Xencor Presents Updated Data from the Phase 1 Study of Vudalimab, PD-1 x CTLA-4 Bispecific Antibody, at the SITC Annual Meeting

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-- Vudalimab was generally well-tolerated; objective responses observed across multiple tumor types --

-- Confirmed partial responses observed in two of four evaluable castration-resistant prostate cancer patients with measurable disease --

-- Additional complete response observed in patient with advanced BRCA1+ high-grade serous ovarian cancer --

MONROVIA, Calif.--(BUSINESS WIRE)--Nov. 12, 2021-- Xencor, Inc. (NASDAQ:XNCR), a clinical-stage biopharmaceutical company developing engineered monoclonal antibodies and cytokines for the treatment of cancer and autoimmune diseases, today reported data from its Phase 1 study evaluating vudalimab (XmAb®717), a PD-1 x CTLA-4 bispecific antibody, in patients with advanced solid tumors (DUET-2). The updated results, predominantly from the study's expansion cohorts, are presented in a poster titled, "Preliminary clinical experience with XmAb20717, a PD-1 x CTLA-4 bispecific antibody, in patients with advanced solid tumors" at the 36th Annual Meeting of the Society for Immunotherapy of Cancer (SITC).

"Data from early-stage studies suggest that PD-1 and CTLA-4 inhibition has promise in prostate cancer, an area with high unmet need and without much checkpoint use. Dual targeting of these checkpoints through a bispecific antibody with a differentiated tolerability profile could meet an important unmet clinical need. In our Phase 1 study, we have observed vudalimab to be generally well tolerated, with lower rates of some types of immunotherapy-related adverse events, and to have encouraging clinical activity," said Allen Yang, M.D., Ph.D., senior vice president and chief medical officer at Xencor. "We are now enrolling a Phase 2 study of vudalimab for patients with metastatic castration-resistant prostate cancer, as a monotherapy or in combination, depending on molecular subtype. In addition, we are initiating a second Phase 2 study in patients with advanced pelvic tumors, including clinically defined high risk mCRPC and certain gynecologic malignancies, which represent another opportunity for vudalimab's dual targeting of PD-1 and CTLA-4 to address an unmet need."

At the data cut off, 110 patients had been treated at the 10 mg/kg recommended dose level in dose-escalation (n=7) and in five dose expansion cohorts: melanoma (n=20), renal cell carcinoma (RCC, n=21), non-small cell lung cancer (NSCLC, n=20), castration-resistant prostate cancer (CRPC, n=21) and other cancers without approved checkpoint therapies (n=21). 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 safety analysis includes all 110 patients, who were a median of 65 years old and were heavily pretreated, having a median of four prior systemic therapies. 65% of patients had received at least one prior checkpoint therapy, and 25% had received at least two prior checkpoint therapies.

- Vudalimab was generally well-tolerated, and the most common treatment-related adverse events were immune-related adverse events (irAEs). The most common irAEs of any grade were rash (45.5%), pruritus (30.9%), transaminase increases (23.6%), diarrhea (11.8%), hypothyroidism (9.1%), infusion related reaction (8.2%) and myalgia (8.2%).
- As previously reported, 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, and 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 78 evaluable patients receiving any amount of vudalimab, who had been followed for at least two cycles prior to data cut.

- A complete response was observed in a patient with BRCA1+ high-grade serous ovarian cancer, who had received multiple prior treatments, including olaparib and nivolumab in the metastatic setting. The patient had a partial response after Cycle 4, and by Cycle 18 of treatment all lesions had resolved except a lesion in the abdominal wall, which later showed no cancer cells upon biopsy.
- A confirmed complete response was observed in a patient with melanoma during dose-escalation at the 10 mg/kg dose level, as previously reported.

Partial responses were observed in patients with melanoma (n=2), RCC (n=3), NSCLC (n=2) and CRPC (n=2). The objective response rate across cohorts was 14.1% (11/78). All responses in patients with melanoma and CRPC and two responses in patients with RCC were confirmed. All

responders, except those with CRPC, had received prior checkpoint inhibitor therapy.

- Of the 12 efficacy-evaluable patients with CRPC, four had measurable disease and follow-up RECIST assessments, including the two CRPC responders.
- Six additional patients with CRPC, but without measurable disease, experienced a best overall response of non-CR/non-PD, as stable disease cannot be determined without measurable disease.
- The two CRPC responders had visceral and nodal metastases, had response durations of 41.3 and 27.0 weeks, were without progression on bone scans and had confirmed prostate-specific antigen (PSA) reductions of more than 50% from baseline. Among twelve patients with baseline and follow-up PSA assessments, including the two responders, 33% (4/12) had PSA reductions greater than 50%.

The median duration of response, unadjusted, for all responders was 18.3 weeks. The median duration of response, unadjusted, for patients with RCC was 24.1 weeks, and two patients remained on treatment.

Pharmacodynamic analysis indicated that activation and 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. Baseline serum levels of the cytokines IL-6, IL-8 and IL-10 trended lower in patients who achieved a response on study. Low baseline tumor expression of myeloid recruitment genes (CXCL3 and CXCL8) was also associated with clinical benefit.

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

About Vudalimab (XmAb®717)

Vudalimab (XmAb®717) is an XmAb 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 approach to dual checkpoint/co-stimulation reduces the need for the multiple antibodies and allows for more selective targeting of T cells with high checkpoint expression, which may potentially improve the therapeutic index of combination immunotherapies. In preclinical studies, dual blockade of PD-1 and CTLA-4 with vudalimab significantly enhanced T cell proliferation and activation, and anti-tumor activity in vivo. Xencor has initiated a Phase 2 clinical study of vudalimab in patients with metastatic castration resistant prostate cancer (mCRPC), as a monotherapy or in combination depending on subtype, and a Phase 2 clinical study in patients with advanced gynecologic and genitourinary malignancies, as well as clinically defined high-risk mCRPC.

About Xencor, Inc.

Xencor is a clinical-stage biopharmaceutical company developing engineered monoclonal antibodies and cytokines for the treatment of cancer and autoimmune diseases. Currently, 22 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 proteins resulting 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 the clinical trial data for vudalimab generally, planned clinical trials, the quotations from Xencor's senior vice president and chief medical 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, 2020 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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