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UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

Form 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.**
For the fiscal year ended December 31, 2018

☐ **TRANSITION REPORTS PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.**
For the transition period from to

Commission File Number: 001-37937

XENETIC BIOSCIENCES, INC.
(Exact name of registrant as specified in its charter)

Nevada	**45-2952962**
(State or other jurisdiction of incorporation or organization)	**(IRS Employer Identification No.)**

40 Speen Street, Suite 102
Framingham, MA 01701
(Address of principal executive offices and zip code)

781-778-7720
(Registrant's telephone number, including area code)

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

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, $0.001 par value per share	The NASDAQ Stock Market LLC

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

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 ☒

Indicate by check mark whether the registrant (1) has filed all reports required 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 ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically 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 ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405) 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: Yes ☐ No ☒

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

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☒
(Do not check if a 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 provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Exchange Act Rule 12b-2): ☐

The aggregate market value of the voting and non-voting common stock held by non-affiliates of the registrant as of June 29, 2018, the last business day of the registrant's most recently completely second fiscal quarter, based upon the closing price of the registrant's common stock on the NASDAQ Capital Market on that date of $4.08, was approximately $16,464,779. For purposes of this computation, all officers, directors, and 10% beneficial owners of the registrant are deemed to be affiliates. Such determination should not be deemed to be an admission that such officers, directors or 10% beneficial owners are, in fact, affiliates of the registrant.

As of March 15, 2019, the number of outstanding shares of the registrant's common stock was 10,443,889.

DOCUMENTS INCORPORATED BY REFERENCE

Information required in response to Part III of Form 10-K (Items 10, 11, 12, 13 and 14) is hereby incorporated by reference to portions of the registrant's definitive proxy statement, information statement or an amendment to this Annual report on Form 10-K for its 2019 Annual Meeting of Stockholders. The registrant intends to file a definitive proxy statement, information statement or an amendment to this Annual Report on Form 10-K with the Securities and Exchange Commission no later than 120 days after the end of the registrant's fiscal year ended December 31, 2018.

XENETIC BIOSCIENCES, INC.
2018 ANNUAL REPORT ON FORM 10-K

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K ("Annual Report") contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 27A of the Securities Act of 1933, as amended. All statements contained in this Annual Report other than statements of historical fact, including statements regarding our future results of operations and financial position, our business strategy and plans, future revenues, projected costs, prospects and our objectives for future operations, are forward-looking statements. These forward-looking statements include, but are not limited to, statements concerning our plans to develop our proposed drug candidates; our expectations regarding the nature, timing and extent of clinical trials and proposed clinical trials including the timing of generating clinical data from these trials; our expectations regarding the timing for proposed submissions of regulatory filings, including but not limited to any Investigational New Drug ("IND") filing or any New Drug Application ("NDA"); the nature, timing and extent of collaboration arrangements; the expected results pursuant to collaboration arrangements including the receipts of future payments that may arise pursuant to collaboration arrangements; the outcome of our plans to obtain regulatory approval of our drug candidates; the outcome of our plans for the commercialization of our drug candidates; our plans to address certain markets, engage third party manufacturers, and evaluate additional drug candidates for subsequent commercial development, and the likelihood and extent of competition to our drug candidates; the development of the CAR T ("Chimeric Antigen Receptor T Cell") technology; and the risk that the acquisition of the CAR T technology may not be completed on the terms or in the timeframe expected by the Company.

In some cases, these statements may be identified by terminology such as "may," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "predict," "potential," or "continue," or the negative of such terms and other comparable terminology. Although we believe that the expectations reflected in the forward-looking statements contained herein are reasonable, we cannot guarantee future results, the levels of activity, performance or achievements. These statements involve known and unknown risks and uncertainties that may cause our or our industry's results, levels of activity, performance or achievements to be materially different from those expressed or implied by forward-looking statements.

Some factors that could cause actual results to differ materially include without limitation:

- our need to raise additional working capital in the very near term for the purpose of developing products and technologies and to continue as a going concern;
- our ability to finance our business;
- our ability to successfully execute, manage and integrate key acquisitions and mergers, including the acquisition of the CAR T technology;
- product development and commercialization risks, including our ability to successfully develop the CAR T technology;
- our ability to successfully commercialize our current and future drug candidates;
- our ability to achieve milestone and other payments associated with our co-development collaborations and strategic arrangements;
- the impact of new technologies on our drug candidates and our competition;
- changes in laws or regulations of governmental agencies;
- interruptions or cancellation of existing contracts;
- impact of competitive products and pricing;
- product demand and market acceptance and risks;
- the presence of competitors with greater financial resources;
- continued availability of supplies or materials used in manufacturing at the current prices;
- the ability of management to execute plans and motivate personnel in the execution of those plans;
- our ability to attract and retain key personnel;
- adverse publicity related to our products or the Company itself;
- adverse claims relating to our intellectual property;
- the adoption of new, or changes in, accounting principles;
- the costs inherent with complying with statutes and regulations applicable to public reporting companies, such as the Sarbanes-Oxley Act of 2002;
- other new lines of business that the Company may enter in the future; and
- other factors set forth in the Risk Factors section of this Annual Report on Form 10-K and in subsequent filings we make with the Securities and Exchange Commission.

These factors are not necessarily all of the important factors that could cause actual results to differ materially from those expressed in the forward-looking statements in this Annual Report. Other unknown or unpredictable factors also could have material adverse effects on our future results, including, but not limited to, those discussed in the section titled "Risk Factors." The forward-looking statements in this Annual Report are made only as of the date of this Annual Report, and we do not undertake any obligation to publicly update any forward-looking statements to reflect subsequent events or circumstances. We intend that all forward-looking statements be subject to the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995.

As used in this Annual Report, unless otherwise indicated, all references herein to "Xenetic," the "Company," "we" or "us" refer to Xenetic Biosciences, Inc. and its wholly-owned subsidiaries.

Our brand and product names, including but not limited to Virexxa®, OncoHist™, PolyXen™, ErepoXen™, ImuXen™, and PulmoXen™ contained in this Annual Report are trademarks, registered trademarks or service marks of Xenetic Biosciences, Inc. and/or its subsidiaries in the United States of America ("USA" or "U.S.") and certain other countries. All other company and product names may be trademarks of the respective companies with which they are associated.

PART I

ITEM 1 – BUSINESS

Overview

We are a biopharmaceutical company focused on the discovery, research and development of next-generation biological drugs and novel oncology therapeutics. We have an extensive patent portfolio of over 170 issued patents in the U.S. and worldwide, covering various aspects of our PolyXen™ platform technology and advanced polymer conjugate technologies, as well as our proprietary biologic drugs and novel oncology drug candidates. We believe our portfolio positions us well for strategic partnership and commercialization opportunities. Our objective is to leverage our portfolio to maximize opportunities to out-license assets from our portfolio in order to generate working capital to both build long-term stockholder value and provide us with the funding necessary for clinical development of our oncology drug candidates through market launch.

We incorporate our patented and proprietary technologies into a number of drug candidates currently under development with biotechnology and pharmaceutical industry collaborators to create what we believe will be next-generation biologic drugs with improved pharmacological properties over existing therapeutics. While we primarily focus on researching and developing oncology drugs, we also have significant interests in drugs being developed by our collaborators to treat other conditions.

Our most advanced investigational drug candidate is oncology therapeutic XBIO-101 (sodium cridanimod) for the treatment of progestin resistant endometrial cancer. We have exclusive rights to develop and commercialize XBIO-101 worldwide, except for specified countries in the Commonwealth of Independent States ("CIS"). XBIO-101 has been granted orphan drug designation by the U.S. Food and Drug Administration ("FDA") for the potential treatment of progesterone receptor negative ("PrR-") endometrial cancer in conjunction with progesterone therapy. We commenced a Phase II trial for XBIO-101 under an IND in 2017, with the first patient dosed in October 2017. We closed patient enrollment in the trial in March 2019 as a result of slower than expected progress on the trial resulting from patient enrollment and retention challenges.

Our lead proprietary technology is PolyXen™, an enabling platform technology which can be applied to protein or peptide therapeutics. It employs the natural polymer polysialic acid ("PSA") to prolong a drug's circulating half-life and potentially improve other pharmacological properties. PolyXen has been demonstrated in human clinical trials to confer prolonged half-life on biotherapeutics such as recombinant human erythropoietin and recombinant Factor VIII ("rFVIII"). We believe this technology may be applied to a variety of drug candidates to enhance the properties of the therapeutic, potentially providing advantages over competing products.

Our drug candidates have resulted from our research activities or that of our collaborators and are in the development stage. As a result, we continue to commit a significant amount of our resources to our research and development activities and anticipate continuing to do so for the near future. To date, none of our drug candidates have received regulatory marketing authorization in the U.S. by the FDA nor in any other territories by any applicable agencies. Although we hold a broad patent portfolio, because of capital constraints the focus of our internal development efforts in 2018 was limited to research and development of our primary product candidate XBIO-101.

We were incorporated under the laws of the State of Nevada in August 2011. We, directly or indirectly, through our wholly-owned subsidiary, Xenetic Biosciences (U.K.) Limited ("Xenetic U.K."), and its wholly-owned subsidiaries, Lipoxen Technologies Limited ("Lipoxen"), Xenetic Bioscience, Incorporated ("XTI") and SymbioTec, GmbH ("SymbioTec"), own various U.S. federal trademark registrations and applications, and unregistered trademarks and service marks, including but not limited to Virexxa®, OncoHist™, PolyXen, ErepoXen™, ImuXen™, and PulmoXen™.

Our Strategy

We recently announced our plans to acquire the XCART platform, a novel CAR T technology engineered to target patient- and tumor-specific neoantigens (referred to herein as "XCART") (See Recent Developments for a description of the transaction and technology.) The acquisition of the platform technology is expected to close in the first half of 2019, and the Company plans to initially apply the XCART technology to develop cell-based therapeutics for the treatment of B-cell Lymphomas. We believe these personalized T cell therapies have the potential to offer cancer patients substantial benefits over the existing standard of care and currently approved CAR T therapies. We anticipate that our primary focus once the transaction is completed will be on advancing this technology through regulatory approval and commercialization.

Our strategy is to develop oncology drug candidates through regulatory approval and commercialization, and to opportunistically pursue a continuous and ongoing out-licensing effort for our PolyXen platform technology to drive incremental shareholder value and generate working capital to assist in providing the funding required to support our drug development efforts.

We intend to pursue orphan drug designations and accelerated approval pathways for relevant oncology indications as appropriate in both the U.S. and Europe. If our orphan oncology drug candidates are granted orphan drug designation, then we may benefit from certain key advantages of orphan status including certain market exclusivities.

We intend to opportunistically advance our PolyXen platform technology by entering into collaborative out-license arrangements with global pharmaceutical companies who could apply the necessary resources for advancing drug candidates through to worldwide commercialization, or by entering into arrangements with other partners that would in-license our technology on a restrictive-market basis. The latter arrangement would provide support to the Company in the form of access to partner-generated clinical data, which is informative when contemplating potential monetization of our proprietary technology in larger markets.

We intend to advance development of our drug candidates primarily through the use of contract manufacturing and contract research organizations ("CROs") in order to efficiently manage our resources. Continuous pipeline growth and advancement of out-licensed drug candidates is dependent, in part, on our ability to raise sufficient capital and to advance our existing co-development collaborations and strategic arrangements as well as enter into new such arrangements.

Recent Developments

XCART Technology

On March 1, 2019, we entered into an agreement to acquire the XCART platform technology (the "Transaction") a proximity-based screening platform capable of identifying CAR constructs that can target patient-specific tumor neoantigens, with a demonstrated proof of mechanism in B-cell Non-Hodgkin lymphomas. The XCART technology, developed by The Scripps Research Institute (the "Institute") in collaboration with the Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry ("IBCH"), is believed to have the potential to significantly enhance the safety and efficacy of cell therapy for B-cell lymphomas by generating patient- and tumor-specific CAR T cells.

The XCART technology platform was designed by its originators to utilize an established screening technique to identify peptide ligands that bind specifically to the unique B-cell receptor ("BCR") on the surface of an individual patient's malignant tumor cells. The peptide is then inserted into the antigen-binding domain of a CAR, and a subsequent transduction/transfection process is used to engineer the patient's T cells into a CAR T format which redirects the patient's T cells to attack the tumor. Essentially, the XCART screening platform is the inverse of a typical CAR T screening protocol wherein libraries of highly specific antibody domains are screened against a given target. In the case of XCART screening, the target is itself an antibody domain, and hence highly specific by its nature. The XCART technology creates the possibility of personalized treatment of lymphomas utilizing a CAR with an antigen-binding domain that should only recognize, and only be recognized by, the unique BCR of a particular patient's B-cell lymphoma. An expected result for XCART is limited off-tumor toxicities, such as B-cell aplasia. Our clinical development program will seek to confirm the early preclinical results, and to demonstrate a more attractive safety profile than existing therapies.

In connection with the Transaction, we entered into a Share Purchase Agreement (the "Share Purchase Agreement") pursuant to which we will purchase all of the issued and outstanding shares of capital stock of Hesperix SA, a Swiss corporation ("Hesperix"), as well as additional transaction documents. Concurrent with the Share Purchase Agreement, we also entered into an assignment agreement with OPKO Pharmaceuticals, LLC ("OPKO") (the "OPKO Assignment Agreement") pursuant to which the Company will acquire and accept all of OPKO's right, title and interest in an Intellectual Property License Agreement entered into between the Institute and OPKO related to the XCART technology. In total, we will issue 7.5 million shares of our common stock in the Transaction, including 4.875 million shares to be issued to the shareholders of Hesperix and 2.625 million shares of common stock to be issued in connection with the OPKO Assignment Agreement. The closing of the Transaction is subject to customary closing conditions as well as conditions regarding (i) the Company having adequate financing to fund its future working capital obligations following the closing and (ii) the Company obtaining necessary and appropriate stockholder approvals, evidencing among other matters, approval of the Share Purchase Agreement and the transactions contemplated thereunder, including the issuance of the transaction shares. Subject to the satisfaction of the closing conditions, the Transaction is expected to close in the first half of 2019.

We intend to pursue development efforts of the XCART technology once the acquisition is consummated and pursue other development efforts around CAR T technology. We also plan to pursue collaborations with immuno-oncology ("I-O") companies in which we would seek to use XBIO-101 in combination with approved or developmental I-O compounds such as checkpoint inhibitors subject to adequate funding.

Closing of Patient Enrollment in XBIO-101 Phase II EC Trial

We commenced the Phase II trial for XBIO-101 in 2017, with the first patient dosed in October 2017. We closed patient enrollment in the trial in March 2019 as a result of slower than expected progress on the trial resulting from patient enrollment and retention challenges. We are in the process of identifying development paths for XBIO-101, particularly those that can efficiently leverage our existing human data and regulatory status to extend development into I-O settings.

Our Technology and Drug Candidates

The Technologies

We incorporate our patented and proprietary technologies into a number of drug candidates which are currently under development with our biotechnology and pharmaceutical collaborators, with the goal of creating what we believe will be the next generation of biologic drugs and therapeutics. While we primarily focus on researching and developing oncology drugs, we also have ownership and other economic interests in drugs being developed by our collaborators to treat other conditions. Our patent portfolio spans four core proprietary technologies including two platforms, small molecules and biologics covering multiple drug candidates and indications including XBIO-101, PolyXen, OncoHist and ImuXen. We have primarily been focused on the advancement of XBIO-101 through clinical trials. We have not been actively pursuing development efforts for PolyXen, OncoHist and ImuXen due to capital restraints. We anticipate that the focus of our future internal development efforts will be limited to research and development of our XCART technology as well as potential I-O applications for our product candidate XBIO-101.

XBIO-101 — A small molecule therapeutic with the potential to confer sensitivity to hormone therapeutics upon cancer cells that are otherwise insensitive to such treatments. XBIO-101 (sodium cridanimod) belongs to a class of low-molecular weight synthetic interferon inducers. In addition to its immunomodulatory properties, XBIO-101 has been shown to increase levels of progesterone receptor, or PrR, expression in tumor tissue of patients who are PrR-, and thus may restore sensitivity of non-responsive endometrial cancers to hormonal (e.g., progestin) therapy. Based on preclinical observations, XBIO-101 may also be therapeutically relevant in other hormone therapy resistant cancers, such as triple-negative breast cancer. XBIO-101 has been granted an orphan drug designation by the FDA for the potential treatment of progesterone receptor negative endometrial cancer in conjunction with progesterone therapy. Sodium cridanimod has been the subject of numerous nonclinical studies as well as 21 foreign controlled clinical trials totaling 750 subjects, which supported marketing authorizations in ex-Soviet territories, as well as enablement of our active US IND. We believe that XBIO-101 may also have utility, alone or in combination, in immuno-oncology approaches. The Company is therefore seeking to advance the compound in collaboration with I-O focused partners.

PolyXen	An enabling biological platform technology designed to extend the circulation time of drug molecules in the human body by chemically attaching polysialic acid, or PSA, to the drug molecule by a process termed polysialylation, thereby creating potentially superior next generation therapeutic candidates. PSA, a biopolymer, comprising a chain of sialic acid molecules, is a natural constituent of the human body, although we obtain our PSA from a bacterial source.
OncoHist	A novel therapeutic platform technology that utilizes the properties of modified human histone H1.3 for targeted cell apoptosis (programmed cell death), which may enable OncoHist to treat a broad range of cancer indications. OncoHist, unlike many competing oncology therapies, is based on a molecule occurring naturally in the human body, primarily in the cell nucleus, and is therefore hypothesized to be better tolerated and less immunogenic than other oncology therapies.
ImuXen	A novel liposomal co-entrapment encapsulation technology designed to maximize both cell and immune system mediated responses. The technology is based on the co-entrapment of the nominated antigen(s) in a liposomal vesicle. The technology when applied may create new vaccines and improve the use and efficacy of certain existing human vaccines.

Though we hold a broad patent portfolio, the focus of our internal development efforts in 2018 was limited to research and development of XBIO-101.

Research, Outside Services and Collaborations

Through partner efforts, we are developing our pipeline of next-generation bio-therapeutics and novel oncology drugs based on our XBIO-101 and PolyXen proprietary technologies. In order to do this while efficiently managing our overhead, we rely on the services of contract manufacturers and CROs and our strategic collaborations. We currently do not have in-house research facilities to pursue these initiatives. Accordingly, continuous pipeline growth and advancement of our technologies and drug candidates is dependent on several important collaborations and strategic arrangements including our arrangements with:

- PJSC Pharmsynthez (“Pharmsynthez”), a Russian pharmaceutical company and presently our majority stockholder;
- Serum Institute of India Limited (“Serum Institute”), one of the world’s largest vaccine manufacturers and one of India’s largest biotech companies, as well as a beneficial owner of over 5% of our common stock; and
- Takeda Pharmaceuticals Co. Ltd (formerly Shire plc) (“Takeda”), a global biopharmaceutical leader.

Accordingly, in addition to pursuing the development of our pipeline of next-generation bio-therapeutics and novel oncology drugs, we also have significant interests in drug candidates being developed by our collaborators to treat other conditions. We may collect milestone payments and royalties pursuant to these collaborations to the extent that these drugs are successfully developed and marketed. However, other than potential royalty payments under a sublicense with Takeda, we do not anticipate any milestone or royalty payments in the near term, if at all. For further detail, please read the section titled “Significant Co-Development Collaborations and Strategic Arrangements” below.

Our Drug Candidate Pipeline

Our product pipeline contains a number of drug candidates under development with our biotechnology and pharmaceutical collaborators. The following discussion summarizes key information regarding our current drug candidates, organized by our internal programs and our collaborators’ programs:

XBIO-101

XBIO-101 is our most advanced internal candidate with an orphan drug designation from the FDA for the potential treatment of progesterone receptor negative endometrial cancer in conjunction with progesterone therapy. An IND application was submitted for XBIO-101 and is in effect for our Phase II clinical trial in the U.S.

We acquired certain IP rights with respect to XBIO-101, and the worldwide rights to develop, market and license XBIO-101 for certain uses, except for excluded uses within the CIS, from AS Kevelt ("Kevelt"), a wholly-owned subsidiary of Pharmsynthez. We also acquired Kevelt's orphan drug designation from the FDA for the use of XBIO-101 in the treatment of PrR- endometrial cancer in conjunction with progesterone therapy.

XBIO-101 (sodium cridanimod), belongs to a class of low-molecular weight synthetic interferon, or IFN, inducers and is primarily used in a wide range of therapeutic areas such as antiviral, antibacterial, antitumor, and inflammatory indications due to its ability to modify or regulate one or more immune system functions. We believe XBIO-101 may also prove to be therapeutically relevant in hormone-resistant cancers by increasing the levels of PrR expression in tumor tissue of patients who are PrR deficient. As such, it may restore the sensitivity of non-responsive endometrial cancers to hormonal (e.g., progestin) therapy. Accordingly, we were pursuing the use of XBIO-101 for the treatment of endometrial cancer.

Our decision to investigate XBIO-101 for the treatment of endometrial cancer was based in part on the history of sodium cridanimod in preclinical and clinical research conducted by others, including prior clinical trials conducted and completed in Russia that assessed the efficacy and safety of sodium cridanimod. Sodium cridanimod has been authorized for medicinal use in the Russian Federation for over 20 years with millions of doses estimated to have been sold for the treatment of non-cancer indications. XBIO-101 is also known under the brand names Neovir, Camedon and Primavir.

The extensive clinical testing conducted by others, as well as the marketing history of sodium cridanimod, provided support for our authorization to proceed directly with a Phase II efficacy study under our U.S. IND for the use of sodium cridanimod in conjunction with progestin therapy in patients with progestin resistant, recurrent or persistent endometrial cancer. We commenced the Phase II trial under the IND in 2017, with the first patient dosed in October 2017. We closed patient enrollment of the trial in March 2019 as a result of slower than expected progress on the trial resulting from patient enrollment and retention challenges. We are in the process of identifying development paths for XBIO-101, particularly those that can efficiently leverage our existing human data and regulatory status to extend development into immune-oncology settings.

ErepoXen

ErepoXen, or polysialylated erythropoietin ("PSA-EPO"), uses our PolyXen platform technology for the treatment of anemia in chronic kidney disease ("CKD") patients. It is designed to reduce the dosing frequency by extending the circulating half-life of the therapeutic in the body. We terminated our clinical development efforts of ErepoXen and continue to seek out-license opportunities for the drug candidate in our licensed territories.

We have collaboration agreements with SynBio LLC ("SynBio") and Serum Institute to develop and launch ErepoXen in limited markets pursuant to which we will collect royalties if they are successful in these efforts.

Serum Institute conducted Phase I and Phase II clinical trials in 95 human subjects. These safety trials, which had no significant drug-related adverse events, provided us with the data to commence a Phase II, repeat dosing, ICH compliant clinical trial for ErepoXen in Australia, New Zealand and South Africa for CKD patients not on dialysis. We completed three cohorts of this study and then terminated the study. Each cohort represents an increased dose of ErepoXen that is given on a repeat schedule until therapeutic levels of hemoglobin are achieved. In our study, there were no serious Treatment Emergent Adverse Events ("TEAE") related to ErepoXen in either cohort 1 or 2. There was one serious TEAE in cohort 3 judged to be possibly related, but not unexpected given the safety profile of other Erythropoietin Stimulating Agents.

In addition, Serum Institute finished Phase I/II clinical trials in India of ErepoXen for in-center-dialysis patients. Serum Institute has submitted a clinical trial application to conduct a Phase II(b)/III clinical trial for PSA-EPO in India.

SynBio received regulatory approval to commence ErepoXen Phase II(b)/III human clinical trials in Russia, is currently recruiting patients and intends to commence the commercialization and marketing stages of ErepoXen in the Russian and CIS markets subject to approval in such markets.

Drug Candidates in the Pipeline that are not Currently Active Internally or with Third Party Collaborators

OncoHist

Our drug candidate OncoHist, which has clinical proof of concept, utilizes the properties of modified human histone H1.3 for targeted cell killing. We were previously researching and developing OncoHist for the treatment of relapsed or resistant acute myeloid leukemia ("AML"). Currently, all our development efforts regarding OncoHist remain on hold due to capital constraints. We would expect to file an IND application for OncoHist for AML once we are able to raise sufficient capital and reactivate our development efforts.

We have a sponsored research agreement with Dana Farber Cancer Institute intended to elucidate OncoHist's mechanism of action as well as to characterize the responsiveness of various AML cell lines to OncoHist. Dr. Richard Stone, MD, Professor of Medicine at Harvard Medical School and Clinical Director of the Adult Leukemia Program at Dana-Farber Cancer Institute, presented data at the 2014 American Society of Hematology meeting (*Blood*, 2014 124(21):3604 OncoHist, an rh Histone 1.3, Is Cytotoxic to Acute Myeloid Leukemia Cells and Results in Altered Downstream Signaling).

We have completed non-clinical toxicity studies and had a productive, in-person pre-IND meeting with the FDA in August 2015 where manufacturing and clinical matters were addressed, including guidance from the FDA regarding inclusion of an additional indication besides AML in our proposed Phase I clinical trial. However, our efforts in developing this drug candidate have been on hold since 2016 due to our focus on other product candidates and limited capital resources.

Pipeline Expansion Opportunities

Operating under licenses from us within their home markets, our collaborators can potentially generate preclinical and clinical data related to our technologies across a wide spectrum of therapeutic areas. Under these agreements, we retain all rights for major markets and co-own the clinical data. We therefore have the opportunity to utilize the data in our decision-making process regarding development and commercialization in major markets. We expect to be able to utilize the results from substantially all of our clinical toxicity data and other clinical data generated in the development of XBIO-101 and PolyXen, and potentially for OncoHist, and ImuXen, if any, for a variety of orphan oncology indications and next generation biologic drugs.

For example, we believe that we may be able to develop XBIO-101 for other indications. Results from preclinical and exploratory studies conducted by a collaborative partner suggest that XBIO-101 can up-regulate (i.e., increase the levels of) estrogen receptor ("ER") in certain tissue types. Proof of concept studies are being planned to investigate additional therapeutic opportunities for XBIO-101 in hormone therapy resistant tumor types other than endometrial cancer.

We are in the process of identifying development paths for XBIO-101, particularly those that can efficiently leverage our existing human data and regulatory status to extend development into immuno-oncology settings. We are seeking partners for conducting preclinical and Phase I – Phase II studies, such as human clinical dose ranging and biomarker studies of XBIO-101, alone and in combination with I-O therapeutics including checkpoint inhibitors.

We also believe that the nature of our technologies, including the PolyXen platform, will allow us to pursue additional drug candidates for new indications based on existing and future scientific data.

Significant Co-Development Collaborations and Strategic Arrangements

Takeda Pharmaceuticals Co. Ltd. ("Takeda") (f/k/a Shire plc)

We are a party to an exclusive research, development and license agreement with Baxalta US Inc. and Baxalta AB (collectively "Baxalta"), wholly-owned subsidiaries of Takeda, related to the development of a novel series of polysialylated blood coagulation factors. This collaboration with Takeda relies on the Company's PolyXen technology to conjugate PSA to therapeutic blood-clotting factors, with the goal of improving the pharmacokinetic profile and extending the active life of these biologic molecules. The agreement grants Takeda a worldwide, exclusive, royalty-bearing license to our PSA patented and proprietary technology in combination with Takeda's proprietary molecules designed for the treatment of blood and bleeding disorders. The first program under this agreement was a next generation Factor VIII protein product candidate.

In May 2017, we announced that Takeda had terminated further development of SHP656, its polysialylated rFVIII drug candidate for the treatment of hemophilia, being developed using our proprietary PolyXen technology. While Takeda's Phase I/II trial demonstrated SHP656's efficacy and pharmacokinetic data commensurate with the profile of an extended half-life rFVIII product, the pre-defined once-weekly dosing criterion set forth in the research, development, license and supply agreement was not met. To our knowledge, there were no drug-related adverse events, serious adverse events, or rFVIII inhibitors reported to date. Though the trial's pre-defined once-weekly dosing criterion was not met, we intend to continue to explore the potential for future collaborations with Takeda and Takeda has commenced a new, undisclosed project under the agreement.

In October 2017, we entered into a right to sublicense agreement (the "Sublicense Agreement") with Baxalta. Pursuant to the sublicense agreement, we granted to Baxalta the right to grant a nonexclusive sublicense to licensed patents in connection with products related to the treatment of blood and bleeding disorders ("Covered Products"). Pursuant to the sublicense agreement, Baxalta paid us a one-time payment of seven million five hundred thousand dollars ($7,500,000) in November 2017 and agreed to pay us single digit royalty payments based upon net sales of the Covered Products throughout the term, each of which is conditioned upon the performance of the sublicense contemplated by the sublicense agreement. No royalties have been received to date.

SynBio LLC

In August 2011, we entered into a stock subscription and collaborative development agreement with SynBio (the "Co-Development Agreement"), pursuant to which we granted SynBio an exclusive license to develop, market and commercialize certain drug candidates utilizing molecules based on our PolyXen and OncoHist platform technologies in Russia and the CIS, collectively referred to herein as the SynBio Market. In exchange for our granting to SynBio those certain license rights, SynBio granted an exclusive license to us to use any SynBio preclinical and clinical data generated by SynBio and to engage in the development and commercialization of drug candidates that may arise from the collaboration in any territory outside of the SynBio Market based upon the Co-Development Agreement.

We hope and expect to mitigate certain technical and commercial risks of drug development by working in collaboration with SynBio. Under the Co-Development Agreement, SynBio is responsible for progressing six new product candidates through human proof of concept trials in Russia as primary validation for the initiation of European Medicines Agency ("EMA") or FDA clinical trials by us.

The primary goal of the Co-Development Agreement is to research and develop drug candidates for planned commercialization using SynBio and our combined respective expertise and technologies. Drug candidates must meet the success criteria as decided upon by a joint steering committee, which includes representation from both SynBio and us, where we have the right to appoint the chair who has the casting vote. Once a potential drug candidate is selected, clinical trials will be separately conducted by each company in their respective territories with the goal to achieve regulatory approval of the products for commercial sale.

SynBio is wholly responsible for funding and conducting their own research and clinical development activities in Russia, and we are wholly responsible for funding and conducting our own research and clinical development activities in the U.S., Europe and elsewhere outside the SynBio Market. There are no milestones or other research-related payments provided for under the Co-Development Agreement other than fees for the provision of each party's respective research supplies based on their technology. For the years ended December 31, 2018 and 2017, we have recognized no supply service revenues in connection with the Co-Development Agreement. Among other provisions, the parties may terminate the Co-Development Agreement in relation to a particular product upon 30 days' written notice, if such party, in its reasonable opinion, believes that a third-party IP right exists, which would have a material effect on the research and/or development of the relevant product. Further, the parties may terminate the Co-Development Agreement if the other party is in material breach of the Co-Development Agreement and, in the case of a breach capable of remedy, the breach is not remedied within 90 days of receiving notice specifying the breach and requiring its remedy, or if the other party becomes insolvent. The parties also may terminate the Co-Development Agreement by immediate written notice to the other party in relation to a specific product such if product does not meet the relevant success criteria for the product.

