XBiotech Highlights Third Quarter Developments for 2018

October 31, 2018

Company Provides Updated Overview including on its Clinical and Discovery Pipeline as well as Other Corporate Initiatives

AUSTIN, Texas, Oct. 31, 2018 (GLOBE NEWSWIRE) -- XBiotech Inc. (NASDAQ: XBIT) today provided an update on recent company developments in its third quarter Form 10-Q filing with the SEC. The Company reports that it continues to make important progress in its clinical and pre-clinical programs in addition to other corporate initiatives.

John Simard, XBiotech's President & CEO, commented, "I am pleased with our performance during Q3 and I am positive about the prospects for substantive advances in our programs."

Further information with respect to the Company's recent developments and other items is set forth in the Form 10-Q filed today. A summary of key events included in the Management's Discussion and Analysis section of the Form 10-Q is provided below:

Clinical Programs

Atopic Dermatitis

In April 2018, XBiotech announced the launch of a Phase 2, open label clinical trial to evaluate the Company's True Human™ monoclonal antibody, bermekimab, in patients with moderate to severe Atopic Dermatitis (AD). The study utilizes the Company's new pre-filled syringes to deliver bermekimab therapy via subcutaneous injection. This ongoing study is evaluating the safety and efficacy of bermekimab in two groups of AD patients: those receiving 4 weekly 200mg treatments and those receiving 8 weekly 400mg treatments. The relatively short duration treatment regimen compares with the 16 week treatment for the only approved biological therapy in AD. During Q3, we announced successful completion and positive interim findings for the first cohort of this study, which involved nine patients who received the low dose (200mg/weekly) and four treatments with bermekimab. The Company reported that the 200mg subcutaneous injections were well-tolerated and that bermekimab treatment was associated with statistically significant improvement in several endpoints assessing efficacy. Enrollment was completed during Q3, totaling 37 patients, with 28 patients in the second, higher-dose cohort. Completion of the study and results analysis is expected around year end 2018 or early 2019.

Hidradenitis Suppurativa

During Q3, XBiotech announced enrollment of the first patient in its Phase 2, open label clinical study to evaluate bermekimab in patients with moderate to severe Hidradenitis Suppurativa (HS). U.S. recruitment in this study was completed in Q3 with enrollment rates exceeding expectations. The very robust enrollment is viewed by the Company as evidencing the strong desire for new treatment options in HS and the potential marketability for HS bermekimab therapy should it successfully advance through marketing approval. Importantly, the clinical study is evaluating bermekimab in two distinct patient populations: those that have failed anti-TNF therapy and in patients that have had no prior anti-TNF treatment history (the only approved biological drug to treat HS is the anti-TNF drug, Humira.). HS patients are being treated with 13 weekly subcutaneous injections of bermekimab. It was previously demonstrated in the Company's double blind, placebo-controlled study of patients with HS that bermekimab, when administered as an intravenous therapy, was effective for treating HS patients who failed or were ineligible for anti-TNF therapy. The Company projects completion of the current study and a results read-out during the first quarter of 2019.

Pancreatic Cancer

XBiotech is evaluating bermekimab in combination with chemotherapy for the treatment of patients with pancreatic cancer. A clinical study headed by Dr. Andrew Hendifar, MD is being conducted at Cedars-Sinai Medical Center, Los Angeles, CA to examine the safety of bermekimab in combination with Onivyde (nanoliposomal irinotecan) and 5-fluorouracil (5FU)/folinic acid (leucovorin) for pancreatic cancer patients with wasting syndrome. Enrollment is expected to be completed around year end 2018. Bermekimab is believed to block tumor-related inflammation that is involved in neovascularization and tissue matrix remodeling, which is a crucial process for the growth and spread of tumors. As well, bermekimab may block tumor related inflammation that causes central nervous system (CNS) mediated metabolic dysregulation that can lead to wasting. The molecular target of bermekimab, IL-1α, may also be involved in tumor metastasis. In a Phase III randomized study in advanced cancer patients, patients that achieved the primary endpoint (as defined in Hickish et al., Lancet Oncology 2017) had lower incidence of disease progression. In another Phase III cancer study, bermekimab treatment was associated with a significant increase in lean body mass. Patients with pancreatic cancer often suffer from aggressive disease progression and wasting. The disease is known for its rapid mortality and high degree of morbidity. Bermekimab may also improve the anti-tumor activity of the cytotoxic chemotherapy and help patients endure longer exposure to these agents by reducing the inflammatory response caused by the treatment. Although the mechanism of cachexia in pancreatic cancer is not fully understood, bermekimab could help reduce this debilitating symptom by enabling patients to maintain and/or gain lean body mass during cancer treatment.

