HEMISPHERX BIOPHARMA INC Form 424B3 October 12, 2017

Filed Pursuant to Rule

424(b)(3)

Registration No. 333-220756

PROSPECTUS

HEMISPHERX BIOPHARMA, INC.

5,407,759 Shares of Common Stock

Issuable Upon Exercise of Outstanding Warrants

This prospectus relates to the resale of an aggregate of 5,407,759 shares of our common stock, which may be offered for sale from time to time by the selling stockholders (the "Selling Stockholders") named in this prospectus, that they may receive if they exercise their outstanding warrants (the "Warrants").

We are not selling any shares of common stock under this prospectus and will not receive any proceeds from the sale of common stock by the Selling Stockholders. To the extent the Warrants are exercised for cash, if at all, we will receive the exercise price of the Warrants. The Selling Stockholders or their pledgees, assignees or successors-in-interest may offer and sell or otherwise dispose of the shares of common stock described in this prospectus from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices. The shares of common stock may be sold in one or more transactions, at fixed prices, at prevailing market prices at the time of sale or at negotiated prices. The Selling Stockholders will be responsible for any underwriting fees, discounts and commissions due to underwriters, brokers-dealers or agents. We will bear all costs, expenses and fees in connection with the registration of the shares. Please see the section titled "Plan of Distribution" of this prospectus for a more complete description of how the offered common stock may be sold.

You should carefully read this prospectus and any prospectus supplement before you invest. You also should read the documents we have referred you to in the "Where You Can Find More Information" and the "Incorporation by Reference" sections of this prospectus for information about us and our financial statements.

Our common stock is traded on the NYSE American under the symbol "HEB." On October 10, 2017, the last reported sale price for our common stock on the NYSE American was \$0.34 per share.

Investing in our securities involves a high degree of risk. See "Risk Factors" on page 5 of this Prospectus.

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

The date of this prospectus is October 12, 2017

TABLE OF CONTENTS

3
6
6
9
9
9
12
13
13
13
14

Neither we nor the Selling Stockholders have authorized any dealer, salesman or other person to provide you with information other than the information contained in or incorporated by reference into this prospectus. This prospectus does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, the common stock offered by this prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the front cover of the prospectus, or that the information contained in any document incorporated by reference into this prospectus is accurate as of any date other than the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus contains forward-looking statements that are subject to a number of risks and uncertainties, many of which are beyond our control. See "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements".

PROSPECTUS SUMMARY

This summary description about us and our business highlights selected information contained elsewhere in this prospectus or incorporated by reference into this prospectus. It does not contain all the information you should consider before investing in our securities. Important information is incorporated by reference into this prospectus. To understand this offering fully, you should read carefully the entire prospectus, including "Risk Factors," together with the additional information described under "Incorporation By Reference."

Unless otherwise stated or the context otherwise requires, references in this prospectus to "Hemispherx", "we", "us", "our" and "ours" refer to Hemispherx Biopharma, Inc.

About Hemispherx

We are a specialty pharmaceutical company headquartered 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 disorders. We were first formed in 1966 and in the early 1970s were 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.

Our flagship products include Alferon N Injection® and the experimental therapeutic Ampligen®. Alferon N Injection® is approved for a category of STD infection, and Ampligen® represents an experimental RNA being developed for globally important viral diseases and disorders of the immune system. Hemispherx' platform technology includes components for potential treatment of various severely debilitating and life threatening diseases.

The chart below provides an overview of clinical indications for both Ampligen® and Alferon® currently under development.

We own and operate a 30,000 sq. ft. facility in New Brunswick, NJ with the objective of producing Alferon® and Ampligen® upon FDA approval. As part of our objectives to achieve our commercial goals and increase stockholder value, we are in the process of selling an underutilized building adjacent to our New Jersey manufacturing facility site. We do not believe that the sale of this building will have an impact on the production of our products.

