to an aggregate of $1,000,000 in funds should we be unable to obtain additional financing, if needed. Under the Standby Financing Agreement, we will use our best efforts in 2009 to obtain one or more additional financing agreements on such terms as our Board deems to be reasonable and appropriate in order to maintain our operations. If at any time after December 1, 2009 and prior to June 30, 2010 a majority of our independent Directors deems that in the event a financing of at least $2.5 Million has not been obtained and additional funds are needed to maintain our operations, we will send a written notice to each of the Individuals informing them of the total amount of additional funds required and the specific amount that will be required from each Individual. Within fifteen calendar days after receipt of the notice, the Individuals will be required to pay us their respective amount. We will then issue to them one year 15% senior secured notes for their respective amounts (the "Notes"). Interest will be paid monthly in our Common Stock. Repayment of the principal and interest under the Notes will be secured by all of our assets. We will not, without the consent of the Individuals, (i) incur any new debt senior or pari passu to the Notes or (ii) encumber or grant a security interest in any assets. Upon 20 business days written notice, we may prepay the Notes in cash at any time at 105% of the then outstanding principal amount of the Notes, plus any accrued but unpaid interest.

For agreeing to be obligated to loan us money, each Individual received 10 year warrants (the "Commitment Warrants") to purchase our common stock at the rate of $50,000 worth in warrants per $100,000 committed. The exercise price of these warrants is $0.51 (125% of the market closing price of our Common Stock on the date that Agreement was executed). These warrants vested immediately. If and when we notify the Individuals that we are consummating the Standby Financing, upon each Individual's payment of his committed amount, he will receive additional 10 year warrants to purchase our Common Stock at the rate of $50,000 worth in warrants per $100,000 paid. The exercise price of the warrants will be the closing market price of our Common Stock on the day we receive the funds from the Individuals. These warrants will vest immediately. While any portion of the Notes are outstanding, Individuals will have weighted average anti-dilution rights with regard to the exercise price of all warrants issued pursuant to the Standby Financing, except that these rights will not apply if the securities are issued to employees, Board members, corporate and scientific advisors, select vendors, pursuant to the Purchase Agreement with Fusion Capital or part of a corporate or strategic alliance.

If we are unable to obtain sufficient financing from the sale of securities to Fusion Capital and/or the Standby Financing Agreement and if we are unable to commercialize and sell Ampligen(R), Alferon N Injection(R) or other products, we 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(R) products. In this regard we previously registered $50,000,000 worth of our securities in a universal

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shelf registration statement, none of which has been designated or issued. 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 the financing we require be unavailable or prohibitively expensive when we require it, the consequences could be a material adverse effect on our ability to develop our products or continue our operations.

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

Our finished goods inventory of Alferon N Injection(R) reached it's expiration date in March 2008. As a result, we have no product to sell at this time. The FDA has 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(R) 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(R) 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(R) NDA. Work on the Alferon N Injection(R) is expected to resume in mid-2009 under the condition that adequate funding is obtained, which means that we may not have any Alferon N Injection(R) product commercially available until 2010.

In 2007, we averaged Alferon N Injection(R) sales of approximately $77,000 per month. However with no FDA approval to extend the expiration date of our finished good inventory, we will no longer receive these monthly revenues. In addition, 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(R) enhances the effectiveness of different drug combinations on avian influenza, preliminary testing in the laboratory is not necessarily predictive of successful results in clinical testing or human treatment.

