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Registration Statement No. 333-201813

Free Writing Prospectus

XBiotech Inc. ("XBiotech") has filed a registration statement (including a preliminary prospectus) with the Securities and Exchange Commission, or SEC, for the offering to which this communication relates. Before you invest, you should read the prospectus in that registration statement and other documents XBiotech Inc. has filed with the SEC for more complete information about XBiotech Inc. and this offering. You may get these documents for free by visiting EDGAR on the SEC Web site at www.sec.gov. Alternatively, we or WR Hambrecht + Co will arrange to send you the prospectus if you request it by calling WR Hambrecht + Co toll-free 1-800-673-6476.

On March 27, 2015, W.R. Hambrecht + Co made available on its website a research report prepared by Crystal Research Associates. The research report can be viewed at www.wrhambrecht.com.

The research report contains forward-looking statements that involve substantial risks and uncertainties. In some cases, you can identify forward-looking statements by the following words: "believe," "may," "would," "will," "estimate," "continue," "anticipate," "intend," "expect," "predict," "potential" and similar expressions, although not all forward-looking statements contain these words. These statements related to future events or XBiotech's future growth, financial performance or condition and involve known and unknown risks, uncertainties and other factors that could cause actual results to differ materially from those expressed or implied by these forward-looking statements. These risks, uncertainties and other factors are described more fully in XBiotech's most recent prospectus filed with the SEC, particularly in the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." In light of the significant uncertainties in the forward-looking statements, you should not place undue reliance on these statements or regard these statements as a representation or warranty by any person that XBiotech will achieve its objectives and plans in any specified timeframe, or at all. The forward-looking statements contained in this research report represent estimates and assumptions only as of the date of this research report and, except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this research report.

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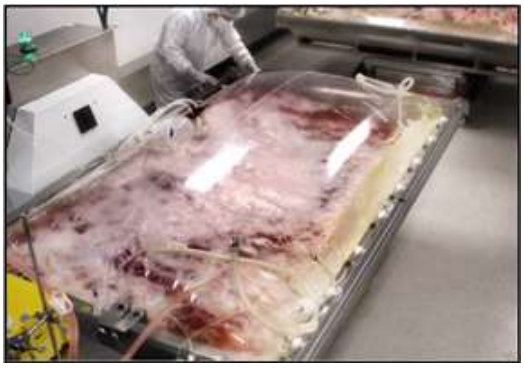
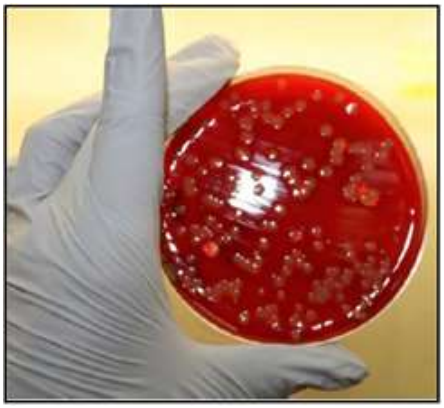
XBiotech's Novel 1,000-Liter Bioreactor for Antibody Production



Screening Bacteria Colonies for MRSA at XBiotech's Laboratories



Company Description

XBiotech Inc. ("XBiotech" or "the Company") is engaged in discovering, developing, and translating natural human immunity into novel therapeutic antibody products. These "true human" **antibodies†** may enable faster development of potentially safer, more efficacious antibody therapies. Moreover, XBiotech has developed a streamlined approach to biologics manufacturing that is believed to offer lower development costs, shorter lead times, greater reliability, and more flexible production than conventional techniques. The Company's product development centers on the use of its True Human™ antibodies, which are cloned directly from a human gene, as opposed to using antibodies that are engineered or derived from animal immunization procedures. XBiotech's lead True Human™ antibody therapy, Xilonix™, is currently in Phase III clinical trials for advanced colorectal cancer in both the U.S. and Europe. Proof-of-concept for the Company's True Human™ therapeutic has also been established with favorable data to date in non-small-cell lung cancer (NSCLC), vascular disease, **pyoderma gangrenosum (PG)**, acne, psoriasis, and type 2 diabetes. Additionally, XBiotech recently filed an IND for a Phase I/II study to assess its True Human™ antibody therapy for the treatment of *Staphylococcus aureus* infections, which is currently on clinical hold, and has begun using the True Human™ technology to develop a therapy for Ebola virus infection. The Company recently received blood donations from Ebola-recovered patients, which contain high levels of anti-Ebola antibodies. XBiotech is a Canadian company headquartered in the U.S., with wholly owned subsidiaries in the U.S., Switzerland, Germany, and Japan.

Key Points

- XBiotech addresses a growing market for targeted immunotherapies. By 2019, global sales of **monoclonal antibodies (MAbs)** are forecast to top $122 billion, up from $63 billion in 2013. Moreover, five of the 10 bestselling biotechnology drugs in the U.S. during 2013 were therapeutic MAbs, each with annual sales over $6 billion.
- By using human-derived genes, True Human™ antibodies are not likely to be detected by the immune system as foreign, and thus, are expected to offer improved safety, efficacy, and commercial value versus existing antibody therapeutics, including those currently referred to as "fully human."
- XBiotech holds 39 issued and over 100 pending patent applications in various global jurisdictions. Its lead product candidate has intellectual property coverage in the U.S., Japan, Europe, and 14 other countries.
- XBiotech has skilled leadership, including CEO John Simard, who was founder of CTL ImmunoTherapies and AlleCure, and a Board of Directors that includes the former CEO/chairman of Novartis, Dr. Vasella, who has been ranked among Europe's and the world's most influential leaders by both *Time* and the *Financial Times*; the former EVP of operations at Amgen, Dr. Bonanni; and Thorpe McKenzie, co-founder of Tiger Management (TIGER fund).
- As of Dec. 31, 2014, XBiotech reported cash of ~$57.3 million. The Company has raised over $130 million in private rounds to date, and filed an S-1 registration statement with the SEC in Feb. 2015.

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Executive Overview

XBiotech Inc. (“XBiotech” or “the Company”) is a biotechnology company focused on translating natural human immunity into new medicines that have the potential to be more effective, safer, and less costly than conventional therapeutic approaches. The Company’s most advanced clinical program targets colorectal cancer for which two Phase III studies are currently underway: one in the U.S. for advanced refractory colorectal cancer and another in Europe for symptomatic colorectal cancer. XBiotech also has a pipeline of antibody therapeutics at the clinical stage for indications including non-small-cell lung cancer (NSCLC), type 2 diabetes, vascular disease (**restenosis**), pyoderma gangrenosum (PG), acne, psoriasis, and methicillin-resistant *Staphylococcus aureus* (MRSA).

Need for Next-Generation, Human Antibodies

A plethora of antibody-based therapeutics have emerged in recent years due to the medically beneficial properties of antibodies—in particular, their ability to selectively target certain diseases in a potentially safer and more effective manner than small molecule drugs. The key to an antibody’s effectiveness at fighting off an illness is in its ability to bind to a target antigen with a high degree of specificity and with high affinity—meaning each antibody binds only to one particular type of **antigen**. However, people do not innately possess an antibody for every possible foreign pathogen, virus, bacteria, allergen, and so on that enters the body. Rather, as part of antibody-mediated immunity, the body’s circulating **B-cells** go through a process of **somatic hypermutation (SHM)**, or genetic rearrangement, after antigen recognition and co-stimulation by helper T-cells. Through this natural process, an enormous diversity of antibodies can be created from a limited set of genes (Source: Li, Z., et al., “The generation of antibody diversity through somatic hypermutation and class switch recombination,” *Genes & Dev.*, 2004, 18: 1-11). Ultimately, what the B-cell can create is an antibody with a protein sequence unique only to that cell. These sequences are not encoded in the human genome; they are not hereditary.

As part of this process, the immune system regulates newly created antibodies through a system of selection and deletion, whereby cells producing good and tolerable antibodies are able to proliferate but cells producing “bad antibodies,” or antibodies that are harmful to or otherwise incompatible with the body, are removed. XBiotech estimates that the vast majority of cells producing new antibodies in the body are in fact deleted through a process of programmed cell death, or **apoptosis**. As a result, there appears to be a clever, essential method by which the body selects cells that produce the necessary and safe antibodies and removes those that are harmful—a process that, to the Company’s knowledge, cannot yet be reproduced in current antibody therapeutics, even those labeled as “fully human.”

Fully human antibodies, such as AbbVie Inc.’s (ABBV-NYSE) Humira® (the bestselling therapeutic in 2013 with roughly $11 billion in annual sales), are the latest in a string of attempts to engineer therapeutic antibodies that mimic natural human immunity, despite being laboratory-derived. Over time, antibody production has evolved from initially using **murine** (mouse) antibodies, which were strongly immunogenic due to the body recognizing murine DNA as a foreign molecule and launching an immune response against it, to next using **chimeric** antibodies and humanized antibodies, which had varying levels of **xenogeneic** content (illustrated in Figure 6 [page 15]), to, most recently, using fully human antibodies. The latter are made from human DNA but the antibody’s gene sequences are modified and rearranged in the laboratory in order to achieve the desired specificities and affinities—bypassing the natural process of antibody selection and deletion that is used by the immune system to ensure the production of tolerable antibodies.

As a result, while their risk of side effects are lower than murine or chimeric antibodies, fully human antibodies continue to present immunogenicity and tolerability concerns, including hypersensitivity reactions and loss of efficacy due to neutralization of the therapeutic (Source: Harding, et al., “The immunogenicity of humanized and fully human antibodies: Residual immunogenicity resides in the CDR regions,” *MAbs*, 2010, Vol. 2[3], 256–265). Humira® (adalimumab), for example, is associated with potentially serious side effects such as infusion site reactions and hypersensitivity (strong allergic) reactions, immunosuppression, and increased risk of infections, certain cancers, and worsening heart failure, among other outcomes (Sources: *Nature Reviews Drug Discovery*, 2010, Vol. 9, 325-338; and the U.S. National Institutes of Health [NIH]).

XBiotech's Solution: True Human™ Antibodies

XBiotech is pioneering the next generation of antibody therapeutics using antibodies derived directly from a human body, which a human immune system has already naturally pre-screened for tolerability. Rather than building gene sequences ex vivo, the Company screens blood samples from donors in order to discover highly specific, high-affinity antibodies present in the samples. When the right antibodies capable of neutralizing a particular disease antigen are found, XBiotech obtains a tissue sample from the individual donor, distinguishes the clinically relevant antibodies from trillions of irrelevant background antibody molecules in the donor's blood, and then clones the antibody-producing gene.

XBiotech's technology has been validated in a number of clinical trials, including a landmark study conducted at the University of Texas MD Anderson Cancer Center (ranked the second-best hospital in the U.S. for cancer care by the *U.S. News and World Report*). This study used a True Human™ antibody, called MABp1 or Xilonix™, which worked to block the activity of **interleukin-1** alpha (IL-1a), a pro-inflammatory protein in the body. The IL-1a gene is present in healthy individuals and has a beneficial role as part of the immune response to injury. However, in disease states, IL-1a has a negative impact as a result of stimulating local and systemic inflammation and swelling, damaging tissues, lowering pain thresholds, triggering **angiogenesis** (the formation of new blood vessels, which is undesirable around tumor cells that use the increased blood supply to grow), and causing tumor stromal remodeling, tumor invasiveness, **metastasis**, anxiety, and **cachexia** (severe weakness and wasting of the body due to illness). In this clinical trial, XBiotech administered Xilonix™ to patients with severe advanced cancers for which prior treatments had failed or were no longer working.

Results showed that Xilonix™ was well tolerated, with no dose-limiting toxicities or immunogenicity. As reported in the *Lancet Oncology* (May 2014, Vol. 15[6]: 656–666), Phase I participants collectively received over 300 infusions of MABp1 with no infusion-site reactions, no dose reductions nor delays for toxicity, and no indication that patients were developing antibodies against the drug. The Company found it was able to safely administer the highest dose used in the trial, which was 3.75 mg/kg every two weeks. Moreover, this trial is believed to represent the first time that a recovery in patients' lean body mass (an indication of recovery from cachexia) was observed in an advanced, refractory cancer population, and was also the first time that a physical recovery of this nature has been prognostic for extended survival. Greater details of trial data are provided on pages 22-24.

Product Pipeline

Figure 1
XBIOTECH'S CLINICAL PROGRAMS SNAPSHOT

Phase III Studies

- Symptomatic Colorectal Cancer (EU Registration)
- Advanced Colorectal Cancer (U.S. Registration)

Phase II

- Vascular Disease (Randomized)
- Non-small-cell Lung Cancer (NSCLC)
- Diabetes
- Psoriasis
- Acne
- Pyoderma Gangrenosum (orphan indication)

Phase I/II and Preclinical

- Advanced Solid Cancer
- Infectious Disease

Source: XBiotech Inc.

To date, the MABp1 therapy has been administered to patients over 700 times in seven clinical trials spanning the U.S. and Europe, and has shown a therapeutic benefit in an array of inflammatory-driven indications, including colorectal cancer and other tumors, vascular disease, diabetes, and multiple dermatological disorders. XBiotech's current product pipeline is summarized in Figure 1. There are currently two ongoing Phase III trials for colorectal cancer in Europe and the U.S., which are scheduled for completion in 2015 and 2016, respectively, and an ongoing Phase II trial in PG that is also scheduled to complete during 2015.

Beyond those indications listed in Figure 1 and detailed in this report, XBiotech continues to identify potential therapeutic antibodies present in natural human immunity that may hold promise for commercial production. Using XBiotech's novel method for screening and cloning genetic material, a simple blood draw of an individual who has demonstrated an immunity to a particular disease may yield sufficient critical genetic information to enable development of a new antibody therapy for the benefit of all those who suffer from the disease.

To this end, the Company has recently initiated a development program to treat methicillin-resistant *Staphylococcus aureus* (MRSA) infections using a True Human™ antibody. XBiotech identified its antibody now in development for MRSA in 2013 after screening the blood of hundreds of individuals. It is estimated that one-third of people already have *S. aureus* in their bodies, especially in the nasal cavities, and that 2.7% of these are MRSA strains. Following the submission of an Investigational New Drug (IND) application to the FDA in December 2014, the study is currently on clinical hold while, at the request of the FDA, the Company completes an animal toxicology study. XBiotech aims to conclude the toxicology study in the first half of 2015 and commence a randomized, double-blind, dose-escalation Phase I/II clinical trial of its antibody against *S. aureus*, subject to FDA approval.

XBiotech has also recently begun using its True Human™ antibody technology to begin development of a therapy for Ebola virus infection. In January and February 2015, the Company received blood donations from Ebola-recovered patients, which have been confirmed to contain high levels of anti-Ebola antibodies. A product candidate derived from this blood is expected to enter animal studies in 2015.

Production Efficiencies

Part of XBiotech's competitive advantage in the field of antibody therapeutics stems from the Company's proprietary manufacturing techniques supporting the time- and cost-effective development of complex natural human antibodies. XBiotech has deployed a new commercial manufacturing framework that uses components such as disposable yet durable **bioreactor** systems that do not require much servicing, internally-designed bioreactor platforms, and a largely disposable downstream process for antibody purification. The Company believes that its minimalist production infrastructure offers greater flexibility than standard processes, particularly including the ability to scale-up production to meet evolving market demands that may arise as XBiotech begins commercializing products in the future. Moreover, to the Company's knowledge, it can identify and manufacture antibody therapeutics with less infrastructure, reduced capital and operations costs, and in a faster timeframe than competitors. Details and illustrations of XBiotech's manufacturing are provided on pages 18-20 of the Core Story.

Headquarters and Employees

XBiotech Inc. was incorporated in Canada in 2005. The Company's global headquarters, research and development space, and current **Good Manufacturing Practices (GMP)** production operations are located in Austin, Texas, where XBiotech is also in the process of building a new, large-scale manufacturing facility. The new facility is located on 48 acres approximately five miles from Austin's central business district. It is being equipped with production space to support commercial manufacturing requirements as well as quality control, laboratories, and administrative offices.

The Company maintains four wholly owned subsidiaries for operations in various global jurisdictions: (1) XBiotech USA, Inc.; (2) XBiotech Switzerland AG; (3) XBiotech Japan K.K.; and (4) XBiotech Germany GmbH. As of March 9, 2015, XBiotech employed 56 individuals, 14 of whom held a Ph.D. or M.D. (or equivalent) degree.

Growth Strategy

XBiotech seeks to fundamentally change the way therapeutic antibodies are developed and commercialized by reducing the time to market and cost of development, and by increasing the safety, tolerability, and efficacy of targeted antibody therapeutics. To do so, the Company is focusing on the following strategies in the near term:

- Obtain regulatory approval, and begin commercial production, for the sale of Xilonix™ in the U.S. and Europe;
- Continue its research and clinical work on infectious diseases, including *S. aureus*;
- Review its clinical results for vascular disease (restenosis), diabetes, psoriasis, and acne, and determine additional research or clinical studies that it may conduct in the future;
- Discover new therapeutic True Human™ antibody therapies using the Company's proprietary process; and
- Leverage its novel manufacturing technology.

XBiotech has been primarily funded through private equity transactions, which have raised net cash proceeds for the Company of over $130 million to date. Going forward, XBiotech plans to become a publicly traded biotechnology company on the NASDAQ stock exchange. Proceeds from the Company's initial public offering (IPO) are earmarked for completing the ongoing Phase III trials of Xilonix™ in the U.S. and Europe as well as the other ongoing clinical trials in PG and *S. aureus*. Additionally, proceeds are targeted toward plant and equipment infrastructure to complete construction of the new manufacturing and laboratory facility in Austin, Texas, as well as other working capital and general corporate purposes. XBiotech further plans to conduct an IPO of its common stock. The offering is expected to commence after the U.S. Securities and Exchange Commission (SEC) completes the review process of XBiotech's registration statement, which was publicly filed with the SEC on February 2, 2015, and amended on March 10, 2015, subject to market and other conditions.

Regarding XBiotech's plans for post-approval marketing and sales (if the Company is successful in its product development efforts for Xilonix™ or other candidates), the Company has not yet established a sales, marketing, or distribution organization but intends to establish such a network in the U.S. and Europe for targeting oncologists and the medical community. In other foreign jurisdictions outside of the U.S. and EU, XBiotech will likely seek to enter into license, distribution, marketing, or other similar agreements with third parties.

Milestones

Recent Milestones

Corporate

- Appointed Dr. Daniel Vasella, former CEO and chairman of Novartis AG, to the Company's Board of Directors. Dr. Vasella has been ranked among Europe's and the world's most influential leaders by both *Time* magazine and the *Financial Times*.
- Entered into a strategic relationship with McKesson/US Oncology to gain access to a more extensive network of cancer treatment centers through which to enroll patients for the Phase III oncology studies
- Established subsidiaries in Frankfurt, Germany, and Tokyo, Japan, in order to facilitate clinical operations in these jurisdictions
- Publicly filed a registration statement with the SEC in order to conduct an IPO of its common stock, the offering of which is subject to SEC review and market conditions

Manufacturing

- Began construction on a new, 42,000-square-foot manufacturing facility in Austin, Texas, that is intended to accommodate large-scale commercial production. XBiotech estimates total costs for construction to be in the range of only roughly $10 million to $12 million due to its low-infrastructure manufacturing technologies.

Clinical Development

- Reported favorable interim data in its Phase III U.S. registration trial for Xilonix™ in colorectal cancer
- Conducted data analysis for five key clinical programs initially launched in 2011 targeting oncology, cardiovascular disease, type 2 diabetes, psoriasis, and acne
- Published results in the May 2014 issue of *Lancet Oncology* from a Phase I/II clinical trial conducted at the University of Texas MD Anderson Cancer Center in advanced cancers that demonstrated the favorable safety profile of Xilonix™ as well as showed patients' improved symptoms and a significant recovery in lean body mass that appeared to correlate with improvements in overall survival (which, to the Company's knowledge, is the first ever reported observations of lean body mass recovery in refractory cancer patients)
- Received FDA **Fast Track** Designations in both colorectal cancer and in vascular disease
- Worked with the European Medicines Agency (EMA) to design a regulatory path with new clinical endpoints for Xilonix™ in advanced colorectal cancer that may be faster and more informative than other methods. The Phase III trial ongoing in Europe uses novel radiographic techniques to measure patients' physical recovery, which may be more informative in the patient population, and establish a new more valuable surrogate compared to RECIST criteria.
- Launched a Phase II clinical trial in pyoderma gangrenosum (PG), which is currently ongoing
- Filed an IND for a Phase I/II study of the True Human™ antibody therapy to treat *S. aureus* infections, which is currently subject to clinical hold
- Began development of a True Human™ therapy for Ebola virus infection

Potential Milestones

- Complete Phase III studies in colorectal cancer in Europe during 2015 and in the U.S. during 2016
- Complete the ongoing Phase II trial in PG
- Complete an animal toxicology study, as requested by the FDA, come off of clinical hold, and commence the planned Phase I/II randomized clinical study to assess the True Human™ antibody therapy for the treatment of serious infections due to S. *aureus*, subject to FDA approval

Intellectual Property

XBiotech's strategy is to seek international intellectual property protection for each discovery, technology platform, and therapeutic product and process, which is intended to cover and protect key aspects of the Company's technology and products. To date, XBiotech's patent portfolio consists of 16 patent families, which includes 39 issued/allowed patents and more than 100 pending patent applications. These patents and applications are on file in multiple countries around the world. XBiotech reports that its lead product candidate has intellectual property coverage in the U.S., Japan, Europe, and 14 other countries.

