HEMISPHERX BIOPHARMA INC
Form 10-K
March 30, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

[X] ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2017

OR

[ ] TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from _____ to _____

Commission File No. 000-27072

HEMISPHERX BIOPHARMA, INC.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization)	52-0845822 (I.R.S. Employer Identification Number)

860 N. Orange Avenue, Suite B, Orlando, Florida (Address of principal executive offices)	32801 (Zip Code)

Registrant's telephone number, including area code: (215) 988-0080

Securities registered pursuant to Section 12(b) of the Act:

Common Stock, $.001 par value

Securities registered pursuant to Section 12(g) of the Act:

(Title of Each Class)

NONE

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes [ ] No [X]

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes [ ] No [X]

Indicate by check mark whether the registrant (1) has filed all reports to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes [X] No [ ]

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes [X] No [ ]

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. [ ]

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

[ ]	Large accelerated filer	[ ]	Accelerated filer
[ ]	Non-accelerated filer	[X]	Smaller reporting company
		[ ]	Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards pursuant to Section 13(a) of the Exchange Act. [ ]

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes [ ] No [X]

The aggregate market value of Common Stock held by non-affiliates at June 30, 2017, the last business day of the registrant's most recently completed second fiscal quarter was $14,478,834.

The number of shares of the registrant's Common Stock outstanding as of March 26, 2018 was 37,715,230.

DOCUMENTS INCORPORATED BY REFERENCE: None.

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CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

Certain statements in this Annual Report on Form 10-K (the "Form 10-K"), including statements under "Item 1-Business," "Item 1A-Risk Factors" and "Item 3-Legal Proceedings" in PART I and "Item 7-Management's Discussion and Analysis of Financial Condition and Result of Operations" in PART II, constitute "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and the Private Securities Litigation Reform Act of 1995. 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. Forward-looking statements reflect our views as of the date that they are made with respect to future events and are based on assumptions. 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. We discuss many of these risks, uncertainties and other important factors in greater detail under the "Risk Factor" sections in this Form 10-K. 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. 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. All statements other than statements of historical fact included in this Form 10-K regarding our financial position, business strategy and plans or objectives for future operations are forward-looking statements.

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") for 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 AdministracionNacional de Medicamentos, Alimentos y TecnologiaMedica ("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 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 in pancreatic cancer. 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 most likely 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 May 2016, we entered into a five year agreement with myTomorrows, a Netherlands based company, for the commencement and management of an Early Access Program ("EAP") in Europe and Turkey (the "Territory") related to CFS. Pursuant to the agreement, myTomorrows, as our exclusive service provider and distributor in the Territory, is performing EAP activities. In January 2017, we announced that the EAP has been extended to pancreatic cancer patients beginning in the Netherlands. In June 2017, we signed an amendment to provide support services to Hemispherx with respect to the execution of the 511-Program ("511-Services") and that the 511-Services shall be rendered free of charge. In February 2018, we signed an amendment to extend the territory to cover Canada to treat pancreatic cancer patients, pending government approval. In March 2018, we signed an amendment to which myTomorrows will be our exclusive service provider for special access activities in Canada for the supply of Ampligen® for the treatment of ME/CFS. No assurance can be given that we can sufficiently supply product should we experience an unexpected demand for Ampligen® in our clinical studies, the commercial launch in Argentina or pursuant to the EAP.

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 for 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.

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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.

We believe, and are investigating, Ampligen®'s potential role in enhancing the activity of influenza vaccines. While certain studies involving rodents, non-human primates (monkeys) and healthy human subjects indicate that Ampligen® may enhance the activity of influenza vaccines by conferring increased cross-reactivity or cross-protection, further studies will be required and no assurance can be given that Ampligen® will assist in the development of a universal vaccine for influenza or other viruses.

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.

PART I

ITEM 1. Business

GENERAL

Hemispherx Biopharma, Inc. and its subsidiaries (collectively, “Hemispherx”, “Company”, “we” or “us”) are a specialty pharmaceutical company headquartered in Orlando, Florida and engaged in the development of new drug therapies based on natural immune system enhancing technologies for the treatment of viral and immune based disorders. 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.

We 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 recently sold our main facility while obtaining a long term lease with a buy-back option on the facility. In addition, we sold an underutilized, unencumbered, and wholly owned building adjacent to our manufacturing facility site noted above. We do not believe that the sale of these buildings will have an impact on the production of our products. Please see “Part 2. Properties” below.

In February 2013, we received a Complete Response Letter (“CRL”) from the FDA for the NDA for Ampligen® for Chronic Fatigue Syndrome ("CFS") without further confirmatory clinical trials. Please see the discussion in "Our Products - Ampligen®" below for more detail.

We are committed to a focused business plan oriented toward finding senior co-development partners with the capital and expertise needed to commercialize the many potential therapeutic aspects of our experimental drugs and our FDA approved drug Alferon® N.

With keeping to our austerity plan to reserve capital we have relocated our principal executive office from a large expensive corporate space in center city Philadelphia to 860 N. Orange Avenue, Suite B, Orlando, FL 32801.

AVAILABLE INFORMATION

We file our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Exchange Act electronically with the Securities and Exchange Commission, or SEC. The public may read or copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is http://www.sec.gov.

You may obtain a free copy of our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and amendments to those reports on the day of filing with the SEC on our website on the World Wide Web at http://www.hemispherx.net under the Investor Relations tab for SEC Filings or by contacting the Investor Relations Department by calling 888-557-6480 or sending an e-mail message to ir@hemispherx.net.

OUR PRODUCTS

Our primary pharmaceutical product platform consists of our experimental compound, Ampligen®, and our FDA approved natural interferon product, Alferon N Injection®.

