XBiotech Inc.
Form 10-K
March 14, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 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

Commission file number 001-37437

XBIOTECH INC.

(Exact name of Registrant as specified in its charter)

British Columbia, Canada	N/A
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)

5217 Winnebago Ln, Austin, TX 78744

(Address of principal executive offices, including zip code)

Telephone Number (512) 386-2900

(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, par value $0.0001 per share	NASDAQ Global Market

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 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 such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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:

Large accelerated filer Accelerated filer Non-accelerated filer 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 Rule 12b-2 of the Act). Yes No

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of December 31, 2018, was approximately $130,631,560, based upon the closing sales price for the registrant's common stock, as reported on the NASDAQ Global Market. The calculation of the aggregate market value of voting and non-voting common equity excludes 10,184,898 shares of common stock the registrant held by executive officers, directors and shareholders that the registrant concluded were affiliates of the registrant on that date. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of management or policies of the registrant or that such person is controlled by or under common control with the registrant.

As of March 13, 2019, 36,047,606 shares of the registrant's Common Stock were outstanding.

Documents incorporated by reference:

Certain portions, as expressly described in this Annual Report on Form 10-K, of the registrant's Proxy Statement for the 2018 Annual Meeting of the Stockholders, to be filed not later than 120 days after the end of the year covered by this Annual Report, are incorporated by reference into Part III of this Annual Report where indicated.

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CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This annual report contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this annual report, including, without limitation, statements regarding the assumptions we make about our business and economic model, our dividend policy, business strategy and other plans and objectives for our future operations, are forward-looking statements.

These forward-looking statements include declarations regarding our management's beliefs and current expectations. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "would," "could," "expects," "plans," "contemplate," "anticipates," "believes," "estimates," "predicts," "projects," "intend" or "continue" or the negative of such terms or other comparable terminology, although not all forward-looking statements contain these identifying words. Forward-looking statements are subject to inherent risks and uncertainties in predicting future results and conditions that could cause the actual results to differ materially from those projected in these forward-looking statements. Some, but not all, of the forward-looking statements contained in this annual report include, among other things, statements about the following:

- *our ability to obtain regulatory approval to market and sell Xilonix™ in the United States, Europe and elsewhere;*
- *the initiation, timing, cost, progress and success of our research and development programs, preclinical studies and clinical trials for Xilonix™ and other product candidates;*
- *our ability to advance product candidates into, and successfully complete, clinical trials;*
- *our ability to successfully commercialize the sale of Xilonix™ in the United States, Europe and elsewhere;*
- *our ability to recruit sufficient numbers of patients for our future clinical trials for our pharmaceutical products;*
- *our ability to achieve profitability;*
- *our ability to obtain funding for our operations, including research funding;*
- *our ability to identify additional new products using our True Human™ antibody discovery platform;*
- *the implementation of our business model and strategic plans;*

- *our ability to develop and commercialize product candidates for orphan and niche indications independently;*

- *our commercialization, marketing and manufacturing capabilities and strategy;*

- *our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others;*

- *our expectations regarding federal, state and foreign regulatory requirements;*

- *the therapeutic benefits, effectiveness and safety of our product candidates;*
- *the accuracy of our estimates of the size and characteristics of the markets that may be addressed by our products and product candidates;*
- *the rate and degree of market acceptance and clinical utility of Xilonix™ and future products, if any;*
- *the timing of and our collaborators' ability to obtain and maintain regulatory approvals for our product candidates;*
- *our expectations regarding market risk, including interest rate changes and foreign currency fluctuations;*
- *our belief in the sufficiency of our cash flows to meet our needs for at least the next 12 to 24 months;*
- *our expectations regarding the timing during which we will be an emerging growth company under the JOBS Act;*
- *our ability to engage and retain the employees required to grow our business;*
- *our future financial performance and projected expenditures;*
- *developments relating to our competitors and our industry, including the success of competing therapies that are or become available; and*
- *estimates of our expenses, future revenue, capital requirements and our needs for additional financing.*

You should also read the matters described in the "Risk Factors" and the other cautionary statements made in this annual report as being applicable to all related forward-looking statements wherever they appear in this annual report. We cannot assure you that the forward-looking statements in this annual report will prove to be accurate and therefore you are encouraged not to place undue reliance on forward-looking statements. You should read this annual report completely.

PART I

ITEM 1 BUSINESS

Overview

XBiotech Inc. (“XBiotech” or the “Company) is a pre-market biopharmaceutical company engaged in discovering and developing True Human™ monoclonal antibodies for treating a variety of diseases. True Human™ monoclonal antibodies are those which occur naturally in human beings—as opposed to being derived from animal immunization or otherwise engineered. We believe that naturally occurring monoclonal antibodies have the potential to be safer and more effective than their non-naturally occurring counterparts. XBiotech is focused on developing its True Human™ pipeline and manufacturing system.

The majority of our efforts to date have been concentrated on developing our lead product candidate, bermekimab (also known as MABp1, Xilonix™, CA-18C3, CV-18C3, RA-18C3, and T2-18C3), a therapeutic antibody which specifically neutralizes interleukin-1 alpha (IL-1a). IL-1a is a pro-inflammatory protein produced by leukocytes and other cells, where it plays a key role in inflammation. When unchecked, inflammation can contribute to the development and progression of a variety of different diseases, such as cancer, vascular disease, inflammatory skin disease, and diabetes. Our clinical studies have shown that blocking IL-1a with our lead product candidate may have a beneficial effect on several diseases.

In the second quarter of 2018, XBiotech launched a multi-center phase 2, open label, dose escalation clinical trial evaluating the safety and efficacy of bermekimab in the treatment of patients with moderate to severe atopic dermatitis. This study was the first to utilize the Company’s new pre-filled syringes to deliver bermekimab therapy via a subcutaneous injection. In 2018, the Company released its first production lot of pre-filled syringes, which contain a highly concentrated formulation of bermekimab, allowing dosing of 400mg in a single, convenient injection. In December 2018, the Company announced topline results from the study which enrolled a total of 38 patients at 9 different dermatology centers across the U.S. Ten patients completed 4 weekly 200mg injections of bermekimab in the low dose group, at which point a safety assessment showed the dose to be well tolerated with no dose limiting toxicities. This was followed by enrollment of 28 patients in the high dose cohort, which received 8 weekly 400mg injections of bermekimab. The study met all primary and secondary endpoints and clinically and statistically significant improvement was seen for all clinical endpoints in the high dose group. Results of this study were presented at the American Academy of Dermatology’s (AAD) Annual Meeting held in March 2019 by Eric Simpson, M.D, M.C.R. Professor of Dermatology at Oregon Health & Science University, School of Medicine. The presented findings demonstrated that bermekimab treatment resulted in rapid and significant improvement of disease in patients with moderate-to-severe Atopic Dermatitis. After 7 weeks of treatment, 71% of patients that received a 400mg weekly bermekimab regimen had at least 75% reduction in their disease, as measured by the Eczema Area and Severity Index (EASI) score. Moreover, within 7 weeks, using patient reported Numerical Rating Scale (NRS) for itch and pain, patients receiving the 400mg bermekimab treatment regimen had 71% reduction in itch and an 84% reduction in pain. The Company plans to further pursue clinical development of bermekimab as a treatment for atopic dermatitis.

In the third quarter of 2018, the Company announced enrollment of the first patient in a phase 2, open label clinical study to evaluate safety and efficacy of bermekimab in patients with moderate to severe Hidradenitis Suppurativa (HS). With enrollment rates exceeding expectation, XBiotech announced enrollment completion within the same quarter with a total of 42 patients treated in the study. The study consisted of two treatment groups- those who had failed prior anti-TNF therapy (n=24); and those with no prior anti-TNF treatment history (n=18), all of which received 400mg subcutaneous weekly doses of bermekimab via the Company's new pre-filled syringes in a 12-week treatment regimen. The study was conducted at eleven different dermatology research centers across the U.S. Bermekimab was well tolerated with no safety concerns. The findings of this study were also recently presented at the AAD annual meeting by Alice Gottlieb, M.D., Ph.D., Chair of the study and Clinical Professor of Dermatology, Department of Dermatology, Icahn School of Medicine at Mount Sinai in New York. The presented findings showed that by week 12 of treatment, 63% of patients who have previously failed anti-TNF therapy achieved a positive Hidradenitis Suppurativa Clinical Response (HiSCR) score (the accepted measure of disease severity in HS); similarly, 61% of patients with no prior anti-TNF therapy achieved positive HiSCR. These results translated into a 46% ($p<0.001$) and 60% ($p=0.005$) mean reduction in the number of abscesses and inflammatory nodules, respectively, for the two groups. Another key finding was that 67% and 72% of patients achieved a clinically meaningful reduction in pain by week 12. These results confirm previous findings from a completed phase II, double-blind, placebo-controlled, investigator-sponsored study evaluating bermekimab for the treatment of HS. The data from this study, which has been published in the *Journal of Investigative Dermatology*, is from 20 patients treated with moderate to severe HS that had progressed on standard therapies. Patients received bermekimab for 12 weeks and were followed for an additional 12 weeks to observe durability of treatment. Results demonstrated a response rate in patients treated with bermekimab versus placebo of 60% vs 10%, respectively ($p=0.035$). The Company plans to further pursue clinical development of bermekimab as a treatment for hidradenitis suppurativa.

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An investigator sponsored study that was launched in 2017 at Cedars Sinai Medical Center located in Los Angeles, California for bermekimab to be used in combination with Onivyde (Irinotecan liposome injection) and 5-fluorouracil/folinic acid for treatment of advanced pancreatic adenocarcinoma has nearly completed enrollment. Andrew Hendifar, M.D., Principal Investigator of the study, Medical Oncology lead for the Gastrointestinal Disease Research Group at Cedars-Sinai and Co-Director of Pancreas Oncology, is leading the study and has enrolled nearly all 16 patients at the Cedars-Sinai Medical Center. The Phase I study will determine a maximum tolerated dose as well as assess efficacy. Other studies with bermekimab in oncology are also being considered and these will be announced if and when further progress is made in these directions.

We have also investigated our lead product candidate in clinical trials for other inflammatory conditions, including vascular disease (which led to fast track designation from the FDA to develop bermekimab as a therapy to reduce the need for re-intervention after treatment of peripheral vascular disease with angioplasty or other endovascular methods of treatment), type II diabetes, acne, psoriasis, and pyoderma gangrenosum (PG). Data from each of these trials have been published in journals, with the exception of PG. A listing of these publications is included in the *Summary of Clinical Findings to Date* section of this document.

The Company previously conducted a Phase I/II study evaluating dosing, safety and efficacy of its novel antibody, 514G3. 514G3 was developed from a healthy human donor with natural antibodies effective at neutralizing Methicillin-resistant *Staphylococcus aureus* (MRSA) and non-MRSA forms of *Staphylococcus aureus (S. aureus)*. 514G3 works to eliminate the principle immune evasion mechanism of the bacteria, allowing white blood cells to detect and destroy the bacteria. 514G3 has potential to treat all strains of MRSA and can be used without consideration for strain-specific resistance to various antibiotics. As a True Human monoclonal antibody, 514G3 is expected to be well tolerated without the side effects or risks of antibiotics, including the lack of risk of antibiotic resistance. This proprietary antibody received Fast Track Designation by the FDA for the treatment of all forms of *S. aureus* infections, including Methicillin-resistant *S. aureus* (MRSA). Top line results from the Phase I/II study were announced in April 2017 and reported a reduction in adverse events and shorter hospitalization associated with the 514G3 therapy, even with 514G3-treated subjects tending to be sicker than those receiving placebo. Pre-clinical research involving 514G3 was published in January 2018 in the journal PLOS ONE in a manuscript titled, "*A Natural Human Monoclonal Antibody Targeting Staphylococcus Protein A Protects Against Staphylococcus aureus (S. aureus) Bacteremia*." Throughout 2018, XBiotech continued to reestablish and optimize manufacturing production of 514G3. The Company is continuing to improve yields and processing efficiencies, and to reduce overall cost of production for 514G3 to support its initiatives to potentially use 514G3 as a prophylaxis.

In 2017, data was presented at the American Heart Association's Scientific Sessions which provided the first evidence that IL-1 is associated with Neutrophil Extracellular Traps (NETs) and plays a key role in endothelial activation and thrombogenesis. The data stems from a Material Transfer Agreement (MTA) signed in 2016 with Brigham and Women's Hospital and Massachusetts General Hospital in which Dr. Peter Libby, a renowned Cardiovascular medicine specialist at Brigham and Women's Hospital (BWH) and the Mallinckrodt Professor of Medicine at Harvard Medical School, was named principal investigator of the research. The study researched the influence of NETs on the endothelial cell (EC) functions related to erosion-associated thrombosis. The data shows that exposure of human saphenous veins ECs (HSVECs) to NETs cause an increase in expression of cell surface adhesions such as VCAM-1 and ICAM-1, which may participate in atherogenesis. In conclusion, it was found that NETs act to increase thrombogenicity in vitro through a response mediated by IL-1 . These data suggest a potentially important role for

bermekimab therapy in heart disease. Findings from this research were published in August 2018 in a journal of the American Heart Association (AHA), *Atherosclerosis, Thrombosis, and Vascular Biology*, in an article titled, *Neutrophil Extracellular Traps Induce Endothelial Cell Activation and Tissue Factor Production Through Interleukin-1 and Cathepsin G*. The publication highlights findings that point toward a white blood cell-derived interleukin-1 alpha (IL-1) as a cause of blood clots that could lead to heart attacks or strokes via an intriguing mechanism whereby NETs, released from neutrophils, are laden with IL-1 that is capable of activating cells of the artery wall in a way that in turn activates blood clotting mechanisms and recruits further white blood cells. These published findings not only broaden bermekimab's potential treatment opportunity in heart disease, but also expands treatment opportunities for other inflammatory diseases in which NETs play a deleterious role, such as cancer and pulmonary, autoimmune and gastrointestinal diseases.

