Xencor Reports Initial Dose-Escalation Data from Phase 1 Study of XmAb®104, PD-1 x ICOS Bispecific Antibody, in Advanced Solid Tumors

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MONROVIA, Calif.--(BUSINESS WIRE)--May 26, 2022-- Xencor, Inc. (NASDAQ:XNCR), a clinical-stage biopharmaceutical company developing engineered antibodies and cytokines for the treatment of cancer and autoimmune diseases, today reported initial dose-escalation data from the Phase 1 study evaluating XmAb®104, a PD-1 x ICOS bispecific antibody, in patients with advanced solid tumors (DUET-3). These results will be presented at the Annual Meeting of the American Society of Clinical Oncology (ASCO), during the poster session “Developmental Therapeutics—Immunotherapy” on Sunday, June 5, 2022, from 8:00 a.m. to 11 a.m. CDT in Hall A at McCormick Place in Chicago.

DUET-3 is an ongoing Phase 1 study of XmAb104 to assess the candidate’s safety and tolerability profile in patients with advanced solid tumors and to determine the maximum tolerated dose (MTD). The expansion portion of the study is currently enrolling patients with colorectal cancer (CRC), head and neck squamous cell carcinoma (HNSCC), non-squamous non-small cell lung cancer (NSCLC), sarcoma, melanoma and clear-cell renal cell carcinoma (RCC) and is randomizing patients 1:1 to receive 10 mg/kg intravenous XmAb104 every two weeks as monotherapy or in combination with ipilimumab.

“XmAb104 is engineered to selectively engage T cells that express both PD-1 and ICOS, important regulators of T cell activity, and we have observed biomarker activity consistent with engagement of both receptors. XmAb104 has been well tolerated and is exhibiting a distinct safety profile compared to other clinical ICOS programs, which, along with early anti-tumor activity in patients, supports its evaluation in expansion cohorts,” said Allen Yang, M.D., Ph.D., senior vice president and chief medical officer at Xencor. “The ongoing expansion portion of the study is testing XmAb104, with or without the anti-CTLA-4 antibody ipilimumab, as CTLA-4 blockade has been found to increase the frequency of ICOS-expressing T cells in multiple solid tumor types.”

Additionally, a trial-in-progress poster, “A phase 2, multicenter, parallel-group, open-label study of vudalimab (XmAb20717), a PD-1 x CTLA-4 bispecific antibody, alone or in combination with chemotherapy or targeted therapy in patients with molecularly defined subtypes of metastatic castration-resistant prostate cancer,” will be presented during the session “Genitourinary Cancer—Prostate, Testicular, and Penile” on Monday, June 6, 2022, from 1:15 p.m. to 4:15 p.m. CDT in Hall A.

Posters will be archived under "Events & Presentations" in the Investors section of the Company's website located at www.xencor.com, at the time of the formal presentations at ASCO.

Key Highlights from DUET-3 (Abstract #2604)

At the data cut off on April 15, 2022, 62 patients had been treated in nine dose-escalation cohorts escalating from 0.002 to 15 mg/kg of XmAb104 administered every other week in four-week cycles. Patients were a median age of 63 years and had a median of three prior systemic therapies. 62.9% of patients had received at least one prior checkpoint therapy, and 91.9% of patients had Stage IV disease.

Patients presented with the following primary tumor types: CRC (n=14), pancreatic adenocarcinoma (n=8), soft tissue sarcoma (n=8), melanoma (n=6), HNSCC (n=5), RCC (n=4), endometrial cancer (n=2), NSCLC (n=2) and other solid tumor types (n=8). Of the patients with CRC, eight were microsatellite stable (MSS), three were microsatellite instable (MSI) and three were not defined. Most patients had tumors generally not considered to be sensitive to checkpoint inhibition.

