Xencor Presents Initial Data from Phase 1 Study of XmAb®13676 in B-cell Malignancies at the ASH Annual Meeting

December 9, 2019

-- Live webcast to review initial clinical data at 8:30 p.m. EST tonight --

MONROVIA, Calif.--(BUSINESS WIRE)--Dec. 9, 2019-- Xencor, Inc. (NASDAQ:XNCR), a clinical-stage biopharmaceutical company developing monoclonal antibodies for the treatment of cancer, autoimmune disease, asthma and allergic diseases, today announced initial data from its ongoing Phase 1 dose-escalation study of XmAb®13676, a CD20 x CD3 bispecific antibody, in patients with B-cell malignancies. Data are being presented by Krish Patel, M.D., Director of the Lymphoma Program at Swedish Cancer Institute, in a poster session today from 6:00 p.m. to 8:00 p.m. EST at the 61st American Society of Hematology (ASH) Annual Meeting in Orlando, Florida.

“XmAb13676 has been generally well tolerated and has demonstrated encouraging clinical activity in patients with advanced non-Hodgkin’s lymphoma as a monotherapy in initial dose escalation cohorts. This activity supports the potential of XmAb13676 in lymphoma treatment, and we are planning additional studies as a monotherapy and in combination with other agents,” said Bassil Dahiyat, Ph.D., president and chief executive officer at Xencor. “Dose escalation and optimization of dosing schedule, using a priming dose and step-up regimen, are ongoing.”

Key Highlights

At data cut off in November 2019, 45 patients with relapsed/refractory non-Hodgkin’s lymphoma (r/r NHL) had received doses of XmAb13676 ranging from 0.7 to 170 mcg/kg, and 8 patients with relapsed/refractory chronic lymphocytic leukemia (r/r CLL) had received doses ranging from 0.7 to 20 mcg/kg. The study was designed in two parts: Part A to establish an initial priming dose with flat dosing regimens and Part B to escalate dosing on subsequent administrations to the priming dose. Prophylactic treatment for cytokine release syndrome (CRS) was mandated prior to each dose of XmAb13676.

XmAb13676 was generally well tolerated, and a priming dose of 45 mcg/kg was chosen for continued dose escalation in Part B for patients with NHL.

Safety was evaluated in all 53 patients. The most common treatment-emergent adverse events (AEs) were pyrexia (55%), CRS (53%) and anemia (41%). CRS was more frequent and generally higher grade on the first dose. Three patients (6%) experienced Grade 3 or 4 CRS on the first dose, all prior to the implementation of step-up dosing. AEs consistent with the symptoms of CRS, but not reported as such, were observed in an additional 23% of patients and were mild to moderate in severity.

CRS Grades by NHL Dose Groups in Treatment Cycle 1

First dose (Cycle 1, Day 1 [C1D1])

	No CRS	Grade 1	Grade 2	≥ Grade 3
> 45 mcg/kg	50.0%	13.6%	27.2%	9.1%
≤ 45 mcg/kg	42.9%	14.3%	42.9%	0%

Doses on Days 8, 15 or 22 (C1D8, C1D15 or C1D22)

	No CRS	Grade 1	Grade 2	≥ Grade 3
> 45 mcg/kg	87.3%	9.5%	3.2%	0%
≤ 45 mcg/kg	95.3%	4.7%	0%	0%

Nervous system disorders, which were observed in 49% of patients, were mild or moderate in severity, and the most common of these events were dizziness (17%), headache (17%), paresthesia (9%) and lethargy (6%). One patient experienced short-term encephalopathy during a CRS event (Grade 2), and one patient lost consciousness during a bowel movement. Grade 3 or 4 AEs experienced by more than 5% of patients, other than CRS, included anemia (23%), neutropenia (15%), thrombocytopenia (11%), lymphopenia (9%) and hypokalemia (6%).

Eighteen patients with diffuse large B-cell lymphoma (DLBCL) who received doses of 80 to 170 mcg/kg are included in the analysis to describe clinical activity. These patients had a median age of 63.5 years, a median of three prior systemic therapies and had been diagnosed a median of 21.5 months prior to treatment. The objective response rate was 39% (n=7), and the complete response rate was 28% (n=5). XmAb13676 demonstrated clinical activity in an apparent dose-dependent manner. At dose levels with clinical activity for patients with DLBCL, 80 to 170 mcg/kg, a complete response was observed in one patient (20%; n=1/5) with follicular lymphoma (FL). Additional complete responses have been observed in Waldenström macroglobulinemia (n=1) and Richter transformation of CLL (n=1), both at 20 mcg/kg, the highest dose administered in the ongoing Part A of the study for patients with CLL.

The poster will be made available under Archived Scientific Presentations on the Events & Presentations page in the Investors section of www.xencor.com.

Webcast Information

Xencor will provide an overview of these data in a live webcast presentation at 8:30 p.m. EST on Monday, December 9, 2019. The webcast can also be accessed on the Events & Presentations page in the Investors section of www.xencor.com, and it will remain archived for 30 days.

About XmAb®13676

XmAb®13676 is a tumor-targeted antibody that contains both a CD20 binding domain and a T-cell binding domain (CD3) in a Phase 1 clinical trial for the treatment of B-cell malignancies. An 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 on XmAb13676. CD20 is highly expressed on B-cell tumors, including in chronic lymphocytic leukemia (CLL) and non-Hodgkin's lymphoma (NHL). Engagement of CD3 by XmAb13676 activates T cells for highly potent and targeted killing of CD20-expressing tumor cells.

About XmAb® Bispecific Fc Technology

XmAb® bispecific Fc domains enable the rapid design and simplified development of bispecific antibodies, and other protein structures, that bind two or more different targets simultaneously using an engineered heterodimer Fc domain. Seven XmAb bispecific antibodies are being evaluated in Phase 1 clinical studies conducted by Xencor or its pharmaceutical partners.

- **CD3 bispecific antibodies** contain an anti-tumor associated antigen binding domain and a second binding domain targeted to CD3, an activating receptor on T cells, with the goal to recruit or activate T cells against the antigen target. Candidates in clinical development include XmAb14045 (CD123 x CD3), XmAb13676 (CD20 x CD3), XmAb18087 (SSTR2 x CD3) and Amgen's AMG 424 (CD38 x CD3).
- **Tumor microenvironment (TME) activator bispecific antibodies** promote tumor-selective T-cell activation by targeting multiple checkpoints or co-stimulating receptors. These candidates incorporate Xencor's Xtend™ technology for longer half-life in their design. Candidates in clinical development include XmAb20717 (PD1 x CTLA4), XmAb22841 (CTLA4 x LAG3) and XmAb23104 (PD1 x ICOS).
- **Cytokine candidates** are built on a heterodimeric Fc domain and have their potencies tuned to improve therapeutic index. These candidates incorporate Xtend technology for longer half-life.

About Xencor, Inc.

Xencor is a clinical-stage biopharmaceutical company developing engineered monoclonal antibodies for the treatment of cancer, autoimmune diseases, asthma and allergic diseases. Currently, 14 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 president and chief executive officer and any expectations relating to Xencor's financial expectations and business, the timing and success of clinical trials, future product candidates, Xencor's research and development programs, partnering efforts and capital requirements. 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, 2018 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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Source: Xencor, Inc.

Charles Liles
626-737-8118
cliles@xencor.com

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