

HEMISPHERX BIOPHARMA INC  
Form 424B5  
May 28, 2010

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Registration No. 333-159856

PROSPECTUS SUPPLEMENT  
(To Prospectus Dated June 22, 2009)

32,000,000 Shares  
HEMISPHERX BIOPHARMA, INC.  
Common Stock

We have entered into a sales agreement with the Maxim Group LLC relating to shares of our common stock offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the sales agreement, we may offer and sell up to the maximum of 32,000,000 shares of our common stock, \$0.001 par value per share, from time to time through the Maxim Group LLC, acting as agent. Our common stock is listed on the NYSE Amex under the ticker symbol "HEB". Sales of shares of our common stock under this prospectus supplement, if any, may be made by any method permitted by law deemed to be an "at the market" offering as defined in Rule 415 under the Securities Act of 1933, as amended (the "Securities Act"), which includes sales made directly on the NYSE Amex, the existing trading market for our common stock, or sales made to or through a market maker other than on an exchange. With our express written consent, the sales agent may also sell shares of our common stock in privately negotiated transactions. The sales agent will make all sales on a best efforts basis using commercially reasonable efforts consistent with its normal trading and sales practices, on terms mutually agreed upon by the sales agent and us. The last reported sale price of our common stock on the NYSE Amex on May 25, 2010 was \$0.64 per share.

You should read "Risk Factors" beginning on page S-3 of this prospectus supplement and the risk factors described in other documents incorporated by reference herein before buying our securities.

The Maxim Group LLC will be entitled to compensation at a fixed commission rate of 4.0% of the gross sales price per share sold, up to aggregate gross proceeds of \$10,000,000, and, thereafter, at a fixed commission rate of 3.0% of the gross sales price per share sold. In connection with the sale of the common stock on our behalf, the Maxim Group LLC may be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation of the Maxim Group LLC may be deemed to be underwriting commissions or discounts.

We have agreed to indemnify the sales agent and its controlling persons against certain liabilities, including liabilities under the Securities Act. If we are unable to provide this indemnification, we will contribute to payments the sales agent and its controlling persons may be required to make in respect of those liabilities.

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

Maxim Group LLC

The date of this prospectus supplement is May 28, 2010.

TABLE OF CONTENTS  
Prospectus Supplement

	Page
About This Prospectus Supplement	S-1
Prospectus Supplement Summary	S-1
The Offering	S-2
Risk Factors	S-3
Special Note Regarding Forward-Looking Statements	S-3
Use of Proceeds	S-4
Price Range of Our Common Stock	S-4
Dividend Policy	S-4
Dilution	S-5
Plan of Distribution	S-6
Legal Matters	S-7
Experts	S-7
Where You Can Find More Information	S-7
Important Information Incorporated by Reference	S-7

Prospectus

	Page
Prospectus Summary	2
Risk Factors	4
Special Note Regarding Forward-Looking Statements	18
Ratio Of Earnings To Fixed Charges	19
Use of Proceeds	19
Description of Capital Stock	19
Description of Warrants	22
Description of Debt Securities	23
Plan of Distribution	35
Legal Matters	37
Experts	37
Where You Can Find More Information	38
Information Incorporated By Reference	38

## ABOUT THIS PROSPECTUS SUPPLEMENT

We provide information to you about this offering of shares of our common stock in this prospectus supplement, which describes the specific details regarding this offering, and in the accompanying prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this “prospectus,” we are referring to both documents combined.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not, and the Maxim Group LLC has not, authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus supplement or the accompanying prospectus. These documents do not constitute an offer to sell or solicitation of an offer to buy these shares of common stock in any circumstance under which the offer or solicitation is unlawful. The information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein are accurate only as of their respective dates, regardless of the time of delivery of this prospectus supplement or the sale of our common stock. If information in this prospectus supplement, or information incorporated by reference in this prospectus supplement and the accompanying prospectus that is of a more recent date than the accompanying prospectus, is inconsistent with the accompanying prospectus, this prospectus supplement, or the information incorporated by reference in this prospectus supplement and the accompanying prospectus, will apply and will supersede that information in the accompanying prospectus. References in this prospectus supplement to “Hemispherx,” “we,” “our” or “us” refer to Hemispherx Biopharma, Inc. and its subsidiaries.

## PROSPECTUS SUPPLEMENT SUMMARY

This summary does not contain all of the information that you should consider before investing in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including “Risk Factors,” and the financial statements and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment in our common stock.