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

The Offering

Common Stock offered by Selling Stockholders:	5,407,759 Shares of common stock, \$0.001 par value per share, issuable upon exercise of Warrants.
Common Stock Outstanding:	31,319,672 Shares of common stock outstanding as of October 10, 2017.
Use of Proceeds:	We will not receive any of the proceeds from the sale of any shares of common stock by the Selling Stockholders. However, we will receive proceeds from the exercise of the Warrants if and when they are exercised in cash. See "Use of Proceeds".
Risk Factors: NYSE American trading symbol:	Investing in our common stock involves a high degree of risk. Please see "Risk Factors" and the risk factors set forth in the documents incorporated by reference herein for a discussion of risks to consider before deciding to purchase shares of our common stock. HEB

5

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before deciding whether to purchase shares of our common stock, you should carefully consider the risks and uncertainties described under "Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, any subsequent Quarterly Reports on Form 10-Q and our other filings with the Securities and Exchange Commission (the "SEC"), all of which are incorporated by reference herein (please see "Incorporation by Reference"). If any of these risks actually occur, our business, financial condition and results of operations could be materially and adversely affected and we may not be able to achieve our goals, the value of our securities could decline and you could lose some or all of your investment. Additional risks not presently known to us or that we currently deem immaterial may also impair our business operations.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

Certain statements in this prospectus and in the other filings incorporated by reference herein, constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended which we refer to as the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements reflect our current views with respect to future events and are based on assumptions and are subject to risks, uncertainties and other important factors. We discuss many of these risks, uncertainties and other important factors in greater detail under the "Risk Factor" sections in our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and in subsequent Quarterly Reports on Form 10-Q, as well as other filings we make with the SEC (collectively, our "SEC Filings"), all of which are incorporated by reference herein. As the foregoing risks 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, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should carefully read the risks, uncertainties and other important factors in our SEC Filings completely and with the understanding that our actual future results may be materially different from what we expect. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our business, results of operations and financial condition. 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. Any statements in this prospectus, and in the other filings incorporated by reference herein about our expectations, beliefs, plans, objectives, assumptions or future events or performance that are not historical facts are forward-looking statements. You can identify these forward-looking statements by the use of words or phrases such as "believe", "may", "could", "will", "estimate", "continue", "anticipate", "intend", "seek", "plan", "expect", "

Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are risks and uncertainties inherent in our business including, without limitation: our ability to adequately fund our projects as we will need additional funding to proceed with our objectives, the potential therapeutic effect of our products, the possibility of obtaining regulatory approval, our ability to find senior co-development partners with the capital and expertise needed to commercialize our products and to enter into arrangements with them on commercially reasonable terms, our ability to manufacture and sell any products, our ability to enter into arrangements with third party vendors, market acceptance of our products, our ability to earn a profit from sales or licenses of any drugs, our ability to discover new drugs in the future, changing market conditions, changes in laws and regulations affecting our industry, and issues related to our New Brunswick, New Jersey facility. We have disclosed that in February 2013, we received a Complete Response from the U.S. Food and Drug Administration (the "FDA") declining to approve our Ampligen® New Drug Application ("NDA") for Chronic Fatigue Syndrome Treatment, sometimes referred to as myalgic encephalomyelitis/chronic fatigue syndrome ("ME/CFS"), stating that we should conduct at least one additional clinical trial, complete various nonclinical studies and perform a number of data analyses. Accordingly, the remaining steps to potentially gain FDA approval of the Ampligen® NDA, the final results of these and other ongoing activities could vary materially from our expectations and could adversely affect the chances for approval of the Ampligen® NDA. These activities and the ultimate outcomes are subject to a variety of risks and uncertainties, including but not limited to risks that (i) the FDA may ask for additional data, information or studies to be completed or provided; and (ii) the FDA may require additional work related to the commercial manufacturing process to be completed or may, in the course of the inspection of manufacturing facilities, identify issues to be resolved. With regard to our NDA for Ampligen® to treat ME/CFS, as noted above, there are additional steps which the FDA has advised Hemispherx to take in our seeking approval. The final results of these and other ongoing activities, and of the FDA review, could vary materially from Hemispherx' expectations and could adversely affect the chances for approval of the Ampligen® NDA. Any failure to satisfy the FDA's requirements could significantly delay, or preclude outright, approval of our drugs for commercial sale in the United States.