In April 2018, the Company obtained an exclusive worldwide license from a Swiss biotechnology Company for the development of the anti-NY-ESO-1 monoclonal antibody, 12D7. The 12D7 antibody targets NY-ESO-1, a cancer-related protein commonly found in many kinds of aggressive tumors. The therapeutic use of 12D7 offers the potential to target advanced tumors by activating cellular immunity or antibody directed immune responses against tumors. A 12D7 therapy may be combined with other therapies that unleash the immune system to produce anti-cancer responses. The Company made considerable strides in the cell line development of cells producing 12D7. These cells will be scaled up to make parental cell banks and grown for process development purposes. This NYESO-1 antibody has the potential to stimulate the body to produce a highly specific immune response against tumors, and may be used to enhance the specificity and potential efficacy of checkpoint inhibitor therapies.

Our True Human antibody therapeutics are developed in-house using our proprietary discovery platform. Identifying True Human antibodies useful for therapeutics may involve screening thousands of blood donors. To distinguish the clinically relevant antibodies from irrelevant background antibody molecules in donor bloods, we use our Super High Stringency Antibody Mining (SHSAM™) technology. After we identify donors, we undertake the complex process of identifying the unique genes for producing the native antibody. Once the nucleic acid sequence is isolated, we are able to introduce these sequences into engineered production cells to manufacture large quantities of product candidate for use in humans. All patents and other intellectual property relating to both the composition of matter and methods of use of our True Human antibodies were developed internally by us. We manufacture these antibodies using a proprietary expression system licensed from Lonza Sales AG. The manufacturing process we have developed incorporates both proprietary and non-proprietary technology.

In 2018, XBiotech completed consolidation of its operations in its new headquarter facility in Austin, Texas. The Company previously occupied three building locations totaling almost 90,000 square feet of space. Operations are now exclusively housed in a custom-built 33,000 square foot facility that includes a new large scale manufacturing operation, R&D laboratories and administrative space. The move has enabled significant reduction in operating costs while maintaining all R&D and operational capabilities in an improved Good Manufacturing Practices (GMP) environment. The new facility is built on a 48 acre property, which is wholly owned by the Company. In December 2018, the Company announced its first successful GMP audit of the new facility by Eurofins Amatsigroup. The audit was conducted in connection with XBiotech’s distribution in Europe of its US-manufactured biological drug product. The Company regularly ships drug product manufactured at the new facility to clinics in various countries in the European Union and the United Kingdom. Drugs manufactured outside of Europe may only be distributed in Europe through a qualified organization that can assure quality of drug product and manufacturing practices (in this case, Amatsigroup). XBiotech currently produces all of its clinical drug material and plans to manufacture any potential commercial drug product from its Austin headquarters.

XBiotech made important advances in its pre-clinical R&D programs in 2018. This includes in vivo work to test and select its lead anti *C. difficile* antibody candidates that target cell surface antigen of the pathogenic bacterium. The Company has successfully optimized an aggressive initial infection and relapse models to test these antibodies both in a prophylactic and therapeutic manner. The Company also continues to make progress in development of True Human antibodies for the treatment and prevention of influenza by targeting two key surface moieties on influenza, hemagglutinin and neuraminidase. The Company has identified lead antibodies that bind to several influenza strains within two subgroups of influenza A and is currently in the process of identifying broadly neutralizing antibodies that target both groups. The company has also selected two lead, broadly neutralizing antibodies against neuraminidase

protein, and is currently in the process of optimizing antibody expression in CHO to allow for future large-scale manufacture of these antibodies. During 2018, the Company also made progress in its herpes zoster (shingles) discovery program. It has now identified its lead anti-herpes zoster antibody against a surface protein of the virus. This antibody was identified from an initial in vitro assay performed by a clinical research organization, and will be characterized further in house in the year 2019.

XBiotech continues to optimize its upstream and downstream manufacturing processes. Considerable manufacturing milestones were achieved in 2018, including an increase in bioreactor media volume to maximize cell culture capacity at harvest, an increase in bioreactor run-time to maximize product yield, and minimization of processing time by streamlining downstream manufacturing processes. In addition, scale up towards achieving full capacity production runs in the current manufacturing facility is planned for 2019. This will include a four-fold increase in syringe output capacity per drug product lot by third quarter 2019.

A Background on Therapeutic Antibodies

A century ago scientists and physicians envisioned being able to custom design therapeutic agents that were highly specific for a single biological target. By selectively attacking disease while sparing healthy tissue, these “magic bullets” were thought to be ideal therapeutic agents. It was not until the early 1970’s, however, that this vision was realized when Kohler and Milstein developed a ground-breaking method for making target-specific monoclonal antibodies—a Nobel prize-winning endeavor. Using this new approach, numerous monoclonal antibody-based research, diagnostic, and therapeutic products have been developed.

Kohler and Milstein’s discovery was based on their knowledge that the immune system of higher animals produces antibodies as a method of protecting them from various, potentially damaging, agents, such as viruses, bacteria, and diseased cells. White blood cells, known as B cells, produce billions of different types of antibodies, each with a unique potential to selectively attach to and neutralize different disease targets. The vast array of possible treatments based on antibodies led to the development of what is now a major industry around the use of therapeutic antibodies.

True Human™ Antibodies

White blood cells in the human body secrete billions of different antibodies that circulate through the blood to react and protect us from toxins, infectious agents or even other unwanted substances produced by our body. True Human™ antibodies, as the name implies, are simply those that are derived from a natural antibody identified from the blood of an individual. To develop a True Human™ antibody therapy, donors are screened to find an individual that has a specific antibody that matches the desired characteristics needed to obtain the intended medical benefit. White blood cells from that individual are obtained, the unique gene that produced the antibody is cloned, and the genetic information is used to produce an exact replica of the antibody sequence. A True Human™ antibody is, therefore, not to be confused with other marketed antibodies, such as so-called “fully human” antibodies—where antibody reactivity is developed through gene sequence engineering in the laboratory.

Fundamental Science of True Human™ Antibodies

To appreciate the background safety and tolerability of True Human™ antibodies, it is important to consider the fundamental biology of natural antibody production.

Billions of different white blood cells secrete billions of unique antibodies every day into circulation. The vast number of different antibodies (and cells that produce them), are essential to enable adequate molecular diversity to ward off a vast range of potential infectious or toxic threats. In other words, since antibodies act to bind and thereby neutralize

unwanted agents, any given circulating antibody must be able to react with a potentially limitless number of existing or evolving disease entities.

The staggering number of different antibodies needed to achieve this level of preparedness, however, is a daunting concept from a genetics point of view. If an individual antibody gene was needed to encode each of a billion different antibodies, there would be approximately 20,000 times as many genes needed just for antibodies as there would be needed to encode the rest of the entire human genome. Individual cells would need to be gigantic, and monumental resources of the body would be required to make, copy and maintain all of the DNA. Clearly, the system of antibodies could not have evolved to protect us, had not an elegant solution emerged to deal with this genetic conundrum.

Thus, a hallmark of the immune physiology of all vertebrates (all have antibodies) is the ability to recombine and selectively mutate a relatively small number of gene segments to create a phenomenal and effectively unlimited number of antibody genes. By rearranging, recombining and mutating the genetic code, specialized white blood cells, or B lymphocytes, are able to create an unlimited array of antibody genes. The consequence of this genetic engineering, however, is that each antibody gene is unique to the individual B lymphocyte that created it—and no copy of the gene exists in the human germline. The only place to find a unique antibody gene is in the individual cells that created it.

The extraordinary process of gene rearrangement and mutation results in a multitude of unique B lymphocytes and consequently an incredibly diverse repertoire of antibodies in any given individual.

Elucidating the mechanisms behind the production of unique antibody genes must be considered one of the major achievements of medical research in the 20th century. Yet unfolding this mystery created another problem to solve: If antibodies were not produced from genes encoded in the human genome and the products of these genes were new to the body, why were these antibody molecules not recognized by the immune system as foreign substances—like any other foreign substance that they were intended to eradicate? How could the body distinguish the apparently “foreign” antibody molecules from the bona fide infectious intruders?

Unraveling the genetics of antibody production led to another major advance in medicine: the discovery of how an endless array of antibody proteins could be made in a way that individual molecules were always tolerated by the body.

In the early 1990s, research began to demonstrate that the production of antibodies was not an unregulated process. Rather, it was learned that the antibodies produced by each and every B lymphocyte were subject to intense scrutiny. Studies showed that B lymphocytes which produced acceptable antibodies were stimulated to grow while those that produced “autoreactive” antibodies were not. B lymphocytes that produced “good” antibodies were stimulated to proliferate, and enabled to produce copious amounts of antibody in the event it was needed to ward off a harmful agent. B lymphocytes that rearranged genes to produce antibodies that were ineffective or were autoreactive were given signals that instructed them to engage in a process of programmed cell death. Thus B lymphocytes producing harmful or useless antibodies are simply killed off. This mechanism for creating antibody diversity on the one hand, while protecting the individual from a mass of unwanted or intolerable antibody molecules on the other, was as elegant as it was fundamental to the success of vertebrate immune physiology.

This process of “selection” has been elucidated in great detail. There can be no more important feature of immune physiology than the process of selection. Selection is a fundamental step to enable the body to produce an extremely diverse set of antibody molecules without, in the process, producing an array of novel molecules that cause harm.

Industry Context

Until now each and every therapeutic antibody on the market has been derived from animals and/or through gene sequence modification in the laboratory to produce a desired antibody reactivity. Marketed antibodies to date, described as “fully human”, are not derived from human gene sequences that have undergone the crucial process of selection in a human.

Without exception, all marketed products to date that are described as “fully human”, are in fact engineered and are not selected based on natural tolerance in the human body. The use of the term “fully human” to describe these products has thus created considerable confusion. To our knowledge, there are at present no True Human™ antibodies manufactured, using recombinant protein technology, currently marketed. If successful in clinical development, our lead product candidate is expected to be the first True Human™ therapeutic antibody to be commercialized.

Platform Technology

Our True Human antibody therapeutics are developed in-house using our proprietary discovery platform. There are significant technical challenges in identifying and cloning genes for True Human™ antibodies. A key problem to overcome can be to first identify individuals with the desired antibody reactivity. This can involve screening thousands of blood donors to enable the identification of a single, clinically relevant antibody—discovered from literally trillions of irrelevant background antibody molecules in the blood of donors. To distinguish the clinically relevant antibodies from irrelevant background antibody molecules in donor bloods, we use our Super High Stringency Antibody Mining (SHSAM™) technology. White blood cells from that individual can then be isolated, and the unique gene that produced the native antibody obtained. We currently obtain blood donor samples through a Research and Collaboration Agreement with the South Texas Blood & Tissue Center, a Texas 501(c)(3) non-profit corporation. See "Intellectual Property- Other Commercial Licenses."

Novel cloning technologies developed at XBiotech have enabled us to clone the crucial antibody gene sequences from these donors in order to reproduce a True Human™ antibody for use in clinical therapy. A True Human™ monoclonal antibody should therefore not be confused with other marketed therapeutic monoclonal antibodies, such as those currently referred to as “fully human” antibodies.

Market Opportunity

We have a number of indications in various stages of clinical or pre-clinical development with significant market opportunities. These include dermatology, oncology and other inflammatory conditions, as well as infectious disease indications. The potential market opportunities in these various indications are vast and we believe our research and manufacturing technologies, designed to more rapidly, cost-effectively and flexibly produce new therapies, will be advantageous in each market space.

Our Strategy

Our objective is to fundamentally change the way drugs are developed and commercialized, and become a leading biopharmaceutical company focused on the discovery, development and commercialization of therapeutic True Human™ antibodies. The key goals of our business strategy are to:

- Obtain regulatory approval to market and sell our lead product candidate and/or our other product candidates in the United States, Europe and other markets, and begin commercial sale;
- Continue our research and clinical work on infectious diseases, including S. *aureus*;
- Advance our pipeline of therapeutic antibodies and other possible clinical programs in strategic therapeutic areas;
- Discover other True Human™ antibody therapies using our proprietary platform; and
- Leverage our manufacturing technology.

Product Pipeline

Our product development status for the fourth quarter of 2018 was as follows:

Competition

The therapeutic antibody space is dynamic as there continues to be a highly active commercial pipeline of therapeutic antibodies globally, involving a complex array of development cycles as products reach the end of their patent life and as new candidate products proceed into pivotal studies and approach registration. There are numerous independent reviews on the subject in both trade journals and academic press (one such example being Reichert JM, Antibodies to watch in 2018 MAbs. 2018 Jan 4:1-21).