### Our Business

We are a specialty pharmaceutical company based in Philadelphia, Pennsylvania and engaged in the clinical development 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 natural interferon and 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. We have three domestic subsidiaries BioPro Corp., BioAegean Corp., and Core BioTech Corp., all of which are incorporated in Delaware and are dormant. Our foreign subsidiary is Hemispherx Biopharma Europe N.V./S.A. established in Belgium in 1998, which has no activity. All significant intercompany balances and transactions have been eliminated in consolidation.

Our current strategic focus is derived from four applications of our two core pharmaceutical technology platforms Ampligen® and Alferon N Injection®. The commercial focus for Ampligen® includes application as a treatment for Chronic Fatigue Syndrome (“CFS”) and as an influenza vaccine enhancer (adjuvant) for both therapeutic and preventative vaccine development. Alferon N Injection® is a Food and Drug Administration (“FDA”) approved product with an indication for refractory or recurring genital warts. Alferon® LDO (Low Dose Oral) is a formulation currently under development targeting influenza.



We own and operate a 43,000 sq. ft. FDA approved facility in New Brunswick, New Jersey that was primarily designed to produce Alferon®. We are currently undertaking a major capital improvement program to enhance our manufacturing capability for Alferon N Injection®, Alferon® LDO and Ampligen®. The planned capital improvements include upgrade to the ventilation and electrical distribution systems; upgrade of the high pressure boiler to support process equipment and battery management system; building a utility mezzanine to support the installation of a new water and waste treatment process.

#### Our Corporate Information

Our principal executive offices are located at One Penn Center, 1617 JFK Boulevard, Philadelphia, Pennsylvania 19103, and our telephone number is 215-988-0080, and our website can be accessed at [www.hemispherx.net](http://www.hemispherx.net). Information contained in our website does not constitute part of this prospectus supplement or the accompanying prospectus.

### THE OFFERING

Offering price and proceeds:	Variable at-the-market pricing, with aggregate gross proceeds from the sale of up to 32,000,000 shares.
Manner of offering:	“At-the-market” offering that may be made from time to time through our agent, the Maxim Group LLC. See “Plan of Distribution” on page S-6.
Use of proceed:	We intend to use the net proceeds from this offering to meet our working capital needs as well as to offset the costs related to capital improvements and clinical programs. See “Use of Proceeds”.
Risk factors:	You should read the “Risk Factors” section of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement for a discussion of risks to consider before deciding to purchase shares of our common stock.
NYSE Amex trading symbol:	HEB

## RISK FACTORS

Investment in our common stock involves a high degree of risk. In addition to the other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus, you should carefully consider the risks described below and in the section entitled “Risk Factors” in our Annual Report on Form 10-K for our most recent fiscal year filed with the Securities and Exchange Commission, and in other reports we file with the Securities and Exchange Commission that are incorporated by reference herein, before making an investment decision. The risks and uncertainties described therein and below could adversely affect our business, operating results and financial condition, as well as cause the value of our common stock to decline. You may lose all or part of your investment as a result. You should also refer to the other information contained in this prospectus supplement and the accompanying prospectus, or incorporated by reference, including our financial statements and the notes to those statements, and the information set forth under the caption “Special Note Regarding Forward-Looking Statements.” The risks described below and contained in our Annual Report on Form 10-K and in our other periodic reports are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business operations.

### Risks Related to this Offering

We will have broad discretion in how we use the proceeds, and we may use the proceeds in ways in which you and other stockholders may disagree.

We plan to use the net proceeds from the sale of shares of our common stock in this offering to meet our working capital needs, as well as for general corporate purposes. Pending these uses, we intend to invest the net proceeds in investment grade, interest bearing securities. Our management will have broad discretion in the application of the proceeds from this offering and could spend the proceeds in ways that do not necessarily improve our operating results or enhance the value of our common stock.

Investors in this offering will suffer immediate and substantial dilution in the net tangible book value per share of our common stock.

Because the assumed price per share of our common stock in this offering is substantially higher than the net tangible book value per share of common stock, investors in this offering will suffer immediate and substantial dilution in the net tangible book value per share of common stock. Assuming we sold all 32,000,000 shares at an assumed price to the public of \$0.64 per share, the last reported sale price of our common stock on May 25, 2010, and after deducting the estimated commissions and offering expenses payable by us, if you purchase shares in this offering, you will suffer immediate and substantial dilution of approximately \$0.17 per share in the net tangible book value of our common stock.

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Because the risk factors referred to above and our Annual Report on Form 10-K for our most recent fiscal year filed with the Securities and Exchange Commission and in other reports we file with the Securities and Exchange Commission that are incorporated by reference herein, 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. 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. 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.