Research & Development

Overview

During Q3 XBiotech continued to consolidate operations at its Winnebago campus facility. All personnel and operations with the exception of in vivo research activities were successfully transferred and are now operating at the Winnebago campus. During Q3, the Company completed design and received city permits for constructing an annex building to house a new animal research facility at its Winnebago campus. This new facility will mark the final stage of the Company's move to consolidate operations and transfer its R&D group from the East Riverside Drive location to the Winnebago campus. XBiotech's new annex facility will include a state-of-the-art "biobubble" for working with infectious diseases, will house a Class II containment work space for pathogenic virus culture and propagation, and will include a lab for screening human blood donations and conducting the first stage of discovery work for identifying new antibody therapies. R&D activities in the new facility are planned to commence during Q1 2019.

C. difficile

XBiotech continues to make progress with its key pre-clinical R&D programs. In vivo testing of the C. difficile prophylaxis is ongoing. The Company's scientists have established what we believe is a more challenging model for the disease. The strain of C. difficile now being used in pre-clinical development work produces a more aggressive and lethal form of disease. We believe that the new model will better establish the potential for our True Human antibody to prevent or treat human infections with C. difficile.

Influenza
The Company continues to progress with developing its True Human antibodies for the treatment and prevention of influenza. XBiotech has focused on developing antibodies that target hemagglutinin and neuraminidase, two key surface moieties of the influenza virus. These key antibodies have been genetically introduced in cell lines to enable manufacturing production. A highly specific selection process has been ongoing during Q3 to identify True Human antibodies that target precise regions of the Hemagglutinin. This process, which is expected to allow the antibody therapy to be effective in a broader range of virus strains, is proceeding as planned and is expected to continue through 2018.

Anti-Tumor Antibody 12D7G
XBiotech's manufacturing development group has progressed with advancing the 12-D7G antibody cell line production system. During the quarter, the gene for 12D7G was synthesized and inserted into a cell line, which was used to produce the first set of stable clones for potential manufacturing. The candidate production cells are undergoing further selection and a high-producing cell line suitable for clinical or commercial production is expected by year end. The True Human antibody 12D7G binds to a tumor-related protein, NYESO-1, for which it has the potential to stimulate the body to produce a highly specific immune response against tumors. 12D7G is a candidate immunotherapy that could be used to enhance the specificity and potential efficacy of checkpoint inhibitor therapies.

Manufacturing

Highlights
XBiotech continues to optimize its upstream and downstream manufacturing processes. Process development work is ongoing to increase bioreactor volume and running time for its cell culture systems, to enhance yields and reduce costs. Ongoing optimization of our manufacturing technology reflects our continued effort to establish the lowest possible cost of goods. We believe that lowering the cost of goods for monoclonal antibodies opens up new and larger potential areas of unmet medical need. We believe that considerable opportunities exist for safe and effective medicines derived from human antibody immunity; and that some of these opportunities will require competitive pricing that will be enabled by reduced cost of goods.

This year the Company invested in plant and equipment infrastructure and product formulation development to enable the launch of syringes that are pre-filled with bermekimab for use in subcutaneous injection. A new filling machine capable of loading syringes with bermekimab was installed at the Winnebago manufacturing center. The filling line operation was also transferred from the East Riverside Drive facility to the new filling suite at XBiotech's Winnebago campus. The first release of bermekimab-filled syringes (pre-filled and ready for use in the clinic) occurred during Q3. These syringes are already being used successfully in two ongoing clinical trials. The Company is increasing the output capacity for the syringes with a target capability to fill 1,200 syringes per day, with an annual production capacity of about 300,000 units by 2019. We believe this will be adequate output to support a market launch should an approval be granted.

During the third quarter XBiotech began to reestablish and optimize manufacturing production of its monoclonal antibody, 514G3, for the treatment or prevention of Staphylococcus aureus (S. aureus) infections including MRSA. The Company expects to improve yields and processing efficiencies, and to reduce overall cost of production for 514G3 to support its initiatives to potentially use 514G3 as a prophylaxis.

Strategic Direction

Highlights
XBiotech is in clinical development with bermekimab for therapeutic indications including oncology, cardiovascular medicine, and dermatology. The Company's anti-infective antibody, 514G3, is in clinical development to treat S. aureus infections. Other anti-infectious disease antibodies are in pre-clinical development and are not expected to enter clinical studies before 2020.