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

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

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

We need to preserve and acquire enforceable patents covering the use of Ampligen(R) for a particular disease in order to obtain exclusive rights for the commercial sale of Ampligen(R) for such disease. We obtained all rights to Alferon N Injection(R), and we plan to preserve and acquire enforceable patents covering its use for existing and potentially new diseases. Our success depends, in large part, on our ability to preserve and obtain patent protection for our

products and to obtain and preserve our trade secrets and expertise. Certain of our know-how and technology is not patentable, particularly the procedures for the manufacture of our experimental drug, Ampligen(R), which is carried out according to standard operating procedure manuals. We also have been issued patents on the use of Ampligen(R) in combination with certain other drugs for the treatment of chronic Hepatitis B virus, chronic Hepatitis C virus, and a patent which affords protection on the use of Ampligen(R) in patients with Chronic Fatigue Syndrome. We have not yet been issued any patents in the United States for the use of Ampligen(R) as a sole treatment for any of the cancers, which we have sought to target. With regard to Alferon N Injection(R), we have acquired from ISI its patents for natural alpha interferon produced from human peripheral blood leukocytes and its production process and we have filed a patent application for the use of Alferon(R) 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.

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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(R)-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.

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

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

There are a limited number of manufacturers in the United States available to provide the polymers for use in manufacturing Ampligen(R). 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(R) 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(R) and the commercial production of Alferon N Injection(R) and other products which we may commercially produce are subject to fluctuation depending on a variety of

factors beyond our control, including competitive factors, changes in technology, and FDA and other governmental regulations and there can be no assurance that we will be able to obtain such products and materials on terms acceptable to us or at all.

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

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

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We have limited manufacturing experience and capacity.

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

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

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

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

The pharmaceutical and biotechnology industries are subject to rapid and substantial technological change. Technological competition from pharmaceutical and biotechnology companies, universities, governmental entities and others diversifying into the field is intense and is expected to increase. Most of these entities have significantly greater research and development capabilities than us, as well as substantial marketing, financial and managerial resources, and represent significant competition for us. There can be no assurance that developments by others will not render our products or technologies obsolete or noncompetitive or that we will be able to keep pace with technological developments.

Our products may be subject to substantial competition.

Ampligen(R). Competitors may be developing technologies that are, or in the future may be, the basis for competitive products. Some of these potential products may have an entirely different approach or means of accomplishing similar therapeutic effects to products being developed by us. These competing products may be more effective and less costly than our products. In addition, conventional drug therapy, surgery and other more familiar treatments may offer competition to our products. Furthermore, many of our competitors have significantly greater experience than us in pre-clinical testing and human clinical trials of pharmaceutical products and in obtaining FDA, HPB and other regulatory approvals of products. Accordingly, our competitors may succeed in obtaining FDA, HPB or other regulatory product approvals more rapidly than us.
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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(R) on the immune system, we cannot assure that we will be able to compete.

ALFERON N Injection(R). 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(R) currently competes with Schering's injectable recombinant alpha interferon product (INTRON(R) A) for the treatment of genital warts. 3M Pharmaceuticals also offer competition from its immune-response modifier, Aldara(R), 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, VeregenTM, which is indicated for the topical treatment of external genital and perianal warts. Alferon N Injection(R) also competes with surgical, chemical, and other methods of treating genital warts. We cannot assess the impact products developed by our competitors, or advances in other methods of the treatment of genital warts, will have on the commercial viability of Alferon N Injection(R). If and when we obtain additional approvals of uses of this product, we expect to compete primarily on the basis of product performance. Our 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(R) for the treatment of new indications, we will be able to achieve any significant penetration into those markets. In addition, because certain competitive products are not dependent on a source of human blood cells, such products may be able to be produced in greater volume and at a lower cost than Alferon N Injection(R). Currently, our wholesale price on a per unit basis of Alferon N Injection(R) is

higher than that of the competitive recombinant alpha and beta interferon products.

General. Other companies may succeed in developing products earlier than we do, obtaining approvals for such products from the FDA more rapidly than we do, or developing products that are more effective than those we may develop. While we will attempt to expand our technological capabilities in order to remain competitive, there can be no assurance that research and development by others or other medical advances will not render our technology or products obsolete or non-competitive or result in treatments or cures superior to any therapy we develop.

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

Ampligen(R). We believe that Ampligen(R) has been generally well tolerated with a low incidence of clinical toxicity, particularly given the severely debilitating or life threatening diseases that have been treated. A mild flushing reaction has been observed in approximately 15-20% 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(R) in certain clinical situations and therefore, could adversely affect potential revenues and physician/patient acceptability of our product.