Ampligen®

Ampligen® is approved for sale in Argentina and is an experimental drug currently undergoing clinical development for the treatment of CFS in the United States of America. Over its developmental history, Ampligen® has received various designations, including Orphan Drug Product Designation (FDA), Treatment protocol (e.g., “Expanded Access” or “Compassionate” use authorization) with Cost Recovery Authorization (FDA) and “promising” clinical outcome recognition based on the evaluation of certain summary clinical reports (“AHRQ” or Agency for Healthcare Research and Quality). Ampligen® represents the first drug in the class of large (macromolecular) RNA (nucleic acid) molecules to apply for NDA review. Based on the results of published, peer reviewed pre-clinical studies and clinical trials, we believe that Ampligen® may have broad-spectrum anti-viral and anti-cancer properties.

We believe that nucleic acid compounds represent a potential new class of pharmaceutical products as they are designed to act at the molecular level for treatment of human diseases. There are two forms of nucleic acids, DNA and RNA. DNA is a group of naturally occurring molecules found in chromosomes, the cell’s genetic machinery. RNA is a group of naturally occurring informational molecules which orchestrate a cell’s behavior which, in turn, regulates the action of groups of cells, including the cells which compromise the body’s immune system. RNA directs the production of proteins and regulates certain cell activities including the activation of an otherwise dormant cellular defense against viruses and tumors. Our drug technology utilizes specifically-configured RNA. Our double-stranded RNA drug product, trademarked Ampligen®, is an experimental, unapproved drug in the United States, that is administered intravenously. Ampligen® has been assigned the generic name rintatolimod by the United States Adopted Names Council (USANC) and has the chemical designation poly(I):poly(C_{12}U).

Clinical trials of Ampligen® already conducted by us include studies of the potential treatment of CFS, Hepatitis B, HIV and cancer patients with renal cell carcinoma and malignant melanoma. All of these potential uses will require additional clinical trials to generate the safety and effectiveness data necessary to support regulatory approval.

In February 2013, we received a Complete Response Letter ("CRL") from the FDA for Ampligen® for CFS. In its CRL, the FDA communicated that Hemispherx should conduct at least one additional clinical trial, complete various nonclinical studies and perform a number of data analyses. We are actively engaged with the FDA, and have had several meetings in order to reach an agreement on the path forward. Until we reach an agreement with the FDA regarding the design of a study, we are unable to reasonably estimate the nature or costs necessary to obtain FDA clearance or anticipated completion dates of any additional clinical study or studies.

The FDA authorized an open-label treatment protocol, ("AMP-511"), allowing patient access to Ampligen® for treatment in an open-label safety study under which severely debilitated CFS patients have the opportunity to be on Ampligen® to treat this very serious and chronic condition. The data collected from the AMP-511 protocol through a consortium group of clinical sites provide safety information regarding the use of Ampligen® in patients with CFS. We are establishing an enlarged data base of clinical safety information which we believe will provide further documentation regarding the absence of autoimmune disease associated with Ampligen® treatment. We believe that continued efforts to understand existing data, and to advance the development of new data and information, will ultimately support our future filings for Ampligen® and/or the design of future clinical studies. In 2015, we engaged an independent certified public accountant to recalculate the cost per dose consistent with the current guidelines, utilizing the costs to produce a vial. In October 2016, the FDA granted our request to implement the new cost which was initiated during the quarter ended March 31, 2017.As of December 31, 2017, there are 17 patients participating in this open-label treatment protocol.

In August 2016, we received approval of our NDA from ANMAT for commercial sale of rintatolimod (U.S. tradename: Ampligen®) in the Argentine Republic for the treatment of ME/CFS. The product will be marketed by GP Pharm, our commercial partner in Latin America. 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 most likely will need additional funds to manufacture product at a sufficient level for a commercial launch.

In May 2016, we entered into a five year agreement with myTomorrows, a Netherlands based company, for the commencement and management of an Early Access Program ("EAP") in Europe and Turkey (the "Territory") related to CFS. Subsequently we have made amendments to the original agreement in January 2017, June 2017, February 2018 and March 2018. Pursuant to the original agreement and the amendments myTomorrow's will manage all Early Access Programs and Special Access Programme's in Europe, Canada and Turkey to treat pancreatic cancer and ME/CFS patients. myTomorrows will also provide support services to Hemispherx with respect to the execution of the 511-cost recovery Program to treat ME/CFS patients in the USA.

In August, 2017 we announced that we have commenced full data analysis of an intranasal human safety study of Ampligen® plus FluMist® known as AMP-600. The study was previously closed, but the initiation of full data analysis awaited the FDA's evaluation of preliminary reports of blinded study findings. That evaluation was completed per formal notification from the FDA in August, 2017. Intranasal Ampligen was generally well-tolerated in the study.

Alferon N Injection®

Alferon N Injection® is the registered trademark for our injectable formulation of natural alpha interferon, which was approved by the FDA for the treatment of certain categories of genital warts. Alferon® is the only natural-source, multi-species alpha interferon currently approved for sale in the U.S. for the intralesional (within lesions) treatment of refractory (resistant to other treatment) or recurring external genital warts in patients 18 years of age or older. Certain types of human papilloma viruses ("HPV") cause genital warts, a sexually transmitted disease ("STD"). The U.S. Centers for Disease Control and Prevention ("CDC") estimates that "*approximately twenty million Americans are currently infected with HPV with another six million becoming newly infected each year. HPV is so common that at least 50% of sexually active men and women get it at some point in their lives.*" Although they do not usually result in death, genital warts commonly recur, causing significant morbidity and entail substantial health care costs.

Interferons are a group of proteins produced and secreted by cells to combat diseases. Researchers have identified four major classes of human interferon: alpha, beta, gamma and omega. Alferon N Injection® contains a multi-species form of alpha interferon. The world-wide market for injectable alpha interferon-based products has experienced rapid growth and various alpha interferon injectable products are approved for many major medical uses worldwide. Alpha interferons are manufactured commercially in three ways: by genetic engineering, by cell culture, and from human white blood cells. All three of these types of alpha interferon are or were approved for commercial sale in the U.S. Our natural alpha interferon is produced from human white blood cells.