S-3

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## USE OF PROCEEDS

We plan to use the net proceeds from the sale of shares of our common stock in this offering to meet our working capital needs, as well as to offset the costs related to capital improvements at our New Brunswick, NJ manufacturing facility and clinical programs utilizing Ampligen® and Alferon®. Pending these uses, we intend to invest the net proceeds in investment grade, interest bearing securities.

## PRICE RANGE OF OUR COMMON STOCK

Our common stock is traded on the NYSE Amex under the symbol “HEB”. The following table sets forth, for the periods indicated, the reported high and low sales prices per share of our common stock as reported by the NYSE Amex:

Fiscal Year Ended December 31, 2008	High	Low
First Quarter	\$ 0.89	\$ 0.62
Second Quarter	\$ 0.90	\$ 0.65
Third Quarter	\$ 1.07	\$ 0.33
Fourth Quarter	\$ 0.66	\$ 0.31
Fiscal Year Ending December 31, 2009	High	Low
First Quarter	\$ 0.80	\$ 0.32
Second Quarter	\$ 3.75	\$ 0.46
Third Quarter	\$ 3.31	\$ 1.90
Fourth Quarter	\$ 1.95	\$ 0.56
Fiscal Year Ending December 31, 2010	High	Low
First Quarter	\$ 0.83	\$ 0.57
Second Quarter (through May 25, 2010)	\$ 0.81	\$ 0.64

As of May 25, 2010, the closing price of our common stock as reported by the NYSE Amex was \$0.64 per share and there were approximately 220 holders of record of our common stock. This does not include the number of persons whose stock is in nominee or “street name” accounts through brokers.

## DIVIDEND POLICY

We have never declared or paid any cash dividends on our common stock. We currently intend to retain any future earnings to finance the growth and development of our business. Therefore, we do not anticipate that we will declare or pay any cash dividends on our common stock in the foreseeable future. Any future determination to pay cash dividends will be at the discretion of our Board of Directors and will depend on our financial condition, results of operations, capital requirements, restrictions under any existing indebtedness and other factors the Board of Directors deems relevant.



## DILUTION

If you purchase shares of our common stock from us, your interest will be diluted to the extent of the difference between the public offering price per share you pay and the net tangible book value per share of our common stock immediately after this offering. Our net tangible book value as of March 31, 2010, was approximately \$57,558,000, or \$0.43 per share of common stock. Net tangible book value per share is calculated by subtracting our total liabilities from our total tangible assets, which is total assets less intangible assets of approximately \$838,000, and dividing this amount by the 132,860,602 issued and outstanding shares of common stock outstanding as of March 31, 2010. Assuming we sold all 32,000,000 shares at an assumed price to the public of \$0.64 per share, the last reported sale price of our common stock on May 25, 2010, and after deducting the estimated commissions and offering expenses of payable by us, our adjusted net tangible book value as of March 31, 2010 would have been approximately \$77,084,000, or \$0.47 per share of common stock. This would represent an immediate increase in the net tangible book value of approximately \$0.04 per share to our existing stockholders and an immediate and substantial dilution in the net tangible book value of \$0.17 per share of common stock to new investors. The following table illustrates this calculation on a per share basis:

	Existing Stockholders (Approx.)	New Investors (Approx.)
Assumed public offering price per share		\$ 0.64
Net tangible book value per share as of March 31, 2010	\$ 57,558,000	
Increase per share attributable to investors participating in this offering	\$ 0.04	
As adjusted net tangible book value per share after this offering		\$ 77,084,000
Dilution per share to investors participating in this offering		\$ 0.17

The information in the table above is provided for illustrative purposes and assumes that all 32,000,000 shares of common stock offered hereby is sold at a price of \$0.64 per share, the last reported sale price of our common stock on May 25, 2010. The shares, if any, sold pursuant to the sales agreement will be sold from time to time at various prices that will depend largely on the market price of our common stock at the time of sale. An increase, or decrease, of \$0.25 per share in the price at which the shares are sold from the assumed offering price of \$0.64 per share shown in the table above, assuming all 32,000,000 shares of common stock offered are sold at that price, would increase (or decrease) our adjusted net tangible book value per share after the offering by approximately \$7,760,000 and \$0.04 per share, respectively, and the dilution in net tangible book value per share new investors in this offering by approximately \$27,286,000 and \$0.38 per share, respectively, after deducting the estimated commissions of the Maxim Group LLC and estimated aggregate offering expenses payable by us.