In furtherance of our co-development clinical objectives, on December 31, 2014, we granted SynBio a warrant to purchase 204,394 shares of our common stock that contain vesting triggers based on the achievement by SynBio of certain clinical development objectives within specific timeframes (the "SynBio 2014 Warrant"). Simultaneously with the issuance of the SynBio 2014 Warrant, we granted additional warrants to purchase 9,697 aggregate new shares of our common stock to SynBio and Pharmsynthez non-director designees under the same terms and conditions of the SynBio 2014 Warrant. No warrants were exercised during the years ended December 31, 2018 and 2017. The vesting criteria for the SynBio 2014 warrants were not met and, as a result, the warrants expired during the year ended December 31, 2018.

In 2017, SynBio became a wholly-owned subsidiary of Pharmsynthez and all ownership percentages previously held by SynBio are combined with Pharmsynthez.

PJSC Pharmsynthez

In November 2009, we entered into a collaborative research and development license agreement with Pharmsynthez (the "Pharmsynthez Arrangement") pursuant to which we granted an exclusive license to Pharmsynthez to develop, commercialize and market six product candidates based on our PolyXen and ImuXen technology anywhere within Russia and the CIS, as well as certain clinical and research data developed by us on the six product candidates. In exchange, Pharmsynthez granted us an exclusive license to use any preclinical and clinical data developed by Pharmsynthez, within the scope of the Pharmsynthez Arrangement, and to engage in further research, development and commercialization of drug candidates in any territory outside of Russia and the CIS at our own expense.

We expect to mitigate certain risks of drug development by reviewing human clinical data arising out of this collaboration with Pharmsynthez before we take a particular drug candidate into FDA and EMA trials. Under the Pharmsynthez Arrangement, Pharmsynthez is responsible for progressing six new drug candidates through human proof of concept trials in Russia as primary validation prior to the initiation of EMA/FDA clinical trials by us outside of Russia. A joint steering committee, where we have the right to appoint the chair who has the casting vote, was established to facilitate the communication of scientific data and to assist generally with each party's research decisions and to monitor research and development progress under the Pharmsynthez Arrangement.

Pharmsynthez is wholly responsible for funding and conducting its own research and clinical development activities in Russia. We are wholly responsible for funding and conducting our own research and clinical development activities in the U.S., Europe and the rest of the world outside of Russia and the ex-CIS regions. There are no milestones or other research related payments provided for under the Pharmsynthez Arrangement other than royalties. Among other provisions, the parties may terminate the agreement in relation to a particular product upon 30 days' written notice, if such party, in its reasonable opinion, believe that a third-party intellectual property right exists which would have a material effect on the research and/or development of the relevant product. Further, the parties may terminate the agreement if the other party is in material breach of the agreement and, in the case of a breach capable of remedy, the breach is not remedied within 90 days of receiving notice specifying the breach and requiring its remedy, or if the other party becomes insolvent. The parties also may terminate the agreement by immediate written notice to the other party in relation to a specific product if such product does not meet the relevant success criteria for the product.

Pharmsynthez is an affiliate of the Company and our majority stockholder. On February 27, 2017, Pharmsynthez acquired 100% of SynBio. As a result, SynBio's ownership stake is reflected as part of Pharmsynthez' share ownership. Pharmsynthez directly, and indirectly through SynBio, has a share ownership in the Company of approximately 57.1% of the total issued and outstanding common stock as of December 31, 2018. In addition to its common stock ownership, Pharmsynthez holds outstanding warrants to purchase our common stock, approximately 1.5 million shares of our issued and outstanding Series B Preferred Stock (as defined in Note 9, *Stockholders' Equity*), and all of our issued and outstanding Series A Preferred Stock (as defined in Note 9, *Stockholders' Equity*) through SynBio.

Serum Institute

In August 2011, we entered into a collaborative research and development agreement (the "Serum Agreement") with Serum Institute amending and restating a series of earlier agreements and providing Serum Institute an exclusive license to use our PolyXen technology to research and develop one potential commercial product, PSA-EPO. Serum Institute is responsible for conducting all preclinical and clinical trials required to achieve regulatory approvals within territories outside of certain predetermined territories assigned to us, which include the U.S., the European Economic Area, and Japan, among other territories, at Serum Institute's own expense. Royalty payments are payable by Serum Institute to us for net sales to certain customers in the Serum Institute sales territory. Royalty payments are payable by us to Serum Institute for net sales received by us over the term of the license. No royalty, revenue or expense was recognized by us related to the Serum Institute arrangement during the years ended December 31, 2018 and 2017. There are no milestone or other research-related payments due under the Serum Agreement.

Through December 31, 2018, we and Serum Institute continued to engage in research and development activities with no resultant commercial products. Among other reasons, the parties may terminate the Serum Agreement by written notice if the other party is in material breach of the Serum Agreement and, in the case of a breach capable of remedy, the breach is not remedied within 90 days of the other party receiving notice specifying the breach and requiring its remedy.

In furtherance of our co-development clinical objectives, on December 31, 2014, we granted to Serum Institute certain warrants to purchase 96,970 shares of our common stock that contain vesting triggers based on the achievement by Serum Institute of certain clinical development objectives within specific timeframes ("Serum 2014 Warrant"). Simultaneously with the issuance of the Serum 2014 Warrant, we issued additional warrants to purchase an aggregate of 4,852 shares of our common stock to Serum Institute non-director designees under the same terms and conditions of the Serum 2014 Warrant. The Serum 2014 Warrant expires on December 30, 2019 and no warrants were exercised during any of the years ended December 31, 2018 and 2017.

In addition, the Serum Agreement allows for Serum Institute to nominate a non-executive director to our Board of Directors as long as Serum Institute or its subsidiaries holds at least 6% of our common stock. Serum Institute is a related party of ours, with a share ownership of approximately 6.7% of our total issued common stock as of December 31, 2018.

Our Intellectual Property

We strive to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to our business, including seeking, maintaining and defending patent rights, whether developed internally or licensed from our collaborators or other third-parties. Our policy is to seek to protect our proprietary position by, among other methods, filing patent applications in the U.S. and in jurisdictions outside of the U.S. covering our proprietary technology, inventions, improvements and product candidates that are important to the development and implementation of our business. We also rely on trade secrets and know-how relating to our proprietary technology and product candidates, continuing innovation, and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of oncology. We also plan to rely on data exclusivity, market exclusivity, and patent term extensions when available. Our commercial success will depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions, and improvements; to preserve the confidentiality of our trade secrets; to obtain and maintain licenses to use intellectual property owned by third-parties; to defend and enforce our proprietary rights, including any patents that we may own in the future; and to operate without infringing on the valid and enforceable patents and other proprietary rights of third-parties.

Our drug candidates are in various stages of development, each protected by patent and pending patent applications in the U.S. with the U.S. Patent and Trademark Office ("USPTO") and in certain other developed countries. Our first issued patents begin to expire starting in 2022 with the majority of the existing issued patents expiring between 2025 and 2030.

Our patent strategy is to file patent applications on innovations and improvements in those jurisdictions that comprise the major pharmaceutical markets in the world or locations where a pharmaceutical may be manufactured. These jurisdictions include, but are not limited to, the U.S., U.K., Australia, Japan, Canada, South Korea, China, India, Russia and certain other countries in the European Union ("E.U.") and Asia, though we do not necessarily file a patent application in each of these jurisdictions for every patent family.

As of February 28, 2019, we directly or indirectly own, through our wholly-owned subsidiary, Xenetic U.K., and its wholly-owned subsidiaries, Lipoxen, XTI and SymbioTec, more than 170 U.S. and international patents that cover various aspects of our technologies. We have filed patent applications, and plan to file additional patent applications, covering various aspects of our PolyXen platform technology covering polysialylation and advanced polymer conjugate technologies, respectively, as well as our other product candidates, including XBIO-101. More specifically, our patents and patent applications cover polymer architecture, drug conjugates, formulations, methods of manufacturing polymers and polymer conjugates and methods of administering polymer conjugates. We may also file additional patent applications, where possible, for XBIO-101 and OncoHist for additional uses and indications.

Our patent portfolio contains patents and patent applications that encompass our OncoHist platform technology including use of histones for the treatment of different cancers. The OncoHist patent portfolio, acquired as part of our acquisition of SymbioTec in January 2012, includes OncoHist, a bis-Met histone H1.3. In addition, our licensed patent portfolio includes patents issued in jurisdictions outside of the U.S. and licensed patent applications pending in jurisdictions outside of the U.S. that are foreign counterparts to one or more of the foregoing U.S. patents and patent applications. The OncoHist portfolio also includes patents that cover the use of a histone protein as an antibiotic and to treat thrombocytopenia and further as an antimicrobial component of a personal care product.

We have received patent protection for certain therapeutics that use our PolyXen technology linking the specific therapeutic to a PSA. These include, but are not limited to, PSA-EPO, PSA-insulin and PSA-insulin like protein, SHP656 (PSA-rFVIII), PSA-DNase I and PSA-granulocyte colony stimulating factor (PSA-GCSF). Further patents cover methods to prepare proteins that are linked to a PSA. These method patents include those that link a PSA to a protein in a high pH solution as well as patents that use a process for producing an aldehyde derivative of a sialic acid through the opening and oxidation of a sialic acid unit. For instance, we have patent protection for a PSA linkage that can be at the N-terminus.

We have received patent protection for the production of PSA and the removal of endotoxin during the purification process. The removal of endotoxin occurs through the addition of a high pH solution to the PSA and a process to separate a polydisperse ionically charged polysaccharide, such as PSA, into fractions of different average molecular weight. This is accomplished through the use of a column and elution buffers with different and constant ionic strength and pH, resulting in a fractionated polysaccharide that has a molecular weight polydispersity of 1.1 or lower.

Issued patents can provide protection for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance, and the legal term of patents in the countries in which they are obtained. In general, patents issued for applications filed in the United States can provide exclusionary rights for 20 years from the earliest effective filing date. In addition, in certain instances, the term of an issued U.S. patent that covers or claims an FDA approved product can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, which is called patent term extension. The restoration period cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. The term of patents outside of the U.S. varies in accordance with the laws of the foreign jurisdiction, but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country, and the validity and enforceability of the patent.

In certain situations, where we work with drugs covered by one or more patents, our ability to develop and commercialize our technologies may be affected by limitations of our access to these proprietary drugs. Even if we believe we are free to work with a proprietary drug, we cannot guarantee that we will not be accused of, or be determined to be, infringing a third-party's rights and be prohibited from working with the drug or found liable for damages. Any such restriction on access or liability for damages would have a material adverse effect on our business, results of operations and financial condition.

The patent positions of pharmaceutical and biotechnology companies, such as ours, are uncertain and involve complex legal and factual issues. There can be no assurance that patents that have issued will be held valid and enforceable in a court of law. Even for patents that are held valid and enforceable, the legal process associated with obtaining such a judgment is time consuming and costly. Additionally, issued patents can be subject to opposition or other proceedings that can result in the revocation of the patent or maintenance of the patent in amended form (and potentially in a form that renders the patent without commercially relevant and/or broad coverage). Further, our competitors may be able to circumvent and otherwise design around our patents. Even if a patent is issued and enforceable, because development and commercialization of pharmaceutical products can be subject to substantial delays, patents may expire early and provide only a short period of protection, if any, following the commercialization of products encompassed by our patent(s). We may have to participate in interference proceedings declared by the USPTO, which could result in a loss of the patent and/or substantial cost to us. Further, we understand that if any of our pending patent applications do not issue, or are deemed invalid following issuance, we may lose valuable IP protection.

U.S. and foreign patent rights and other proprietary rights exist that are owned by third-parties and relate to pharmaceutical compositions and reagents, medical devices and equipment and methods for preparation, packaging and delivery of pharmaceutical compositions. We cannot predict with any certainty which, if any, of these rights will be considered relevant to our technology by authorities in the various jurisdictions where such rights exist, nor can we predict with certainty which, if any, of these rights will or may be asserted against us by third-parties. We could incur substantial costs in defending ourselves and our partners against any such claims. Furthermore, parties making such claims may be able to obtain injunctive or other equitable relief, which could effectively block our ability to develop or commercialize some or all of our products in the U.S. and in other countries and could result in the award of substantial damages. In the event of a claim of infringement, we or our partners may be required to obtain one or more licenses from third-parties. There can be no assurance that we can obtain a license to any technology that we determine we require on reasonable terms, if at all, or that we could develop or otherwise obtain alternative technology. The failure to obtain licenses, if required, may have a material adverse effect on our business, results of operations and financial condition. Further, we may not be able to obtain IP licenses related to the development of our drug candidates on a commercially reasonable basis, if at all.

It is our policy to require our employees and consultants, outside scientific collaborators, sponsored researchers and other advisors who receive confidential information from us to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third-parties except in specific circumstances. The agreements provide that all inventions conceived by an employee shall be our property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

Manufacturing and Supply

We do not have the capability to manufacture our own materials necessary to support our drug candidate development programs nor do we intend to acquire such capability as part of our present business strategy. We currently have agreements in place with Serum Institute whereby Serum Institute produces clinical materials for use in the development of drug candidates involving our PolyXen technology. We are currently dependent on Kevelt for clinical materials with respect to our XBIO-101 research program.

Government Regulation

General

Government authorities in the U.S., at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of products such as those we are developing. Generally, a new drug must be approved by the FDA through the NDA process and a new biologic must be licensed by the FDA through the biologics license application ("BLA") process before it may be legally marketed in the U.S.

U.S. Regulation

Drug Development Process

In the U.S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA"), and in the case of biologics, also under the Public Health Service Act, and their implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, license revocation, a clinical hold, warning letters or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

The process required by the FDA before a drug or biologic may be marketed in the U.S. generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in accordance with Good Laboratory Practices ("GLP") regulations and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practice ("GCP") regulations to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA or BLA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current Good Manufacturing Practices ("cGMP") requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA or BLA.

Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. The sponsor will also include a protocol detailing, among other things, the objectives of the first phase of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if the first phase lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns about ongoing or proposed clinical trials or noncompliance with specific FDA requirements, and the trials may not begin or continue until the FDA notifies the sponsor that the hold has been lifted.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP regulations. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and timely safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events. An institutional review board (IRB) at each institution participating in the clinical trial must review and approve each protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each trial subject or his or her legal representative, monitor the study until completed and otherwise comply with IRB regulations.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- ***Phase I***: The drug candidate is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

- ***Phase II***: This phase involves clinical trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and appropriate dosage.

- ***Phase III***: Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These clinical trials are intended to establish the overall risk-benefit ratio of the drug candidate and provide, if appropriate, an adequate basis for product labeling.

Post-approval trials, sometimes referred to as Phase IV studies, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase IV clinical trials as a condition of approval of an NDA or BLA.

The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug. In addition, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

While the IND is active and before approval, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or in-vitro testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

There are also requirements governing the reporting of ongoing clinical trials and completed trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products are required to register and disclose specified clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, trial sites and investigators and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved.

U.S. Market Approval Process

The results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA or BLA requesting approval to market the product. The submission of an NDA or BLA is subject to the payment of user fees; a waiver of such fees may be obtained under certain limited circumstances. The FDA reviews all NDAs and BLAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA may request additional information rather than accept an NDA or BLA for filing. In this event, the NDA or BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA may refer the NDA or BLA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The approval process is lengthy and often difficult, and the FDA may refuse to approve an NDA or BLA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data and information. Even if such data and information are submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. The FDA reviews a BLA to determine, among other things whether the product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. Before approving an NDA or BLA, the FDA will inspect the facility or facilities where the product is manufactured.

After the FDA evaluates an NDA or BLA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA or BLA identified by the FDA and may require additional clinical data, such as an additional pivotal Phase 3 trial or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a Complete Response Letter is issued, the sponsor must resubmit the NDA or BLA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA or BLA does not satisfy the criteria for approval.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require a sponsor to conduct Phase 4 testing, which involves clinical trials designed to further assess a drug's safety and effectiveness after NDA or BLA approval, and may require testing and surveillance programs to monitor the safety of approved products which have been commercialized. The FDA may also place other conditions on approval including the requirement for a risk evaluation and mitigation strategy (REMS) to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA or BLA must submit a proposed REMS. The FDA will not approve the NDA or BLA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Marketing approval may be withdrawn for noncompliance with regulatory requirements or if problems occur following initial marketing.

Orphan Drug Act

The Orphan Drug Act provides incentives to manufacturers to develop and market drugs or biologics for rare diseases and conditions affecting fewer than 200,000 persons in the U.S. at the time of application for orphan drug designation, or for a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug or biologic will be recovered from sales in the U.S. The first developer to receive FDA marketing approval for an orphan drug is entitled to a seven-year exclusive marketing period in the U.S. for that product. However, a drug that the FDA considers to be clinically superior to, or different from, another approved orphan drug, even though for the same indication, may also obtain approval in the U.S. during the seven-year exclusive marketing period. In addition, holders of exclusivity for orphan drugs are expected to assure the availability of sufficient quantities of their orphan drugs to meet the needs of patients. Failure to do so could result in the withdrawal of marketing exclusivity for the drug.

Pediatric Information

Under the Pediatric Research Equity Act of 2007 ("PREA"), NDAs or BLAs or supplements to NDAs or BLAs must contain data to assess the safety and effectiveness of the drug for the claimed indication(s) in all relevant pediatric sub-populations and to support dosing and administration for each pediatric sub-population for which the drug is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan drug designation has been granted. The Best Pharmaceuticals for Children Act ("BPCA") provides sponsors of NDAs with an additional six-month period of market exclusivity for all unexpired patent or non-patent exclusivity on all forms of the drug containing the active moiety if the sponsor submits results of pediatric studies specifically requested by the FDA under BPCA within required timeframes. The Biologics Price Competition and Innovation Act provides sponsors of BLAs an additional six-month extension for all unexpired non-patent market exclusivity on all forms of the biologic containing the active moiety pursuant to the BPCA if the conditions under the BPCA are met.

The Food and Drug Administration Safety and Innovation Act ("FDASIA"), which was signed into law on July 9, 2012, amended the FDCA. FDASIA requires that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan ("PSP") within sixty days of an end-of-Phase II meeting or as may be agreed between the sponsor and FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, and/or other clinical development programs.

Expedited Development and Review Programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a Fast Track product at any time during the clinical development of the product. Unique to a Fast Track product, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Fast Track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process. Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product designated for priority review in an effort to facilitate the review. Additionally, a product may be eligible for accelerated approval. Drug or biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. If the FDA concludes that a drug shown to be effective can be safely used only if distribution or use is restricted, it will require such post-marketing restrictions as it deems necessary to assure safe use of the drug, such as distribution restricted to certain facilities or physicians with special training or experience; or distribution conditioned on the performance of specified medical procedures.

FDASIA established a new category of drugs and biologics referred to as "breakthrough therapies" that may be eligible to receive Breakthrough Therapy Designation. A sponsor may seek FDA designation of a drug or biologic candidate as a "breakthrough therapy" if the product is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance. The Breakthrough Therapy Designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met. If a product is designated as breakthrough therapy, the FDA will expedite the development and review of such drug. All requests for breakthrough therapy designation will be reviewed within 60 days of receipt, and the FDA will either grant or deny the request.

Post-Approval Requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements or standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, certain manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Drug and biologics manufacturers and other entities involved in the manufacture and distribution of approved drugs and biologics are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP regulations and other laws and regulations.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of our drug candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA or BLA plus the time between the submission date of an NDA or BLA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA or BLA.

Marketing exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application (ANDA), or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of regulatory market exclusivity in the U.S. under the BPCA. Pediatric exclusivity provides for an additional six months of marketing exclusivity if a sponsor conducts clinical trials in children as addressed in the section named “Pediatric Information” above. In addition, orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances.

Foreign Regulation

In addition to regulations in the U.S., we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our drug candidates.

Whether or not we obtain FDA approval for our drug candidates, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the drug candidates in those countries. Certain countries outside of the U.S. have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a CTA must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and the IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical study development may proceed.

The requirements and process governing the conduct of clinical trials, product approval and licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational drug or biological product under European Union regulatory systems, we must submit a marketing authorization application. The application used to file the NDA or BLA in the U.S. is similar to that required in the European Union, with the exception of, among other things, country-specific document requirements. The European Union also provides opportunities for market exclusivity. For example, in the European Union, upon receiving marketing authorization, new chemical entities generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic product can be marketed until the expiration of the market exclusivity. However, there is no guarantee that a product will be considered by the European Union's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity. Products receiving orphan designation in the European Union can receive ten years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. An orphan product can also obtain an additional two years of market exclusivity in the European Union for pediatric studies. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

The criteria for designating an "orphan medicinal product" in the European Union are similar in principle to those in the U.S. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. The application for orphan drug designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the marketing authorization application if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. In addition, marketing authorization may be granted to a similar product for the same indication at any time if:

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- the applicant consents to a second orphan medicinal product application; or
- the applicant cannot supply enough orphan medicinal product.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical studies, product licensing or approval, pricing and reimbursement vary from country to country. In all cases, again, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Other Regulatory Matters

Manufacturing, sales, promotion and other activities following product approval are also potentially subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the U.S., the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments. In the U.S., sales, marketing and scientific/educational programs must also comply with state and federal fraud and abuse laws, including state and federal anti-kickback, false claims, data privacy and security and physician payment transparency laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively the Affordable Care Act. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities are also potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with regulatory requirements may subject us to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts. In addition, even if a firm complies with FDA and other requirements, new information regarding the safety or efficacy of a product could lead the FDA to modify or withdraw product approval. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Environmental Regulation

In addition to being subject to extensive regulation by the FDA, we must also comply with environmental regulation insofar as such regulation applies to us or our drug candidates. Our costs of compliance with environmental regulation as applied to similar pharmaceutical companies are minimal, since we do not currently, nor do we intend to, engage in the manufacturing of any of our drug candidates. We currently use unaffiliated manufacturers to produce all of our drug candidate material and receive final material from such manufacturer, without any involvement on our part in the manufacturing process at any stage of the process.

Although we believe that our safety procedures for using, handling, storing and disposing of our drug candidate materials comply with the environmental standards required by state and federal laws and regulations, we cannot completely eliminate the risk of accidental contamination or injury from these materials. We do not carry a specific insurance policy to mitigate this risk to us or to the environment.

Research and Development Expenses

Research and development activities include personnel costs, research supplies, clinical and preclinical study costs. Such expenses related to the research and development of our drug candidates totaled $2.9 million for the year ended December 31, 2018 and $4.1 million for the year ended December 31, 2017.

Employees

At December 31, 2018, we employed four full-time employees. We are not a party to any collective bargaining agreement with our employees; nor are any of our employees a member of any labor unions. We are subject to certain statutory and contractual obligations in instances where we terminate U.K.-based employees. These obligations, which are ordinary and customary in the U.K., generally range from one to 12 months of wages for terminated employees and would not be expected to represent a material adverse effect to us.

To complement our own professional staff, we utilize specialists in regulatory affairs, pharmacovigilance, process engineering, manufacturing, quality assurance, preclinical and clinical development, accounting and business development. These individuals include scientific advisors as well as independent consultants.

COMPETITION

The pharmaceutical and biotechnology industries are characterized by intense competition and rely heavily on the ability to move quickly, adapt to changing medical and market needs, and to develop and maintain strong intellectual property positions. We believe that the development experience of our scientific and management team, as well as the strength and promise of our drug candidates, provide us with a competitive advantage; nevertheless, we face potential competition from a myriad of sources many of which operate with greater resources and more mature products. These include pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions. Competition is intense and is expected to increase.

Product and Technology Specific Competition

XBIO-101 for Endometrial Cancer ("EC") and Triple Negative Breast Cancer ("TNBC")

Current standard of care treatments for EC and TNBC include radiation, surgery as well as certain chemotherapeutic and antineoplastic agents, particularly platinum-based agents, including but not limited to Taxol, Taxane, anthracycline, carboplatin, doxorubicin, cisplatin, ifosfamide, and topotecan.

A number of additional therapeutic classes are in development worldwide, including but not limited to antibodies, antibody-drug conjugates and immunotherapies. Additionally, there are a number of targeted agents including PARP inhibitors and other agents that target the PI3K/Akt/mTOR pathway and other kinase inhibitors. The aforementioned therapeutics and therapeutic classes may be used either alone or in combination.

PSA for Drug Delivery

Current competing platforms include PEGylation, Fc-fusion, albumin-fusion, HESylation, PASylation, depot and CTP-fusion, among others.

We also expect to compete with academic institutions and other smaller pharmaceutical companies during the drug development stage of our progress. In addition to competing with universities and other research institutions in the development of drug products, therapies, technologies and processes, we may compete with other companies in acquiring rights to products or technologies from universities. There can be no assurance that our products or drug candidates will be more effective or achieve greater market acceptance than competitive products, or that these companies will not succeed in developing products and technologies that are more effective than those being developed for us or that would render our products and technologies less competitive or obsolete.

Available Information

Our website address is www.xeneticbio.com. The information on, or that can be accessed through, our website is not part of this Annual Report on Form 10-K. 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 are available, free of charge, on or through our website as soon as practicable after we electronically file such forms, or furnish them to, the SEC. The public may read and copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Information on the operations of the Public Reference Room can be obtained by calling 1-800-SEC-0330. The SEC maintains an internet site that contains reports, proxy and information statements and other information regarding our filings at www.sec.gov.

In addition to disclosing current information pursuant to Section 13 or 15(d) of the Exchange Act and for reports of information required to be disclosed by Regulation FD through our SEC filings, we also intend to disclose such current information through our investor relations website, press releases, public conference calls and webcasts.

ITEM 1A – RISK FACTORS

Our business is subject to numerous risks. You should consider carefully the risks and uncertainties described below, in addition to other information contained in this Annual Report as well as our other public filings with the Securities and Exchange Commission. Any of the following risks could have a material adverse effect on our business, financial condition, results of operations and prospects and cause the trading price of our common stock to decline.

Risks Related to Our Financial Condition and Capital Requirements

We have never been profitable and may never achieve or sustain profitability.

We are a clinical stage biopharmaceutical company with a limited operating history. Pharmaceutical product and technology development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have focused primarily on developing our drug candidates, XBIO-101 and PolyXen, our biological platform technology, and researching additional drug candidates. We have no products approved for commercial sale and have generated only limited revenue to date. Due to capital constraints in 2018 we focused solely on the development of XBIO-101. We continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we have never been profitable and we may not achieve profitability in the foreseeable future, if at all. Our ability to generate profits in the future will depend on a number of factors, including:

- Funding the costs relating to the research and development, regulatory approval, commercialization and sale and marketing of our drug candidates and technologies;
- Market acceptance of our drug candidates and technologies;
- Costs of acquiring and developing new drug candidates and technologies;
- Ability to bring our drug candidates to market;
- General and administrative costs relating to our operations;
- Increases in our research and development costs;
- Charges related to purchases of technology or other assets;
- Establishing, maintaining and protecting our intellectual property rights;
- Attracting, hiring and retaining qualified personnel; and
- Our ability to raise additional capital.

As of December 31, 2018, we had an accumulated deficit of approximately $153.2 million. Substantial doubt exists about our ability to continue as a going concern as a result of anticipated capital needs. We expect to incur additional significant operating losses as we expand our research and development activities and our commercialization, marketing and sales efforts. We may also encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. In addition, because of the numerous risks and uncertainties associated with pharmaceutical product development, including that our current drug candidates may not achieve the clinical endpoints of applicable trials, we are unable to predict the timing or amount of increased expenses, and if or when we will achieve or maintain profitability. If we are unable to generate sufficient revenue from our operations to pay expenses or we are unable to obtain additional financing on commercially reasonable terms, our business, financial condition and results of operations may be materially and adversely affected.

Our independent registered public accounting firm and the Company have expressed substantial doubt about our ability to continue as a going concern.

We have concluded there is substantial doubt about our ability to continue as a going concern. As described in their audit report, our auditors have included an explanatory paragraph that states that we have incurred recurring losses and negative cash flows from operations since inception and have an accumulated deficit at December 31, 2018 of $153.2 million. These matters raise substantial doubt about our ability to continue as a going concern. Our consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty. If we cannot continue as a viable entity, our stockholders may lose some or all of their investment in us.

We will require substantial additional funding to achieve our goals. Failure to obtain this necessary capital when needed on acceptable terms, or at all, may force us to delay, limit or terminate our product development efforts, other operations or commercialization efforts.

Developing drug candidates is an expensive, risky and lengthy process, and we expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, continue and initiate clinical trials of, and seek marketing approval for, our drug candidates.

As of December 31, 2018, we had cash and cash equivalents of $0.6 million. We expect that we will require additional capital to complete clinical trials, obtain regulatory approval for, and to commercialize, our drug candidates, including our other preclinical drug candidates and our future drug candidates. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, third-party funding, marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or a combination of these approaches. In any event, we will require additional capital to pursue preclinical and clinical activities, pursue regulatory approval for, and to commercialize, our longer term pipeline drug candidates. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our drug candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may negatively impact the holdings or the rights of our stockholders, and the issuance of additional securities, whether equity or debt, by us or the possibility of such issuance may cause the market price of our shares to decline. The incurrence of indebtedness could result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue our clinical development program or the commercialization of any drug candidates. We may also be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could harm our business, financial condition and results of operations.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or drug candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity and debt financings, as well as selectively continuing to enter into collaborations, strategic alliances and licensing arrangements. We do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, equity interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, and may be secured by all or a portion of our assets.

If we raise funds by selectively continuing to enter into collaborations, strategic alliances or licensing arrangements with third-parties, we may have to relinquish additional valuable rights to our technologies, future revenue streams, research programs or drug candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market drug candidates that we would otherwise prefer to develop and market ourselves. If we are unable to raise additional funds through collaborations, strategic alliances or licensing arrangements, we may be required to terminate product development or future commercialization efforts or to cease operations altogether.

Risks Related to the Transaction

We cannot assure you that the proposed Transaction will be completed on a timely basis or at all or that the Company will recognize the anticipated benefits of the Transaction.

On March 1, 2019, we entered into an agreement to acquire the novel CAR T platform technology, called "XCART," a proximity-based screening platform capable of identifying CAR constructs that can target patient-specific tumor neoantigens, with a demonstrated proof of mechanism in B-cell Non-Hodgkin lymphomas. The XCART technology, developed by the Institute in collaboration with the IBCH, is believed to have the potential to significantly enhance the safety and efficacy of cell therapy for B-cell lymphomas by generating patient- and tumor-specific CAR T cells.

There are a number of risks and uncertainties relating to the Transaction. For example, the Transaction may not be completed, or may not be completed in the time frame, on the terms or in the manner currently anticipated and the Company may not recognize the anticipated benefits of the Transaction, as a result of a number of factors, including the following:

- that one or more closing conditions to the Transaction, including certain regulatory approvals, may not be satisfied or waived, on a timely basis or otherwise, that the required approval by the stockholders of the Company may not be obtained, and the Company may not have adequate financing to fund its future working capital obligations of the Company following the closing;
- unexpected costs, charges or expenses resulting from the Transaction;
- uncertainty of the expected financial performance of the Company following completion of the Transaction;
- the ability of the Company to implement its business strategy; and
- the occurrence of any event that could give rise to termination of the Transaction.