The potential advantages of natural alpha interferon over recombinant (synthetic) interferon produced and marketed by other pharmaceutical firms may be based upon their respective molecular compositions. Natural alpha interferon is composed of a family of proteins containing many molecular species of interferon. In contrast, commercial recombinant alpha interferon products each contain only a single species. Researchers have reported that the various species of interferons may have differing antiviral activity depending upon the type of virus. Natural alpha interferon presents a broad complement of species, which we believe may account for its higher activity in laboratory studies. Natural alpha interferon is also glycosylated (partially covered with sugar molecules). Such glycosylation is not present on the currently U.S. marketed recombinant alpha interferons. We believe that the absence of glycosylation may be, in part, responsible for the production of interferon-neutralizing antibodies seen in patients treated with recombinant alpha interferon. Although cell culture-derived interferon is also composed of multiple glycosylated alpha interferon species, the types and relative quantity of these species are different from our natural alpha interferon.

Alferon N Injection® [Interferon alfa-n3 (human leukocyte derived)] is a highly purified, natural-source, glycosylated, multi-species alpha interferon product. There are essentially no neutralizing antibodies observed against Alferon N Injection® to date and the product has a relatively low side-effect profile. The recombinant DNA derived alpha interferon formulations have been reported to have decreased effectiveness after one year, probably due to neutralizing antibody formation.

See “Manufacturing” and “Marketing/Distribution” sections below for more details on the manufacture and marketing/distribution of Alferon N Injection®.

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HISTORICAL COSTS RELATED TO OUR PRODUCTS

The following table sets forth the costs related to our major products for each of the prior three years. Our aggregate expenses from the time that we first started developing nucleic acid pharmaceutical technology in the mid 1980's through March 2003 were substantially related to the development of Ampligen®, and from that date through the current period were substantially related to Ampligen® and Alferon®.

	(dollars in thousands) Year Ended December 31, 2017			
	Ampligen® NDA	Alferon N® Injection®	Other	Total
Costs and Expenses				
Production costs	$—	$ 1,183	$ —	$1,183
Research and development	3,629	469	—	4,098
General and administrative	4,815	1,757	—	6,572
Total	$8,444	$ 3,409	$ —	$11,853

	(dollars in thousands) Year Ended December 31, 2016			
	Ampligen® NDA	Alferon N® Injection®	Other	Total
Costs and Expenses				
Production costs	$—	$ 1,108	$ —	$1,108
Research and development	4,368	739	—	5,107
General and administrative	5,628	2,053	—	7,681
Total	$9,996	$ 3,900	$ —	$13,896

	(dollars in thousands) Year Ended December 31, 2015			
	Ampligen® NDA	Alferon N® Injection®	Other	Total
Costs and Expenses				
Production costs	$—	$ 1,598	$ —	$1,598
Research and development	3,452	4,586	—	8,038
General and administrative	2,560	4,587	—	7,147
Total	$6,012	$ 10,771	$ —	$16,783

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PATENTS AND NON-PATENT EXCLUSIVITY RIGHTS

As of December 31, 2017, we had 50 patents worldwide with 7 additional pending patent applications comprising our intellectual property. Please see “Note 5: Patents, Trademark Rights and Other Intangibles (FASB ASC 350 General Intangibles Other than Goodwill)” under Notes to Consolidated Financial Statements for more information on these patents.

We continually review our patents’ rights to determine whether they have continuing value. Such review includes an analysis of the patent’s ultimate revenue and profitability potential. In addition, Management’s review addresses whether each patent continues to fit into our strategic business plans for Ampligen® and Alferon N Injection®. One U.S. patent relating to our Alferon® product expired on April 2, 2013 (#5,503,828) and another on October 14, 2014 (#5,676,942) (see discussion below on patent #5,503,828 and #5,676,942).

In 2016, we received a new Ampligen® composition of matter patent in the US (9,315,538 B2). In 2015, we were granted a new composition of matter patent (#2340307) by the European Patent Office and we received twenty-eight new patents in various EU countries. In 2014, we were granted a new composition of matter patent in the United States (#8,722,874) covering Ampligen® formulations.

Alferon® composition patent #5,503,828 which expired in April 2013, related to the manufacturing process for Alferon® Active Pharmaceutical Ingredient (“API”), a complex mixture of natural interferon species that is manufactured from human leukocytes obtained from human blood donors. In addition, while it is the current standard by the FDA to treat biological drug products like interferon as “Well Characterized” biologics, a process for which chemical entities can have their identity, purity, impurities, potency, and quality controlled by chemical testing, Alferon®, as a natural interferon, does not lend itself well to such testing. Moreover, FDA continues to require that each lot of Alferon® we produce be tested and released by the FDA before it can be distributed for commercial sales. Because of the complexity of the Alferon® manufacturing process and these additional regulatory requirements, we believe that potential manufacturers of generic, or so-called “bio-similar,” drug products are focused on developing recombinant interferon products, rather than natural interferon products. For these reasons, we believe the expiration of this Alferon® composition patent in April 2013 should have no or little impact on the Company. Additionally, at the receipt of the FDA certification for the revised Alferon® manufacturing process and techniques in New Brunswick, NJ, it is our intention to file for additional patent protection.

Alferon® patent #5,676,942 which expired on October 14, 2014 and Alferon® patent #5,989,441 which was set to expire on December 22, 2017, but was allowed to lapse beforehand, related to a manufacturing methodology which is no longer in use. For this reason, we believe the expiration of these Alferon® patents should have no impact on the Company.