Alferon N Injection(R). At present, Alferon N Injection(R) is only approved for the 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(R), patients did not experience serious side effects; however, there can be no assurance that unexpected or unacceptable side effects will not be found in the future for this use or other potential uses of Alferon N Injection(R) which could threaten or limit such product's usefulness.

We may be subject to product liability claims from the use of Ampligen(R), Alferon N Injection(R), or other of our products which could negatively affect our future operations. We 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(R) or other of our products results in adverse effects. This liability might result from claims made directly by patients, hospitals, clinics or other consumers, or by pharmaceutical companies or others manufacturing these products on our behalf. Our future operations may be negatively affected from the litigation costs, settlement expenses and lost

product sales inherent to these claims. While we will continue to attempt to take appropriate precautions, we cannot assure that we will avoid significant product liability exposure.

On November 28, 2008, as we disclosed in an 8-K, we suspended product liability insurance for Alferon(R) N and Ampligen(R) until we receive regulatory clearance for Ampligen(R). We now require third parties to indemnify us in conjunction with all overseas emergency sales of Ampligen(R) and Alferon(R) LDO. We concluded that years of successfully addressing the limited number of product liability claims filed against Ampligen(R) and Alferon(R) 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.

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Currently, without product liability coverage for Ampligen(R) and Alferon(R) 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(R), and his knowledge of our overall activities, including patents and clinical trials. As a result of our implementation of the Employee Wage Or Hours Reduction Program, our staff has agreed to take a portion of their compensation in shares of our Common Stock. While we believe that our employees are dedicated to us and while we have incentivised them to remain with us through the establishment of a Bonus Pool that would award them money in the event that the FDA approves our NDA for Ampligen(R), we cannot assure that they will remain with us. 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(R). 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.

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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; o 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 (formerly, the American Stock Exchange). For the 12-month period ended December 31, 2008, the price of our common stock has ranged from $0.25 to $1.20 per share. We expect the price of our common stock to remain volatile. The average daily trading volume of our common stock varies significantly. Our relatively low average volume and low average number of transactions per day may affect the ability of our stockholders to sell their shares in the public market at prevailing prices and a more active market may never develop.

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

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The sale of our common stock to Fusion Capital may cause dilution and the sale of the shares of common stock acquired by Fusion Capital could cause the price of our common stock to decline.

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 the date of this Prospectus we have sold an aggregate of 4,377,515 shares to Fusion Capital (exclusive of any shares issued as a commitment fee) under the Purchase Agreement for gross proceeds of approximately $1,860,000, leaving 15,622,485 shares (exclusive of additional shares issuable as a commitment fee). The number of shares ultimately offered for sale by Fusion Capital under this Prospectus is dependent upon the number of shares purchased by Fusion Capital under the agreement. The purchase price for the common stock to be sold to Fusion Capital pursuant to the Purchase Agreement will fluctuate based on the price of our common stock. It is anticipated that shares offered pursuant to this Prospectus could be sold over a period of up to 16 months after the date hereof. Depending upon market conditions at the time, a sale of shares by Fusion Capital at any given time could cause the trading price of our common stock to decline. Fusion Capital may ultimately purchase all, some or none of the 15,622,485 shares (exclusive of additional shares issued or to be issued as a commitment fee) registered herein but not yet issued. After it has acquired such shares, it may sell all, some or none of such shares. Therefore, sales to Fusion Capital by us under the Purchase Agreement may result in substantial dilution to the interests of other holders of our common stock. The sale of a substantial number of shares of our common stock 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.

In addition to the shares registered for Fusion Capital, we have previously registered 135% 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 the warrants is less than the market price of the common stock, the holders of the warrants are likely to exercise them and sell the underlying shares of common stock and to the extent that the conversion price and exercise price of these securities are adjusted pursuant to anti-dilution protection, the securities could be exercisable or convertible for even more shares of common stock. We also may issue shares to be used to meet our capital requirements or use shares to compensate employees, consultants and/or directors. In this regard, we previously registered $50,000,000 worth of our securities in a universal shelf registration statement, none of which has been designated or issued. 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 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.