We believe True Human™ therapeutic antibodies have important differentiating factors from other monoclonal antibodies currently marketed. The unique activity of our lead anti-cancer therapeutic has the potential ability to both improve well-being and extend life. We feel our product candidates will be highly differentiated in the market place for therapeutics in various indications including but not limited to cancer and dermatology. However, regardless of the potential advantages or uniqueness of our lead product candidate in the market, we do expect these products to compete head-to-head with the numerous existing candidate antibody products in development, including emerging biosimilar therapeutic antibodies.

Current Clinical and/or Regulatory Activity

Phase II Study for Atopic Dermatitis (AD)

The Company recently completed a phase 2, open label, multi-center clinical study to evaluate safety and efficacy of bermekimab in patients with moderate to severe Atopic Dermatitis (AD). Thirty eight patients in two treatment groups received a low (n=10) or high (n=28) dose of bermekimab once weekly for either a 4 or 7-week treatment regimen, respectively. The study met all primary and secondary endpoints and clinically and statistically significant improvement was seen for all clinical endpoints in the high dose group. Study findings demonstrated that bermekimab treatment resulted in rapid and significant improvement of disease in patients with moderate-to-severe AD. After only 7 weeks of treatment, 71% of patients that received a 400mg weekly bermekimab regimen had at least 75% reduction in their disease, as measured by the Eczema Area and Severity Index (EASI) score. Moreover, within 7 weeks, using patient reported Numerical Rating Scale (NRS) for itch and pain, patients receiving the 400mg bermekimab treatment regimen had 71% reduction in itch and an 84% reduction in pain. The Company plans to further pursue clinical development of bermekimab as a treatment for atopic dermatitis.

Phase II Study for Hidradenitis Suppurativa (HS)

The Company recently completed a phase 2, open label, multi-center clinical study to evaluate safety and efficacy of bermekimab in patients with moderate to severe Hidradenitis Suppurativa (HS). The study enrolled 42 patients at eleven different dermatology clinics in the U.S., each receiving 400mg subcutaneous weekly subcutaneous doses of bermekimab in a 12-week treatment regimen. There were two treatment groups: those who had failed prior anti-TNF therapy (n=24); and those with no prior anti-TNF treatment history (n=18). Bermekimab was well-tolerated with no safety concerns. Statistically significant improvement was seen for all efficacy endpoints in both groups, with the exception of Hospital Anxiety and Depression Scale (HADS) in the anti-TNF naïve group (using an alpha level of .05 (5%)). Study results showed that by week 12 of treatment, 63% of patients who have previously failed anti-TNF therapy achieved a positive HiSCR (the accepted measure of disease severity in HS); similarly, 61% of patients with no prior anti-TNF therapy achieved positive HiSCR. These results translated into a 46% ($p<0.001$) and 60% ($p=0.005$) reduction in the number of abscesses and inflammatory nodules, respectively, for the two groups. Another key finding was that 67% and 72% of patients achieved a clinically meaningful reduction in pain by week 12.

These results confirm previous findings from a completed phase II, double-blind, placebo-controlled, investigator-sponsored study evaluating bermekimab for the treatment of HS. The data from this study, which has been published in the *Journal of Investigative Dermatology*, is from 20 patients treated with moderate to severe HS that had progressed on standard therapies. Patients received bermekimab for 12 weeks and were followed for an additional 12 weeks to observe durability of treatment. Results demonstrated a response rate in patients treated with bermekimab versus placebo of 60% vs 10%, respectively ($p=0.035$). The Company plans to further pursue clinical development of bermekimab as a treatment for hidradenitis suppurativa.

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Phase I Pancreatic Cancer Combination Study

An investigator sponsored study that was launched in 2017 at Cedars Sinai Medical Center located in Los Angeles, California for bermekimab to be used in combination with Onivyde (Irinotecan liposome injection) and 5-fluorouracil/folinic acid for treatment of advanced pancreatic adenocarcinoma has nearly completed enrollment. Andrew Hendifar, M.D., Principal Investigator of the study, Medical Oncology lead for the Gastrointestinal Disease Research Group at Cedars-Sinai and Co-Director of Pancreas Oncology, is leading the study and has enrolled nearly all 16 patients at the Cedars-Sinai Medical Center. The Phase I study will determine a maximum tolerated dose as well as assess efficacy. Other studies with bermekimab in oncology are also being considered and these will be announced if and when further progress is made in these directions.

Summary of Clinical Findings to Date

Safety

Our lead product under development is derived from a natural human immune response. We expected that this would facilitate better tolerability when used as a therapeutic compared to humanized or “fully human” monoclonal antibodies. Antibody therapies are known to be associated with significant risk for infusion reactions, including serious anaphylactic reactions. We believe that these reactions are the result of using antibodies that were not derived from natural human immunity but rather had engineered specificities. Based on scientific principles of antibody physiology, a fundamentally important premise was that our True Human™ antibody therapy should be safer and result in less infusion-related complications than engineered human antibodies when used in clinical studies.

Therapeutic monoclonal antibodies, even those so-called “fully human,” have been associated with infusion reactions. Comparably administration of our lead product candidate is associated with a reduced number of infusion related reactions and injection site reactions.

To date the Company has 9 publications from 7 of its clinical studies. The table below outlines each of these publications.

Indication	Journal	Title
Oncology	Oncoimmunology	Interleukin-1 receptor antagonist levels predict favorable outcome after bermekimab, a first-in-class true human interleukin-1 antibody, in a phase III randomized study of advanced colorectal cancer

Oncology	The Lancet Oncology	MABp1 as a novel antibody treatment for advanced colorectal cancer: a randomized, double-blind, placebo-controlled, phase 3 study
Oncology	The Lancet Oncology	MABp1, a first-in-class true human antibody targeting interleukin-1 in refractory cancers: an open-label, phase 1 dose-escalation and expansion study
Oncology	Investigational New Drugs	Xilonix, a novel true human antibody targeting the inflammatory cytokine interleukin-1 alpha, in non-small cell lung cancer
Psoriasis	JAMA Dermatology	Open-label trial of MABp1, a true human monoclonal antibody targeting interleukin 1 , for the treatment of psoriasis
Acne	Journal of Drugs in Dermatology	An open label, phase 2 study of MABp1 monotherapy for the treatment of acne vulgaris and psychiatric comorbidity
Cardiovascular	Journal of Vascular Surgery	A randomized phase II study of Xilonix, a targeted therapy against interleukin 1 , for the prevention of superficial femoral artery restenosis after percutaneous revascularization
Diabetes	Journal of Diabetes and Its Complications	Safety, pharmacokinetics, and preliminary efficacy of a specific anti-IL-1alpha therapeutic antibody (MABp1) in patients with type 2 diabetes mellitus
Hidradenitis Suppurativa	Journal of Investigative Dermatology	MABp1 Targeting Interleukin-1Alpha for Moderate to Severe Hidradenitis Suppurativa not Eligible for Adalimumab: A Randomized Study

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Intellectual Property

XBiotech has developed a large international intellectual property (IP) portfolio to protect important aspects of its technology, services and products, including patents, trademarks and trade secrets. As of December 31, 2018, XBiotech's patent portfolio consisted of 21 patent families, and included 137 issued patents and 112 pending patent applications (of which 11 were allowed) in various countries around the world. XBiotech's IP portfolio is designed to protect XBiotech's drug products, therapies, and discovery technology. It includes patents and applications that protect bermekimab (also known as MABp1) as a composition of matter and methods of using anti-IL-1a antibodies for the treatment of various diseases including cancer, vascular disorders, inflammatory skin diseases, diabetes, and arthritis. XBiotech's IP portfolio also includes patents and applications directed to our proprietary antibody discovery platform, as well as treating and preventing *S. aureus* infections.

XBiotech owns the rights to the patent families described in more detail below.

A. Interleukin-1 Alpha Antibodies and Methods of Use. This patent family relates to the development of IL-1a-specific True Human™ monoclonal antibodies, including MABp1. As of December 31, 2018, XBiotech has been granted 35 patents in this family; including nine in the U.S., and others in Australia, Canada, Chile, China, Europe, Hong Kong, India, Indonesia, Israel, Japan, South Korea, Malaysia, Mexico, New Zealand, the Philippines, Russia, Singapore, and South Africa. As of December 31, 2018, this family has 11 pending patent applications (US, Brazil, Philippines, Israel, Indonesia, Malaysia, Europe, Japan, China, Canada, and India). Unless extended, patents in this family expire in 2029.

B. Treatment of Cancer with Anti- IL-1 Antibodies. This patent family relates to the use of anti-IL-1 antibodies to inhibit the metastatic potential of tumors by interrupting the role that tumor-derived IL-1 plays in tumor metastasis. As of December 31, 2018, XBiotech has been granted five patents for this family; including one in Australia, one in Canada, two in Japan, and one in Europe. As of December 31, 2018, this family has three pending patent applications (US, China, and Hong Kong). Unless extended, patents in this family expire in 2027.

C. Treatment of Neoplastic Diseases. This patent family relates to the administration of anti-IL-1 antibodies to treat various tumor-associated diseases and the administration of a monoclonal antibody that specifically binds IL-1 to reduce the size of tumors in human patients suffering from cancer. As of December 31, 2018, XBiotech has been granted 13 patents for this family including three in Australia, two in Europe, one in Indonesia, one in Japan, one in South Korea, one in Mexico, one in New Zealand, one in the Philippines, one in Singapore, and one in South Africa. As of December 31, 2018, this family has 13 pending patent applications (two in the US, two in Israel, two in China, Europe, Philippines, Japan, Mexico, Russia, Hong Kong, and Korea of which 2 (Israel and Russia) have been allowed. Unless extended, patents in this family expire in 2027.

D. Diagnosis, Treatment, and Prevention of Vascular Disorders. This patent family relates to methods of diagnosing, treating and preventing a variety of vascular disorder using IL-1a autoantibody. As of December 31, 2018, XBiotech has been granted seven patents in this family, including two in the U.S., one in Australia, one in Canada, one in Europe and two in Japan. As of December 31, 2018, this family has two pending patent applications (China). Unless extended, patents in this family expire in 2026.

E. IL-1 Alpha Immunization Induces Autoantibodies Protective Against Atherosclerosis. This patent family relates to the use of IL-1 in a vaccine to generate anti-IL-1a antibodies to protect against atherosclerosis. As of December 31, 2018, XBiotech has been granted patents for this family in Australia and Europe. Unless extended, patents in this family expire in 2027.

F. Targeting Pathogenic Monocytes. This patent family relates to the discovery that IL-1 is expressed on the proinflammatory, disease-associated CD14+CD16+ monocyte subset in humans, and describes targeting IL-1 to deplete these pathogenic cells or to modulate their function. As of December 31, 2018, XBiotech has been granted five patents in this family; including two in the U.S., one in Australia, one in Canada, and one in Japan. As of December 31, 2018, this family has one pending patent application in Europe. Unless extended, patents in this family expire in 2029.

G. Arthritis Treatment. This patent family relates to the administration of anti-IL-1 antibodies to treat conditions associated with arthritis. As of December 31, 2018, XBiotech has been granted seven patents in this family, including three in Australia, one in Europe, two in Japan, and one in Israel. As of December 31, 2018, this family has seven pending patent applications (US, Canada, China, Hong Kong, Israel, and two in Korea). Unless extended, patents in this family expire in 2031.

H. Cachexia Treatment. This patent family relates to the administration of anti-IL-1 antibodies to treat cachexia. As of December 31, 2018, XBiotech has been granted eight patents in this family, including one in the U.S., one in Australia, one in Europe, one in Japan, one in Mexico, one in the Philippines, one in Russia, and one in South Africa. As of December 31, 2018, this family has six pending patent applications (US, Canada, China, Hong Kong, Israel, and Korea, of which two (US and Israel) have been allowed. Unless extended, patents in this family expire in 2032.

I. Treatment of Diabetes. This patent family relates to the administration of anti- IL-1 antibodies to treat diabetes. As of December 31, 2018, XBiotech has been granted two U.S. patents. Unless extended, patents in this family expire in 2033.

J. Treating Vascular Disease and Complications Thereof. This patent family relates to the administration of IL-1 targeting agents to reduce the chance or severity of a major adverse clinical event occurring in a patient who has received or is expected to receive surgical treatment for a stenosed blood vessel. As of December 31, 2018, XBiotech has been granted three patents, including one in Australia, one in Russia, and one in South Africa. As of December 31, 2018, this family has 11 pending patent applications (US, Canada, China, two in Europe, Israel, Japan, Mexico, New Zealand, Korea, and Hong Kong, of which one (Japan) has been allowed. Unless extended, patents in this family expire in 2033.

K. Treatment of Inflammatory Skin Disease and Psychiatric Conditions. This patent family relates to the administration of anti-IL-1 antibodies to treat inflammatory skin diseases such as acne and psoriasis, as well as to treat psychiatric conditions such as anxiety. As of December 31, 2018, XBiotech has been granted seven patents in this family, including two in the U.S., two in Australia, one in Europe, and two in Japan. As of December 31, 2018, this family has 12 pending patent applications (US, Australia, two in Canada, two in China, two in Europe, Hong Kong, Japan, and two in Korea) of which one has been allowed (Australia). Unless extended, patents in this family expire in 2033.

L. Methods, compositions, and kits for reducing anti-antibody responses. This patent family relates to methods and compositions for reducing immune system-mediated reactions to allotypic determinants on administered antibody products. As of December 31, 2018, XBiotech has been granted one Australian patent in this family. Unless extended, patents in this family expire in 2030.

