Xencor Presents Updated Data From the DUET-2 Phase 1 Study of XmAb20717, PD-1 x CTLA-4 Bispecific Antibody, at the SITC Annual Meeting

November 9, 2020

-- XmAb20717 was generally well-tolerated; 19% objective response rate (ORR) observed across cohorts at the recommended dose level --

-- Early clinical activity, including prostate-specific antigen (PSA) reductions in patients with advanced prostate cancer, support initiation of new Phase 1b study in 2021--

MONROVIA, Calif.--(BUSINESS WIRE)--Nov. 9, 2020-- Xencor, Inc. (NASDAQ:XNCR), a clinical-stage biopharmaceutical company developing engineered monoclonal antibodies for the treatment of cancer and autoimmune diseases, today reported data from its ongoing Phase 1 study evaluating XmAb®20717, a PD-1 x CTLA-4 bispecific antibody and Xencor's first tumor microenvironment activator, in patients with advanced solid tumors (DUET-2). The preliminary results from the study's expansion cohorts will be presented in a poster titled, "Preliminary safety, pharmacokinetics/pharmacodynamics, and antitumor activity of XmAb20717, a PD-1 x CTLA-4 bispecific antibody, in patients with advanced solid tumors" at the 35th Annual Meeting of the Society for Immunotherapy of Cancer (SITC) by Elaine Shum, M.D., Assistant Professor in the Division of Medical Oncology and Hematology at the NYU Perlmutter Cancer Center.

"We are observing activity across multiple tumor types in patients who have already been treated with a checkpoint inhibitor, a difficult-to-treat patient population," said Bassil Dahiyat, Ph.D., president and chief executive officer at Xencor. "XmAb20717 continues to be tolerable throughout our expansion cohorts, and importantly in our study we are observing lower rates of some types of immunotherapy-related adverse events, including colitis, than are typically seen with CTLA-4 blockade."

"Though data are early, we are especially encouraged by initial activity in patients with metastatic castration-resistant prostate cancer. In the first half of 2021, we plan to initiate a Phase 1b study of XmAb20717 for patients with certain molecular subtypes of mCRPC, as a monotherapy or in combination depending on the subtype, as these patients represent a high unmet medical need," said Allen Yang, M.D., Ph.D., senior vice president and chief medical officer at Xencor. "We are also planning additional cohorts in selected populations within DUET-2, based on clinical activity and unmet medical need. Data are also still maturing in cohorts of patients with renal cell carcinoma, and those with cancers without approved checkpoint therapies, including prostate cancer. We will provide further updates in the coming months."

Initial Dose Escalation

In the study's escalation phase, 34 patients have been treated with doses escalating from 0.15 to 10 mg/kg. As previously reported, a dose of 10 mg/kg was identified as the recommended dose for the multi-cohort, parallel-group expansion phase, based on an observation of consistent proliferation of both CD8+ and CD4+ T cells, indicative of dual checkpoint blockade, and a complete response (CR) in one patient with melanoma. The study currently is enrolling patients at a dose of 15 mg/kg.

Multi-Cohort Dose Expansion

At the data cut off on September 30, 2020, 89 patients had been treated at the recommended dose in five dose expansion cohorts: melanoma (n=20), renal cell carcinoma (RCC, n=11), non-small cell lung cancer (NSCLC, n=20), castration-resistant prostate cancer (CRPC, n=18) and other cancers without approved checkpoint therapies (n=20).

The safety analysis included 96 patients treated at the 10 mg/kg dose level, which includes seven patients from the dose-escalation phase of the study. Patients were a median of 65.5 years old and were heavily pretreated, having a median of four prior systemic therapies. 56% of patients had received at least one prior checkpoint therapy. XmAb20717 was generally well-tolerated, and the most common treatment-related adverse events were immune-related adverse events (irAEs). With exceptions for rash and increases in transaminases, other Grade 3 or higher irAEs were reported for no more than three patients each. The most common AEs of any grade were rash (36.5%), pruritus (25.0%), transaminase increases (17.7%), diarrhea (9.4%), infusion related reaction (8.3%) and fatigue (6.3%), as well as hypothyroidism, myalgia and pneumonitis (5.2% each). Immune-mediated pancreatitis (Grade 5) was reported for one patient with RCC, whose cancer had already metastasized to the pancreas at baseline and progressed on study. Grade 5 myocarditis and respiratory failure were reported for a patient with NSCLC who had a history of significant cardiac events, including atrial fibrillation and the insertion of a dual-chamber pacemaker.