We also have disclosed that, in August 2016, we received approval of our NDA from Administracion Nacional de Medicamentos, Alimentos y Tecnologia Medica ("ANMAT") for commercial sale of rintatolimod (U.S. tradename: Ampligen®) in the Argentine Republic for the treatment of severe ME/CFS. The product will be marketed by GP

Pharm, our commercial partner in Latin America. We believe, but cannot assure, that this approval provides a platform for potential commercial sales in certain countries within the European Union under regulations that support cross-border pharmaceutical sales of licensed drugs. In Europe, approval in a country with a stringent regulatory process in place, such as Argentina, should add further validation for the product as the Early Access Program as discussed below and underway in Europe. ANMAT approval is only an initial, but important, step in the overall successful commercialization of our product. There are a number of actions that must occur before we could be able to commence commercial sales in Argentina. Commercialization in Argentina will require, among other things, an appropriate reimbursement level, appropriate marketing strategies, completion of manufacturing preparations for launch (including possible requirements for approval of final manufacturing) and we will need additional funds to manufacture product at a sufficient level for a commercial launch. There are no assurances as to whether or when such multiple subsequent steps will be successfully performed to result in an overall successful commercialization and product launch. Approval of rintatolimod for ME/CFS in the Argentine Republic does not in any way suggest that the Ampligen® NDA in the United States or any comparable application filed in the European Union or elsewhere will obtain commercial approval.

We also have disclosed that, in January 2017, the EAP through our agreement with myTomorrows designed to enable access of Ampligen® to ME/CFS patients has been extended to pancreatic cancer patients beginning in the Netherlands. myTomorrows is our exclusive service provider in Europe and Turkey and will manage all EAP activities relating to the pancreatic cancer extension of the program. No assurance can be given that Ampligen® will prove effective in the treatment of pancreatic cancer.

Our overall objectives include plans to continue seeking approval for commercialization of Ampligen® in the United States and abroad as well as seeking to broaden commercial therapeutic indications of Alferon N Injection® presently approved in the United States and Argentina. We continue to pursue senior co-development partners with the capital and expertise needed to commercialize our products and to enter into arrangements with them on commercially reasonable terms. Our ability to commercialize our products, widen commercial therapeutic indications of Alferon N Injection® and/or capitalize on our collaborations with research laboratories to examine our products are subject to a number of significant risks and uncertainties including, but not limited to our ability to enter into more definitive agreements with some of the research laboratories and others that we are collaborating with, to fund and conduct additional testing and studies, whether or not such testing is successful or requires additional testing and meets the requirements of the FDA and comparable foreign regulatory agencies. We do not know when, if ever, our products will be generally available for commercial sale for any indication.

We outsource certain components of our manufacturing, quality control, marketing and distribution while maintaining control over the entire process through our quality assurance and regulatory groups. We cannot provide any guarantee that the facility or our contract manufacturer will necessarily pass an FDA pre-approval inspection for Alferon® manufacture.

