Xencor Announces XmAb Drug Candidates in Autoimmune Disease with Near-Term Clinical Plans and Shares Clinical Progress in Early-Stage Oncology Programs

September 9, 2024

– Phase 1 healthy volunteer study of half-life extended anti-TL1A antibody XmAb942 to dose first subject in Q4 2024, with data anticipated in the first half of 2025 –

– XmAb® T-cell engagers plamotamab (CD20 x CD3) and XmAb657 (CD19 x CD3) to be evaluated in autoimmune diseases, with respective Phase 1b/2a and Phase 1 studies to initiate in 2025 –

– Ongoing Phase 1 dose escalation of XmAb819 (ENPP3 x CD3) in advanced clear cell renal cell carcinoma shows initial encouraging clinical activity including RECIST responses –

– Management hosting webcast and conference call at 8:00 a.m. ET / 5:00 a.m. PT today –

PASADENA, Calif.--(BUSINESS WIRE)--Sep. 9, 2024-- Xencor, Inc. (NASDAQ: XNCR), a clinical-stage biopharmaceutical company developing engineered antibodies for the treatment of cancer and other serious diseases, today announced four new XmAb® programs in development for the treatment of patients with autoimmune diseases and provided updates from dose-escalation studies evaluating its first-in-class oncology programs, including XmAb819 (ENPP3 x CD3) in patients with advanced clear cell renal cell carcinoma and XmAb808 (B7-H3 x CD28) in patients with advanced solid tumors.

“Xencor’s clinical pipeline of XmAb bispecific T-cell engagers and newly announced autoimmune programs have multiple near-term milestones and offer a balance of opportunities to deliver novel treatment options that could potentially make a real difference in patients’ lives. The foundation of our portfolio is world-class protein engineering, using our XmAb platforms to potentially solve complex engineering problems and rationally build drug candidates that address specific clinical opportunities,” said Bassil Dahiyat, Ph.D., president and chief executive officer at Xencor. “Our goal is clear—fully leverage our protein engineering strengths and reduce exposure to biological uncertainties to increase our overall opportunities for clinical success.”

Clinical Progress Updates in Early-Stage Oncology Programs: XmAb819 (ENPP3 x CD3) and XmAb808 (B7-H3 x CD28)

XmAb819: ENPP3 x CD3 bispecific T-cell engager in Phase 1 dose escalation for patients with advanced clear-cell renal cell carcinoma (ccRCC)

XmAb819 is designed to engage the immune system, activating T cells for highly potent and targeted killing of tumor cells expressing ENPP3, an antigen highly expressed on kidney cancers. Xencor’s XmAb 2+1 multivalent format used in XmAb819 enables greater selectivity of ENPP3-expressing tumor cells compared to normal cells, which express lower levels of ENPP3.

- ***Clinical update:*** Initial evidence of anti-tumor activity has been observed in recent dose-escalation cohorts in the ongoing Phase 1 study, including RECIST responses, and the duration of treatment for several patients in earlier dose cohorts has extended beyond one year. Cytokine release syndrome remains manageable, and the tolerability profile from recent dose cohorts, including no maximum tolerated dose being reached, supports continued dose escalation toward target dose levels.
- ***Guidance:*** The Company continues to anticipate reaching target dose levels by year end and plans to provide a clinical update around initiation of the first dose expansion cohort during the first half of 2025.

XmAb808: B7-H3 x CD28 bispecific T-cell engager in Phase 1 dose escalation in advanced solid tumors

XmAb808 is a tumor-selective, co-stimulatory CD28 bispecific antibody that binds to the broadly expressed tumor antigen B7-H3 and is constructed with the XmAb 2+1 format. Co-stimulation is required for T cells to achieve full activation, and targeted CD28 bispecific antibodies may provide conditional co-stimulation of T cells when the antibodies are bound to tumor cells.

- ***Clinical update:*** The majority of patients enrolled into the ongoing Phase 1 dose-escalation study are men with metastatic castration-resistant prostate cancer (mCRPC). In this group of patients, prostate specific antigen (PSA) declines have been observed during the four-week monotherapy safety run-in period. Tolerability from recent dose cohorts remains supportive of continued dose escalation in combination with pembrolizumab.

- ***Guidance:*** The Company continues to anticipate reaching target dose levels by year end and plans to provide a clinical update around initiation of dose expansion cohorts during the first half of 2025.

