January 29, 2015

Xencor Reports XmAb®7195 Top-line Interim Phase 1a Results Showing Rapid Reduction of Serum IgE in Healthy Volunteers

- 90% of subjects had reduction of free IgE to below the limit of detection by the end of XmAb7195 infusion, including at lowest dose evaluated of 0.3 mg/kg -
- Dose limiting toxicity of thrombocytopenia observed at 3.0 mg/kg -
- Enrollment continues in Part 2 of trial for high IgE subjects -
- Conference call today at 8:30 a.m. ET -

MONROVIA, Calif., Jan. 29, 2015 /PRNewswire/ -- Xencor, Inc. (NASDAQ: XNCR), a clinical-stage biopharmaceutical company developing engineered monoclonal antibodies for the treatment of asthma and allergic diseases, autoimmune diseases and cancer, today reported top-line interim results from a Phase 1a study for XmAb®7195. The data show rapid reduction of circulating free IgE levels to below the limit of detection in 90% of XmAb7195 treated subjects that had detectable free IgE pre-dose, including those at the lowest dose evaluated of 0.3 mg/kg. Total IgE levels were also reduced in a parallel fashion. A dose limiting toxicity of transient, asymptomatic thrombocytopenia was observed at the 3.0 mg/kg dose. Two subjects with high pre-dose IgE levels (above 400 IU/mL) were treated with XmAb7195, one each at 0.75 mg/kg and 3.0 mg/kg doses, and both had reduction of free IgE levels to below the limit of detection lasting for at least one week. XmAb7195 is an anti-IgE monoclonal antibody containing Xencor's proprietary XmAb Immune Inhibitor Fc domain that targets FcγRIIb, which results in rapid clearance of free and total IgE and inhibition of the function of IgE expressing B cells.

"These results demonstrate for the first time that XmAb7195's first-in-class mechanism of action which targets IgE and FcγRIIb can be effective at reducing both free and total IgE from the circulation in humans," said Paul Foster, M.D., chief medical officer of Xencor. "XmAb7195 was very potent, reducing IgE to the assay detection limit at even our lowest dose of 0.3 mg/kg. In addition, for the two subjects enrolled who happened to have IgE above 400 IU/mL, one each at 0.75 mg/kg and 3.0 mg/kg, it reduced free IgE below the detection limit for at least a week. These data will help us determine a dose regimen with acceptable activity and safety profiles as we proceed with future clinical development."

XmAb7195 has been administered to 30 subjects in Part 1 of the study in single doses ranging from 0.3 to 3.0 mg/kg. 29 of 30 (97%) subjects had detectable free IgE levels pre-dose. Of these, 26 subjects (90%) had reduction of free IgE levels to below the detectable limit of the assay (< 10 ng/mL) at the end of the XmAb7195 infusion with reduction lasting for at least one week following a single infusion. Total IgE was reduced to below the limit of detection (< 2.0 IU/mL) in 26 of 30 (87%) subjects with detectable total IgE pre-dose. Total IgE reduction differentiates XmAb7195 from other anti-IgE therapeutic antibodies, which actually increase total IgE levels. Because total IgE assays, unlike free IgE assays, are readily available to clinicians, the effect of XmAb7195 on total IgE levels could enable for the first time simple monitoring, and potentially adjustment, of treatment effect.

"IgE is a key mediator of allergic symptoms whose reduction is correlated to clinical response in allergic asthma, and these results support our clinical development plans for XmAb7195 to treat allergic diseases. While this study explores two of the three mechanisms of XmAb7195, the rapid clearance via FcgRIIb-expressing cells and the binding to soluble IgE, assessing its third mechanism, the suppression of IgE production by immune cells, will require longer duration studies" said Bassil Dahiyat, Ph.D., president and chief executive officer of Xencor. "In addition to continuing the high IgE subject portion of this study, we are planning a multi-dose Phase 1b study and are developing a subcutaneous formulation of XmAb7195."

Dosing through the first three cohorts (0.3, 1.0 and 3.0 mg/kg) resulted in observations of two apparent dose-related toxicities: urticaria and thrombocytopenia. There were no other adverse events that occurred in more than two XmAb7195 treated subjects. There were no serious adverse events reported and no subject discontinued the trial early.

As a result of the laboratory finding of transient, asymptomatic thrombocytopenia in all six subjects receiving XmAb7195 in the 3.0 mg/kg dose cohort, thrombocytopenia was deemed a dose limiting toxicity and the two remaining cohorts were subsequently enrolled at a reduced dose of 0.75 mg/kg. The decrease in platelet count was transient with a nadir by 24 hours post-dose, recovery starting by 48 hours post-dose and near full platelet count recovery by study day eight in all cases, at which time serum drug concentrations still exceeded levels that eliminate detectable IgE. There was no apparent relationship of thrombocytopenia to known polymorphisms of Fcg receptors IIa or IIb. No evidence of thrombocytopenia has been observed in any of the clinical trials of XmAb5871, an anti-CD19 antibody with the identical XmAb Immune Inhibitor Fc domain as that of XmAb7195.