With respect to Ampligen®, the main U.S. CFS treatment patent (#6,130,206) expired October 10, 2017 (we believe that the expiration of this patent will have minimal impact on us; see detail on U.S. 8,722,874 below). Our main patents covering HIV treatment (#4,820,696, #5,063,209, and #5,091,374) expired on April 11, 2006, November 5, 2008, and February 25, 2009, respectively. Our U.S. Ampligen® Trademark (#73/617,687) has been renewed through December 6, 2018. New therapeutic use patent applications are pending. On May 13, 2014, the United States Patent Office issued patent U.S. 8,722,874 titled "*Double-Stranded Ribonucleic Acids with Rugged Physiochemical Structure and Highly Specific Biologic Activity*" to inventors Carter, et al. and assignee Hemispherx. The patent claims a novel form of rugged dsRNA. Rugged dsRNA are nucleic acids with a unique composition and physical characteristic identified with high specificity of binding to Toll-Like Receptor 3 (TLR3), thereby conveying an important range of therapeutic opportunities. The newly discovered form of dsRNA has increased bioactivity and binding affinity to the TLR 3 receptor because of its reduced tendency to form branched dsRNA which can inhibit receptor binding. Pharmaceutical formulations containing the newly discovered nucleic acid as active ingredients and methods of treatment with those formulations are also described in the issued patent. Hemispherx believes that the issuance of U.S. Patent 8,722,874 will help ensure that Hemispherx retains patent protection for novel formulations of Ampligen® products until at least 2029.

In September 2015, the European Patent Office granted the European version of U.S. Patent 8,722,874 with the same title as shown above to inventors Carter, et al. and assignee Hemispherx.

In addition to our patent rights relating to Ampligen®, the FDA has granted "orphan drug status" to the drug for CFS, HIV/AIDS, renal cell carcinoma and malignant melanoma. Orphan drug status grants us protection against the potential subsequent approval of other sponsors' versions of the drug for these uses for a period of seven years following FDA approval of Ampligen® for each of these designated uses. The first NDA approval for Ampligen® as a new chemical entity will also qualify for four or five years of non-patent exclusivity during which abbreviated new drug applications seeking approval to market generic versions of the drug cannot be submitted to the FDA. (See "Government Regulation" below.)

In May 2011, a new United States Patent 7,943,147 was granted for the use of Ampligen® as a vaccine adjuvant for use with seasonal influenza vaccine to induce an enhanced immune response against H5N1 avian influenza.

RESEARCH AND DEVELOPMENT ("R&D")

Our general focus during the past three fiscal years has been on the clinical development of new drug therapies based on natural immune system enhancing technologies for the treatment of viral and immune based disorders.

The following table summarizes our research and development costs for the years 2017, 2016 and 2015 by project (in thousands):

	2017	2016	2015
Ampligen® New Drug Application for the treatment of CFS	$3,629	$4,368	$3,452
Alferon N Injection®	469	739	4,586
Other projects	—	—	—
Total research and development	$4,098	$5,107	$8,038

Due to the inherent uncertainty involved in the design and conduct of clinical trials and the applicable regulatory requirements, including the factors discussed above in "Our Products", we cannot predict what additional studies and/or additional testing or information may be required by the FDA. Accordingly, we are unable to estimate the nature, timing, costs and necessary efforts to complete these projects nor the anticipated completion dates. In addition, we have no basis for estimating when material net cash inflows may commence. We have yet to generate significant revenues from the sale of these developmental products. As of December 31, 2017, we had approximately $2,107,000

in Cash, Cash Equivalents and Marketable Securities, (inclusive of approximately $695,000 in Marketable Securities). Please see ITEM 1A. Risk Factors; "*We will require additional financing which may not be available*" below.

In its CRL, the FDA communicated that Hemispherx should conduct at least one additional clinical trial, complete various nonclinical studies and perform a number of data analyses. We are actively engaged with the FDA, and have had several meetings in order to reach an agreement on the path forward. . At this point in time, we cannot predict how long it would take to run an additional trial and submit the data to the FDA for approval of the drug product. We anticipate that the time and cost to undertake clinical trial(s), studies and data analysis are beyond our current financial resources without gaining access to additional funding. Please see "*We most likely will require additional financing which may not be available.*" in Item 1A. Risk Factors below.

Chronic Fatigue Syndrome ("CFS")

Chronic Fatigue Syndrome ("CFS"), also known as Chronic Fatigue Immune Dysfunction Syndrome ("CFIDS") and Myalgic Encephalomyelitis ("ME"), is a serious and debilitating chronic illness and a major public health problem. CFS is recognized by both the government and private sector as a significant unmet medical need, including the U.S. National Institutes of Health ("NIH"), FDA and the CDC. The CDC states on its website at http://www.cdc.gov/cfs/index.html that "*Chronic fatigue syndrome, or CFS, is a devastating and complex disorder characterized by overwhelming fatigue that is not improved by bed rest and that may be worsened by physical or mental activity. People with CFS most often function at a significantly lower level of activity than they were capable of before the onset of illness.*"

Many severe CFS patients become completely disabled or totally bedridden and are afflicted with severe pain and mental confusion even at rest. CFS is characterized by incapacitating fatigue with profound exhaustion and extremely poor stamina, sleep difficulties and problems with concentration and short-term memory. It is also accompanied by flu-like symptoms, pain in the joints and muscles, tender lymph nodes, sore throat and new headaches. A distinctive characteristic of the illness is a worsening of symptoms following physical or mental exertion, which do not subside with rest.

In June 2012**,** U.S. Senators Robert P. Casey, Richard Blumenthal and Kay R. Hagan sent a letter to Health and Human Services Secretary Kathleen Sebelius requesting the FDA hold a stakeholders meeting on CFS. Senators Casey and Hagan were serving at the time on the Committee on Health, Education, Labor& Pensions, which has Congressional oversight responsibility for FDA. The letter stated, "*CFS/ME" represents a significant unmet medical need, one that confers on patients a lifetime of illness. A stakeholder meeting would be of great benefit, as it would offer an opportunity to examine existing treatment protocols known to FDA, address how risk/benefit determinations should be made in relation to CFS/ME treatments and identify a path forward for regulatory science in this area*."