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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 8.9% of our common stock, the Plan's threshold will be 20%, instead of 15%. The Rights will expire on November 19, 2012, and may be redeemed prior thereto at $.01 per Right under certain circumstances.

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

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Certain statements in this Prospectus constitute "forwarding-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities and Exchange Act of 1995 (collectively, the "Reform Act"). Certain, but not necessarily all, of such forward-looking statements can be identified by the use of forward-looking

terminology such as "believes," "expects," "may," "will," "should," or "anticipates" or the negative thereof or other variations thereon or comparable terminology, or by discussions of strategy that involve risks and uncertainties. All statements other than statements of historical fact, included in this Prospectus regarding our financial position, business strategy and plans or objectives for future operations are forward-looking statements. Without limiting the broader description of forward-looking statements above, we specifically note that statements regarding potential drugs, their potential therapeutic effect, the possibility of obtaining regulatory approval, our ability to manufacture and sell any products, market acceptance or our ability to earn a profit from sales or licenses of any drugs or our ability to discover new drugs in the future are all forward-looking in nature.

Such forward-looking statements involve known and unknown risks, uncertainties and other factors, including but not limited to, the risk factors discussed 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.

BUSINESS

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2008, incorporated by reference into this Prospectus, contains information about us, including audited financial statements for our fiscal year ended December 31, 2008. Please refer to this report for additional information.

SELLING STOCKHOLDER

The following table presents information regarding the selling stockholder, Fusion Capital. Neither the selling stockholder nor any of its affiliates has held a position or office, or had any other material relationship, with us. However, in July 2005 we entered into a prior common stock purchase agreement with Fusion Capital, pursuant to which we sold an aggregate of 8,791,838 shares for total gross proceeds of $20,000,000. In April 2006 we entered into a prior common stock purchase agreement with Fusion Capital, pursuant to which we sold an aggregate of 10,682,032 shares for total gross proceeds of approximately $19,739,000 through November, 2007. Each of these transactions was substantially similar to the transaction set forth herein.

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Selling Stockholder	Shares Beneficially Owned Before Offering	Percentage of Outstanding Shares Beneficially Owned Before Offering (1)	Shares to be Sold in the Offering Assuming The Company Issues The Maximum Remaining Number of Shares Under the Purchase Agreement (1)	P Outs Bene Af
Fusion Capital Fund II, LLC (2)	1,098,814 (3)	1.5%	21,300,000 (3)	L

(1) Applicable percentage of ownership is based on 74,960,278 shares of our common stock outstanding as of August 1, 2008 (prior to the commencement of the offering), together with securities exercisable or convertible into shares of Common Stock within sixty (60) days of that date for the selling stockholder. Beneficial ownership is determined in accordance with the rules of the SEC and generally includes voting or investment power with respect to securities. Shares of common stock are deemed to be beneficially owned by the person holding such securities for the purpose of computing the percentage of ownership of such person, but are not treated as outstanding for the purpose of computing the percentage ownership of any other person.

(2) Steven G. Martin and Joshua B. Scheinfeld, the principals of Fusion Capital, are deemed to be beneficial owners of all of the shares of common stock owned by Fusion Capital. Messrs. Martin and Scheinfeld have shared voting and disposition power over the shares being offered under this Prospectus.

(3) We have included in this Prospectus 21,300,000 shares in the aggregate. The numbers in the above table are as of August 1, 2008, prior to the commencement of the offering. As of the date of the Prospectus, the 21,300,000 shares consist of the following:4,377,515 shares which we have issued and sold to Fusion Capital, 15,622,485 shares which are not presently issued and which we may sell to Fusion Capital at our discretion, 690,300 shares we have issued to Fusion Capital as a commitment fee and 609,700 shares we may issue to Fusion Capital as a commitment fee. Therefore, we may issue to Fusion Capital up to an additional 16,232,185 shares under the Purchase Agreement but Fusion Capital does not presently beneficially own those shares as determined in accordance with the rules of the SEC. Prior to entering into the Purchase Agreement Fusion Capital owned 448,814 of our shares that it previously acquired.