The information in the foregoing table does not take into account further dilution to new investors that could occur upon the exercise of outstanding options having a per share exercise price less than the price per share at which new investors purchase the shares offered hereby. As of May 25, 2010, there were 132,813,489 shares of common stock outstanding, which does not include:

• 8,817,912 shares of our common stock issuable upon exercise of outstanding stock options under our stock option plans as of May 25, 2010, at a weighted average exercise price of \$2.57;

• 106,920 shares of restricted stock; and

• 4,557,252 shares of our common stock issuable upon exercise of outstanding warrants as of May 25, 2010 at a weighted average price of \$1.81 per share.

S-5

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## PLAN OF DISTRIBUTION

We have entered into a sales agreement with the Maxim Group LLC (“Maxim”). Subject to the terms and conditions of the sales agreement, we may offer and sell up to 32,000,000 shares of our common stock from time to time through Maxim. Sales of the shares, if any, will be made by means of ordinary brokers’ transactions on the NYSE Amex at market prices. Additionally, under the terms of the sales agreement, we may also sell shares of our common stock through Maxim, as sales agent, on the NYSE Amex at negotiated prices or at prices related to the prevailing market price. With our express written consent, Maxim also may also sell shares of our common stock in privately negotiated transactions. As sales agent, Maxim will not engage in any transactions that stabilize our common stock.

Maxim, as sales agent, will use its commercially reasonable efforts to sell shares of common stock on our behalf on a daily basis or as otherwise agreed upon by us and Maxim. We will designate the maximum amount of shares of common stock to be sold through Maxim on a daily basis or otherwise as we and Maxim agree. We may instruct Maxim not to sell shares of common stock if the sales cannot be effected at or above the price designated by us in any such instruction. We or Maxim may suspend the offering of shares of common stock by notifying the other.

We will pay Maxim a commission equal to 3.0% of the gross sales price per share sold, up to aggregate gross proceeds of \$10,000,000, and, thereafter, at a fixed commission rate of 4.0% of the gross sales price per share sold. The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of the shares. All expenses of the offering will be paid by us. We estimate that the expenses of the offering payable by us, excluding discounts and commissions, will be approximately \$139,600. We have also agreed to reimburse Maxim for certain of its expenses in an amount not to exceed \$100,000.

Settlement for sales of common stock will occur on the third business day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sale of common stock on our behalf, Maxim may be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation paid to Maxim may be deemed to be underwriting commissions or discounts. We have agreed to indemnify Maxim against certain liabilities, including liabilities under the Securities Act, or to contribute to payments that Maxim may be required to make. Maxim may engage in transactions with, or perform other services for, us in the ordinary course of business.

Our shares are traded on the NYSE Amex under the symbol “HEB”.

In compliance with the guidelines of the Financial Industry Regulatory Authority, Inc. (“FINRA”), the maximum discount or commission to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate offering price of the shares offered pursuant to this prospectus supplement.

In connection with any future sales of common stock made under the sales agreement or terms agreement, Regulation M may require that Maxim observe certain restrictions with respect to its trading of our common stock. Such restrictions could negatively impact the liquidity in our common stock.

The offering of common stock pursuant to the sales agreement will terminate upon the earlier of (i) the sale of all 32,000,000 shares of common stock subject to the sales agreement or (ii) the termination of the sales agreement by either Maxim or us.



## LEGAL MATTERS

The validity of the common stock offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by Silverman Sclar Shin & Byrne PLLC, New York, New York. Certain legal matters in connection with the offering of the common stock will be passed upon for Maxim Group LLC by Goodwin Procter LLP, New York, New York.

## EXPERTS

The financial statements incorporated in this prospectus supplement by reference from the Company's Annual Report on Form 10-K have been audited by McGladrey & Pullen LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference (which report expresses an unqualified opinion on the consolidated financial statements). Such financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

## WHERE YOU CAN FIND MORE INFORMATION

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

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

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

## IMPORTANT INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" the information that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be an important part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the following documents and any future filing made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 prior to the termination of the offering:

- Annual Report on Form 10-K for the fiscal year ended December 31, 2009; and
- Quarterly Report on Form 10-Q for the period ended March 31, 2010; and

• The description of our Common Stock contained in our registration statement on Form S-1, SEC File No. 333-117178, and any amendment or report filed for the purpose of updating this description filed subsequent to the date of this prospectus and prior to the termination of this offering.

S-7

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You may request a copy of these filings, at no cost, by writing or telephoning us at the following address:

Investor Relations  
One Penn Center, 1617 JFK Blvd., Suite 660  
Philadelphia, PA 19103  
Phone: 215-988-0080  
Fax: 215-988-1739  
Email: [ir@hemispherx.net](mailto:ir@hemispherx.net)

You should rely only on the information incorporated by reference or provided in this prospectus. We have not authorized anyone else to provide you with different information. We will not make offers to sell these shares in any jurisdiction where the offer is not permitted.