M. Identifying Affinity-Matured Human Antibodies. This patent family relates to methods and compositions for identifying affinity-matured True Human™ monoclonal antibodies from donors. As of December 31, 2018, XBiotech has been granted eight patents in this family (four in the U.S., one in Australia, one in China, one in Russia, and one in Hong Kong)). As of December 31, 2018, this family has 13 pending patent applications (US, Australia, Canada, China, Europe, India, two in Israel, Japan, two in Mexico, Korea, and Russia, of which two (Israel and Mexico) have been allowed. Unless extended, patents in this family expire in 2032.

N. Compositions and Methods for Treating *S. Aureus* Infections. This patent family relates to antibodies for preventing and treating *S. aureus* infections. As of December 31, 2018, XBiotech has been granted thirteen patents in this family, including three in the U.S, one in Australia, one in China, one in Colombia, one in Japan, one in Mexico, one in the Philippines, one in Russia, one in Singapore, one in South Africa, and one in South Korea. As of December 31, 2018, this family has 20 pending patent applications (US, Australia, Brazil, Canada, China, Chile, Europe, India, Indonesia, Israel, Japan, Malaysia, Mexico, New Zealand, Philippines, two in Hong Kong, Singapore, Korea, and Russia) of which one (US) has been allowed. Unless extended, patents in this family expire in 2035.

O. Treatment of Hidradenitis Suppurativa. This patent family relates to the use of antibodies (Abs) which specifically bind interleukin-1 (IL-1) to treat hidradenitis suppurativa. As of December 31, 2018, XBiotech has one pending U.S. application and one pending international patent application. Unless extended, patents in this family expire in 2038.

P. Treatment of *S. Aureus* Infections. This patent family relates to the use of antibodies (Abs) which specifically bind interleukin-1 (IL-1) for treating *S. aureus* bloodstream infections in human patients. As of December 31, 2018, XBiotech has one pending international patent application. Unless extended, patents in this family expire in 2038.

Q. Treatment of Atopic Dermatitis. This patent family relates to the use of antibodies (Abs) which specifically bind interleukin-1alpha (IL-1) to treat various symptoms of atopic dermatitis. As of December 31, 2018, XBiotech has three pending U.S. applications. Unless extended, patents in this family expire in 2039.

XBiotech has licensed exclusive rights to the intellectual property described below.

R. Antibacterial antibodies and Methods of Use. This patent family relates to antibodies for preventing and treating *S. aureus* infections. XBiotech acquired the use of patents within this family pursuant to its exclusive license agreement with STROX Biopharmaceuticals, LLC. As of December 31, 2018, this patent family includes two patents in the U.S., each expiring in 2019, unless extended.

S. Staphylococcus Aureus-Specific Antibody Preparations. This patent family relates to antibodies for preventing and treating *S. aureus* infections. XBiotech acquired use of patents within this family pursuant to its exclusive license agreement with STROX Biopharmaceuticals, LLC. As of December 31, 2018, this patent family includes one Australian and one Israeli patent. As of December 31, 2018, this family has two pending patent applications (Canada and India). Unless extended, patents in this family expire in 2029.

T. Monoclonal Human Tumor-Specific Antibody. This patent family relates generally to human tumor-specific antibodies as well as fragments, derivatives and variants thereof that recognize tumor-associated antigen NY-ESO-1. XBiotech acquired the use of patents within this family pursuant to its exclusive license agreement with CT Atlantic AG. As of December 31, 2018, this patent family includes pending applications in Brazil, Canada (allowed), and Europe and 13 issued patents, including one in the U.S., one in Australia, two in Europe, one in China, one in Israel, one in India, one in Japan, one in South Korea, one in New Zealand, one in Mexico, one in Russia, and one in South Africa. Unless extended, patents in this family expire in 2028.

U. Combination Therapy including Tumor Associated Antigen-Binding Antibodies. This patent family relates generally to a combination therapy including tumor associated antigen binding antibodies. XBiotech acquired the use of patents within this family pursuant to its exclusive license agreement with CT Atlantic AG. As of December 31, 2018, this patent family includes pending applications in Canada (allowed), India, and the U.S. and four issued patents, including one in China, one in Europe, one in Japan, and one in South Korea. Unless extended, patents in this family expire in 2032.

ITEM 1A RISK FACTORS

Risks Related to our Financial Condition and Capital Requirements

We have incurred significant losses every quarter since our inception and anticipate that we will continue to incur significant losses in the future.

We are a pre-market pharmaceutical company with no revenue and a limited operating history. Investment in pharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval or become commercially viable. We do not have any products approved by regulatory authorities for marketing or commercial sale and have not generated any revenue from product sales, or otherwise, to date, and we continue to incur significant research, development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred losses in every reporting period since our inception in 2005. For the years ended December 31, 2016, 2017, and 2018, we reported a net loss of $52.8 million, $33.2 million and $21.1 million respectively. As of December 31, 2018, we had an accumulated deficit since inception of approximately $237.7 million.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate these losses will increase as we continue the research and development of, and seek regulatory approvals for our lead product candidate in various indications and any of our other product candidates, and potentially begin to commercialize any products that may achieve regulatory approval. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our financial condition. The amount of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. Our prior losses and expected future losses have had, and will continue to have, an adverse effect on our financial condition. If our lead product candidate or any other product candidate fails in clinical trials or does not gain regulatory approval, or if approved and fails to achieve market acceptance, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. We will need to raise significant additional funding, which may not be available on acceptable terms, if at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

Since inception, we have dedicated a majority of our resources to the discovery and development of our proprietary preclinical and clinical product candidates, and we expect to continue to expend substantial resources doing so for the foreseeable future. These expenditures will include costs associated with conducting research and development, manufacturing product candidates and products approved for sale, conducting preclinical experiments and clinical trials and obtaining and maintaining regulatory approvals, as well as commercializing any products later approved for sale. During the year ending December 31, 2018, we recognized approximately $15.7 million in expenses associated with research and development and clinical trials.

We completed our initial public offering on April 15, 2015 and a registered direct offering in March 2017. However, the net proceeds from these offerings and cash on hand may not be sufficient to complete clinical development of any of our product candidates nor may it be sufficient to commercialize any product candidate. Accordingly, we may require substantial additional capital beyond the offering to continue our clinical development and potential commercialization activities. Our future capital requirements depend on many factors, including but not limited to:

- the number and characteristics of the future product candidates we pursue;
- the scope, progress, results and costs of researching and developing any of our future product candidates, and conducting preclinical research and clinical trials;
- the timing of, and the costs involved in, obtaining regulatory approvals for any future product candidates we develop;
- the cost of future commercialization activities for our lead product candidate and the cost of commercializing any future products approved for sale;
- the cost of manufacturing our future products; and
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patents, including litigation costs and the outcome of any such litigation.

We are unable to accurately estimate the funds we will actually require to complete research and development of our product candidates or the funds required to commercialize any resulting product in the future or the funds that will be required to meet other expenses. Our operating plan may change as a result of many factors currently unknown to us, and our expenses may be higher than expected. We may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. Raising funds in the future may present additional challenges and future financing may not be available in sufficient amounts or on terms acceptable to us, if at all.

Raising additional capital may cause dilution to our existing shareholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

The terms of any financing arrangements we enter into may adversely affect the holdings or the rights of our shareholders and the issuance of additional securities, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our shareholders. The incurrence of indebtedness would result in increased fixed payment obligations and, potentially, the imposition of restrictive covenants. Those covenants may include 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. We could also be required to seek funds through arrangements with collaborators or otherwise at an earlier stage than otherwise would be desirable resulting in the loss of rights to some of our product candidates or other unfavorable terms, any of which may have a material adverse effect on our business, operating results and prospects. Additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our products.

Risks Related to Our Business

We currently have no source of product revenue and may never become profitable.

To date, we have not generated any revenues from commercial product sales, or otherwise. Our ability to generate revenue in the future from product sales and achieve profitability will depend upon our ability, alone or with any future collaborators, to commercialize products successfully, including our lead product candidate or any future product candidates that we may develop, in-license or acquire in the future. Even if we are able to achieve regulatory approval successfully for our lead product candidate or any future product candidates, we do not know when any of these products will generate revenue from product sales, if at all. Our ability to generate revenue from product sales from our lead product candidate or any of our other product candidates also depends on a number of additional factors, including our ability to:

- complete development activities, including the necessary clinical trials;
- complete and submit new drug applications, or NDAs, to the US Food and Drug Administration, or FDA, and obtain regulatory approval for indications for which there is a commercial market;
- complete and submit applications to, and obtain regulatory approval from, foreign regulatory authorities such as the European Medicines Agency, or EMA;
- establish our manufacturing operations;
- develop a commercial organization capable of sales, marketing and distribution for our lead product candidate and any products for which we obtain marketing approval and intend to sell ourselves in the markets in which we choose to commercialize on our own;
- find suitable distribution partners to help us market, sell and distribute our approved products in other markets;
- obtain coverage and adequate reimbursement from third-party payers, including government and private payers;
- achieve market acceptance for our products, if any;

- establish, maintain and protect our intellectual property rights; and

- attract, hire and retain qualified personnel.

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In addition, because of the numerous risks and uncertainties associated with pharmaceutical product development, including that our lead product candidate or any other product candidates may not advance through development or achieve the endpoints of applicable clinical trials, we are unable to predict the timing or amount of increased expenses, or when or if we will be able to achieve or maintain profitability. In addition, our expenses could increase beyond expectations if we decide to or are required by the FDA, or foreign regulatory authorities, to perform studies or trials in addition to those that we currently anticipate. Even if we are able to complete the development and regulatory process for our lead product candidate or any other product candidates, we anticipate incurring significant costs associated with commercializing these products.

Even if we are able to generate revenues from the sale of our lead product candidate or any other product candidates that may be approved, we may not become profitable and may need to obtain additional funding to continue operations. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations.

Our future success is dependent on the regulatory approval and commercialization of our lead product candidate and any of our other product candidates.

We do not have any products that have gained regulatory approval. The Company's Phase III symptomatic colorectal cancer study has been completed and XBiotech proceeded with the submission of a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) in March 2016. In May 2017, the Company announced that it received a negative opinion from the EMA's Committee for Medicinal Products for Human Use ("CHMP") for the MAA in Europe. XBiotech subsequently pursued the EMA's re-examination procedure in which new Rapporteurs were assigned to reevaluate the initial opinion after receiving the Company's grounds for re-examination. In September 2017, the CHMP issued its opinion on the re-examination of the Company's MAA and maintained its initial negative opinion issued in May 2017. In June 2017, XBiotech reported discontinuation of its second Phase III study, a double-blind placebo controlled study for improving survival in metastatic colorectal cancer, following the Independent Data Monitoring Committee's (IDMC) second prospectively planned, unblinded interim analysis at 75% of events in the study.

As a result, our ability to finance our operations and generate revenue, are substantially dependent on our ability to obtain regulatory approval for, and, if approved, to successfully commercialize our lead product candidate in a timely manner. We cannot commercialize our lead product candidate or our other product candidates in the U.S. without first obtaining regulatory approval for each product from the FDA; similarly, we cannot commercialize our lead product candidate or our other product candidates outside of the U.S. without obtaining regulatory approval from comparable foreign regulatory authorities, including the EMA. The FDA review process typically takes years to complete and approval is never guaranteed. Before obtaining regulatory approvals for the commercial sale of our lead product candidate or any of our other potential product candidates for a target indication, we must demonstrate with substantial evidence gathered in preclinical and well-controlled clinical studies, including two well-controlled Phase III studies, and, with respect to approval in the U.S. to the satisfaction of the FDA, and in Europe, to the satisfaction of the EMA, that the product candidate is safe and effective for use for that target indication; and that the manufacturing facilities, processes and controls are adequate. Obtaining regulatory approval for marketing of our lead product

candidate or our future product candidates in one country does not ensure we will be able to obtain regulatory approval in other countries. A failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in other countries.

Even if our lead product candidate or any of our other product candidates were to successfully obtain approval from the FDA or comparable foreign regulatory authorities, any approval might contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, or may be subject to burdensome post-approval studies or risk management requirements. If we are unable to obtain regulatory approval for our lead product candidate in one or more jurisdictions, or any approval contains significant limitations, we may not be able to obtain sufficient funding or generate sufficient revenue to continue the development of any of our other product candidates that we are developing or may discover, in-license, develop or acquire in the future. Also, any regulatory approval of our lead product candidate or our other product candidates, once obtained, may be withdrawn. Furthermore, even if we obtain regulatory approval for our lead product candidate or our other product candidates, its commercial success will depend on a number of factors, including the following:

- development of a commercial organization within XBiotech or establishment of a commercial collaboration with a commercial infrastructure;

- establishment of commercially viable pricing and obtaining approval for adequate reimbursement from third-party and government payers;

- our ability to manufacture quantities of our lead product candidate using commercially satisfactory processes and at a scale sufficient to meet anticipated demand and enable us to reduce our cost of manufacturing;

- our success in educating physicians and patients about the benefits, administration and use of our lead product candidate;

- the availability, perceived advantages, relative cost, relative safety and relative efficacy of alternative and competing treatments;

- the effectiveness of our own or our potential strategic collaborators' marketing, sales and distribution strategy and operations;

- acceptance as a safe and effective therapy by patients and the medical community; and

- a continued acceptable safety profile following approval.