Figure 2 (page 10) summarizes a selection of XBiotech's key patent families and applications by therapeutic area, as well as notes the specific processes, discoveries, or entities covered by and protected by each family or application. This is not a complete listing of XBiotech's intellectual property portfolio.

Figure 2

XBIOTECH'S KEY PATENT FAMILIES AND DISCOVERIES

General

Interleukin-1 Alpha Antibodies and Methods of Use

Development of fully human MAbs with a very high binding affinity for human IL-1

Describes functional characteristics, binding affinity studies, and additional related studies

Methods, Compositions, and Kits for Reducing Anti-antibody Responses

Development of methods to reduce the potential undesirable immune response to an administered antibody

Identifying Affinity Mature Human Antibodies

Method of identifying antigen-specific variable-regions of antibodies that occur in low frequencies in humans

Use of these methods and variable regions for the construction of antigen-specific human MAbs

Oncology

Treatment of Cancer with Anti-IL-1 Antibodies

Use of anti-IL1 antibodies to both inhibit metastatic potential of tumors and cause tumor cytotoxicity

Cancer Treatment

Discovery that administration of a anti-IL-1 MAbs to a patient suffering from cancer reduces the size of tumors

Treatment of Neoplastic Diseases

Discovery that a MAb that specifically binds IL-1 is useful for treating various tumor-associated diseases

Cachexia Treatment

Discovery that an anti-IL-1 agent can improve the symptoms of cachexia, including reversing lean body mass loss.

Treatment of Cachexia by Targeting Interleukin-1

Use of IL-1 targeting agents for improving the symptoms of cachexia in human patients

Inflammation and Autoimmune

Targeting Pathogenic Monocytes

Discovery that IL-1 is expressed on a pro-inflammatory, disease-associated monocyte subset in humans; .

Use of anti-IL1 antibodies to deplete or modulate the function of such cells

Arthritis Treatment

Discovery that anti-IL-1 antibody administration in human subject with arthritis decreases the number of pathogenic monocytes, while reducing inflammation without any observed major side effects.

Treatment of Dermatological Pathologies

Discovery that an anti-IL-1 MAb reduces skin inflammation, and its usefulness for treating inflammatory skin diseases including psoriasis vulgaris and acne vulgaris

Cardiovascular

Diagnosis, Treatment, and Prevention of Vascular Disorders Using IL-1 Autoantibodies

Use of IL-1 autoantibody concentration to assess risks of atherosclerosis in individuals

Use of IL-1 autoantibodies to reduce the risk and progression of certain types of vascular disease

IL-1 Immunization Induces Autoantibodies Protective Against Atherosclerosis

Process to increase IL-1 autoantibody concentration in mammals by immunization with IL-1

Use of this process to reduce the risk, severity, or progression of atherosclerosis-related diseases

Sources: XBiotech Inc. and Crystal Research Associates, LLC.

Company Leadership

Executive Management and Key Leadership

Figure 3 summarizes the Company's executive leadership, followed by brief biographies.

Figure 3

MANAGEMENT

John Simard	Chairman, President, and Chief Executive Officer (CEO)
David J. Combs, Ph.D.	Vice President, Manufacturing
Norma I. Gonzalez	Vice President, Quality
Queena Han, CPA	Vice President, Finance and Human Resources
Sushma Shivaswamy, Ph.D.	Senior Director of Research and Development (R&D)
Michael Stecher, M.D.	Medical Director

Source: XBiotech Inc.

John Simard, Chairman, President, and Chief Executive Officer (CEO)

Mr. Simard founded XBiotech in 2005. Prior to XBiotech, he was founder and CEO of the therapeutic vaccine developer CTL ImmunoTherapies Corp., headquartered in Los Angeles with over 100 scientists and support staff. Mr. Simard also founded AlleCure Corp., of Valencia, California, a developer of immune-modulating therapies. In 2001, AlleCure and CTL ImmunoTherapies merged to form MannKind Corp., where Mr. Simard served as corporate vice president and member of the Board. Mr. Simard invented the core technologies which form the basis for each of the commercialization programs at XBiotech. Operationally, he has championed an integrated approach to drug development, undertaking R&D, manufacturing, and clinical regulatory programs under one roof, which he has used as an effective means to conserve capital and control timelines. Mr. Simard holds a degree in biochemistry from the University of Saskatchewan and attended graduate studies in medical biophysics/immunology at the University of Toronto. He has numerous patents related to cancer therapy, therapeutic vaccines, and therapeutic antibodies as well as substantial peer-reviewed scientific publications and the textbook *Immune Response Genes*.

David J. Combs, Ph.D., Vice President, Manufacturing

Dr. Combs has served XBiotech since April 2010, initially as manufacturing process development scientist and now as vice president, manufacturing. Dr. Combs oversees a team that manages all aspects of the manufacturing program—from initiation of cell culture process to fill and finish of drug product. Dr. Combs also oversees a team of research scientists working on both upstream and downstream process development, including media development and product purification technology. In addition, he heads up efforts to develop a custom bioreactor system that will reduce XBiotech's capital requirements for manufacturing expansion. Dr. Combs previously worked for the Cancer Research Institute at Scott and White Memorial Hospital where he served as senior scientist in charge of preclinical development, process development, manufacturing, and formulation of immunotoxins used for clinical trials. While at Scott and White, Dr. Combs was involved in the design and set up of a current Good Manufacturing Practices (cGMP) facility and has extensive experience designing and running bioreactors used for the production of therapeutics. Dr. Combs has a B.Sc. in biology from Tarleton State University and a Ph.D. in cellular and molecular biology from the University of Texas at Austin.

Norma I. Gonzalez, Vice President, Quality

Ms. Gonzalez has served as XBiotech's vice president of quality since February 2008. Ms. Gonzalez was one of the first employees to join XBiotech's operation in Austin, Texas, in 2008. She played a crucial role in launching XBiotech's manufacturing program and establishing the Company's bioreactor system for the production of clinical trial drug product. Ms. Gonzalez transitioned to developing a full quality program, to enable cGMP compliance and growth of the Company's manufacturing program. She continues to prepare the Company to enable pivotal study and commercial scale production. Before joining XBiotech, Ms. Gonzalez was director of quality at Carbomedics, a global manufacturer of heart valves. During her tenure at Carbomedics, Ms. Gonzalez held various roles including director of R&D, director of manufacturing mechanical heart valve, and director of tissue valve and quality. Prior to Carbomedics, Ms. Gonzalez worked for Shiley Caribbean as a quality control and manufacturing manager as well as at Baxter-Travenol as a microbiology/quality control supervisor. Ms. Gonzalez holds a B.Sc. in biology from the University of Puerto Rico.

Queena Han, CPA, Vice President, Finance and Human Resources

Ms. Han has served XBiotech since 2008 as controller, and more recently, as vice president of finance and human resources. Ms. Han is responsible for reporting, auditing, taxation, internal control, insurance, legal and regulatory compliance regarding all financial functions, and maintenance of cash flow position. She serves as a liaison among directors, investors, and the Company. She is also responsible for all aspects of human resources within the Company. Ms. Han has over 20 years of experience in accounting and finance, and has held several executive positions. Prior to joining XBiotech, she served as chief financial officer (CFO) for a public company with a nationwide pay phone hardware and service business. Ms. Han has a B.A. in accounting and holds the Chartered Professional Accountants (CPA) designation in Canada. She is a professional member of SHRM and holds the Human Resource Management Certification from the University of Texas at Austin.

Sushma Shivaswamy, Ph.D., Senior Director of Research and Development (R&D)

Dr. Shivaswamy has been with XBiotech since May 2009 when she joined as a senior research scientist and quickly advanced to lead the R&D group as director of research. The multidisciplinary R&D group has pioneered development of the Company's technology platform for discovery of True Human™ antibodies and new approaches for screening human blood for novel True Human™ antibodies based on super-high-stringency mining technology. Dr. Shivaswamy has an academic background in regulation of eukaryotic gene expression and molecular genetics. Prior to joining XBiotech, she was a postdoctoral researcher at the Center for Systems and Synthetic Biology at the University of Texas at Austin. She has a Ph.D. in molecular biology from the Center for Cellular and Molecular Biology, India.

Michael Stecher, M.D., Medical Director

Dr. Stecher has served as XBiotech's medical director since June 2010. Dr. Stecher has worked to develop the clinical trial program to treat chronic inflammatory diseases through targeting the interleukin-1 system and collaborated with an acclaimed group of international physician researchers and scientists to help produce breakthrough clinical data on diseases characterized by chronic inflammatory processes. Dr. Stecher is board certified in family medicine and is a graduate from the University of Kansas School of Medicine. He completed his work in family practice medicine at Austin Brackenridge Hospital where he served as chief resident of family medicine.

Board of Directors

The Board of Directors oversees the conduct of and supervises the Company's management. Figure 4 provides a summary of Board members, followed by brief biographies.

Figure 4

BOARD OF DIRECTORS

John Simard	Chairman, President, and Chief Executive Officer (CEO)
Fabrizio Bonanni, Ph.D.	Board Member
Thorpe McKenzie	Board Member
Daniel Vasella, M.D.	Board Member

Source: XBiotech Inc.

John Simard, Chairman, President, and Chief Executive Officer (CEO)

Biography provided on page 11.

Fabrizio Bonanni, Ph.D., Board Member

Dr. Bonanni served senior operating roles at Amgen Inc. (AMGN-NASDAQ) from 1999 to 2012. This included serving as executive vice president, operations from 2007 to 2012. Prior to overseeing operations, he served as senior vice president, manufacturing, and senior vice president, quality and compliance. Earlier, Dr. Bonanni held various management positions at Baxter International, Inc. (BAX-NYSE) from 1974 to 1999, including positions as corporate vice president, regulatory and clinical affairs and corporate vice president, quality system.

Thorpe McKenzie, Board Member

Mr. McKenzie is managing director of Pointer Management Company, Chattanooga, Tennessee, which he co-founded in 1990 to invest in hedge funds and similar types of partnerships utilizing a fund of funds approach. From 1982 until 1990, he was a private investor in New York City, and a director of several public and private companies. From 1980 until 1982, he was founding general partner of TIGER, a global hedge fund. From 1971 until 1980, he was a vice president of Kidder, Peabody & Co., Inc. in New York. Mr. McKenzie is a graduate of the University of North Carolina in Chapel Hill, and the Wharton Graduate division of the University of Pennsylvania in Philadelphia.

Daniel Vasella, M.D., Board Member

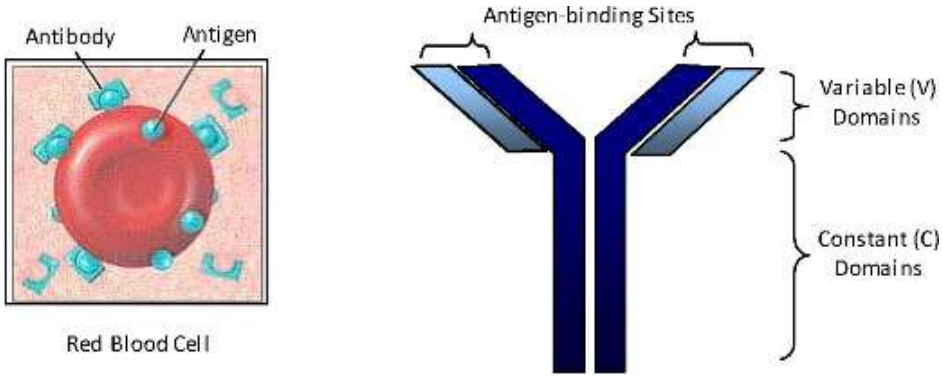
Dr. Vasella has served as a director since November 4, 2014. He is the honorary chairman and former chairman and CEO of Novartis AG (NVS-NYSE), a company that engages in the R&D, manufacture, and marketing of healthcare products worldwide. Dr. Vasella served as chairman of Novartis from 1999 to February 2013 and as CEO from 1996 to January 2010. From 1992 to 1996, Dr. Vasella held the positions of CEO, chief operating officer, senior vice president and head of worldwide development, and head of corporate marketing at Sandoz Pharma AG. Dr. Vasella is a director of American Express Company (AXP-NYSE), PepsiCo, Inc. (PEP-NYSE), a member of the International Business Leaders Advisory Council for the Mayor of Shanghai, a foreign honorary member of the Academy of Arts and Sciences, a trustee of the Carnegie Endowment for International Peace, and a member of several industry associations and educational institutions.

Core Story

ANTIBODY THERAPEUTICS

An antibody is a critical component of the human immune system. It is a specific type of protein produced by B-cells circulating in the blood in response to the presence of an antigen, or foreign molecule, found on diseased cells, viruses, fungi, bacteria, and toxins, among other abnormal substances. When a circulating B-cell comes into contact with foreign disease antigens in the blood, it can create Y-shaped antibodies that uniquely recognize and attach to those particular antigens, marking them for destruction by other components of the immune system. Each antibody has a unique binding site that attaches to the complementary site of a foreign antigen, as illustrated on the red blood cell in Figure 5.

Figure 5
ANTIBODY STRUCTURE



Sources: A.D.A.M., Inc. (ADAM-NASDAQ) and Crystal Research Associates, LLC.

The variable region gives the antibody its specificity for binding to antigens, meaning its ability to single out a specific antigen from many similar targets. Only the tips of the variable regions on the arms of the Y, called antigen-binding sites, have the structures known as **complementarity-determining regions (CDRs)** that recognize and attach to antigens. The amino acid sequence in the CDRs varies greatly among different antibodies, giving the antibody its affinity for a specific antigen. This high level of specificity makes antibody therapies attractive as potential treatments against particular antigens.

By binding to an antigen, antibodies disable the undesired protein or signal other immune defenses, such as leading the antigen to a macrophage (a type of large white blood cell) that can ingest and destroy it. Moreover, B-cells can manufacture more of the same antibody very quickly if recurrent antigens appear. In this manner, antibodies are part of the natural, primary immune system humans use to fight off illnesses. Vaccines, for example, capitalize on this characteristic by “training” B-cells to recognize and react to select foreign disease molecules.

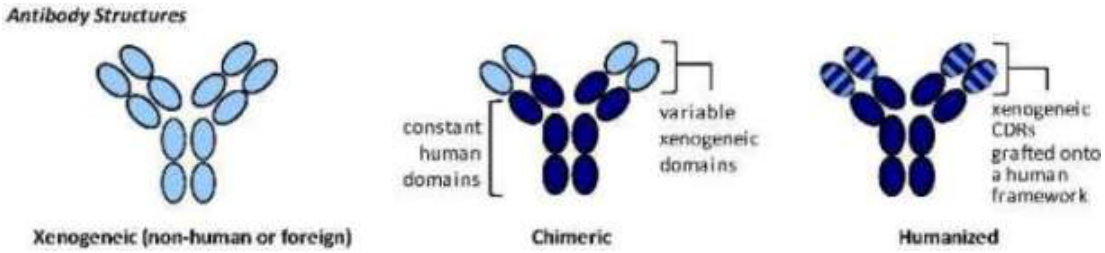
Development of Antibodies for Medical Use

In the field of new drug development, many researchers emphasize creating antibody-based therapeutics due to the medically beneficial properties of antibodies—in particular, their ability to selectively target certain diseases in a potentially safer and more effective manner than traditional small molecule drugs. Such antibody products have been mass-produced in a number of ways, from being grown in cell culture to being cultured in live animal hosts, with the amount of actual human antibody included in the antibody product varying based on the method of production.

Early therapeutic antibodies were derived from murine (mice) cells, which have had utility in certain applications, but have also been plagued by reduced efficacy and heightened safety concerns due to the immune system's recognition of these non-human murine antibodies as "foreign." For example, as early as the 1970s, scientists Georges Köhler and César Milstein began using antibodies as therapeutic agents. In order to produce large amounts of monoclonal antibodies (MAbs), Köhler and Milstein fused rodent B-cells with tumor cells (**myelomas**) to produce a **hybridoma**. A hybridoma leverages a cancer cell's ability to reproduce with an immune cell's ability to make antibodies. These antibodies were expected to be able to treat a range of diseases due to their target specificity. However, because they were developed in laboratory animals, these monoclonal antibodies (MAbs), when injected into people, are recognized by the immune system as foreign. This recognition can cause an immune response against the administered antibodies, reducing or eliminating efficacy. In the case of mouse-derived (murine) antibodies, this is known as the human anti-mouse antibody (H.A.M.A.) response.

To improve upon the safety and efficacy of therapeutic antibodies, scientists began using a variety of protein engineering techniques to "humanize" antibodies. Humanization effectively reduces the xenogeneic (foreign) content of MAbs. During humanization, the antigen-binding portions of mouse antibodies are grafted onto human antibody frameworks, which is known as a chimeric antibody (as shown in Figure 6). Although less immunogenic, chimeric antibodies can still elicit an immune response due to the sizeable non-human sequences present.

Figure 6
ANTIBODY HUMANIZATION



Source: Crystal Research Associates, LLC.

Researchers then focused on development of humanized antibodies that only contain the CDRs of a xenogeneic antibody, grafted onto the framework of a human antibody. This process transfers the antigen-binding properties of a mouse MAb to a predominantly human, non-immunogenic context. As such, it reduces the likelihood of the immune system recognizing the therapeutic antibody as foreign. Taking these advancements a step farther is a class of "fully human" antibodies, which are typically created in one of two ways: (1) transplanting human antibody genes into bacteria-specific viruses known as **phages** that are capable of generating the appropriate antibodies from the newly acquired genes, with one type of antibody per phage; or (2) more commonly, creating a **transgenic** mouse with a human immune system. In this approach, researchers place the gene segments responsible for generating human antibodies into mouse embryonic stem cells and grow the mice to maturity. The target antigen is injected into the transgenic mouse to generate a human antibody against the antigen. The resulting antibody is considered to be fully human due to being made from human genetic material, but it is not derived from the human body itself.

Natural Antibody Selection and Deletion

The human genome is estimated to contain fewer than 100,000 genes, of which only 20,000 to 25,000 genes are believed to be protein-coding genes. With this few protein-creating genes contained in humans' hereditary genetic information, it is not possible to have a gene present in the body to create an antibody against every possible variation of every possible antigen (infectious diseases, toxins, viruses, foreign agents, etc.) in the world, since the key to an antibody's effectiveness at fighting off an illness is in its ability to bind to the target antigen with a high degree of specificity and with high affinity—meaning each antibody binds only to one particular type of antigen. Essentially, a person would need billions of individual genes in order to target the billions of potentially **pathogenic** agents they might encounter.

Lacking a sufficient number of hereditary genes in the body to code an antibody for each unique occasion, researchers believe there is another method of genetic engineering that occurs in the body's B-cells. B-cells are capable of making antibodies with unique variable domains (as shown in Figure 5 [page 14]) that encode specific antigen-binding sites. As part of antibody-mediated immunity, the B-cells, after antigen recognition and co-stimulation by helper T-cells, go through a process of somatic hypermutation (SHM) or genetic rearrangement, whereby an enormous diversity of antibodies can be created from a limited set of genes (Source: Li, Z., et al., "The generation of antibody diversity through somatic hypermutation and class switch recombination," *Genes & Dev.*, 2004, 18: 1-11).

Segments of DNA present in the B-cells are essentially shuffled, recombined, and mutated to produce an infinite number of possible antibody genes that exist only inside those antigen-specific B-cells. Through SHM, the variable antibody domain is reconfigured to generate high-affinity antigen binding sites. Ultimately, what is created is believed to be antibodies with protein sequences unique only to the cell that performed the engineering. These sequences are not encoded in the human genome; they are not hereditary. Moreover, these newly created proteins are tolerated by the body because as the immune system goes through the meticulous process of antibody selection, it also goes through a process of deletion, through which cells producing "bad antibodies," or antibodies that are harmful to or otherwise incompatible with the body, are removed. XBiotech estimates that the vast majority of cells producing new antibodies in the body are in fact "deleted" through a process of programmed cell death, or apoptosis. As a result, there appears to be a clever, innate method by which the body selects cells that produce the necessary and safe antibodies and removes those that are harmful—a process that, to the Company's knowledge, is not yet being reproduced outside the human body.