Our business is substantially dependent on the success of XCART.

Our business depends almost entirely on the successful consummation of the acquisition of the XCART platform technology and its clinical development, regulatory approval and commercialization. It will require substantial clinical development and regulatory approval efforts before we are permitted to commence its commercialization, if ever. The clinical trials and manufacturing and marketing of XCART and any other product candidates will be subject to extensive and rigorous review and regulation by numerous government authorities in the U.S., the European Union and other jurisdictions where we intend to test and, if approved, market our product candidates. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through preclinical testing and clinical trials that the product candidate is safe and effective for use in each target indication, and potentially in specific patient populations. This process can take many years and may include post-marketing studies and surveillance, which would require the expenditure of substantial resources beyond the proceeds we have currently raised. Of the large number of drugs in development for approval in the U.S. and the European Union, only a small percentage successfully complete the FDA or European Medicines Agency, or EMA, regulatory approval processes, as applicable, and are commercialized. Accordingly, even if we are able to obtain the requisite financing to continue to fund our research, development and clinical programs, we cannot assure you that XCART or any of our other product candidates will be successfully developed or commercialized.

Risks Related to the Discovery and Development of our Pharmaceutical Products

We are an early stage company in the business of developing pharmaceutical products including drug candidates and technologies. Given the uncertainty of such development, our business operations may never fully materialize and create value for investors.

We currently do not have any products that have gained marketing approval. We have invested substantially all of our efforts and financial resources developing ErepoXen, OncoHist and, most recently, XBIO-101. Our revenues to date consist primarily of collaboration revenue from a single partner and not from product sales or royalties. Our ability to generate product revenues, which may not occur for several years, if ever, will depend on the successful development and eventual commercialization of our drug candidates. We currently generate no revenues from sales of any drugs, and we may never be able to develop or commercialize a marketable drug. Each of our drug candidates will require development, management of development and manufacturing activities, marketing approval in multiple jurisdictions, obtaining manufacturing supply, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenues from drug sales. We have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the pharmaceutical area. For example, to execute our business plan, we will need to successfully:

- Execute development activities for our drug candidates, including successful enrollment in and completion of clinical trials;
- Obtain required marketing approvals for the development and commercialization of our drug candidates;
- Obtain and maintain patent and trade secret protection or regulatory exclusivity for our drug candidates;
- Protect, leverage and expand our intellectual property portfolio;
- Establish and maintain clinical and commercial manufacturing capabilities or make arrangements with third-party manufacturers for clinical and commercial manufacturing;
- Build and maintain robust sales, distribution and marketing capabilities, either on our own or in collaboration with strategic partners, if our drug candidates are approved;
- Gain acceptance for our drug candidates, if approved, by patients, the medical community and third party payors;
- Effectively compete with other therapies;
- Obtain and maintain healthcare coverages and adequate reimbursement;
- Maintain a continued acceptable safety profile for our drug candidates following approval;
- Develop and maintain any strategic relationships we elect to enter into, if any;
- Enforce and defend intellectual property rights and claims; and
- Manage our spending as costs and expenses increase due to preclinical development, clinical trials, marketing approvals and commercialization.

We may find it difficult to enroll patients in our clinical studies, which could delay or prevent clinical studies of our pharmaceutical products.

Identifying and qualifying patients to participate in clinical studies of our pharmaceutical products is critical to our success. The timing of our clinical studies depends on the speed at which we can recruit patients to participate in testing our pharmaceutical products. We may experience delays. If patients are unwilling to participate in our clinical studies because of negative publicity from adverse events in the biopharmaceutical industries or for other reasons, including competitive clinical studies for similar patient populations, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products may be delayed. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of the clinical studies altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a study, to complete our clinical studies in a timely manner. Patient enrollment is affected by factors including:

- Severity of the disease under investigation;
- Real or perceived availability of alternative treatments;
- Size and nature of the patient population;
- Eligibility criteria for and design of the trial in question;
- Perceived risks and benefits of the drug candidate under study;
- Proximity and availability of clinical sites for prospective patients;
- Ongoing clinical trials of potentially competitive agents;
- Physicians' and patients' perceptions as to the potential advantages of our drug candidates being studied in relation to available therapies or other products under development;
- Our CRO's and our trial sites' efforts to facilitate timely enrollment in clinical trials;
- Patient referral practices of physicians; and
- The need to monitor patients and collect patient data adequately during and after treatment.

We may not be able to initiate or continue clinical studies if we cannot enroll a sufficient number of eligible patients to participate in the clinical studies required by the FDA or other regulatory agencies. Our ability to successfully initiate, enroll and complete a clinical study in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- Difficulty in establishing or managing relationships with CROs and physicians;
- Different standards for the conduct of clinical studies;
- Our inability to locate qualified local consultants, physicians and partners; and
- The potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical studies as planned, we may need to delay, limit or terminate ongoing or planned clinical studies, any of which would have an adverse effect on our business.

We may encounter substantial delays in commencement, enrollment or completion of our clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities, which could prevent us from commercializing our current and future drug candidates on a timely basis, if at all.

Before obtaining marketing approval from regulatory authorities for the sale of our current and future drug candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the drug candidates. We cannot guarantee that any clinical studies will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical studies can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include:

- Delays in reaching a consensus with regulatory agencies on study design;
- Delays in reaching agreement on acceptable terms with prospective CROs and clinical study sites;
- Delays in obtaining required Institutional Review Board, or Independent Ethics Committee approval at each clinical study site;
- Delays in recruiting suitable patients to participate in our clinical studies;
- Imposition of a clinical hold by regulatory agencies, including after an inspection of our clinical study operations or study sites;
- Failure by our CROs, other third-parties or us to adhere to clinical study requirements;
- Failure to perform in accordance with the FDA's GCP, or applicable regulatory requirements in other countries;
- Delays in the testing, validation, manufacturing and delivery of our drug candidates to the clinical sites;
- Delays in having patients complete participation in a study or return for post-treatment follow-up;
- Clinical study sites or patients dropping out of a study;
- Occurrence of serious adverse events associated with the drug candidate that are viewed to outweigh its potential benefits; or
- Changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

Any inability to successfully complete preclinical studies and clinical trials could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our drug candidates, we may need to conduct additional studies to bridge our modified drug candidates to earlier versions. Clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our drug candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our drug candidates and may harm our business, financial condition, results of operations and prospects.

If the results of our clinical studies are inconclusive or if there are safety concerns or adverse events associated with our pharmaceutical products, we may:

- Be delayed in obtaining marketing approval or licenses for our drug candidates, if at all;
- Obtain approval for indications or patient populations that are not as broad as intended or desired;
- Obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- Be subject to changes with the way the product is administered;
- Be required to perform additional clinical studies to support approval or be subject to additional post-marketing testing requirements;
- Have regulatory authorities withdraw their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy;
- Be subject to the addition of labeling statements, such as warnings or contraindications;
- Be sued; or
- Experience damage to our reputation.

As described above, any of these events could prevent us from achieving or maintaining market acceptance of our pharmaceutical products and impair our ability to generate revenues.

Clinical trials may fail to demonstrate the safety and efficacy of our pharmaceutical drug candidates and could prevent or significantly delay regulatory approval.

Before receiving NDA or BLA approval to commercialize a drug candidate, we must demonstrate to the FDA, with substantial evidence from well-controlled clinical trials, that the drug candidate is both safe and effective or the biologic is safe, pure and potent. If these trials or future clinical trials are unsuccessful, our business and reputation could be harmed and our stock price could be adversely affected.

Clinical failure can occur at any stage of clinical development. Clinical trials may produce negative or inconclusive results, and we or any of our current and future collaborators may decide, or regulators may require us, to conduct additional clinical or preclinical testing. We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our drug candidates are as safe and effective for use in a specific patient population as the respective reference products before we can seek regulatory approvals for their commercial sale. Success in early clinical trials does not mean that future larger registration clinical trials will be successful because drug candidates in later-stage clinical trials may fail to demonstrate equivalent safety and efficacy to the satisfaction of the FDA and foreign regulatory agencies despite having progressed through initial clinical trials. Drug candidates that have shown promising results in early clinical trials may still fail in subsequent confirmatory clinical trials. Similarly, the outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical industry, including those with greater resources and experience than us, have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier clinical trials.

In addition, the design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We may be unable to design and execute a clinical trial to support regulatory approval. In some instances, there can be significant variability in safety or efficacy results between different trials of the same drug candidate due to numerous factors, including but not limited to changes in trial protocols, differences in size and type of the patient populations, adherence to the dosing regimen and the rate of dropout among clinical trial participants.

Because of these risks, our research and development efforts, and those of our collaborative partners, may not result in any commercially viable products. If a significant portion of these development efforts is not successfully completed, or if required regulatory approvals are not obtained by us or our partners, or any approved products are not commercially successful, we may not generate significant revenues or become profitable.

Even if we complete the necessary preclinical and clinical studies, we cannot predict when or if we will obtain regulatory approval to commercialize a drug candidate or the approval may be for a more narrow indication than we expect.

A drug candidate cannot be commercialized until the appropriate regulatory authorities have reviewed and approved the drug candidate. Even if our drug candidates demonstrate safety and efficacy in clinical studies, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory advisory group or authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical studies and the review process. Regulatory agencies also may approve a drug candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our drug candidates. Failure to obtain, or a delay in obtaining, regulatory approval to commercialize a drug candidate will impair our ability to generate revenues and harm our business prospects.

Even if we obtain regulatory approval for a drug candidate, our drug candidate will remain subject to regulatory scrutiny.

If our drug candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, efficacy and other post-market information, including both federal and state requirements in the U.S. and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturing facilities are required to comply with extensive FDA, and comparable foreign regulatory authority, requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any, BLA or marketing authorization application, or MAA. Accordingly, we and our collaborators and suppliers must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we or our collaboration partners receive for our drug candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval or may contain requirements for potentially costly additional clinical trials and surveillance to monitor the safety and efficacy of the drug candidate. We will be required to report certain adverse reactions and production problems, if any, to the FDA and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization or increased costs to assure compliance. We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we are not allowed to promote our products for indications or uses for which they do not have approval. If our drug candidates are approved, we must submit new or supplemental applications and obtain approval for certain changes to the approved products, product labeling or manufacturing process. We could also be asked to conduct post-marketing clinical trials to verify the safety and efficacy of our products in general or in specific patient subsets. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval.

If a regulatory agency discovers previously unknown problems with an approved product, such as adverse events of unanticipated severity or frequency or problems with our manufacturing facilities or disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- Issue untitled and warning letters;
- Impose civil or criminal penalties;
- Suspend or withdraw regulatory approval or revoke a license;
- Suspend any of our ongoing clinical trials;
- Refuse to approve pending applications or supplements to approved applications submitted by us;
- Impose restrictions on our operations, including closing our manufacturing facilities; or
- Seize or detain products or require a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be negatively impacted.

The commercial success of any current or future pharmaceutical products will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

Even with the requisite approvals, the commercial success of our pharmaceutical products will depend in part on the medical community, patients, and third-party payors accepting our pharmaceutical products as medically useful, cost-effective, and safe. Any pharmaceutical product that we or our partners bring to the market may not gain market acceptance by physicians, patients, third-party payors and others in the medical community. The degree of market acceptance of these pharmaceutical products, if approved for commercial sale, will depend on a number of factors, including:

- The effectiveness of our approved drug candidates as compared to currently available products;
- Patient willingness to adopt our approved drug candidates in place of current therapies;
- Our ability to provide acceptable evidence of safety and efficacy;
- Relative convenience and ease of administration;
- The prevalence and severity of any adverse side effects;
- Restrictions on use in combination with other products;
- Availability of alternative treatments;
- Pricing and cost-effectiveness assuming either competitive or potential premium pricing requirements, based on the profile of our drug candidates and target markets;
- Effectiveness of our or our partners' sales and marketing strategy;
- Our ability to obtain sufficient third-party coverage or reimbursement; and
- Potential product liability claims.

Even if a potential product displays a favorable efficacy and safety profile in preclinical and clinical studies, market acceptance of the product will not be known until after it is launched. Our efforts to educate the medical community and third-party payors on the benefits of the pharmaceutical products may require a significant amount of resources and may never be successful. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable.

The commercial potential of a pharmaceutical candidate in development is difficult to predict. If the market size for a new drug candidate or technology is significantly smaller than we anticipate, it could significantly and negatively impact our revenue, results of operations and financial condition.

It is very difficult to estimate the commercial potential of pharmaceutical products due to important factors such as safety and efficacy compared to other available technologies or treatments, including changing standards of care, third-party payor reimbursement standards, patient and physician preferences, the availability of competitive alternatives that may emerge either during the long drug development process or after commercial introduction, and the availability of generic versions of our successful drug candidates following approval by government health authorities based on the expiration of regulatory exclusivity or our inability to prevent generic versions from coming to market by asserting our patents. If due to these factors, or others, the market potential for a pharmaceutical product is lower than we anticipated, it could significantly and negatively impact the commercial terms of any collaboration partnership potential for such pharmaceutical product or, if we have already entered into a collaboration for such pharmaceutical product, the revenue potential from royalty and milestone payments could be significantly diminished which would negatively impact our business, financial condition and results of operations.

Failure to obtain or maintain adequate coverage and reimbursement for our drug candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

The success of our drug candidates, if approved, depends on the availability of adequate coverage and reimbursement from third-party payors. In addition, because our drug candidates represent new approaches to the treatment of certain diseases, we cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our drug candidates or assure that coverage and reimbursement will be available for any product that we may develop.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors are critical to new product acceptance.

Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

- A covered benefit under its health plan;
- Safe, effective and medically necessary;
- Appropriate for the specific patient;
- Cost-effective; and
- Neither experimental nor investigational.

In the U.S., no uniform policy of coverage and reimbursement for products exists among third-party payors. As a result, obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of our gene-modifying products. Patients are unlikely to use our drug candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our drug candidates. There is significant uncertainty related to insurance coverage and reimbursement of newly approved products. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our drug candidates.

Moreover, increasing efforts by governmental and third-party payors in the U.S. and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our drug candidates. We expect to experience pricing pressures in connection with the sale of any of our drug candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, cost containment initiatives and additional legislative changes.

We intend to seek approval to market our drug candidates in both the U.S. and in select foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our drug candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, the pricing of pharmaceutical products is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our drug candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a drug candidate. In addition, market acceptance and sales of our drug candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our drug candidates and may be affected by existing and future health care reform measures. Failure to obtain or maintain adequate coverage and reimbursement for our drug candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

We may use our financial and human resources to pursue a particular research program or drug candidate and fail to capitalize on programs or drug candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited resources, we may forego or delay pursuit of opportunities with certain programs or drug candidates or for indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for drug candidates may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through strategic collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such drug candidate, or we may allocate internal resources to a drug candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement. Failure to pursue opportunities with greater commercial potential or relinquishing valuable rights to drug candidates may adversely impact our business, results of operations and prospects.

We may not be successful in our efforts to identify or discover additional pharmaceutical products.

The success of our business depends primarily upon our ability to identify and develop pharmaceutical products. Our research programs may fail to identify potential pharmaceutical products for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential pharmaceutical products or our potential pharmaceutical products may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to identify new pharmaceutical products require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or pharmaceutical products that ultimately prove to be unsuccessful. If we are not successful in our efforts to identify or discover additional pharmaceutical products, it could adversely affect our business, results of operations and prospects.

We may fail to obtain orphan drug designations from the FDA for our drug candidates, and even if we obtain such designations, we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biologic intended to treat a rare disease or condition, which is defined as one occurring in a patient population of fewer than 200,000 in the U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug or biologic will be recovered from sales in the U.S.. In the U.S., orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a full NDA or BLA, to market the same drug or biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity.

OncoHist for AML and XBIO-101 for endometrial cancer have orphan designation in the U.S. While we have not obtained nor have we sought to obtain additional orphan designations for any drug candidate, we believe our products and drug candidates could qualify for additional orphan drug designations for additional indications. We may seek to obtain orphan drug designation for our drug candidates for any qualifying indications they may be approved for in the future. Even if we obtain such designations, we may not be the first to obtain marketing approval of our drug candidate for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the U.S. may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan product is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process. In addition, while we may seek orphan drug designation for our drug candidates, we may never receive such designations.

The market opportunities for our drug candidates may be limited to those patients who are ineligible for or have failed prior treatments and may be small.

Cancer therapies are sometimes characterized as first line, second line or third line, and the FDA often approves new therapies initially only for third line use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapy, usually chemotherapy, hormone therapy, surgery or a combination of these, proves unsuccessful, second line therapy may be administered. Second line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor targeted small molecules or a combination of these. Third line therapies can include bone marrow transplantation, antibody and small molecule targeted therapies, more invasive forms of surgery and new technologies. In markets with approved therapies, we expect to initially seek approval of our drug candidates as a later stage therapy for patients who have failed other approved treatments. Subsequently, for those drugs that prove to be sufficiently beneficial, if any, we would expect to seek approval as a second line therapy and potentially as a first line therapy, but there is no guarantee that our drug candidates, even if approved, would be approved for second line or first line therapy. In addition, we may have to conduct additional clinical trials prior to gaining approval for second line or first line therapy.

Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers in a position to receive later stage therapy and who have the potential to benefit from treatment with our drug candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations or market research and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these cancers. The number of patients may turn out to be lower than expected. In addition, the potentially addressable patient population for our drug candidates may be limited or may not be amenable to treatment with our drug candidates. Even if we obtain significant market share for our drug candidates, we may never achieve profitability without obtaining regulatory approval for additional indications, including use as a first or second line therapy, which may adversely affect our business and results of operations.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

In both the U.S. and certain foreign jurisdictions, there have been a number of legislative and regulatory enactments in recent years that change the healthcare system in ways that could impact our future ability to sell our drug candidates profitably.

Furthermore, there have been and continue to be a number of initiatives at the federal and state level that seek to reduce healthcare costs. Most significantly, in March 2010, the Patient Protection and Affordable Health Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was signed into law, which includes measures that significantly change the way healthcare is financed by both governmental and private insurers. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the ACA. In addition, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Further, on October 12, 2017, President Trump issued another executive order requiring the Secretaries of the Departments of Health and Human Services ("HHS"), Labor, and the Treasury to consider proposing regulations or revising existing guidance to allow more employers to form association health plans that would be allowed to provide coverage across state lines, increase the availability of short-term, limited duration health insurance plans, which are generally not subject to the requirements of the ACA, and increase the availability and permitted use of health reimbursement arrangements. On October 13, 2017, the Department of Justice announced that HHS was immediately stopping its cost sharing reduction payments to insurance companies based on the determination that those payments had not been appropriated by Congress. Furthermore, on December 22, 2017, President Trump signed the Tax Cuts and Jobs Act (the "TCJA") into law that, in addition to overhauling the federal tax system, also, effective as of January 1, 2019, repeals the penalties associated with the individual mandate. Congress or the President of the U.S. also could consider subsequent legislation or executive action to replace or eliminate elements of the ACA. We will continue to evaluate the effect that the ACA and any future measures to modify, repeal or replace the ACA have on our business. We are not able to provide any assurance that the continued healthcare reform debate will not result in legislation, regulation, or executive action by the President of the U.S. that is adverse to our business.

Laws and other reform and cost containment measures that may be proposed and adopted in the future remain uncertain, but may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our future customers and accordingly, our ability to generate revenue, attain profitability, or commercialize our products.

Risks Related to Our Reliance on Third-Parties

If conflicts arise between us and our collaborators or strategic partners, these parties may act in their self-interest, which may limit our ability to implement our strategies.

If conflicts arise between our corporate or academic collaborators or strategic partners and us, the other party may act in its self-interest, which may limit our ability to implement our strategies. Some of our academic collaborators and strategic partners are conducting multiple product development efforts within each area that is the subject of the collaboration with us. Our collaborators or strategic partners, however, may develop, either alone or with others, products in related fields that are competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by the collaborators or strategic partners or to which the collaborators or strategic partners have rights, may result in the withdrawal of partner support for our drug candidates.

Some of our collaborators or strategic partners could also become our competitors in the future. Our collaborators or strategic partners could develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain timely regulatory approvals, terminate their agreements with us prematurely, or fail to devote sufficient resources to the development and commercialization of products. Any of these developments could harm our product development efforts, which may adversely affect our business, results of operations and prospects.

We expect to rely on third-parties to conduct, supervise and monitor our clinical studies, and if these third-parties perform in an unsatisfactory manner, it may harm our business.

We expect to rely on CROs, clinical investigators and clinical study sites to ensure our clinical studies are conducted properly and on time. We will have limited influence over the performance by CROs, clinical investigators and clinical study sites and we will control only certain aspects of our CROs' activities. Nevertheless, we will be responsible for ensuring that each of our clinical studies is conducted in accordance with the applicable protocol, legal, and regulatory requirements and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We, our clinical investigators and our CROs are required to comply with the FDA's GCPs for conducting, recording and reporting the results of clinical trials to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA enforces these GCPs through periodic inspections of study sponsors, principal investigators and clinical trial sites. If we or our CROs or the clinical investigators fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving any marketing applications. Upon inspection, the FDA may determine that our clinical trials did not comply with GCPs. In addition, our future clinical trials will require a sufficient number of test subjects to evaluate the safety and efficacy of our drug candidates. Accordingly, if our CROs or clinical investigators fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical trials, which would delay the regulatory approval process.

Our CROs are not our employees, and we are therefore unable to directly monitor whether or not they devote sufficient time and resources to our clinical and nonclinical programs, which must be conducted in accordance with GCPs and GLPs, respectively. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical studies or other drug development activities that could harm our competitive position. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical studies may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize our pharmaceutical products. As a result, our financial results and the commercial prospects for our pharmaceutical products would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

We may also rely on other third-parties to store and distribute our products for any clinical studies that we may conduct. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our pharmaceutical products or commercialization of our products, if approved, producing additional losses and depriving us of potential product revenue.

Our collaborators or strategic partners may decide to adopt alternative technologies or may be unable to develop commercially viable products with our technology, which would negatively impact our revenues and our strategy to develop these products.

Our collaborators or strategic partners may adopt alternative technologies, which could decrease the marketability of our products. Additionally, because our current or future collaborators or strategic partners are likely to be working on more than one development project, they could choose to shift their resources to projects other than those they are working on with us. If they do so, this would delay our ability to test our technology and would delay or terminate the development of potential products based on our platforms. Further, our collaborators and strategic partners may elect not to develop products arising out of our collaborative and strategic partnering arrangements or to devote sufficient resources to the development, manufacturing, marketing or sale of these products. The failure to develop and commercialize a drug candidate pursuant to our agreements with our current or future collaborator would prevent us from receiving future milestone and royalty payments which would negatively impact our revenues.

We may seek to establish additional collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our drug candidate development programs and the potential commercialization of our drug candidates will require substantial additional cash to fund expenses. For some of our drug candidates, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of those drug candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for any additional collaborations will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by FDA or similar regulatory authorities outside the U.S., the potential market for the subject drug candidate, the costs and complexities of manufacturing and delivering such drug candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative drug candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our drug candidate. The terms of any additional collaborations or other arrangements that we may establish may not be favorable to us.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the drug candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our drug candidates or bring them to market and generate product revenue.

If we enter into one or more collaborations, we may be required to relinquish important rights to and control over the development of our drug candidates or otherwise be subject to unfavorable terms.

Any future collaborations we enter into could subject us to a number of risks, including:

- We may not be able to control the amount and timing of resources that our collaborators devote to the development or commercialization of our drug candidates;
- Collaborators may delay clinical trials, provide insufficient funding, terminate a clinical trial or abandon a drug candidate, repeat or conduct new clinical trials or require a new version of a drug candidate for clinical testing;
- Collaborators may not pursue further development and commercialization of products resulting from the strategic partnering arrangement or may elect to discontinue research and development programs;
- Collaborators may not commit adequate resources to the marketing and distribution of our drug candidates, limiting our potential revenues from these products;
- Disputes may arise between us and our collaborators that result in the delay or termination of the research, development or commercialization of our drug candidates or that result in costly litigation or arbitration that diverts management's attention and consumes resources;
- Collaborators may experience financial difficulties;
- Collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in a manner that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- Business combinations or significant changes in a collaborator's business strategy may also adversely affect a collaborator's willingness or ability to complete its obligations under any arrangement;
- Collaborators could decide to move forward with a competing drug candidate developed either independently or in collaboration with others, including our competitors; and
- Collaborators could terminate the arrangement or allow it to expire, which would delay the development and may increase the cost of developing our drug candidates.

Our contract manufacturers are subject to significant regulation with respect to manufacturing our products. The manufacturing facilities on which we rely may not continue to meet regulatory requirements and have limited capacity.

We currently have relationships with a limited number of suppliers for the manufacturing of our pharmaceutical products. Each supplier may require licenses to manufacture components if such processes are not owned by the supplier or in the public domain and we may be unable to transfer or sublicense the intellectual property rights we may have with respect to such activities.

All entities involved in the preparation of pharmaceutical products for clinical studies or commercial sale, including our existing contract manufacturers for our drug candidates, are subject to extensive regulation. Components of a finished pharmaceutical product approved for commercial sale or used in late-stage clinical studies must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our pharmaceutical products that may not be detectable in final product testing. Our contract manufacturers must supply all necessary documentation in support of an NDA or BLA on a timely basis and must adhere to the FDA's GLP, and cGMP regulations enforced by the FDA through its facilities inspection program. The facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our pharmaceutical products or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our pharmaceutical products or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit the manufacturing facilities of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third-party to implement and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon third-parties with whom we contract could materially harm our business.

If our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a drug candidate, or revocation of a pre-existing approval. As a result, our business, financial condition and results of operations may be materially harmed.

Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in commercial supply. The number of manufacturers with the necessary manufacturing capabilities is limited. In addition, an alternative manufacturer would need to be qualified through an NDA or BLA supplement which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines, which could materially harm our business and results of operations.

These factors could cause the delay of clinical studies, regulatory submissions, required approvals or commercialization of our pharmaceutical products, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical studies may be delayed or we could lose potential revenue, which could materially harm our business and results of operations.

We have no manufacturing, sales, marketing or distribution capabilities, and we may have to invest a significant amount of resources to develop these capabilities.

We have no internal manufacturing capabilities. As a result, for manufacturing we depend on third-party manufacturers, including Kevelt, Pharmsynthez and the Serum Institute, which in turn may rely upon third-parties to manufacture our products. Although our strategy is based on leveraging the ability of collaboration partners to develop and manufacture our products for commercialization in the pharmaceutical marketplace, we will be dependent on collaborations with drug development and manufacturing collaborators. If we are not able to maintain existing collaborative arrangements or establish new arrangements on commercially acceptable terms, we would be required to undertake product manufacturing and development activities at our own expense. This would increase our capital requirements or require us to limit the scope of our development activities. Moreover, we have limited or no experience in conducting full scale bioequivalence or other clinical studies, preparing and submitting regulatory applications, and distributing and marketing pharmaceutical products and as such we are reliant on contract parties for such efforts. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms or at all.

If any of our developmental collaborators breach or terminate their agreements with us or otherwise fail to conduct their collaborative activities in a timely manner, the preclinical and/or clinical development and/or commercialization of our pharmaceutical products will be delayed and we would be required to devote additional resources to product development and commercialization or terminate certain development programs. Also, a license relationship may be terminated at the discretion of our collaborator, or at the end of contract terms, and in some cases with only limited notice to us. The termination of the collaborative arrangement could have a material adverse effect on our business, financial condition and results of operations. There also can be no assurance that disputes will not arise with respect to the ownership of rights to any technology developed with third-parties. These and other possible disagreements with collaborators could lead to delays in the development or commercialization of our pharmaceutical products or could result in litigation or arbitration, which could be time consuming and expensive and could have a material adverse effect on our business, financial condition and results of operations. Even if we decide to perform clinical trials, sales, marketing and distribution functions ourselves, we could face a number of additional related risks, including:

- we may not be able to attract clinical investigators and build effective clinical trials, or a solid marketing department or sales force;
- the cost of establishing an internal clinical trials program, marketing department or sales force may exceed our available financial resources and the revenue generated by any of our current product candidates, if approved, or any other pharmaceutical products that we may develop, in-license or acquire; and
- our direct sales and marketing efforts may not be successful.

Any failure to perform such activities could have a material adverse effect on our business, financial condition and results of our operations.

Our reliance on third-parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third-parties to manufacture our pharmaceutical products, and because we collaborate with various organizations and academic institutions on the development of our pharmaceutical products, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third-parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third-parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

Risks Related to Our Intellectual Property

If we fail to adequately protect or enforce our intellectual property rights, we may be unable to operate effectively.

Our success and ability to compete are substantially dependent on our patents, proprietary formulations and trademarks. Although we believe that the patents and associated trademarks and licenses are valid, there can be no assurance that they will not be challenged and subsequently invalidated and/or canceled. The invalidation or cancellation of any one or all of the patents or trademarks would significantly damage our commercial prospects. Further, we may find it necessary to legally challenge parties infringing our patents or trademarks or licensed trademarks to enforce our rights thereto. There can be no assurance that any of the patents would ultimately be held valid or that efforts to defend any of the patents, trade secrets, know-how or other IP rights would be successful.

The patent positions of pharmaceutical and biotechnology companies, such as ours, are uncertain and involve complex legal and factual issues. We own numerous U.S. and foreign patents and a number of pending patent applications that cover various aspects of our drug candidates and technologies. There can be no assurance that patents that have been issued will be held valid and enforceable in a court of law. Even for patents that are held valid and enforceable, the legal process associated with obtaining such a judgment is time consuming and costly. Additionally, issued patents can be subject to opposition or other proceedings that can result in the revocation of the patent or maintenance of the patent in amended form (and potentially in a form that renders the patent without commercially relevant and/or broad coverage). Further, our competitors may be able to circumvent and otherwise design around our patents. Even if a patent is issued and enforceable, because development and commercialization of pharmaceutical products can be subject to substantial delays, patents may expire early and provide only a short period of protection, if any, following the commercialization of a product encompassed by our patents. We may have to participate in interference proceedings declared by the USPTO, which could result in a loss of the patent and/or substantial cost to us.

We have filed patent applications and plan to file additional patent applications, covering various aspects of our drug candidates and technologies. There can be no assurance that the patent applications for which we apply would actually be issued as patents, or do so with commercially relevant and/or broad coverage. The coverage claimed in a patent application can be significantly reduced before the patent is issued. The scope of our claim coverage can be critical to our ability to enter into licensing transactions with third-parties and our right to receive royalties from our collaboration partnerships. Since publication of discoveries in scientific or patent literature often lags behind the date of such discoveries, we cannot be certain that we were the first inventor of inventions covered by our patents or patent applications. In addition, there is no guarantee that we will be the first to file a patent application directed to an invention.