Safety and Tolerability

Safety was evaluated in all 62 patients. XmAb104 was well tolerated through the highest tested dose cohort, and treatment-related adverse events (TRAE) were mostly mild. The most common TRAEs (>5 patients) were decreased appetite (9.7%), diarrhea (9.7%), fatigue (9.7%) and maculopapular rash (8.1%). Immune-related adverse events were reported for a limited number of patients, were predominantly Grade 1 or 2, and showed no relationship to dose level. Two patients (3.2%) experienced serious TRAEs, including a Grade 3 hyperbilirubinemia and a Grade 4 asymptomatic lipase increase; both events resolved with prednisone. Four patients (6.5%) discontinued from the study due to an adverse event.

No dose-limiting toxicities were observed, and the MTD was not reached. The recommended dose for continued study, based on feasibility of administration at higher dose levels and a review of safety data with investigators, was determined to be 10 mg/kg.

Clinical Activity Highlights

The efficacy analysis included 51 evaluable patients who received any amount of XmAb104 and had at least one post-baseline assessment by RECIST 1.1. At the data cut off, two confirmed partial responses (PR), one unconfirmed PR, and stable disease have been observed:

- A patient with undifferentiated pleomorphic sarcoma, who was immunotherapy naïve, presented with two target lesions in the lung and a subpleural lingular nodule. The patient was enrolled into the 0.2 mg/kg cohort and dose escalated to 0.6 mg/kg. The nodule completely resolved, and a single non-target lesion remained in the lung. The confirmed partial response continued at the time of the data cut (28 months).
- A patient with clear cell RCC, who had previously received treatment with pembrolizumab/axitinib, presented with two target lesions in the ribs, one target lesion in a lymph node, and a non-target lesion in bone. The patient was treated at the 10 mg/kg dose. A partial response was observed at the end of Cycle 2, and the patient remained in response at the time of the data cut (8 months).
- A patient with HNSCC, who had recently received treatment with pembrolizumab, was enrolled into the 1.8 mg/kg dose cohort. Prior therapies also included neo-adjuvant nivolumab, cisplatin, nivolumab and a GAL-3 inhibitor, and the patient experienced disease progression on all prior therapies. Two target lesions in the lung were identified, and the patient experienced a partial response at the end of Cycle 2.
- Two patients with CRC have experienced durable stable disease for over 20 months, both ongoing at the time of data cut. A patient with microsatellite instability high (MSI-H)-CRC was treated at an initial dose of 1.8 mg/kg and dose escalated to 10 mg/kg. Laboratory results indicated a decrease in the tumor marker CEA over time. A second patient, with MSI-H CRC, was treated at the 10 mg/kg dose, and at the time of the data cut, continued to experience stable disease in Cycle 22.

Pharmacokinetics/Pharmacokinetics Assessments

Data from assessments of pharmacokinetics (PK) and pharmacodynamics (PD) will not be shown in the poster presentation. The PK analysis indicated a linear and dose-proportional profile. Biomarker analyses indicated complete receptor saturation on peripheral T cells beginning at the 0.6 mg/kg dose level.

About XmAb®104

XmAb®104 is an investigational XmAb bispecific antibody designed to promote tumor-selective T-cell activation by simultaneously targeting immune checkpoint receptor PD-1 and the immune co-stimulatory receptor ICOS. Xencor's approach to dual checkpoint inhibition and co-stimulation reduces the need for multiple antibodies and allows for more selective targeting of T cells with high target expression, which may potentially improve the therapeutic index of combination immunotherapies. In preclinical studies, dual blockade of PD-1 and ICOS with XmAb104 significantly enhanced T cell proliferation and activation, and anti-tumor activity *in vivo*. XmAb104 is currently being evaluated, as a monotherapy and in combination with ipilimumab, in the expansion portion of a Phase 1 clinical study for the treatment of patients with advanced solid tumors.

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 the clinical trial data for XmAb104 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, 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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Charles Liles
cliles@xencor.com

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

Source: Xencor, Inc.