In April 2013, the FDA, in a series of meetings called Patient Focused Drug Development meetings selected CFS to be the first disease. The two-day meeting with key stakeholders resulted in a report called *The Voice of the Patient*, published in September of 2013. In March 2014, FDA published the first ever Guidance for Industry Chronic Fatigue Syndrome/Myalgic Encephalomyelitis: Developing Drug Products for Treatment.

In February 2015, the Institute of Medicine (IOM) published a report, Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome; Redefining an Illness. The committee was charged by HHS with evaluating the current criteria for the diagnosis of ME/CFS and recommend clinical diagnostic criteria that would address the needs of health care providers, patients, and their caregivers. The primary message of the committee is "*ME/CFS is a serious, chronic, complex, systemic disease that can profoundly affect the lives of patients*." The IOM since published a Report Guide for Clinicians. In October 2015, NIH Director Francis S. Collins, M.D., Ph.D. announced that NIH is strengthening its efforts to advance research on ME/CFS. In an interview with ME Action, December 2015, Collins described the range of possibilities – "*everything from basic science to clinical trials for promising approaches, including Ampligen® and Rituximab*". In 2017 the Norwegian rituximab Phase 3 study in ME/CFS was reported to have failed with no positive treatment effect seen, leaving no other product at the Phase III level other than Ampligen in the regulatory pipeline to treat ME/CFS patients.

Other Diseases

In December 2013, we announced that we were supporting the University of Pittsburgh's Chemokine Modulation Research initiative which includes Ampligen® as an adjuvant. As part of this collaboration, Hemispherx has supplied clinical grade Ampligen® (rintatolimod) to the University. The study, under the leadership of Professor of Surgery Pawel Kalinski, M.D., Ph.D., involved the Chemokine Modulatory regimen developed by Dr. Kalinski's group and successfully completed the Phase 1 dose escalation in patients with resectable colorectal cancer. In the 1st quarter of 2017, Dr. Kalinski relocated to Roswell Park Cancer Institute (RPCI) in Buffalo, NY. Dr. Kalinski is currently working to establish a cancer program at RPCI which will continue to require a supply of Ampligen®. The cancer protocols utilizing Ampligen® at the University of Pittsburgh have been closed except for the ovarian study for which Dr. Edwards is the investigator. This study of recurrent ovarian cancer patients which includes Ampligen® as a component of the treatment regimen has enrolled 10 patients to date.

In July 2015, we submitted an application for orphan drug designation to the European Medicines Agency (EMA) for Alferon® N to treat MERS and in January 2016, the EMA forwarded to us both its Public Summary of Opinion and its record designation approving the Orphan Medicinal Products Designation for Alferon N Injection®, also known as interferon alfa-n3, as a potential treatment of MERS. In addition, we concluded our series of collaborations designed to determine the potential effectiveness of Alferon® N and Ampligen® as potential preventative and/or therapeutic treatments for Ebola related disorders. Although we believe that the threat of both MERS and Ebola globally may reemerge in the future, it appears that the spread of these disorders has somewhat diminished. As a result, we have elected to focus our research and development efforts on other areas at this time.

In January 2017, we announced that 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. In February 2018, the agreement with myTomorrows was extended to cover Canada to treat pancreatic cancer patients, pending government approval.

As of December 31, 2017, 34 pancreatic patients have received treatment with single-agent Ampligen® immuno-oncology therapy in an EAP managed by Amsterdam-based myTomorrows, an international leader in providing physician access to experimental medicines.

In July 2017, we entered into a Material Transfer Agreement with Roswell Park Cancer Institute (RPCI) in Buffalo, NY to continue the cancer studies with Dr. Pawel Kalinski and his associates.

Laboratory experiments do not necessarily indicate clinical benefit. Some of the research both past and present has been, and may in the future be, sponsored in part by contracts or grants from us to various independent research entities.

MANUFACTURING

In January 2017, we entered into a purchase order to replace the previous purchase commitment with Jubilant Hollister-Stier LLC ("Jubilant") pursuant to which Jubilant will manufacture batches of Ampligen® for us. Pursuant to the order, Jubilant will perform tooling and validation activities as well as final fill and finish services. The first lot is expected to be manufactured and released for sale and clinical use in the second quarter of 2018, once all validation activities and release testing are complete.

In July 2016, we reached an agreement with Avrio Biopharmaceuticals, now Nitto Avecia Pharma, Inc. ("Avecia") to serve as an additional contract manufacturer of our experimental drug, Ampligen®. In May 2017, we filed a complaint against Nitto Avecia Pharma Services, Inc. ("NAPS"), the successor to Avrio Biopharmaceuticals, LLC ("Avrio"), primarily for breach of contract. Please see "Item 3: Legal Proceedings" in Part I and Item 1A. Risk Factors *"There are no long-term agreements with suppliers of required materials and services for Ampligen® and there are a limited number of raw material suppliers. If we are unable to obtain the required raw materials and/or services, we may not be able to manufacture Ampligen®"*.

Commercial sales of Alferon® and Alferon® API internationally are projected to begin as soon as the necessary regulatory approvals are obtained. However, commercial sales of Alferon® in the USA will not resume until new batches of commercial filled and finished product are produced and released by the FDA. While the facility is approved by the FDA under the BLA for Alferon®, this status will need to be reaffirmed by an FDA pre-approval inspection. We will also need the FDA's approval to release commercial product once we have submitted satisfactory stability and quality release data. Currently, the manufacturing process is on hold and there is no definitive timetable to have the facility back online. We estimate we will need approximately $10,000,000 to commence the manufacturing process. Due to the Company extending the timeline of Alferon® production to an excess of one year, we reclassified Alferon® work-process-inventory to other assets within our balance sheet as of December 31, 2017. In addition, due to the high cost estimates to bring the facility back online, 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.