An adverse outcome in any judicial proceeding involving IP, including patents, could subject us to significant liabilities to third-parties, require disputed rights to be licensed from or to third-parties or require us to cease using the technology in dispute. In those instances where we seek an IP license from another, we may not be able to obtain the license on a commercially reasonable basis, if at all, thereby raising concerns on our ability to freely commercialize our technologies and/or products. It is also possible that we or our licensors or licensees will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third-parties and are reliant on our licensors or licensees. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If our current or future licensors or licensees fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our licensors or licensees are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised.

Failure to adequately protect or enforce our intellectual property rights could have a material adverse impact on our business, results of operations and prospects.

Issued patents covering our drug candidates could be found invalid or unenforceable if challenged in court.

If we or one of our licensing partners initiated legal proceedings against a third-party to enforce a patent covering one of our drug candidates, the defendant could counterclaim that the patent covering our drug candidate is invalid and/or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third-parties may also raise similar claims before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our drug candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our drug candidates. Such a loss of patent protection would have a material adverse impact on our business.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on drug candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we may not be able to prevent third-parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our inventions in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the U.S. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third-parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Failure to adequately protect our intellectual property rights throughout the world could have a material adverse impact on our business, results of operations and prospects.

If we infringe on the intellectual property rights of others, our business and profitability may be adversely affected.

Our commercial success will also depend, in part, on us and our collaborative partners not infringing on the patents or proprietary rights of others. There can be no assurance that the technologies and products used or developed by our collaborative partners and marketed and sold by us will not infringe such rights. If such infringement occurs and neither we nor our collaborative partner is able to obtain a license from the relevant third-party, we will not be able to continue the development, manufacture, use, or sale of any such infringing technology or product. There can be no assurance that necessary licenses to third-party technology will be available at all, or on commercially reasonable terms. In some cases, litigation or other proceedings may be necessary to defend against or assert claims of infringement or to determine the scope and validity of the proprietary rights of third-parties. Any potential litigation could result in substantial costs to, and diversion of, our resources and could have a material and adverse impact on us. An adverse outcome in any such litigation or proceeding could subject us to significant liabilities, require us to cease using the subject technology or require us to license the subject technology from the third-party, all of which could have a material adverse effect on our business.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third-parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to a number of intellectual property license agreements that are important to our business and we expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license.

We may need to obtain licenses from third-parties to advance our research, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop the affected drug candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current drug candidates or future products, resulting in either an injunction prohibiting the sales, or, with respect to the sales, an obligation on our part to pay royalties and/or other forms of compensation to third-parties.

In many cases, patent prosecution of our licensed technology is controlled solely by the licensor. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using the intellectual property. In certain cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- The scope of rights granted under the license agreement and other interpretation-related issues;
- The extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- The sublicensing of patent and other rights under our collaborative development relationships;
- Our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- The ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- The priority of invention of patented technology.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected drug candidates, which could have a material adverse effect on our business.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and/or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings provoked by third-parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the U.S.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock underlying the units.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity and is, therefore, costly, time-consuming and inherently uncertain. In addition, the U.S. has recently enacted and is currently implementing wide-ranging patent reform legislation. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our and our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents. Provisions of the Leahy-Smith America Invents Act, or the Leahy-Smith Act, adopted in September 2011, which includes a number of significant changes to U.S. patent law, are still being implemented through the adoption of new regulations. The Leahy-Smith Act and its implementation, in addition to any new regulation, could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third-parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

We employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee's former employers or other third-parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may also be subject to claims that former employees, collaborators or other third-parties have an ownership interest in our patents or other intellectual property. We may have in the future ownership disputes arising, for example, from conflicting obligations of consultants or others who are involved in developing our drug candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Our inability to protect our confidential information and trade secrets would harm our business and competitive position.

In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third-parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts both within and outside the U.S. may be less willing or unwilling to protect trade secrets. If a competitor lawfully obtained or independently developed any of our trade secrets, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position and our business.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the U.S. in several stages over the lifetime of the patents and/or applications. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. Non-compliance may result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

Risks Related to Our Business Operations

We operate in an extremely competitive environment and there can be no assurances that competing technologies would not harm our business development.

We are engaged in a rapidly evolving field. Competition from numerous pharmaceutical companies is intense and expected to increase. The large and rapidly growing market for oncology treatments is likely to attract new entrants. Numerous biotechnology and pharmaceutical companies are focused on developing cancer treatments and I-O technologies including CAR T. Many, if not all, of these companies have greater financial and other resources and development capabilities than we do. Many of our competitors also have greater collective experience in undertaking preclinical and clinical testing of products, obtaining regulatory approvals and manufacturing and marketing prescription pharmaceutical products. There can be no assurance that our under-development drug candidates will be more effective or achieve greater market acceptance than competitive products, or that our competitors will not succeed in developing products and technologies that are more effective than those being developed by us or that would render our products and technologies less competitive or obsolete. Additionally, there can be no assurance that the development by others of new or improved drugs will not make our pharmaceutical products superfluous or obsolete.

We are a party to collaboration agreements and other significant agreements which contain complex commercial terms that could result in disputes, litigation or indemnification liability that could adversely affect our business, results of operations and financial condition.

We currently derive, and expect to derive in the foreseeable future, all or much of our revenue from collaboration agreements with biotechnology and pharmaceutical companies. These collaboration agreements contain complex commercial terms, including:

- Clinical development and commercialization obligations that are based on certain commercial reasonableness performance standards that can often be difficult to enforce if disputes arise as to adequacy of our partner's performance;
- Research and development performance and reimbursement obligations for our personnel and other resources allocated to partnered drug candidate development programs;
- Clinical and commercial manufacturing agreements, some of which are priced on an actual cost basis for products supplied by us to our partners with complicated cost allocation formulas and methodologies;
- Intellectual property ownership allocation between us and our partners for improvements and new inventions developed during the course of the collaboration;
- Royalties on drug sales based on a number of complex variables, including net sales calculations, geography, scope of patent claim coverage, patent life, generic competitors, bundled pricing and other factors; and
- Indemnity obligations for intellectual property infringement, product liability and certain other claims.

From time to time, we have informal dispute resolution discussions with third-parties regarding the appropriate interpretation of the complex commercial terms contained in our agreements. One or more disputes may arise or escalate in the future regarding our collaboration agreements, transaction documents, or third-party license agreements that may ultimately result in costly litigation and unfavorable interpretation of contract terms, which would have a material adverse effect on our business, financial condition and results of operations.

Governments may impose price controls, which may adversely affect our future profitability.

We intend to seek approval to market our drug candidates in both the U.S. and in foreign jurisdictions. In some foreign countries and jurisdictions, particularly in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug candidate. To obtain reimbursement or pricing approval in some countries, we may be required to conduct clinical trials to compare the cost effectiveness of our drug candidates to other available therapies, which is time consuming and costly. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

Write-offs related to the impairments of our long-lived assets, including goodwill and indefinite-lived intangible assets, and other non-cash charges such as share-based payments may adversely impact our results of operations.

We may incur significant non-cash charges related to impairments of our long-lived assets, including goodwill and indefinite-lived intangible assets. Although we did not record any such charges during 2018, we are required to perform periodic impairment reviews of those assets at least annually. The carrying value of goodwill on our balance sheet that is subject to impairment reviews was approximately $3.3 million at December 31, 2018 and December 31, 2017 and the carrying value of our indefinite-lived assets was $9.2 million at December 31, 2018 and December 31, 2017. To the extent future reviews conclude that the expected future cash flows generated from our business activities are not sufficient to recover the carrying value of these assets, we will be required to measure and record an impairment charge to write-down these assets to their realizable values and those impairment charges could be equal to the entire carrying value.

We completed our last review during the fourth quarter of 2018 and determined that goodwill and indefinite-lived intangible assets were not impaired as of December 31, 2018. However, there can be no assurance that upon completion of subsequent reviews a material impairment charge will not be recorded. If future periodic reviews determine that our assets are impaired and a write-down is required, it will adversely impact our operating results.

In addition, we recorded non-cash charges of approximately $1.4 million and $1.8 million for share-based expense during the years ended December 31, 2018 and 2017, respectively. In the future, this amount could fluctuate materially as the Company expects to continue to issue share-based payments awards.

Potential new accounting standards or legislative actions may adversely impact our future financial position or results of operations.

Future changes in financial accounting standards may cause adverse, unexpected fluctuations in the timing of the recognition of revenues or expenses, and may affect our financial position or results of operations. New standards may occur in the future and may cause us to be required to make changes in our accounting policies. Compliance with changing regulation of corporate governance and public disclosure may result in additional expenses. Changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, new SEC regulations, Public Company Accounting Oversight Board, or PCAOB, standards and NASDAQ rules, are creating uncertainty for companies such as ours and insurance, accounting and auditing costs are high as a result of this uncertainty and other factors.

We have limited capital resources and currently have only one full time employee in our finance department. We rely on outside consultants to supplement our internal expertise and are committed to maintaining high standards of corporate governance and public disclosure. As a result, we intend to invest all reasonably necessary resources to comply with evolving standards, and this investment may result in increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities.

Varying interpretations of existing standards and rules have occurred with frequency and may cause us to have to restate previously reported result of operations.

Varying interpretations of existing standards of accounting policies or accounting treatments of existing transactions may cause us to have to restate previously reported result of operations.

For example, in January 2014 we completed a transaction that we determined to be a reverse merger business combination. We allocated the purchase price consideration to the assets acquired and liabilities assumed at their estimated fair values as of the date of acquisition. Our determination that the transaction met the criteria for a business combination was based on our best knowledge of the facts and circumstances surrounding the transaction, and required the application of our judgment. Changes to this determination would result in the transaction to be accounted for as a recapitalization, with no goodwill recorded, which could cause a material change in our reported results of operations and could cause the Company to have to amend prior periodic or other filings with the SEC, at further expense to the Company. We may be subject to similar varying interpretations of existing standards of accounting policies or accounting treatments in the future.

In addition, we do not consider the Company to be a development stage entity for financial reporting presentation purposes. A determination that the Company is a development stage entity could cause a material change in our reported results of operations and could cause the Company to have to amend prior periodic or other filings with the SEC, at further expense to the Company.

Tax reform may significantly affect the Company and its stockholders.

On December 22, 2017, the TCJA, which significantly reforms the Internal Revenue Code of 1986, as amended (the "Code"), was signed into law. The TCJA, among other things, includes changes to U.S. federal tax rates, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitations of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitations of the deduction for net operating losses ("NOLs") to 80% of current year taxable income and elimination of NOL carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, modifying or repealing many business deductions and credits and putting into effect the migration from a "worldwide" system of taxation to a territorial system. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will adjust their policies in response to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is uncertain and could be adverse.

Due to the potential for changes to tax laws and regulations or changes to the interpretation thereof (including regulations and interpretations pertaining to the TCJA), the ambiguity of tax laws and regulations, the subjectivity of factual interpretations and other factors, our estimates of effective tax rate and income tax assets and liabilities may be incorrect and our financial statements could be adversely affected. The impact of these factors referenced in the first sentence of this paragraph may be substantially different from period-to-period.

In addition, the amount of income taxes we pay is subject to ongoing audits by U.S. federal, state and local tax authorities and by non-U.S. tax authorities. If audits result in payments or assessments different from our reserves, our future results may include unfavorable adjustments to our tax liabilities and our financial statements could be adversely affected. Any further significant changes to the tax system in the U.S. or in other jurisdictions (including changes in the taxation of international income as further described below) could adversely affect our financial statements.

Our ability to use potential future operating losses and our federal and state NOL carryforwards to offset taxable income from revenue generated from operations or corporate collaborations could be limited.

The use of our NOL carryforwards may have limitations resulting from certain future ownership changes or other factors under the Code and other taxing authorities. The TCJA changed both the federal deferred tax value of the NOL carryforwards and the rules of utilization of federal NOL carryforwards. The TCJA lowered the corporate tax rate from 35% to 21% effective for our 2018 fiscal year. For NOL carryforwards generated in years prior to 2018, there is no annual limitation on the utilization and the carryforward period remains at 20 years. However, NOL carryforwards generated in years after 2017 will only be available to offset 80% of future taxable income in any single year but will not expire.

If our NOL carryforwards are limited, and we have taxable income which exceeds the available NOL carryforwards for that period, we would incur an income tax liability even though NOL carryforwards may be available in future years prior to their expiration. Any such income tax liability may adversely affect our future cash flow, financial position and financial results.

Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.

We are highly dependent on principal members of our executive team and key employees, the loss of whose services may adversely impact the achievement of our objectives. Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in preclinical or clinical studies may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research and development objectives.

We will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations.

As of December 31, 2018, we had four full-time employees. As we mature, we may need to expand our full-time employee base and to hire more consultants and contractors. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees, all of which may have a material adverse effect on our business, results of operations and prospects. Any future growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional drug candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize drug candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with the regulations of the FDA and non-U.S. regulators, provide accurate information to the FDA and non-U.S. regulators, comply with healthcare fraud and abuse laws and regulations in the U.S. and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained in the course of clinical studies, which could result in regulatory sanctions and cause serious harm to our reputation or could cause regulatory agencies not to approve our drug candidates. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability and costs. If the use of our drug candidates harms patients, or is perceived to harm patients even when such harm is unrelated to our drug candidates, our regulatory approvals could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims.

The use of our drug candidates in clinical studies and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. There is a risk that our drug candidates may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- Impairment of our business reputation;
- Withdrawal of clinical study participants;
- Costs due to related litigation;
- Distraction of management's attention from our primary business;
- Substantial monetary awards to patients or other claimants;
- The inability to commercialize our drug candidates; and
- Decreased demand for our drug candidates, if approved for commercial sale,

all of which may have a material adverse effect on our business, results of operations and prospects.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third-parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

The workers' compensation insurance we maintain to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions, which may have a material adverse effect on our business and results of operations.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. Any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected, which may have material adverse effect on our business and results of operations.

Failure in our information technology systems, including by cybersecurity attacks or other data security incidents, could significantly disrupt our operations.

Our operations depend, in part, on the continued performance of our information technology systems. Our information technology systems are potentially vulnerable to physical or electronic break-ins, computer viruses and similar disruptions. Failure of our information technology systems could adversely affect our business, profitability and financial condition.

A successful cybersecurity attack or other data security incident could result in the misappropriation and/or loss of confidential or personal information, create system interruptions, or deploy malicious software that attacks our systems. It is possible that a cybersecurity attack might not be noticed for some period of time. The occurrence of a cybersecurity attack or incident could result in business interruptions from the disruption of our information technology systems, or negative publicity resulting in reputational damage with our clinical trial participants, customers, stockholders and other stakeholders and/or increased costs to prevent, respond to or mitigate cybersecurity events. In addition, the unauthorized dissemination of sensitive personal information or proprietary or confidential information could expose us or other third-parties to regulatory fines or penalties, litigation and potential liability, or otherwise harm our business.

Risks Related to Our Common Stock

An active, liquid and orderly market for our common stock may not develop.

Our common stock trades on The NASDAQ Capital Markets. An active trading market for our common stock may never develop or be sustained. If an active market for our common stock does not continue to develop or is not sustained, it may be difficult for investors in our common stock to sell shares without depressing the market price for the shares or to sell the shares at all. An inactive market may also impair our ability to raise capital by selling common stock and may impair our ability to acquire other businesses, applications or technologies using our common stock as consideration, which, in turn, could materially adversely affect our business.

The market price of our stock may be highly volatile, and you may not be able to sell shares of our stock.

Companies trading in the stock market in general have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our stock, regardless of our actual operating performance.

The market price of our stock may be volatile. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- Adverse results or delays in preclinical or clinical studies;
- Inability to obtain additional funding;
- Any delay in filing an IND or BLA for any of our drug candidates and any adverse development or perceived adverse development with respect to the FDA's review of that IND or BLA;
- Failure to develop successfully our drug candidates;
- Failure to maintain our existing strategic collaborations or enter into new collaborations;
- Failure by us or our licensors and strategic collaboration partners to prosecute, maintain or enforce our intellectual property rights;
- Changes in laws or regulations applicable to future products;
- Inability to obtain adequate product supply for our drug candidates or the inability to do so at acceptable prices;
- Adverse regulatory decisions;
- Introduction of new products, services or technologies by our competitors;
- Failure to meet or exceed financial projections we may provide to the public;
- Failure to meet or exceed the financial projections of the investment community;
- The perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- Announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic collaboration partner or our competitors;
- Disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- Additions or departures of key scientific or management personnel;
- Significant lawsuits, including patent or stockholder litigation;
- Changes in the market valuations of similar companies;
- Sales of our common stock by us or our stockholders in the future; and
- Trading volume of our common stock.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of March 15, 2019, our executive officers, directors, affiliates and other principal stockholders beneficially own approximately 78.1% of our outstanding common stock. Therefore, these stockholders will have the ability to influence us through their ownership positions. Further, our majority stockholder, Pharmsynthez, has beneficial ownership of approximately 9.3 million shares of common stock. These shares represent ownership of approximately 64.8% of our common stock as of March 15, 2019. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

We have entered into several agreements with our major stockholders.

We have entered into several agreements with our major stockholders. Some of the agreement parties may be considered affiliates of ours, which may result in conflicts of interest. In addition, these arrangements may not have been negotiated at arm's length and may contain terms and conditions that are not in our best interest and would not otherwise be applicable if we entered into arrangements with a third-party not affiliated with us.

Our preferred stock has rights, preferences and privileges that are not held by, and are preferential to, the rights of our common stockholders, which could result in the interests of the holders of our preferred stock differing from those of our common stockholders.

The holders of our preferred stock have the right to receive a liquidation preference entitling them to be paid out of our assets available for distribution to stockholders before any payment may be made to holders of any common stock or any series of preferred stock ranked junior to such class of preferred stock. The existence of a liquidation preference may reduce the value of our common stock, make it harder for us to sell shares of common stock in offerings in the future, or prevent or delay a change of control. Additionally, each share of Series A preferred stock is convertible into one share of common stock and each share of Series B preferred stock is convertible into two shares of common stock, subject to certain adjustments, which may cause substantial dilution to our common stockholders. The preferential rights could result in divergent interests between the holders of shares of preferred stock and holders of our common stock. In addition, our majority shareholder, Pharmsynthez holds shares consisting of the majority of our Series B Preferred Stock and all of our Series A Preferred Stock. The interests of these preferred holders may differ from the interests of our security holders as a whole.

The issuance of future shares of common stock may result in dilution to our stockholders.

As of March 15, 2019, we had 10,443,889 shares of common stock excluding:

- 970,000 shares of common stock underlying outstanding Series A Preferred Stock, which are convertible into common stock on a one-for-one basis;
- 1,804,394 shares of common stock underlying outstanding Series B Preferred Stock, which are convertible into common stock on a one-for-two basis;
- 509,000 shares of common stock issuable upon the exercise of outstanding pre-funded warrants;
- 5,240,427 shares of common stock issuable upon the exercise of outstanding warrants;
- 1,833,011 shares of common stock issuable upon the exercise of outstanding options;
- 50,000 shares of common stock underlying outstanding restricted stock units;
- 88,817 shares of common stock issuable in connection with the common stock awards; and
- 7,500,000 shares of common stock to be issued in connection with the Transaction including 4,875,000 shares of common stock to be issued to the shareholders of Hesperix and 2,625,000 shares of common stock to be issued in connection with the OPKO Assignment Agreement.

The issuance of these shares of common stock and the sale of these shares of common stock, or even the potential of such issuance and sale, may have a depressive effect on the market price of our common stock and the issuance of such common stock will cause dilution to our stockholders.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

We do not intend to pay dividends on our common stock or preferred stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividends on our common stock or preferred stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to common or preferred stockholders will therefore be limited to the appreciation of their stock.

ITEM 1B – UNRESOLVED STAFF COMMENTS

Not Applicable.

ITEM 2 – PROPERTIES

We occupied a facility consisting of approximately 4,000 square feet in the Ledgemont Technology Center in Lexington, Massachusetts. The premises were divided into approximately 50% laboratory and 50% office space and were leased by our subsidiary, Xenetic Bioscience, Incorporated. The lease provided for an initial term of 61 months which commenced in January 2014 and expired on January 31, 2019. Commencing February 1, 2019, we occupy a facility consisting of approximately 1,700 square feet of office space at 40 Speen Street in Framingham, Massachusetts. The sublease is for 21 months through September 2020. We believe that this space is adequate for our current needs and that if additional space is required, it can be obtained at commercially reasonable terms nearby.

In addition, we lease 450 sq. ft. of office space in Miami, Florida. The lease provided for an initial term of 12 months, which commenced on December 1, 2016, and was extended for an additional two years through November 30, 2019. We believe that this space is adequate for our current needs and that if additional space is required, it can be obtained at commercially reasonable terms either within its current space or nearby.

ITEM 3 – LEGAL PROCEEDINGS

From time to time, we may be a party to litigation and subject to claims incident to the ordinary course of business. Although the results of litigation and claims cannot be predicted with certainty, we currently believe that the final outcome of these ordinary course matters will not have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

There are no matters, as of December 31, 2018, that, in the opinion of management, might have a material adverse effect on our financial position, results of operations or cash flows.

ITEM 4 – MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5 – MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our common stock is listed for trading on The NASDAQ Capital Market under the symbol "XBIO."

Holders of Record

As of March 15, 2019, there were 410 holders of record of our common stock.

Dividends

There are no restrictions in our articles of incorporation or bylaws that prevent us from declaring dividends. The Nevada Revised Statutes, however, do prohibit us from declaring dividends where after giving effect to the distribution of the dividend:

- We would not be able to pay our debts as they become due in the usual course of business; or
- Our total assets would be less than the sum of our total liabilities plus the amount that would be needed to satisfy the rights of stockholders who have preferential rights superior to those receiving the distribution.

We have never previously declared or paid any cash dividends on our common stock. We currently intend to retain earnings and profits, if any, to support our business strategy and do not intend to pay any cash dividends within the foreseeable future. Any future determination to pay cash dividends will be at the sole discretion of our Board of Directors and will depend upon the financial condition of the Company, our operating results, capital requirements, general business conditions and any other factors that the Board of Directors deems relevant.

Recent Sales of Unregistered Securities

None.

Repurchases of Equity Securities of the Issuer

During 2018 and 2017, we did not repurchase any of our outstanding securities.

ITEM 6 – SELECTED FINANCIAL DATA

We are not required to provide the information required by this Item because we are a smaller reporting company.

ITEM 7 – MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

BUSINESS OVERVIEW

Our Phase II trial for our novel oncology product, XBIO-101, commenced patient dosing in October 2017. We closed patient enrollment of the trial in March 2019 as a result of slower than expected progress on the trial resulting from patient enrollment and retention challenges.

We continue to commit a significant amount of our resources to our research and development activities and anticipate continuing to do so for the near future. Although we hold a broad patent portfolio, the focus of our internal development efforts during 2018 was limited to research and development of XBIO-101 due to capital constraints.

On March 1, 2019, the Company entered into an agreement to acquire the novel ("Chimeric Antigen Receptor ("CAR") T platform technology, referred to herein as "XCART," (the "Transaction") a proximity-based screening platform capable of identifying CAR constructs that can target patient-specific tumor neoantigens, with a demonstrated proof of mechanism in B-cell Non-Hodgkin lymphomas. The XCART technology, developed by the Scripps Research Institute (the "Institute") in collaboration with the Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry ("IBCH"), is believed to have the potential to significantly enhance the safety and efficacy of cell therapy for B-cell lymphomas by generating patient- and tumor-specific CAR T cells. The closing of the Transaction is subject to customary closing conditions as well as conditions regarding (i) the Company having adequate financing to fund its future working capital obligations following the closing and (ii) the Company obtaining necessary and appropriate stockholder approvals, evidencing among other matters, approval of the Share Purchase Agreement and the transactions contemplated thereunder, including the issuance of the transaction shares. Subject to the satisfaction of the closing conditions, the transaction is expected to close in the first half of 2019.

Critical Accounting Estimates

The preparation of our financial statements in conformity with United States ("U.S.") generally accepted accounting principles ("U.S. GAAP") requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amounts of revenue, costs and expenses during the reporting period. On an ongoing basis, we evaluate our estimates that are based on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. The result of these evaluations forms the basis for making judgments about the carrying values of assets and liabilities and the reported amount of expenses that are not readily apparent from other sources. Because future events and their effects cannot be determined with certainty, actual results and outcomes could differ materially from our estimates, judgments and assumptions.

Management believes that the following accounting estimates are the most critical to aid in fully understanding and evaluating our reported financial results, and they require management's most difficult subjective or complex judgments, resulting from the need to make estimates about the effect of matters that are inherently uncertain. The following narrative describes these critical accounting estimates, judgments and assumptions and the effect if actual results differ from these assumptions.

Revenue Recognition

We enter into supply, license and collaboration arrangements with pharmaceutical and biotechnology partners, some of which include royalty agreements based on potential net sales of approved commercial pharmaceutical products.

Effective January 1, 2018, we adopted Accounting Standards Codification ("ASC") Topic 606, *Revenue from Contracts with Customers* ("ASC 606"), using the modified retrospective transition method. Under this method, results for reporting periods beginning after January 1, 2018 are presented under ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with ASC 605. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. We did not have any revenue generating contracts with customers and, therefore, the adoption of this new revenue standard did not have a material impact on the consolidated financial statements. Under ASC 605, we recognized revenue when all of the following criteria were met: (i) persuasive evidence of an arrangement existed; (ii) delivery had occurred or services had been rendered; (iii) the seller's price to the buyer was fixed or determinable; and (iv) collectability was reasonably assured.

The terms of our license agreements may include delivery of an IP license to a collaboration partner. We may be compensated under license arrangements through a combination of non-refundable upfront receipts, development and regulatory objective receipts and royalty receipts on future product sales by partners. We anticipate recognizing non-refundable upfront license payments and development and regulatory milestone payments received by us in license and collaboration arrangements that include future obligations, such as supply obligations, ratably over our expected performance period under each respective arrangement. We make our best estimate of the period over which we expect to fulfil our performance obligations, which may include technology transfer assistance, research activities, clinical development activities, and manufacturing activities from development through the commercialization of the product. Given the uncertainties of these collaboration arrangements, significant judgment is required to determine the duration of the performance period.

When we enter into an arrangement to sublicense some of our patents, we will consider the performance obligations to determine if there is a single element or multiple elements to the arrangement as we determine the proper method and timing of revenue recognition. We consider the terms of the license or sublicense for such elements as price adjustments or refund clauses in addition to any performance obligations for us to provide such as services, patent defense costs, technology support, marketing or sales assistance or any other elements to the arrangement that could constitute an additional deliverable to us that could change the timing of the revenue recognition. Non-refundable upfront license and sublicense fees received, whereby continued performance or future obligations are considered inconsequential or perfunctory to the relevant licensed technology, are recognized as revenue upon delivery of the technology.

We expect to recognize royalty revenue in the period of sale, based on the underlying contract terms, provided that the reported sales are reliably measurable, we have no remaining performance obligations, and all other revenue recognition criteria are met.

We anticipate reimbursements for research and development services completed by us related to the collaboration agreements to be recognized in operations as revenue on a gross basis.

Our license, sublicense and collaboration agreements with certain collaboration partners could also provide for future milestone receipts to us based solely upon the performance of the respective collaboration partner in consideration of deadline extensions or upon the achievement of specified sales volumes of approved drugs. For such receipts, we expect to recognize the receipts as revenue when earned under the applicable contract terms on a performance basis or ratably over the term of the agreement. These receipts may also be recognized as revenue when continued performance or future obligations by us are considered inconsequential or perfunctory.

Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue at a point in time, or over time, as it satisfies a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract, determine those that are performance obligations, and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

As part of the accounting for these arrangements, we must use significant judgment to determine: a) the number of performance obligations based on the determination under step (ii) above; b) the transaction price under step (iii) above; and c) the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above. We use judgment to determine whether milestones or other variable consideration should be included in the transaction price as described further below. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. In developing the stand-alone price for a performance obligation, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. We validate the stand-alone selling price for performance obligations by evaluating whether changes in the key assumptions used to determine the stand-alone selling prices will have a significant effect on the allocation of transaction price between multiple performance obligations. We recognize a contract asset or liability for the difference between our performance (i.e., the goods or services transferred to the customer) and the customer's performance (i.e., the consideration paid by, and unconditionally due from, the customer).

Research and Development Expenses

Research and development expenses consist of expenses incurred in performing research and development activities, including compensation and benefits, facilities expenses, overhead expenses, clinical trial and related clinical manufacturing expenses, fees paid to Clinical Research Organizations ("CROs") and contract manufacturing organizations and other outside expenses. We expense research and development costs as incurred. We expense upfront, non-refundable payments made for research and development services as obligations are incurred. The value ascribed to intangible assets acquired but which have not met capitalization criteria is expensed as research and development at the time of acquisition.

We are required to estimate accrued research and development expenses at each reporting period. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met. However, some require advanced payments. We make estimates of accrued expenses as of each balance sheet date in the financial statements based on facts and circumstances known at that time. We periodically confirm the accuracy of the estimates with the service providers and make adjustments, if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- program managers in connection with overall program management of clinical trials;
- CROs in connection with clinical trials; and
- investigative sites in connection with clinical trials.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple research institutions and CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or prepaid accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Share-based Expense

Share-based expense includes grants of options and restricted stock units ("RSUs") to employees and non-employees to purchase shares of common stock, Joint Share Ownership Plan ("JSOP") awards to employees, as well as agreements to issue common stock in exchange for services provided by non-employees.

Share-based expense is based on the estimated fair value of the option or calculated using the Black-Scholes option pricing model. Determining the appropriate fair value model and related assumptions requires judgment, including estimating share price volatility and expected terms of the awards. The expected volatility rates are estimated based on our actual volatility and of comparable public companies over the expected term of the option. The expected terms represent the time that options are expected to be outstanding. We account for forfeitures as they occur and not at the time of grant. The Company has not paid dividends and does not anticipate paying cash dividends in the foreseeable future and, accordingly, uses an expected dividend yield of zero. The risk-free interest rate is based on the rate of U.S. Treasury securities with maturities consistent with the estimated expected term of the awards. Upon exercise, stock options are redeemed for newly issued shares of common stock. RSUs are redeemed for newly issued shares of common stock as the vesting and settlement provisions of the grant are met.

For employee options that vest based solely on service conditions, the fair value measurement date is generally on the date of grant and the related compensation expense is recognized on a straight-line basis over the requisite vesting period of the awards. For non-employee options, the fair value measurement date is the earlier of the date the performance of services is complete or the date the performance commitment has been reached. We generally determine that the fair value of the stock options is more reliably measurable than the fair value of the services received. Compensation expense related to stock options granted to non-employees that vest based solely on service conditions is subject to re-measurement at each reporting period until the options vest and is recognized on a straight-line basis over requisite vesting period of the awards.