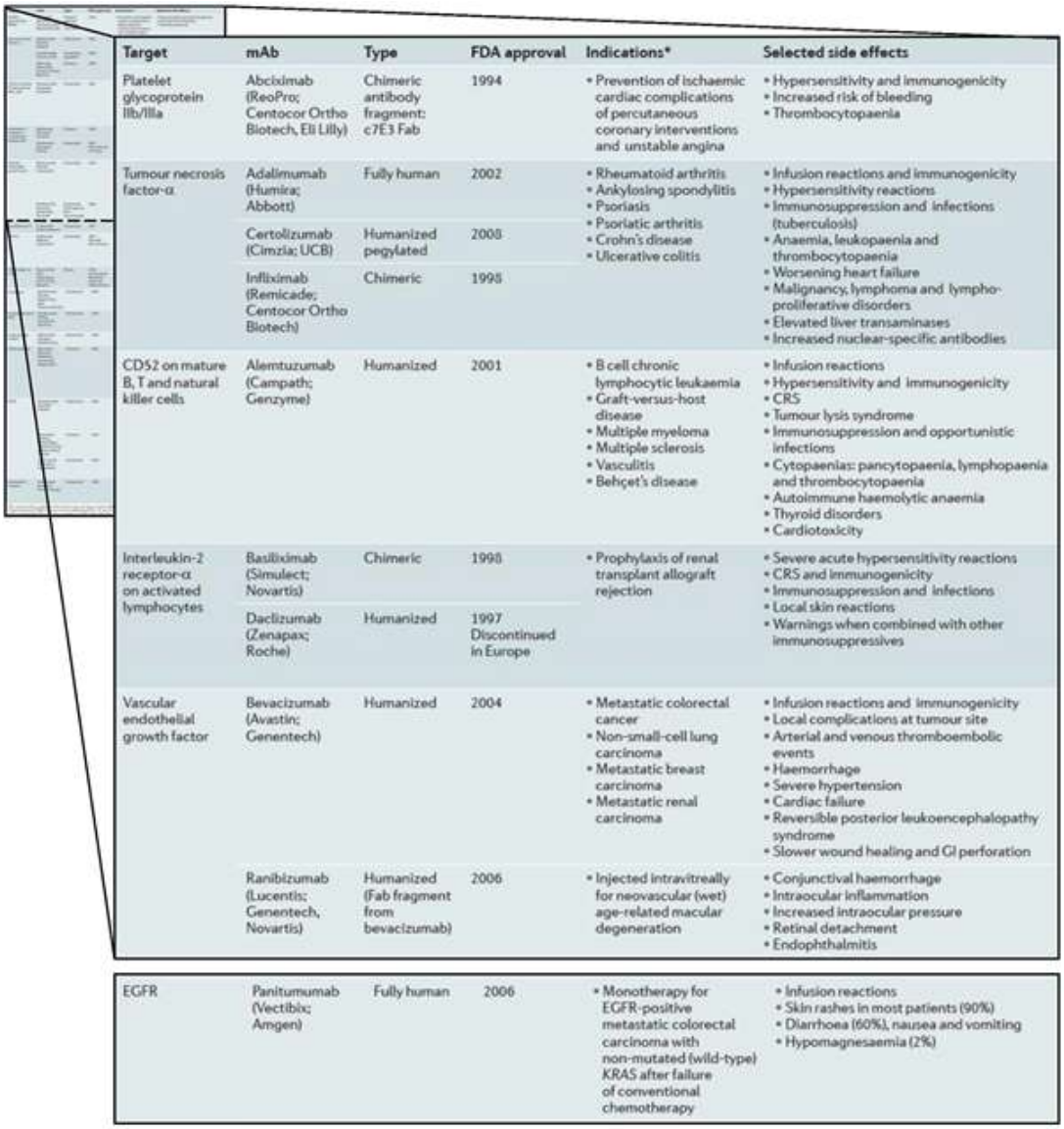
Current Antibody Development Technologies Continue to Pose Safety and Efficacy Concerns

As previously described, despite their name, fully human antibodies are not truly human in that they are not derived out of the immune system's natural processes of selection and deletion, but rather, are engineered in the laboratory. Thus while their risk of side effects are lower than murine or chimeric antibodies, fully human antibodies continue to present immunogenicity and tolerability concerns, including hypersensitivity reactions and loss of efficacy due to neutralization of the therapeutic (Source: Harding, et al., "The immunogenicity of humanized and fully human antibodies: Residual immunogenicity resides in the CDR regions," *MAbs*, 2010, Vol. 2[3], 256–265).

For example, the fully human MAb Adalimumab (approved by the U.S. Food and Drug Administration in 2002) treats a range of conditions, including rheumatoid arthritis, ankylosing spondylitis, psoriasis, ulcerative colitis, and Crohn's disease, but is associated with potentially serious side effects such as infusion site reactions and hypersensitivity (strong allergic) reactions, immunosuppression, and increased risk of infections, certain cancers, and worsening heart failure, among other outcomes (Sources: *Nature Reviews Drug Discovery*, 2010, Vol. 9, 325-338; and the U.S. National Institutes of Health [NIH]). Adalimumab is sold as Humira® by AbbVie Inc. and topped $10.6 billion in sales for 2013 (Source: FirstWord Pharma's "FirstWord Lists – Pharma's 50 biggest selling drugs: AbbVie's Humira joins the $10 billion club," March 2014).

Figure 7 (page 17) contains an excerpt from a table published in *Nature Reviews Drug Discovery* that demonstrates the need for improved next-generation therapeutic antibody development (Source: Trevor T. Hansel, Harald Kropshofer, Thomas Singer, Jane A. Mitchell & Andrew J. T. George, *Nature Reviews Drug Discovery* Vol. 9, 325-338 [April 2010]). The full table of data for 20 therapeutic antibodies is available here: www.nature.com/nrd/journal/v9/n4/fig_tab/nrd3003_T1.html.

Figure 7
EXCERPT OF "TABLE 1: SIDE EFFECTS OF LICENSED MONOCLONAL ANTIBODIES"



Target	mAb	Type	FDA approval	Indications*	Selected side effects
Platelet glycoprotein IIb/IIIa	Abciximab (ReoPro; Centocor Ortho Biotech, Eli Lilly)	Chimeric antibody fragment: c7E3 Fab	1994	• Prevention of ischaemic cardiac complications of percutaneous coronary interventions and unstable angina	• Hypersensitivity and immunogenicity • Increased risk of bleeding • Thrombocytopaenia
Tumour necrosis factor-α	Adalimumab (Humira; Abbott)	Fully human	2002	• Rheumatoid arthritis • Ankylosing spondylitis • Psoriasis • Psoriatic arthritis • Crohn's disease • Ulcerative colitis	• Infusion reactions and immunogenicity • Hypersensitivity reactions • Immunosuppression and infections (tuberculosis) • Anaemia, leukopaenia and thrombocytopaenia • Worsening heart failure • Malignancy, lymphoma and lympho-proliferative disorders • Elevated liver transaminases • Increased nuclear-specific antibodies
	Certolizumab (Cimzia; UCB)	Humanized pegylated	2008		
	Infliximab (Remicade; Centocor Ortho Biotech)	Chimeric	1998		
CD52 on mature B, T and natural killer cells	Alemtuzumab (Campath; Genzyme)	Humanized	2001	• B cell chronic lymphocytic leukaemia • Graft-versus-host disease • Multiple myeloma • Multiple sclerosis • Vasculitis • Behçet's disease	• Infusion reactions • Hypersensitivity and immunogenicity • CRS • Tumour lysis syndrome • Immunosuppression and opportunistic infections • Cytopaenias: pancytopaenia, lymphopaenia and thrombocytopaenia • Autoimmune haemolytic anaemia • Thyroid disorders • Cardiotoxicity
Interleukin-2 receptor-α on activated lymphocytes	Basiliximab (Simulect; Novartis)	Chimeric	1998	• Prophylaxis of renal transplant allograft rejection	• Severe acute hypersensitivity reactions • CRS and immunogenicity • Immunosuppression and infections • Local skin reactions • Warnings when combined with other immunosuppressives
	Daclizumab (Zenapax; Roche)	Humanized	1997 Discontinued in Europe		
Vascular endothelial growth factor	Bevacizumab (Avastin; Genentech)	Humanized	2004	• Metastatic colorectal cancer • Non-small-cell lung carcinoma • Metastatic breast carcinoma • Metastatic renal carcinoma	• Infusion reactions and immunogenicity • Local complications at tumour site • Arterial and venous thromboembolic events • Haemorrhage • Severe hypertension • Cardiac failure • Reversible posterior leukoencephalopathy syndrome • Slower wound healing and GI perforation
	Ranibizumab (Lucentis; Genentech, Novartis)	Humanized (Fab fragment from bevacizumab)	2006	• Injected intravitreally for neovascular (wet) age-related macular degeneration	• Conjunctival haemorrhage • Intraocular inflammation • Increased intraocular pressure • Retinal detachment • Endophthalmitis
EGFR	Panitumumab (Vectibix; Amgen)	Fully human	2006	• Monotherapy for EGFR-positive metastatic colorectal carcinoma with non-mutated (wild-type) *KRAS* after failure of conventional chemotherapy	• Infusion reactions • Skin rashes in most patients (90%) • Diarrhoea (60%), nausea and vomiting • Hypomagnesaemia (2%)

Source: Trevor T. Hansel, Harald Kropshofer, Thomas Singer, Jane A. Mitchell & Andrew J. T. George, Nature Reviews Drug Discovery Vol. 9, 325-338 (2010).

XBIOTECH'S SOLUTION: TRUE HUMAN™ ANTIBODY DEVELOPMENT

As previously detailed, technologies for producing humanized antibodies to date have centered on the creation of high-affinity antibodies by modifying gene sequences out of the human body. As a result, these antibodies have not undergone natural biological processes of antibody selection and deletion, which are used by the immune system to ensure the production of safe and effective antibodies. Thus, while being marketed as "fully human" or otherwise, existing antibody therapies are not likely to have undergone natural selection for tolerability in humans.

As an alternative to engineering synthetic antibodies in live mice or mouse cell lines, XBiotech's product development uses the Company's therapeutic antibodies that are derived from natural human immunity. Termed "True Human™," these antibody genes are cloned directly from a human gene using XBiotech's proprietary technology. By removing the xenogeneic content and processes, True Human™ antibodies are not likely to be detected by the immune system as foreign and thus are expected to offer improved safety, efficacy, and commercial value versus existing antibody therapeutics, including those currently referred to as "fully human."

Identification and Production of True Human™ Antibodies

The crux of XBiotech's approach is improving the safety of antibody therapeutics by using antibodies directly from a human body, which have already been vetted by the body and are thus anticipated to be safe and tolerable. To do this, XBiotech has screened thousands of blood donors using its Super High Stringency Antibody Mining (SHSAM™) technology. The Company first seeks to identify highly specific, high-affinity antibodies in blood samples, and when the right antibodies are found, XBiotech obtains a tissue sample from the individual donor. The SHSAM™ technology is used to distinguish the clinically relevant antibodies from trillions of irrelevant background antibody molecules in the donor's blood.

After thousands of blood samples have been screened and the specific antibody gene in a particular sample's rare cell is identified, XBiotech's next step in its True Human™ antibody development is to faithfully clone the gene in order to reproduce it for use in clinical therapy. In doing so, the cloned gene has already been naturally pre-screened for tolerability in humans as a result of the original gene having survived the immune system's process of selecting and growing optimal antibodies while removing harmful antibodies. This method of first finding in human blood donors, and then reproducing by cloning, antibodies with the desired characteristics for use against specific diseases is considerably different from past approaches of engineering the desired characteristics through gene manipulation in a laboratory. Moreover, XBiotech believes that it has refined its manufacturing process such that it can convert DNA into therapeutic antibody product at a sufficient commercial scale (thousands of doses) in a more efficient manner than conventional manufacturing processes.

XBiotech's In-House Manufacturing Technology

Figure 8

XBIOTECH'S DRUG VIALS READY FOR SHIPMENT TO CLINICAL TRIAL SITES

Source: XBiotech Inc.

In 2008, XBiotech began building its own approach to biologics manufacturing, in an aim to reduce the infrastructure required versus standard industry processes. Rather than implementing complex, capital- and labor-intensive bioreactor systems, the Company sought to streamline and simplify production in a minimalist manner. Today, XBiotech has deployed a new commercial manufacturing framework that uses components such as disposable yet durable bioreactor systems that do not require much servicing, internally-designed bioreactor platforms, and a largely disposable downstream process for antibody purification. As a consequence of using simple, disposable technology engineered in-house, XBiotech's manufacturing technology could likely provide the Company with a number of competitive advantages, as outlined in Figure 9 (page 19), as well as help create a new paradigm for flexible and efficient biologics manufacture.

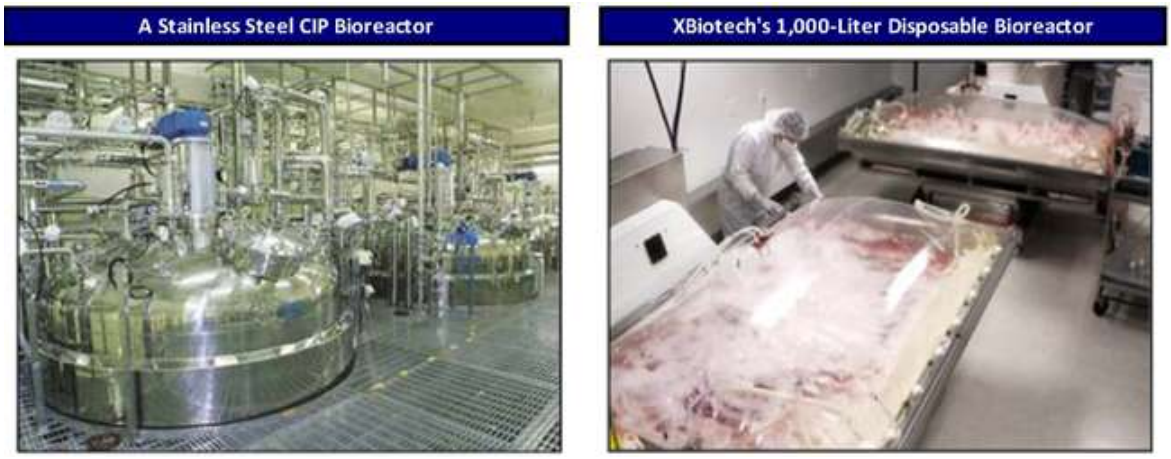
Figure 9
A SELECTION OF POTENTIAL COMPETITIVE ADVANTAGES TO XBIOTECH'S MANUFACTURING TECHNOLOGY

- A more reliable production process with less risk of contamination, due to using disposable components, as well as simpler quality compliance
- Minimal plant infrastructure capable of high and efficient levels of production
- Fewer capital costs for constructing a facility to manage disposable plastic bioreactors versus a facility for stainless steel bioreactor systems with a similar level of output
- Reduced maintenance and operation costs
- Shorter lead times
- Considerable production flexibility compared to industry standard manufacturing systems

Source: XBiotech Inc.

Figure 10 illustrates XBiotech's bioreactors versus the clean-in-place (CIP), stainless steel bioreactors that are representative of typical biomanufacturing setups. The bioreactor is the apparatus in which a biological process occurs. For XBiotech, the bioreactor is where antibody-producing cells are harnessed to proliferate and secrete the desired antibody, which is then harvested, purified, and finished as a drug product via subsequent downstream processes. XBiotech's disposable bioreactors, as shown on the right side of Figure 10, are essentially large, single-use plastic bags that have been pre-sterilized and are discarded after each use. They have a 1,000-liter capacity and, importantly, are expected to facilitate flexible and scalable production including a ramp-up from clinical-scale manufacturing to that required to support commercialization.

Figure 10
XBIOTECH'S BIOREACTOR TECHNOLOGY VERSUS TYPICAL CAPITAL EQUIPMENT

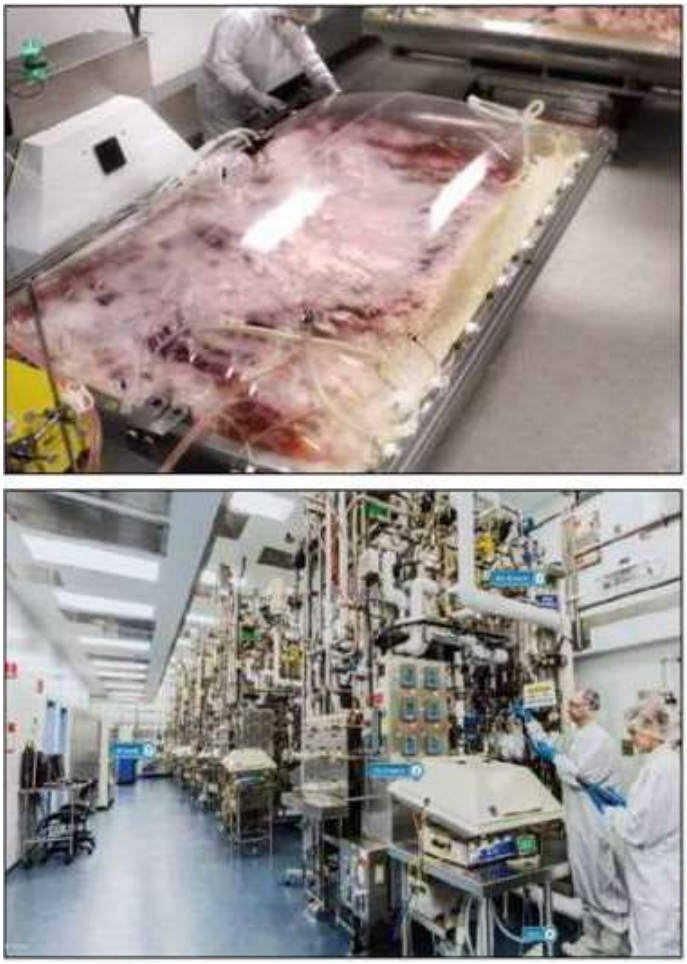


Source: XBiotech Inc.

To date, XBiotech's drug production has been limited to production for use in the Company's clinical trials. All manufacture occurs in-house at XBiotech's Good Manufacturing Practices (GMP) facility in Austin, Texas. The Company broke ground on a new manufacturing facility intended to accommodate larger-scale commercial production in September 2014. The new site is located on a 48-acre parcel of land approximately five miles from Austin's central business district. Construction is ongoing, for which XBiotech estimates total costs (including manufacturing equipment) to be in the range of roughly $10 million to $12 million versus the hundreds of millions that a new manufacturing facility built to industry standards could cost, and XBiotech's new facility is forecast to be capable of producing several hundred thousand doses of antibody annually. The facility is scheduled to be approximately 42,000 square feet and include laboratories, quality control rooms, and administrative offices as well as production areas. Construction is predicted to be complete by late 2015, and the Company expects to begin operating in the new facility in early 2016.

Figure 11
COMPARISON OF XBIOTECH'S MANUFACTURING EQUIPMENT TO THAT OF A COMPETITIVE LARGE-SCALE MANUFACTURER

The single "bag" reactor employed by XBiotech (above image) is stated by the Company to have the same operating capacity and potential output as the row of complex, costly machines on the manufacturing floor of a competitive operation (lower image) . XBiotech believes that existing manufacturing practices are relics of an old biotech industry, and that its approach may likely present a new and more efficient method.



Source: XBiotech Inc.

Potential to Disrupt the Status Quo of Antibody Therapeutics

To XBiotech's knowledge, its lead product candidate using a True Human™ antibody—Xilonix™ for the treatment of colorectal cancer—is expected to be the only marketed product that is a true human antibody. The Company views the current class of fully human antibodies as misleading and believes there is considerable opportunity to develop next-generation antibody products that could offer improved safety, tolerability, and efficacy. This is an important facet of XBiotech's technology and product development, as the "fully human" designation applied to antibodies that have been engineered in the laboratory rather than derived from natural human processes of antibody selection and deletion serves to downplay the inherent safety risks of immunogenic, infusion-site, or anaphylactic reactions that exist with such products. A key issue for the Company is ensuring that there is a proper differentiation of safety and tolerability expectations for antibody platforms, and that there is a means for distinguishing its True Human™ antibodies from existing fully human products, whose name likely incorrectly implies that they have reached the highest standard of antibody humanization.