The production of new Alferon® API inventory will not commence until the validation phase is complete. While the facility is approved by FDA under the Biological License Application ("BLA") for Alferon®, this status will need to be reaffirmed by a successful Pre-Approval Inspection by the FDA prior to commercial sale of newly produced inventory product. If and when the Company obtains a reaffirmation of FDA BLA status and has begun production of new Alferon® API, it will need FDA approval as to the quality and stability of the final product to allow commercial sales to resume. We will need additional funds to finance the revalidation process in our facility to initiate commercial manufacturing, thereby readying ourselves for an FDA Pre-Approval Inspection. If we are unable to gain the necessary FDA approvals related to the manufacturing process and/or final product of new Alferon® inventory, our operations most likely will be materially and/or adversely affected. In light of these contingencies, there can be no assurances that the approved Alferon N Injection® product will be returned to production on a timely basis, if at all, or that if and when it is again made commercially available, it will return to prior sales levels. In addition, we are currently readying the New Brunswick facility to start manufacturing polymers used for the production of Ampligen to satisfy our future needs, supplementing the polymers we have on hand. While we anticipate that we will be able to commence manufacturing polymers at the New Brunswick facility, we will need additional funding to continue manufacturing. There cannot be any guarantee that we will obtain adequate funds to sustain manufacturing at the New Brunswick facility or that the facility will be able to manufacture sufficient lots for the commercial launch of Ampligen.

USE OF PROCEEDS

We will not receive any of the proceeds from the sale of any shares of common stock by the Selling Stockholders. However, we will receive proceeds from the exercise of the Warrants if and when they are exercised in cash. As of the date of this prospectus, the exercise prices of the Warrants are above the current trading price of our common stock.

MARKET PRICE OF OUR COMMON STOCK

The following table sets forth the high and low prices for our common stock for the last two fiscal years and the first two quarters of 2017 as reported by the NYSE American. The following prices give retroactive effect to the 12-to-1 reverse stock split effected on August 26, 2016.

	High	Low
COMMON STOCK		
Time Period:		
January 1, 2017 through March 31, 2017	\$0.93	\$0.39
April 1, 2017 through June 30, 2017	\$0.84	\$0.45
July 1, 2017 through September 30, 2017	\$0.74	\$0.30
January 1, 2016 through March 31, 2016	\$2.40	\$0.78
April 1, 2016 through June 30, 2016	\$1.92	\$1.24
July 1, 2016 through September 30, 2016	\$2.64	\$1.24
October 1, 2016 through December 31, 2016	\$1.26	\$0.65
January 1, 2015 through March 31, 2015	\$3.96	\$2.52
April 1, 2015 through June 30, 2015	\$3.48	\$2.40
July 1, 2015 through September 30, 2015	\$2.52	\$1.68
October 1, 2015 through December 31, 2015	\$2.52 \$2.16	\$0.72

On October 10, 2017, the last sale price for our common stock on the NYSE American was \$0.34 per share.

SELLING STOCKHOLDERS

The shares of common stock being offered by the Selling Stockholders pursuant to this prospectus are those issuable upon exercise of Warrants previously issued to the Selling Stockholders and identified below (the "Warrant Shares").

We are registering the Warrant Shares in order to permit the Selling Stockholders to offer the shares for resale from time to time. Except for the ownership of shares acquired in a registered direct offering and the Warrants, the Selling Stockholders have not had any material relationship with us within the past three years.

The table below lists the Selling Stockholders and other information regarding the beneficial ownership of our common stock by each of the Selling Stockholders, and is based on 31,319,672 shares of our common stock outstanding on October 10, 2017. The number of shares listed as beneficially owned by each Selling Stockholder is based on its ownership of shares and Warrants as of October 10, 2017 and assumes exercise of the Warrants held by the Selling Stockholders on that date, without regard to any limitations on exercises.

The Warrants held by the Selling Stockholders consist of:

- Series A Warrants dated August 23, 2017 exercisable for an aggregate of 2,370,000 shares of common stock at an (i) exercise price of \$0.45 per share, initially exercisable on December 1, 2017 and expiring on March 6, 2022 ("Series A December Investor Warrants");
- Series A Warrants dated August 23, 2017 exercisable for an aggregate of 130,000 shares of common stock at an
- (ii) exercise price of \$0.45 per share, initially exercisable on January 10, 2018 and expiring on March 6, 2022 ("Series A January Investor Warrants");
- Series B Warrants dated August 23, 2017 exercisable for an aggregate of 2,384,000 shares of common stock at an (iii) exercise price of \$0.45 per share, initially exercisable on December 1, 2017 and expiring three months thereafter ("Series B December Investor Warrants");
- Series B Warrants dated August 23, 2017 exercisable for an aggregate of 416,000 shares of common stock at an (iv) exercise price of \$0.45 per share, initially exercisable on January 10, 2018 and expiring three months thereafter ("Series B January Investor Warrants"); and
- Warrants dated June 1, 2017 exercisable for an aggregate of 107,759 shares of common stock at an exercise price (v) of \$0.625 per share, initially exercisable on December 1, 2017 and expiring on June 1, 2022 (the "PA Warrants").