S-8

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32,000,000 Shares  
HEMISPHERX BIOPHARMA, INC.  
Common Stock

PROSPECTUS SUPPLEMENT

Maxim Group LLC  
May 28, 2010

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\$150,000,000

HEMISPHERX BIOPHARMA, INC.

Common Stock  
Preferred Stock  
Warrants  
Debt Securities

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

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

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

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

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

The date of this prospectus is June 22, 2009.

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TABLE OF CONTENTS

	Page
Prospectus Summary	2
Risk Factors	4
Special Note Regarding Forward-Looking Statements	18
Ratio Of Earnings To Fixed Charges	19
Use of Proceeds	19
Description of Capital Stock	19
Description of Warrants	22
Description of Debt Securities	23
Plan of Distribution	35
Legal Matters	37
Experts	37
Where You Can Find More Information	38
Information Incorporated By Reference	38

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## PROSPECTUS SUMMARY

### Important Notice about the Information Presented in this Prospectus

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

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

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

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

### About Hemispherx

We are a specialty pharmaceutical company engaged in the clinical development, manufacture, marketing and distribution of new drug therapies based on natural immune system enhancing technologies for the treatment of viral and immune based chronic disorders. We were founded in the early 1970s doing contract research for the National Institutes of Health. Since that time, we have established a strong foundation of laboratory, pre-clinical, and clinical data with respect to the development of nucleic acids to enhance the natural antiviral defense system of the human body and to aid the development of therapeutic products for the treatment of certain chronic diseases.

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

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

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

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

## RISK FACTORS

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

### Risks Associated With Our Business

No assurance of successful product development.

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

Alferon N Injection®. Although Alferon N Injection® is approved for marketing in the United States for the intra-lesional treatment of refractory or recurring external genital warts in patients 18 years of age or older, to date it has not been approved for other indications. We face many of the risks discussed above, with regard to developing this product for use to treat other ailments.

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

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

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

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

If Ampligen® or one of our other products does not receive regulatory approval in the U.S. or elsewhere, our operations most likely will be materially adversely affected.

Alferon® LDO is undergoing pre-clinical testing for possible prophylaxis against avian flu. Additional studies are anticipated for swine H1N1. While the studies to date have been encouraging. Preliminary testing in the laboratory and animals is not necessarily predictive of successful results in clinical testing or human treatment. No assurance can be given that similar results will be observed in clinical trials. Use of Alferon® as a possible treatment of avian flu requires prior regulatory approval. Only the FDA can determine whether a drug is safe, effective or promising for treating a specific application. As discussed in the prior risk factor, obtaining regulatory approvals is a rigorous and lengthy process.

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

We began operations in 1966 and last reported net profit from 1985 through 1987. Since 1987, we have incurred substantial operating losses, as we pursued our clinical trial effort to get our experimental drug, Ampligen®, approved. As of March 31, 2009, our accumulated deficit was approximately \$200,496,000. We have not yet generated significant revenues from our products and may incur substantial and increased losses in the future. We cannot assure that we will ever achieve significant revenues from product sales or become profitable. We require, and will continue to require, the commitment of substantial resources to develop our products. We cannot assure that our product development efforts will be successfully completed or that required regulatory approvals will be obtained or that any products will be manufactured and marketed successfully, or be profitable.

We may require additional financing which may not be available.

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

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

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

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

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

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

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

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



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

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

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

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

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

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

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

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

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

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

We have limited marketing and sales capability. If we are unable to obtain additional distributors and our current and future distributors do not market our products successfully, we may not generate significant revenues or become profitable.

We have limited marketing and sales capability. We are dependent upon existing and, possibly future, marketing agreements and third party distribution agreements for our products in order to generate significant revenues and become profitable. As a result, any revenues received by us will be dependent in large part on the efforts of third parties, and there is no assurance that these efforts will be successful.

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

We cannot assure that our U.S. or foreign marketing strategy will be successful or that we will be able to establish future marketing or third party distribution agreements on terms acceptable to us, or that the cost of establishing these arrangements will not exceed any product revenues. Our inability to establish viable marketing and sales capabilities would most likely have a materially adverse effect on us.

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

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

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

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

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

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

We have limited manufacturing experience.

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

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

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

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

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

Our products may be subject to substantial competition.