Accordingly, XBiotech has contacted the U.S. Adopted Names Council (USANC) to discuss creating a new nomenclature for describing and differentiating True Human™ antibodies from fully human antibodies. The USANC is the body responsible for selecting simple, informative, and unique nonproprietary names for drugs in the health professions by establishing logical terminology based on pharmacological and/or chemical relationships. It is sponsored by the American Medical Association, U.S. Pharmacopeial Convention, and American Pharmacists Association, as well as maintains a relationship with the FDA and the World Health Organization. Discussions between USANC and XBiotech to establish this new nomenclature are ongoing.

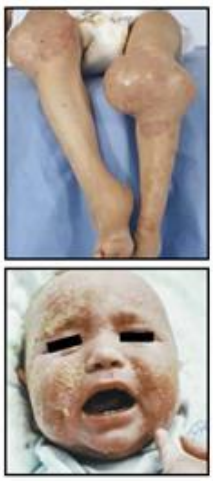
Clinical Validation of XBiotech's MABp1 Therapeutic Antibody

The True Human™ technology has been validated in a number of clinical trials to date. As detailed on the following pages, these have entailed the use of a True Human™ monoclonal antibody (MAb) targeting and neutralizing interleukin-1 alpha (IL-1a), a pro-inflammatory protein made primarily in immune cells. The IL-1a gene is present in healthy individuals and provides the genetic instructions for making the IL-1a protein, which has a beneficial role in cell-to-cell communication, including protecting the body from foreign pathogens by stimulating the activity of genes involved in inflammation and immunity, as well as has a role in bone resorption by helping break down and remove unneeded bone tissue (Source: the U.S. National Library of Medicine).

IL-1a is generally produced as part of the immune response to injury; however, in many disease states, too much IL-1a has been found to be negatively involved in disease progression as a result of stimulating local and systemic inflammation and swelling, damaging tissues, lowering pain thresholds, and leading to other adverse side effects (as illustrated in Figure 12). Blocking IL-1a may have particular utility in inflammatory skin conditions, such as acne, eczema, psoriasis, and pyoderma gangrenosum (PG), where the protein is associated with the skin's epidermal cells called keratinocytes. Recent research from a number of companies has been directed at ways to inhibit IL-1 receptors or neutralize either IL-1a or IL-1ß in order to improve outcomes in a wide variety of diseases (Source: Dinarello, C. et al, "Treating inflammation by blocking interleukin-1 in a broad spectrum of diseases," *Nature Reviews Drug Discovery*, August 2012, Vol. 11(8): 633–652). IL-1a's contribution to tumor progression and spread is detailed under the 2010 MD Anderson Cancer Center Study on pages 22-24.

The Company's anti-IL-1a MABp1 antibody therapy was derived from an individual who had a natural IL-1a immunity, and whose immunity could be cloned via XBiotech's proprietary processes and reproduced as a True Human™ anti-IL-1a antibody. In preclinical work, MABp1 has shown that it can neutralize IL-1a, prevent binding to the IL-1 receptor type 1, and block the activities of IL-1a in the body (Source: *The Lancet Oncology*, May 2014, Vol. 15[6]: 656–666). To date, MABp1 had been administered to patients over 700 times in seven different clinical trials spanning the U.S. and Europe. Figure 13 (page 22) lists XBiotech's completed and enrolling clinical trials.

Figure 12
OVERACTIVE IL-1 AT BIRTH



Source: New England Journal of Medicine, June 4, 2009; 360(23): 2426-2437.

Figure 13
LIST OF ENROLLING OR COMPLETED CLINICAL STUDIES

The MABp1 anti-IL-1a therapeutic antibody has been assigned different names depending on the clinical indication, such as MABp1, Xilonix™, CA-18C3, CV-18C3, RA-18C3, T2-18C3, etc. Each of these, however, contain the same True Human™ antibody MABp1.

Study Title	Enrolling	Completed
Study of MABp1 in patients with Advanced Cancers		X
Study of CA-18C3 in Subjects with Advanced Hematologic Malignancies		X
Open Label, Randomized Study of the Safety, Pharmacokinetics, and Preliminary Efficacy of an Anti-Inflammatory Therapeutic Antibody (CV-18C3) in Reducing Restenosis in Patients Undergoing Percutaneous Femoro-Popliteal Revascularization		X
Open Label Study of the Safety, Pharmacokinetics, and Efficacy of a True Human™ Anti-Inflammatory Therapeutic Antibody (RA-18C3) in Subjects with Moderate to Severe Plaque Psoriasis		X
Study of the Safety and Pharmacokinetics of an Anti-Inflammatory Therapeutic Antibody (MABp1) in Patients with Type 2 Diabetes Mellitus		X
Open Label Study of the Safety, Pharmacokinetics, and Efficacy of a True Human™ Anti -Inflammatory Therapeutic Antibody (RA-18C3) in Subjects with Moderate to Severe Acne Vulgaris		X
A Phase II Open Label Study of RA-18C3 in Subjects with Pyoderma Gangrenosum	X	
A Phase III Double Blind, Placebo Controlled Study of Xilonix™ for Improving Survival in Metastatic Colorectal Cancer (U.S.)	X	
A Phase III Double Blind, Placebo Controlled Study of Xilonix™ in Symptomatic Colorectal Cancer Patients Refractory to Standard Therapy (Europe)	X	

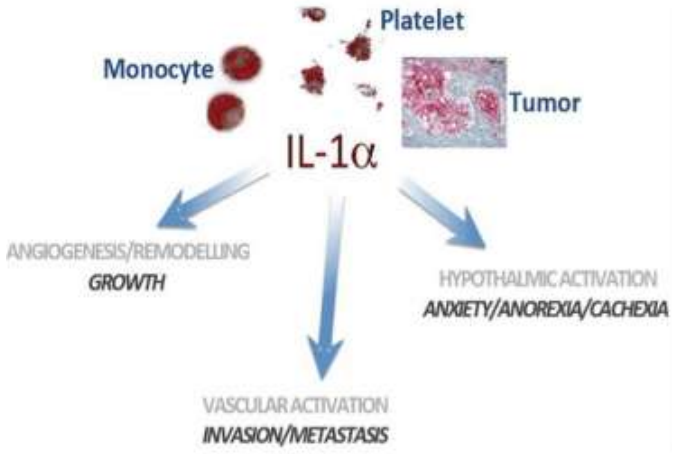
Source: XBiotech Inc.

2010 MD Anderson Cancer Center Study

From March 2010 to July 2012, XBiotech enrolled 52 patients with 18 different types of metastatic cancer in a Phase I clinical trial of MABp1. The trial was conducted at the University of Texas' MD Anderson Cancer Center (Houston, Texas), which is one of the U.S. leading comprehensive cancer centers. MD Anderson is currently ranked as the second-best hospital in the U.S. for cancer care according to the *U.S. News and World Report's* "America's Best Hospitals" list, and has been included in the top two cancer centers for the past 25 years.

In this open-label, dose-escalation trial, the Company sought to evaluate the safety and tolerability of its anti-IL-1a MABp1 antibody in an advanced, refractory (treatment-resistant) cancer population. This population was suitable for an IL-1a-targeting antibody due to the known harm that pathological inflammation can cause in cancer patients. The immune system's **inflammatory cascade**, which begins with the IL-1a response, triggers angiogenesis (the formation of new blood vessels, which is undesirable around tumor cells that use the increased blood supply to grow), tumor stromal remodeling, tumor invasiveness, metastasis, and cachexia (severe weakness and wasting of the body due to illness) (Source: *The Lancet Oncology*, May 2014, Vol. 15[6]: 656–666). Altering these actions could have a beneficial effect on a patient's cancer treatment, particularly for individuals who are in advanced stages of disease where existing options are few and frequently create more side effects than benefits. IL-1a is deemed to be an appropriate therapeutic antibody target for a variety of reasons, including those listed following Figure 14 on page 23:

Figure 14
HIGHLIGHTS OF IL-1a ACTIVITY PROMOTING TUMOR GROWTH AND SPREAD



Source: XBiotech Inc.

- NSAIDs—a class of common anti-inflammatory medications—have not shown sufficient potency or specificity against cancer-associated inflammation;
- IL-1a is an early and very active component in the inflammatory cascade, thus targeting this protein may have more effect than targeting other cellular components, such as the overexpression of vascular endothelial growth factor (VEGF) that occurs further downstream; and
- IL-1a is present on both **leukocytes** (white blood cells) and platelets, with platelet-associated IL-1a having also been linked to cerebrovascular inflammation and exacerbated synovial inflammation and damage.

In developing the MABp1 program, XBiotech has sought to help downregulate the inflammatory processes that are either triggered or exacerbated by IL-1a.

Phase I Advanced Cancer Trial Outcomes

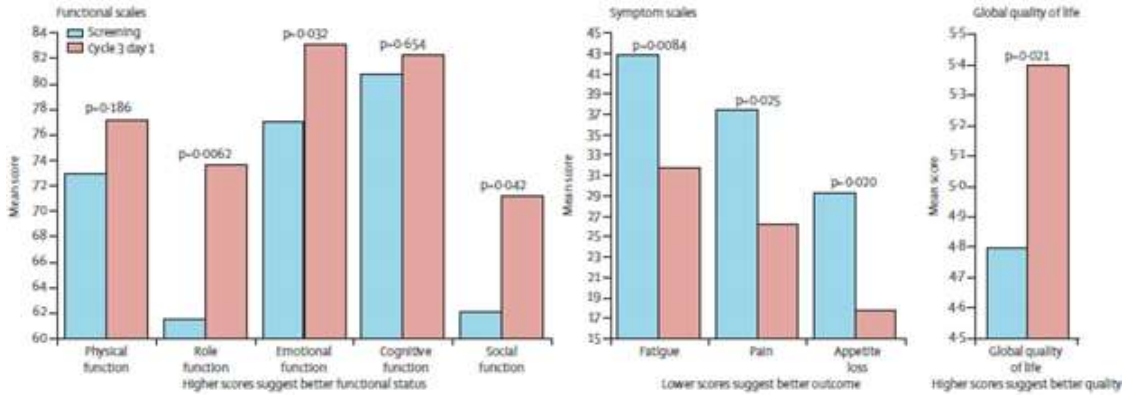
The study's outcomes demonstrated that MABp1 was well tolerated, with no dose-limiting toxicities or immunogenicity. As reported in a published article of the trial's protocol and findings (*The Lancet Oncology*, May 2014, Vol. 15[6]: 656–666), Phase I participants collectively received over 300 infusions of MABp1 with no infusion-site reactions, no dose reductions nor delays for toxicity, and no indication that patients were developing antibodies against the drug. The Company found it was able to safely administer the highest dose used in the trial, which was 3.75 mg/kg every two weeks. The most common adverse events noted during the trial were **proteinuria**, nausea, and fatigue, though it is possible these symptoms were unrelated to the MABp1 therapy and were rather related to the patient's disease. One patient with non-small-cell lung cancer developed pneumonia that was only possibly related to the MABp1 infusion.

In addition to the safety and tolerability data, another important finding from this Phase I trial was that some patients began to see physical improvements in quality of life factors, including pain levels, fatigue, appetite, and weight (as shown in Figure 15 [page 24]). The patients enrolled in this trial had an average age of 61 and were very sick from advanced stages of cancer. In the six months before the trial started, 77% of a 30-patient subset had been losing weight. At week 8 scans, these patients' lean body mass had increased by a mean of 1.02 kg. Figure 16 (page 24) illustrates the change in lean body mass for these 30 patients, with some individuals even showing a 10% to 15% increase in lean body mass over the course of treatment. Lean body mass is an important indicator of recovery from cachexia (wasting away of muscle), as lean body mass is a measure of weight gain due to increases in tissue rather than fat. Cachexia in advanced cancer is known to correlate with poor survival outcomes.

Findings from the trial further suggested that physical recovery could be associated with improvements in survival, particularly in colorectal cancer, which was the tumor type of 27% of the Phase I participants. An interesting outcome of the study was that the Company began to notice that, although all of the patients had advanced disease with tumor metastasis for which it is difficult to predict who will do well and who will not, it could be possible to predict survival outcomes based on the patients' lean body mass recovery.

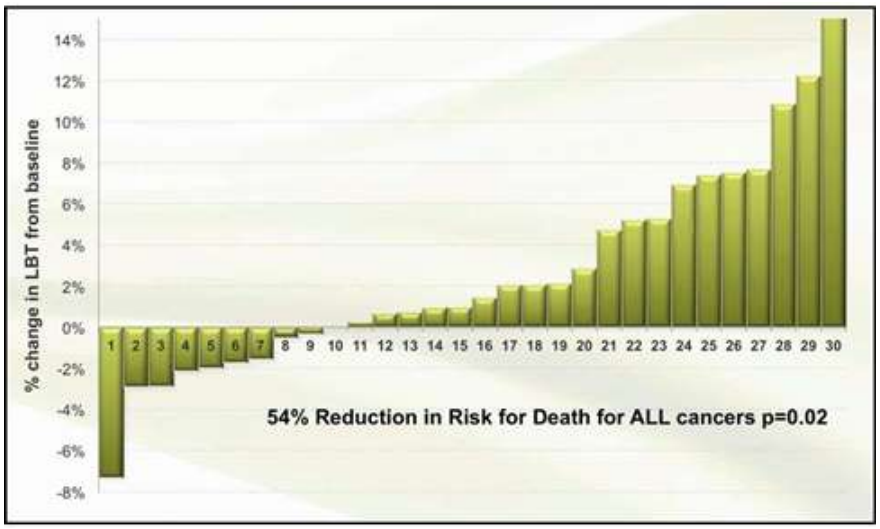
Collectively, the colorectal cancer patients in the trial exhibited a median overall survival of 8.7 months versus the 5 months to 6 months that is typical in this patient population using placebo or regorafenib (Stivarga® from Bayer HealthCare). These findings formed the basis for XBiotech's continued development of MABp1 for colorectal cancer under the trade name Xilonix™. Moreover, colorectal cancer patients in the trial who also showed an increase in lean body mass had a median overall survival of 19.3 months versus 6.6 months in this that lost lean body mass during the study.

Figure 15
CHANGE IN QUALITY OF LIFE AS ASSESSED BY THE EUROPEAN ORGANIZATION FOR RESEARCH AND TREATMENT OF CANCER QUALITY OF LIFE QUESTIONNAIRE



*Source: Figure 4 from Hong, David et al., MABp1, a first-in-class true human antibody targeting interleukin-1*a *in refractory cancers: an open-label, phase 1 dose-escalation and expansion study, The Lancet Oncology, May 2014, Vol. 15[6]: 656–666.*

Figure 16
INDIVIDUAL CHANGES IN LEAN BODY MASS BETWEEN BASELINE AND WEEK 8



Source: XBiotech Inc. and the Lancet Oncology (May 2014).

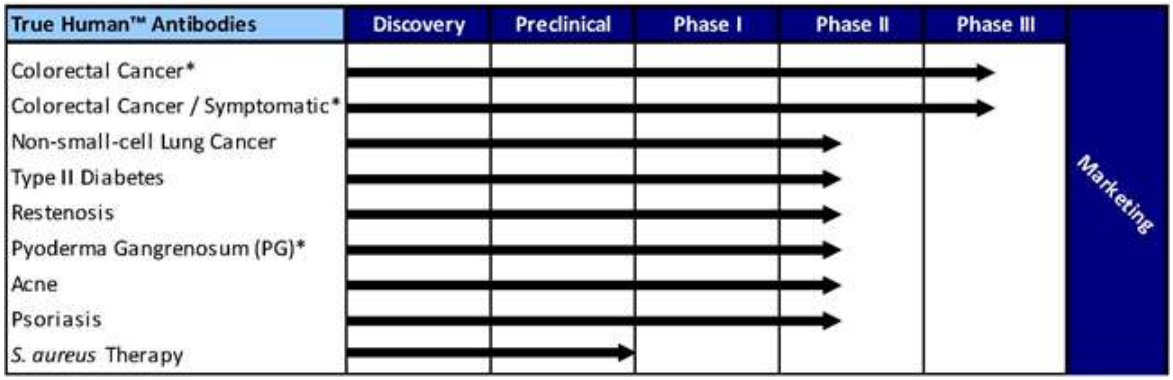
PRODUCT DEVELOPMENT

In addition to the 2010 MD Anderson advanced cancers trial detailed on pages 22-24, the MABp1 therapy has been evaluated in a number of Phase I and Phase II studies for indications including diabetes, vascular disease, acne, psoriasis, and pyoderma gangrenosum (PG). As shown in Figure 17, the lead indication to date is colorectal cancer treatment using XBiotech's Xilonix™ (MABp1) product candidate, and the Company is currently conducting two Phase III studies for colorectal cancer in the U.S. and Europe.

XBiotech has developed a second True Human™ antibody candidate, which targets methicillin-resistant *Staphylococcus aureus* (MRSA). In December 2014, XBiotech filed an IND application for a Phase I/II randomized clinical study to assess this antibody for the treatment of serious infections due to *S. aureus*, which is subject to a clinical hold pending the completion of an animal toxicology study. XBiotech is also currently conducting a Phase II trial for pyoderma gangrenosum (PG).

The Company is currently reviewing the results that it obtained from its studies of MABp1 in patients with diabetes, restenosis, acne, and psoriasis, and is determining additional research or clinical studies that it may conduct in the future in these areas.

Figure 17
XBIOTECH'S PIPELINE



** Ongoing trial*

Source: XBiotech Inc.

Xilonix™ for Colorectal Cancer

In 2013, the FDA granted Fast Track designation for Xilonix™ (MABp1) in colorectal cancer. Fast Track is reserved for products that demonstrate the potential to treat a serious or life-threatening condition that has unmet medical needs. Fast Track designation, which was mandated by the FDA Modernization Act of 1997, can expedite the review of new therapeutic agents. At present, there are two Phase III registration studies underway for Xilonix™ in the colorectal cancer indication: (1) a Phase III U.S. trial in patients with advanced, refractory colorectal cancer; and (2) a Phase III European trial in patients with symptomatic colorectal cancer. Each of these are detailed below.

U.S. Phase III Trial in Colorectal Cancer

XBiotech began its randomized Phase III trial in the U.S. in March 2013. The study originally sought to enroll patients who have colorectal cancer complicated with cachexia. Patient recruitment occurs at over 60 cancer centers across the U.S. In September 2014, the Company opted to temporarily halt this trial in order to revise the protocol and allow for faster patient enrollment. The 40 patients already enrolled were randomized 1:1 between Xilonix™ and a control arm. XBiotech intends for its new protocol to randomize patients 2:1 between Xilonix™ and placebo, and to open enrollment for all advanced, refractory colorectal cancer patients regardless of weight loss. The FDA has agreed to these amendments and the Company aims to begin treating patients under the new protocol in March 2015, with complete enrollment expected in 2016.

The interruption in this study allowed for the Company to perform an interim analysis on the intended primary and secondary endpoints of the study for the 40 patients enrolled up to that point. XBiotech reported that these patients receiving Xilonix™ had a hazard ratio for risk of death of 0.33 (p=0.11) compared with controls, which is considered to show improved survival in the Xilonix™-treated group compared to controls (Source: XBiotech Inc.'s September 2, 2014, press release). Based on a model for predicting the statistical significance of this survival benefit over the projected complete course of the study, XBiotech believes that, although these findings were not statistically significant due to the relatively small number of patients (statistical model was designed for 656 patients), if current effects continue, it could achieve a significant survival benefit beyond what is necessary for product registration.

European Phase III Trial in Symptomatic Colorectal Cancer

The European Phase III study aims to evaluate Xilonix™ as an anticancer therapy in patients with symptomatic colorectal cancer. This trial began in July 2014, and is recruiting at least 276 patients from roughly 40 clinical trial sites. Trials sites are located in a number of different EU member countries, including the UK, France, Germany, Poland, and Belgium, and could likely soon also include sites in Russia in order to facilitate future product registration there as well.

The primary objective of this study is to assess the efficacy of Xilonix™ in reversing symptoms in patients with symptomatic colorectal cancer including reversal of muscle loss (cachexia, which will be assessed with a type of X-ray called a DEXA scanner), fatigue, appetite loss, and pain (which will be measured with a questionnaire completed by patients). By blocking IL-1a, Xilonix™ is anticipated to not only slow tumor growth but also improve each of these symptoms. The efficacy of the therapy will be measured by assessing the change in these symptoms for patients treated with Xilonix™ versus those treated with placebo. The trial is on track for completion of enrollment in 2015, and may enable product registration by the EMA and Russian regulatory authorities.

