Xilio Therapeutics Announces Preclinical Data Demonstrating Anti-Tumor Activity and Tolerability of XTX301, a Tumor-Selective IL-12, at Society for Immunotherapy in Cancer Annual Meeting

November 12, 2021

WALTHAM, Mass., Nov. 12, 2021 (GLOBE NEWSWIRE) -- Xilio Therapeutics, Inc. (Nasdaq:XLO), a biotechnology company developing tumor-selective immuno-oncology therapies for patients with cancer, today announced data from preclinical studies of XTX301, an engineered tumor-selective interleukin-12 (IL-12) product candidate, demonstrating selective anti-tumor activity and favorable tolerability with minimal systemic activity. These data are highlighted in a poster at the Society for Immunotherapy in Cancer's 36 th Annual Meeting (SITC), which is being held virtually and in Washington, D.C., from November 10-14, 2021. In addition, Xilio will present an overview (poster #519) of its Phase 1/2 clinical trial design of XTX101, its tumor-selective anti-CTLA-4 monoclonal antibody product candidate, in patients with solid tumors.

"The presentations at SITC exemplify the progress we've made at Xilio in 2021 with our pipeline of clinical and preclinical-stage tumor selective antibody and cytokine product candidates," said Martin Huber, M.D., president of R&D and chief medical officer of Xilio. "IL-12 has the potential to be a meaningful treatment for patients with cancer, but current therapies are encumbered with severe toxicities due to their peripheral activity, leading to sub-optimal dosing and limited efficacy. Using our GPS platform, we have engineered XTX301 to achieve systemic delivery of tumor-selective IL-12, while avoiding the known side effect challenges. These preclinical data showcase our engineering efforts to activate XTX301 only when it is within the tumor microenvironment, resulting in the potential to achieve an optimized therapeutic index and enhanced anti-tumor activity. We look forward to further advancing this program, with plans to submit an investigational new drug application to the FDA in the second half of 2022."

XTX301, a Protein-Engineered IL-12, Exhibits Tumor-Selective Activity in Mice Without Peripheral Toxicities and is Well Tolerated in Non-human Primates (#719)
Data reported in the poster build upon earlier preclinical findings reported by Xilio, which demonstrated that XTX301 was activated in a protease-dependent manner, including in human tumor samples *ex vivo*. Key findings from the poster are from preclinical studies in mouse and non-human primate (NHP) models, including comparisons between XTX301 and XTX300, a non-masked control version of XTX301, as well as corresponding murine surrogate molecules mXTX301 and mXTX300. In these preclinical studies:

- XTX301 showed no detectable binding to IL-12 receptors in its masked form. Cleavage of the masked molecule by matrix metalloproteinases (MMPs) restored binding of XTX301 to IL-12 receptors, demonstrating that the masking domain prevents interaction with the receptor.
- XTX301 demonstrated equivalent *in vitro* potency compared to the non-masked control.
- XTX301 became pharmacologically active upon MMP cleavage in primary human immune cells.
- mXTX301 demonstrated up to 90% tumor growth inhibition in mouse models, was well-tolerated and induced minimal peripheral immune activation.
- mXTX301 induced an approximately three-fold increase in immune infiltrate within tumors compared to the vehicle control and approximately 150-fold less peripheral immune activation, thereby avoiding the body weight loss and morbidity in mice that was associated with doses of non-masked control required for tumor growth inhibition.
- In an NHP model, XTX301 was well-tolerated, with minimal systemic toxicity observed at doses up to 1.5 mg/kg. In addition, XTX301 exhibited minimal elevation in liver enzymes and peripheral T cell and natural killer (NK) cell activation, showing a 50-fold improvement in tolerability compared to the non-masked control.

About XTX301
Xilio has leveraged its geographically precise solutions (GPS) platform to engineer XTX301, a novel IL-12 product candidate that is masked with a protein domain to prevent binding to IL-12 receptors and downstream signaling activity until the masking domain is cleaved off by tumor microenvironment-associated proteases. In preclinical studies, XTX301 has demonstrated protease-dependent activation in human tumor cells ex vivo and has been well-tolerated with minimal systemic activity in studies in non-human primates.

About Xilio Therapeutics
Xilio Therapeutics is a biotechnology company focused on harnessing the immune system to achieve deep and durable clinical responses to improve the lives of patients with cancer. The company is using its proprietary geographically precise solutions (GPS) platform to rapidly engineer novel molecules, including cytokines and other biologics, that are designed to optimize their therapeutic index. These molecules are designed to localize activity within the tumor microenvironment without systemic effect, resulting in the potential to achieve enhanced anti-tumor activity. Xilio is building a pipeline of wholly-owned, tumor-selective, GPS-enabled cytokine and checkpoint inhibitor product candidates, including XTX101, a tumor-selective anti-CTLA-4 monoclonal antibody; XTX202, a tumor-selective IL-2; XTX301, a tumor-selective IL-12; and XTX401, a tumor-selective IL-15. For more information, please visit www.xiliotx.com.

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans, strategies, timelines and expectations for Xilio Therapeutics' current or future approved

product candidates, including plans to submit an investigational new drug application for XTX301 to the U.S. Food and Drug Administration; the potential benefits of any of Xilio Therapeutics' current or future product candidates in treating patients; and Xilio Therapeutics' strategy, goals and anticipated financial performance, milestones, business plans and focus. The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks and uncertainties related to ongoing and planned research and development activities, including initiating, conducting or completing preclinical studies and clinical trials and the timing and results of such preclinical studies or clinical trials; the delay of any current or planned preclinical studies or clinical trials or the development of Xilio Therapeutics' current or future product candidates; preclinical and clinical supply of current or future product candidates; Xilio Therapeutics' advancement of multiple early-stage efforts; Xilio Therapeutics' ability to successfully demonstrate the safety and efficacy of its product candidates and gain approval of its product candidates on a timely basis, if at all; the preclinical and clinical results for Xilio Therapeutics' product candidates, which may not support further development of such product candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of current or future clinical trials; Xilio Therapeutics' ability to obtain, maintain and enforce patent and other intellectual property protection for current or future product candidates; Xilio Therapeutics' ability to obtain and maintain sufficient cash resources to fund current or future operating expenses and capital expenditure requirements; and the impact of the COVID-19 pandemic on Xilio Therapeutics' business, operations, strategy, goals and anticipated milestones. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Xilio Therapeutics' filings with the U.S. Securities and Exchange Commission (SEC), including Xilio Therapeutics' final prospectus related to its initial public offering, and any other filings that Xilio Therapeutics makes with the SEC in the future. Any forward-looking statements contained in this press release represent Xilio Therapeutics' views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Xilio Therapeutics explicitly disclaims any obligation to update any forward-looking statements.

For Investor Inquiries:
Monique Allaire,
THRUST Strategic Communications
monique@thrustsc.com

For Media Inquiries:
Dan Budwick, 1AB
dan@1abmedia.com