Many of these factors are beyond our control. If we are unable to successfully commercialize our lead product candidate, we may not be able to earn sufficient revenues to continue our business.

New laws or regulations may be promulgated or modified in the United States, in Europe, or other jurisdictions that could impact our ability to receive the necessary approvals to successfully market and commercialize our lead product candidate or any of our other product candidates.

The pharmaceutical and biotechnology industry is one of the most regulated on a state, federal and international level. There are a number of laws, regulations, and court decisions which impact the daily activities of our business. As a result, we must ensure that strategies and planning in relation to our product candidates are in line with the current regulations governing our industry. When there are changes in leadership, whether within the U.S., or elsewhere, we must anticipate the possibility of shifts in regulatory policies as they pertain to our business. New or modified regulations may impact our ability to quickly respond with updates to our programs. While we may be able to anticipate certain changes, policy statements often are not always translated into actionable legislation. We continue to track updates and changes internally to ensure we are in compliance with regulatory authority guidelines and

expectations. Court decisions at both the state and federal level can also impact the way in which we operate and make specific product related program decisions. New laws, regulations, or court orders could materially alter or impact our ability to receive necessary approvals from regulatory authorities to market and commercialize our lead product candidate or any of our other product candidates.

We submitted a Marketing Authorization Application to the EMA for our lead product candidate after successfully completing a Phase III study in Europe which was ultimately denied by the Agency. Even if the EMA or FDA approves our lead product candidate in the future, there are a number of obstacles to consider in the post-marketing approval and commercialization processes in Europe and/or the U.S.

In March 2016, we submitted a Marketing Authorization Application to the EMA Committee for Human Medicinal Products, or CHMP, for the Phase III study of our lead product candidate completed in Europe during Q4 2015. In May 2017, the Company announced that it received a negative opinion from the EMA's Committee for Medicinal Products for Human Use ("CHMP") for the MAA in Europe. XBiotech subsequently pursued the EMA's re-examination procedure in which new Rapporteurs were assigned to reevaluate the initial opinion after receiving the Company's grounds for re-examination. In September 2017, the CHMP issued its opinion on the re-examination of the Company's MAA and maintained its initial negative opinion issued in May 2017. In June 2017, XBiotech reported discontinuation of its second Phase III study, a double-blind placebo controlled study for improving survival in metastatic colorectal cancer, following the Independent Data Monitoring Committee's (IDMC) second prospectively planned, unblinded interim analysis at 75% of events in the study. Therefore, the Company does not currently have any marketing applications under review with any regulatory agencies.

During the EMA's assessment period, our manufacturing facilities were audited. They were determined, by the EMA, to have met the standards of Good Manufacturing Practices, (GMP) in October 2016. Additionally, our new manufacturing facility, which opened in September 2016, must go through validation with the appropriate regulatory agency prior to commercial production. The new facility might fail validation or not meet regulatory standards for a commercial manufacturing facility. Also, during the assessment period, our clinical research sites engaged to recruit patients into the clinical trial were audited to ensure standards of Good Clinical Practice, (GCP). Even though there were no major findings resulting from the audit of the selected clinical research site, this was merely a sampling by the EMA and may not be representative of other research sites that participated in the clinical trial.

If the Company does seek approval in the EU in the future, we must also gain reimbursement approval in specific EU countries, as well as, buy-in from patients and health care professionals alike for the use of lead product candidate or our other product candidates to treat any relevant indication(s). If we do not receive reimbursement from countries or private payers in the EU, our lead product candidate may not reach or be accessible to patients or health care professionals. Even if our lead product candidate or our other product candidates is approved for reimbursement in EU countries, it may not always maintain its reimbursement status. There are a number of scenarios where we may encounter tight price controls, continuous negotiations, and other variety of outcomes that could challenge our ability to effectively sell the product in certain EU countries. Some countries may decide to no longer reimburse our lead product candidate or our other product candidates for a number of reasons. Further, patients and health care professionals may reject one lead product candidate or our other product candidates as a standard of care treatment for any relevant indication(s). If patients and healthcare professionals reject one of our product candidates, then it will be difficult to generate revenue for the company. There will be a similar scenario if the Company seeks approval in the U.S.

If one of our product candidates is approved by the EMA and/or FDA, we do not have a sufficient number of personnel engaged as employees to conduct an effective marketing and commercialization strategy. We would need to build a larger team to execute wide-ranging commercialization efforts in the EU and or U.S. As a result, we must build an in-house team of seasoned commercialization professionals, or pursue a strategic partnership through a contractual arrangement with an organization with the appropriate expertise, or a combination of both. The cost-benefit of such an arrangement may not actualize profit and generate revenues on a short-term basis. If we entrusted commercialization to an outside organization, there may be any number of issues that arise that we cannot foresee. We may not find a suitable strategic partner or fail to identify appropriate candidates to hire onto a commercialization team, thus potentially limiting our ability to effectively commercialize our lead product candidate.

Because the results of earlier clinical trials are not necessarily predictive of future results, product candidates we advance into clinical trials, may not have favorable results in later clinical trials or receive regulatory approval.

Success in preclinical testing and early clinical trials does not ensure that later clinical trials will generate adequate data to demonstrate the efficacy and safety of an investigational drug. A number of companies in the pharmaceutical and biotechnology industries, including those with greater resources and experience, have suffered significant setbacks in clinical trials, even after seeing promising results in earlier clinical trials. Despite the results reported in earlier clinical trials for our lead product candidate, we do not know whether the clinical trials we are conducting, or

may conduct, will demonstrate adequate efficacy and safety to result in regulatory approval to market our lead product candidate or any of our other product candidates in any particular jurisdiction. Even if we believe that we have adequate data to support an application for regulatory approval to market our product candidates, the FDA or other comparable foreign regulatory authorities may not agree and could require us to conduct additional research studies, including late-stage clinical trials. If late-stage clinical trials do not produce favorable results, our ability to achieve regulatory approval for any of our product candidates may be adversely impacted.

If we are unable to enroll subjects in clinical trials, we will be unable to complete these trials on a timely basis.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of subjects to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, ability to obtain and maintain patient consents, risk that enrolled subjects will drop out before completion, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. Furthermore, we rely on Clinical Research Organizations (CRO's) and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and while we have agreements governing their committed activities, we have limited influence over their actual, day-to-day performance. We may experience delays in starting-up clinical trial sites in a timely manner, enrolling subjects in our trials, and may not be able to enroll a sufficient number of subjects to complete the trials.

If we experience delays in the completion or if there is termination of, any clinical trial of our lead product candidate or any future product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, and jeopardize our ability to commence product sales, which would impair our ability to generate revenues and may harm our business, results of operations, financial condition and cash flows and future prospects. In addition, many of the factors that could cause a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our lead product candidate or our other product candidates.

The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our lead product candidate or our other product candidates, our business may fail.

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable, but typically takes several years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities and any shifts in regulatory policy. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate, and it is possible that neither our lead product candidates nor any other product candidates we are developing or may discover, in-license or acquire and seek to develop in the future will ever obtain regulatory approval.

Our product candidates could fail to receive marketing approval from the FDA or a comparable foreign regulatory authority for many reasons, including but not limited to:

- disagreement over the design or implementation of our clinical trials;
- failure to demonstrate that a product candidate is safe and effective;
- failure of clinical trials to meet the level of statistical significance required for approval;
- failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- disagreement over our interpretation of data from preclinical studies or clinical trials;

- disagreement over whether to accept efficacy results from clinical trial sites outside the United States where the standard of care is potentially different from that in the United States;

- the insufficiency of data collected from clinical trials of our lead product candidate or our other product candidates to support the submission and filing of an NDA or other submission or to obtain regulatory approval;

- irreparable or critical compliance issues relating to our manufacturing and/clinical trial processes; or

- changes in the approval policies or regulations that render our preclinical and clinical data insufficient for approval.

The FDA or a comparable foreign regulatory authority may require more information, including additional preclinical or clinical data to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program altogether. Even if we do obtain regulatory approval, our lead product candidate or our other product candidates may be approved for fewer or more limited indications than we request, approved contingent on the performance of costly post-marketing clinical trials, or approved with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. In addition, if our lead product candidate or our other product candidate produces undesirable side effects or safety issues, the FDA may require the establishment of Risk Evaluation Mitigation Strategies, or REMS, or a comparable foreign regulatory authority may require the establishment of a similar strategy, that may, restrict distribution of our products and impose burdensome implementation requirements. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Even if we believe any completed, current or planned clinical trials are successful, the FDA or a comparable foreign regulatory authority may not agree that our completed clinical trials provide adequate data on the safety or efficacy of our lead product candidate or our other product candidates, permitting us to proceed to additional clinical trials. Approval by comparable foreign regulatory authorities does not ensure approval by the FDA and approval by one or more foreign regulatory authorities does not ensure approval by regulatory authorities in other countries or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative impact on the regulatory process in others. We may not be able to file for regulatory approvals, and even if we file we may not receive the necessary approvals to commercialize our products in any market.

Our lead product candidate or our other product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following any marketing approval.

Undesirable side effects caused by our lead product candidate or our other product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authority. If toxicities occur in our current or future clinical trials they could cause delay or even the discontinuation of further development of our lead product candidate or other product candidates, which would impair our ability to generate revenues and would have a material adverse effect our business, results of operations, financial condition and cash flows and future prospects. There can be no assurance that side effects from our lead product candidate or our other product candidates in future clinical trials or that side effects in general will not prompt the discontinued development or possible market approval of our lead product candidate or other product candidates. If serious side effects or other safety or toxicity issues are experienced in our clinical trials in the future, we may not receive approval to market our lead product candidate or any other product candidates, which could prevent us from ever generating revenues or achieving profitability. Results of our trials could reveal an unacceptably high severity and prevalence of side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Any of these occurrences may have a material adverse effect on our business, results of operations, financial condition and cash flows and future prospects.

Additionally, if our lead product candidate or any of our other product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such product, a number of potentially significant negative consequences could result, including:

- we may be forced to suspend marketing of such product;
- regulatory authorities may withdraw their approvals of such product;

- regulatory authorities may require additional warnings on the label that could diminish the usage or otherwise limit the commercial success of such product;

- the FDA or other regulatory bodies may issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings about such product;

- the FDA may require the establishment or modification of REMS or a comparable foreign regulatory authority may require the establishment or modification of a similar strategy that may, for instance, restrict distribution of our product and impose burdensome implementation requirements on us;

- we may be required to change the way the product is administered or conduct additional clinical trials;

- we could be sued and held liable for harm caused to subjects or patients;

- we may be subject to litigation or product liability claims; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved.

Even if our lead product candidate or our other product candidates receive regulatory approval, they may still face future development and regulatory difficulties.

Even if we obtain regulatory approval for our lead product candidate or another product candidate, it would be subject to ongoing requirements by the FDA and comparable foreign regulatory authorities governing the manufacture, quality control, further development, labeling, packaging, storage, distribution, safety surveillance, import, export, advertising, promotion, recordkeeping and reporting of safety and other post-market information. The safety profile of any product will continue to be closely monitored by the FDA and comparable foreign regulatory authorities after approval. If the FDA or comparable foreign regulatory authorities become aware of new safety information after approval of our lead product candidate or any other product candidate, they may require labeling changes or establishment of a REMS or similar strategy, impose significant restrictions on a product's indicated uses or marketing, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. For example, the label ultimately approved for our lead product candidate, if it achieves marketing approval, may include restrictions on use.

In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practices, or cGMP, and other regulations. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, our manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. If we, our product candidates or our manufacturing facilities for our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- impose restrictions on the marketing or manufacturing of the product candidates;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;

- require us or any future collaborator to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products, or require us to initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our lead product candidate or any other product candidates and generate revenue.

The FDA strictly regulates the advertising and promotion of drug products, and drug products may only be marketed or promoted for their FDA approved uses, consistent with the product's approved labeling. Advertising and promotion of any product candidate that obtains approval in the U.S., and is covered by federal insurance programs such as Medicare or Medicaid, will be heavily scrutinized by the FDA, the Department of Justice, (DOJ), the Office of Inspector General of the Department of Health and Human Services, (HHS), state attorneys general, members of Congress and the public. Violations, including promotion of our products for unapproved or off-label uses, are subject to enforcement letters, inquiries and investigations, and civil, criminal and/or administrative sanctions by the FDA and/or the DOJ. Additionally, advertising and promotion of, any product candidate that obtains approval outside of the U.S. will be heavily scrutinized by comparable foreign regulatory authorities.

In the U.S., engaging in impermissible promotion of our future products for off-label uses can also subject us to false claims litigation under federal and state statutes, which can lead to civil, criminal and/or administrative penalties and fines and corporate integrity agreements that materially restrict the manner in which we promote or distribute our drug products. The federal False Claims Act, allows any individual to bring a lawsuit against a pharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims, or causing to present such false or fraudulent claims, for payment by a federal program, such as Medicare or Medicaid. If the government prevails in the lawsuit, the individual may share in any fines or settlement funds. Since 2004, False Claims Act lawsuits against pharmaceutical companies have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements based on certain sales practices promoting off-label drug uses. This growth in litigation has increased the risk that a pharmaceutical company will have to defend a false claims action, pay settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations, and be excluded from Medicare, Medicaid and other federal and state healthcare programs. If we do not lawfully promote our approved products, we may become subject to such litigation and, if we are not successful in defending against such actions, those actions could have a material adverse effect on our business, results of operations, financial condition and cash flows and future prospects.

