Xencor Presents Initial Data From the Phase 1 Study of Tidutamab in Neuroendocrine Tumors at NANETS' Multidisciplinary NET Medical Virtual Symposium

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MONROVIA, Calif.--(BUSINESS WIRE)--Oct. 2, 2020-- Xencor, Inc. (NASDAQ:XNCR), a clinical-stage biopharmaceutical company developing engineered monoclonal antibodies for the treatment of cancer and autoimmune diseases, today announced initial data from its ongoing Phase 1 study of tidutamab (XmAb®18087), an SSTR2 x CD3 bispecific antibody, in patients with neuroendocrine tumors (NETs). The data were presented at the North American Neuroendocrine Tumor Society's 2020 Multidisciplinary NET Medical Virtual Symposium (NANETS).

"NETs affecting the pancreas or gastrointestinal tract, called GEP-NETs, are typically an indolent, slow-growing tumor type. Tumor reduction is rarely observed in response to the limited number of approved treatment options, and progression-free and overall survival rates are ultimately the most significant factor in determining clinical benefit for patients," said Allen Yang, M.D., Ph.D., senior vice president and chief medical officer at Xencor. "Preliminary data from the study indicate that tidutamab, which redirects cytotoxic T cells to tumors, was well-tolerated. Anticipated dose-dependent T-cell proliferation and meaningful biological activity were observed in escalation cohorts and with the initial patients enrolled into the study's expansion."

"Tidutamab is the first XmAb CD3 bispecific antibody evaluated in patients with solid tumors, and we are encouraged by the low rate and grade of cytokine release syndrome, which has been limited to Grade 1 and Grade 2 in this study. Consistent with our experiences with other CD3 bispecific antibodies in hematologic malignancies, cytokine production decreased after subsequent dosing," said Bassil Dahiyat, Ph.D., president and chief executive officer at Xencor. "Considering that tidutamab induces sustained activation of cytotoxic T cells and engagement of the SSTR2 target, as designed, and its encouraging safety profile, we will initiate a new study in Merkel cell carcinoma and small cell lung cancer, SSTR2-expressing tumor types known to be responsive to immunotherapy, as we continue our study in NETs and gastrointestinal stromal tumors."

A poster with initial data from the study is available in the NANETS Virtual Poster Hall, and it will be made available under Archived Scientific Presentations on the Events & Presentations page in the Investors section of www.xencor.com. In addition to the poster, these initial results will be presented during the Clinical Abstracts session, which begins at 2:00 p.m. ET on Saturday, October 3, 2020.

Key Highlights

The primary objectives of the Phase 1 study are to determine the safety and tolerability profile of tidutamab in patients with advanced, well-differentiated NETs of pancreatic, gastrointestinal, lung and undetermined origin, and to identify the maximum tolerated dose and/or recommended dosing regimen for continued study.

At data cut-off in August 2020, 27 patients with neuroendocrine tumors, with the initial lesion location in the pancreas (56%), intestine (15%), lung (15%), and other GEP-NET or unknown (14%), received doses of tidutamab ranging from 0.1 to 2.0 mcg/kg. Dosing in the study includes a lower priming dose, followed by a higher repeated dose on subsequent dosing days. Patients had a median age of 61.0 years and a median of four prior lines of systemic therapies. Fifty-six percent of patients received prior peptide receptor radionuclide therapy. Prophylaxis for cytokine release syndrome (CRS) was required prior to at least the first four doses of tidutamab.

Tidutamab was generally well tolerated at the recommended dose identified for the expansion portion of the study, a 0.3 mcg/kg priming dose and subsequent 1.0 mcg/kg repeated doses (the 0.3/1.0 mcg/kg dose). All 27 patients treated were included in the safety analysis. The most common treatment-related Grade 3 or Grade 4 adverse events across all doses were lymphopenia (41%), gamma-glutamyl transferase increases (19%), vomiting (19%), transaminase increases (19%) and nausea (15%). Dose-limiting toxicities of nausea and vomiting were observed in the 1.0/2.0 mcg/kg cohort. CRS was observed in 41% of patients and was limited to Grade 1 and Grade 2 and also to the first two doses.

Analysis of peripheral blood biomarkers indicated that tidutamab induced acute and sustained T-cell activation at the recommended dose for expansion. CD8-positive effector T cells showed a dose-dependent increase in proliferation (Ki67) and activation (PD-1) markers that began within 48 hours of the first dose and persisted at least seven weeks, as measured at cycle 2, day 22.

Fourteen patients, including 12 across the first three dose-escalation cohorts (0.1/0.1, 0.1/0.3 and 0.3/1.0 mcg/kg) and two in the expansion cohort (0.3/1.0 mcg/kg), were included in the analysis to describe clinical activity. The best overall response was stable disease, with a disease control rate of 43% and a median duration of treatment of approximately seven months. Completion of enrollment in the expansion cohort and longer follow-up are required to evaluate progression-free survival and the clinical utility of tidutamab in this NET patient population.

Xencor plans to initiate an additional clinical study in patients with Merkel cell carcinoma and small cell lung cancer, SSTR2-expressing tumor types known to be responsive to immunotherapy, in early 2021.

About Tidutamab

Tidutamab (XmAb®18087) is a tumor-targeted bispecific antibody that contains both an SSTR2 binding domain and a T-cell binding domain (CD3). An XmAb® bispecific Fc domain serves as the scaffold for the two antigen binding domains and confers long circulating half-life, stability and ease of manufacture on tidutamab. SSTR2 (somatostatin receptor 2) is an antigen highly expressed on some solid tumors, and engagement of CD3 by tidutamab activates T cells for highly potent and targeted killing of SSTR2-expressing tumor cells. Tidutamab is being evaluated in an ongoing Phase 1 study, which is enrolling patients with neuroendocrine tumors (NETs) and gastrointestinal stromal tumors (GISTs).

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 chief medical officer and any statements relating to the timing, expectations and success of clinical trials, 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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