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The Fusion Transaction

General

On July 2, 2008, we entered into a Common Stock Purchase Agreement with Fusion Capital Fund II, LLC, an Illinois limited liability company. Under the Purchase Agreement, Fusion Capital is obligated, under certain conditions, to purchase shares from us in an aggregate amount of up to $30 million from time to time over a 25 month period from August 21, 2008. Under the terms of the Purchase Agreement, Fusion Capital has received a commitment fee consisting of 650,000 shares of our common stock. Also, we will issue to Fusion Capital up to an additional 650,000 shares as a commitment fee pro rata as we receive the $30 million of future funding. We originally registered herein 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 April 23, 2009, we have sold an aggregate of 4,377,515 shares to Fusion Capital (exclusive of any shares issued as a commitment fee) under the Purchase Agreement for gross proceeds of approximately $1,860,000.

Our common stock is quoted on the NYSE Amex (formerly, the American Stock Exchange) under the symbol "HEB." In connection with this transaction, under the rules of the NYSE Amex, we may not issue more than 14,823,651 shares (19.99% of our outstanding shares as of July 2, 2008, the date of the Purchase Agreement) without first obtaining the approval of our stockholders. Under the Purchase Agreement and a Registration Rights Agreement with Fusion Capital we are required to register and have included in the offering pursuant to this

Prospectus (1) 650,000 shares which have already been issued, (2) an additional 650,000 shares which we may issue in the future as a commitment fee pro rata as we receive up to the $30 million of future funding and (3) at least 13,523,651 shares which we may sell to Fusion Capital after this registration statement is declared effective. In the aggregate, this is 14,823,651 or 19.99% of our outstanding shares on July 2, 2008, the date of the Purchase Agreement.

Under the Purchase Agreement, we have the right but not the obligation to sell more than the 20,000,000 shares to Fusion Capital (excluding the 1,300,000 shares we have issued or may issue to Fusion Capital as a commitment fee). This 21,300,000 shares is greater than 19.99% of our outstanding shares of common stock as of the date of the Purchase Agreement. The number of shares ultimately offered for sale by Fusion Capital is dependent upon the number of shares purchased by Fusion Capital under the Purchase Agreement. On November 11, 2008, at our Annual Meeting of Stockholders we received stockholder approval of the Purchase Agreement in order to be in compliance with the NYSE Amex rules permitting us to sell more than 14,823,651 or 19.99% of our outstanding shares on July 2, 2008, the date of the Purchase Agreement.

As of the date of this Prospectus, we do not have any plans or intent to sell to Fusion Capital any shares beyond the 20,000,000 shares offered hereby (excluding the 1,300,000 shares we have issued or may issue to Fusion Capital as a commitment fee). However, if we elect to sell more than the 20,000,000 shares, which we have the right but not the obligation to do, we must first register under the Securities Act any additional shares we may elect to sell to Fusion Capital before we can sell such additional shares, which could cause substantial dilution to our stockholders.

Generally, we have the right but not the obligation from time to time to sell our shares to Fusion Capital in amounts between $120,000 and $1.0 million depending on certain conditions. We have the right to control the timing and amount of any sales of our shares to Fusion Capital. The purchase price of
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the shares will be determined based upon the market price of our shares without any fixed discount at the time of each sale. Fusion Capital does not have the right nor the obligation to purchase any shares of our common stock on any business day that the price of our common stock is below $0.40. There are no negative covenants, restrictions on future fundings, penalties or liquidated damages in the Purchase Agreement or the Registration Rights Agreement. The Purchase Agreement may be terminated by us at any time at our discretion without any cost to us.

The number of shares ultimately offered for sale by Fusion Capital is dependent upon the number of shares purchased by Fusion Capital under the Purchase Agreement.