The fair value of common stock awards issued in exchange for services provided by non-employees is generally determined by using the fair value of the services provided, as this provides the most reliable measure of the fair value of the awards. Share-based expense is recognized as services are rendered on a straight-line basis. The assumptions used in calculating the fair value of the common stock awards represent our best estimates and involve inherent uncertainties and the application of our judgment. As a result, if factors change and we use different assumptions, share-based expense related to the common stock awards could be materially different in the future.

Warrants

In connection with certain financing, consulting and collaboration arrangements, we issued warrants to purchase shares of our common stock. Outstanding warrants are standalone instruments that are not puttable or mandatorily redeemable by the holder and are classified as equity awards. We measure the fair value of the awards using the Black-Scholes option pricing model, which requires the input of subjective assumptions and judgments, including estimating the expected term of the awards and the share price volatility, at each reporting period until the measurement date is reached. The expected term is deemed to be the contractual life of the warrant and we determine the expected volatility based on a weighted-average of the historical volatility of a peer group of comparable publicly traded companies with drug candidates in similar stages of development to our drug candidates in conjunction with our historical volatility.

All other warrants are recorded at fair value as expense on a straight-line basis over the requisite service period or at the date of issuance, if there is not a service period or if service has already been rendered. For warrants that contain vesting triggers based on the achievement of certain objectives, we apply judgment to estimate the probability and timing of the achievement of those objectives. These estimates involve inherent uncertainties, and as a result, if the probability or timing of the achievement of those objectives change, expense related warrants could be materially different in the future.

Warrants issued to collaboration partners in conjunction with the issuance of common stock are initially recorded at fair value as a reduction of additional paid-in capital of the common stock issued.

For warrants issued in connection with financing arrangements the Company allocates the proceeds based on the relative fair value of the award and other instrument(s).

Goodwill and Indefinite-lived Intangible Assets

Goodwill

Goodwill is not amortized but is reviewed for impairment annually as of October 1, or when events or changes in the business environment indicate that all, or a portion, of the carrying value of the reporting unit may no longer be recoverable. Under this method, we compare the fair value of our reporting unit to its carrying value. If the fair value is less than the carrying amount, a more detailed analysis is performed to determine if goodwill is impaired. An impairment loss, if any, is measured as the excess of the carrying value of goodwill over the fair value of goodwill. We also have the option to first assess qualitative factors to determine whether the existence of events or circumstances leads us to determine that it is more likely than not (that is, a likelihood of more than 50%) that goodwill is impaired. If we choose to first assess qualitative factors and it is determined that it is not more likely than not goodwill is impaired, we are not required to take further action to test for impairment. We also have the option to bypass the qualitative assessment and perform only the quantitative impairment test, which we may choose to do in some periods but not in others. As the option to perform the qualitative assessment is not a permanent election, we reassess this option during each annual impairment review.

We determine our reporting unit by identifying the components of our operating segment with similar economic characteristics based on quantitative and qualitative factors that have discrete financial information available. We determined that we have one reporting unit as of October 1, 2018 and 2017, the dates of our annual impairment reviews. Based on our annual impairment reviews, we used the quantitative method and determined no adjustment to the carrying value of goodwill would be necessary as the fair value of our reporting unit exceeded its respective carrying value as of October 1, 2018 and 2017, respectively. There can be no assurance that future events will not result in an impairment of goodwill.

Indefinite-lived Intangible Assets

Our indefinite-lived intangible assets consist of acquired in-process research and development ("IPR&D"). IPR&D intangible assets are considered indefinite-lived intangible assets until completion or abandonment of the associated research and development efforts. IPR&D is not amortized but is reviewed for impairment annually as of October 1, or when events or changes in the business environment indicate the carrying value may be impaired. If the fair value of the intangible asset is less than the carrying amount, we perform a quantitative test to determine the fair value. The impairment loss, if any, is measured as the excess of the carrying value of the intangible asset over its fair value. We also have the option to first assess qualitative factors to determine whether the existence of events or circumstances leads us to determine that it is more likely than not (that is, a likelihood of more than 50%) that our indefinite-lived intangible asset is impaired. If we choose to first assess qualitative factors and it is determined that it is not more likely than not our indefinite-lived intangible asset is impaired, we are not required to take further action to test for impairment. We also have the option to bypass the qualitative assessment and perform only the quantitative impairment test, which we may choose to do in some periods but not in others. As the option to perform the qualitative assessment is not a permanent election, we reassess this option during each annual impairment review. During 2018 and 2017, we used the quantitative method and determined the fair value of the indefinite-lived intangible asset exceeded its carrying value as of October 1, 2018 and 2017.

Significant judgments are inherent in the calculation of fair value. With the assistance of an independent third party, we calculated the fair value of our IPR&D by using the Multi-Period Excess-Earnings Method (the "MPEEM") which is a form of the income approach. Under the MPEEM, the fair value of an intangible asset is equal to the present value of the asset's incremental after-tax cash flows (excess earnings) remaining after deducting the market rates of return on the estimated value of contributory assets (contributory charge) over its remaining useful life. This method requires us to make long-term projections of the amount and timing of income and expenses related to development and commercialization of the acquired intangible asset and assumptions regarding the rate of return on contributory assets, the weighted average cost of capital and the discount rate for estimated future after-tax cash flows. Specifically, this method took into account our estimates of future incremental milestone payments that may be achieved upon completion of clinical trial stages, regulatory approval and sales goals upon commercialization, as well as our expected royalty income based on sales upon commercialization. Projected expenses are based on our forecasted spend required to complete the development of our IPR&D, which will require the Company to raise further capital to fund the development. Our projections are estimates subject to change based on several factors including the results of clinical trials and delays in regulatory approval. The discount rate used is commensurate with the uncertainties associated with the economic estimates described above and reflects the stage of development, the time and resources needed to complete the development of the product and the risks of advancement through regulatory approval processes.

Key assumptions utilized in the fair valuation of our indefinite-lived intangible asset are as follows:

- Discount rate – 45.0%
- Estimated aggregate milestone receipts – approximately $300 million
- Royalty rates – 10% of net sales

While we believe reasonable estimates and appropriate assumptions were utilized to calculate the fair value of IPR&D, it is possible a material change could occur. Use of different estimates and judgments could yield materially different results in our analysis and could result in materially different asset values or expense.

There can be no assurance that we will be able to successfully develop and complete the acquired IPR&D program and profitably commercialize the underlying drug candidates before our competitors develop and commercialize similar products, or at all. Moreover, if the acquired IPR&D program fails or is abandoned during development, then we may not realize the value we have estimated and recorded in our financial statements on the acquisition date, and we may also not recover the research and development investment made since the acquisition date to further develop that program. If such circumstances were to occur, our future operating results could be materially adversely impacted.

We did not record an impairment charge as a result of our goodwill or indefinite-lived intangible asset impairment tests in 2018 or 2017. We will continue to closely monitor the performance of our indefinite-lived intangible asset and reporting unit. If the business experiences adverse changes in our key assumptions and judgments, we will perform an interim goodwill and/or indefinite-lived intangible asset impairment analysis. There can be no assurance that future events will not result in an impairment of our goodwill or indefinite-lived intangible asset. As a result of the going concern uncertainty discussed under *Liquidity and Capital Resources* below, the recoverability and classification of the Company's intangible assets and goodwill could be adversely affected.

RESULTS OF OPERATIONS

The table below sets forth the comparison of our historical results of operations for the year ended December 31, 2018 to the year ended December 31, 2017.

Description	2018	2017	Increase (Decrease)	Percentage Change
Revenues:				
Licenses and collaboration services	$ –	$ 7,585,000	$ (7,585,000)	(100.0)%
Operating costs and expenses:				
Cost of research and development revenue	–	(156,119)	(156,119)	(100.0)%
Research and development	(2,883,952)	(4,060,000)	(1,176,048)	(29.0)%
General and administrative	(4,392,375)	(6,937,643)	(2,545,268)	(36.7)%
Loss from operations	$ (7,276,327)	$ (3,568,762)	$ 3,707,565	103.9 %
Other income (expense):				
Other expense	(24,640)	(24,552)	88	0.4 %
Interest income (expense)	509	(1,818)	(2,327)	(128.0)%
Net loss	$ (7,300,458)	$ (3,595,132)	$ 3,705,326	103.1 %

Revenue

For the year ended December 31, 2017, revenue represented license and collaboration services. We did not receive any license or collaboration service revenue for the year ended December 31, 2018.

In October 2017, we entered into a Right to Sublicense Agreement (the "Sublicense Agreement") with Baxalta Incorporated, Baxalta US Inc., and Baxalta GmbH (collectively, with their affiliates "Baxalta") wholly-owned subsidiaries of Takeda Pharmaceuticals Co., Ltd. ("Takeda"), formerly Shire plc. Pursuant to the Sublicense Agreement, Baxalta paid us a one-time payment of seven million five hundred thousand dollars ($7,500,000) in November 2017 and agreed to pay us single digit royalty payments based upon net sales of the licensed patents in connection with products related to the treatment of blood and bleeding disorders ("Covered Products") throughout the term, each of which is conditioned upon the performance of the sublicense contemplated by the Sublicense Agreement. We recognized revenue of $7.5 million in 2017 related to this payment.

Research and development revenue represents collaboration services related to research and development programs conducted on behalf of third-parties in 2017.

Cost of Revenue

There was no cost of revenue for the year ended December 31, 2018. Cost of research and development revenue represents collaboration services related to research and development programs conducted on behalf of third-parties in 2017.

Research and Development Expense

R&D expenses decreased $1.2 million, or 29.0% to $2.9 million from $4.1 million in the comparable period in 2017. The table below sets forth the research and development expenses incurred by category of expense for the years ended December 31, 2018 and 2017.

	Year ended December 31,	
Category of Expense	**2018**	**2017**
Outside services and Contract Research Organizations	$ 2,242,658	$ 3,094,583
Share-based expense	203,031	101,400
Personnel costs	280,118	568,376
Other	158,145	295,641
Total research and development expense	$ 2,883,952	$ 4,060,000

The decrease in outside services and contract research organizations expense was primarily due to our internal development efforts being solely focused on our oncology product, XBIO-101, during the year ended December 31, 2018 due to capital constraints. For the year ended December 31, 2017 outside services and contract research organizations included costs associated with other programs and development efforts but such costs were not continued in 2018. Share-based expense increased during the year ended December 31, 2018 as compared to the same period in the prior year primarily due to expense related to warrants issued to Serum Institute in 2016. Salaries and wages decreased during the year ended December 31, 2018 as we reduced our R&D headcount in the second half of fiscal year 2017 due to our limited internal development efforts. Other expense decreased during the year ended December 31, 2018 primarily due to lower laboratory costs in 2018 as we discontinued our internal development efforts in the second half of 2017.

General and Administrative Expense

General and administrative expenses decreased by approximately $2.5 million or 36.7% for the year ended December 31, 2018 to $4.4 million from $6.9 million in the comparable period in 2017. Employee-related costs, including shared-based costs and travel, legal, accounting, investor and public relations costs all decreased during the year ended December 31, 2018 compared to the year ended December 31, 2017 as we significantly reduced our discretionary spending due to our capital constraints. In addition, expense for the year ended December 31, 2017 included approximately $0.6 million in accrued severance related to a settlement agreement with our former Chief Executive Officer who separated from the Company in November 2017.

Other Expense

Other expense was approximately $25,000 for the year ended December 31, 2018 and was relatively unchanged from the prior year.

Interest Income (Expense)

We earned $500 of net interest income for the year ended December 31, 2018 compared to net interest expense of $2,000 in the year ended December 31, 2017 due to lower interest expense on our operating lease.

Liquidity and Capital Resources

We incurred a net loss of approximately $7.3 million for the year ended December 31, 2018 and had an accumulated deficit of $153.2 million at December 31, 2018 as compared to an accumulated deficit of approximately $145.9 million at December 31, 2017. Working capital (deficit) was approximately $(0.4) million and $3.9 million at December 31, 2018 and December 31, 2017, respectively. During the year ended December 31, 2018, our working capital decreased by $4.3 million due primarily to outflows for general operating costs and costs related to our XBIO-101 Phase II clinical trial. These cash outflows were partially offset by approximately $1.5 million of proceeds received from the exercise of warrants during the year ended December 31, 2018. We expect to continue incurring losses for the foreseeable future and will need to raise additional capital or pursue other strategic alternatives in the very near term in order to continue the pursuit of our business plan and continue as a going concern.

Our principal source of liquidity consists of cash. At December 31, 2018, we had approximately $0.6 million in cash and $1.6 million in accounts payable and accrued expenses. At December 31, 2017, we had approximately $5.5 million in cash and $1.9 million in accounts payable and accrued expenses.

We have historically relied upon sales of our equity securities to fund our operations. Since 2005, we have raised approximately $60.0 million in proceeds from offerings of our common and preferred stock. We have also received approximately $20.0 million from revenue producing activities from 2005 through December 31, 2018, including two cash payments from Takeda in 2017: a $3.0 million clinical milestone payment in January 2017; and a $7.5 million sublicense payment in November 2017. More than 90% of the milestone and sublicense revenue received to date has been from a single collaborator, Takeda. We expect the majority of our funding through equity or equity-linked instruments, debt financings, corporate collaborations, related party funding and/or licensing agreements to continue as a trend for the foreseeable future.

We estimate that our existing resources will only be able to fund our planned operations, existing obligations and contractual commitments through the first half of 2019. This estimate is based on our current expectations regarding projected staffing expenses, working capital requirements, costs to close the XCART transaction, capital expenditure plans and anticipated revenues. Given our current working capital constraints, we have attempted to minimize cash commitments and expenditures for external research and development and general and administrative services to the greatest extent practicable. We will need to raise additional working capital in the very near term in order to fund our future operations, including our development efforts associated with the XCART platform technology.

We have no committed sources of additional capital. Our management believes that we have access to capital resources through possible public or private equity offerings, debt financings, corporate collaborations, related party funding or other means. On March 5, 2019, we raised $3.1 million in a registered direct common stock offering resulting in $2.7 million of net proceeds to the Company. However, we have not secured any commitment for additional financing at this time. The terms, timing and extent of any future financing will depend upon several factors including the achievement of progress in our clinical development programs, our ability to identify and enter into licensing or other strategic arrangements and factors related to financial, economic and market conditions, many of which are beyond our control.

Management evaluates whether there are conditions or events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern within one year after the date that the financial statements are issued. We have incurred substantial losses since our inception, and we expect to continue to incur operating losses in the near-term. These factors raise substantial doubt about our ability to continue as a going concern. As a result, our independent registered public accounting firm included an explanatory paragraph in its report on our audited financial statements for the year ended December 31, 2018 expressing doubt as to our ability to continue as a going concern. We will need to raise additional capital in order to sustain our operations. If we are unable to secure additional funds on a timely basis or on acceptable terms, we may be required to defer, reduce or eliminate significant planned expenditures, restructure, curtail or eliminate some or all of our development programs or other operations, reduce general and administrative expenses, and delay or cease the purchase of clinical research services, dispose of technology or assets, pursue an acquisition of our company by another party at a price that may result in a loss on investment for our stockholders, enter into arrangements that may require us to relinquish rights to certain of our drug candidates, technologies or potential markets, file for bankruptcy or cease operations altogether.

We continue to seek appropriate out-license arrangements for all of our technologies but are currently unable to reliably predict whether or when we may enter into an agreement. Due to the uncertainties inherent in the clinical research process and unknown future market conditions, there can be no assurance any of our technologies will lead to any future income.

Cash Flows from Operating Activities

Cash flows used in operating activities for the year ended December 31, 2018 totaled approximately $6.5 million, which was primarily due to our $7.3 million net loss for the period offset by non-cash charges of $1.4 million. Cash flows from operating activities for the year ended December 31, 2017 was $1.5 million due to the receipt of the $3.0 million clinical milestone payment from Takeda in January 2017. Cash flow from this clinical milestone payment was substantially offset by our net loss of $3.6 million, which included $1.8 million of non-cash share-based expense.

Cash Flows from Investing Activities

Cash flows provided by investing activities for the year ended December 31, 2018 totaled approximately $23,000, which represented proceeds from the sale of laboratory equipment.

Cash flows used in investing activities for the year ended December 31, 2017 included approximately $9,000 for the purchase of assets consisting primarily of computer equipment.

As of December 31, 2018, there were no material commitments for capital expenditures.

Cash Flow from Financing Activities

Cash flows from financing activities for the year ended December 31, 2018 totaled approximately $1.5 million representing proceeds from the exercise of warrants.

For the year ended December 31, 2017, there were no significant cash sources or uses from financing activities.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements that have or are reasonably likely to have a current or future material effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources.

Contractual Obligations

Contractual obligations represent future cash commitments and liabilities under agreements with third-parties and exclude contingent liabilities for which we cannot reasonably predict future payment. Our contractual obligations result from property leases for office space. Although we do have obligations for CRO services, the table below excludes potential payments we may be required to make under our agreements with CROs because timing of payments and actual amounts paid under those agreements may be different depending on the timing of receipt of goods or services or changes to agreed-upon terms or amounts for some obligations, and those agreements are cancelable upon written notice by the Company and therefore, not long-term liabilities. The contracts also contain variable costs that are hard to predict as they are based on such things as patients enrolled and clinical trial sites, which can vary and, therefore, are also not included in the table below. Additionally, the expected timing of payment of the obligations presented below is estimated based on current information.

The following table represents our contractual obligations as of December 31, 2018, aggregated by type:

	Payments Due by Period				
	Total	Less than 1 year	1 – 3 years	3 – 5 years	More than 5 years
Operating lease obligations	$ 24,583	$ 24,583	$ –	$ –	$ –
Total	$ 24,583	$ 24,583	$ –	$ –	$ –

On January 7, 2019, we entered into a new office lease in Framingham, MA. The sublease is for 21 months through September 30, 2020 with a total contractual obligation of approximately $50,000.

Recent Accounting Standards

Refer to Note 2, *Summary of Significant Accounting Policies*, of the accompanying financial statements in Item 8 herein.

ITEM 7A – QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are not required to provide the information required by this Item because we are a smaller reporting company.

ITEM 8 - FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and Board of Directors of
Xenetic Biosciences, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Xenetic Biosciences, Inc. (the "Company") as of December 31, 2018 and 2017, and the related consolidated statements of comprehensive loss, stockholder's equity and cash flows for each of the two years in the period ended December 31, 2018 and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2018, in conformity with accounting principles generally accepted in the United States of America.

Explanatory Paragraph/Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As more fully described in Note 1 to the financial statements, the Company has had recurring net losses and continues to experience negative cash flows from operations. These conditions raise substantial doubt about its ability to continue as a going concern. Management's plans regarding those matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Marcum llp

Marcum llp

We have served as the Company's auditor since 2015.

Boston, Massachusetts
March 29, 2019

XENETIC BIOSCIENCES, INC.
CONSOLIDATED BALANCE SHEETS

	December 31, 2018	December 31, 2017
ASSETS		
Current assets:		
Cash	$ 571,605	$ 5,533,062
Restricted cash	66,510	66,510
Prepaid expenses and other	555,856	285,005
Total current assets	1,193,971	5,884,577
Property and equipment, net	4,956	27,846
Goodwill	3,283,379	3,283,379
Indefinite-lived intangible assets	9,243,128	9,243,128
Other assets	705,660	724,713
Total assets	$ 14,431,094	$ 19,163,643
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 934,147	$ 786,779
Accrued expenses	664,029	1,135,653
Other current liabilities	1,612	21,234
Total current liabilities	1,599,788	1,943,666
Deferred tax liability	2,918,518	2,918,518
Total liabilities	$ 4,518,306	$ 4,862,184
Commitments and contingent liabilities (Note 12)		
Stockholders' equity:		
Preferred stock, 10,000,000 shares authorized		
Series B, $0.001 par value: 1,804,394 and 2,120,742 shares issued and outstanding as of December 31, 2018 and December 31, 2017, respectively	1,804	2,120
Series A, $0.001 par value: 970,000 shares issued and outstanding as of December 31, 2018 and December 31, 2017	970	970
Common stock, $0.001 par value; 45,454,546 shares authorized as of December 31, 2018 and December 31, 2017; 9,727,774 and 9,041,426 shares issued as of December 31, 2018 and December 31, 2017, respectively; 9,403,889 and 8,717,541 shares outstanding as of December 31, 2018 and December 31, 2017, respectively	9,726	9,040
Additional paid in capital	168,161,329	165,249,912
Accumulated deficit	(153,233,595)	(145,933,137)
Accumulated other comprehensive income	253,734	253,734
Treasury stock	(5,281,180)	(5,281,180)
Total stockholders' equity	9,912,788	14,301,459
Total liabilities and stockholders' equity	$ 14,431,094	$ 19,163,643

The accompanying notes are an integral part of these consolidated financial statements.

XENETIC BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

	FOR THE YEARS ENDED DECEMBER 31,	
	2018	**2017**
Revenue		
Licenses	$ –	$ 7,500,000
Collaboration services	–	85,000
Total revenue	–	7,585,000
Operating costs and expenses:		
Cost of research and development revenue	–	(156,119)
Research and development	(2,883,952)	(4,060,000)
General and administrative	(4,392,375)	(6,937,643)
Loss from operations	(7,276,327)	(3,568,762)
Other income (expense):		
Other expense	(24,640)	(24,552)
Interest income (expense)	509	(1,818)
Total other expense	(24,131)	(26,370)
Net loss	$ (7,300,458)	$ (3,595,132)
Basic and diluted loss per share	$ (0.80)	$ (0.41)
Weighted-average shares of common stock outstanding, basic and diluted	9,070,883	8,665,763

The accompanying notes are an integral part of these consolidated financial statements.

XENETIC BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY

	Preferred Stock		Common Stock						
	Number of Shares	Par Value ($0.001)	Number of Shares	Par Value ($0.001)	Additional Paid in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Treasury Stock	Total Stockholders' Equity
Balance as of January 1, 2017	3,275,742	$ 3,275	8,731,029	$ 8,730	$ 163,522,921	$ (142,338,005)	$ 253,734	$ (5,281,180)	$ 16,169,475
Conversion of notes	–	–	125,397	125	(125)	–	–	–	–
Conversion of Series B preferred stock to shares of common stock	(185,000)	(185)	185,000	185	–	–	–	–	–
Share-based expense	–	–	–	–	1,784,129	–	–	–	1,784,129
Common stock awards to vendors	–	–	–	–	69,303	–	–	–	69,303
Warrant expense	–	–	–	–	(126,316)	–	–	–	(126,316)
Net loss	–	–	–	–	–	(3,595,132)	–	–	(3,595,132)
Balance as of December 31, 2017	3,090,742	$ 3,090	9,041,426	$ 9,040	$ 165,249,912	$ (145,933,137)	$ 253,734	$ (5,281,180)	$ 14,301,459
Exercise of warrants	–	–	370,000	370	1,479,630	–	–	–	1,480,000
Conversion of Series B preferred stock to shares of common stock	(316,348)	(316)	316,348	316	–	–	–	–	–
Share-based expense	–	–	–	–	1,351,873	–	–	–	1,351,873
Common stock awards to vendors	–	–	–	–	69,708	–	–	–	69,708
Warrant expense	–	–	–	–	10,206	–	–	–	10,206
Net loss	–	–	–	–	–	(7,300,458)	–	–	(7,300,458)
Balance as of December 31, 2018	2,774,394	$ 2,774	9,727,774	$ 9,726	$ 168,161,329	$ (153,233,595)	$ 253,734	$ (5,281,180)	$ 9,912,788

The accompanying notes are an integral part of these consolidated financial statements.

XENETIC BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS

	FOR THE YEARS ENDED DECEMBER 31,	
	2018	**2017**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (7,300,458)	$ (3,595,132)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:		
Depreciation	15,827	23,784
Gain on sale of property and equipment	(15,437)	–
Share-based expense	1,351,873	1,784,129
Warrant-based expense for services	10,206	(126,316)
Vendor share-based payments	69,708	135,280
Changes in operating assets and liabilities:		
Accounts receivable	–	3,000,000
Prepaid expenses and other assets	(251,798)	280,633
Accounts payable, accrued expenses and other liabilities	(343,878)	(8,183)
Net cash (used in) provided by operating activities	(6,463,957)	1,494,195
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property and equipment	–	(9,264)
Proceeds from sale of property and equipment	22,500	–
Net cash provided by (used in) investing activities	22,500	(9,264)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from exercise of warrants	1,480,000	–
Net cash provided by financing activities	1,480,000	–
Net change in cash and restricted cash	(4,961,457)	1,484,931
Cash and restricted cash at beginning of period	5,599,572	4,114,641
Cash and restricted cash at end of period	$ 638,115	$ 5,599,572
SUPPLEMENTAL CASH FLOW INFORMATION:		
Cash paid for interest	$ 599	$ 1,932
SUPPLEMENTAL SCHEDULE OF NON-CASH INVESTING AND FINANCING ACTIVITIES:		
Conversion of Series B preferred stock to common stock	$ 316	$ 185
Reclassification of common shares issuable to accounts payable	$ –	$ 65,977
Issuance of common stock for promissory note converted in 2016	$ –	$ 125

The accompanying notes are an integral part of these consolidated financial statements.

1. The Company

Background

Xenetic Biosciences, Inc. ("Xenetic" or the "Company"), incorporated in the state of Nevada and based in Framingham, Massachusetts, is a biopharmaceutical company focused on the discovery, research and development of next generation biological drugs and novel oncology therapeutics. The Company's 170+ patent portfolio covers next generation biologic drugs and novel oncology drug therapeutics and provides protection for its current drug candidates and positions it well for strategic partnership and commercialization opportunities. The Company's objective is to leverage its portfolio to maximize opportunities to out-license assets from its portfolio in order to generate working capital to both build long-term stockholder value and provide the Company with the funding necessary for clinical development of its oncology drug candidates through market launch.

Xenetic incorporates its patented and proprietary technologies into a number of drug candidates under development with biotechnology and pharmaceutical industry collaborators to create what the Company believes will be the next-generation biologic drugs with improved pharmacological properties over existing therapeutics. While the Company primarily focuses on researching and developing oncology drugs, it also has significant interests in drugs being developed by its collaborators to treat other conditions.

Xenetic's most advanced investigational drug candidate is oncology therapeutic XBIO-101 (sodium cridanimod) for the treatment of progestin resistant endometrial cancer. The Company has exclusive rights to develop and commercialize XBIO-101 worldwide, except for specified countries in the Commonwealth of Independent States ("CIS"). XBIO-101 has been granted orphan drug designation by the United States ("U.S.") Food and Drug Administration ("FDA") for the potential treatment of progesterone receptor negative ("PrR-") endometrial cancer in conjunction with progesterone therapy. The Company's Phase II trial for XBIO-101 commenced patient dosing in October 2017. The Company closed patient enrollment in the trial in March 2019 as a result of slower than expected progress on the trial resulting from patient enrollment and retention challenges.

Xenetic's lead proprietary technology is PolyXen™, an enabling platform technology which can be applied to protein or peptide therapeutics. It employs the natural polymer polysialic acid ("PSA") to prolong a drug's circulating half-life and potentially improve other pharmacological properties. PolyXen has been demonstrated in human clinical trials to confer prolonged half-life on biotherapeutics such as recombinant human erythropoietin and recombinant Factor VIII ("rFVIII"). The Company believes this technology may be applied to a variety of drug candidates to enhance the properties of the therapeutic, potentially providing advantages over competing products.

On March 1, 2019, the Company entered into an agreement to acquire the novel CAR T ("Chimeric Antigen Receptor T Cell") platform technology, referred to herein as "XCART," (the "Transaction") a proximity-based screening platform capable of identifying CAR constructs that can target patient-specific tumor neoantigens, with a demonstrated proof of mechanism in B-cell Non-Hodgkin lymphomas. The XCART technology, developed by The Scripps Research Institute (the "Institute") in collaboration with the Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry ("IBCH"), is believed to have the potential to significantly enhance the safety and efficacy of cell therapy for B-cell lymphomas by generating patient- and tumor-specific CAR T cells.

The XCART technology platform was designed by its originators to utilize an established screening technique to identify peptide ligands that bind specifically to the unique B-cell receptor ("BCR") on the surface of an individual patient's malignant tumor cells. The peptide is then inserted into the antigen-binding domain of a CAR, and a subsequent transduction/transfection process is used to engineer the patient's T cells into a CAR T format which redirects the patient's T cells to attack the tumor. Essentially, the XCART screening platform is the inverse of a typical CAR T screening protocol wherein libraries of highly specific antibody domains are screened against a given target. In the case of XCART screening, the target is itself an antibody domain, and hence highly specific by its nature. The XCART technology creates the possibility of personalized treatment of lymphomas utilizing a CAR with an antigen-binding domain that should only recognize, and only be recognized by, the unique BCR of a particular patient's B-cell lymphoma. An expected result for XCART is limited off-tumor toxicities, such as B-cell aplasia. Xenetic's clinical development program will seek to confirm the early preclinical results, and to demonstrate a more attractive safety profile than existing therapies.

The closing of the Transaction is subject to customary closing conditions as well as conditions regarding (i) the Company having adequate financing to fund its future working capital obligations following the closing and (ii) the Company obtaining necessary and appropriate stockholder approvals, evidencing among other matters, approval of the Share Purchase Agreement and the transactions contemplated thereunder, including the issuance of shares of the Company's common stock. Subject to the satisfaction of the closing conditions, the Transaction is expected to close in the first half of 2019. See Note 14 "*Subsequent Events*".

Xenetic's drug candidates have resulted from its research activities or those of its collaborators and are in the development stage. As a result, the Company continues to commit a significant amount of its resources to its research and development activities and anticipates continuing to do so for the near future. To date, none of the Company's drug candidates have received regulatory marketing authorization in the U.S. by the FDA nor in any other territories by any applicable agencies. Although the Company holds a broad patent portfolio, the focus of its internal development efforts was limited in 2018 to research and development of its primary product candidate XBIO-101 due to capital constraints. The Company intends to pursue development efforts of the XCART technology once the acquisition is consummated and pursue other developments efforts around CAR T technology. The Company also plans to research potential utilities for XBIO-101 alone or in combination, in immuno-oncology approaches and will continue to look for potential partner and out-licensing opportunities for its platform technologies subject to adequate funding.

The Company, directly or indirectly, through its wholly-owned subsidiary, Xenetic UK, and the wholly-owned subsidiaries of Xenetic Biosciences (U.K.) Limited ("Xenetic UK"), Lipoxen Technologies Limited ("Lipoxen"), Xenetic Bioscience, Incorporated and SymbioTec, GmbH ("SymbioTec"), owns various U.S. federal trademark registrations and applications, and unregistered trademarks and service marks, including but not limited to Virexxa®, OncoHist™, PolyXen™, ErepoXen™, ImuXen™, and PulmoXen™, which may be used throughout this Annual Report. All other company and product names may be trademarks of the respective companies with which they are associated.

Going Concern and Management's Plan

The Company incurred a net loss of approximately $7.3 million for the year ended December 31, 2018. The Company had an accumulated deficit of approximately $153.2 million as of December 31, 2018 as compared to an accumulated deficit of approximately $145.9 million as of December 31, 2017. Working capital (deficit) was approximately $(0.4) million at December 31, 2018 and approximately $3.9 million at December 31, 2017. The Company expects to continue incurring losses for the foreseeable future and will need to raise additional capital or pursue other strategic alternatives in the very near term in order to continue pursuit of its business plan and continue as a going concern.