Licensing/Collaborations/Joint Ventures

To maximize the availability of Ampligen® to patients on a worldwide basis, we have embarked on a strategy to license the product and/or to collaborate and/or create a joint venture with companies that have the demonstrated capabilities and commitment to successfully gain approval and commercialize Ampligen® in their respective

territories of the world. Ideal partners would have the following characteristics: well established global and regional experience and coverage, robust commercial infrastructure, strong track record of successful development and registration of in-licensed products, as well as a therapeutic area fit (ME/CFS, immuno-oncology, etc.).

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MARKETING/DISTRIBUTION

If we are unable to achieve licensing, collaboration and/or joint ventures, our marketing strategy for Ampligen® will be to be part of the differing health care systems around the world along with the different marketing and distribution systems that are used to supply pharmaceutical products to those systems. We expect that, subject to receipt of FDA, ANMAT and/or other regulatory approval, Ampligen® may be utilized in four medical arenas: physicians' offices, clinics, hospitals, and the home treatment setting. In preparation for the FDA's consideration of our Ampligen® NDA, we undertook early stage development of pre-launch and launch driven marketing plans focusing on audience development, medical support and payer reimbursement initiatives which could facilitate product acceptance and utilization at the time of regulatory approval, if obtained. Similarly, we continued to consider distribution scenarios for the Specialty Pharmacy/Infusion channel which could provide market access, offer 3PL (third party logistics) capabilities and provide the requisite risk management control mechanisms. It is our intent to utilize third party service providers to execute elements of both the marketing/sales and distribution plans. As a possible option, we considered a plan to utilize a small group of Managed Market account managers to introduce the product to payor, employer and government account audiences. We believe that this approach could establish a market presence and facilitate the generation of revenue without incurring the substantial costs associated with a traditional sales force. Furthermore, Management believes that any approach considered should enable us to retain multiple options for future marketing strategies.

In May 2016, we entered into a five year exclusive Renewed Sales, Marketing, Distribution and Supply Agreement (the "Agreement") with GP Pharm. Under this Agreement, GP Pharm is responsible for gaining regulatory approval in Argentina for Ampligen® to treat CFS in Argentina and for commercializing Ampligen® for this indication in Argentina. We granted GP Pharm the right to expand rights to sell this experimental therapeutic into other Latin America countries based upon GP Pharm achieving certain performance milestones. We also granted GP Pharm an option to market Alferon N Injection® in Argentina and other Latin America countries.

In January 2017, the ANMAT granted a five year extension to a previous approval to sale and distribute Alferon N Injection® (under the brand name "Naturaferon") in Argentina. This extends the approval until 2022. In February 2013, we received the ANMAT approval for the treatment of refractory patients that failed or were intolerant to treatment with recombinant interferon, with Naturaferon® in Argentina.

In August 2017, we extended our agreement with Asembia, formerly Armada Healthcare, LLC, to undertake the marketing, education and sales of Alferon N Injection® throughout the United States.

In August 2017, we extended our agreement with specialty distributor, BioRidgePharma, LLC ("BioRidge") to warehouse, ship, and distribute Alferon N Injection® on an exclusive basis in support of U.S. sales.

In May 2016, we entered into an amended and restated five year agreement (the “Impatients Agreement”) with Impatients, N.V. (“myTomorrows”), a Netherlands based company, for the commencement and management of an Early Access Program (“EAP”) in Europe and Turkey (the “Territory”) related to CFS. Pursuant to the agreement, myTomorrows, as our exclusive service provider and distributor in the Territory, is performing EAP activities. These activities will be directed to (a) the education of physicians and patients regarding the possibility of early access to innovative medical treatments not yet the subject of a Marketing Authorization (regulatory approval) through named-patient use, compassionate use, expanded access and hospital exemption, (b) patient and physician outreach related to a patient-physician platform, (c) the securing of Early Access Approvals (exemptions and/or waivers required by regulatory authorities for medical treatments prior to Marketing Authorization) for the use of such treatments, (d) the distribution and sale of such treatments pursuant to such Early Access Approvals, (e) pharmacovigilance (drug safety) activities and/or (f) the collection of data such as patient-reported outcomes, doctor-reported experiences and registry data. We are supporting these efforts and supplying Ampligen® to myTomorrows at a predetermined transfer price. In the event that we receive Marketing Authorization in any country in the Territory, we will pay myTomorrows a royalty on products sold. Pursuant to the Impatients Agreement, the royalty would be a percentage of Net Sales (as defined in the Impatients Agreement) of Ampligen® sold in the Territory where Marketing Authorization was obtained, and the maximum royalty would be a percentage of Net Sales. The formula to determine the percentage of Net Sales will be based on the number of patients that are entered into the EAP. The Company believes that disclosure of the exact maximum royalty rate and royalty termination date could cause competitive harm. However, to assist the public in gauging these terms, the actual maximum royalty rate is somewhere between 2% and 10% and the royalty termination date is somewhere between five and fifteen years from the First Commercial Sale of a product within a specific country. The parties established a Joint Steering Committee comprised of representatives of both parties to oversee the EAP. No assurance can be given that activities under the EAP will result in Marketing Authorization or the sale of substantial amounts of Ampligen® in the Territory. In 2017, the Company commenced sales of recently manufactured Ampligen® in international programs.

In January 2017, we announced that 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.

In June 2017, we signed an amendment to the EAP with myTomorrows. This amendment is for myTomorrows to provide support services to Hemispherx with respect to the execution of the 511-Program ("511-Services"). The 511-Services shall be rendered for a period of six months to be renewed with additional 6 month periods with written mutual consent, or until termination of the 511-Program. The 511-Services shall be rendered free of charge.

In February 2018, we signed an amendment to the EAP with myTomorrows. This amendment extended the territory to cover Canada to treat pancreatic cancer patients, pending government approval.