Purchase Of Shares Under The Purchase Agreement

Under the common stock purchase agreement, on any business day selected by us, we may direct Fusion Capital to purchase up to $120,000 of our common stock. The purchase price per share is equal to the lesser of:

- the lowest sale price of our common stock on the purchase date; or
- the average of the three (3) lowest closing sale prices of our common stock during the twelve (12) consecutive business days prior to the date of a purchase by Fusion Capital.

The purchase price will be equitably adjusted for any reorganization, recapitalization, non-cash dividend, stock split, or other similar transaction occurring during the business days used to compute the purchase price. We may direct Fusion Capital to make multiple purchases from time to time in our sole

discretion; no sooner then every two business days.

Our Right To Increase the Amount to be Purchased

In addition to purchases of up to $120,000 from time to time, we may also from time to time elect on any single business day selected by us to require Fusion Capital to purchase our shares in an amount up to $150,000 provided that our share price is not below $0.80 during the two business days prior to and on the purchase date. We may increase this amount to up to $250,000 if our share price is not below $1.25 during the two business days prior to and on the purchase date. This amount may also be increased to up to $500,000 if our share price is not below $1.75 during the two business days prior to and on the purchase date. This amount may also be increased to up to $1,000,000 if our share price is not below $4.00 during the two business days prior to and on the purchase date. We may direct Fusion Capital to make multiple large purchases from time to time in our sole discretion; however, at least two business days must have passed since the most recent large purchase was completed. The price at which our common stock would be purchased in this type of larger purchases will be the lesser of (i) the lowest sale price of our common stock on the purchase date and (ii) the lowest purchase price (as described above) during the previous ten business days prior to the purchase date.

Minimum Purchase Price

Under the common stock purchase agreement, we have set a minimum purchase price ("floor price") of $0.40. However, Fusion Capital does not have the right nor the obligation to purchase any shares of our common stock in the event that the purchase price would be less the floor price. Specifically, Fusion Capital does not have the right or the obligation to purchase shares of our common stock on any business day that the market price of our common stock is below $0.40.

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Events of Default

Generally, Fusion Capital may terminate the common stock purchase agreement without any liability or payment to us upon the occurrence of any of the following events of default:

- the effectiveness of the registration statement of which this Prospectus is a part of lapses for any reason (including, without limitation, the issuance of a stop order) or is unavailable to Fusion Capital for sale of our common stock offered hereby and such lapse or unavailability continues for a period of ten consecutive business days or for more than an aggregate of 30 business days in any 365-day period;

- suspension by the NYSE Amex of our common stock from trading for a period of three consecutive business days;

- the de-listing of our common stock from the NYSE Amex provided our common stock is not immediately thereafter trading on the Nasdaq OTC Bulletin Board Market, the Nasdaq Global Market, the Nasdaq Capital Market, or the New York Stock Exchange;

- the transfer agent`s failure for five business days to issue to Fusion Capital shares of our common stock which Fusion Capital is entitled to under the common stock purchase agreement;

- any material breach of the representations or warranties or covenants contained in the common stock purchase agreement or any related agreements which has or which could have a material adverse effect on us subject to a cure period of five business days; or

o any participation or threatened participation in insolvency or bankruptcy proceedings by or against us.

Our Termination Rights

We have the unconditional right at any time for any reason to give notice to Fusion Capital terminating the Purchase Agreement without any cost to us.

No Short-Selling or Hedging by Fusion Capital

Fusion Capital has agreed that neither it nor any of its affiliates shall engage in any direct or indirect short-selling or hedging of our common stock during any time prior to the termination of the common stock purchase agreement.