The Company believes that it has access to capital resources through possible public or private equity offerings, debt financings, corporate collaborations, related party funding or other means. On March 5, 2019, the Company raised $3.1 million in a registered direct common stock offering resulting in $2.7 million of net proceeds to the Company. However, it has not secured any commitment for additional financing at this time. The terms, timing and extent of any future financing will depend upon several factors, including the achievement of progress in its clinical development programs, its ability to identify and enter into licensing or other strategic arrangements, and factors related to financial, economic and market conditions, many of which are beyond its control.

While these consolidated financial statements have been prepared on a going concern basis, if the Company does not successfully raise additional working capital, there can be no assurance that the Company will be able to continue its operations and these conditions raise substantial doubt about its ability to continue as a going concern. Under such circumstances, the Company would have to further reduce the planned scale of, or possibly suspend, some or all of its preclinical development initiatives and clinical trials. In addition, the Company would have to continue to reduce its general and administrative and other operating expenses and delay or cease the purchase of clinical research services if and until the Company is able to obtain additional financing. The accompanying consolidated financial statements do not include any adjustments related to the recoverability or classification of asset carrying amounts or the amounts and classification of liabilities that may result should the Company be unable to continue as a going concern.

2. Summary of Significant Accounting Policies

Preparation of Financial Statements

These consolidated financial statements have been prepared on the assumption that the Company will be able to realize its assets and discharge its liabilities in the normal course of business. This assumption is presently uncertain and contingent upon the Company's ability to raise additional working capital. The financial statements do not include any adjustments relating to recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might be necessary should the Company be unable to continue as a going concern.

Principles of Consolidation

The consolidated financial statements of the Company include the accounts of Xenetic UK and its wholly-owned subsidiaries: Lipoxen, Xenetic Bioscience, Incorporated, and SymbioTec. All material intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The consolidated financial statements and accompanying notes are prepared in accordance with U.S. generally accepted accounting principles ("U.S. GAAP"). The preparation of the financial statements in accordance with U.S. GAAP requires management to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities, the reported amounts of revenue, costs and expenses in the financial statements and disclosures in the accompanying notes. Actual results and outcomes may differ materially from management's estimates, judgments and assumptions.

Functional Currency Change

Effective April 1, 2015, the functional currency of the Company's foreign subsidiaries changed from the British Pound Sterling to the U.S. dollar. The change in functional currency was applied on a prospective basis. Therefore, any gains and losses that were previously recorded in accumulated other comprehensive income remain unchanged.

Foreign Currency Transactions

Realized and unrealized gains and losses resulting from foreign currency transactions arising from exchange rate fluctuations on balances denominated in currencies other than the functional currencies are recognized in "Other income (expense)" in the consolidated statements of comprehensive loss. Monetary assets and liabilities that are denominated in a currency other than the functional currency are re-measured to the functional currency using the exchange rate at the balance sheet date and gains or losses are recorded in the consolidated statements of comprehensive loss.

Fair Value of Financial Instruments

The Company applies the following fair value hierarchy, which prioritizes the inputs used to measure fair value into three levels and bases the categorization within the hierarchy upon the lowest level of input that is available and significant to the fair value measurement. Level 1 inputs are quoted prices in active markets for identical assets or liabilities that the reporting entity has the ability to access at the measurement date. Level 2 utilizes quoted market prices in markets that are not active, broker or dealer quotations, or alternative pricing sources with reasonable levels of price transparency. Level 3 inputs are unobservable inputs for the asset or liability in which there is little, if any, market activity for the asset or liability at the measurement date. See Note 7, *Fair Value Measurements*, for discussion of the Company's fair value measurements.

Cash and Cash Equivalents

The Company considers all highly liquid investments with maturities of 90 days or less from the date of purchase to be cash equivalents. Investments with original maturities of greater than 90 days from the date of purchase but less than one year from the balance sheet date are classified as short-term investments, while investments with maturities of one year or beyond from the balance sheet date are classified as long-term investments. Management determines the appropriate classification of its cash equivalents and investment securities at the time of purchase and re-evaluates such determination as of each balance sheet date.

Restricted Cash

As of December 31, 2018 and 2017, restricted cash represents a certificate of deposit that matures annually and secures the Company's outstanding letter of credit of approximately $0.1 million for its former operating lease in Lexington, Massachusetts (the "Lexington Lease"). The Lexington Lease expired in January 2019 and the letter of credit is required to be maintained through May 1, 2019.

In November 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash* that changes the presentation of restricted cash and cash equivalents on the statement of cash flows. Restricted cash and restricted cash equivalents are included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 was effective for the Company in the first quarter of fiscal 2018. Adoption of this standard resulted in reclassification of restricted cash in the consolidated statements of cash flows for the year ended December 31, 2017.

Concentration of Credit Risk

Financial instruments that subject the Company to concentrations of credit risk include cash and cash equivalents. The Company maintains cash and cash equivalents with various major financial institutions. The Company performs periodic evaluations of the relative credit standing of these financial institutions and limits the amount of credit exposure with any one institution.

Property and Equipment

The Company records property and equipment at cost less accumulated depreciation. Expenditures for major renewals and improvements which extend the life or usefulness of the asset are capitalized. Items of an ordinary repair or maintenance nature are charged directly to operating expense as incurred. The Company calculates depreciation using the straight-line method over the estimated useful lives of the assets:

Asset Classification	Estimated Useful Life
Laboratory equipment	3 years
Office and computer equipment	3 years
Leasehold improvements	5 years or the remaining term of the lease, if shorter
Furniture and fixtures	5 years

The Company eliminates the cost of assets retired or otherwise disposed of, along with the corresponding accumulated depreciation, from the related accounts, and the resulting gain or loss is reflected in the results of operations.

Indefinite-Lived Intangible Assets

Acquired indefinite-lived intangible assets consist of in-process research and development ("IPR&D") related to the Company's business combination with SymbioTec, which was recorded at fair value on the acquisition date. IPR&D intangible assets are considered indefinite-lived intangible assets until completion or abandonment of the associated research and development efforts. Substantial additional research and development may be required before the Company's IPR&D reaches technological feasibility. Upon completion of the IPR&D project, the IPR&D assets will be amortized over their estimated useful lives.

The Company assesses intangible assets with indefinite lives for impairment at least annually as of October 1, or when events or changes in the business environment indicate the carrying value may be impaired. The Company also has the option to first assess qualitative factors to determine whether the existence of events orcircumstances leads the Company to determine that it is more likely than not (that is, a likelihood of more than 50%) that the acquired IPR&D is impaired. If the Company chooses to first assess the qualitative factors and it is determined that it is not more likely than not acquired IPR&D is impaired, the Company is not required to take further action to test for impairment. The Company also has the option to bypass the qualitative assessment and perform only the quantitative impairment test, which the Company may choose to perform in some periods but not in others.

No impairment was recorded during the years ended December 31, 2018 and 2017.

Goodwill

Goodwill is comprised of the purchase price of business combinations in excess of the fair value assigned at acquisition to the net tangible and identifiable intangible assets acquired. Goodwill is not amortized. The Company assesses goodwill for impairment at least annually, or when events or changes in the business environment indicate the carrying value may not be fully recoverable. The Company also has the option to first assess qualitative factors to determine whether the existence of events or circumstances leads the Company to determine that it is more likely than not (that is, a likelihood of more than 50%) that goodwill is impaired. If the Company chooses to first assess qualitative factors and it is determined that it is not more likely than not goodwill is impaired, the Company is not required to take further action to test for impairment. The Company also has the option to bypass the qualitative assessment and perform only the quantitative impairment test, which the Company may choose to do in some periods but not in others. The Company performs its annual impairment review as of October 1.

No impairment was recorded during the years ended December 31, 2018 and 2017.

Impairment of Long-Lived Assets

The Company reviews long-lived assets to be held and used, including property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying amount of the assets or asset group may not be fully recoverable. No such impairments were recorded during the years ended December 31, 2018 and 2017.

Evaluation of recoverability is based on an estimate of undiscounted future cash flows resulting from the use of the asset or asset group and its eventual disposition. Impairment, if any, is calculated as the amount by which an asset's carrying value exceeds its fair value, typically using discounted cash flows to determine fair value.

Revenue Recognition

The Company enters into supply, license and collaboration arrangements with pharmaceutical and biotechnology partners, some of which include royalty agreements based on potential net sales of approved commercial pharmaceutical products.

Effective January 1, 2018, the Company adopted Accounting Standards Codification ("ASC") Topic 606, *Revenue from Contracts with Customers* ("ASC 606"), using the modified retrospective transition method. Under this method, results for reporting periods beginning after January 1, 2018 are presented under ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with ASC 605. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. The Company did not have any revenue generating contracts with customers and, therefore, the adoption of this new revenue standard did not have a material impact on the consolidated financial statements. Under ASC 605, the Company recognized revenue when all of the following criteria were met: (i) persuasive evidence of an arrangement existed; (ii) delivery had occurred or services had been rendered; (iii) the seller's price to the buyer was fixed or determinable; and (iv) collectability was reasonably assured.

The terms of the Company's license agreements may include delivery of an IP license to a collaboration partner. The Company may be compensated under license arrangements through a combination of non-refundable upfront receipts, development and regulatory objective receipts and royalty receipts on future product sales by partners. The Company anticipates recognizing non-refundable upfront license payments and development and regulatory milestone payments received by the Company in license and collaboration arrangements that include future obligations, such as supply obligations, ratably over the Company's expected performance period under each respective arrangement. The Company makes its best estimate of the period over which the Company expects to fulfil the Company's performance obligations, which may include technology transfer assistance, research activities, clinical development activities, and manufacturing activities from development through the commercialization of the product. Given the uncertainties of these collaboration arrangements, significant judgment is required to determine the duration of the performance period.

When the Company enters into an arrangement to sublicense some of its patents, it will consider the performance obligations to determine if there is a single element or multiple elements to the arrangement as it determines the proper method and timing of revenue recognition. The Company considers the terms of the license or sublicense for such elements as price adjustments or refund clauses in addition to any performance obligations for it to provide such as services, patent defense costs, technology support, marketing or sales assistance or any other elements to the arrangement that could constitute an additional deliverable to it that could change the timing of the revenue recognition. Non-refundable upfront license and sublicense fees received, whereby continued performance or future obligations are considered inconsequential or perfunctory to the relevant licensed technology, are recognized as revenue upon delivery of the technology.

The Company expects to recognize royalty revenue in the period of sale, based on the underlying contract terms, provided that the reported sales are reliably measurable, the Company has no remaining performance obligations, and all other revenue recognition criteria are met.

The Company anticipates reimbursements for research and development services completed by the Company related to the collaboration agreements to be recognized in operations as revenue on a gross basis.

The Company's license and collaboration agreements with certain collaboration partners could also provide for future milestone receipts to the Company based solely upon the performance of the respective collaboration partner in consideration of deadline extensions or upon the achievement of specified sales volumes of approved drugs. For such receipts, the Company expects to recognize the receipts as revenue when earned under the applicable contract terms on a performance basis or ratably over the term of the agreement. These receipts may also be recognized as revenue when continued performance or future obligations by the Company are considered inconsequential or perfunctory.

Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue at a point in time, or over time, as it satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that it will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract, determine those that are performance obligations, and assess whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

As part of the accounting for these arrangements, the Company must use significant judgment to determine: a) the number of performance obligations based on the determination under step (ii) above; b) the transaction price under step (iii) above; and c) the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above. The Company uses judgment to determine whether milestones or other variable consideration should be included in the transaction price as described further below. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. In developing the stand-alone price for a performance obligation, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. The Company validates the stand-alone selling price for performance obligations by evaluating whether changes in the key assumptions used to determine the stand-alone selling prices will have a significant effect on the allocation of transaction price between multiple performance obligations. The Company recognizes a contract asset or liability for the difference between the Company's performance (i.e., the goods or services transferred to the customer) and the customer's performance (i.e., the consideration paid by, and unconditionally due from, the customer).

See also Note 3, *Significant Strategic Drug Development Collaborations – Related Parties*.

Research and Development Expenses

Research and development expenses consist of expenses incurred in performing research and development activities, including compensation and benefits, facilities expenses, overhead expenses, clinical trial and related clinical manufacturing expenses, fees paid to contract research organizations ("CROs") and contract manufacturing organizations and other outside expenses. The Company expenses research and development costs as incurred. The Company expenses upfront, non-refundable payments made for research and development services as obligations are incurred. The value ascribed to intangible assets acquired but which have not met capitalization criteria is expensed as research and development at the time of acquisition.

The Company is required to estimate accrued research and development expenses at each reporting period. This process involves reviewing open contracts and purchase orders, communicating with Company personnel to identify services that have been performed on its behalf and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of actual costs. The majority of the Company's service providers invoice it in arrears for services performed, on a pre-determined schedule or when contractual milestones are met. However, some require advanced payments. The Company makes estimates of accrued expenses as of each balance sheet date in the financial statements based on facts and circumstances known at that time. The Company periodically confirms the accuracy of the estimates with the service providers and makes adjustments, if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- program managers in connection with overall program management of clinical trials;
- CROs in connection with clinical trials; and
- investigative sites in connection with clinical trials.

The Company bases its expenses related to clinical trials on its estimates of the services received and efforts expended pursuant to quotes and contracts with multiple research institutions and CROs that conduct and manage clinical trials on the Company's behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company adjusts the accrual or prepaid accordingly. Although it does not expect its estimates to be materially different from amounts actually incurred, the Company's understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to the Company's prior estimates of accrued research and development expenses. As of December 31, 2018, the Company has recorded accrued program expense of approximately $0.2 million as a component of accrued expenses. In addition, the Company has recorded approximately $0.4 million of deposits held with our clinical trial vendors as a component of prepaid expenses and other current assets as of December 31, 2018. At December 31, 2017, the Company had recorded $33,000 as a component of deferred program expenses as a component of prepaid expenses and other current assets.

Share-based Expense

Stock options and restricted stock units

The Company grants share-based payments in the form of options and restricted stock units ("RSUs") to employees and non-employees, Joint Share Ownership Plan ("JSOP") awards to employees, as well as agreements to issue common stock in exchange for services provided by non-employees.

Share-based expense is based on the estimated fair value of the option or calculated using the Black-Scholes option pricing model. Determining the appropriate fair value model and related assumptions requires judgment, including estimating share price volatility and expected terms of the awards. The expected volatility rates are estimated based on the actual volatility of the Company and of comparable public companies over the expected term of the option. The expected terms represent the time that options are expected to be outstanding. The Company accounts for forfeitures as they occur and not at the time of grant. The Company has not paid dividends and does not anticipate paying cash dividends in the foreseeable future and, accordingly, uses an expected dividend yield of zero. The risk-free interest rate is based on the rate of U.S. Treasury securities with maturities consistent with the estimated expected term of the awards. Upon exercise, stock options are redeemed for newly issued shares of common stock. RSUs are redeemed for newly issued shares of common stock as the vesting and settlement provisions of the grant are met.

For employee options that vest based solely on service conditions, the fair value measurement date is generally on the date of grant and the related compensation expense is recognized on a straight-line basis over the requisite vesting period of the awards.

For non-employee options, the fair value measurement date is the earlier of the date the performance of services is complete or the date the performance commitment has been reached. The Company generally determines that the fair value of the stock options is more reliably measurable than the fair value of the services received. Compensation expense related to stock options granted to non-employees that vest based solely on service conditions is subject to re-measurement at each reporting period until the options vest and is recognized on a straight-line basis over the requisite vesting period of the awards.

The Company adopted FASB issued ASU 2016-09, *Compensation – Stock Compensation (Topic 718)* ("ASU 2016-09") effective January 1, 2017. ASU 2016-09 simplifies several aspects of employee share-based payment accounting, including income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. The adoption of this standard did not have a material impact on the Company's financial statements or related disclosures as:

- There have been no stock option exercises as a U.S. company and, therefore, there are no excess tax benefits related to windfalls. Moreover, the Company maintains a full valuation allowance and expects to do so for the foreseeable future;
- The Company has elected to account for forfeitures as they occur, which the Company adopted using a modified retrospective approach and there was no material cumulative effect adjustment to be recorded to opening retained earnings; and
- The Company will classify cash paid to taxing authorities arising from the withholding of shares from employees in cash flows from financing activities.

Common stock awards

The Company grants common stock awards to non-employees in exchange for services provided. The Company measures the fair value of these awards using the fair value of the services provided, as this provides the most reliable measure of the fair value of the awards granted. The fair value measurement date of these awards is generally the date the performance of services is complete. The fair value of the awards is recognized on a straight-line basis as services are rendered. The share-based payments related to common stock awards for the settlement of services provided by non-employees is recorded on the consolidated statement of comprehensive loss in the same manner and charged to the same account as if such settlements had been made in cash.

Warrants

In connection with certain financing, consulting and collaboration arrangements, the Company has issued warrants to purchase shares of its common stock. The outstanding warrants are standalone instruments that are not puttable or mandatorily redeemable by the holder and are classified as equity awards. The Company measures the fair value of the awards using the Black-Scholes option pricing model as of the measurement date. Warrants issued to collaboration partners in conjunction with the issuance of common stock are initially recorded at fair value as a reduction in additional paid-in capital of the common stock issued. All other warrants are recorded at fair value as expense on a straight-line basis over the requisite service period or at the date of issuance, if there is not a service period or if service has already been rendered. Warrants granted in connection with ongoing arrangements are more fully described in Note 9, *Stockholders' Equity.*

Income Taxes

The Company accounts for income taxes using the asset and liability method. Under this method, deferred tax assets and liabilities are determined based on temporary differences resulting from the different treatment of items for tax and financial reporting purposes. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to reverse. Additionally, the Company must assess the likelihood that deferred tax assets will be recovered as deductions from future taxable income. The Company evaluates the recoverability of its deferred tax assets on a quarterly basis.

Basic and Diluted Net Loss per Share

The Company computes basic net loss per share by dividing net loss applicable to common stockholders by the weighted-average number of shares of common stock outstanding during the period. The Company computes diluted net loss per share after giving consideration to the dilutive effect of stock options that are outstanding during the period, except where such non-participating securities would be anti-dilutive. The Company's JSOP awards, prior to exercise, are considered treasury shares by the Company and thus do not impact the Company's net loss per share calculation. As of December 31, 2018 and 2017, there were approximately 0.3 million JSOP awards issued.

For the years ended December 31, 2018 and 2017, basic and diluted net loss per share are the same for each year due to the Company's net loss position. Potentially dilutive, non-participating securities have not been included in the calculations of diluted net loss per share, as their inclusion would be anti-dilutive. As of December 31, 2018 and 2017, approximately 0.8 million and 0.6 million potentially dilutive securities, respectively, were deemed anti-dilutive.

Segment Information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, who is the Company's Chief Executive Officer, in making decisions on how to allocate resources and assess performance. The Company views its operations and manages its business in one operating segment.

Operating Leases

The Company leases administrative and laboratory facilities under operating leases. Lease agreements may include rent holidays, rent escalation clauses and tenant improvement allowances. The Company recognizes scheduled rent increases on a straight-line basis over the lease term beginning with the date the Company takes possession of the leased space.

Acquisitions

The Company has a history of engaging in acquisition transactions that require the Company to evaluate whether the transaction meets the criteria of a business combination and, in some cases, whether it meets the definition of a reverse merger. If the transaction does not meet the business combination requirements, the transaction is accounted for as an asset acquisition or recapitalization and no goodwill is recognized. If the acquisition meets the definition of a business combination, the Company allocates the purchase price, including any contingent consideration, to the assets acquired and the liabilities assumed at their estimated fair values as of the date of the acquisition with any excess of the purchase price paid over the estimated fair value of net assets acquired recorded as goodwill. The fair value of the assets acquired and liabilities assumed is typically determined by using either estimates of replacement costs or discounted cash flow valuation methods.

When determining the fair value of tangible assets acquired, the Company estimates the cost to replace the asset with a new asset, taking into consideration such factors as age, condition and the economic useful life of the asset. When determining the fair value of intangible assets acquired, the Company uses judgment to estimate the applicable discount rate, growth rates and the timing and amount of future cash flows. The fair value of assets acquired and liabilities assumed is typically determined using the assistance of an independent third-party specialist.

Business combination related costs are expensed in the period in which the costs are incurred. Asset acquisition related costs are generally capitalized as a component of cost of the assets acquired.

Recent Accounting Standards

In June 2018, the FASB issued ASU 2018-07*, Compensation – Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting.* ASU 2018-07 expands the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. An entity should apply the requirements of Topic 718 to nonemployees awards except for specific guidance on inputs to an option pricing model and the attribution of cost. ASU 2018-07 specifies that Topic 718 applies to all share-based payment transactions in which a grantor acquires goods or services to be used or consumed in a grantor's own operations by issuing share-based payment awards, and that Topic 718 does not apply to share-based payments used to effectively provide (1) financing to the issuer or (2) awards granted in conjunction with selling goods or services to customers as part of a contract accounted for under Topic 606 *Revenue from Contracts with Customers.* ASU 2018-07 is effective for the Company in the first quarter of fiscal 2019. The adoption of ASU 2018-07 is not expected to have a significant impact on the Company's consolidated financial statements.

In January 2017, the FASB issued ASU 2017-04: *Intangibles — Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment* that eliminates the requirement to calculate implied fair value of goodwill to measure a goodwill impairment charge. Instead, the new guidance will require entities to take an impairment charge based on the excess of a reporting unit's carrying amount over its fair value. The guidance is effective for the Company no later than 2020. The adoption of this guidance is not expected to have a material impact on the Company's consolidated financial statements.

In February 2016, FASB issued ASU 2016-02, *Leases (Topic 842)* ("ASU 2016-02"). ASU 2016-02 will require lessees to recognize a lease liability and a right-of-use asset for all leases, with the exception of short-term leases, at the commencement date. This guidance is effective for annual reporting periods beginning after December 15, 2018, including interim periods within those annual periods. Early application is permitted. The adoption of ASU 2016-02 is not expected to have a significant impact on the Company's consolidated financial statements.

The Company has considered other recent accounting standards and concluded that they are either not applicable to the business, or that no material effect is expected on the consolidated financial statements as a result of future adoption.

3. Significant Strategic Drug Development Collaborations – Related Parties

Takeda Pharmaceutical Co. Ltd., ("Takeda") (formerly Shire plc)

The Company is party to an exclusive research, development and license agreement with Baxalta US Inc. and Baxalta AB, wholly-owned subsidiaries of Takeda, related to the development of a novel series of polysialylated blood coagulation factors. Takeda acquired Shire plc in January 2019. This collaboration with Takeda relies on the Company's PolyXen technology to conjugate PSA with therapeutic blood-clotting factors, with the goal of improving the pharmacokinetic profile and extending the half-life of these biologic molecules. The agreement grants Takeda a worldwide, exclusive, royalty-bearing license to the Company's PSA patented and proprietary technology in combination with Takeda's proprietary molecules designed for the treatment of blood and bleeding disorders. The first program under this agreement was a next generation rFVIII protein product candidate ("SHP656").

In December 2016, Takeda reached a milestone of its Phase I/II clinical trial for the treatment of hemophilia with SHP656, triggering a $3.0 million payment to be paid to the Company pursuant to the agreement with Takeda. The Company determined the milestone to be non-substantive because all significant performance obligations to achieve the contingent payments were the responsibility of Takeda with only negligible amount by the Company of effort to fulfill its obligations, specifically assistance on a research committee. As the amount allocable to the remaining performance period was negligible, the Company recognized the full $3.0 million in milestone revenue in connection with this collaboration during the year ended December 31, 2016. The payment was made in January 2017.

In May 2017 Takeda provided an update on the Phase I/II clinical study indicating that SHP656's efficacy and pharmacokinetic data commensurate with the profile of an extended half-life rFVIII product. Additionally, to the Company's knowledge, there were no drug-related adverse events, serious adverse events, or rFVIII inhibitors reported. However, the pre-defined once-weekly dosing criterion was not met and the rFVIII program was terminated by Takeda.

On October 27, 2017, the Company entered into a Right of Sublicense Agreement (the "Sublicense Agreement") with Baxalta Incorporated, Baxalta US Inc., and Baxalta GmbH (collectively, with their affiliates, "Baxalta") wholly-owned subsidiaries of Takeda. Pursuant to the Sublicense Agreement, the Company granted to Baxalta the right to grant a nonexclusive sublicense to certain patents related to the Company's PolyXen technology that were previously exclusively licensed to Baxalta in connection with products related to the treatment of blood and bleeding disorders ("Covered Products.") Pursuant to the Sublicense Agreement, Baxalta (i) paid the Company a one-time payment of seven million five hundred thousand dollars ($7,500,000) in November 2017 and (ii) agreed to pay to the Company single digit royalty payments based upon net sales of the Covered Products throughout the term. The Company recognized the full $7.5 million as license revenue in connection with this Sublicense Agreement during the year ended December 31, 2017. There have been no royalty payments under the Sublicense Agreement to date.

SynBio LLC

In August 2011, SynBio LLC ("SynBio") and the Company entered into a stock subscription and collaborative development of pharmaceutical products agreement (the "Co-Development Agreement"). The Company granted an exclusive license to SynBio to develop pharmaceutical products using certain molecule(s) based on SynBio's technology and the Company's proprietary technology (PolyXen, OncoHist and ImuXen) that prolongs the active life and/or improves the pharmacokinetics of certain therapeutic proteins and peptides (as well as conventional drugs). In return, SynBio granted an exclusive license to the Company to use the preclinical and clinical data generated by SynBio in certain agreed products and engage in the development of commercial candidates.

SynBio and the Company are each responsible for funding their own research activities. There are no milestone or other research-related payments due under the agreement other than fees for the supply of each company's respective research supplies based on their technology, which, when provided, are due to mutual convenience and not representative of an ongoing or recurring obligation to supply research supplies. Serum Institute of India Limited ("Serum Institute") has agreed to directly provide the research supplies to SynBio, where the Company is not liable for any failure to supply the research supplies as a result of any act or fault of Serum Institute. Upon successful commercialization of any resultant products, the Company is entitled to receive royalties on sales in certain territories and pay royalties to SynBio for sales outside those certain territories.

Through December 31, 2018, the Company and SynBio continued to engage in research and development activities with no resultant commercial products. The Company did not recognize revenue in connection with the Co-Development Agreement during the years ended December 31, 2018 and 2017.

In 2017, SynBio became a wholly-owned subsidiary of Pharmsynthez and all ownership percentages previously held by SynBio are combined with Pharmsynthez. See Note 9, *Stockholders' Equity.*

Serum Institute of India Limited

In August 2011, the Company entered into a collaborative research and development agreement with Serum Institute providing Serum Institute an exclusive license to use the Company's PolyXen technology to research and develop one potential commercial product, Polysialylated Erythropoietin ("PSA-EPO"). Serum Institute is responsible for conducting all preclinical and clinical trials required to achieve regulatory approvals within the certain predetermined territories at Serum Institute's own expense. Royalty payments are payable by Serum Institute to the Company for net sales to certain customers in the Serum Institute sales territory. Royalty payments are payable by the Company to Serum Institute for net sales received by the Company over the term of the license. There are no milestone or other research-related payments due under the collaborative arrangement.

Through December 31, 2018, the Company and Serum Institute continued to engage in research and development activities with no resultant commercial products. No royalty revenue or expense was recognized by the Company related to the Serum Institute arrangement during the years ended December 31, 2018 and 2017.

Serum Institute is a related party of the Company with a share ownership of approximately 6.7% and 7.2% of the total issued common stock of the Company as of December 31, 2018 and 2017, respectively. In addition to its' common stock ownership, Serum Institute holds outstanding warrants to purchase the Company's common stock. See Note 9, *Stockholders' Equity.*

PJSC Pharmsynthez

In November 2009, the Company entered into a collaborative research and development license agreement with Pharmsynthez (the "Pharmsynthez Arrangement") pursuant to which the Company granted an exclusive license to Pharmsynthez to develop, commercialize and market six drug candidates based on the Company's PolyXen and ImuXen technology in certain territories. In exchange, Pharmsynthez granted an exclusive license to the Company to use any preclinical and clinical data developed by Pharmsynthez, within the scope of the Pharmsynthez Arrangement, and to engage in further research, development and commercialization of drug candidates outside of certain territories at the Company's own expense.

Pharmsynthez is an affiliate and controlling stockholder of the Company with a share ownership of approximately 57.1% and 61.5% of the total issued common stock of the Company as of December 31, 2018 and 2017, respectively. In addition to its common stock ownership, Pharmsynthez holds outstanding warrants to purchase the Company's common stock, approximately 1.5 million shares of the Company's issued and outstanding Series B Preferred Stock, and all of the Company's issued and outstanding Series A Preferred Stock through its wholly-owned subsidiary, SynBio. See Note 9, *Stockholders' Equity*.

4. Property and Equipment, net

Property and equipment, net consists of the following:

	December 31, 2018	December 31, 2017
Laboratory equipment	$ –	$ 264,583
Office and computer equipment	42,289	46,634
Leasehold improvements	26,841	26,841
Furniture and fixtures	20,263	20,263
Property and equipment – at cost	89,393	358,321
Less accumulated depreciation	(84,437)	(330,475)
Property and equipment – net	$ 4,956	$ 27,846

Depreciation expense was approximately $16,000 and $24,000 for the years ended December 31, 2018 and 2017, respectively. During the year ended December 31, 2018, the Company sold certain laboratory equipment for $22,500 resulting in an approximate $15,000 gain.

5. Goodwill, Indefinite-Lived Intangible Assets and Other Long-Term Assets

Goodwill

A reconciliation of the change in the carrying value of goodwill is as follows:

Balance as of January 1, 2017	$ 3,283,379
No changes	–
Balance as of December 31, 2017	$ 3,283,379
No changes	–
Balance as of December 31, 2018	$ 3,283,379

As of October 1, 2018 and 2017, the dates of the Company's annual impairment review, the fair value of the Company's goodwill balance exceeded its carrying value.

Indefinite-Lived Intangible Assets

The Company's indefinite-lived intangible asset, OncoHist, is IPR&D relating to the Company's business combination with SymbioTec in 2012. The carrying value of OncoHist was approximately $9.2 million as of December 31, 2018 and 2017. No impairment was recorded during the years ended December 31, 2018 and 2017. OncoHist is not yet commercialized and, therefore, has not yet begun to be amortized as of December 31, 2018.

Other Long-Term Assets

On September 15, 2016, the Company issued approximately 0.2 million shares of common stock to Serum Institute in exchange for approximately $0.8 million of research and development and clinical PSA supply as well as settlement of approximately $0.2 million of prior purchases of PSA supply. Approximately $0.1 million of the clinical supply was utilized and expensed during the year ended December 31, 2017. No clinical supply was utilized during the year ended December 31, 2018. The Company has classified the remaining $0.7 million as long-term as it does not anticipate utilizing the majority of the PSA supply within the next 12 months.