Existing government regulations may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our lead product candidate or any other product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and/or be subject to fines or enhanced government oversight and reporting obligations, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Failure to obtain regulatory approval in foreign jurisdictions would prevent our lead product candidate or any other product candidates from being marketed in those jurisdictions.

In order to market and sell our products in the European Union and many other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the U.S. generally includes all of the risks associated with obtaining FDA approval. Additionally, in many countries outside the U.S., it is required that the product be approved for reimbursement before the product can be effectively commercialized in that country. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. We may not obtain approvals from regulatory authorities outside the U.S. on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the U.S. does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. A failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market. If we are unable to obtain approval of our lead product candidate for any of our other product candidates by regulatory authorities in the European Union or another jurisdiction, the commercial prospects of that product candidate may be significantly diminished and our business prospects could decline.

Even if we are able to commercialize our lead product candidate or our other product candidates, the products may not receive coverage and adequate reimbursement from third-party payers, which could harm our business.

Our ability to commercialize any products successfully will depend, in part, on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government authorities, private health insurers, health maintenance organizations and third-party payers. Patients who are prescribed medications for the treatment of their conditions generally rely on third-party payers to reimburse all or part of the costs associated with their prescription drugs. Coverage and adequate reimbursement from government healthcare programs, such as Medicare and Medicaid, and private health insurers are critical to new product acceptance. Patients are unlikely to use our lead product candidate or our other product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. A primary trend in the US healthcare industry and elsewhere is cost containment. As a result, government authorities and other third-party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payers are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Third-party payers may also seek additional clinical evidence, beyond the data required to obtain marketing approval, demonstrating clinical benefits and value in specific patient populations before covering our products for those patients. We cannot be sure that coverage and adequate reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or are available only at limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, obtaining coverage does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sales and distribution. Interim reimbursement levels for new drugs, if applicable, may also be insufficient to cover our costs, and may only be temporary. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used. Reimbursement rates may also be based in part on existing reimbursement amounts for lower cost drugs or may be bundled into the payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payers and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. Coverage and reimbursement for drug products can differ significantly from payer to payer. As a result, the coverage and reimbursement determination process is often a time-consuming and costly process with no assurance that coverage and adequate reimbursement will be obtained or applied consistently. Third-party payers often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payers for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

We have never marketed a drug before, and if we are unable to establish an effective sales force and marketing infrastructure, or enter into acceptable third-party sales and marketing or licensing arrangements, we may be

unable to generate any revenue.

We do not currently have a comprehensive infrastructure for the sales, marketing and distribution of pharmaceutical drug products. The cost of establishing and maintaining such an infrastructure may exceed the cost-effectiveness of doing so. In order to market any products that may be approved by the FDA and comparable foreign regulatory authorities, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services for which we would incur substantial costs. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue and may not become profitable. We will be competing with many companies that have extensive and well-funded sales and marketing operations. Without an internal commercial organization or the support of a third party to perform sales and marketing functions, or a combination of both, we may be unable to compete successfully against more established companies.

Our lead product candidate and our other product candidates, if approved, may not achieve adequate market acceptance among physicians, patients, and healthcare payers and others in the medical community necessary for commercial success.

Even if we obtain regulatory approval for our lead product candidate or any of our other product candidates, such product(s) may not gain market acceptance among physicians, healthcare payers, patients or the medical community within the U.S. or globally. Our commercial success also depends on coverage and adequate reimbursement of our product candidates by third-party payers, including government payers, generally, which may be difficult or time-consuming to obtain, may be limited in scope and may not be obtained in all jurisdictions in which we may seek to market our products. Market acceptance of any of our product candidates for which we receive approval depends on a number of factors, including:

- the efficacy and safety of such product candidates as demonstrated in clinical trials;
- the clinical indications for which the product candidate is approved;
- acceptance by physicians and patients of the product candidate as a safe and effective treatment;
- the potential and perceived advantages of product candidates over alternative treatments;
- the safety of product candidates seen in a broader patient group, including a product candidate's use outside the approved indications;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA or other regulatory authorities;
- the timing of market introduction of our products as well as competitive products;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage and adequate reimbursement and pricing by third-party payers and government authorities;
- relative convenience and ease of administration;

- the effectiveness of our sales and marketing efforts and those of our collaborators; and

- unfavorable publicity relating to the product candidate or the Company.

If any of our product candidates are approved but fail to achieve market acceptance among physicians, patients, or healthcare payers, we will not be able to generate significant revenues, which would compromise our ability to become profitable.

Our research programs may not succeed.

In the last couple of years, XBiotech has positioned itself with a pipeline of potential drug candidates at all stages of development, from pre-clinical through Phase III clinical trial stage. Even though we have many drugs in development at this time, none of these research programs may succeed. There are several reasons why a drug program may fail:

- In the development stage, we may be unable to develop a therapy, which would mean us succeeding in isolating appropriate antibodies to reach the clinical trial stage

- Any partnerships for the development of antibodies could fail to produce results that would necessitate clinical trials

- We may not receive approval from regulatory bodies to move from early stage clinical trials to later stage clinical trials

- Even if we are able to move to later stage clinical trials, it may prove to be difficult to enroll patients into the studies according to schedule, or at all

- During the clinical trial, there could be unexpected serious adverse events causing severe injury or death in patients, requiring us to cease further enrollment or causing regulatory authorities to place the trial on clinical hold for an indefinite period of time

- If a clinical trial is completed, we may not have the appropriate personnel to submit a marketing application to regulatory authorities for approval, and to further respond to the variety of follow up questions that regulatory authorities may have during the review process

- Regulatory authorities may reject drug candidates for a variety of reasons, preventing us from proceeding with marketing and commercialization of approved products

- We may run out of the funds necessary to complete development for any of our potential drug candidates

Even an effective drug candidate might not be commercially successful.

Even if we ultimately succeed in creating a safe and effective drug, as determined by regulatory authorities, based on our current product pipeline, there is no assurance it would be commercially successful. Competitive products might become available faster or with lower costs or adverse risks to patients, resulting in few sales of any product developed by XBiotech. Occurrences of certain disease indications, such as those in our pipeline, might become sufficiently rare, or victims might be sufficiently impoverished, that commercial production is uneconomic Furthermore, we must have sufficient buy-in from patients and healthcare professionals to guarantee market exposure for our drug candidates. If the end-users are not reached with our products, then it will be difficult to generate revenue from our development efforts. And even though we could obtain regulatory approval for any of our drug candidates, it is not necessarily the case that government or third-party payers will decide to add our products to their respective prescription drug formularies for reimbursement, thus inhibiting the ability for our drug candidates to reach the target patient populations, and health care professionals serving those patients.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current lead product candidate or our other product candidates to treat any relevant indication(s). There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing our future product candidates. Some of these competitive products and therapies are based on scientific approaches that

are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

More established companies may have a competitive advantage over us due to their greater size, cash flows and institutional experience. Compared to us, many of our competitors may have significantly greater financial, technical and human resources. As a result of these factors, our competitors may obtain regulatory approval of their products before we do, which will limit our ability to develop or commercialize our lead product candidate or any of our other product candidates. In addition, many companies are developing new therapeutics to supplant or expand upon the standard of care for a number of diseases, as a result, we cannot predict what the standard of care will be as our product candidates progress through clinical development.

Our failure to successfully identify, acquire, develop and commercialize additional product candidates or approved products other than our lead product candidate could impair our ability to grow.

Although a substantial amount of our efforts will focus on the continued clinical testing and potential approval of our most advanced lead product candidate, a key element of our growth strategy is to acquire, develop and/or market additional products and product candidates. All of these potential product candidates remain in the discovery and clinical study stages. Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Because our internal research capabilities are limited, we may be dependent upon pharmaceutical and biotechnology companies, academic scientists and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify, select and acquire promising pharmaceutical product candidates and products. The process of proposing, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of product candidates and approved products. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. Any product candidate that we acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot provide assurance that any products that we develop or approved products that we acquire will be manufactured profitably or achieve market acceptance.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our lead product candidate and any other product candidates in clinical trials and will face an even greater risk if we commercially sell any products that we may develop. Product liability claims may be brought against us by subjects enrolled in our clinical trials, patients, healthcare providers or others using, administering or selling our products. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- termination of clinical trial sites or entire clinical trial programs;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to clinical trial subjects or patients;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize our product candidates.

We will obtain insurance coverage for products to include the sale of commercial products if we obtain marketing approval for our lead product candidate or our other product candidates, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us, particularly if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

We will need to expand our operations and grow the size of our organization in the future, and we may experience difficulties in managing this growth.

As of March 13, 2019, we had 56 employees. As our development and commercialization plans and strategies develop, or as a result of any future acquisitions, we will need additional managerial, operational, sales, marketing, scientific, and financial headcount and other resources. Our management, personnel and systems currently in place may not be adequate to support this future growth. Future growth would impose significant added responsibilities on members of management, including:

- managing our clinical trials effectively, which we anticipate potentially being conducted at numerous clinical sites on a global scale;
- identifying, recruiting, maintaining, motivating and integrating additional employees with the expertise and experience we will require;
- managing our internal development efforts effectively while complying with our contractual obligations to licensors, licensees, contractors and other third parties;
- managing additional relationships with various strategic partners, suppliers and other third parties;
- improving our managerial, development, operational and finance reporting systems and procedures; and
- expanding our facilities.

Our failure to accomplish any of these tasks could prevent us from successfully growing our Company.

We are highly dependent on our Chief Executive Officer.

Our future success depends in significant part on the continued service of our Chief Executive Officer, John Simard. Mr. Simard is critical to the strategic direction and overall management of our company as well as our research and development process. Although we have an employment agreement with Mr. Simard, it has no specific duration. The loss of Mr. Simard could adversely affect our business, financial condition and operating results.

We depend on key personnel to operate our business, and many members of our current management team are new. If we are unable to retain, attract and integrate qualified personnel, our ability to develop and successfully grow our business could be harmed.

In addition to the continued services of Mr. Simard, we believe that our future success is highly dependent on the contributions of our significant employees, as well as our ability to attract and retain highly skilled and experienced sales, research and development and other personnel in the United States and abroad. Some of our significant employees include our Medical Director, our Chief Scientific Officer, our Vice President of Quality Assurance, our Vice President of Quality Control, and our Vice President of Finance and Human Resources. Changes in our management team may be disruptive to our business.

All of our employees, including our Chief Executive Officer, are free to terminate their employment relationship with us at any time, subject to any applicable notice requirements, and their knowledge of our business and industry may be difficult to replace. If one or more of our executive officers or significant employees leaves, we may not be able to fully integrate new personnel or replicate the prior working relationships, and our operations could suffer. Qualified individuals with the breadth of skills and experience in the pharmaceutical industry that we require are in high demand, and we may incur significant costs to attract them. Many of the other pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Our failure to attract and retain key personnel could impede the achievement of our research, development and commercialization objectives.

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 in the U.S. and elsewhere, including, as a result of our leased laboratory space, 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.

Although we maintain insurance for employee injury to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological or hazardous materials. 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 may also result in substantial fines, penalties or other sanctions.

Business disruptions could seriously harm our future revenues and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. We do not carry insurance for all categories of risk that our business may encounter. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-parties to supply various items which are critical for producing our product candidates. Our ability to produce clinical supplies of product candidates could be disrupted, if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. The ultimate impact on us, our significant suppliers and our general infrastructure of being consolidated in certain geographical areas is unknown, but our operations and financial condition could suffer in the event of a major earthquake, fire or other natural disaster. Further, any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our business, results of operations, financial condition and cash flows from future prospects.

Risks Related to Intellectual Property

If we are unable to obtain or protect intellectual property rights, our competitive position could be harmed.

We depend on our ability to protect our proprietary technology. We rely on trade secret, patent, copyright and trademark laws, and confidentiality, licensing and other agreements with employees and third parties, all of which offer only limited protection. Our commercial success will depend in large part on our ability to obtain and maintain patent protection in the U.S. and other countries with respect to our proprietary technology and products. Where we deem appropriate, we seek to protect our proprietary position by filing patent applications in the U.S. and abroad related to our novel technologies and products that are important to our business. The patent positions of biotechnology and pharmaceutical companies generally are highly uncertain, involve complex legal and factual questions and have in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patents, including those patent rights licensed to us by third parties, are highly uncertain.

The steps we have taken to protect our proprietary rights may not be adequate to preclude misappropriation of our proprietary information or infringement of our intellectual property rights, both inside and outside the U.S. The rights already granted under any of our currently issued patents and those that may be granted under future issued patents may not provide us with the proprietary protection or competitive advantages we are seeking. If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection obtained is not sufficient, our competitors could develop and commercialize technology and products similar or superior to ours, and our ability to successfully commercialize our technology and products may be adversely affected.

