Xencor Presents Preclinical Data from Multiple XmAb® Research Programs at the SITC Annual Meeting

November 3, 2023

PASADENA, Calif.--(BUSINESS WIRE)--Nov. 3, 2023-- Xencor, Inc. (NASDAQ: XNCR), a clinical-stage biopharmaceutical company developing engineered antibodies and cytokines for the treatment of cancer and autoimmune diseases, today presented data from multiple preclinical-stage XmAb® programs at the 38th Annual Meeting of the Society for Immunotherapy of Cancer (SITC) in San Diego.

“Xencor aims to stay on the leading edge of molecular engineering, using and improving upon our XmAb technologies to create molecules with enhanced functionality or new therapeutic mechanisms. At SITC, we are presenting new preclinical data from two research-stage programs —engineered, decoy-resistant IL18-Fc fusions and our multi-valent NK cell engagers targeted to MICA and MICB, which are tumor antigens upregulated in the tumor microenvironment,” said John Desjarlais, Ph.D., executive vice president and chief scientific officer at Xencor. “Later this year, we expect to submit an investigational new drug application for XmAb541, an XmAb 2+1 format CLDN6 x CD3 bispecific antibody that we are developing for patients with ovarian cancer and other tumor types. We are also developing additional CD3 and CD28 T cell engaging bispecific antibodies against solid tumor targets.”

Posters will be available in the poster hall and virtually to registrants of the SITC Annual Meeting. In the poster hall, odd-numbered posters will be displayed on Friday, November 3, and even-numbered posters will be displayed on Saturday, November 4. Xencor’s posters will be archived under "Events & Presentations" in the Investors section of the Company's website located at www.xencor.com.

Clinical Trials in Progress

Abstract 764, “A Phase 1, first-in-human (FIH), open-label, dose-finding and expansion study of XmAb808, a B7H3 x CD28 bispecific antibody, in combination with pembrolizumab in patients with advanced solid tumors”

Xencor is conducting a Phase 1 study of XmAb808 in patients with advanced solid tumors. XmAb808 is a tumor-selective, co-stimulatory XmAb 2+1 bispecific antibody designed to bind to the broadly expressed tumor antigen B7-H3 and selectively to the CD28 T-cell co-receptor only when bound to tumor cells, which was demonstrated *in vitro*. Strong potentiation of checkpoint and CD3 cytotoxic activity was also observed *in vivo*. XmAb808 is a wholly owned Xencor program.

The clinical trials in progress poster reviews the design of XmAb808 and the rationale of using CD28 bispecific antibodies to expand the utility of checkpoint blockade and CD3 T cell engagers. The poster also provides study objectives, key eligibility criteria and study schema.

Preclinical Programs

Abstract 1060, “Optimally engineered IL18-Fc fusion proteins balance potency and pharmacokinetics to promote strong anti-tumor activity”

IL-18 is a proinflammatory cytokine that modulates both the innate and adaptive immune responses. 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 induces a negative feedback loop with its high affinity natural inhibitor, IL18BP, which was upregulated in early phase clinical studies and may have limited IL-18’s clinical performance.

Xencor engineered stabilized, potency-modulated IL-18 cytokines fused to an XmAb heterodimeric Fc domain with Xtend™ Fc technology for longer half-life (IL18-Fc). In addition, Xencor engineered bispecific IL18-Fc cytokines targeted to PD-1, a checkpoint receptor on T cells. Importantly, these molecules were engineered to avoid binding IL18BP.

Xencor’s IL18-Fc fusions and PD1 x IL18-Fc bispecific inhibited tumor growth in a dose- and potency-dependent manner, outperforming a wild-type IL18-Fc fusion, *in vivo*. Further preclinical studies of the engineered IL18-Fc fusions demonstrated pharmacodynamic profiles similar to wild-type IL18-Fc. Notably, a set of surviving tumor-engrafted mice, which had previously received engineered IL18-Fc fusions, had no tumor growth upon rechallenge.

Abstract 1193, “Synergistic targeting of multiple activating pathways with Natural Killer cell Engagers”

Xencor’s XmAb natural killer cell engagers (NKEs) are multifunctional antibodies that target multiple activating receptors on the surface of NK cells and bind to tumor-associated antigens.

MICA and MICB (MICA/B) are stress-induced tumor antigens expressed in a range of cancers. MICA/B antigens are recognized by NKG2D, an activating receptor on NK and CD8+ T cells. While membrane-bound, MICA/B is immuno-stimulatory; however, the cleaved and soluble form, found in

the tumor microenvironment, prevents NKG2D from recognizing tumor cells. Xencor engineered anti-MICA/B antibodies with enhanced effector function in order to block the cleavage of MICA/B antigens and promote NK cell engagement. These antibodies increased MICA/B membrane surface density and led to tumor cell killing with MICA/B binding to NKG2D on immune cells. To enhance the anti-tumor activity, Xencor engineered multi-specific NK cell-engaging antibodies that simultaneously target MICA/B antigens and an orthogonal activating receptor on NK cells, NKp46. These multi-specific NK cell-engaging antibodies demonstrated enhanced functional activity compared to the antibodies targeting only MICA/B.

About Xencor

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 Xencor preclinical programs and clinical trials, the quotations from Xencor's executive vice president and chief scientific officer, 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, 2022, 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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