6. Accrued Expenses

Accrued expenses consist of the following:

	December 31, 2018	December 31, 2017
Accrued payroll and benefits	$ 53,541	$ 723,488
Accrued professional fees	394,075	389,086
Accrued research costs	205,067	11,477
Other	11,346	11,602
	$ 664,029	$ 1,135,653

On November 2, 2017, the Company entered into a Settlement Agreement with M. Scott Maguire, former Chief Executive Officer of the Company (the "Settlement Agreement"), which terminated the Employment Agreement dated November 3, 2009, between Xenetic UK and Mr. Maguire. Pursuant to the terms of the Settlement Agreement, Mr. Maguire continued to receive his current base salary and benefits for a period of 12 months, received a lump sum termination payment of £30,000 and was reimbursed for certain tax liabilities as described in the Settlement Agreement. As of December 31, 2017, the Company expensed approximately $0.4 million of accrued payroll and benefits related to future payments required to be made to Mr. Maguire in accordance with the Settlement Agreement. All obligations to Mr. Maguire were paid as of December 31, 2018. Additionally, Mr. Maguire's unvested stock options vested on October 31, 2018, upon the terms and conditions specified in the Settlement Agreement, and Mr. Maguire will have until June 10, 2020 to exercise the vested options.

7. Fair Value Measurements

ASC Topic 820, *Fair Value Measurement,* defines fair value as the price that would be received to sell an asset or be paid to transfer a liability in an orderly transaction between market participants at the measurement date. The Company applies the following fair value hierarchy, which prioritizes the inputs used to measure fair value into three levels and bases the categorization within the hierarchy upon the lowest level of input that is available and significant to the fair value measurement. Level 1 inputs are quoted prices in active markets for identical assets or liabilities that the reporting entity has the ability to access at the measurement date. Level 2 utilizes quoted market prices in markets that are not active, broker or dealer quotations, or alternative pricing sources with reasonable levels of price transparency. Level 3 inputs are unobservable inputs for the asset or liability in which there is little, if any, market activity for the asset or liability at the measurement date.

The carrying amount of certain of the Company's financial instruments approximate fair value due to their short maturities.

There were no financial instruments classified as Level 3 in the fair value hierarchy during the years ended December 31, 2018 and 2017.

8. Income Taxes

Deferred tax assets and liabilities are determined based on temporary differences resulting from the different treatment of items for tax and financial reporting purposes. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to reverse. Additionally, the Company must assess the likelihood that deferred tax assets will be recovered as deductions from future taxable income. The Company has provided a full valuation allowance on the Company's deferred tax assets because the Company believes it is more likely than not that its deferred tax assets will not be realized. The Company evaluates the recoverability of its deferred tax assets on a quarterly basis. Currently, there is no provision for income taxes as the Company has incurred losses to date.

The components of loss before income taxes are as follows:

	Year ended December 31,	
	2018	2017
Domestic (U.S.)	$ (3,824,673)	$ (5,889,926)
Foreign (U.K.)	(3,379,268)	2,398,830
Foreign (Germany)	(96,517)	(104,036)
Loss before income taxes	$ (7,300,458)	$ (3,595,132)

The reconciliation of income tax benefit at the U.S. corporation tax rate, being the rate applicable to the country of domicile of the Company to net income tax benefit is as follows:

	Year ended December 31,	
	2018	2017
Federal	$ (1,533,096)	$ (1,222,345)
State	(238,952)	(303,315)
Increase in tax losses not recognized	1,695,482	(359,833)
Permanent differences, net	40,015	162,543
Foreign rate differential	124,294	(383,601)
Share-based payments, net	20,441	(22,087)
Changes per enacted tax reform	–	2,320,059
Enhanced research and development tax credits	(108,184)	(191,421)
Net provision (benefit) for income taxes	$ –	$ –

Deferred tax assets and liabilities reflect the net tax effect of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets are as follows:

	Year ended December 31,	
	2018	2017
Deferred tax assets:		
U.K. net operating loss carryforwards	$ 8,039,343	$ 7,641,719
U.K. capital loss carryforwards	1,298,303	1,378,643
U.S. federal net operating loss carryforwards	3,184,691	2,606,017
IPR&D	6,108,078	6,776,473
Share-based payments	1,859,357	1,527,615
Enhanced research and development tax credits	1,109,026	1,060,200
Germany net operating loss carryforwards	524,093	516,401
U.S. state net operating loss carryforwards	1,298,745	1,057,856
Accrued expenses	59,979	198,067
Depreciation	3,283	1,948
Other	–	–
Total deferred tax assets before valuation allowance	23,484,898	22,764,939
Valuation allowance for deferred tax assets	(23,484,898)	(22,764,939)
Deferred tax liabilities:		
Indefinite-lived intangible asset	(2,918,518)	(2,918,518)
Debt discount	–	–
Total deferred tax liabilities	(2,918,518)	(2,918,518)
Net deferred liability	$ (2,918,518)	$ (2,918,518)

For the years ended December 31, 2018 and 2017, the Company had U.K. net operating loss carryforwards of approximately $47.3 million and $45.0 million, respectively, U.S. federal net operating loss carryforwards of approximately $16.5 million and $13.5 million, respectively, U.S. state net operating loss carryforwards of approximately $16.2 million and $13.3 million, respectively, and Germany net operating loss carryforwards of approximately $1.7 million and $1.6 million, respectively. The U.K. and Germany net operating loss carryforwards can be carried forward indefinitely. $3.0 million of the U.S. federal net operating loss carryforwards can be carried forward indefinitely and the remaining U.S. federal and state net operating loss carryforwards begin to expire in 2032.

The Company's ability to use its operating loss carryforwards and tax credits generated in the U.S. to offset future taxable income is subject to restrictions under Section 382 of the U.S. Internal Revenue Code (the "Code"). These restrictions may limit the future use of the operating loss carryforwards and tax credits if certain ownership changes described in the Code occur. Future changes in stock ownership may occur that would create further limitations on the Company's use of the operating loss carryforwards and tax credits. In such a situation, the Company may be required to pay income taxes, even though significant operating loss carryforwards and tax credits exist.

The Company's ability to use its operating loss carryforwards and tax credits generated in the U.K. are subject to restrictions under U.K. tax legislation. These regulations may limit the future use of operating loss carryforwards if there is a change in ownership and a change in the nature or conduct of the business carried on by the Company, and in certain circumstances where there is a change in the nature or conduct of the business only. In such cases the carryforwards would cease to be available to set against future income.

On December 22, 2017, the U.S. enacted new tax reform ("Tax Cuts and Jobs Act"). The Tax Cuts and Jobs Act contains provisions with separate effective dates but is generally effective for taxable years beginning after December 31, 2017. Beginning with the year ending December 31, 2018, the corporate statutory rates on U.S. earnings were reduced from 34% to 21%. The impact of the rate reduction for the year ending December 31, 2017, was approximately $2.3 million relating to the revaluation of the net deferred tax assets. Other than the reduction in statutory rate, the Company does not anticipate the regulations will have a material impact on income taxes in future years. The Tax Cuts and Jobs Act also contains a provision requiring companies to repatriate all aggregate post 1986 earnings and profits of foreign corporations. The Company estimated that the repatriation will be zero under a provisional basis under SAB118. The final calculations under tax reform resulted in no change to the amounts estimated.

The Company's ability to use its operating loss carryforwards and tax credits generated in Germany are also subject to restrictions under German tax legislation. These regulations may limit the future use of operating loss carryforwards if there is a change in ownership. In such cases the carryforwards would cease to be available to set against future income.

As of December 31, 2018 and 2017, the Company did not record any uncertain tax positions.

The Company files income tax returns in the U.S. federal tax jurisdiction and Massachusetts state tax jurisdiction, and certain foreign tax jurisdictions. The Company is subject to examination by the U.S. federal, state, foreign, and local income tax authorities for calendar tax years ending 2013 through 2018 due to available net operating loss carryforwards and research and development tax credits arising in those years. The Company has not been notified of any examinations by the Internal Revenue Service or any other tax authorities as of December 31, 2018. The Company has not recorded any interest or penalties for unrecognized tax benefits since its inception.

Potential 382 Limitation

The Company's net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service. The Company's ability to utilize its net operating loss ("NOL") and research and development credit ("R&D") carryforwards may be substantially limited due to ownership changes that may have occurred or that could occur in the future, as required by Section 382 of the Code, as well as similar state provisions. These ownership changes may limit the amount of NOL and R&D credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change, as defined in Section 382 of the Code, results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50% of the outstanding stock of a company by certain stockholders or public groups.

The Company has not completed a study to assess whether one or more ownership changes have occurred since it became a loss corporation as defined in Section 382 of the Code, but the Company believes that it is likely that an ownership change has occurred. If the Company has experienced an ownership change, utilization of the NOL and R&D credit carryforwards would be subject to an annual limitation, which is determined by first multiplying the value of the Company's common stock at the time of the ownership change by the applicable long-term, tax-exempt rate, and then could be subject to additional adjustments, as required. Any such limitation may result in the expiration of a portion of the NOL or R&D credit carryforwards before utilization. Until a study is completed, and any limitation known, no amounts are being considered as an uncertain tax position or disclosed as an unrecognized tax benefit. Any carryforwards that expire prior to utilization as a result of such limitations will be removed from deferred tax assets with a corresponding adjustment to the valuation allowance. Due to the existence of the valuation allowance, it is not expected that any potential limitation will have a material impact on the Company's operating results.

From time to time the Company may be assessed interest or penalties by major tax jurisdictions, namely the Commonwealth of Massachusetts. As of December 31, 2018, the Company had no material unrecognized tax benefits and no adjustments to liabilities or operations were required. No interest and penalties have been recognized by the Company to date.

The Company's net operating loss carryforwards are subject to review and possible adjustment by the Internal Revenue Service and are subject to certain limitations in the event of cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%.

9. Stockholders' Equity

Common Stock

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to dividends when and if declared by the Board of Directors. In the event of any voluntary or involuntary liquidation, dissolution or winding-up of the Company, the holders of common stock are entitled to share ratably in the assets of the Company available for distribution.

In March 2017, the Company issued approximately 0.1 million shares of the Company's common stock to Pharmsynthez in connection with the conversion by Pharmsynthez of its $500,000, 10% convertible promissory note as a result of the Company's underwritten public offering in November 2016 and Pharmsynthez subsequently exercising its rights to the shares. The shares issued to Pharmsynthez represent both owed principal and accrued interest.

The holders of Series B Preferred Stock converted approximately 0.3 million shares and 0.2 million shares into the same number of shares of common stock during the years ended December 31, 2018 and December 31, 2017, respectively.

During the year ended December 31, 2018, 0.4 million warrants were exercised resulting in the issuance of 0.4 million shares of common stock. There were no exercises of warrants during the year ended December 31, 2017.

Series A Preferred Stock

The Company has designated 1,000,000 shares as Series A preferred stock with each share having a par value of $0.001 and stated value of $4.80 (the "Series A Preferred Stock"). The following is a summary of the material terms of the Series A Preferred Stock.

Liquidation. Upon any dissolution, liquidation or winding up, whether voluntary or involuntary, holders of Series A Preferred Stock will be entitled to receive distributions out of the Company's assets, of an amount equal to $4.80 per share of Series A Preferred Stock (as adjusted for stock splits, combinations, reorganizations and the like) plus any accrued and unpaid dividends thereon before any distributions shall be made on the common stock or any series of preferred stock ranked junior to the Series A Preferred Stock.

Dividends. Holders of the Series A Preferred Stock are entitled to receive a non-cumulative, annual cash dividend of $0.24 per share of Series A Preferred Stock, when and if declared by the Company's Board, out of the Company's assets legally available therefor. No dividends or other distribution will be made on the common stock or any series of preferred stock ranked junior to the Series A Preferred Stock unless the dividend on the Series A Preferred Stock has been paid current and a reserve has been made for the next calendar year. The Company's ability to pay dividends on Series A Preferred Stock is subject to restrictions in the Company's Series B Preferred Stock, which ranks senior to the Series A Preferred Stock in right of payment.

Conversion. Each share of Series A Preferred Stock is convertible, at any time and from time to time at the option of the holder thereof, with a minimum of 61 days' advance notice to the Company, into one share of common stock.

Stock Dividends and Stock Splits. If Xenetic pays a stock dividend or otherwise makes a distribution payable in shares of common stock on shares of common stock or any other common stock equivalents, subdivides or combines outstanding common stock, or reclassifies common stock, the conversion rate will be adjusted to match the conversion rate immediately before such event.

Fundamental Transaction. If Xenetic effects a reorganization, undergoes a change in control event, or enters into any plan or arrangement contemplating the Company's dissolution, then upon any subsequent conversion of Series A Preferred Stock, the holder thereof shall have the right to receive, for each share of common stock that would have been issuable upon such conversion immediately prior to the occurrence of such transaction, the number of shares of the successor's or acquiring corporation's common stock or of the Company's common stock, if Xenetic is the surviving corporation, and any additional consideration receivable as a result of such transaction by a holder of the number of shares of common stock into which Series A Preferred Stock is convertible immediately prior to such transaction. A change in control event means a sale of all or substantially all of the Company's assets or an acquisition of the Company by another entity by means of any transaction or series of related transactions (including, without limitation, a reorganization, consolidated or merger) that results in the transfer of fifty percent (50%) or more of the outstanding voting power of the Company.

Voting Rights. Except as otherwise provided in the Series A Preferred Stock amended and restated certificate of designation or required by law, the Series A Preferred Stock has no voting rights. The holders of Series A Preferred Stock have voting rights as to proposals that specifically affect their shares by law, in which they will vote separately and the vote necessary to approve such proposals will be as set by law.

Fractional Shares. No fractional shares of common stock will be issued upon conversion of Series A Preferred Stock. Rather, the Company will round up to the next whole share.

Redemption. Upon 30 days prior written notice, the Company may require the holder of any Series A Preferred Stock to convert any or all of such holder's Series A Preferred Stock to common stock at a rate of one share of Series A Preferred Stock to one share of common stock.

As of December 31, 2018 and 2017, there were approximately 1.0 million shares of Series A Preferred Stock issued and outstanding which are convertible into the same number of shares of common stock.

Series B Preferred Stock

The Company has designated 2,500,000 shares as Series B preferred stock with each share having a stated value of $4.00 per share (the "Series B Preferred Stock").

The following is a summary of the material terms of the Company's Series B Preferred Stock.

Liquidation. Upon any dissolution, liquidation or winding up, whether voluntary or involuntary, holders of Series B Preferred Stock will be entitled to receive distributions out of the Company's assets, of an amount equal to $4.00 per share of Series B Preferred Stock (as adjusted for stock splits, combinations, reorganizations and the like) plus any accrued and unpaid dividends thereon and any other fees or liquidated damages then due and owing thereon under the amended and restated certificate of designation before any distributions shall be made on the common stock or any series of preferred stock ranked junior to the Series B Preferred Stock, which includes Series A Preferred Stock. A fundamental transaction or change of control under the amended and restated certificate of designation shall constitute a liquidation for purposes of this right. Xenetic will give each holder of Series B Preferred Stock written notice of any liquidation at least 30 days before any meeting of stockholders to approve such liquidation or at least 45 days before the date of such liquidation if no meeting is to be held.

Dividends. Subject to any preferential rights of any outstanding series of preferred stock created by the Company's Board from time to time, the holders of shares of the Company's Series B Preferred Stock will be entitled to such cash dividends, non-cumulative, as may be declared from time to time by the Company's Board on shares of the Company's common stock (on an as-converted basis) from funds available therefore. The Company shall not directly or indirectly pay or declare any dividend or make any distribution upon, nor shall any distribution be made in respect of, any junior securities, including Series A Preferred Stock, as long as any dividends due on the Series B Preferred Stock remain unpaid, nor shall any monies be set aside for or applied to the purchase or redemption of any junior securities or shares pari passu with the Series B Preferred Stock.

Conversion. Each share of Series B Preferred Stock is convertible, at any time and from time to time at the option of the holder thereof, into one share of common stock, subject to the adjustments described below.

Stock Dividends and Stock Splits. If Xenetic pays a stock dividend or otherwise makes a distribution payable in shares of common stock on shares of common stock or any other common stock equivalents, subdivides or combines outstanding common stock, or reclassifies common stock, the conversion rate will be adjusted to match the conversion rate immediately before such event.

Fundamental Transaction. If Xenetic effects a reorganization, undergoes a change in control event, or enters into any plan or arrangement contemplating the Company's dissolution, then upon any subsequent conversion of Series B Preferred Stock, the holder thereof shall have the right to receive, for each share of common stock that would have been issuable upon such conversion immediately prior to the occurrence of such transaction, the number of shares of the successor's or acquiring corporation's common stock or of the Company's common stock, if Xenetic is the surviving corporation, and any additional consideration receivable as a result of such transaction by a holder of the number of shares of common stock into which Series B Preferred Stock is convertible immediately prior to such transaction. A change in control event means a sale of all or substantially all of the Company's assets or an acquisition of the Company by another entity by means of any transaction or series of related transactions (including, without limitation, a reorganization, consolidated or merger) that results in the transfer of thirty-three percent (33%) or more of the outstanding voting power of the Company, with the exception of acquisition of additional voting capital stock by Pharmsynthez or its affiliates.

Subsequent Equity Sales. The Series B Preferred Stock has full ratchet price based anti-dilution protection, subject to customary carve outs, in the event of a down-round financing at a price per share below the stated value of the Series B Preferred Stock. There is no bifurcation of the embedded conversion option being clearly and closely related to the host instrument. Subsequent to year end, the Company entered into a down-round financing event resulting in an adjustment to the conversion ratio. See Note 14 Subsequent Events for further details.

Voting Rights. Except as otherwise provided in the Series B Preferred Stock second amended and restated certificate of designation or required by law, the Series B Preferred Stock has no voting rights. However, as long as any Series B Preferred Stock remains outstanding, the amended and restated certificate of designation provides that the Company shall not, without the affirmative vote of all then-outstanding Series B Preferred Stock, (a) alter or change adversely the powers, preferences or rights given to the Series B Preferred Stock or alter or amend the certificate of designation, (b) authorize or create any class of stock ranking as to dividends, redemption or distribution of assets upon a liquidation senior to, or otherwise pari passu with, the Series B Preferred Stock, (c) amend its certificate of incorporation or other charter documents in any manner that adversely affects any rights of the holders of Series B Preferred Stock, (d) increase the number of authorized shares of Series B Preferred Stock, or (e) enter into any agreement with respect to any of the foregoing. The holders of Series B Preferred Stock have voting rights as to proposals that specifically affect their shares by law, in which they will vote separately and the vote necessary to approve such proposals will be as set by law.

Fractional Shares. No fractional shares of common stock will be issued upon conversion of Series B Preferred Stock. Rather, the Company will, at its election, round up to the next whole share or pay a cash adjustment.

As of December 31, 2018 and 2017, there were approximately 1.8 million and approximately 2.1 million shares of Series B Preferred Stock issued and outstanding which are convertible into the same number of shares of common stock. The holders of Series B Preferred Stock converted approximately 0.3 million shares and 0.2 million shares into the same number of shares of common stock during the years ended December 31, 2018 and December 31, 2017, respectively.

Warrants Related to Collaboration and Consulting Agreements

In connection with certain of the Company's collaboration agreements and consulting arrangements, the Company has issued warrants to purchase shares of common stock as payment for services. As of December 31, 2018 and December 31, 2017, warrants to purchase 539,202 and 646,249 shares of common stock were outstanding, respectively. The fair value of these warrants was determined at each issuance date using the Black-Scholes option pricing model. The warrants are subject to re-measurement at each reporting period until the measurement date is reached. Expense is recognized on a straight-line basis over the expected service period or at the date of issuance, if there is not a service period. For the years ended December 31, 2018 and 2017, the Company recognized expense of approximately $10,000 and a gain of approximately $0.1 million, respectively, related to collaboration and consulting warrants.

On December 31, 2014, SynBio was granted a warrant to purchase 204,394 new shares of common stock at an exercise price of $25.41 per share ("SynBio 2014 Warrant"). The SynBio 2014 Warrant is exercisable in four equal tranches, each with separate non-market, performance-based vesting criteria. The Company uses its judgment to assess the probability and timing of SynBio achieving these vesting criteria and estimated that it is not probable that the vesting criteria for any tranche will be achieved. None of the vesting criteria were met and, therefore, these warrants were forfeited. As a result, the Company did not recognize expense related to this warrant during the years ended December 31, 2018 and 2017.

In connection with the SynBio 2014 Warrant grant, warrants to purchase 9,697 aggregate new shares of common stock were issued to SynBio and Pharmsynthez non-director designees ("SynBio Partner Warrants") on December 31, 2014 under the same terms and conditions of the SynBio 2014 Warrant. The vesting criteria for any tranche were not met and, as a result, the Company did not recognize expense related to the SynBio Partner Warrants during the years ended December 31, 2018 and 2017.

On December 31, 2014, the Company granted Serum Institute a warrant to purchase 96,970 new shares of common stock at an exercise price of $7.92 per share, as adjusted ("Serum Institute 2014 Warrant"). The Serum Institute 2014 Warrant is exercisable in two equal tranches, each with separate non-market, performance-based vesting criteria. The Company uses its judgment to assess the probability and timing of Serum Institute achieving these vesting criteria and estimated that it is probable that the vesting criteria will be achieved for each tranche. These judgments are reassessed at each reporting period until the measurement date is reached.

In connection with the Serum Institute 2014 Warrant grant, warrants to purchase 4,852 aggregate new shares of common stock were issued to Serum Institute non-director designees ("Serum Institute Partner Warrants") on December 31, 2014 under the same terms and conditions of the Serum Institute 2014 Warrant.

In 2016, the Company issued 212,122 warrants to purchase shares of common stock to Serum Institute with an exercise price of $7.92. The new warrants were fully vested and expensed at the time of grant.

The Company recognized warrant expense (income) of approximately $10,000 and $(0.1) million during the years ended December 31, 2018 and 2017, respectively, related to the Serum Institute 2014 Warrant and Serum Institute Partner Warrants. No collaboration or consulting service warrants were exercised or granted during the years ended December 31, 2018 and 2017. These warrants have an average weighted exercise price of $10.41 and expiration dates ranging from December 2019 through May 2021.

Warrants Related to Financing Arrangements

As of December 31, 2018 and 2017 there were outstanding warrants related to financing agreements to purchase an aggregate of 3,152,225 shares and 3,522,225 shares of Common Stock at an average weighted exercise price of $4.33 and $4.30, respectively. During the year ended December 31, 2018, warrants to purchase 370,000 shares of common stock were exercised resulting in approximately $1.5 million of net proceeds to the Company. There were no warrants exercised during the year ended December 31, 2017. No warrants related to financing agreements were granted during the years ended December 31, 2018 and 2017. These warrants have expiration dates ranging from July 1, 2020 through November 2021.

10. Share-Based Expense

Total share-based expense related to stock options, RSUs, common stock awards, and non-financing warrants was approximately $1.4 million and $1.8 million for the years ended December 31, 2018 and 2017, respectively. (See Note 9, *Stockholders' Equity* for a discussion of the non-financing warrants.)

Share-based expense is classified in the consolidated statements of comprehensive loss as follows:

	Year Ended December 31,	
	2018	**2017**
Research and development expenses	$ 203,030	$ 101,401
General and administrative expenses	1,228,757	1,691,692
	$ 1,431,787	$ 1,793,093

Stock Option Modifications

During the year ended December 31, 2017 the Company modified certain former employee stock option awards to extend the expiry dates through March 31, 2018. As a result of the modification, the Company recognized approximately $4,000 in incremental compensation expense during the year ended December 31, 2017, which was charged to general and administrative expense in the consolidated statements of comprehensive loss.

In November 2017, the Company accelerated the vesting and extended the exercise period post termination for certain employees, including the Company's former Chief Executive Officer. These modifications resulted in a change in incremental value and catch up of share-based amortization of approximately $0.2 million, which was charged to general and administrative expense.

Stock Options

The Company grants stock option awards and RSUs to employees and non-employees with varying vesting terms under the Xenetic Biosciences, Inc. Amended and Restated Equity Incentive Plan ("Stock Plan"). The Company measures the fair value of stock option awards using the Black-Scholes option pricing model, which uses the assumptions noted in the tables below, including the risk-free interest rate, expected term, share price volatility, dividend yield and forfeiture rate. The risk-free interest rate is based upon the U.S. Treasury yield curve in effect at the time of grant, with a term that approximates the expected life of the option. For employee stock options issued in 2018 and 2017 that qualify as "plain vanilla" stock options, the expected term is based on the simplified method. The Company has a limited history of stock option exercises, which does not provide a reasonable basis for the Company to estimate the expected term of employee stock options. For all other employee stock options, the Company estimates the expected life using judgment based on the anticipated research and development milestones of the Company's clinical projects and behavior of the Company's employees. The expected life of non-employee options is the contractual life of the option. The Company determines the expected volatility based on a blended volatility rate of its own historical volatility with that of comparable publicly traded companies with drug candidates in similar therapeutic areas and stages of nonclinical and clinical development to the Company's drug candidates. The Company has applied an expected dividend yield of 0% as the Company has not historically declared a dividend and does not anticipate declaring a dividend during the expected life of the options. Effective January 1, 2017, the Company adopted ASU 2016-09 and elected to account for forfeitures as they occur.

Employee Stock Options

During the years ended December 31, 2018 and 2017, 100,000 and 700,000 total stock options to purchase shares of common stock were granted by the Company, respectively. The weighted average grant date fair value per option share was $2.63 and $2.70, respectively. No stock options were exercised during the years ended December 31, 2018 and 2017.

During the years ended December 31, 2018 and 2017, 524,540 and 340,930 total stock options vested, with total fair values of approximately $1.6 million and $1.9 million, respectively. As of December 31, 2018, there was approximately $1.0 million of unrecognized share-based payments related to employee stock options that are expected to vest. The Company expects to recognize this expense over a weighted-average period of approximately 1.3 years.

Key assumptions used in the Black-Scholes option pricing model for options granted to employees during the years ending December 31, 2018 and 2017 are as follows:

	Year Ended December 31,	
	2018	**2017**
Weighted-average expected dividend yield (%)	–	–
Weighted-average expected volatility (%)	118.03	111.37
Weighted-average risk-free interest rate (%)	2.90	1.79
Weighted-average expected life of option (years)	5.90	5.36
Weighted-average exercise price ($)	3.05	3.34

The following is a summary of employee stock option activity for the years ended December 31, 2018 and 2017:

	Number of shares	**Weighted-average exercise price**	**Weighted-average remaining life (years)**	**Aggregate intrinsic value**
Outstanding as of January 1, 2017	1,193,712	$ 4.43	8.94	$ 526,073
Granted	700,000	3.34		
Expired	(113,343)	4.61		
Outstanding as of December 31, 2017	1,780,369	3.99	8.53	$ 5,273
Granted	100,000	3.05		
Expired	(110,929)	5.73		
Outstanding as of December 31, 2018	1,769,440	$ 3.83	8.17	$ –
Vested or expected to vest as of December 31, 2018	1,744,440	$ 3.85	8.16	$ –
Exercisable as of December 31, 2017	731,895	$ 4.84	7.44	$ 5,273
Exercisable as of December 31, 2018	1,152,173	$ 4.11	7.92	$ –

A summary of the status of the Company's non-vested employee stock option shares as of December 31, 2018, and the changes during the year ended December 31, 2018, is as follows:

	Number of shares	**Weighted-average grant date fair value**
Balance as of January 1, 2018	1,048,474	$ 2.86
Granted	100,000	$ 2.63
Forfeited	(6,667)	$ 2.91
Vested	(524,540)	$ 3.05
Balance as of December 31, 2018	617,267	$ 2.65

Restricted Stock Units

For the year ended December 31, 2017, the Company granted 50,000 RSUs. There were no RSU grants for the year ended December 31, 2018. The RSUs vest annually over a 3-year period and had a grant date fair value of $2.11. During the year ended December 31, 2018, 16,667 RSUs were vested and none expired.

Non-Employee Stock Options

Share-based expense related to stock options granted to non-employees is recognized as the services are rendered on a straight-line basis. The Company determined that the fair value of the stock options is more reliably measurable than the fair value of the services received. Compensation expense related to stock options granted to non-employees is subject to re-measurement at each reporting period until the options vest.

During the year ended December 31, 2018, 10,000 total stock options to purchase shares of common stock were granted by the Company to non-employees. No options were granted to non-employees and none were exercised during the year ended December 31, 2017.

During the year ended December 31, 2018 and 2017, 10,000 and 10,101 total stock options vested, with total fair values of approximately $36,000 and $0.1 million, respectively. As of December 31, 2018, all non-employees stock options had vested. For the years ended December 31, 2018 and 2017, the Company recognized approximately $36,000 and $0.1 million, respectively, of compensation expense related to non-employee options.

The following is a summary of non-employee stock option activity for the years ended December 31, 2018 and 2017:

	Number of shares	Weighted-average exercise price	Weighted-average remaining life (years)	Aggregate intrinsic value
Outstanding as of January 1, 2017	57,442	$ 7.57	7.23	$ –
Expired	(723)	10.34		
Outstanding as of December 31, 2017	56,719	7.53	6.31	$ –
Granted	10,000	1.93		
Expired	(3,148)	18.25		
Outstanding as of December 31, 2018	63,571	$ 6.12	5.40	$ –
Vested or expected to vest as of December 31, 2018	63,571	$ 6.12	5.40	$ –
Exercisable as of December 31, 2017	56,719	$ 7.53	6.31	$ –
Exercisable as of December 31, 2018	63,571	$ 6.12	5.40	$ –

A summary of the status of the Company's non-vested non-employee stock option shares as of December 31, 2018, and the changes during the year ended December 31, 2018 is as follows:

	Number of shares	Weighted-average grant date fair value
Balance as of January 1, 2018	–	$ –
Granted	10,000	$ 1.73
Vested	(10,000)	$ 1.73
Balance as of December 31, 2018	–	$ –

Common Stock Awards

The Company granted common stock awards to non-employees in exchange for services provided. The Company measures the fair value of these awards using the fair value of the services provided or the fair value of the awards granted, whichever is more reliably measurable. The fair value measurement date of these awards is generally the date the performance of services is complete. The fair value of the awards is recognized as services are rendered on a straight-line basis. A summary of the Company's common stock awards granted and issued during the years ended December 31, 2018 and 2017 are as follows:

	Number of shares
Balance as of January 1, 2017	29,790
Granted	41,800
Issued	(8,773)
Balance as of December 31, 2017	62,817
Granted	26,000
Issued	–
Balance as of December 31, 2018	88,817

The Company granted 26,000 and 41,800 shares of common stock during the years ended December 31, 2018 and 2017, respectively, in exchange for professional services. As all services were rendered in each respective period, expense related to common stock awards of approximately $0.1 million and $0.1 million was recognized during the years ended December 31, 2018 and 2017, respectively. The balance of the common stock awards has not been issued as of December 31, 2018.