Effect of Performance of the Purchase Agreement on Our Stockholders

All 21,300,000 shares offered in this Prospectus are expected to be freely tradable and will be sold over a period of up to 16 months from the date of this Prospectus. The sale by Fusion Capital of a significant amount of shares at any given time could cause the market price of our common stock to decline and to be highly volatile. We may sell to Fusion Capital all, some or none of the remaining 15,622,485 shares of common stock not yet sold or issued but part of this offering. After Fusion Capital has acquired any of such shares, it may sell all, some or none of such shares. Therefore, sales to Fusion Capital by us under the agreement may result in substantial dilution to the interests of other holders of our common stock. 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. The number of shares ultimately offered for sale by Fusion Capital under this Prospectus is dependent upon the number of shares purchased by Fusion Capital under the Purchase Agreement. The following table sets forth the amount of proceeds we would receive from Fusion Capital from the sale of the remaining 15,622,485 shares at varying purchase prices:

Assumed Average Purchase Price	Number of Remaining Shares to be Issued if Full Purchase	Percentage of Outstanding Shares After Giving Effect to the Issuance of Such Shares to Fusion Capital(1)	Proceeds from the Shares to Fusion C the Second Column Purchase Agreement
$0.40	15,622,485	16.0%	$ 6,248,994
$0.48 (2)	15,622,485	16.0%	$ 7,498,793
$0.75	15,622,485	16.0%	$ 11,716,864

$1.00	15,622,485	16.0%	$ 15,622,485
$1.50	15,622,485	16.0%	$ 23,433,728
$2.00	14,070,000	14.4%	$ 28,140,000

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(1) The denominator is based on the number of remaining shares to be issued as listed in the second column plus the 83,529,962 shares outstanding as of April 23, 2009, which includes 5,067,815 shares previously issued to Fusion Capital in connection with the Purchase Agreement. The numerator is based on the number of remaining shares sold under the Purchase Agreement at the corresponding assumed purchase price set forth in the adjacent column.

(2) Closing sale price of our shares on April 23, 2009.

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PLAN OF DISTRIBUTION

The common stock offered by this Prospectus is being offered by Fusion Capital Fund II, LLC, the selling stockholder. The common stock may be sold or distributed from time to time by the selling stockholder directly to one or more purchasers or through brokers, dealers, or underwriters who may act solely as agents at market prices prevailing at the time of sale, at prices related to the prevailing market prices, at negotiated prices, or at fixed prices, which may be changed. The sale of the common stock offered by this Prospectus may be effected in one or more of the following methods:

- ordinary brokers' transactions;
- transactions involving cross or block trades;
- through brokers, dealers, or underwriters who may act solely as agents;
- "at the market" into an existing market for the common stock;
- in other ways not involving market makers or established business markets, including direct sales to purchasers or sales effected through agents;
- in privately negotiated transactions; or
- any combination of the foregoing.

In order to comply with the securities laws of certain states, if applicable, the shares may be sold only through registered or licensed brokers or dealers. In addition, in certain states, the shares may not be sold unless they have been registered or qualified for sale in the state or an exemption from the registration or qualification requirement is available and complied with.

Brokers, dealers, underwriters, or agents participating in the distribution of the shares as agents may receive compensation in the form of commissions, discounts, or concessions from the selling stockholder and/or purchasers of the common stock for whom the broker-dealers may act as agent. The compensation paid to a particular broker-dealer may be less than or in excess of customary commissions.

Fusion Capital is an "underwriter" within the meaning of the Securities Act.

Neither we nor Fusion Capital can presently estimate the amount of compensation that any agent will receive. We know of no existing arrangements between Fusion Capital, any other stockholder, broker, dealer, underwriter, or

agent relating to the sale or distribution of the shares offered by this Prospectus. At the time a particular offer of shares is made, a prospectus supplement, if required, will be distributed that will set forth the names of any agents, underwriters, or dealers and any compensation from the selling stockholder, and any other required information.

We will pay all of the expenses incident to the registration, offering, and sale of the shares to the public other than commissions or discounts of underwriters, broker-dealers, or agents. We have also agreed to indemnify Fusion Capital and related persons against specified liabilities, including liabilities under the Securities Act.

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Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers, and controlling persons, we have been advised that in the opinion of the SEC this indemnification is against public policy as expressed in the Securities Act and is therefore, unenforceable.

