Xencor Presents Data from Multiple Preclinical XmAb® Cytokine Programs at the American Association for Cancer Research (AACR) Annual Meeting 2022

April 8, 2022

MONROVIA, Calif.--(BUSINESS WIRE)--Apr. 8, 2022-- Xencor, Inc. (NASDAQ: XNCR), a clinical-stage biopharmaceutical company developing engineered antibodies and cytokines for the treatment of cancer and autoimmune diseases, today announced the presentation of new data from its preclinical-stage IL-18 and LAG3-targeted IL-15 cytokine programs at the American Association for Cancer Research (AACR) Annual Meeting 2022.

"XmAb® cytokines are engineered to be long acting and more drug-like in order to overcome inherent limitations facing cytokine therapeutics. At AACR, we are presenting two additions to our wholly owned cytokine portfolio -- a decoy-resistant and potency-reduced IL18-Fc fusion protein, and a LAG-3 targeted IL15/IL15Rα-Fc fusion protein, which is biased toward binding and activating LAG-3-positive lymphocytes that are more likely to be tumor-reactive," said John Desjarlais, Ph.D., senior vice president and chief scientific officer at Xencor. "Later this year we plan to submit an investigational new drug application for XmAb662, our wholly owned, reduced-potency IL12-Fc cytokine, which has demonstrated remarkable preclinical anti-tumor activity and improved therapeutic index in vivo."

The posters will be archived under "Events & Presentations" in the Investors section of the Company's website located at www.xencor.com.

Abstract 2080, "LAG3-targeted IL15/IL15Rα-Fc (LAG3 x IL15) fusion proteins for preferential TIL expansion"

- Session: Immunomodulatory Agents and Interventions 1
- Date and Time: Monday, April 11, 2022, 1:30 - 5:00 p.m. CDT
- Location: Exhibit Halls D-H, Section 38, Board 18

IL-2 and IL-15 are cytokines that cause the activation and proliferation of T cells and NK cells. Their therapeutic potential has been well established in preclinical models and clinical studies; however, when given systemically, these potent cytokines have historically provided a poor therapeutic window, as they are not well tolerated and are quickly cleared from circulation.

Xencor engineered LAG3-targeted IL15/IL15Rα-Fc cytokine/antibody fusion proteins (LAG-3 x IL-15) for selective activation of LAG3-positive immune cells, which may potentially avoid systemic toxicities arising from off-target activation and expansion of peripheral immune cells. An XmAb heterodimeric Fc domain serves as a molecular scaffold, and Xtend™ technology promotes longer circulating half-life. LAG-3 is an immune checkpoint expressed on tumor-infiltrating lymphocytes (TILs), is frequently co-expressed with PD-1 and has limited expression in normal peripheral immune cells. Recently, anti-LAG3 agents have generated promising results in clinical studies, and LAG-3 x IL-15 agents could be combined with anti-PD1 agents. Xencor's LAG-3 x IL-15 candidate molecules demonstrated high selectivity for LAG3-positive cell populations in multiple *in vitro* and *in vivo* models.

Abstract 3515, "Engineered IL18 heterodimeric Fc-fusions featuring improved stability, reduced potency, and insensitivity to IL18BP"

- Session: Immunomodulatory Agents and Interventions 2
- Date and Time: Tuesday, April 12, 2022, 1:30 - 5:00 p.m. CDT
- Location: Exhibit Halls D-H, Section 37, Board 17

IL-18 is a proinflammatory cytokine that modulates both the innate and adaptive immune responses. IL-18 receptor 1, the primary co-receptor for IL-18, is overexpressed on activated T cells and NK cells, which are critical for anti-tumor responses. Additional preclinical studies of IL-18 have demonstrated its anti-tumor activity, including synergy with immune checkpoint inhibitors and CAR-T therapies. In contrast with other potent cytokines, IL-18 has been well tolerated in clinical trials but demonstrated a lack of efficacy despite heavy dosing. IL-18 participates in a negative feedback loop with a high affinity natural inhibitor, IL18BP, which was observed to be upregulated in early phase clinical studies and may have directly resulted in IL-18's limited clinical performance.

Xencor engineered stabilized, potency-reduced, monovalent IL-18 cytokines fused to an XmAb heterodimeric Fc domain with Xtend Fc technology for longer half-life. Importantly, these cytokine-Fc fusions were engineered to not bind its inhibitor, IL18BP. In a preclinical mouse model of graft-versus-host disease, an analog of the candidate XmAb143 led to the expansion and proliferation of target immune cells and induced high levels of interferon gamma. Further, it was well tolerated in non-human primates and exhibited favorable pharmacokinetics, such as slow receptor-mediated clearance.

About Xencor, Inc.

Xencor is a clinical-stage biopharmaceutical company developing engineered antibodies and cytokines for the treatment of patients with cancer and autoimmune diseases. More than 20 candidates engineered with Xencor's XmAb® technology are in clinical development, and three XmAb medicines are marketed by partners. Xencor's XmAb engineering technology enables small changes to a protein's structure that result in new mechanisms of therapeutic action. For more information, please visit www.xencor.com.

Forward-Looking Statements

Certain statements contained in this press release may constitute forward-looking statements within the meaning of applicable securities laws. Forward-looking statements include statements that are not purely statements of historical fact, and can generally be identified by the use of words such as “potential,” “can,” “will,” “plan,” “may,” “could,” “would,” “expect,” “anticipate,” “seek,” “look forward,” “believe,” “committed,” “investigational,” and similar terms, or by express or implied discussions relating to Xencor’s business, including, but not limited to, statements regarding planned additional clinical trials and other statements that are not purely statements of historical fact. Such statements are made on the basis of the current beliefs, expectations, and assumptions of the management of Xencor and are subject to significant known and unknown risks, uncertainties and other factors that may cause actual results, performance or achievements and the timing of events to be materially different from those implied by such statements, and therefore these statements should not be read as guarantees of future performance or results. Such risks include, without limitation, the risks associated with the process of discovering, developing, manufacturing and commercializing drugs that are safe and effective for use as human therapeutics and other risks, including the ability of publicly disclosed preliminary clinical trial data to support continued clinical development and regulatory approval for specific treatments, in each case as described in Xencor's public securities filings. For a discussion of these and other factors, please refer to Xencor's annual report on Form 10-K for the year ended December 31, 2021 as well as Xencor's subsequent filings with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, as amended to date. All forward-looking statements are qualified in their entirety by this cautionary statement and Xencor undertakes no obligation to revise or update this press release to reflect events or circumstances after the date hereof, except as required by law.

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