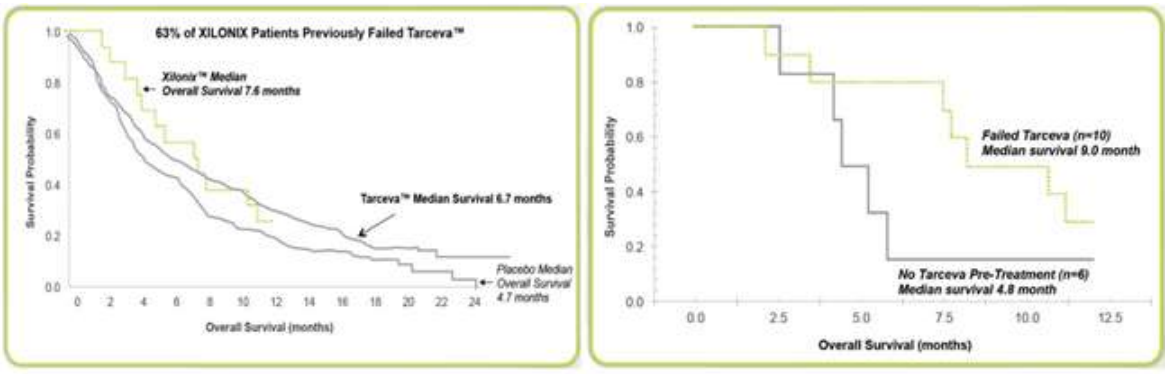
Non-Small-Cell Lung Cancer (NSCLC)

The Phase I study at MD Anderson Cancer Center (as detailed on pages 22-24) included a cohort of 16 patients with advanced non-small-cell lung cancer (NSCLC) who were treated with MABp1 (or Xilonix™) as part of the dose-escalation trial and followed for 24 months. Each of these patients had previously received multiple chemotherapy rounds and had shown to be refractory (resistant) to current treatments. Of this group, 10 individuals (63% of the cohort) had shown disease progression while taking a well-known anti-EGFR inhibitor therapy, erlotinib, which is marketed as Tarceva® from Astellas Pharma, Inc. and Genentech Inc.

As was the case for patients enrolled in the MD Anderson trial who had other tumors (colorectal, pancreatic, renal cell, etc.), Xilonix™ did not appear to have toxicity at any dose level in the NSCLC cohort and there were no infusion reactions reported. However, patients in this cohort did self-report improvements in pain, fatigue, appetite, and physical functions, including showing an average increase in lean body mass. In addition, investigators found that patients who had previously failed anti-EGFR therapy with Tarceva® had better outcomes on substantially all pharmacodynamics and self-reported measures with Xilonix™. Importantly, data suggest that prior treatment with anti-EGFR therapy (even if the treatment failed) was associated with a greater median survival when subsequently treated with Xilonix™. To illustrate, the median overall survival for all patients in the cohort (everyone received Xilonix™) was 7.6 months, which increased to 9.4 months for patients who also had pre-treatment with anti-EGFR therapy and decreased to 4.8 months for patients who had not previously been exposed to the anti-EGFR, as shown in Figure 18 (page 27) (Source: XBiotech Inc.). Based on third-party studies, Tarceva® alone is estimated to extend survival by roughly 6.7 months for patients with locally advanced or metastatic NSCLC (Source: "FDA Approval for Erlotinib Hydrochloride," National Cancer Institute, July 2013).

Figure 18
XILONIX™ OUTCOMES ARE IMPROVED WITH ANTI-EGFR PRE-TREATMENT

Note: The comparison of overall survival with Xilonix™ versus Tarceva® should be viewed with caution, since patient populations, supportive care, or other factors may have been different between the two studies, making direct comparison difficult.



Source: XBiotech Inc.

Type 2 Diabetes

In type 2 diabetes, XBiotech conducted a Phase II pilot study of MABp1, which was led by the University Hospital's (Basel, Switzerland) Head of Endocrinology, Diabetes, and Metabolism, Dr. Marc Donath, who is an endocrinologist and expert on the role of inflammatory disease in diabetes. This trial studied MABp1 in seven patients with type 2 diabetes and was conducted with appropriate due diligence and authorization equivalent to the FDA's IND, under the Swiss regulatory authority SwissMedic. The clinical study assessed safety and pharmacokinetics of MABp1 in the diabetic patient population. The study also examined patients to determine if their diabetes improved, including assessing pancreas function and glucose control.

Patients were given a low dose of MABp1 intravenously every two weeks for a total of four doses (Days 0, 14, 28, and 42). To be eligible for treatment, patients needed to have been diagnosed with type 2 diabetes according to American Diabetes Association's diagnostic criteria at least three months prior to the study.

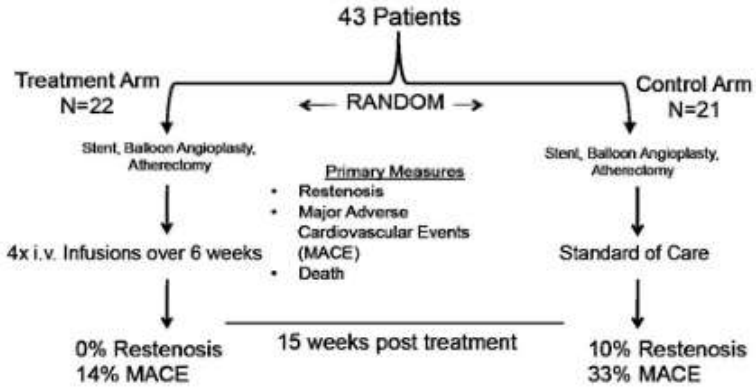
To examine the trend of glycated hemoglobin (HbA1c) levels along the study time points, a trend analysis was performed on patients who completed all visits. Compared to baseline, after the 60 days period of treatment, HbA1c was reduced by 0.14±0.21% (p=0.15), fasting C-peptide was increased by 88% (p=0.03), pro-insulin by 48% (p=0.03), and insulin by 74% (P=0.11). Systolic blood pressure decreased by 11 mmHg (p=0.2). Both HbA1c and blood pressure rebounded to baseline levels 30 days after the end of MABp1 application. Treatment with MABp1 was well tolerated and no adverse events occurred during the study. This increase in HbA1c after removal of the drug further suggested the activity for antibody therapy in these type 2 diabetic patients.

Vascular Disease

In 2012, XBiotech received a Fast Track designation from the FDA for the use of MABp1 antibody therapy as a means to reduce the need for re-intervention after **superficial femoral artery** revascularization. The superficial femoral artery branches off from the femoral artery in the thigh. This is the portion of the femoral artery commonly used for catheters, wires, or drawing blood. Revascularization is the process by which obstructed or disrupted blood vessels (in this case, those located in the superficial femoral artery) are surgically replaced or unblocked in order to restore blood circulation to the affected area. The Company received Fast Track status in this indication after showing favorable interim data from a Phase II study of MABp1 in patients undergoing revascularization of the superficial femoral artery in the leg. The study sought to demonstrate the ability of MABp1 antibody therapy at helping to reduce the likelihood of adverse events in this patient population, all of whom had symptomatic peripheral vascular disease characterized by pain, gangrene, or claudication (an exercise-induced leg cramp cause by artery obstruction).

Patients in the active drug arm were given infusions of MABp1 on days 0, 14, 28, and 42 along with the **standard of care** following surgical intervention. Patients in the control arm received only the standard of care following surgery. Results in peripheral vascular disease have shown a trend toward reducing restenosis (reducing abnormal narrowing of arteries post-surgery) and reducing the incidence of Major Adverse Cardiac Events (MACE), such as heart attack and stroke, in MABp1-treated patients. Figure 19 illustrates the trial design and major outcomes, which suggested a beneficial treatment effect at 15 weeks. At this point, the rate of restenosis and MACE was lower in the MABp1-treated patients than in the control arm. XBiotech believes that data supports the potential that MABp1 may have both a local therapeutic effect as well as an impact on underlying systemic vascular disease.

Figure 19
RANDOMIZED PHASE II STUDY DESIGN AND OUTCOMES IN VASCULAR DISEASE



Source: XBiotech Inc.

Dermatology

Pyoderma Gangrenosum (PG)

Figure 20
CLASSIC PYODERMA GANGRENOSUM

Source: British Medical Journal, 2006 Jul 22; 333(7560): 181–184.

Pyoderma gangrenosum (PG) is a rare immune disorder causing large, painful ulcerative sores to develop on the skin (as shown in Figure 20). People with underlying inflammatory conditions, such as inflammatory bowel disease or rheumatoid arthritis, have a higher risk of the onset of PG. Though this disease is not commonly fatal, it is highly debilitating and painful. Patients may experience a diminished quality of life due to the large lesions on their bodies, and disease recurrence and scarring after immunosuppressive therapy is possible. PG affects approximately 1 in 100,000 persons each year in the U.S., making this an orphan indication for drug development.

An orphan disease is one affecting fewer than 200,000 people in the U.S. An orphan drug is an FDA designation given to products intended to treat orphan diseases. Orphan drug development is incentivized by the FDA through providing makers of orphan drugs with seven years of marketing exclusivity and other incentives designed to expedite clinical development and time to market, such as federal grants, tax credits, and filing fee waivers.

Ongoing Phase II Trial in PG

XBiotech is conducting an open-label Phase II trial to measure the safety and efficacy of MABp1 at wound healing in patients with PG. The primary endpoint of the study is a 28-day assessment from baseline by both the clinician and patient, with the option for patients to continue in up to two additional 28-day cycles if desired. Ten patients are expected to participate in the trial. Thus far, XBiotech reports that wound healing results have been favorable. XBiotech plans to evaluate patient responses in the first half of 2015, and based on these results, may elect to seek breakthrough designation with the FDA. If a drug is designated as breakthrough therapy, the FDA can expedite the development and review of such drug. Approval of MABp1 in PG, combined with the Company's work in acne and psoriasis, could help open up the dermatology market for XBiotech.

Figure 21 illustrates images taken of a patient during the current Phase II study. This patient was given three cycles of MABp1. Each 28-day cycle consisted of a MABp1 administered intravenously the first week and weekly subcutaneous doses for the next three weeks.

Figure 21
PG IMPROVEMENT WITH MABp1

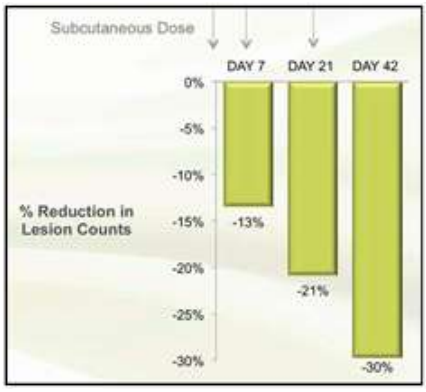
Source: XBiotech Inc.

Acne

The role of IL-1a in acne suggests that an anti-IL-1a antibody therapy may help reduce inflammatory acne lesions, as well as depression and other acne-related conditions, due to an impact on the chronic inflammatory process. As detailed on page 21, IL-1a starts the inflammation response and then sends a message to the brain to give the injury response, thus it is possible that the anxiety and depression frequently associated with acne is not solely from looking in the mirror but may actually be physiologically related to the inflammatory process.

To this end, XBiotech has completed a Phase II exploratory study of MABp1 in moderate to severe acne, and found that patients had significant improvement in facial lesions (data shown in Figure 22) and also had improved scores on the Hospital Anxiety and Depression (HADS) questionnaire following MABp1 injections. The Company reports that, prior to taking MABp1 injections, some patients were considered to have clinical levels of anxiety and were on medication. Within three weeks after the first injection, researchers saw average anxiety and depression scores for the patients in the study decrease to match levels for the general population. After three MABp1 injections (56 days), scores were less than those for the general population (p-value of 0.004) (Source: XBiotech Inc.).

Figure 22
REDUCED FACIAL INFLAMMATORY LESION COUNTS



Source: XBiotech Inc.

Acne may represent a considerable market opportunity for XBiotech, given the favorable safety and tolerability profile of MABp1 shown to date. Existing medications for severe acne that cannot be controlled through over-the-counter means center on the use of isotretinoin (brand names Claravis, Accutane, and others), which is a high-risk product. Common side effects of isotretinoin are dry skin, rashes, upset stomach, eye discomfort, bone and joint pain, and nosebleeds; though, the distribution of this medicine is carefully controlled due to rare but serious risks of fetal abnormalities, suicide, depression, anxiety, and other mental and behavioral changes. A more tolerable alternative to treating

moderate to severe acne without exacerbating the associated psychological conditions is needed. XBiotech anticipates needing a large-scale trial in order to establish the database of safety information required for this indication, which could be a possible path for the Company in the future. Present efforts are focused more toward colorectal cancer and like indications where smaller trials are sufficient and there is a faster time to market.

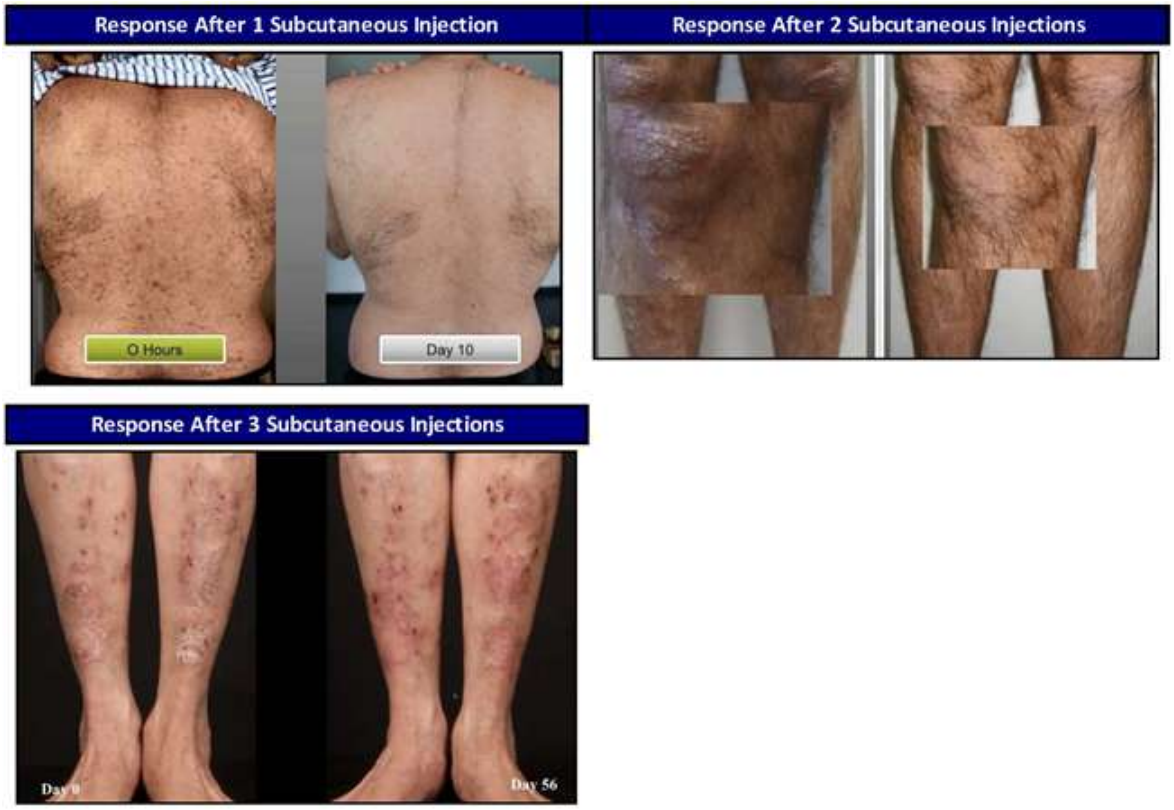
Psoriasis

Figure 23
OVERALL DECLINE IN PASI SCORE

Source: XBiotech Inc.

XBiotech began a Phase II study of MABp1 in moderate to severe plaque psoriasis after seeing favorable results of the therapy used on a compassionate basis in a 48-year-old male suffering from psoriasis. The Company reports that this patient had a nearly complete resolution of his psoriatic lesions within 10 days of MABp1 administration (as shown in Figure 24, top left). Outcomes of the Phase II exploratory study also showed rapid improvement in patients' psoriasis after receiving three subcutaneous injections of the anti-IL-1a antibody. After 35 days, there was an average improvement of 43% in scores on the Psoriasis Area and Severity Index (PASI), as shown in Figure 23. Figure 24 depicts additional favorable outcomes that XBiotech experienced with MABp1 in its psoriasis study.

Figure 24
MABp1 ANTIBODY THERAPY EFFICACY IN PSORIASIS



Source: XBiotech Inc.

Infectious Disease

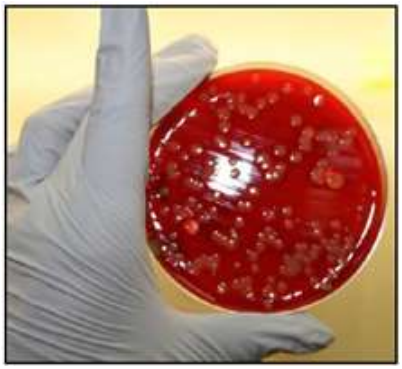
Methicillin-Resistant Staphylococcus Aureus (MRSA)

MRSA is a common bacterial infection that occurs in patients with weakened immune systems, and is resistant to the most common antibiotics, such as methicillin, amoxicillin, penicillin, and oxacillin. MRSA can cause a variety of infections, ranging from superficial skin eruptions to urinary tract infections, pneumonia, and other life-threatening illnesses. XBiotech had initiated a development program to treat MRSA infections using a True Human™ antibody. Note that this is not the same antibody product used in the Company's aforementioned development programs (MABp1). XBiotech identified its True Human™ antibody now in development for MRSA in 2013 after screening the blood of hundreds of individuals. It is estimated that one-third of people already have *S. aureus* in their bodies, especially in the nasal cavities, and that 2.7% of these are MRSA strains.

XBiotech screened blood samples for antibodies that targeted *S. aureus*'s immune-evasion mechanisms. Once such antibodies were found in the blood, the Company identified and cloned the genes responsible for producing these particular antibodies. To XBiotech's knowledge, the True Human™ antibody it is now developing is specific against the *S. aureus* evasion capabilities and is highly resistant to manipulation from the bacteria. The antibody may be able to bind to and neutralize the *S. aureus* bacteria, even blocking its ability to evade the immune system.

Figure 25

BACTERIA COLONIES BEING SCREENED FOR MRSA AT XBIOTECH'S LABORATORIES



Source: XBiotech Inc.

Going forward, XBiotech aims to commence a randomized, double-blind, dose-escalation Phase I/II clinical trial of its antibody against *Staphylococcus*, following the submission of an Investigational New Drug (IND) application to the FDA in December 2014. The study is currently on hold while, at the request of the FDA, an animal toxicology study is conducted, which XBiotech hopes to conclude during the first half of 2015. Upon successful completion of this toxicology study, the clinical trial would likely enroll approximately 50 patients who are hospitalized with *S. aureus* infections, and seek to measure the anti-*Staphylococcus* antibody's impact on hospitalization length.

Additional Potential Pipeline Applications

Ultimately, XBiotech's ability to identify and clone novel antibody proteins could lead to an array of important future discoveries. For example, the Company believes that it is possible to use its approach to create therapeutics for deadly infectious diseases, such as Ebola, where survivors of the disease have generated neutralizing, anti-Ebola antibodies in their own blood to prevent re-infection with the virus. In January and February 2015, the Company received blood samples from Ebola-recovered patients, which have now been confirmed by XBiotech to contain high levels of anti-Ebola antibodies. The Company intends to begin animal studies with a product candidate derived from this blood sample in 2015.

MARKET OPPORTUNITIES

The global market for therapeutic monoclonal antibodies (MAbs) was valued at roughly $63.4 billion in 2013 and is expected to reach $122.6 billion by 2019—representing a compound annual growth rate (CAGR) of 12.2% (Source: BCC Research's *Antibody Drugs: Technologies and Global Markets*, January 2015). Other analysts value the global MAbs market at an estimated $80 billion, and forecast that it could produce one of the biotechnology industry's fastest CAGRs (Source: Research in China's *Global and China Monoclonal Antibody Industry Report, 2014-2019*, October 2014). Growth factors in the therapeutic antibody market include the advancement of MAb technology, increased adoption and acceptance of therapeutic antibodies, and a rise in incidence of various diseases that MAbs target (Source: Persistent Market Research's *Next-Generation Antibody Therapeutics Market: Global Industry Analysis and Forecast to 2020*, November 2014).

Another factor driving antibody research and development is the commercial potential of these therapies. By some estimates, 80% of the antibodies that were expected to be approved from 2011 to 2015 appeared to have significant commercial potential (Source: Insight Pharma Reports' *Monoclonal Antibodies in the Pipeline: A Segment of Major Growth*, March 2011). To that end, 5 of the 10 bestselling biotechnology drugs in the U.S. during 2013 were therapeutic MAbs, each with sales over $6 billion (as shown in Figure 26) (Source: FiercePharma's *The 10 Best-Selling Drugs of 2013*, March 2014). The top 10 best-selling MAbs accounted for $58.1 billion in revenues during that year (Source: Research in China's *Global and China Monoclonal Antibody Industry Report, 2014-2019*, October 2014).