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

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

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

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

Ampligen®. We believe that Ampligen® has been generally well tolerated with a low incidence of clinical toxicity, particularly given the severely debilitating or life threatening diseases that have been treated. A mild flushing reaction has been observed in approximately 15-20% of patients treated in our various studies. This reaction is occasionally accompanied by a rapid heart beat, a tightness of the chest, urticaria (swelling of the skin), anxiety, shortness of breath, subjective reports of "feeling hot", sweating and nausea. The reaction is usually infusion-rate related and can generally be controlled by reducing the rate of infusion. Other adverse side effects include liver enzyme level elevations, diarrhea, itching, asthma, low blood pressure, photophobia, rash, transient visual disturbances, slow or irregular heart rate, decreases in platelets and white blood cell counts, anemia, dizziness, confusion, elevation of kidney function tests, occasional temporary hair loss and various flu-like symptoms, including fever, chills, fatigue, muscular aches, joint pains, headaches, nausea and vomiting. These flu-like side effects typically subside within several months. One or more of the potential side effects might deter usage of Ampligen® in certain clinical situations and therefore, could adversely affect potential revenues and physician/patient acceptability of our product.

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

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

We face an inherent business risk of exposure to product liability claims in the event that the use of Ampligen® or other of our products results in adverse effects. This liability might result from claims made directly by patients, hospitals, clinics or other consumers, or by pharmaceutical companies or others manufacturing these products on our behalf. Our future operations may be negatively affected from the litigation costs, settlement expenses and lost product sales inherent to these claims. While we will continue to attempt to take appropriate precautions, we cannot assure that we will avoid significant product liability exposure.

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

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

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

Our success is dependent on the continued efforts of our staff, especially certain doctors and researchers along with the continued efforts of Dr. William A. Carter because of his position as a pioneer in the field of nucleic acid drugs, his being the co-inventor of Ampligen®, and his knowledge of our overall activities, including patents and clinical trials. The loss of the services of personnel key to our operations or Dr. Carter could have a material adverse effect on our operations and chances for success. As a cash conservation measure, we have elected to discontinue the Key Man life insurance in the amount of \$2,000,000 on the life of Dr. Carter until we receive regulatory clearance for Ampligen®. An employment agreement continues to exist with Dr. Carter that, as amended, runs until December 31, 2010. However, Dr. Carter has the right to terminate his employment upon not less than 30 days prior written notice. The loss of Dr. Carter or other personnel or the failure to recruit additional personnel as needed could have a materially adverse effect on our ability to achieve our objectives.

Uncertainty of health care reimbursement for our products.

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

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

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

Risks Associated With an Investment in Our Common Stock

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

The market price of our common stock has been and is likely to be volatile. This is especially true given the current significant instability in the financial markets. In addition to general economic, political and market conditions, the price and trading volume of our stock could fluctuate widely in response to many factors, including:



- announcements of the results of clinical trials by us or our competitors;
  - adverse reactions to products;
- governmental approvals, delays in expected governmental approvals or withdrawals of any prior governmental approvals or public or regulatory agency concerns regarding the safety or effectiveness of our products;
  - changes in U.S. or foreign regulatory policy during the period of product development;
- developments in patent or other proprietary rights, including any third party challenges of our intellectual property rights;
  - announcements of technological innovations by us or our competitors;
  - announcements of new products or new contracts by us or our competitors;
- actual or anticipated variations in our operating results due to the level of development expenses and other factors;
  - changes in financial estimates by securities analysts and whether our earnings meet or exceed the estimates;
    - conditions and trends in the pharmaceutical and other industries;
    - new accounting standards;
    - overall investment market fluctuation; and
  - occurrence of any of the risks described in these "Risk Factors."

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

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

Our stock price may be adversely affected if a significant amount of shares are sold in the public market.

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

We also previously registered 35% of 3,615,514 shares issuable upon exercise of warrants related to our former convertible debentures and 14,442,294 shares issuable upon exercise of certain other warrants. To the extent the exercise price of our outstanding warrants is less than the market price of the common stock, the holders of the warrants are likely to exercise them and sell the underlying shares of common stock and to the extent that the exercise price of certain of these warrants are adjusted pursuant to anti-dilution protection, the warrants could be exercisable or convertible for even more shares of common stock. We also may issue shares pursuant to this prospectus or otherwise to be used to meet our capital requirements or use shares to compensate employees, consultants and/or directors. We are unable to estimate the amount, timing or nature of future sales of outstanding common stock or instruments convertible into or exercisable for our common stock.