With respect to patent rights, we do not know whether our pending patent applications for any of our technologies or product candidates will result in the issuance of patents that protect such technologies or products candidates, or if any of our issued patents will effectively prevent others from commercializing competitive technologies and products. Our pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Further, the examination process may require us to narrow the claims for our pending patent applications, which may limit the scope of patent protection that may be obtained if these applications issue. Because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, issued patents that we own or have licensed from third parties may be challenged in the courts or patent offices in the U.S. and abroad. Such challenges may result in the loss of patent protection, the narrowing of claims in such patents or the invalidity or unenforceability of such patents, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection for our technology and products. Protecting against the unauthorized use of our patented technology, trademarks and other intellectual property rights is expensive, difficult and, in some cases, not be possible. In some cases, it may be difficult or impossible to detect third-party infringement or misappropriation of our intellectual property rights, even in relation to issued patent claims, and proving any such infringement may be even more difficult.

Intellectual property rights do not necessarily address all potential threats to any competitive advantage we may have.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- Others may be able to make compounds that are the same as or similar to our lead product candidate or our future product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.

- We might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed.

- We or any of our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions.

- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.

It is possible that our pending patent applications will not lead to issued patents.

- Issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.

- Our competitors might conduct research and development activities in the U.S. and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.

- We may not develop additional proprietary technologies that are patentable.

- The patents of others may have an adverse effect on our business.

Our technology may be found to infringe upon third-party intellectual property rights.

Third parties, may in the future, assert claims or initiate litigation related to their patent, copyright, trademark and other intellectual property rights in technology that is important to us. The asserted claims and/or litigation could include claims against us, our licensors or our suppliers alleging infringement of intellectual property rights with respect to our products or components of those products. Regardless of the merit of the claims, they could be time consuming, result in costly litigation and diversion of technical and management personnel, or require us to develop a non-infringing technology or enter into license agreements. We cannot assure you that licenses will be available on acceptable terms, if at all. Furthermore, because of the potential for significant damage awards, which are not necessarily predictable, it is not unusual to find even arguably unmeritorious claims resulting in large settlements. If any infringement or other intellectual property claim made against us by any third party is successful, or if we fail to develop non-infringing technology or license the proprietary rights on commercially reasonable terms and conditions, our business, operating results and financial condition could be materially and adversely affected.

If our products, methods, processes and other technologies infringe upon the proprietary rights of other parties, we could incur substantial costs and we may have to:

- obtain licenses, which may not be available on commercially reasonable terms, if at all;
- abandon an infringing drug or therapy candidate;
- redesign our products or processes to avoid infringement;
- stop using the subject matter claimed in the patents held by others;
- pay damages; or
- defend litigation or administrative proceedings which may be costly whether we win or lose, and which could result in a substantial diversion of our financial and management resources.

We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property, including patent rights that are important or necessary to the development of our products. It may be necessary for us to use the patented or proprietary technology of a third party to manufacture, or otherwise commercialize, our own technology or products, in which case we would be required to obtain a license from such third party. Licensing such intellectual property may not be available or may not be available on commercially reasonable terms, which could have a material adverse effect on our business and financial condition. Several companies in our industry have licensed U.S. patent nos. 6,331,415 and 7,923,221. These patents appear to relate to antibody production techniques, and have been reported to remain in force until December 18, 2018, unless determined to be invalid or unenforceable before that date. Should a license to these patents be necessary, we cannot be certain that such a license would be available on commercially reasonable terms.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and product candidates, 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. Despite these efforts, 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 inside and outside of the U.S. are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Owning Shares of Our Common Stock

Our share price may be volatile, which could subject us to securities class action lawsuits and prevent you from being able to sell your shares at or above the price at which you purchased them.

Our stock could be subject to wide fluctuations in response to many risk factors listed in this section, and others beyond our control, including:

- results of our clinical trials;
- results of clinical trials of our competitors' products;
- regulatory actions with respect to our products or our competitors' products;
- actual or anticipated fluctuations in our financial condition and operating results;
- actual or anticipated changes in our growth rate relative to our competitors;
- actual or anticipated fluctuations in our competitors' operating results or changes in their growth rate;
- competition from existing products or new products that may emerge;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- issuance of new or updated research or reports by securities analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- delisting of the Company's security from the exchange on which it trades due to the Company not being in compliance with the listing requirements of the exchange;

- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- additions or departures of key management or scientific personnel;
- disputes or other developments related to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other shareholders;
- market conditions for biopharmaceutical stocks in general; and
- general economic and market conditions.

Furthermore, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies. These fluctuations often have been unrelated or disproportionate to the operating performance of those companies. These broad market and industry fluctuations, as well as general economic, political and market conditions such as recessions, interest rate changes or international currency fluctuations, may negatively impact the market price of shares of our common stock. In addition, such fluctuations could subject us to securities class action litigation, which could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business. If the market price of shares of our common stock does not exceed your buying price, you may not realize any return on your investment in us and may lose some or all of your investment.

Insiders continue to have substantial control over our company since our initial public offering in April 2015 and could delay or prevent a change in corporate control.

As of December 31, 2018, our directors, executive officers and principal shareholders, together with their affiliates, beneficially own, in the aggregate, at least 10 million shares or approximately 28% of our outstanding common stock, and could own approximately 12.6 million shares or approximately 35% of our outstanding common stock if they fully exercise their outstanding stock options. As a result, these shareholders, if acting together, have the ability to determine the outcome of matters submitted to our shareholders for approval, including the election of directors and any merger, consolidation or sale of all or substantially all of our assets. In addition, these persons, acting together, have the ability to control the management and affairs of the Company. Accordingly, this concentration of ownership may harm the market price of our common stock by:

- delaying, deferring or preventing a change in control of the Company;
- impeding a merger, consolidation, takeover or other business combination involving the Company; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of the Company.

We have broad discretion in the use of the net proceeds from our initial public offering in April 2015 and subsequent offerings and may not use them effectively.

We intend to continue to allocate the net proceeds that we received from the April 2015 offering and subsequent offerings as described below “Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities—Use of Proceeds from IPO.” However, our management will have broad discretion in the actual application of the net proceeds, and we may elect to allocate proceeds differently from that described in “Use of Proceeds” if we believe it would be in our best interests to do so. Our shareholders may not agree with the manner in which our management chooses to allocate and spend the net proceeds. The failure by our management to apply these funds effectively could have a material adverse effect on our business. We may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

Provisions in our charter documents under Canadian law could make an acquisition of us, which may be beneficial to our shareholders, more difficult.

Our authorized preferred capital stock is available for issuance from time to time at the discretion of our Board of Directors, without shareholder approval. Our Articles of Incorporation (“Articles”) grant our Board of Directors the

authority, subject to the corporate law of British Columbia, to determine or alter the special rights and restrictions granted to or imposed on any wholly unissued series of preferred shares, and such rights may be superior to those of our common stock.

Limitations on the ability to acquire and hold our common stock may be imposed by the Competition Act (Canada). This legislation permits the Commissioner of Competition of Canada to review any acquisition of a significant interest in us. This legislation grants the Commissioner jurisdiction to challenge such an acquisition before the Canadian Competition Tribunal if the Commissioner believes that it would, or would be likely to, result in a substantial lessening or prevention of competition in any market in Canada. The Investment Canada Act (Canada) subjects an acquisition of control of a company by a non-Canadian to government review if the value of our assets as calculated pursuant to the legislation exceeds a threshold amount. A reviewable acquisition may not proceed unless the relevant minister is satisfied that the investment is likely to be a net benefit to Canada.

Any of the foregoing could prevent or delay a change of control and may deprive or limit strategic opportunities for our shareholders to sell their shares and/or affect the market price of our shares.

We may be a passive foreign investment company for US tax purposes which may negatively affect US investors.

For US federal income taxation purposes, we will be a passive foreign investment company (PFIC) if in any taxable year either: (a) 75% or more of our gross income consists of passive income; or (b) 50% or more of the value of our assets is attributable to assets that produce, or are held for the production of, passive income. If we meet either test, our shares held by a US person in that year will be PFIC shares for that year and all subsequent years in which they are held by that person. In previous taxable years, our gross income consisted mostly of interest, and we have been considered a PFIC. We may also be a PFIC in future taxable years. Gain realized by a US investor from the sale of PFIC shares is taxed as ordinary income, as opposed to a capital gain, and subject to an interest charge unless the US person timely made certain tax elections.

We are governed by the corporate laws in British Columbia, Canada which in some cases have a different effect on shareholders than the corporate laws in Delaware, United States.

The material differences between the BCBCA as compared to the Delaware General Corporation Law (DGCL) which may be of most interest to shareholders include the following: (i) for material corporate transactions (i.e. mergers and amalgamations, other extraordinary corporate transactions, amendments to our Articles) the BCBCA generally requires two-thirds majority vote by shareholders, whereas DGCL generally only requires a majority vote of shareholders; (ii) the quorum for shareholders meetings is not prescribed under the BCBCA and is only two persons representing 20% of the issued shares under our Articles, whereas under DGCL, quorum requires a minimum of one-third of the shares entitled to vote to be present and companies' certificates of incorporation frequently require a higher percentage to be present; (iii) under the BCBCA, a holder of 5% or more of our common stock can requisition a special meeting at which any matters that can be voted on at our annual meeting can be considered, whereas the DGCL does not give this right; (iv) our Articles require two-thirds majority vote by shareholders to pass a resolution for one or more directors to be removed, whereas DGCL only requires the affirmative vote of a majority of the shareholders; however, many public company charters limit removal of directors to a removal for cause; and (v) our Articles may be amended by resolution of our directors to alter our authorized share structure, including to consolidate or subdivide any of our shares, whereas under DGCL, a majority vote by shareholders is generally required to amend a corporation's certificate of incorporation and a separate class vote may be required to authorize alterations to a corporation's authorized share structure. We cannot predict if investors will find our common stock less attractive because of these material differences. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our share price may be more volatile.

Future sales, or the possibility of future sales, of a substantial number of our common stock could adversely affect the price of the shares and dilute shareholders.

Future sales of a substantial number of our common stock, or the perception that such sales will occur, could cause a decline in the market price of our common stock. As of December 31, 2018, we had 35,899,772 common stock outstanding.

In the future, we may issue additional common stock or other equity or debt securities convertible into common stock in connection with a financing, acquisition, litigation settlement, employee arrangements or otherwise. Any such issuance could result in substantial dilution to our existing shareholders and could cause our common share price to decline.

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012 (JOBS Act) and we intend to take advantage of reduced disclosure and governance requirements applicable to emerging growth companies, which could result in our common stock being less attractive to investors and adversely affect the market price of our common stock or make it more difficult to raise capital as and when we need it.

We are an "emerging growth company" as that term is used in the JOBS Act, and we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved and exemptions from any rules that the Public Company Accounting Oversight Board may adopt requiring mandatory audit firm rotation or a supplement to the auditor's report on the financial statements. We currently intend to take advantage of some, but not all, of the reduced regulatory and reporting requirements that will be available to us under the JOBS Act, so long as we qualify as an "emerging growth company." For example, so long as we qualify as an "emerging growth company," we may elect not to provide you with certain information, including certain financial information and certain information regarding compensation of our executive officers, that we would otherwise have been required to provide in filings we make with the Securities and Exchange Commission (SEC) which may make it more difficult for investors and securities analysts to evaluate the Company.

We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company, which in certain circumstances could be for up to five years.

Due to the exemptions from various reporting requirements provided to us as an "emerging growth company" we may be less attractive to investors and it may be difficult for us to raise additional capital as and when we need it. Investors may be unable to compare our business with other companies in our industry if they believe that our financial statements are not as transparent as other companies in our industry. If we are unable to raise additional capital as and when we need it, our business, results of operations, financial condition and cash flows and future prospects may be materially and adversely affected.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock.

We will be required to disclose changes made in our internal controls and procedures on a quarterly basis and our management will be required to assess the effectiveness of these controls annually. However, for as long as we are an "emerging growth company" under the JOBS Act, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. We could be an "emerging growth company" for up to five years. An independent assessment of the effectiveness of our internal controls could detect problems that our management's assessment might not.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 2. PROPERTIES

Our operations are based primarily in Austin, Texas. On January 12, 2008, the Company entered a lease agreement to lease its facility in Austin, Texas, USA. On September 15, 2010, the Company entered into a second lease agreement to lease additional space in Austin, Texas, USA. On March 20, 2013, the Company extended the lease for another 21 months with the same terms and rental rates as the current lease. To accommodate future potential larger-scale commercial manufacturing needs, the Company purchased 48 acres of industrial-zoned property located five miles from Austin's central business district. In 2016 construction of a new manufacturing facility on this property was completed. The Company continues to prepare this manufacturing facility to produce registration batches of product in the event of potential commercialization in the future.

ITEM 3. LEGAL PROCEEDINGS

On October 23, 2018, the honorable Judge Dustin M. Howell of the 459th Travis County District Court has issued a letter ruling granting the Company's Motion to Dismiss the securities class action complaint brought against XBiotech (Case D-1-GN-17-003063). The District Court has directed the parties to prepare a formal order memorializing the ruling. Two federal cases were previously filed in the U.S. District Court for the Western District of Texas, but both of those cases have also been dismissed. Therefore, there no longer remains any litigation involving the Company.

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.