The efficacy analysis included 42 evaluable patients at the 10 mg/kg dose level. A complete response was observed in a patient with melanoma (1/10), and partial responses were observed in multiple tumor types, including melanoma (2/10), RCC (1/4), NSCLC (2/14), CRPC (1/4), and ovarian cancer (1/5). The objective response rate across cohorts was 19.0% (8/42). Across the expansion cohorts, approximately half of evaluable patients had at least 10% tumor shrinkage from baseline assessments, and nearly all these reductions occurred in patients with prior checkpoint inhibitor treatment. The median duration of response was 119 days at the time of the data cut off, and 24 patients remained on treatment.

Checkpoint therapy induces T-cell proliferation in a patient's peripheral blood, which is evaluated by quantifying the change in the number of T cells expressing the protein Ki67. Measurements were taken at baseline (cycle 1 day 1) and compared to the peak value during the first two cycles of treatment with XmAb20717. Consistent with prior results, proliferation of peripheral T cells began at the 3 mg/kg dose level and increased through the 10 mg/kg level. At the 10 mg/kg level, proliferation of both CD8+ cytotoxic T cells and CD4+ helper T cells was observed, which is consistent with dual PD-1 and CTLA-4 checkpoint inhibition. Additionally, intratumoral pharmacodynamic activity demonstrated increased expression in genes associated with T-cell co-stimulation and activation and gene signatures demonstrating increases in T-cell infiltration and interferon gamma signaling, as expected. The intratumoral biomarker analysis excludes patients whose baseline or subsequent samples are unavailable, which included the eight patients with tumor responses.

Of nine patients with prostate cancer who had baseline and follow-up prostate-specific antigen (PSA) assessments, one achieved a PSA reduction of greater than 50 percent. Two additional patients achieved reductions of greater than 30 percent, one of whom had an unconfirmed partial response by RECIST. Six of these nine patients remained on therapy as of the cut-off date.

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

About XmAb®20717

XmAb®20717 is a bispecific antibody that simultaneously targets immune checkpoint receptors PD-1 and CTLA-4 and is designed to promote tumor-selective T-cell activation. Xencor's XmAb bispecific Fc domain serves as the scaffold for these two antigen binding domains and confers long circulating half-life, stability and ease of manufacture. XmAb bispecific Fc domains have been engineered to eliminate Fc gamma receptor (FcγR) binding, with the intent to prevent activation and/or depletion of T cells via engagement by FcγR-expressing cells. XmAb20717 is being evaluated in an ongoing Phase 1 study.

About Xencor, Inc.

Xencor is a clinical-stage biopharmaceutical company developing engineered monoclonal antibodies for the treatment of cancer and autoimmune diseases. Currently, 18 candidates engineered with Xencor's XmAb® technology are in clinical development internally and with partners. Xencor's XmAb antibody engineering technology enables small changes to the structure of monoclonal antibodies resulting in new mechanisms of therapeutic action. 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 applicable securities laws, including, but not limited to, the quotations from Xencor's chief executive officer and Xencor's chief medical officer and any expectations relating to the timing and success of clinical trials, future product candidates and Xencor's research and development programs. Such statements involve 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 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, 2019 as well as Xencor's subsequent filings with the Securities and Exchange Commission. All forward-looking statements are based on Xencor's current information and belief as well as assumptions made by Xencor. 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. 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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Charles Liles
cliles@xencor.com

Media Contact
Jason I. Spark
Canale Communications
(619) 849-6005
jason@canalecomm.com

Source: Xencor, Inc.