Sales of substantial amounts of our common stock in the public market, including our sale of securities under this Prospectus or pursuant to the Purchase Agreement with Fusion Capital, could cause the market price for our common stock to decrease. Furthermore, a decline in the price of our common stock would likely impede our ability to raise capital through the issuance of additional shares of common stock or other equity securities.

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

Provisions of our Certificate of Incorporation and Delaware law may make it more difficult for someone to acquire control of us or for our stockholders to remove existing management, and might discourage a third party from offering to acquire us, even if a change in control or in management would be beneficial to our stockholders. For example, our Certificate of Incorporation allows us to issue shares of preferred stock without any vote or further action by our stockholders. Our Board of Directors has the authority to fix and determine the relative rights and preferences of preferred stock. Our Board of Directors also has the authority to issue preferred stock without further stockholder approval. As a result, our Board of Directors could authorize the issuance of a series of preferred stock that would grant to holders the preferred right to our assets upon liquidation, the right to receive dividend payments before dividends are distributed to the holders of common stock and the right to the redemption of the shares, together with a premium, prior to the redemption of our common stock. In this regard, in November 2002, we adopted a stockholder rights plan and, under the Plan, our Board of Directors declared a dividend distribution of one Right for each outstanding share of Common Stock to stockholders of record at the close of business on November 29, 2002. Each Right initially entitles holders to buy one unit of preferred stock for \$30.00. The Rights generally are not transferable apart from the common stock and will not be exercisable unless and until a person or group acquires or commences a tender or exchange offer to acquire, beneficial ownership of 15% or more of our common stock. However, for Dr. Carter, our Chief Executive Officer, who already beneficially owns 6.05% of our common stock, the Plan's threshold will be 20%, instead of 15%. The Rights will expire on November 19, 2012, and may be redeemed prior thereto at \$.01 per Right under certain circumstances.



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

#### SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Certain statements in this prospectus constitute “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.

#### RATIO OF EARNINGS TO FIXED CHARGES

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

#### USE OF PROCEEDS

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

#### DESCRIPTION OF CAPITAL STOCK

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

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

#### Common Stock

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

#### Preferred Stock

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

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

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

1. the title and stated value of that preferred stock;
2. the number of shares of that preferred stock offered, the liquidation preference per share and the offering price of that preferred stock;
3. the dividend rate(s), period(s) and/or payment date(s) or method(s) of calculation thereof applicable to that preferred stock;

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

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

#### Transfer Agent and Registrar

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

## DESCRIPTION OF WARRANTS

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

### General

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

### Terms

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

- the title of the warrants;
- the aggregate number of warrants;
- the price or prices at which the warrants will be issued;
- the currencies in which the price or prices of the warrants may be payable;
- the designation, amount and terms of our capital stock or debt securities purchasable upon exercise of the warrants;
- the designation and terms of our other securities, if any, that may be issued in connection with the warrants, and the number of warrants issued with each corresponding security;
- if applicable, the date that the warrants and the securities purchasable upon exercise of the warrants will be separately transferable;
- the prices and currencies for which the securities purchasable upon exercise of the warrants may be purchased;
  - the date that the warrants may first be exercised;
  - the date that the warrants expire;
- the minimum or maximum amount of warrants that may be exercised at any one time;
  - information with respect to book-entry procedures, if any;
  - a discussion of certain federal income tax considerations; and
- any other material terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.