In March 2018, we signed an amendment to the EAP with myTomorrows, pursuant to which myTomorrows will be our exclusive service provider for special access activities in Canada for the supply of Ampligen® for the treatment of ME/CFS.

COMPETITION

RNA based products and toll-like receptors ("TLRs") have demonstrated great promise in pre-clinical and limited clinical applications resulting in active research and development by large pharmaceutical companies and emerging biotech firms. As such, our 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.

These companies and their competing products may be more effective and less costly than our products. In addition, conventional drug therapy, surgery and other more familiar treatments will offer competition to our products. Furthermore, our competitors have significantly greater experience than we do in pre-clinical testing and human clinical trials of pharmaceutical products and in obtaining FDA (in the US), European Medicines Agency ("EMA") and Health Protection Branch ("HPB") (in Canada), and other regulatory approvals of products. Accordingly, our competitors may succeed in obtaining FDA, EMEA and HPB product approvals before we do. If any of our products receive regulatory approvals and we commence commercial sales of our products, we will also be competing with respect to manufacturing efficiency and marketing capabilities, areas in which we have no experience. Our competitors may possess or obtain patent protection or other intellectual property rights that prevent, limit or otherwise adversely affect our ability to develop or exploit our products.

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The major pharmaceutical competitors with biotech capabilities/vaccine franchises include Pfizer, GlaxoSmithKline, Merck & Co., Novartis and AstraZeneca. Biotech competitors include Baxter International, Fletcher/CSI, AVANT Immunotherapeutics, AVI BioPharma and Genta. When we recommence sales of Alferon N Injection®, it will compete with Intron® A, an injectable from Merck & Co., that attempts to kill the virus and prevent reproduction along with topical treatments that are normally applied by a doctor that have a risk of damaging the skin around the wart, such as:

- Aldara®, also known as Imiquimod®, is a cream which is marketed to boost the immune systems in an attempt to rid itself of genital warts;
- Veregen® is a herbal product made from green tea leaves which is self-administered as an ointment and is used to treat external genital warts in adult patients;
- Condylox® Solution (podofilox) and Podofin® (podophyllin resin) are liquids applied externally using a cotton applicator or finger which attempts to destroy genital warts by halting cell growth; and
- Trichloroacetic acid (TCA) or Bichloroacetic acid (BCA) are chemical treatments which attempt to externally “burn off” genital warts.

See “Item 1A-Risk Factors- Our products may be subject to substantial competition”.

GOVERNMENT REGULATION

Regulation by governmental authorities in the U.S. and foreign countries is and will be a significant factor in the manufacture and marketing of Alferon® products and our ongoing research and product development activities. Ampligen® and other products developed from the ongoing research and product development activities will require regulatory clearances prior to commercialization. In particular, new drug products for humans are subject to rigorous pre-clinical and clinical testing as a condition for clearance by the FDA and by similar authorities in foreign countries. The lengthy process of seeking these approvals, and the ongoing process of compliance with applicable statutes and regulations, has and will continue to require the expenditure of substantial resources. Any failure by us or our collaborators or licensees to obtain, or any delay in obtaining, regulatory approvals could materially adversely affect the marketing of any products developed by us and our ability to receive product or royalty revenue. We have received Orphan Drug designation for certain therapeutic indications, which we believe might under certain conditions help to accelerate the process of drug development and commercialization. Alferon N Injection® is only approved for use in intralesional treatment of refractory or recurring external genital warts in patients 18 years of age or older. Use of Alferon N Injection® for other applications requires regulatory approval.

We are subject to various federal, state and local laws, regulations and recommendations relating to such matters as safe working conditions, laboratory and manufacturing practices, the experimental use of animals and the use of and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with our research work. Prior to our construction phase, our laboratory and production facility in New Brunswick, New Jersey was approved for the manufacture of Alferon N Injection®. While our facility

had been granted approval of its BLA by the FDA for the manufacture of Alferon®, this status will need to be reaffirmed as we have completed the facility's enhancements and believe it will again be able to obtain FDA approval. However, there can be no assurance that this facility, or facilities owned and operated by third parties that are utilized in the manufacture of our products, will obtain and/or continue to maintain FDA approval. For information about the current status of our Ampligen® NDA please see "Our Products; Ampligen®" above.

HUMAN RESOURCES

As of March 26, 2018, we had personnel consisting of 25 full-time employees and 2 part-time employees. Eighteen (18) of the combined personnel are engaged in our research, development, clinical, and manufacturing effort with 9 performing regulatory, general administration, data processing, including bio-statistics, financial and investor relations functions. We have no union employees.

While we have been successful in attracting skilled and experienced scientific personnel, there can be no assurance that we will be able to attract or retain the necessary qualified employees and/or consultants in the future.

ITEM 1A: 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 Form 10-K. 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 and finding co-development partners.

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 investigational 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 and Part 1, Item I: “Business; Our Products; Ampligen®” for more information).

Alferon N Injection®. Although Alferon N Injection® is approved for marketing in the United States for the intralesional treatment of refractory or recurring external genital warts in patients 18 years of age or older, to date it has not been approved for other indications. We face many of the risks discussed above, with regard to developing this product for use to treat other ailments (Please see the next Risk Factor and Part 1, Item I: “Business; Our Products; Alferon N Injection®” above for more information).

We are committed to a focused business plan oriented toward finding co-development partners with the necessary capital and expertise required to commercialize the many therapeutic aspects of our experimental drugs and our FDA approved drug Alferon® N. If we are unable to find a suitable co-development partner to assist in the product development and commercialization of our experimental drugs and our FDA approved drug Alferon® N, we may be unable to continue or complete our development and commercialization of our products. In addition, there can be no assurance that such co-development partnerships would be on acceptable terms, or that such partnerships, will be acceptable from a profitability standpoint.