Joint Share Ownership Plan

As of December 31, 2018 and 2017, there were approximately 0.3 million JSOP awards issued and outstanding to two former senior executives, respectively. Under the JSOP, shares in the Company are jointly purchased at fair market value by the participating executives and the trustees of the JSOP trust, with such shares held in the JSOP trust. For U.S. GAAP purposes the awards were valued as employee options and recorded as a reduction in equity as treasury shares until they are exercised by the employee. The JSOP awards are fully vested and have no expiration date. There were no compensation charges during the years ended December 31, 2018 and 2017, respectively.

11. Employee Benefit Plans

The Company has a defined contribution 401(k) savings plan (the "401(k) Plan"). The 401(k) Plan covers substantially all U.S. employees, and allows participants to defer a portion of their annual compensation on a pre-tax basis or make post-tax contributions. Company contributions to the 401(k) Plan may be made at the discretion of the Board of Directors. There were no company contributions to the 401(k) Plan during the year ended December 31, 2018. The Company made contributions of approximately $51,000 to the 401(k) Plan for the year ended December 31, 2017.

In the U.K., the Company has adopted a defined contribution plan (the "UK Plan") which qualifies under the rules established by HM Revenue & Customs. The UK Plan generally allows all U.K. employees to contribute a minimum of 3% of salary with no maximum limit. The Company contributes to the plan between 8% and 12% of the employee's salary, depending upon seniority of the employee. The Company, at its discretion, may also contribute to an employee's personal pension plan. There were no contributions for the years ended December 31, 2018 and December 31, 2017, respectively.

12. Commitments and Contingent Liabilities

Leases

In August 2013, the Company entered into the Lexington Lease to lease office and laboratory space under an operating lease with a commencement date of January 1, 2014 and a termination date of January 31, 2019. With the execution of this lease, the Company is required to maintain a $66,000 letter of credit as a security deposit. The letter of credit is secured by a certificate of deposit, which is classified as restricted cash within the consolidated balance sheets. The letter of credit is required to be maintained through May 1, 2019.

In December 2016, the Company entered into a one-year lease of office space in Miami, Florida, under an operating lease with a commencement date of December 1, 2016, and a termination date of November 30, 2017. The Company renewed this lease in November 2017 for an additional two years with a revised termination date of November 30, 2019.

The Company's contractual commitments under all non-cancelable operating leases as of December 31, 2018, are as follows:

As of December 31,	Total Operating Leases
2019	$ 24,583
2020	–
Total minimum lease payments	$ 24,583

Rent expense is calculated on a straight-line basis over the term of the leases. Rent expense under the Company's operating leases was approximately $0.1 million for the years ended December 31, 2018 and 2017, respectively.

Subsequent to year end, the Lexington Lease expired and the Company relocated its corporate headquarters to Framingham, Massachusetts. The new lease commenced in January 2019 and has a termination date of September 30, 2020. The total contractual commitment of approximately $50,000 associated with the new lease is not reflected in the table above.

Litigation

On August 27, 2015, Eurogentec S.A. ("EGT"), a former supplier of the Company, brought an action against the Company in the Commercial Court of the Canton of Zurich Switzerland (the "Court") alleging nonpayment of invoices for services provided by EGT. The Company requested dismissal of the claim based on the argument that EGT knew, or should have known, that the services provided by EGT should not have been performed or had not been properly performed. On July 12, 2017, the Court rendered a decision in favor of EGT ordering the Company to pay approximately $0.7 million to EGT, representing all amounts that EGT alleged were owed by the Company, plus interest and court and legal fees. The Company had previously recorded $0.6 million related to this contract when the relevant services were provided and accrued an additional $0.1 million related to interest and fees in 2017 as a result of the ruling. In December 2017, the Company entered into a Settlement Agreement and paid approximately $0.6 million to settle all claims associated with this matter.

13. Related Party Transactions

The Company has entered into various research, development, license and supply agreements with Takeda, SynBio, Serum Institute and Pharmsynthez, each a related party whose relationship, ownership, and nature of transactions is disclosed within other sections of these footnotes.

During the year ended December 31, 2017, the Company received research and consulting services from a director of Pharmsynthez, a controlling stockholder of the Company. The total amount of services received was approximately $0.1 million for the year ended December 31, 2017. This consulting agreement was terminated in July 2017.

Please refer to Note 3, *Significant Strategic Drug Development Collaborations – Related Parties* and Note 9, *Stockholder's Equity*, for details on arrangements with collaboration partners that are also related parties.

14. Subsequent Events

The Company performed a review of events subsequent to the balance sheet date through the date the financial statements were issued and determined that there were no such events requiring recognition or disclosure in the financial statements except as described below.

XCART Transaction

On March 1, 2019 (the "Signing Date"), the Company entered into the Share Purchase Agreement with Hesperix, the owners of Hesperix (each, a "Seller" and collectively, the "Sellers"), and Alexey Andreevich Vinogradov, as the representative of each Seller (the "Sellers' Representative"), pursuant to which the Company will purchase from Sellers all of the issued and outstanding shares of capital stock (the "Shares") of Hesperix.

Under the terms of the Share Purchase Agreement, the Company will issue to Sellers an aggregate of Four Million Eight Hundred Seventy-Five Thousand (4,875,000) shares of the Company's common stock (the "Transaction Shares"), regardless of the trading price per share of the Company's common stock at the time of the closing. In addition, the Share Purchase Agreement contains customary representations and warranties relating to each Seller and about the condition of the Company and Hesperix. The Company expects to issue the Transaction Shares pursuant to a registration statement on Form S-4.

The closing of the Transaction is subject to customary closing conditions as well as conditions regarding (i) the Company having adequate financing to fund its future working capital obligations following the closing and (ii) the Company obtaining necessary and appropriate stockholder approvals, evidencing among other matters, approval of the Share Purchase Agreement and the transactions contemplated thereunder, including the issuance of the Transaction Shares. Subject to the satisfaction of the closing conditions, the Transaction is expected to close in the first half of 2019. The Company is currently evaluating the accounting impacts associated with the Transaction.

On the Signing Date and in connection with the Transaction, Hesperix entered into an assignment agreement (the "Hesperix Assignment Agreement") with the IBCH, Pharmsynthez, and certain other parties thereto (collectively, the "Assignors"), pursuant to which, the Assignors have agreed, among other things, to sell, assign, transfer, and convey unto Hesperix all of their individual right, title, and interest throughout the world in and to patents related to "Articles And Methods Directed To Personalized Therapy Of Cancer," and the related know-how. Hesperix has agreed to pay each of IBCH and Pharmsynthez a royalty rate in the low single digit range based on the net sales of products in each country in which, in absence of the Hesperix Assignment Agreement, the manufacture, use, offer for sale, sale, or importation of such product would infringe a valid claim of a patent.

Also on the Signing Date, the Company entered into an assignment agreement (the "OPKO Assignment Agreement") with OPKO Pharmaceuticals, LLC ("OPKO"), pursuant to which the Company will acquire and accept, all of OPKO's right, title and interest in and to that certain Intellectual Property License Agreement (the "IP License Agreement"), entered into between the Institute and OPKO regarding certain patents related to "Articles And Methods Directed To Personalized Therapy Of Cancer" and which the Institute agreed to grant an exclusive royalty-bearing license, to the patent rights owned by the Institute to OPKO and OPKO has agreed to pay the Institute a royalty rate in the low single digit range based on the net sales of products in each country in which, in absence of the IP License Agreement, the manufacture, use, offer for sale, sale, or importation of such product would infringe a valid claim of a patent or pending application.

Under the terms of the OPKO Assignment Agreement and the IP License Agreement, the Company will issue One Million Nine Hundred Sixty-Eight Thousand Seven Hundred Fifty (1,968,750) shares of the Company's common stock to OPKO and Six Hundred Fifty-Six Thousand Two Hundred Fifty (656,250) shares of the Company's common stock to the Institute regardless of the trading price per share of the Company's common stock at the time of the closing. In addition, the OPKO Assignment Agreement contains customary representations and warranties relating to OPKO and the IP License Agreement.

Financing

On March 5, 2019, the Company entered into a Securities Purchase Agreement (the "Purchase Agreement") with certain purchasers who are parties to the Purchase Agreement (the "Purchasers"), pursuant to which the Company offered to the Purchasers, in a registered direct offering, an aggregate of (i) 1,040,000 shares (the "Shares") of common stock, par value $0.001 per share ("Common Stock") and (ii) pre-funded warrants to purchase 509,000 shares of Common Stock (the "Pre-Funded Warrants"). The Pre-Funded Warrants will be exercisable beginning on March 7, 2019 at an exercise price of $0.001 per share. The Shares were sold at a price of $2.00 per share and the Pre-Funded Warrants were sold at a price of $1.999 per Pre-Funded Warrant, which represents the per share purchase price for the Shares less the $0.001 per share exercise price for each such Pre-Funded Warrant. Aggregate gross proceeds to the Company were approximately $3.1 million, before deducting fees to the placement agent and other estimated offering expenses payable by the Company. The Shares and Pre-Funded Warrants were offered by the Company pursuant to an effective shelf registration statement on Form S-3, which the Company originally filed with the Securities and Exchange Commission on September 27, 2018, and was declared effective on October 12, 2018 (File No. 333-227572).

In a concurrent private placement, the Company also sold to the Purchasers a warrant to purchase one share of the Company's Common Stock for each Share and Pre-Funded Warrant purchased in the offering, representing warrants to purchase up to 1,549,000 shares of the Company's Common Stock (the "Purchase Warrants"). The Purchase Warrants will be exercisable beginning on September 8, 2019 (the "Initial Exercise Date") at an exercise price of $2.25 per share and expire on the seven year anniversary of the Initial Exercise Date.

ITEM 9 – CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

ITEM 9A – CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), as of the end of the period covered by this Annual Report on Form 10-K.

Based on this evaluation our management, including our Chief Executive Officer and Chief Financial Officer, concluded that, as of December 31, 2018, our disclosure controls and procedures are designed at a reasonable assurance level and are effective to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate, to allow timely decisions regarding required disclosure.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) of the Exchange Act. Management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, conducted an assessment of the design and effectiveness of our internal control over financial reporting as of the end of the period covered by this Annual Report on Form 10-K. In making its assessment of internal control over financial reporting, management used the criteria set forth by the Committee of Sponsoring Organizations ("COSO") of the Treadway Commission in *Internal Control — Integrated Framework (2013 Framework)*. Based on this assessment, our management concluded that, as of the end of the period covered by this Annual Report on Form 10-K, our internal control over financial reporting was effective based on the criteria set forth by COSO of the Treadway Commission in *Internal Control — Integrated Framework.*

This annual report does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting. Management's report was not subject to attestation by our registered public accounting firm pursuant to an exemption for non-accelerated filers set forth in Section 989G of the Dodd-Frank Wall Street Reform and Consumer Protection Act.

Changes in Internal Control Over Financial Reporting

There have been no changes in our internal control over financial reporting that occurred during the period covered by this Annual Report on Form 10-K that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. The Company's internal control over financial reporting includes those policies and procedures that:

(1) Pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the Company's assets;
(2) Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that the Company's receipts and expenditures are being made only in accordance with authorizations of the Company's management and directors; and
(3) Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the Company's assets that could have a material effect on the financial statements.

Management, including the Company's principal executive and principal financial officers, or persons performing similar functions, does not expect that the Company's internal controls will prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of internal controls can provide absolute assurance that all control issues and instances of fraud, if any, have been detected. Also, any evaluation of the effectiveness of controls in future periods are subject to the risk that those internal controls may become inadequate because of changes in business conditions, or that the degree of compliance with the policies or procedures may deteriorate.

ITEM 9B – OTHER INFORMATION

None.

PART III

ITEM 10 – DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this Item will be set forth in the Company's definitive proxy statement or information statement to be filed with the SEC in connection with the Company's 2019 Annual Meeting of Stockholders within 120 days of the end of the Company's fiscal year ended December 31, 2018 and is incorporated herein by reference, or will be included in an amendment to this Annual Report on Form 10-K.

ITEM 11 – EXECUTIVE COMPENSATION

The information required by this Item will be set forth in the Company's definitive proxy statement or information statement to be filed with the SEC in connection with the Company's 2019 Annual Meeting of Stockholders within 120 days of the end of the Company's fiscal year ended December 31, 2018 and is incorporated herein by reference, or will be included in an amendment to this Annual Report on Form 10-K.

ITEM 12 – SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this Item will be set forth in the Company's definitive proxy statement or information statement to be filed with the SEC in connection with the Company's 2019 Annual Meeting of Stockholders within 120 days of the end of the Company's fiscal year ended December 31, 2018 and is incorporated herein by reference, or will be included in an amendment to this Annual Report on Form 10-K.

ITEM 13 – CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this Item will be set forth in the Company's definitive proxy statement or information statement to be filed with the SEC in connection with the Company's 2019 Annual Meeting of Stockholders within 120 days of the end of the Company's fiscal year ended December 31, 2018 and is incorporated herein by reference, or will be included in an amendment to this Annual Report on Form 10-K.

ITEM 14 – PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this Item will be set forth in the Company's definitive proxy statement or information statement to be filed with the SEC in connection with the Company's 2019 Annual Meeting of Stockholders within 120 days of the end of the Company's fiscal year ended December 31, 2018 and is incorporated herein by reference, or will be included in an amendment to this Annual Report on Form 10-K.

PART IV

ITEM 15 – EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) The following is filed as part of this Annual Report on Form 10-K:

- *Consolidated Financial Statements:* The consolidated financial statements and report of independent registered public accounting firm required by this item are included in Part II, Item 8;
- *Financial Statement Schedules:* All schedules are omitted because they are not applicable or not required, or because the required information is shown either in the consolidated financial statements or in the notes thereto.

(b) **Exhibits:** The exhibits which are filed or furnished with this Annual Report on Form 10-K or which are incorporated herein by reference are set forth in the Exhibit Index beginning on page 67 which is incorporated herein by reference.

ITEM 16 – FORM 10-K SUMMARY

Not applicable.

EXHIBIT INDEX

Exhibit No.	Exhibit Index	Form	Filing Date	Exhibit Number	Filed Herewith
2.1	Order of the High Court of Justice, Chancery Division, entered January 23, 2014	8-K	01/29/2014	2.1	
3.1	Articles of Incorporation	S-1	11/21/2011	3.1	
3.2	Certificate of Amendment to Articles of Incorporation	8-K	02/12/2013	3.1	
3.3	Certificate of Amendment to Articles of Incorporation	8-K	02/27/2013	3.1	
3.4	Certificate of Amendment to Articles of Incorporation	10-Q	01/10/2014	3.1	
3.5	Certificate of Change Pursuant to NRS 78.209	10-Q	01/10/2014	3.2	
3.6	Certificate of Amendment to Articles of Incorporation	8-K	09/30/2015	3.1	
3.7	Amended and Restated Bylaws	8-K	02/27/2017	3.1	
3.8	Form of Amended and Restated Certificate of Designation of Preferences, Rights and Limitations of Series A Preferred Stock	S-1/A	10/27/2016	3.8	
3.9	Second Amended and Restated Certificate of Designation of Preferences, Rights and Limitations of Series B Preferred Stock	S-1/A	10/31/2016	3.9	
4.1	Form of Common Stock Certificate of the Registrant	S-1/A	07/14/2016	4.1	
4.2	Xenetic Biosciences, Inc. Shareholder Voting Agreement dated October 26, 2016 between Xenetic Biosciences Inc. and SynBio, LLC	S-1/A	10/27/2016	4.2	
4.3	SynBio LLC Warrant to Purchase Common Stock of Xenetic Bioscience, Inc.	10-K	04/15/2015	10.2	
4.4	Serum Institute of India Limited Warrant to Purchase Common Stock of Xenetic Bioscience, Inc.	10-K	04/15/2015	10.03	
4.5	Firdaus Jal Dastoor Warrant to Purchase Common Stock of Xenetic Bioscience, Inc.	10-K	04/15/2015	10.04	
4.6	Form of Common Stock Purchase Warrant	8-K	11/16/2015	10.3	
4.7	Form of Management Common Stock Purchase Warrant	8-K	11/16/2015	10.4	
4.8	Form of Amended and Restated Common Stock Purchase Warrant	8-K	11/16/2015	10.6	
4.9	Form of Common Stock Purchase Warrant	8-K	07/08/2016	10.3	
4.10	Form of Common Stock Purchase Warrant	S-1/A	10/31/2016	10.53	
4.11	Form of Ten Percent (10%) Senior Secured Convertible Promissory Note	8-K	11/16/2015	10.2	
4.12	Form of Ten Percent (10%) Junior Secured Convertible Promissory Note – Due Deferral End Date	8-K	07/08/2016	10.2	
4.13	Form of Amended and Restated Ten Percent (10%) Senior Secured Convertible Promissory Note	8-K	11/16/2015	10.5	
4.14	Registration Rights Agreement, dated July 1, 2015, between Xenetic Bioscience, Inc. and OJSC Pharmsynthez	8-K	07/08/2015	10.3	
4.15	Form of First Amendment to Registration Rights Agreement	8-K	11/16/2015	10.8	
10.1	Possible Offer for Xenetic Biosciences plc by General Sales & Leasing, Inc., dated October 21, 2013	8-K	10/21/2013	9.1	
10.2	Recommended Acquisition of Xenetic Biosciences plc by General Sales & Leasing, Inc. including Scheme of Arrangement	8-K/A	11/25/2013	9.1	
10.3	Announcement of Recommended Offer by General Sales and Leasing, Inc. for shares of Xenetic Biosciences plc, dated November 12, 2013	8-K	11/25/2013	9.2	
10.4	Agreement of Conveyance, Transfer and Assignment of Subsidiaries and Assumption of Obligations dated November 12, 2013 between General Sales Inc., Leasing, Inc., Oxbridge Technology Partners, SA, Shift It Media Company and General Aircraft, Inc.	10-K	11/27/2013	9.3	
10.5†	Form of Rules of the Lipoxen plc Unapproved Share Option Plan dated July 18, 2000 (as amended by a resolution of the board of directors of Lipoxen plc passed on March 14, 2006)	10-K	04/15/2014	10.5	
10.6†	Form of Xenetic Biosciences plc 2007 Share Option Scheme and US Addendum (as established in 2007 and by resolution of shareholders in 2010 and awarded by board resolution in 2012)	10-K	04/15/2014	10.6	

Exhibit No.	Exhibit Index	Form	Filing Date	Exhibit Number	Filed Herewith
10.7†	Form of Amended and Restated Xenetic Biosciences, Inc. Equity Incentive Plan, effective November 15, 2017	DEFR14A	11/03/2017	Appendix A	
10.8	Master Clinical Research Services Agreement between Novotech Pty Limited and Xenetic Biosciences plc dated Feb. 6, 2013	10-K	04/15/2014	10.17	
10.9†#	Employment Agreement, dated November 3, 2009, between Lipoxen plc and M. Scott Maguire	10-K/A	02/18/2015	10.01	
10.10	Form of Lease for Ledgemont Research Center, Lexington, Massachusetts dated August 1, 2013 between One Ledgemont LLC and Xenetic Bioscience, Incorporated.	10-K/A	02/18/2015	10.03	
10.11	Stock Purchase Agreement, dated January 29, 2014, between Xenetic Biosciences, Inc. and Baxter Healthcare SA	10-K/A	02/18/2015	10.08	
10.12	Stock Purchase Agreement Amendment No. 1, dated February 14, 2014, between Xenetic Biosciences, Inc. and Baxter Healthcare SA	10-K/A	02/18/2015	10.09	
10.13#	Exclusive Research, Development and License Agreement, dated August 15, 2005, between Lipoxen Technologies Limited, Baxter Healthcare SA and Baxter Healthcare Corporation	10-K/A	02/18/2015	10.10	
10.14#	Letter Agreement, dated December 11, 2006, between Lipoxen Technologies Limited, Baxter Healthcare SA, Baxter Healthcare Corporation and Serum Institute of India Limited	10-K/A	02/18/2015	10.11	
10.15#	Amendment to the Exclusive Research, Development and License Agreement, dated December 13, 2006, between Lipoxen Technologies Limited, Baxter Healthcare SA and Baxter Healthcare Corporation	10-K/A	02/18/2015	10.12	
10.16#	Second Amendment to the Exclusive Research, Development and License Agreement, dated May 28, 2009, between Lipoxen Technologies Limited, Baxter Healthcare SA and Baxter Healthcare Corporation	10-K/A	02/18/2015	10.13	
10.17#	Amendment Number Four to the Exclusive Research, Development and License Agreement, dated August 10, 2010, between Lipoxen Technologies Ltd., Baxter Healthcare SA and Baxter Healthcare Corporation	10-K/A	02/18/2015	10.14	
10.18#	Amendment Number Five to the Exclusive Research, Development and License Agreement, dated September 15, 2010, between Lipoxen Technologies Ltd., Baxter Healthcare SA and Baxter Healthcare Corporation	10-K/A	02/18/2015	10.15	
10.19#	Form of Sixth Amendment to the Exclusive Research, Development and License Agreement, dated January 29, 2014, between Lipoxen Technologies Limited, Baxter Healthcare SA and Baxter Healthcare Corporation	10-K/A	02/18/2015	10.16	
10.20#	Agreement on Co-Development and the Terms of Exclusive License dated August 4, 2011 between Lipoxen plc, Lipoxen Technologies LTD and SynBio LLC	10-K/A	02/18/2015	10.18	
10.21#	Subscription Agreement in respect of ordinary shares in the capital of Lipoxen plc dated August 4, 2011 between SynBio LLC and Lipoxen plc	10-K/A	02/18/2015	10.19	
10.22#	Collaboration, License and Development Agreement, dated November 11, 2009, between Pharmsynthez ZAO and Lipoxen Technologies Ltd.	10-K/A	02/18/2015	10.20	
10.23#	Exclusive Patent and Know How License and Manufacturing Agreement, dated August 4, 2011, between Lipoxen plc, Lipoxen Technologies Ltd and Serum Institute of India Limited	10-K/A	02/18/2015	10.21	
10.24†	Employment Agreement, dated April 30, 2012, between Xenetic Bioscience, Inc. and Dr. Henry Hoppe IV.	10-K/A	02/18/2015	10.23	
10.25	Intellectual Property Assignment between Dmitry Genkin, FDS Pharma, Lipoxen Technologies Limited and Xenetic Biosciences Inc.	10-K	04/15/2015	10.1	
10.26	Securities Purchase Agreement, dated May 2015, between Xenetic Bioscience, Inc. and OJSC Pharmsynthez	8-K	07/08/2015	10.1	

Exhibit No.	Exhibit Index	Form	Filing Date	Exhibit Number	Filed Herewith
10.27	Security Agreement dated July 1, 2015, between Xenetic Bioscience, Inc. and OJSC Pharmsynthez	8-K	07/08/2015	10.4	
10.28	Subsidiary Guarantee dated July 1, 2015, between Xenetic Bioscience, Inc. and OJSC Pharmsynthez	8-K	07/08/2015	10.5	
10.29	Form of Assignment and Assumption Agreement	8-K	07/08/2015	10.7	
10.30#	Settlement Agreement, dated August 27, 2015, between Xenetic Biosciences (UK) Limited, Xenetic Biosciences, Inc., Lipoxen Technologies Limited and Colin Hill	8-K	09/02/2015	10.1	
10.31	Form of Asset Purchase Agreement, dated as of November 13, 2015, by and among Xenetic Biosciences, Inc., Lipoxen Technologies, LTD, a U.K. corporation, AS Kevelt, an Estonian company and OJSC Pharmsynthez	8-K	11/16/2015	10.1	
10.32	Form of First Amendment to Securities Purchase Agreement	8-K	11/16/2015	10.7	
10.33	Form of First Amendment to Security Agreement	8-K	11/16/2015	10.9	
10.34	Form of First Amendment to Subsidiary Guarantee	8-K	11/16/2015	10.10	
10.35	Form of Transition, Services and Resupply Agreement by and among Xenetic Bioscience, Inc., AS Kevelt and OJSC Pharmsynthez	8-K	11/16/2015	10.11	
10.36†	Letter Agreement re. Appointment of Non – Employee, Independent Director of Xenetic Biosciences, Inc. for Roger D. Kornberg dated February 2016	8-K	02/29/2016	10.1	
10.37†	Deferred Salary Security Agreement, dated July 1, 2016 between Xenetic Bioscience, Inc. and M. Scott Maguire	8-K	07/08/2016	10.1	
10.38†	Letter Agreement re. Appointment of Non – Employee, Independent Director of Xenetic Biosciences, Inc. for Jeffrey F. Eisenberg dated July 8, 2016	8-K	07/12/2016	10.1	
10.39†	Letter Agreement re. Appointment of Non – Employee, Independent Director of Xenetic Biosciences, Inc. for Dr. Edward J. Benz dated November 18, 2016	8-K	11/22/2016	10.1	
10.40†	Employment Agreement, dated December 1, 2016, between Xenetic Biosciences, Inc. and Jeffrey Eisenberg	8-K	12/6/2016	10.1	
10.41†	Employment Agreement, dated January 1, 2017 between Xenetic Biosciences, Inc. and Curtis Lockshin	8-K	01/04/2017	10.1	
10.42†	Employment Agreement, dated March 23, 2017 between Xenetic Biosciences, Inc. and James F. Parslow	8-K	04/04/2017	10.1	
10.43†	Stock Option Grant Notice, dated April 3, 2017, between Xenetic Biosciences, Inc. and James F. Parslow	8-K	04/04/2017	10.2	
10.44†	Form of Indemnity Agreement by and between Xenetic Biosciences, Inc. and each of its directors and executive officers	10-Q	08/14/2017	10.1	
10.45†	Amended and Restated Employment Agreement, dated October 26, 2017, between Xenetic Biosciences, Inc. and Jeffrey Eisenberg	10-K	03/30/2018	10.45	
10.46#	Right to Sublicense Agreement, dated October 27, 2017, by and among Xenetic Biosciences, Inc., Baxalta Incorporated, Baxalta US Inc., and Baxalta GmbH	10-K	03/30/2018	10.46	
10.47†	Settlement Agreement, dated November 3, 2017, by and among M. Scott Maguire, Xenetic Biosciences (UK) Limited and Lipoxen Technologies, Limited	10-K	03/30/2018	10.47	
10.48†	Letter Agreement re. Appointment of Non – Employee, Independent Director of Xenetic Biosciences, Inc. for Adam Logal dated October 11, 2017	10-K	03/30/2018	10.48	
10.49†	Letter Agreement re. Appointment of Non – Employee, Independent Director of Xenetic Biosciences, Inc. for James E. Callaway dated October 11, 2017	10-K	03/30/2018	10.49	

Exhibit No.	Exhibit Index	Form	Filing Date	Exhibit Number	Filed Herewith
21.1	List of Subsidiaries				X
23.1	Consent of Marcum LLP				X
24.1	Power of Attorney (included on signature page)				X
31.1	Certification of Principal Executive Officer, as required by Rule 13a-14(a) or Rule 15d-14(a)				X
31.2	Certification of Principal Financial Officer, as required by Rule 13a-14(a) or Rule 15d-14(a)				X
32.1*	Certification of Principal Executive Officer and Principal Financial Officer, as required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 36 of Title 18 of the United States Code (18 U.S.C. §1350)				X
101.INS	XBRL Instance Document.				X
101.SCH	XBRL Taxonomy Extension Schema Document.				X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.				X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.				X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.				X
101.PRE	XRBL Taxonomy Extension Presentation Linkbase Document.				X

† Indicates a management contract or any compensatory plan, contract or arrangement.

Application has been made with the Securities and Exchange Commission to seek confidential treatment of certain confidential material contained in this document. Omitted material for which confidential treatment has been requested has been filed separately with the Securities and Exchange Commission.

* This certification is deemed not filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

XENETIC BIOSCIENCES, INC.

Date: March 29, 2019 By: /s/ JEFFREY F. EISENBERG
Jeffrey F. Eisenberg
Chief Executive Officer

POWER OF ATTORNEY AND SIGNATURES

We, the undersigned officers and directors of Xenetic Biosciences, Inc., hereby severally constitute and appoint Jeffrey F. Eisenberg, our true and lawful attorney, with full power to him, to sign for us in our names in the capacities indicated below, all amendments to this report, and generally to do all things in our names and on our behalf in such capacities to enable Xenetic Biosciences, Inc. to comply with the provisions of the Securities Exchange Act of 1934, as amended, and all requirements of the Securities and Exchange Commission.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities indicated below on the 29th day of March, 2019.

Signature	**Title(s)**
/s/ JEFFREY F. EISENBERG Jeffrey F. Eisenberg	Chief Executive Officer and Director (*Principal Executive Officer)*
/s/ JAMES PARSLOW James Parslow	Chief Financial Officer *(Principal Financial Officer and Principal Accounting Officer*)
/s/ JAMES CALLAWAY James Callaway	Director
/s/ FIRDAUS JAL DASTOOR, FCS Firdaus Jal Dastoor, FCS	Director
/s/ DMITRY GENKIN Dmitry Genkin	Director
/s/ ROMAN KNYAZEV Roman Knyazev	Director
/s/ ROGER KORNBERG Roger Kornberg	Director
/s/ ADAM LOGAL Adam Logal	Director

Exhibit 21.1

SUBSIDIARIES OF REGISTRANT

Subsidiary	**Country / State of Incorporation**
Xenetic Biosciences (UK), Ltd.	United Kingdom registered company
Lipoxen Technologies, Ltd.	United Kingdom registered company
Xenetic Bioscience, Inc.	Delaware
SymbioTec, GmbH	German Registered Company

Exhibit 23.1

INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM'S CONSENT

We consent to the incorporation by reference in the Registration Statement of Xenetic Biosciences, Inc. on Form S-8 File Nos. 333-222272 and 333-218024 and on Form S-3 (File No. 333-227572) of our report dated March 29, 2019, which includes an explanatory paragraph as to the Company's ability to continue as a going concern, with respect to our audits of the consolidated financial statements of Xenetic Biosciences, Inc. as of December 31, 2018 and 2017 and for each of the two years in the period ended December 31, 2018, which report is included in this Annual Report on Form 10-K of Xenetic Biosciences, Inc. for the year ended December 31, 2018.

/s/ Marcum LLP

Marcum LLP
Boston, Massachusetts
March 29, 2019

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO EXCHANGE ACT RULES 13a-14(a) AND 15d-14(a),
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Jeffrey F Eisenberg, certify that:

1. I have reviewed this annual report on Form 10-K of Xenetic Biosciences, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 29, 2019

By: /s/ Jeffrey F Eisenberg
Jeffrey F. Eisenberg
Principal Executive Officer

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO EXCHANGE ACT RULES 13a-14(a) AND 15d-14(a),
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, James Parslow, certify that:

1. I have reviewed this annual report on Form 10-K of Xenetic Biosciences, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 29, 2019

By: /s/ James Parslow
James Parslow
Principal Financial Officer

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Xenetic Biosciences, Inc. (the "Company") for the fiscal year ended December 31, 2018, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), we, the undersigned officers of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 29, 2019

/s/ Jeffrey F. Eisenberg
Jeffrey F. Eisenberg
Chief Executive Officer
(Principal Executive Officer)

/s/James Parslow
James Parslow
Chief Financial Officer
(Principal Financial Officer)