## Exercise of Warrants

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

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

## DESCRIPTION OF DEBT SECURITIES

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

### General

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

- the title and ranking;
    - the aggregate principal amount and any limit on such amount;
    - the price at which such debt securities will be issued;
      - the date on which the debt securities mature;
  - the fixed or variable rate at which the debt securities will bear interest, or the method by which such rate shall be determined;
  - the timing, place and manner of making principal, interest and any premium payments on the debt securities, and, if applicable, where such debt securities may be surrendered for registration of transfer or exchange;
  - the date or dates, if any, after which the debt securities may be converted or exchanged into or for shares of our common stock, preferred stock or another company's securities or properties or cash and the terms of any such conversion or exchange;
    - any redemption or early repayment provisions;
    - any sinking fund or similar provisions;
      - the authorized denominations;
      - any applicable subordination provisions;
    - any guarantees of such securities by our subsidiaries or others;
  - the currency in which we will pay the principal, interest and any premium payments on such debt securities;
  - whether the amount of payments of principal of (and premium, if any) or interest, if any, on the debt securities may be determined with reference to an index, formula or other method and the manner in which such amounts shall be determined;
  - the time period within which, the manner in which and the terms and conditions upon which the purchaser of the securities can select the payment currency;
    - the provisions, if any, granting special rights to the holders of debt securities upon certain events;
  - any additions to or changes in the events of default or covenants of Hemispherx with respect to the debt securities and any change in the right of the trustee or the holders to declare the principal, premium and interest with respect to such securities to be due and payable;
  - whether and under what circumstances we will pay any additional amounts on such debt securities for any tax, assessment or governmental charge and, if so, whether we will have the option to redeem such debt securities instead of paying such amounts;
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- the form (registered and/or bearer securities), any restrictions applicable to the offer, sale or delivery of bearer securities and the terms, if any, upon which bearer securities may be exchanged for registered securities and vice versa;
- the date of any bearer securities or any global security, if other than the date of original issuance of the first security of the series to be issued;
  - the person to whom and manner in which any interest shall be payable;
  - whether such securities will be issued in whole or in part in the form of one or more global securities;
  - the identity of the depositary for global securities;
- whether a temporary security is to be issued with respect to such series and whether any interest payable prior to the issuance of definitive securities of the series will be credited to the account of the persons entitled thereto;
- the terms upon which beneficial interests in a temporary global security may be exchanged in whole or in part for beneficial interests in a definitive global security or for individual definitive securities and the terms upon which such exchanges may be made;
  - the securities exchange(s), if any, on which the securities will be listed;
  - whether any underwriter(s) will act as market maker(s) for the securities;
  - the form (certificated or book-entry);
- the form and/or terms of certificates, documents or conditions which may be necessary, if any, for the debt securities to be issuable in final form; and
  - additional terms not inconsistent with the provisions of the indenture.

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

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

#### Exchange, Registration, Transfer and Payment

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

## Global Debt Securities

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

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

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

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

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

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

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

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

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

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

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

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

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

#### Covenants

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

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

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

#### Consolidation, Merger and Sale of Assets

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

- we are the surviving entity or, in the event that we are not the surviving entity, the entity formed by the transaction (in a consolidation) or the entity which received the transfer of assets is a corporation organized under the laws of any state of the United States or the District of Columbia;
  - such entity assumes all of our obligations under the debt securities and the indenture; and

- immediately after giving effect to the transaction, no event of default, as defined in the indenture, shall have occurred and be continuing.

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

#### Events of Default

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

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

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

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

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

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

#### Discharge of Indenture and Defeasance

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

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

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

- we have paid or deposited with the trustee, in trust an amount of cash or United States government obligations sufficient to pay all outstanding principal of and interest on the then outstanding debt securities of such series at maturity or upon their redemption, as the case may be;
  - such deposit will not result in a breach of, or constitute a default under, the indenture;
- no default or event of default shall have occurred and continue on the date of deposit and no event of default as a result of a bankruptcy or event which with the giving of notice or the lapse of time would become a bankruptcy event of default shall have occurred and be continuing on the 91st day after such date;



- we deliver to the trustee a legal opinion that we have received from, or there has been published by, the United States Internal Revenue Service a ruling, or there has been a change in tax law, in either case to the effect that the holders of the debt securities of such series will not recognize income, gain or loss for Federal income tax purposes as a result of our exercise of such option and shall be subject to Federal income tax on the same amounts and in the same manner and at the same times as would have been the case if such option had not been exercised; and
  - certain other conditions are met.

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

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

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

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

- rights of registration of transfer and exchange of debt securities of such series;
- rights of substitution of mutilated, defaced, destroyed, lost or stolen debt securities of such series;
- rights of holders of debt securities of such series to receive payments of principal thereof and premium, if any, and interest thereon when due;
  - rights, obligations, duties and immunities of the trustee;

- rights of holders of debt securities of such series as beneficiaries with respect to property deposited with the trustee and payable to all or any of them; and
  - our obligations to maintain an office or agency in respect of the debt securities of such series.

#### Transfer and Exchange

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

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

#### Amendment, Supplement and Waiver

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

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

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

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

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

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

#### Replacement Securities

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

#### Regarding the Trustee

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

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

#### Governing Law

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

PLAN OF DISTRIBUTION

We may sell the securities registered under this prospectus:

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

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

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

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

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

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

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

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

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

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

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

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

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

#### LEGAL MATTERS

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

#### EXPERTS

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

### WHERE YOU CAN FIND MORE INFORMATION

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

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

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

### INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" the information that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be an important part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the following documents and any future filing made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 prior to the termination of the offering:

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



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

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

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

HEMISPHERX BIOPHARMA, INC.

\$150,000,000

Common Stock  
Preferred Stock  
Warrants  
Debt Securities

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PROSPECTUS

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June 22, 2009

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