By 2013, 33 MAbs were approved in the U.S., with an additional 338 antibody products in various stages of clinical development. Oncology and autoimmune diseases are the areas of greatest activity, with approximately 170 new MAbs being developed for cancer indications and over 70 MAbs in clinical development for treatment of inflammatory and autoimmune diseases (Source: PhRMA Research's *Biologics: 2013 Report*).

Figure 26
TOP 10 BEST-SELLING THERAPEUTICS OF 2013

Product	Company	Indications	Sales (in $ billions)
Humira® (adalimumab)	AbbVie	Rheumatoid Arthritis, Plaque Psoriasis, Crohn's Disease, Ulcerative Colitis, Psoriatic Arthritis, Ankylosing Spondylitis	$ 11.02
Enbrel® (etanercept)	Pfizer/Amgen	Rheumatoid Arthritis, Plaque Psoriasis, Psoriatic Arthritis, Ankylosing Spondylitis, Juvenile Idiopathic Arthritis	$ 8.78
Remicade® (infliximab)	Janssen (J&J)	Rheumatoid Arthritis, Plaque Psoriasis, Crohn's Disease, Ulcerative Colitis, Psoriatic Arthritis, Ankylosing Spondylitis	$ 8.39
Advair®	GlaxoSmithKline	Asthma/COPD	$ 8.25
Lantus®	Sanofi-Aventis	Diabetes	$ 7.59
Rituxan® (rituximab)	Biogen/Genentech Roche	Oncology (Non-Hodgkin's Lymphoma, Chronic Lymphocytic Leukemia) and Rheumatoid Arthritis	$ 7.50
Avastin® (bevacizumab)	Roche	Colorectal Cancer, Non-small Cell Lung Cancer, Renal Cell Carcinoma, Glioblastoma (brain cancer)	$ 6.75
Herceptin® (trastuzumab)	Roche	Breast Cancer, Gastric Cancer	$ 6.56
Crestor®	AstraZeneca	Cholesterol	$ 6.04
Abilify®	Bristol-Myers Squibb	Schizophrenia	$ 5.50

* Monoclonal Antibodies (MAbs)

Source: FiercePharma's The 10 Best-Selling Drugs of 2013, March 2014.

Monoclonal Antibodies in Oncology

Cancer is among the leading causes of morbidity and mortality worldwide, with approximately 14 million new cases and 8.2 million cancer-related deaths in 2012, with the number of new cases expected to rise by about 70% over the next two decades (Source: World Health Organization). As a serious, prevalent, and highly fatal group of diseases, oncology markets continues to lead new therapeutics development and commercialization, with revenues estimated at nearly $91 billion as of 2013 (Source: IMS Institute for Healthcare Informatics, May 2014). However, as technology advances, the dynamics of the oncology market are subject to change. IMS Health's May 2014 study documented a dramatic shift toward targeted therapies—in essence, cancer medications that are directed specifically to a certain component in the body rather than function as systemic treatments (like many previous chemotherapy options) attacking the body's healthy cells in the quest to eradicate the tumor cells. Targeted therapies, such as XBiotech's True Human™ antibody approach to cancer and other diseases, have the potential to achieve greater efficacy with fewer adverse effects—a highly desirable quality in cancer care. IMS Health states that targeted therapies represented 46% of global oncology sales in 2013, up from only 11% a decade ago (Source: IMS Health's May 6, 2014, Press Release).

The scope of the problem and the size of the potential cancer market has prompted pharmaceutical and biotechnology companies to invest in the oncology sector, with major focus on MAbs. The 2013 market for cancer MAbs was estimated at $23 billion and is expected to reach $33 billion by 2017 (Source: RNCOS' *Cancer Monoclonal Antibodies Market Forecast to 2017*, August 2013).

Over the past couple of decades, the FDA has approved more than a dozen MAbs to treat certain cancers (Source: American Cancer Society, December 2014). In addition, clinical trials of MAbs therapies are being undertaken for almost every type of cancer, as researchers find more antigens linked to each type of cancer. Accordingly, there are 374 experimental cancer drugs in mid-stage trials, of which between 25% and 30% are immunotherapies (Source: Bloomberg's *The Coming Wave of New Cancer-Fighting Drugs*, January 2015).

Colorectal Cancer

Colorectal cancer is one of the most diagnosed cancers in both men (third highest) and women (second highest), resulting in 694,000 deaths during 2012 (Source: World Health Organization). Advancements in treating colorectal cancer have traditionally come from the development of new chemotherapy agents or new combinations of such agents but have recently shifted with the introduction of targeted therapies such as MAbs.

The global market for MAbs in colorectal cancer is estimated to reach $5.5 billion by 2019 (Source: GBI Research's *Monoclonal Antibodies Market in Colorectal Cancer to 2019*, December 2013). There are currently three such treatments approved by the FDA for metastatic colorectal cancer, with the purpose of extending the patient's lifespan: (1) bevacizumab (Avastin®) for advanced bowel cancer, breast cancer, and some other cancers; (2) cetuximab (Erbitux®) for advanced bowel cancer or in trials for other cancers; and (3) panitumumab (Vectibix®) for advanced bowel cancer.

Monoclonal Antibodies in Dermatology

Psoriasis

MAbs have been employed in the treatment of dermatologic disease, with a particular emphasis in the treatment of psoriasis. The systemic psoriasis market is forecast to grow from $5 billion in 2013 to $10.4 billion in 2020, driven by a rising treatment population and the continued uptake of biologics. Although patent expiration and the generation of biosimilar competitors might have a negative effect on the market, it is expected to be offset by the emergence of additional novel therapies (Source: GBI Research's *Systemic Psoriasis Therapeutics in Major Developed Markets to 2020 – Continued Uptake of Biologics and Novel Pipeline Drugs to Drive Growth*). Increased understanding of the **immunopathogenesis** of psoriasis has led to the emergence of new MAb-based therapies targeting the immune cells and molecules that induce and maintain the clinical changes seen in psoriatic plaques. In addition to effectiveness, agents treating psoriasis have enjoyed significant financial status. Humira®, Enbrel®, and Remicade®, each of which target psoriasis among other conditions, were the top three bestselling therapeutic agents in 2013.

Pyoderma Gangrenosum (PG)

In general, the dermatology market is expected to profit from the increased use of biologics, with the clinical development pipeline including MAbs for the treatment of several mild-to-moderate dermatological conditions (Source: Researchandmarkets' *Global Dermatological Drugs Market 2014-2018*, March 2014). More specifically, in recent years a deeper understanding of the underlying basis for dermatological ailments has led to the study and use of MAbs as an effective treatment option for various systemic and cutaneous dermatological diseases in addition to psoriasis, including atopic dermatitis, PG, and various blistering diseases (Source: *Journal of Dermatological Treatment*, Vol. 20[6]:319-27, 2009). Currently, TNF-alpha inhibitors—which include adalimumab (Humira®), infliximab (Remicade®), and etanercept (Enbrel®), among others—are close to first-line agents in the treatment of PG (Source: Medscape). In addition, XOMA Corporation (XOMA-NASDAQ) is assessing the use of gevokizumab, an IL-1ß-modulating antibody that has been granted Orphan Drug designation by the FDA, for the treatment of PG.

Diabetes

The global market for diabetes medications is expected to reach $55.3 billion in 2017, up from an estimated $35.6 billion in 2012 (Source: Visiongain's *Diabetes Treatments: World Drug Market 2013-2023*, April 2013). The growth of the diabetes market is driven by an increase in the worldwide incidence of type 1 and type 2 diabetes, with 9% of adults 18 years and older estimated to have diabetes in 2014. In 2012, diabetes was the direct cause of 1.5 million deaths, with the disease projected to be the seventh-leading cause of death by 2030 (Source: World Health Organization).

Cardiovascular Disease

Cardiovascular disease is the number one cause of death worldwide, with an estimated 17.3 million deaths in 2008, representing 30% of all global deaths. This number is expected to increase, reaching 23.3 million deaths by 2030 (Source: World Health Organization). The world market for cardiovascular drugs is projected to exceed $111.8 billion by the year 2015, driven by an aging population, a significantly large number of patients, and growing incidence of cardiovascular diseases (Source: Global Industry Analysts, Inc.'s *Cardiovascular Drugs: A Global Strategic Business Report*, April 2010). During 2013, four of the top 15 therapeutic classes by sales were cardiovascular related: anti-hypertensive ($49.6 billion), lipid regulators ($28.9 billion), anticoagulants ($24.1 billion), and other cardiovascular ($21.9 billion).

Drug-Resistant Infections: MRSA

The U.S. Centers for Disease Control and Prevention (CDC) estimates that 1 in 20 hospitalized patients contract a healthcare-associated infection. The global rate is calculated at 3.5% to 12% of admissions in developed regions (Source: Kalorama Information's *Healthcare Associated Infection Control Markets: Disinfection, Area, Sterilization, Device Sterilization, Testing-C.diff, Testing-MRSA, Treatments*, June 2014). The global MRSA therapeutics market, estimated at $2.7 billion in 2011, is forecasted to reach $3.5 billion by 2019 due to an increase in the prevalence of MRSA infections and a growth in government and non-government awareness programs (Source: GlobalData's *Methicillin-resistant Staphylococcus aureus [MRSA] Therapeutics - Pipeline Assessment and Market Forecasts to 2019*, June 2012). The market growth is driving the demand for products and services, with the pipeline to treat this condition including both antibiotics and vaccines, in various phases of development. First-in-class molecules account for over 40% of the pipeline, showing that a new generation of medicines is fast emerging, including the use of MAbs.

Competition

By the end of 2013, there were 33 therapeutic monoclonal antibodies (MAbs) approved in the U.S., with over 338 in various stages of clinical development but largely directed at indications in the areas of cancer, immunological and inflammatory diseases, and infectious disease (Source: PhRMA Research's *Biologics: 2013 Report*). Despite the growing interest in the MAb therapeutic field, a large part of the total market is still concentrated in few companies with the top 10 bestselling MAbs accounting for over 72% of the market in 2013.

However, smaller technology-focused companies are expected to continue to be a major source of innovation in the antibody market, both as developers of new technologies and as a source of antibodies for licensing agreements. In addition, as the biologics and MAb market continues to expand, major companies that currently derive only modest revenues from antibody products are expected to make strategic acquisitions to enhance pipelines (Source: Insight Pharma Report's *Monoclonal Antibodies in the Pipeline: A Segment of Major Growth Report— Overview*, March 2011).

As XBiotech's pipeline targets diverse conditions, including cancer, immunological and inflammatory diseases, cardiovascular disease, diabetes, and infectious disease, the Company might encounter a wide range of competition, from existing products (both traditional and biologic agents) being marketed for these indications to new creations in development at pharmaceutical and biotechnology companies and research institutions. XBiotech believes that its novel True Human™ antibody technology, and the cost and competitive advantages of its manufacturing and production process, give the Company a competitive edge over alternative therapy techniques, either approved or in development.

The companies presented below are not intended to be an exhaustive collection of XBiotech's potential competition, but rather are believed to be representative of the type of competition that XBiotech may face as it seeks to commercialize its product candidates going forward.

AbbVie Inc. (ABBV-NYSE)

AbbVie is a global research-based biopharmaceutical company formed in 2013 following its separation from Abbott Laboratories. AbbVie's MAb products include Humira® (adalimumab), a biologic therapy to treat autoimmune diseases; BT-061 (tregalizumab), a Phase II candidate for the treatment of rheumatoid arthritis and psoriasis; and ABT-700, a Phase I candidate for solid tumors. Humira®, the first fully human MAb approved by the FDA, is a TNF-inhibiting anti-inflammatory drug for the treatment of rheumatoid arthritis, plaque psoriasis, Crohn's disease, ulcerative colitis, psoriatic arthritis, and ankylosing spondylitis. Humira® has been one of the bestselling drugs in the past few years, exceeding $10.6 billion in sales for 2013. AbbVie, based in North Chicago, Illinois, employs approximately 25,000 people and markets medicines in more than 170 countries.

Amgen Inc. (AMGN-NASDAQ)

Amgen is a biotechnology company focused on the development and commercialization of human therapeutics in the areas of oncology, hematology, inflammation, bone health, nephrology, cardiovascular, and general medicine. Its MAb line of products includes Vectibix® (panitumumab), a fully human MAb indicated as a first-line (in combination with FOLFOX chemotherapy regimen) or second-line treatment of some forms of metastatic colorectal cancer, and XGEVA® (denosumab) for the treatment of osteoporosis, bone cancer, bone loss, and bone-related problems in patients who have cancer. In addition, the company's products include the biologic Enbrel® (etanercept), co-marketed with Pfizer, a TNF-inhibiting agent for the treatment of rheumatoid arthritis, plaque psoriasis, psoriatic arthritis, ankylosing spondylitis, and juvenile idiopathic arthritis. Enbrel® continues to hold its position as market leader among biologics, with revenues of $8.8 billion in 2013. Amgen's clinical pipeline also includes the rilotumumab in Phase III studies for the treatment of gastric cancer, and brodalumab (jointly developed in collaboration with AstraZeneca Plc [AZN-NYSE]), in Phase III studies for the treatment of psoriasis. Amgen was founded in 1980 and is headquartered in Thousand Oaks, California.

Bristol-Myers Squibb Company (BMY-NYSE)

Bristol-Myers develops and markets biopharmaceutical products in various therapeutic areas, including virology, oncology, neuroscience, metabolics, immunoscience, and cardiovascular disease. One of the company's main oncology products is Erbitux® (cetuximab), a chimeric (mouse/human) MAb used for the treatment of metastatic colorectal cancer, metastatic non-small-cell lung cancer (NSCLC), and head and neck cancer. Erbitux® is produced and marketed in North America in collaboration with Eli Lilly and Company, and is marketed outside of the U.S. and Canada by Merck KGaA. In addition, the company's product line includes the biologic fusion protein Orencia® (abatecep) for lupus nephritis, psoriatic arthritis, and rheumatoid arthritis. The company also has various MAbs in Phase III trials for treatment of cancer, including elotuzumab for relapsed multiple myeloma and nivolumab for metastatic melanoma. The company, headquartered in New York, New York, was formerly known as Bristol-Myers Company and changed its name to Bristol-Myers Squibb Company in 1989.

Celgene Corporation (CELG-NASDAQ)

Celgene is a biopharmaceutical company involved in the development and commercialization of therapies to treat cancer and immune-inflammatory related diseases. The company's products include Otezla® (apremilast), a small molecule for the treatment of psoriatic arthritis and plaque psoriasis. Apremilast is the first oral agent that is FDA approved for the treatment of psoriatic arthritis and offers the convenience of oral dosing compared to treatment with biopharmaceuticals. It is also being tested for its efficacy in treating other chronic inflammatory diseases such as ankylosing spondylitis, Behcet's disease, and rheumatoid arthritis. Celgene was founded in 1980 and is headquartered in Summit, New Jersey.

Eli Lilly and Company (LLY-NYSE)

Eli Lilly develops, manufactures, and sells pharmaceutical products worldwide in a wide range of therapeutic areas, including oncology, endocrinology, neuroscience, and cardiovascular disease. Its oncology products treat pancreatic, metastatic breast, NSCLC, ovarian, bladder, colorectal, and head and neck cancer. The company's MAb-related products include Erbitux® (cetuximab), a chimeric (mouse/human) MAb used for the treatment of metastatic colorectal cancer, metastatic NSCLC, and head and neck cancer (in partnership with Bristol Myers) and Cyramz® (ramucirumab), a fully human MAb approved for the treatment of gastric cancers and NSCLC. In addition, Eli Lilly's pipeline includes the product candidate ixekizumab, a biologic entity that is being studied for the treatment of psoriasis and psoriatic arthritis. Eli Lilly and Company was founded in 1876 and is headquartered in Indianapolis, Indiana.

Johnson & Johnson (JNJ-NYSE)

Johnson & Johnson, together with its subsidiaries, is engaged in the development and sale of various products in the healthcare field worldwide. The company operates in three segments: consumer, pharmaceutical, and medical devices and diagnostic. The Pharmaceutical segment produces anti-infective, antipsychotic, cardiovascular, contraceptive, gastrointestinal, hematology, immunology, infectious diseases, metabolic, neurology, oncology, pain management, thrombosis, and vaccine products, mostly through the operations of its Janssen Pharmaceutical Companies subsidiary. Janssen Biotech Inc. develops solutions in the therapeutic areas of immunology, oncology, and nephrology with a strong emphasis on biologic therapies. Janssen Biotech's product portfolio includes Remicade® (infliximab), a MAb approved for the treatment of plaque psoriasis, rheumatoid arthritis, psoriatic arthritis, Crohn's disease, ankylosing spondylitis, and ulcerative colitis, and one of the top-selling therapeutic agents in 2013 (sales of $8.4 billion). In addition, the company also commercializes Simponi® (golimumab), a biologic treatment for rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis, and Stelara® (ustekinumab), which is approved to treat moderate to severe plaque psoriasis and psoriatic arthritis. Johnson & Johnson was founded in 1885 and is based in New Brunswick, New Jersey.

Novartis AG (NVS-NYSE)

Novartis is a Swiss multinational pharmaceutical company with a pharmaceuticals division that offers patented prescription medicines in various therapeutic areas, including oncology, autoimmune diseases, ophthalmology, neuroscience, and cardiovascular disease. The company's products includes Cosentyx® (secukinumab), a MAb approved for the treatment of moderate-to-severe plaque psoriasis and which is also in clinical trials for the treatment of ankylosing spondylitis and rheumatoid arthritis. In addition, Novartis' Sandoz division, responsible for the company's generics business, is currently developing biosimilars for adalimumab (Phase III for plaque psoriasis), etanercept (Phase III for plaque psoriasis), and rituximab (Phase II for rheumatoid arthritis). Novartis AG was founded in 1895 and is headquartered in Basel, Switzerland.

Pfizer Inc. (PFE-NYSE)

Pfizer develops and commercializes healthcare products worldwide. Its specialty care and oncology segment provides prescription pharmaceutical products for anti-infectives, endocrine disorders, hemophilia, inflammation, ophthalmology, pulmonary arterial hypertension, specialty neuroscience, and vaccines, as well as oncology and oncology-related illnesses. Pfizer's main biologic product is Enbrel® (etanercept), co-marketed with Amgen, a TNF-inhibiting agent for the treatment of rheumatoid arthritis, plaque psoriasis, psoriatic arthritis, ankylosing spondylitis, and juvenile idiopathic arthritis. The company's pipeline also includes Xeljanz® (tofacitinib), a Janus Kinase (JAK) inhibitor in Phase III studies for psoriasis, psoriatic arthritis, and ulcerative colitis. Pfizer Inc. was founded in 1849 and is headquartered in New York, New York.

Roche Holding AG (ROG.VX-SIX)

Roche is a Swiss healthcare company that operates worldwide in two divisions: pharmaceuticals and diagnostics. Roche, the largest oncology company in the world, currently has the largest portfolio of approved MAb treatments, including Avastin® (bevacizumab) for the treatment of brain, colon, kidney, and lung cancers; Herceptin® (trastuzumab) for breast and stomach cancers; Rituxan® (rituximab, through the operations of its wholly owned affiliate Genentech) for chronic lymphocytic leukemia and non-Hodgkin's lymphoma; ACTEMRA® (tocilizumab) for the treatment of rheumatoid arthritis; and MabThera® (Rituximab) for treatment of moderately to severely active rheumatoid arthritis. In addition, the company's pipeline includes RG7221, a MAb in Phase II for colorectal cancer. Roche's headquarters are located in Basel, Switzerland.

XOMA Corporation (XOMA-NASDAQ)

XOMA Corporation discovers and develops antibody-based therapeutics for global distribution. The company's pipeline include gevokizumab, a IL-1ß-modulating antibody for the treatment of inflammatory, ophthalmology, and cardiovascular diseases, including Phase III studies for PG (which was granted Orphan Drug Designation by the FDA), and Phase II for cardiovascular disease and acne. XOMA's proprietary products also include its Xmet program, incorporating a new class of fully human MAbs for treatment of diabetes, as well as several oncology programs. Further, the company licenses multiple antibody discovery, development, and manufacturing technologies. The company was founded in 1981 and is headquartered in Berkeley, California.

Historical Financial Results

Figures 27, 28, and 29 (pages 38-40) summarize XBiotech's key historical financial statements: its Statements of Operations, Balance Sheets, and Statements of Cash Flows, as presented in the Company's amended Form S-1 filed with the U.S. Securities and Exchange Commission (SEC) on March 10, 2015. XBiotech plans to conduct an IPO of its common stock after the SEC completes the review process of its S-1 registration statement, subject to market and other conditions.