Although the Warrants held by the Selling Stockholders are not exercisable until at least December 1, 2017, for purposes of the table below, the Shares of common stock and percentage ownership identified below assume that the Warrants are currently exercisable and thus the shares of common stock underlying the Warrants are deemed to be outstanding and to be beneficially owned by the Selling Stockholders holding the Warrants, but are not treated as outstanding for the purpose of computing the percentage ownership of any other Selling Stockholders.

Under the terms of the Warrants, a Selling Stockholder may not exercise Warrants to the extent that such Selling Stockholder, together with its affiliates, would beneficially own, after such exercise more than 4.99% of the shares of common stock then outstanding (subject to the right of the Selling Stockholder to increase or decrease such beneficial ownership limitation upon notice to us, provided that such limitation cannot exceed 9.99%) and provided that any increase in the beneficial ownership limitation shall not be effective until 61 days after such notice is delivered. The number of shares does not reflect this limitation. The Selling Stockholders may sell all, some or none of their shares in this offering. See "Plan of Distribution."

Name of Selling Stockholder

Shares Beneficially Shares Beneficially Owned Prior to the Owned After Giving Effect to the Offering Offering Number of Percentage Number Maximum Shares of of Shares Number of of Common Beneficially Shares of Shares Owned Stock Common of Owned Prior to the Stock to be Common After Prior to Offering Sold Stock the Pursuant to Owned

Percentage

of Shares

Owned

Giving Effect to the

Beneficially

	Offering			this Prospectus (1)	After the Offering	Offering	
Sabby Healthcare Master Fund, Ltd. (2)(4)	1,590,000	4.9	%	1,590,000	0	0	%
Sabby Volatility Warrant Master Fund, Ltd. (3) (4)	1,060,000	3.3	%	1,060,000	0	0	%
Anson Investments Master Fund LP. (5)	1,562,851	4.9	%	2,650,000	340,909	0.1	%
Michael Vasinkevich (6)(7)	307,891	*		70,043	237,848	*	
Noam Rubinstein (6)(7)	149,024	*		33,944	115,080	*	
Mark Viklund (6)(7)	11,448	*		2,694	8,754	*	
Charles Worthman (6)(7)	4,732	*		1,078	3,654	*	

*Represents beneficial ownership of less than one percent.

We do not know when or in what amounts a Selling Stockholder may offer shares for sale. The Selling Stockholders may choose not to sell any or all of the shares offered by this prospectus. Because the Selling
(1) Stockholders may offer all or some of the shares pursuant to this offering, we cannot estimate the number of the shares that will be held by the Selling Stockholders after completion of the offering. However, for purposes of this table, we have assumed that, after completion of the offering, all of the shares covered by this prospectus will be sold by the Selling Stockholders.

620,000 shares of common stock issuable upon exercise of Series A December Investor Warrants, 424,000 shares
(2) of common stock issuable upon exercise of Series B December Investor Warrants, 130,000 shares of common stock issuable upon exercise of Series A January Investor Warrants and 416,000 shares of common stock issuable upon exercise of Series B January Investor Warrants are registered for sale under this prospectus.

500,000 shares of common stock issuable upon exercise of Series A December Investor Warrants and 560,000(3) shares of common stock issuable upon exercise of Series B December Investor Warrants are registered for sale under this prospectus.