Moderate urticaria was reported in a total of seven XmAb7195 treated subjects with an apparent correlation of dose with frequency of occurrence. In all cases regardless of dose, the signs/symptoms of urticaria were mild, non-diffuse and easily treated with oral antihistamine, and the study drug infusions were continued to completion without worsening of symptoms.

The Company continues to conduct an analysis of safety, pharmacokinetics, immunogenicity and efficacy data of Part 1 of the Phase 1a study and continues to enroll patients in Part 2 of the study.

Conference Call and Webcast
Xencor will host a conference call today at 8:30 a.m. ET to discuss this data. The live call may be accessed by dialing (855) 433-0932 for domestic callers or (484) 756-4280 for international callers, and providing the conference ID number 76049183. A live webcast of the conference call will be available online from the investors section of the Company's website at www.xencor.com. The webcast will be archived on the company website for 30 days.

About the Phase 1a Study of XmAb®7195
The Phase 1a study is a randomized, double-blind, placebo-controlled, single ascending dose trial being conducted in two parts. In the completed Part 1, healthy subjects were enrolled into five consecutive dose cohorts of eight subjects each, randomized to receive a single intravenous (IV) administration of XmAb7195 or matching placebo (6:2). In the ongoing Part 2, otherwise healthy subjects with a history of allergic rhinitis and/or allergic conjunctivitis and/or atopic dermatitis with elevated serum IgE (> 300 IU/mL), will be enrolled into three consecutive dose cohorts of eight subjects each, randomized to a single IV administration of XmAb7195 or matching placebo (6:2). The primary and secondary objectives of the study are to determine the safety and tolerability profile of single-dose IV administration of XmAb7195 and to characterize the pharmacokinetics (PK) and immunogenicity of single-dose IV administration of XmAb7195 respectively. Exploratory objectives include the determination of the effect of XmAb7195 on serum free and total IgE and the effect on basophil surface IgE and basophil FcεRI expression levels.

About XmAb®7195
XmAb7195 is a first-in-class monoclonal antibody that targets IgE with its variable domain and that uses Xencor's XmAb immune inhibitor Fc domain to target FcγRIIb, a receptor that inhibits B cell function. Xencor has demonstrated in multiple animal models that XmAb7195 rapidly reduces free and total IgE and blocks production of IgE by immune cells. Its three mechanisms of action offer a unique approach to IgE reduction for the potential treatment of allergic disease.

About Xencor's XmAb® Immune Inhibitor Technology
FcγRIIb (IIb), also called CD32b, is a receptor for Fc domains on B cells and other immune cells. When engaged, the IIb receptor blocks immune activation pathways and traffics bound soluble antigens out of circulation. Xencor has discovered a series of Fc domain variants with up to a 400-fold increase in binding affinity to FcγRIIb derived from just two amino acid changes. These XmAb Immune Inhibitor Fc domains greatly heighten the properties of IIb receptor engagement and have potential as building blocks for drug candidates in autoimmune, allergic and inflammatory diseases.

About Xencor, Inc.
Xencor is a clinical-stage biopharmaceutical company developing engineered monoclonal antibodies for the treatment of autoimmune diseases, asthma and allergic diseases, and cancer. Currently, eight candidates that have been engineered with Xencor's XmAb® technology are in clinical development internally and with partners. Xencor's internally-discovered programs include: XmAb5871, which completed a Phase 1b/2a clinical trial for the treatment of rheumatoid arthritis and is in preparation for a clinical trial in IgG4-related disease in 2015; XmAb7195 in Phase 1a development for the treatment of asthma; and XmAb5574/MOR208 which has been licensed to Morphosys AG and is in Phase 2 clinical trials for the treatment of acute lymphoblastic leukemia and non-Hodgkin lymphoma. Xencor's XmAb antibody engineering technology enables small changes to the structure of monoclonal antibodies resulting in new mechanisms of therapeutic action. Xencor partners include Merck, Janssen R&D LLC, Alexion, Novo Nordisk and Boehringer Ingelheim. For more information, please visit www.xencor.com.

Forward Looking Statements
Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the U.S. securities laws, including statements associated with XmAb7195, XmAb5871 and Xencor's research, collaborations and its expectations regarding future therapeutic and commercial potential of Xencor's technologies, programs, drug candidates and intellectual property related to Xencor's XmAb® technology. Because such statements are subject to risks and uncertainties, including risks associated with the process of discovering, developing and commercializing drugs that are safe and effective, actual results and the timing of events may differ materially from those expressed or implied by such forward-looking statements. These and other risks concerning Xencor's programs and technology are described in additional detail in Xencor's SEC filings. These forward-looking statements speak as of the date on which they were made, are based upon Xencor's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Xencor disclaims any intention or obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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