Market Information

Our common stock began trading on the NASDAQ Global Select Market on April 15, 2015 under the symbol "XBIT." Prior to that time, there was no established public trading market for our common stock. The following table sets forth the high and low close prices per share for our common stock on the NASDAQ Global Select Market for the periods indicated:

Year Ended December 31, 2015:	High	Low
Second Quarter (commencing April 15, 2015)	$31.50	$17.63
Third Quarter	$20.71	$13.87
Fourth Quarter	$15.77	$7.47

Year Ended December 31, 2016:	High	Low
First Quarter	$10.44	$6.99
Second Quarter	$20.92	$9.46
Third Quarter	$24.90	$12.81
Fourth Quarter	$16.90	$8.90

Year Ended December 31, 2017:	High	Low
First Quarter	$19.20	$9.44
Second Quarter	$17.17	$3.20
Third Quarter	$5.58	$4.14
Fourth Quarter	$4.66	$3.90

Year Ended December 31, 2018:	High	Low
First Quarter	$5.35	$3.92
Second Quarter	$5.13	$4.04
Third Quarter	$4.69	$2.31
Fourth Quarter	$6.27	$3.22

Holders of record

As of March 6, 2019, there were 1,835 holders of record of our common stock. Because many of our shares are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of beneficial holders represented by these record holders.

Dividends

We have never paid or declared any cash dividends on our common stock. We currently intend to retain any earnings for future growth and, therefore, do not expect to pay cash dividends in the foreseeable future.

Use of Proceeds from IPO

On April 14, 2015, our registration statement on Form S-1 (File No. 333-201813) was declared effective by the Securities and Exchange Commission for our initial public offering pursuant to which we sold an aggregate of 4,000,000 shares of our common stock to investors at a price of $19.00 per share. W.R. Hambrecht + Co., Inc. acted as the sole underwriter. The offering commenced as of April 14, 2015 and did not terminate before all of the securities registered in the registration statement were sold. On April 17, 2015, we closed the sale of such shares, resulting in net proceeds to us of approximately $70.6 million after deducting underwriting discounts and commissions of $3.8 million and other offering expenses of approximately $1.6 million. No payments were made by us to directors, officers or persons owning ten percent or more of our common stock or to their associates, or to our affiliates.

ITEM 6. SELECTED FINANCIAL DATA

The following selected consolidated financial data for each of the five years ended December 31, 2017 are derived from our audited consolidated financial statements. The selected consolidated financial data set forth below should be read in conjunction with “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and the financial statements, and the related Notes, included elsewhere in this annual report on Form 10-K. Historical results are not necessarily indicative of future results. Set forth below are our selected consolidated financial data (in thousands, except share and per share amounts)

	Year Ended December 31,				
	2018	2017	2016	2015	2014
Statement of Operations Data					
Operating expenses:					
Research and development	$15,725	$26,424	$42,486	$31,310	$14,329
General and administrative	5,269	7,635	10,277	6,200	7,449
Total operating expenses	20,994	34,059	52,763	37,510	21,778
Loss from operations	(20,994)	(34,059)	(52,763)	(37,510)	(21,778)
Other income (loss):					
Interest income	400	354	49	-	1
Foreign exchange gain (loss)	(548)	555	(47)	6	53
Other income	4	-	-	21	-
Total other income (loss):	(144)	909	2	27	54
Net loss	(21,138)	(33,150)	(52,761)	(37,483)	(21,724)
Net loss per common share—basic and diluted	(0.59)	(0.95)	(1.63)	(1.22)	(0.90)
Weighted average number of common shares—basic and diluted	35,804,304	34,875,814	32,403,391	30,801,994	24,162,700

	As of December 31,				
	2018	2017	2016	2015	2014

Balance sheet data					
Cash and cash equivalents	$15,823	$31,768	$34,324	$91,051	$57,329
Working capital	14,072	30,540	28,967	86,750	54,917
Total assets	44,345	62,972	67,050	109,358	62,177
Total shareholders’ equity	41,398	60,162	59,064	103,050	59,030

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

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes thereto included elsewhere in this annual report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this annual report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this annual report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

XBiotech Inc. ("XBiotech" or the "Company) is a pre-market biopharmaceutical company engaged in discovering and developing True Human™ monoclonal antibodies for treating a variety of diseases. True Human™ monoclonal antibodies are those which occur naturally in human beings—as opposed to being derived from animal immunization or otherwise engineered. We believe that naturally occurring monoclonal antibodies have the potential to be safer and more effective than their non-naturally occurring counterparts. XBiotech is focused on developing its True Human™ pipeline and manufacturing system.

We have never been profitable and, as of December 31, 2018, we had an accumulated deficit of $237.7 million. We had a net loss of $21.1 million for the year ended December 31, 2018, compared to $33.2 million for the year ended December 31, 2017, and $52.8 million for the year ended December 31, 2016. We expect to incur significant and increasing operating losses for the foreseeable future as we advance our drug candidates from discovery through preclinical testing and clinical trials and seek regulatory approval and eventual commercialization. In addition to these increasing research and development expenses, we expect general and administrative costs to increase as we continue to operate as a public company. We will need to generate significant revenues to achieve profitability, and we may never do so. As of December 31, 2018, we had 53 employees.

Revenues

To date, we have not generated any revenue. Our ability to generate revenue and become profitable depends on our ability to successfully commercialize our lead product candidate or any other product candidate we may advance in the future.

Research and Development Expenses

Research and development expense consists of expenses incurred in connection with identifying and developing our drug candidates. These expenses consist primarily of salaries and related expenses, stock-based compensation, the purchase of equipment, laboratory and manufacturing supplies, facility costs, costs for preclinical and clinical research, development of quality control systems, quality assurance programs and manufacturing processes. We charge all research and development expenses to operating expenses as incurred.

Clinical development timelines, likelihood of success and total costs vary widely. We do not currently track our internal research and development costs or our personnel and related costs on an individual drug candidate basis. We use our research and development resources, including employees and our drug discovery technology, across multiple drug development programs. As a result, we cannot state precisely the costs incurred for each of our research and development programs or our clinical and preclinical drug candidates. From inception through December 31, 2018, we have recorded total research and development expenses, including share-based compensation, of $185.7 million. Our total research and development expenses for the year ended December 31, 2018 was $15.7 million, compared to $26.4 million the year ended December 31, 2017, and $42.5 million for the year ended December 31, 2016. Share-based compensation accounted for $0.7 million for the year ended December 31, 2018, $0.4 million for the year ended December 31, 2017 and $2.1 million for the year ended December 31, 2016.

Research and development expenses as a percentage of total operating expenses was 75% for the year ended December 31, 2018, 78% for the year ended December 31, 2017, and 81% for the year ended December 31, 2016. The percentages, *excluding* stock-based compensation, were 78% for the year ended December 31, 2018, 82% for the year ended December 31, 2017 and 86% for the year ended December 31, 2016.

Our clinical development costs decreased with the completion and close-out of large, phase 3 studies that were on-going in previous years.

The clinical research and development costs may increase going forward as we evaluate our pipeline and plan potential new studies.

Based on the results of our preclinical studies, we anticipate that we will select drug candidates and research projects for further development on an ongoing basis in response to their preclinical and clinical success and commercial potential. For research and development candidates in early stages of development, it is premature to estimate when material net cash inflows from these projects might occur.

General and Administrative Expenses

General and administrative expense consists primarily of salaries and related expenses for personnel in administrative, finance, business development and human resource functions, as well as the legal costs of pursuing patent protection of our intellectual property and patent filing and maintenance expenses, share–based compensation, and professional fees for legal services. Our total general and administration expenses was $5.3 million for the year ended December 31, 2018, $7.6 million for the year ended December 31, 2017 and $10.3 million for the year ended December 31, 2016. Share-based compensation accounted for $1.0 million for the year ended December 31, 2018, $2.1 million for the year ended December 31, 2017 and $3.5 million for the year ended December 31, 2016.

Critical Accounting Policies

Our Management’s Discussion and Analysis of Financial Condition and Results of Operations is based on our financial statements, which have been prepared in conformity with generally accepted accounting principles in the United States (US GAAP). The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and expenses incurred during the reported periods.

We base estimates on our historical experience, known trends and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in the notes to our financial statements appearing in this Annual Report on Form 10-K, we believe that the following accounting policies are the most critical to understanding and evaluating our reported financial results.

Stock-Based Compensation

Stock-based awards are measured at fair value at each grant date. We recognize stock-based compensation expenses ratably over the requisite service period of the option award.

Determination of the Fair Value of Stock-Based Compensation Grants

The determination of the fair value of stock-based compensation arrangements is affected by a number of variables, including estimates of the expected stock price volatility, risk-free interest rate and the expected life of the award. We value stock options using the Black-Scholes option-pricing model, which was developed for use in estimating the fair value of traded options that are fully transferable and have no vesting restrictions. Black-Scholes option-pricing model and other option valuation models require the input of highly subjective assumptions, including the expected stock price volatility. If we made different assumptions, our stock-based compensation expenses, net loss, and net loss per common share could be significantly different. Prior to our initial public offering in April 2015, we issued common stock for cash consideration to investors. We believe that such transactions represent the best evidence of fair value of our common stock. Therefore, we used the sales price of our common stock prior to our initial public offering (IPO) in April 2015 as the fair value of our common stock. After our IPO, we determine that the fair value of common stock is equal to the closing price of the Company’s common stock as reported by NASDAQ on the option grant date.

The following summarizes the assumptions used for estimating the fair value of stock options granted during the periods indicated:

	Year Ended December 31,		
	2018	2017	2016
Weighted-average grant date fair value per share	$4.38	$4.85	$7.29
Expected volatility	67% - 80%	65% - 67%	65% - 70%
Risk-free interest rate	2.38% - 3.12%	1.83% - 2.41%	1.09% - 2.44%
Expected life (in years)	1 – 10	5.38 – 10	5 – 10
Dividend yield	–	–	–

We have assumed no dividend yield because we do not expect to pay dividends in the foreseeable future, which is consistent with our past practice. The risk-free interest rate assumption is based on observed interest rates for U.S. Treasury securities with maturities consistent with the expected life of our stock options. The expected life represents the period of time the stock options are expected to be outstanding and is based on the simplified method when the stock option includes “plain vanilla” terms. Under the simplified method, the expected life of an option is presumed to be the midpoint between the vesting date and the end of the agreement term. We used the simplified method due to the lack of sufficient historical exercise data to provide a reasonable basis upon which to otherwise estimate the expected life of the stock options. For stock options that did not include “plain vanilla” terms, we used the contractual life of the stock option as the expected life. Such stock options consisted primarily of options issued to our board of directors that were immediately vested at issuance. Expected volatility is based on historical volatilities for publicly traded stock of comparable companies over the estimated expected life of the stock options. Due to the adoption of ASU No. 2016-09, “Stock Compensation,”, effective January 1, 2017, the Company accounts for forfeitures as they occur rather than on an estimated basis.

Results of Operations

Revenue

We did not record any revenue during the years ended December 31, 2018, 2017 and 2016.

Expenses

Research and Development

Research and Development costs are summarized as follows (in thousands):

	Year Ended December 31,		Increase	% Increase	Year Ended December 31,		Increase	% Increase
	2018	2017	(Decrease)	(Decrease)	2017	2016	(Decrease)	(Decrease)
Salaries and related expenses	$4,178	$6,327	$(2,149)	(34%)	$6,327	$8,402	$(2,075)	(25%)
Laboratory and manufacturing supplies	2,027	2,915	(888)	(30%)	2,915	7,458	(4,543)	(61%)
Clinical trials and sponsored research	2,087	11,129	(9,042)	(81%)	11,129	19,792	(8,663)	(44%)
Stock-based compensation	696	413	283	69%	413	2,095	(1,682)	(80%)
Other	6,737	5,640	1,097	19%	5,640	4,739	901	19%
Total	$15,725	$26,424	$(10,699)	(40%)	$26,424	$42,486	$(16,062)	(38%)

We do not currently track our internal research and development costs or our personnel and related costs on an individual drug candidate basis. We use our research and development resources, including employees and our drug discovery technology, across multiple drug development programs. As a result, we cannot state precisely the costs incurred for each of our research and development programs or our clinical and preclinical drug candidates.

Research and development expenses decreased by 40% to $15.7 million for year ended December 31, 2018 compared to $26.4 million for the year ended December 31, 2017. The decrease in research and development expenses for the year ended December 31, 2018 compared to the year ended December 31, 2017 was due to a $9 million decrease of clinical trial activities and sponsored research expenses. In addition, there was a decrease in laboratory and manufacturing supplies expense due to the decrease of manufacturing. The decrease is also due to $2.1 million of salaries and related expenses in 2018. We had an offsetting increase in stock–based compensation due to the issuance of stock options to employees.

Research and development expenses decreased by 38% to $26.4 million for year ended December 31, 2017 compared to $42.5 million for the year ended December 31, 2016. The decrease in research and development expenses for the year ended December 31, 2017 compared to the year ended December 31, 2016 was due to a $8.7 million decrease of clinical trial activities and sponsored research expense, related to the completion of all active trials. In addition, there was a decrease in laboratory and manufacturing supplies expense due to a reduction in clinical trial drug manufacturing. Salary and related expenses also decreased due to the reduction of our research and development workforce from 96 to 44. The decrease of stock-based compensation expenses was mainly due to the forfeiture of terminated employees' stock options.

General and Administrative

General and administrative costs are summarized as follows (in thousands):

	Year Ended December 31,		Increase	% Increase	Year Ended December 31,		Increase	% Increase
	2018	2017	(Decrease)	(Decrease)	2017	2016	(Decrease)	(Decrease)
Salaries and related expenses	$							