Figure 27

XBiotech Inc.

CONSOLIDATED STATEMENTS OF OPERATIONS

(in thousands, except share and per share data)

	Year Ended December 31,		
	2012	2013	2014
Operating expenses:			
Research and development	$ 13,334	$ 7,935	$ 14,329
General and administrative	1,829	1,990	7,449
Total operating expenses	15,163	9,925	21,778
Loss from operations	(15,163)	(9,925)	(21,778)
Other income (loss):			
Interest income	3	1	1
Foreign exchange gain (loss)	—	(3)	53
Total other income (loss)	3	(2)	54
Net loss	$ (15,160)	$ (9,927)	$ (21,724)
Net loss per share—basic and diluted	$ (0.71)	$ (0.45)	$ (0.90)
Shares used to compute basic and diluted net loss per share	21,294,369	22,220,416	24,162,700

Source: XBiotech Inc.

Figure 28

XBiotech Inc.

CONSOLIDATED BALANCE SHEETS

(in thousands, except share data)

	December 31	
	2013	2014
Assets		
Current assets:		
Cash and cash equivalents	$ 7,244	$ 57,329
Prepaid expenses and other current assets	449	411
Deferred offering costs	—	324
Total current assets	7,693	58,064
Property and equipment, net	3,380	4,113
Total assets	$ 11,073	$ 62,177
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable	$ 561	$ 1,629
Accrued expenses	284	1,518
Total current liabilities	845	3,147
Shareholders' equity:		
Preferred stock, no par value, unlimited shares authorized, no shares outstanding	—	—
Common stock, no par value, unlimited shares authorized, 22,752,101 and 27,546,632 shares outstanding at December 31, 2013 and 2014, respectively	81,807	152,351
Accumulated other comprehensive loss	(135)	(153)
Accumulated deficit	(71,444)	(93,168)
Total shareholders' equity	10,228	59,030
Total liabilities and shareholders' equity	$ 11,073	$ 62,177

Source: XBiotech Inc.

Figure 29

XBiotech Inc.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(In Thousands)

	Year Ended December 31, 2012	2013	2014
Operating activities			
Net loss	$(15,160)	$ (9,927)	$(21,724)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	946	784	664
Share-based compensation expense	2,816	739	7,020
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(49)	(252)	38
Accounts payable	(199)	103	1,068
Accrued expenses	80	(326)	1,234
Deferred rent	(68)	(29)	—
Net cash used in operating activities	(11,634)	(8,908)	(11,700)
Investing activities			
Purchase of property and equipment	(550)	(59)	(1,397)
Net cash used in investing activities	(550)	(59)	(1,397)
Financing activities			
Issuance of common stock and warrants, net	7,148	12,045	63,374
Issuance of common stock under stock option plan	135	—	150
Deferred offering costs	—	—	(324)
Net cash provided by financing activities	7,283	12,045	63,200
Effect of foreign exchange rate on cash	—	(1)	(18)
Net change in cash and cash equivalents	(4,901)	3,077	50,085
Cash and cash equivalents beginning of period	9,068	4,167	7,244
Cash and cash equivalents end of period	$ 4,167	$ 7,244	$ 57,329

Source: XBiotech Inc.

Risks and Disclosures

This Executive Informational Overview® (EIO) has been prepared by XBiotech Inc. ("XBiotech" or "the Company") with the assistance of Crystal Research Associates, LLC ("CRA") based upon information provided by the Company. CRA has not independently verified such information. Some of the information in this EIO relates to future events or future business and financial performance. Such statements constitute forward-looking information within the meaning of the Private Securities Litigation Act of 1995. Such statements can only be predictions and the actual events or results may differ from those discussed due to the risks described in XBiotech's statements in its public and investor materials as well as regulatory forms filed from time to time.

The content of this report with respect to XBiotech has been compiled primarily from information available to the public released by the Company through news releases, investor presentations, and other materials released from time to time. XBiotech is solely responsible for the accuracy of this information. Information as to other companies has been prepared from publicly available information and has not been independently verified by XBiotech or CRA. Certain summaries of activities and outcomes have been condensed to aid the reader in gaining a general understanding. CRA assumes no responsibility to update the information contained in this report. In addition, CRA has been compensated in cash of forty-five thousand U.S. dollars for its work in creating this report and other services.

Investors should carefully consider the risks and information about XBiotech's business, as described below. Investors should not interpret the order in which considerations are presented in this or other filings as an indication of their relative importance. The risks and uncertainties overviewed below are not the only risks that the Company faces. Additional risks and uncertainties not presently known to XBiotech or that it currently believes to be immaterial may also adversely affect the Company's business. If any of such risks and uncertainties develops into an actual event, XBiotech's business, financial condition, and results of operations could be materially and adversely affected, and the trading price of the Company's shares could decline.

This report is published solely for information purposes and is not to be construed as an offer to sell or the solicitation of an offer to buy any security in any state. Past performance does not guarantee future performance. Additional information about XBiotech, as well as copies of this report, can be obtained by calling (512) 386-2900.

RISKS RELATED TO XBIOTECH'S FINANCIAL CONDITION AND CAPITAL REQUIREMENTS

XBiotech has incurred significant operating losses in every quarter since its inception and anticipates that it will continue to incur significant operating losses in the future.

XBiotech is a clinical-stage 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 effect or an acceptable safety profile, gain regulatory approval, or become commercially viable. XBiotech does not have any products approved by regulatory authorities for marketing or commercial sale and has not generated any revenue from product sales, or otherwise, to date, and the Company continues to incur significant research and development (R&D) and other expenses related to its ongoing operations. As a result, the Company is not profitable and has incurred losses in every reporting period since its inception in 2005. For the years ended December 31, 2012 and December 31, 2013, XBiotech reported a net loss of $15.2 million and $9.9 million, respectively. For the nine months ended September 30, 2014, the Company reported a net loss of $15.8 million. As of September 30, 2014, the Company had an accumulated deficit since inception of $87.3 million.

XBiotech expects to continue to incur significant expenses and operating losses for the foreseeable future. The Company anticipates these losses to increase as it continues the R&D of, and seeks regulatory approvals for, Xilonix™ and any of its future product candidates, and potentially begins to commercialize any products that may achieve regulatory approval. XBiotech may encounter unforeseen expenses, difficulties, complications, delays, and other unknown factors that may adversely affect its financial condition. The size of future net losses will depend, in part, on the rate of future growth of its expenses and its ability to generate revenues. Prior losses and expected

future losses have had and will continue to have an adverse effect on financial condition. If Xilonix™ or any future product candidate fails in clinical trials or does not gain regulatory approval, or if approved, fails to achieve market acceptance, XBiotech may never become profitable. Even if the Company achieves profitability in the future, it may not be able to sustain profitability in subsequent periods.

XBiotech has a limited operating history, which may make it difficult for potential investors to evaluate the success of its business to date and to assess its future viability.

XBiotech's operations began in March 2005, and the Company has only a limited operating history upon which to evaluate its business and prospects. In addition, as a development-stage company, it has limited experience and has not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. For example, to execute XBiotech's business plan, it will need to successfully accomplish the following:

- Obtain regulatory approval to market and sell Xilonix™ in the U.S. and/or in Europe;
- Successfully commercialize the sale of Xilonix™ in the U.S. and/or Europe;
- Develop and commercialize other product candidates, including antibodies to treat vascular disease, non-small cell lung cancer (NSCLC), pyoderma gangrenosum (PG), and *Staphylococcus aureus* (*S. aureus*) infections;
- Build and maintain a strong intellectual property (IP) portfolio;
- Develop and maintain successful strategic relationships; and
- Manage costs associated with R&D, clinical trials, regulatory approvals, and marketing.

If XBiotech is unsuccessful in accomplishing these objectives, it may not be able to develop drug candidates, raise capital, expand its business, or continue operations.

XBiotech will need to raise additional funding, which may not be available on acceptable terms, if at all. Failure to obtain this necessary capital when needed may force the Company to delay, limit, or terminate its product development efforts or other operations.

Since inception, XBiotech has dedicated most of its resources to discovery and development of proprietary preclinical and clinical product candidates, and expects to continue to expend substantial resources doing so for the foreseeable future. These expenditures will include costs associated with R&D, manufacturing of product candidates and products approved for sale, conducting preclinical and clinical trials, and obtaining and maintaining regulatory approvals, as well as commercializing any products later approved for sale. During the fiscal year ended December 31, 2014, the Company recognized approximately $14.3 million in expenses associated with R&D and clinical trials, of which $1.3 million is attributable to stock-based compensation. Accordingly, XBiotech will likely require substantial additional capital to continue clinical development and potential commercialization activities. Future capital requirements depend on many factors, including but not limited to the following:

- the number and characteristics of the future product candidates the Company pursues;
- the scope, progress, results, and costs of independently researching and developing any future product candidates and conducting preclinical research and clinical trials as well as obtaining regulatory approvals for any future product candidates;
- the cost of future commercialization activities for Xilonix™ and any other future products approved for sale;
- the cost of manufacturing future products, if any;
- the Company's ability to maintain existing collaborations and to establish new collaborations, licensing, or other arrangements and the financial terms of such agreements; and

- the costs involved in preparing, filing, prosecuting, maintaining, defending, and enforcing patents, including litigation costs and the outcome of such litigation.

XBiotech is unable to estimate the funds it will actually require to complete R&D of its product candidates or the funds required to commercialize any resulting product in the future. The Company 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, if at all.

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

The terms of any financing arrangements the Company enters into may adversely affect the holdings or the rights of its shareholders and the issuance of additional securities, whether equity or debt, by XBiotech, or the possibility of such issuance, may cause the market price of the Company's shares to decline. The sale of additional equity or convertible securities would dilute all 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 XBiotech's ability to incur additional debt, limitations on its ability to acquire, sell, or license IP rights, and other operating restrictions that could adversely impact the Company's ability to conduct business. XBiotech 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 its product candidates or other unfavorable terms, any of which may have a material adverse effect on business, operating results, and prospects. Additional fundraising efforts may also divert management from day-to-day activities, which may adversely affect the Company's ability to develop and commercialize products.

RISKS RELATED TO XBIOTECH'S BUSINESS

XBiotech currently has no source of product revenue and may never become profitable.

To date, XBiotech has not generated revenues from commercial product sales, or otherwise. Its ability to generate revenue from product sales and achieve profitability will depend on its ability, alone or with future collaborators, to successfully commercialize products, including Xilonix™ or any future product candidates that it may develop, in-license, or acquire in the future. Even if XBiotech is able to successfully achieve regulatory approval for Xilonix™ or any future product candidates, the Company does not know when any of these products will generate revenue from product sales, if at all. Its ability to generate revenue from product sales from Xilonix™ or any future product candidates also depends on a number of additional factors, including XBiotech's ability to do the following:

- complete development activities, including the necessary clinical trials, and complete and submit New Drug Applications (NDAs) to the U.S. Food and Drug Administration (FDA);
- submit applications to, and obtain regulatory approval from, domestic and foreign regulatory authorities;
- establish manufacturing operations and develop a commercial organization capable of sales, marketing, and distribution for Xilonix™ and any products for which XBiotech obtains marketing approval and intends to sell by itself in the markets in which it chooses to commercialize on its own;
- find suitable distribution partners to help market, sell, and distribute approved products in other markets;
- obtain coverage and adequate reimbursement from third-party payors, including government and private payors;
- achieve market acceptance for the Company's products, if any;
- establish, maintain, and protect IP rights; and
- attract, hire, and retain qualified personnel.

In addition, because of the numerous risks and uncertainties associated with pharmaceutical product development, including that Xilonix™ or any future product candidates may not advance through development or achieve the endpoints of applicable clinical trials, XBiotech is unable to predict the timing or amount of increased expenses, or when or if it will be able to achieve or maintain profitability. In addition, expenses could increase beyond expectations if the Company decides to or is required by the FDA, or foreign regulatory authorities, to perform studies or trials in addition to those currently anticipated. Even if XBiotech is able to complete the development and regulatory process for Xilonix™ or any future product candidates, it anticipates incurring significant costs associated with commercializing these products.

Even if XBiotech is able to generate revenues from the sale of Xilonix™ or any future product candidates that may be approved, the Company may not become profitable and may need to obtain additional funding to continue operations. If XBiotech fails to become profitable or is unable to sustain profitability on a continuing basis, then it may be unable to continue operations at planned levels and be forced to reduce operations.

Future success is dependent on the regulatory approval and commercialization of Xilonix™ and any future product candidates.

XBiotech does not have any products that have gained regulatory approval. Xilonix™, the lead product, is currently in two Phase III clinical trials in the U.S. and Europe. As a result, XBiotech's near-term prospects, including an ability to finance operations and generate revenue, are substantially dependent on its ability to obtain regulatory approval for and successfully commercialize Xilonix™ in a timely manner. XBiotech cannot commercialize Xilonix™ or future product candidates in the U.S. or elsewhere without first obtaining regulatory approval for the product. Review processes typically take years to complete and approval is never guaranteed. Before obtaining regulatory approvals for the commercial sale of Xilonix™ or any future product candidates for a target indication, XBiotech must demonstrate with substantial evidence gathered in preclinical and well-controlled clinical studies, generally including two well-controlled Phase III trials, and, with respect to approval in the U.S., to the satisfaction of the FDA, 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 Xilonix™ or future product candidates in one country does not ensure regulatory approval in other countries, but a failure or delay in obtaining approval in one country may have a negative effect on the regulatory process in other countries.

Even if Xilonix™ or future product candidates were to successfully obtain approval from the FDA and 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 study or risk management requirements. If XBiotech is unable to obtain approval for Xilonix™ in one or more jurisdictions, or any approval contains significant limitations, the Company may not be able to obtain sufficient funding or generate sufficient revenue to continue development of any of future product candidate that it may discover, in-license, develop, or acquire. Also, any regulatory approval of Xilonix™ or future product candidates, once obtained, may be withdrawn. Furthermore, even if XBiotech obtains regulatory approval for Xilonix™, the commercial success of Xilonix™ will depend on a number of factors, including the following:

- development of a commercial organization or a commercial collaboration with a commercial infrastructure;
- establishment of commercially viable pricing and adequate reimbursement from third-party payors;
- an ability to manufacture quantities of Xilonix™ using commercially sufficient processes and at a scale sufficient to meet anticipated demand and enable XBiotech to reduce its cost of manufacturing;
- success in educating physicians and patients about the benefits, administration, and use of Xilonix™;
- the availability, perceived advantages, relative cost, relative safety, and relative efficacy of alternative and competing treatments;
- the effectiveness of marketing, sales, and distribution strategy and operations;
- acceptance of Xilonix™ as safe and effective by patients and the medical community; and

- a continued acceptable safety profile of Xilonix™ following approval.

Many of these factors are beyond the Company's control. If XBiotech is unable to successfully commercialize Xilonix™, it may not be able to earn sufficient revenues to continue its business.

Because the results of earlier clinical trials are not necessarily predictive of future results, Xilonix™ which is currently in Phase III clinical trials, or any future product candidate that XBiotech advances 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 Xilonix™, XBiotech does not know whether the clinical trials it is conducting, or may conduct, will demonstrate adequate efficacy and safety to result in regulatory approval to market Xilonix™ or any future product candidates in any particular jurisdiction. Even if the Company believes that it has adequate data to support an application for regulatory approval to market its product candidates, FDA or other applicable foreign regulatory authorities may not agree and may require additional clinical trials. If later-stage trials do not produce favorable results, the Company's ability to achieve regulatory approval for any of its product candidates may be adversely impacted.

If XBiotech is unable to enroll subjects in trials, it 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 consent, risk that enrolled subjects will drop out before completion, competing 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 being investigated. Furthermore, XBiotech relies on Clinical Research Organizations (CROs) and clinical trial sites to ensure the proper and timely conduct of clinical trials, and while the Company has agreements governing their committed activities, it has limited influence over their actual performance.

If XBiotech experiences delays in the completion or termination of any clinical trial of Xilonix™ or any future product candidates, the commercial prospects of its candidates will be harmed and its ability to generate product revenues from any of these candidates will be delayed. In addition, delays in completing clinical trials will increase costs, slow down product development and approval processes, could shorten any periods during which XBiotech may have the exclusive right to commercialize its candidates, could allow competitors to bring products to market before the Company does, and could jeopardize XBiotech's ability to commence product sales, which would impair its ability to generate revenues and may harm its business, results of operations, financial condition, cash flows, and future prospects. In addition, many of the factors that could delay the commencement or completion of trials may also ultimately lead to the denial of regulatory approval of Xilonix™ or future product candidates.

The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time consuming, and inherently unpredictable, and if XBiotech is ultimately unable to obtain regulatory approval for Xilonix™ or future product candidates, its business will fail.

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable, but typically takes many years following the commencement of preclinical studies and clinical trials and depends on numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a candidate's clinical development and may vary among jurisdictions. XBiotech has not obtained regulatory approval for any product candidate, and it is possible that neither Xilonix™ nor any future product candidates will ever obtain regulatory approval. The Company's product candidates could fail to receive approval from the FDA or a comparable foreign regulatory authority for many reasons, including the following (on page 46):

- disagreement over the design or implementation of clinical trials;
- failure to demonstrate that a product candidate is safe and effective for its proposed indication;

- 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 interpretation of data from preclinical studies or clinical trials;
- disagreement over whether to accept efficacy results from clinical trial sites outside the U.S. where the standard of care is potentially different from that in the U.S.;
- an insufficiency of data collected from clinical trials of Xilonix™ or future product candidates to support the submission and filing of an NDA or other submission or to obtain regulatory approval;
- disapproval of manufacturing processes; or
- changes in approval policies or regulations that render the Company's preclinical and clinical data insufficient.

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 commercialization, or XBiotech may decide to abandon the development program altogether. Even if the Company does obtain regulatory approval, Xilonix™ or future product candidates may be approved for fewer or more limited indications than requested; approval may be contingent on the performance of costly post-marketing clinical trials; or approval may not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. In addition, if Xilonix™ or future product candidates produce undesirable side effects or safety issues, the FDA may require the establishment of Risk Evaluation Mitigation Strategies (REMS), or a comparable foreign regulatory authority may require the establishment of a similar strategy, that may, restrict distribution of XBiotech's products and impose burdensome implementation requirements on the Company. Any of the foregoing scenarios could materially harm the commercial prospects for XBiotech's product candidates. XBiotech may not be able to file for regulatory approvals and, even if it does file, it may not receive the necessary approvals to commercialize products in any market.

Xilonix™ or future 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 Xilonix™ or future product candidates could cause XBiotech 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. For example, even though Xilonix™ administered orally has generally been well tolerated by patients in earlier-stage clinical trials, in animal toxicity studies certain side effects, including severe ulcerations to the gastrointestinal tract of dogs and adverse effects to the ocular lens of some animals, occurred. There can be no assurance that these toxicities in animals will not occur in humans. If these toxicities do occur in future clinical trials, they could delay or even cause discontinuance of further development of Xilonix™ or future product candidates, which would impair the Company's ability to generate revenues and would have a material adverse effect business, results of operations, financial condition, cash flows, and future prospects. To date, the most common side effect of Xilonix™ noted in clinical trials is mild gastrointestinal upset including mild diarrhea, nausea, and gastric pain. No severe side effects have been noted to date. There can be no assurance that side effects from Xilonix™ in future clinical trials will be continue to be mild or that side effects in general will not prompt the discontinued development of Xilonix™ or future product candidates. As a result of these side effects or further safety or toxicity issues that XBiotech may experience in clinical trials in the future, the Company may not receive approval to market Xilonix™ or any future product candidates, which could prevent it from ever generating revenues or achieving profitability. Trial results could reveal an unacceptably high severity and prevalence of side effects. In such an event, trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could cease further development of or deny approval of such 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 business, results of operations, financial condition and cash flows, and future prospects.

Additionally, if Xilonix™ or any future product candidates receives marketing approval, and XBiotech or others later identify undesirable side effects caused by such product, a number of potentially significant negative consequences could result, including that the Company may be forced to suspend marketing of such product; regulatory authorities may withdraw their approvals, may require additional warnings on the label that could limit the use or commercial success of such product, may issue safety alerts, Dear Healthcare Provider letters, press releases, or other communications containing warnings about such product, may require the establishment or modification of REMS or a similar strategy that may, for instance, restrict distribution of XBiotech's products and impose burdensome implementation requirements; the Company may be required to change the way the product is administered or conduct additional clinical trials; could be sued and held liable for harm caused to subjects or patients; or may be subject to litigation or product liability claims; and XBiotech's reputation may suffer. Any of these events could impede market acceptance of the particular product candidate, if approved.

Even if Xilonix™ or future product candidates receive regulatory approval, they may still face future development and regulatory difficulties.