Fusion Capital and its affiliates have agreed not to engage in any direct or indirect short selling or hedging of our common stock during the term of the common stock purchase agreement.

We have advised Fusion Capital that while it is engaged in a distribution of the shares included in this Prospectus it is required to comply with Regulation M promulgated under the Securities Exchange Act of 1934, as amended. With certain exceptions, Regulation M precludes the selling stockholder, any affiliated purchasers, and any broker-dealer or other person who participates in the distribution from bidding for or purchasing, or attempting to induce any person to bid for or purchase any security which is the subject of the distribution until the entire distribution is complete. Regulation M also prohibits any bids or purchases made in order to stabilize the price of a security in connection with the distribution of that security. All of the foregoing may affect the marketability of the shares offered hereby this Prospectus.

This offering will terminate on the date that all shares offered by this Prospectus have been sold by Fusion Capital.

USE OF PROCEEDS

We will not receive any proceeds from the sale of the shares of common stock offered by the selling stockholder. However, we may receive proceeds from the sale of shares of our common stock to Fusion Capital under the Purchase Agreement. We will apply such proceeds, if any, to fund infrastructure growth including manufacturing, regulatory compliance, market development or general operating costs.

SEC POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling the company pursuant to the foregoing provisions, we have been informed that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

DESCRIPTION OF SECURITIES BEING REGISTERED

The following section does not purport to be complete and is qualified in all respects by reference to the detailed provisions of our certificate of incorporation and by-laws, as amended and restated, copies of which have been

filed with the Securities and Exchange Commission.

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Our authorized capital stock consist of: (i) 200,000,000 shares of common stock, $.001 par value; and (ii) 5,000,000 shares of preferred stock, $.01 par value. 83,529,962 shares of common stock were issued and outstanding as of the date of this Prospectus.

Common Stock

Shares of our common stock are entitled to one vote per share, either in person or by proxy, on all matters that may be voted upon by the owners of our shares at meetings of our stockholders. There is no provision for cumulative voting with respect to the election of directors by the holders of common stock. Therefore, the holder of more than 50% of our shares of outstanding common stock can, if they choose to do so, elect all of our directors. In this event, the holders of the remaining shares of common stock will not be able to elect any directors.

The holders of common stock:

- have equal rights to dividends from funds legally available therefore, when and if declared by our board of directors;
- are entitled to share ratably in all of our assets available for distribution to holders of common stock upon liquidation, dissolution or winding up of our affairs; and
- do not have preemptive rights, conversion rights, or redemption of sinking fund provisions.

The outstanding shares of our common stock are duly authorized, validly issued, fully paid and nonassessable.

Anti-Takeover Provisions

Delaware Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law, as amended, which restricts certain business combinations with interested stockholders even if such a combination would be beneficial to all stockholders. In general, Section 203 would require a two-thirds vote of stockholders for any business combination (such as a merger or sale of all or substantially all of our assets) between us and an "interested stockholder" unless such transaction is approved by a majority of the disinterested directors or meets certain other requirements. An "interested stockholder" is a person who, together with affiliates and associates, owns (or within three years, did own) 15% or more of our voting stock. These provisions could deprive stockholders of an opportunity to receive a premium for their common stock as part of a sale of us or may otherwise discourage a potential acquirer from attempting to obtain control of us.

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Certificate of Incorporation

Provisions of our Certificate of Incorporation 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.

Shareholder rights plan

In November, 2002 we adopted a shareholder 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 William A. Carter, M.D., our chief executive officer, who already beneficial owns 8.9% 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.

The rights have certain anti-takeover effects. The rights will cause substantial dilution to a person or group that attempts to acquire us on terms not approved by our Board of Directors. The rights should not interfere with any merger or business combination approved by the Board of Directors.

LEGAL MATTERS

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

EXPERTS

The financial statements, 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.

HEMISPHERX BIOPHARMA, INC.

21,300,000 Shares of
Common Stock

PROSPECTUS

April 24, 2009