The use of monoclonal antibodies as prophylaxis (i.e. to prevent disease) has not generally been considered a large or highly profitable business. The cost to produce antibodies is generally too large for them to be ideal for use in disease prevention, especially when the incidence of most diseases is not frequent enough among the general population to justify relatively high unit costs. To date, therefore, most marketed monoclonal antibodies have been for therapeutic use only (to treat patients already afflicted by disease). We believe there are two crucial components for the ideal medical and commercial success of monoclonal antibodies for use in prophylaxis: a high incidence of the target disease in the population; and strong evidence of significant clinical benefit as a result of therapy. We believe that the aforementioned situation potentially exists for XBiotech's product candidates being administered prophylactically to patients with end-stage renal disease (ESRD) who are undergoing maintenance hemodialysis. In patients undergoing hemodialysis, there is a high relative incidence of cardiovascular and infectious disease-related morbidity and mortality compared to the general population. With bermekimab and 514G3, the Company has product candidates that could potentially reduce the incidence of cardiovascular and infectious disease mortality and morbidity, respectively, in this population.

Cardiovascular Risk in ESRD
Major adverse cardiovascular events (MACE) account for a 20% annual mortality rate in ESRD patients undergoing hemodialysis; only 35% of patients on maintenance hemodialysis will survive five years[1]. MACE is by far the leading cause of death and morbidity in this population. Clinical data, a body of scientific research, and recent discoveries (from Dr. Peter Libby's group: Folco et al. Arterioscler Thromb Vasc Biol. 2018;38:1901-1912) suggest a potential role for bermekimab in reducing MACE in ESRD patients. More than 500,000 patients are currently undergoing maintenance hemodialysis in the United States for the treatment of ESRD. Reducing cardiovascular risk in patients with ESRD is thus a major unmet medical need—for which there are no approved therapies. The successful application of bermekimab as a prophylaxis in patients receiving maintenance hemodialysis would thus represent a very important breakthrough for management of this disease.

***S. aureus* infections in ESRD**
The incidence of S. aureus infection in patients undergoing hemodialysis is about one hundred times that of the general population, and the bacteria accounts for about 10% of all-cause mortality in the hemodialysis population. Each year an estimated 37,000 hemodialysis patients will develop S. aureus infections. Of the 500,000 patients currently receiving hemodialysis in the United States, it is expected that about 40,000 will die from S. aureus infections over their hemodialysis careers[2].

We believe that should we be able to demonstrate 514G3 to reduce incidence of mortality and morbidity due to S. aureus that it would be a groundbreaking approach to reducing burden of infectious disease in patients undergoing maintenance hemodialysis.

Dermatology

XBiotech has two ongoing clinical studies in dermatology, to assess bermekimab therapy in patients with Atopic dermatitis (AD) and hidradenitis suppurativa (HS). The Company believes that there continues to be considerable unmet medical need for effective treatment of both AD and HS. Moreover, recent FDA approvals of other biological agents to treat AD and HS have provided clinical study endpoints that we believe reduce uncertainty for our clinical study designs; therefore, these endpoints are included in XBiotech's current studies. Based on outcomes of the ongoing studies, XBiotech expects to initially focus on only one indication (AD or HS) to conduct pivotal registration stud(ies). The market for dupilumab (the recently approved AD biological drug) has been estimated to be as much as US$5 billion[3], and Humira (the recently approved biological drug for HS) is expected to generate US$21 billion in sales by 2020[4]. Marketing approvals in either AD or HS indications for bermekimab would represent a very significant entry into the market.

Oncology

XBiotech continues to analyze data generated from its Phase III studies in oncology, particularly with respect to stratifying the groups to better understand which patients are likely to benefit most from bermekimab therapy. In Q3, these analyses have provided important information suggesting that patient selection based on biomarkers could significantly enhance response rates (response as defined in Hickish et al., Lancet Oncology 2017) to bermekimab therapy by nearly 50%. Analysis and manuscript preparation of these findings is being performed by our scientific board members, including leading oncologist Dr. Razelle Kurzrock, and others. The findings will be submitted for peer review and described in their entirety upon successful publication. The Company believes that these findings may provide a rationale for seeking registration or conducting further clinical work based on a biomarker-defined subgroup. The Company plans to seek FDA guidance based on these findings.

Other Developments

Scientific Board

During the quarter, XBiotech announced the addition of two leading physicians and researchers to its Scientific Advisory Board (SAB): Dr. Alice Gottlieb and Dr. Peter Libby. Both of these extraordinary scientists are world-recognized leaders in their fields.