XmAb Drug Candidates for the Treatment of Patients with Autoimmune and Inflammatory Diseases and Planned Clinical Studies: Plamotamab (CD20 x CD3), XmAb657 (CD19 x CD3), XmAb942 (Xtend™ TL1A) and the XmAb TL1A x IL-23 Program

Plamotamab: CD20 x CD3 bispecific T-cell engager to be evaluated in patients with multi-drug resistant rheumatoid arthritis (MDR-RA), with Phase 1b/2a study anticipated to initiate in the first half of 2025

Xencor plans to initiate a Phase 1b/2a proof-of-concept study for plamotamab in MDR-RA in the first half of 2025. The Phase 1b portion of the study will select a priming and step-up dose regimen based on the regimen established in oncology, and will assess the initial safety, efficacy, and biomarkers of plamotamab in patients with MDR-RA. The selected dose regimen will then be evaluated in the randomized Phase 2a portion, with efficacy determined at week 24.

Xencor previously completed a Phase 1 clinical study of plamotamab in hematologic cancers, completing enrollment in late 2023. Results from the study showed favorable tolerability and comparable preliminary efficacy data, when cross compared to results from studies of a competitor molecule within the class, with similar patient baseline characteristics. Based on these clinical outcomes, significant B-cell depletion observed in preclinical studies, and the emergent biology supportive of B-cell targeted T cell engagers for the treatment of patients with autoimmune diseases, Xencor plans to evaluate plamotamab in MDR-RA, in which patients progressed through two prior lines of therapy.

XmAb657: Rationally designed CD19 x CD3 bispecific T-cell engager for patients with autoimmune diseases, with first-in-human Phase 1 study anticipated to initiate in the second half of 2025

Xencor has leveraged its XmAb protein engineering platforms to create XmAb657, a potent, potentially long-acting CD19 x CD3 bispecific antibody, utilizing the XmAb 2+1 bispecific antibody format and Xtend™ Fc technology. In non-human primate studies, a single dose of XmAb657 deeply reduced B cells by over 99.98% in the peripheral compartment, bone marrow and lymph nodes, which was sustained for at least 28 days. Half-life was estimated to be 15 days, which indicates a potential for durable B-cell depletion in clinical studies. XmAb657 was well tolerated preclinically, with no clinical signs of cytokine release syndrome. Xencor plans to initiate a first-in-human study during the second half of 2025.

XmAb942: A novel high-affinity anti-TL1A antibody designed for extended half-life, under development for the treatment of inflammatory bowel diseases (IBD), with first-in-human Phase 1 study anticipated to initiate in the fourth quarter 2024

XmAb942 is a monospecific anti-TL1A antibody, utilizing Xencor's Xtend Fc domain and proprietary Fc silencing technology, with potentially class-leading potency, and is under development for patients with IBD. The two most common forms of IBD are Crohn's disease and ulcerative colitis. Half-life preclinically was greater than 22 days, potentially supporting an 8- to 12-week dosing regimen in humans. An abstract with preclinical characterization was accepted for presentation at the United Europe Gastroenterology Week (UEGW) in Vienna, Austria on Tuesday, October 15. Xencor anticipates dosing the first subject in a first-in-human, single-ascending dose study of XmAb942 in the fourth quarter of 2024, with interim data during the first half of 2025.

XmAb TL1A x IL-23 Program: Potential first-in-class bispecific antibody to combine two validated biological pathways of interest into one drug candidate for the treatment of IBD, leveraging Xencor's world-class protein engineering

An expertly engineered XmAb TL1A x IL-23p19 bispecific antibody could potentially provide dual targeting of important inflammatory pathways for autoimmune and inflammatory disease, while avoiding the complexities of dosing and formulary access for two separate TL1A and IL23 targeted drugs. Xencor anticipates initiating first-in-human studies during 2026.

Conference Call and Webcast

Xencor will host a conference call and webcast today at 8:00 a.m. ET (5:00 a.m. PT) to review the topics outlined in this news release.

The live webcast may be accessed through "Events & Presentations" in the Investors section of the Company's website, located at investors.xencor.com. Telephone participants may register to receive a dial-in number and unique passcode that can be used to access the conference call. A recording will be available for at least 30 days.

About Xencor

Xencor is a clinical-stage biopharmaceutical company developing engineered antibodies for the treatment of patients with cancer and other serious diseases. More than 20 candidates engineered with Xencor's XmAb® technology are in clinical development, and multiple 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 expectations for clinical progress, planned presentations of clinical data, new XmAb candidates and programs, planned and in process clinical trials, the quotations from Xencor's president and chief executive 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, 2023 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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For Investors:
Charles Liles
cliles@xencor.com
(626) 737-8118

For Media:
Cassidy McClain
Inizio Evoke
cassidy.mcclain@inizioevoke.com
(619) 694-6291

Source: Xencor, Inc.