Even if XBiotech obtains regulatory approval for Xilonix™ or a future 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. If XBiotech or a regulatory agency discovers 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, including recall or withdrawal of the product from the market or suspension of manufacturing. Additional outcomes of a failure to comply with regulatory agencies' requirements could include that the agencies issue warning letters or untitled letters; impose restrictions on marketing or manufacturing; mandate modifications to promotional materials or require corrective information provided to healthcare practitioners; require XBiotech 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 XBiotech; 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 a product recall. The occurrence of any event or penalty described above may inhibit the Company's ability to commercialize Xilonix™ or any future 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. will be heavily scrutinized by the FDA, the Department of Justice, the Office of Inspector General of the Department of Health and Human Services, state attorneys general, members of Congress, and the public. Violations, including promotion of products for unapproved or off-label uses, are subject to enforcement letters, inquiries and investigations, and civil, criminal and/or administrative sanctions as well as potentially to false claims litigation under federal and state statutes, which can lead to civil, criminal, and/or administrative penalties and fines and agreements that materially restrict the manner in which XBiotech promotes or distributes its drug products. If XBiotech does not lawfully promote its approved products, it may become subject to such litigation and, if it is not successful in defending against such actions, those actions could have a material adverse effect the Company's business, results of operations, financial condition and cash flows, and future prospects. 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.

Existing government regulations may change and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of Xilonix™ or any future product candidates. If XBiotech is slow or unable to adapt to such changes, or if it is not able to maintain regulatory compliance, it may lose any marketing approval that it may have obtained and/or be subject to fines or enhanced government oversight and reporting obligations, which would adversely affect its business, prospects, and ability to achieve or sustain profitability.

Failure to obtain regulatory approval in international jurisdictions would prevent Xilonix™ or any future product candidates from being marketed outside the U.S.

In order to market and sell products in the European Union and many other jurisdictions, XBiotech 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. In addition, in many countries outside the U.S., it is required that the product be approved for reimbursement before the product can be approved for sale in that country. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties, and costs and could delay or prevent the introduction of products in certain countries. XBiotech may not obtain approvals from foreign regulatory authorities on a timely basis, if at all. Approval by the FDA does not ensure foreign regulatory approval, and approval by one regulatory authority outside the U.S. does not ensure approval by other regulatory authorities outside the U.S. or 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. XBiotech may not be able to file for marketing approvals and may not receive necessary approvals to commercialize products in any market. If it is unable to obtain approval of Xilonix™ or any future product candidates by regulatory authorities in the European Union or another jurisdiction, the commercial prospects of that product candidate may be significantly diminished and business prospects could decline.

Even if XBiotech is able to commercialize Xilonix™ or future product candidates, the products may not receive coverage and adequate reimbursement from third-party payors, which could harm business.

XBiotech's 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 payors. Patients who are prescribed medications for the treatment of their conditions generally rely on third-party payors 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 Xilonix™ or the Company's future product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of the product candidates. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. As a result, government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Third-party payors 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 products for those patients. XBiotech cannot be sure that coverage and adequate reimbursement will be available for any product that it commercializes 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 the Company obtains marketing approval. If coverage and reimbursement are not available or are available only at limited levels, XBiotech may not be able to successfully commercialize any product candidate for which it obtains 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 its costs, including R&D, manufacture, sales and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover 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 and 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 payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices. Coverage and reimbursement for drug products can differ significantly from payor to payor. 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 payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. An inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for any approved products could have a material adverse effect on operating results, ability to raise capital, and overall financial condition.

XBiotech has never marketed a drug before, and if it is unable to establish an effective sales force and marketing infrastructure, or enter into acceptable third-party sales and marketing or licensing arrangements, it may be unable to generate any revenue.

XBiotech does not currently have an infrastructure for the sales, marketing, and distribution of pharmaceutical drug products and the cost of establishing and maintaining such an infrastructure may exceed the cost-effectiveness of doing so. In order to market any approved products, XBiotech must build its sales, marketing, managerial, and other non-technical capabilities or make arrangements with third parties for these services. If the Company is unable to establish adequate sales, marketing, and distribution capabilities, whether independently or with third parties, it may not be able to generate product revenue and may not become profitable as it will be competing with many companies that currently have extensive and well-funded sales and marketing operations.

Xilonix™ and future product candidates, if approved, may not achieve adequate acceptance among physicians, patients, healthcare payors, and others in the medical community necessary for commercial success.

Even if XBiotech obtains regulatory approval for Xilonix™ or any future product candidates, the candidate may not gain acceptance among physicians, healthcare payors, patients, or the medical community. Market acceptance of any product candidates for which XBiotech receives approval depends on a number of factors, including efficacy and safety as demonstrated in clinical trials; the approved clinical indications; acceptance by physicians and patients as being a safe and effective treatment; potential and perceived advantages over alternative treatments; safety as seen in a broader patient group, including use outside the approved indications; the prevalence and severity of any side effects; regulatory authorities' product labeling or product insert requirements; the timing of market introduction versus competitive products; the cost of treatment in relation to alternative treatments; the availability of coverage and adequate reimbursement and pricing by third-party payors and government authorities; relative convenience and ease of administration; the effectiveness of sales and marketing efforts; and favorable or unfavorable publicity relating to the product candidate. If any of XBiotech's product candidates are approved but fail to achieve market acceptance among physicians, patients, or healthcare payors, the Company will not be able to generate significant revenues, which would compromise its ability to become profitable.

XBiotech's Ebola research may not succeed.

XBiotech has received blood donations from two patients that had each recently recovered from Ebola infection. The blood donations are to be used in development of a True Human™ antibody therapeutic that could be used to treat patients infected by the virus. In the case of one patient, the Company agreed to comply with the patient's wishes that in the event an Ebola therapy derived from the donation was marketed, a percentage of the gross proceeds of all sales from such product would be used to provide drugs at no cost for those persons unable to afford therapy. However, there is no assurance that XBiotech will be able to develop a therapy. Even if the Company succeeds in isolating appropriate antibodies, the regulatory process to determine their safety and effectiveness would likely take years to complete at substantial expense, with no assurance that a drug will ever be approved for marketing.

Even an effective Ebola drug might not be commercially successful.

Even if XBiotech ultimately succeeds in creating a safe and effective drug based on human antibodies that resist Ebola, 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 Ebola might become sufficiently rare, or victims of Ebola might be sufficiently impoverished, making commercial production uneconomic. XBiotech's promises regarding donation of five percent of any gross revenues from an Ebola drug developed using the blood sample it recently received may adversely impact XBiotech and its shareholders. In addition, the Company received the blood donations from two patients that had each recently recovered from Ebola infection through its contractual relationship with the South Texas Blood & Tissue Center (STBTC), a 501(c) not for profit organization, and has an obligation to pay STBTC a royalty on any Ebola product that is developed based on these donations, which could further impact the profitability of this drug.

XBiotech faces substantial competition, which may result in others discovering, developing, or commercializing products before or more successfully than the Company.

The development and commercialization of new drug products is highly competitive. XBiotech faces competition with respect to Xilonix™, and will likely face competition with respect to future product candidates, from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations. 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 XBiotech is developing product candidates. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to the Company's approach, and others are based on entirely different approaches. More established entities may have a competitive advantage over XBiotech due to their greater size, cash flows, and institutional experience. Compared to XBiotech, many competitors may have significantly greater financial, technical, and human resources, and as a result, may obtain regulatory approval of their products before the Company does, which will limit its ability to develop or commercialize Xilonix™ or any future product candidates. In addition, many companies are developing new therapeutics, and XBiotech cannot predict what the standard of care will be as its product candidates progress through clinical development.

A failure to successfully identify, acquire, develop, and commercialize additional product candidates or approved products other than Xilonix™ could impair XBiotech's ability to grow.

Although a substantial amount of the Company's efforts focus on the continued clinical testing and potential approval of Xilonix™, a key element of XBiotech's 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 the Company's internal research capabilities are limited, it may be dependent upon pharmaceutical and biotechnology companies, academic scientists, and other researchers to sell or license products or technology to XBiotech. The success of this strategy depends partly upon XBiotech's 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 for the license or acquisition of product candidates and approved products. XBiotech has limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses, and technologies. Moreover, the Company may devote resources to potential acquisitions or in-licensing opportunities that are never completed or may fail to realize the anticipated benefits of such efforts. Any product candidate acquired 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 candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, XBiotech cannot provide assurance that any products that it develops or approved products that it acquires will be manufactured profitably or achieve market acceptance.

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

XBiotech faces an inherent risk of product liability exposure related to the testing of Xilonix™ and any future product candidates in clinical trials and will face an even greater risk if it commercially sells any products that it may develop. Product liability claims may be brought against the Company by subjects enrolled in clinical trials, patients, healthcare providers, or others using, administering, or selling the products. If XBiotech cannot successfully defend against claims that its product candidates or products caused injuries, the Company could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in decreased demand for product candidates; termination of clinical trial sites or entire trial programs; injury to reputation and significant negative media attention; withdrawal of clinical trial participants; significant costs to defend the related litigation; substantial monetary awards to trial subjects or patients; loss of revenue; diversion of management and scientific resources from business operations; and the inability to commercialize product candidates.

XBiotech intends to obtain insurance coverage for products to include the sale of commercial products if it obtains marketing approval for Xilonix™ or future product candidates, but 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 the Company, particularly if judgments exceed its insurance coverage, could decrease cash and adversely affect the business.

XBiotech will need to expand and grow, and may experience difficulties in managing this growth.

As of March 9, 2015, XBiotech had 56 employees. As development and commercialization plans and strategies develop, or as a result of any future acquisitions, XBiotech will need additional managerial, operational, sales, marketing, scientific, and financial headcount and other resources. Management, personnel, and systems currently in place may not be adequate to support this future growth. Future growth could impose significant added responsibilities on members of management, including the following, any failure of which could prevent XBiotech from successfully growing its company:

- managing clinical trials effectively, which the Company anticipates conducting at numerous clinical sites;
- identifying, recruiting, maintaining, motivating, and integrating employees with expertise and experience;
- managing internal development efforts effectively while complying with contractual obligations to licensors, licensees, contractors, and other third parties;
- managing additional relationships with various strategic partners, suppliers, and other third parties;
- improving managerial, development, operational, and finance reporting systems and procedures; and
- expanding facilities.

XBiotech is highly dependent on its Chief Executive Officer (CEO).

The Company’s future success depends in significant part on the continued service of its CEO, Mr. John Simard. Mr. Simard is critical to the strategic direction and overall management of the Company as well as to its R&D process. Although XBiotech has an employment agreement with Mr. Simard, it has no specific duration. The loss of Mr. Simard could adversely affect the Company’s business, financial condition, and operating results.

XBiotech depends on key personnel to operate its business, and many members of its current management team are new. If the Company is unable to retain, attract, and integrate qualified personnel, its ability to develop and successfully grow its business could be harmed.

In addition to the services of Mr. Simard, XBiotech believes that its future success is highly dependent on the contributions of its significant employees, as well as its ability to attract and retain highly skilled and experienced sales, R&D, and other personnel in the U.S. and abroad. Some significant employees include the medical director, vice president of manufacturing, vice president of quality, director of research, director of quality control, vice president of finance, and human resources. Changes in management may be disruptive to the business.

All employees, including executive officers, are free to terminate their employment relationship with XBiotech at any time, and their knowledge of the Company's business and industry may be difficult to replace. If one or more executive officers or significant employees leave, the Company may not be able to fully integrate new personnel or replicate the prior working relationships, and XBiotech's operations could suffer. Qualified individuals with the breadth of skills and experience in the pharmaceutical industry are in high demand, and the Company may incur significant costs to attract them. Many competitive pharmaceutical companies may have greater financial and other resources, different risk profiles, and a longer history in the industry than XBiotech. They also may provide more diverse opportunities and better chances for career advancement. Competition for qualified personnel is particularly intense in the Austin, Texas, area, where the Company's headquarters are located. A failure to retain key personnel could impede the achievement of R&D and commercialization objectives.

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

XBiotech is subject to numerous environmental, health, and safety laws and regulations in the U.S. and Canada, including, as a result of its leased laboratory space, those governing laboratory procedures and the handling, use, storage, treatment, and disposal of hazardous materials and wastes. The Company's operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Its operations also produce hazardous waste products. XBiotech generally contracts with third parties for the disposal of these materials and wastes. XBiotech cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from the use of hazardous materials, the Company could be held liable for any resulting damages, and any liability could exceed its resources. XBiotech also could incur significant costs associated with civil or criminal fines and penalties.

Although the Company maintains workers' compensation insurance to cover costs and expenses it may incur due to injuries to employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. The Company does not maintain insurance for environmental liability or toxic tort claims that may be asserted against it in connection with the storage or disposal of biological or hazardous materials. XBiotech may also 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 R&D or production efforts. Failure to comply may result in substantial fines, penalties, or other sanctions.

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

XBiotech's 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 the Company is predominantly self-insured. XBiotech does not carry insurance for all categories of risk that its business may encounter. The occurrence of any of these business disruptions could seriously harm operations and financial condition and increase costs and expenses. XBiotech relies on third-party manufacturers to produce its product candidates. An ability to obtain 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 XBiotech, its significant suppliers, and its general infrastructure of being consolidated in certain geographical areas is unknown, but its 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 the Company to pay substantial amounts, which would adversely affect its business, results of operations, financial condition, and cash flows from future prospects.

RISKS RELATED TO INTELLECTUAL PROPERTY (IP)

If XBiotech is unable to obtain or protect IP rights, its competitive position could be harmed.

XBiotech depends on its ability to protect its proprietary technology. XBiotech relies 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. Commercial success will depend in large part on the Company's ability to obtain and maintain patent protection in the U.S. and other countries with respect to its proprietary technology and products. Where XBiotech has the right to do so under its license agreements, it seeks to protect its proprietary position by filing patent applications in the U.S. and abroad related to its novel technologies and products that are important to the 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 XBiotech's patents, including those patent rights licensed to the Company by third parties, are highly uncertain.

The steps XBiotech has taken to protect its proprietary rights may not be adequate to preclude misappropriation of proprietary information or infringement of IP rights, both inside and outside the U.S. The rights already granted under any of the Company's currently issued patents and those that may be granted under future issued patents may not provide the proprietary protection or competitive advantages sought. If XBiotech is unable to obtain and maintain patent protection for its technology and products, or if the scope of the patent protection obtained is not sufficient, competitors could develop and commercialize technology and products similar or superior, and XBiotech's ability to successfully commercialize its technology and products may be adversely affected.

With respect to patent rights, XBiotech does not know whether any of the pending patent applications for any of its discovered or licensed compounds will result in the issuance of patents that protect its technology or products, or if any of its issued patents will effectively prevent others from commercializing competitive technologies and products. The Company's pending 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 XBiotech or its future potential licensor(s) to narrow the claims for its 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 the Company owns or has licensed from third parties may be challenged in 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 XBiotech's ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection for the Company's technology and products. Protecting against the unauthorized use of patented technology, trademarks, and other IP rights is expensive, difficult, and may in some cases not be possible. In some cases, it may be difficult or impossible to detect third-party infringement or misappropriation of IP rights, even in relation to issued patent claims, and proving any such infringement may be even more difficult.

IP rights do not necessarily address all potential threats to any competitive advantage XBiotech may have.

The degree of future protection afforded by IP rights is uncertain because IP rights have limitations, and may not adequately protect XBiotech's business or permit it to maintain a competitive advantage. The examples listed below are illustrative.

- Others may be able to make compounds that are the same as or similar to MABp1 or XBiotech's future product candidates but that are not covered by the claims of the patents that the Company owns or has exclusively licensed.
- XBiotech might not have been the first to make the inventions covered by the issued patent or pending patent application that it owns or has exclusively licensed.

- XBiotech or any of its licensors or strategic partners might not have been the first to file patent applications covering certain of its inventions.
- Others may independently develop similar or alternative technologies or duplicate any of the Company's technologies without infringing its IP rights.
- It is possible that XBiotech's pending patent applications will not lead to issued patents.
- Issued patents that the Company owns or has exclusively licensed may not provide any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by competitors.
- Competitors might conduct R&D in the U.S. and other countries that provide a safe harbor from patent infringement claims for certain R&D activities, as well as in countries where XBiotech does not have patent rights, and then use the information learned from such activities to develop competitive products for sale in the Company's major commercial markets.
- XBiotech may not develop additional proprietary technologies that are patentable.
- The patents of others may have an adverse effect on the Company's business.

Glossary

Angiogenesis—The development of new blood vessels.

Antibodies—Blood proteins produced in response to and counteracting a specific antigen. Antibodies combine chemically with substances that the body recognizes as alien, such as bacteria, viruses, and foreign substances in the blood.

Antigen—Any substance that antagonizes or stimulates the immune system to produce antibodies.

Apoptosis—The death of cells that occurs as a normal and controlled part of an organism's growth or development.

B-Cell—Also called a B lymphocyte, a B-cell is developed in bone marrow. It circulates in the blood and lymph and, upon encountering a particular foreign antigen, differentiates into a clone of plasma cells that secrete a specific antibody and a clone of memory cells that make the antibody on subsequent encounters.

Bioreactor—An apparatus in which a biological reaction or process is carried out, especially on an industrial scale.

Cachexia—Weakness and wasting of the body due to severe chronic illness.

Chimeric—A type of antibody that is mostly human and partially mouse.

Complementarity-determining Regions (CDRs)—Part of the variable chains in immunoglobulins (antibodies) and T-cell receptors, generated by B-cells and T-cells respectively, where these molecules bind to their specific antigen.

Fast Track—The FDA Fast Track Designation is a designation of the United States Food and Drug Administration (FDA) that facilitates the development, and expedites the review, of drugs which treat a serious or life-threatening condition and fill an unmet medical need.

Good Manufacturing Practices (GMP)—Regulations established by the FDA for all domestic and foreign manufacturers. These require the establishment of a quality system meeting requirements related to the methods, controls, and facilities used for designing, manufacturing, packaging, labeling, storing, installing, and servicing products and medical devices intended for human use.

Hybridoma—A hybrid cell produced by the fusion of an antibody-producing lymphocyte with a tumor cell and used to culture continuously a specific monoclonal antibody.

Immunopathogenesis—The process of development of a disease in which an immune response or the products of an immune reaction are involved.

Inflammatory Cascade—The inflammatory process involves a complex biological cascade of molecular and cellular signals that alter physiological responses. At the site of an injury, cells release molecular signals that cause a number of changes in the affected area: dilation of blood vessels, increased blood flow, increased vascular permeability, exudation of fluids containing proteins like immunoglobulins (antibodies), and invasion by leukocytes (white blood cells).

Interleukin-1 (IL-1)—A type of biological response modifier that stimulates immune system cells that fight disease, and is involved in inflammatory responses. IL-1 is a natural cytokine released by monocytes, macrophages, T-cells, and other immune cells.

Leukocyte—A colorless cell that circulates in the blood and body fluids and is involved in counteracting foreign substances and disease; a white blood cell. There are several types, all amoeboid cells with a nucleus, including lymphocytes, granulocytes, monocytes, and macrophages.

Metastasis—The development of secondary malignant growths at a distance from a primary site of cancer.

Monoclonal Antibodies (MAbs)—A type of antibody that binds to a specific target. The inherent selectivity of MAbs makes them ideally suited for targeting specific cells, such as cancer cells or certain viruses, while bypassing most normal tissue.

Murine—Of or relating to mice and rats.

Myelomas—A malignant tumor of the bone marrow.

Pathogenic—Capable of causing or producing disease.

Phage—Short for bacteriophage, a virus that lives within a bacteria. A virus for which the natural host is a bacterial cell.

Proteinuria—The presence of abnormally large amounts of protein in the urine, usually resulting from kidney disease but sometimes from fever, excessive exercise, or another abnormal condition.

Pyoderma Gangrenosum (PG)—A rare condition that causes tissue to become necrotic, and results in deep ulcers that usually occur on the legs. When they occur, they can lead to chronic wounds. Ulcers usually initially look like small bug bites or papules before progressing to larger ulcers.

Restenosis—The recurrence of stenosis, which is an abnormal narrowing of an artery or valve after corrective surgery leading to restricted blood flow.

Somatic Hypermutation (SHM)—A cellular mechanism by which the immune system adapts to the new foreign elements that confront it (e.g., microbes).

Standard of Care—A diagnostic and treatment process that a clinician should follow for a certain type of patient, illness, or clinical circumstance.

Superficial Femoral Artery—Part of the main artery of the thigh, supplying blood to the leg.

Transgenic—Of, relating to, or denoting an organism that contains genetic material into which DNA from an unrelated organism has been artificially introduced.

Xenogeneic—Denoting, relating to, or involving tissues or cells belonging to individuals of different species.

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