Dr. Alice Gottlieb, M.D., Ph.D. is internationally recognized for her expertise and trail-blazing work in the development of biological therapies to treat skin diseases. She has played leading roles in the clinical development of therapies including etanercept, infliximab, ustekinumab and secukinumab. Dr. Gottlieb is working to help guide development of bermekimab for the treatment of skin diseases. She currently serves as Study Chair for XBiotech's ongoing Phase 2 study in hidradenitis suppurativa.

Dr. Peter Libby, M.D. is the Mallinckrodt Professor of Medicine at Harvard Medical School and clinical cardiologist at Brigham and Women's Hospital. Dr. Libby is collaborating with XBiotech on basic research into the mechanism of inflammation and the use of bermekimab to treat cardiovascular disease. Pioneering research by Dr. Libby and his team was recently published in the journal of the American Heart Association, Arteriosclerosis, Thrombosis, and Vascular Biology. The breakthrough findings of this research showed that bermekimab could potentially be used to prevent heart attacks and strokes.

Intellectual Property

XBiotech continues to aggressively expand its already extensive patent portfolio. During the quarter the Company was awarded 4 new patents and 7 patent allowances. A Canadian patent and Russian patent both cover bermekimab. Two European patents were awarded, one covering the use of IL-1α-specific antibodies for the treatment of dermatological pathologies and the other the use of IL-1α-specific antibodies for the treatment of cancer-associated cachexia. Patent applications allowed in Q3 include one each in Australia, Canada, Israel, Mexico, the Philippines, Russia, and South Korea. The allowed Australian application relates to using IL-1α-specific antibodies to treat arthritis. The allowed Canadian application relates to using IL-1α-specific antibodies to reduce a subset of blood cells that contribute to inflammatory diseases. The allowed Israeli and Mexican applications each cover key aspects of the Company's innovative True Human ™ antibody discovery platform. The allowed Russian application relates to using IL-1α-specific antibodies to treat vascular diseases and complications thereof, and the allowed Philippines application relates to the Company's antibody for treating S.aureus infections, 514G3.

About True Human™ Therapeutic Antibodies

XBiotech's True Human™ antibodies are derived without modification from individuals who possess natural immunity to certain diseases. With discovery and clinical programs across multiple disease areas, XBiotech's True Human antibodies have the potential to harness the body's natural immunity to fight disease with increased safety, efficacy and tolerability.

About XBiotech

XBiotech is a fully integrated global biosciences company dedicated to pioneering the discovery, development and commercialization of therapeutic antibodies based on its True Human™ proprietary technologyXBiotech currently is advancing a robust pipeline of antibody therapies to redefine the standards of care in oncology, inflammatory conditions and infectious diseases. Headquartered in Austin, Texas, XBiotech also is leading the development of innovative biotech manufacturing technologies designed to more rapidly, cost-effectively and flexibly produce new therapies urgently needed by patients worldwide. For more information, visit www.xbiotech.com.

Cautionary Note on Forward-Looking Statements

This press release contains forward-looking statements, including declarations regarding management's beliefs and expectations that involve substantial risks and uncertainties. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "would," "could," "expects," "plans," "contemplate," "anticipates," "believes," "estimates," "predicts," "projects," "intend" or "continue" or the negative of such terms or other comparable terminology, although not all forward-looking statements contain these identifying words. Forward-looking statements are subject to inherent risks and uncertainties in predicting future results and conditions that could cause the actual results to differ materially from those projected in these forward-looking statements. These risks and uncertainties are subject to the disclosures set forth in the "Risk Factors" section of certain of our SEC filings. Forward-looking statements are not guarantees of future performance, and our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate, may differ materially from the forward-looking statements contained in this press release. Any forward-looking statements that we make in this press release speak only as of the date of this press release. We assume no obligation to update our forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

Contact
Ashley Otero
aotero@xbiotech.com
512-386-2930

[1] USRDS 2013 Annual Data Report: Atlas of End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2014.

[2] Vandecasteele et al. *Staphylococcus aureus* Infections in Hemodialysis: What a Nephrologist Should Know. Clin. J. Am. Soc. Nephrology. August 2009, 4 (8) 1388-1400

[3] https://www.mdmag.com/medical-news/promising-atopic-dermatitis-and-asthma-drug-fast-tracked-by-fda

[4] https://www.reuters.com/article/us-abbvie-results/abbvie-says-humira-sales-will-balloon-to-21-billion-in-2020-shares-rise-idUSKBN1CW1JK

XBiotech Inc.