Sabby Management, LLC is the investment manager of Sabby Healthcare Master Fund, Ltd. and Sabby Volatility Warrant Master Fund, Ltd. and shares voting and investment power with respect to these shares in this capacity. As (4) manager of Sabby Management, LLC, Hal Mintz also shares voting and investment power on behalf of each of the foregoing Selling Stockholder. Each of Sabby Management, LLC and Hal Mintz disclaims beneficial ownership over the securities listed except to the extent of their pecuniary interest therein.

1,250,000 shares of common stock issuable upon exercise of Series A December Investor Warrants and 1,400,000 shares of common stock issuable upon exercise of Series B December Investor Warrants are registered for sale under this prospectus. Anson Advisors Inc and Anson Funds Management LP, the Co-Investment Advisers of Anson Investments Master Fund LP ("Anson") hold voting and dispositive power over the Common Shares held by

(5) Anson Investments Master Fund LP ("Anson"), hold voting and dispositive power over the Common Shares held by Anson. Bruce Winson is the managing member of Anson Management GP LLC, which is the general partner of Anson Funds Management LP. Moez Kassam and Adam Spears are directors of Anson Advisors Inc. Mr. Winson, Mr. Kassam and Mr. Spears each disclaim beneficial ownership of these Common Shares except to the extent of their pecuniary interest therein.

(6) All of the shares for these Selling Stockholders registered for sale under this prospectus are issuable upon conversion of PA Warrants.

The Selling Stockholder is an affiliate of H.C. Wainwright & Co., LLC, a broker-dealer and the placement agent in (7) the private offerings in which the Warrants were sold, and at the time of the acquisition of the Warrants by the Selling Stockholder, such Selling Stockholder did not have any arrangements or understandings with any person to distribute such securities. The Selling Stockholder received the warrants as compensation for the private offerings.

PLAN OF DISTRIBUTION

Each Selling Stockholder and any of their pledgees, assignees and successors-in-interest may, from time to time, sell any or all of their common stock covered hereby on the principal trading market or any other stock exchange, market or trading facility on which our common stock is traded or in private transactions. These sales may be at fixed or negotiated prices. A Selling Stockholder may use any one or more of the following methods when selling securities:

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

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

purchases by a broker-dealer as principal and resale by the broker-dealer for its account;

an exchange distribution in accordance with the rules of the applicable exchange;

privately negotiated transactions;

settlement of short sales;

in transactions through broker-dealers that agree with the Selling Stockholders to sell a specified number of such common stock at a stipulated price per share;

through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;

a combination of any such methods of sale; or

any other method permitted pursuant to applicable law.

The Selling Stockholders may also sell common stock under Rule 144 or any other exemption from registration under the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by the Selling Stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the Selling Stockholders (or, if any broker-dealer acts as agent for the purchaser of common stock, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with FINRA Rule 2440; and in the case of a principal transaction a markup or markdown in compliance with FINRA IM-2440.

In connection with the sale of common stock therein, the Selling Stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of common stock in the course of hedging the positions they assume. The Selling Stockholders may also sell common stock short and deliver these shares to close out their short positions, or loan or pledge common stock to broker-dealers that in turn may sell these shares. The Selling Stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or create one or more derivative securities which require the delivery to such broker-dealer or other financial institution of common stock offered by this prospectus, which common stock such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

12

The Selling Stockholders and any broker-dealers or agents that are involved in selling the common stock may be deemed to be "underwriters" within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the common stock purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Each Selling Stockholder has informed us that it does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the common stock.

We are required to pay certain fees and expenses incurred by us incident to the registration of the common stock. We have agreed to indemnify the Selling Stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

Because Selling Stockholders may be deemed to be "underwriters" within the meaning of the Securities Act, they will be subject to the prospectus delivery requirements of the Securities Act including Rule 172 thereunder. In addition, any common stock covered by this prospectus which qualify for sale pursuant to Rule 144 under the Securities Act may be sold under Rule 144 rather than under this prospectus.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the resale shares may not simultaneously engage in market making activities with respect to the common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the Selling Stockholders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of the common stock by the Selling Stockholders or any other person. We will make copies of this prospectus available to the Selling Stockholders and have informed them of the need to deliver a copy of this prospectus to each purchaser at or prior to the time of the sale (including by compliance with Rule 172 under the Securities Act).