Our drug and related technologies are investigational and subject to regulatory approval. If we are unable to obtain regulatory approval in a timely manner, or at all, our operations will be materially harmed and our stock adversely affected.

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

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, the Agency for the European Medicines Agency ("EMA") in Europe and the AdministracionNacional de Medicamentos, Alimentos y TecnologiaMedica ("ANMAT") in Argentina. 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 and efficacious. While Ampligen® is authorized for use in clinical trials in the U.S., 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. In addition, although Ampligen® has been authorized by the FDA for treatment use under certain conditions, including provision for cost recovery, there can be no assurance that such authorization will continue in effect.

While we received approval of our Argentinian NDA from ANMAT for commercial sale of rintatolimod (U.S. tradename: Ampligen®) in the Argentine Republic for the treatment of severe ME/CFS, 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 would be able to commence commercial sales in Argentina.

On February 1, 2013, we received a CRL from the FDA for our Ampligen® NDA for the treatment of CFS. The FDA communicated that we should conduct at least one additional clinical trial, complete various nonclinical studies and perform a number of data analysis. For more detailed information about the current status of our Ampligen® NDA please see Part 1, Item I: "Business; Our Products; Ampligen®" above.

The FDA's regulatory review and approval process is extensive, lengthy, expensive and inherently uncertain. To receive approval for a product candidate, we must, among other things, demonstrate to the FDA's satisfaction with substantial evidence from well-controlled pre-clinical and clinical trials that the product candidate is both safe and effective for each indication for which approval is sought. Before we can sell Ampligen® for any use, or promote Alferon® for any use other than as Alferon N Injection® for treatment of refractory or recurring genital warts, we will need to file the appropriate NDA with the FDA in the U.S. and the appropriate regulatory agency outside of the U.S. where we intend to market and sell such products. At present the only NDA we have filed with the FDA is the NDA for the use of Ampligen® to treat CFS. As discussed in the prior paragraph, the FDA issued a CRL for this NDA and indicated that we needed to conduct additional work. Therefore, ultimate FDA approval, if any, may be delayed by several years and may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be successful or considered sufficient by the FDA for approval or even to make our applications approvable. If any of these outcomes occur, we may be forced to abandon one or more of our future applications for approval, which might significantly harm our business and prospects. As a result, we cannot predict if or when we might receive regulatory approval for the use of Ampligen® to treat CFS or for the use of any other products. Even if regulatory approval from the FDA is received for the use of Ampligen® to treat CFS or eventually, for the use of any other product, any approvals that we obtain could contain significant limitations in the form of narrow indications, patient populations, warnings, precautions or contra-indications or other conditions of use,

or the requirement that we implement a risk evaluation and mitigation strategy. In such an event, our ability to generate revenues from such products could be greatly reduced and our business could be harmed.

Even if we believe that data collected from our preclinical studies and clinical trials of our product candidate are promising, this data has not been, and may not be in the future, sufficient to support marketing approval by the FDA, and regulatory interpretation of these data and procedures may continue to be unfavorable.

To the extent that we are required by the FDA, pursuant to the Ampligen® NDA, to conduct additional studies and take additional actions, approval of any applications that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be successful or considered sufficient by the FDA for approval or even to make our applications approvable. If any of these outcomes occur, we may be forced to abandon one or more of our future applications for approval, which might significantly harm our business and prospects. As a result, we cannot predict when or whether regulatory approval will be obtained for any product candidate we develop.

Obtaining approval of a NDA by the FDA, or a comparable foreign regulatory authority, is inherently uncertain. Even after completing clinical trials and other studies, a product candidate could fail to receive regulatory approval for many reasons, including the following:

- not be able to demonstrate to the satisfaction of the FDA that our product candidate is safe and effective for any indication;
- the FDA may disagree with the design or implementation of our clinical trials or other studies;
- the results of the clinical trials or other studies may not demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA may disagree with our interpretation of data from clinical trials or other studies;
- the data collected from clinical trials and other studies of a product candidate may not be sufficient to support the submission of a NDA;
- the approval policies or regulations of the FDA may significantly change in a manner rendering our clinical and other study data insufficient for approval; and
- the FDA may not approve the proposed manufacturing processes and facilities for a product candidate.

In 2012, FDA reviewers raised certain questions about the status of our existing lots of older Work-In-Process Alferon® materials and Alferon® Active Pharmaceutical Product ("API"), which would need to be released by the FDA before those materials could be used in commercial product. After conducting all of the appropriate tests on samples of the inventory during 2013, we concluded that we could not alleviate certain questions the FDA had about the older Work-In-Process Alferon N Injection®. Accordingly, these lots were not submitted to the FDA to request release for commercial sale and their remaining dollar value was written-off. In the absence of FDA approvals for product manufactured from existing inventory, commercial sales of Alferon® will not resume until new batches of Alferon® inventory and API can be produced, filled and finished, and released by the FDA for commercial sale. (Please see Part 1, Item I: "Business; Our Products; Manufacturing" above for more information).

If we are unable to gain necessary FDA approvals related to Ampligen® and Alferon® on a timely basis, our operations most likely will be materially and/or adversely affected. Additionally, if we are unable to generate the additional data, successfully complete inspections or obtain approvals as required by the FDA on a timely manner, or at all, or determine that any of our clinical studies are not cost/justified to undertake or if, for that or any other reason, Ampligen®, Alferon® or one of our other products or production processes do not receive necessary regulatory approval in the U.S. or elsewhere:

our ability to generate revenues to sustain our operations will be substantially impaired, which would increase the likelihood that we would need to obtain additional financing for our other development efforts;
our reputation among investors might be harmed, which might make it more difficult for us to obtain equity capital on attractive terms or at all; and
our profitability would be delayed, our business will be materially harmed and our stock price may be adversely affected.

Biotechnology stock prices, including our stock price, have declined significantly in certain instances where companies have failed to meet expectations with respect to FDA approval or the timing for FDA approval.