LEGAL MATTERS

Certain legal matters in connection with our common stock offered hereby will be passed upon for us by Silverman Shin & Byrne PLLC.

EXPERTS

The consolidated financial statements incorporated in this Prospectus by reference from the Company's Annual Report on Form 10-K for the year ended December 31, 2016, have been audited by RSM US LLP, an independent registered

public accounting firm, as stated in their report incorporated herein by reference. Such consolidated financial statements have been 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

We are required to file annual and quarterly reports and other information with the SEC. You may read and copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Room 1580, Washington, D.C., 20549. Please call 1-800-SEC-0330 for further information on the operation of the Public Reference Room. Our filings will also be available to the public from commercial document retrieval services and at the web site maintained by the SEC at http://www.sec.gov. Except as described below, our reports and other information that we have filed, or may in the future file, with the SEC are not incorporated by reference into and do not constitute part of this prospectus.

We have filed with the SEC a registration statement on Form S-1 (including the exhibits, schedules and amendments thereto) under the Securities Act, with respect to the shares of our common stock that may be issued upon exercise of Warrants. This prospectus does not contain all of the information set forth in the registration statement and the exhibits and schedules thereto. For further information with respect to the common stock offered hereby, we refer you to the registration statement and the exhibits and schedules filed therewith. Statements contained in this prospectus as to the contents of any contract, agreement or any other document are summaries of the material terms of such contract, agreement or other document and are not necessarily complete. With respect to each of these contracts, agreements or other documents filed as an exhibit to the registration statement, reference is made to the exhibits for a more complete description of the matter involved.

13

We also maintain a website at *www.hemispherx.net* through which you can access our filings with the Commission. The information contained in, or accessible through, our website is not a part of this prospectus.

INCORPORATION BY REFERENCE

We "incorporate by reference" information from other documents that we file with the SEC into this prospectus, which means that we disclose important information to you by referring you to those documents. The information incorporated by reference is deemed to be part of this prospectus except for any information that is superseded by information included directly in this prospectus, and the information that we file later with the SEC will automatically supersede this information. Any statement contained in this prospectus or any prospectus supplement or a document incorporated by reference in this prospectus or in any prospectus supplement will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or in any other subsequently filed document that is incorporated by reference in this prospectus to the extent that a statement contained in this prospectus or superseded the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus. You should not assume that the information in this prospectus is current as of the date other than the date on the cover page of this prospectus.

The following documents previously filed by us with the SEC are incorporated by reference in this prospectus:

Our Annual Report on Form 10-K for the year ended December 31, 2016;

Our quarterly reports on Form 10-Q for the quarters ended March 31, 2017 and June 30, 2017;

Our Current Reports on Form 8-K filed with the Commission on January 17, 2017, February 1, 2017, February 3, 2017, April 3, 2017, June, 1, 2017, June 22, 2017, August 15, 2017, August 23, 2017, August 29, 2017 and September 14, 2017; and amended Current Report on Form 8-K/A filed with the Commission on May 8, 2017

Our definitive proxy statement on Schedule 14A filed on July 18, 2017; and

A 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.

We are also incorporating by reference into this prospectus any additional documents that we may file with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the effective date of the registration statement and prior to the termination of the offering.

You may request a copy of any document incorporated by reference in this prospectus and any exhibit specifically incorporated by reference in those documents, at no cost, by writing or telephoning us at the following address or phone number:

Hemispherx Biopharma, Inc.

1617 JFK Boulevard, Ste. 500

Philadelphia, Pennsylvania 19103

Attention: Corporate Secretary

(215) 988-0800

14