Xilio Therapeutics to Present Preclinical Data Highlighting Anti-Tumor Activity and Tolerability of XTX202 at the 2021 ASCO Annual Meeting

Data demonstrated that XTX202, an engineered, tumor-selective IL-2, increased tumor growth inhibition without dose-limiting toxicities in preclinical studies

Company plans to submit IND application for XTX202 in second half of 2021

WALTHAM, Mass., May 20, 2021 – Xilio Therapeutics, a biotechnology company developing tumor-selective immuno-oncology therapies for patients with cancer, announced today the presentation of data from preclinical studies of XTX202, its tumor-selective interleukin-2 (IL-2) product candidate, demonstrating selective anti-tumor activity and favorable tolerability with no systemic toxicity observed. The data will be reported in a poster entitled "*XTX202, a protein-engineered IL-2, exhibits tumor-selective activity in mice without peripheral toxicities in non-human primates*" at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting. The poster will be made available on the ASCO Annual Meeting website at the start of the meeting on June 4, 2021 at 9am ET.

Xilio is leveraging its proprietary platform to engineer novel molecules that are designed to be activated in the tumor microenvironment (TME) and have the potential to result in localized, tumor-selective clinical activity without dose-limiting toxicities. XTX202, Xilio's lead cytokine product candidate, is an engineered form of IL-2 that is masked with a protein domain to prevent binding activity until cleaved off by TME-associated proteases.

"The power of IL-2 to activate the immune system as a cancer therapeutic is promising, but utility of IL-2 agents has historically been greatly reduced due to toxicities," said Rónán O'Hagan, Ph.D., chief scientific officer of Xilio. "We have engineered XTX202 to overcome those challenges, with key features designed to ensure it is released and activated locally within the TME, where it selectively binds to IL-2 receptors on immune cells. We are excited to present these data which, for the first time, demonstrate selective tumor-inhibition and favorable tolerability of XTX202 in preclinical models. With these data, we plan to complete IND-enabling studies and submit an IND application in the second half of 2021 to evaluate XTX202 in patients with solid tumors."

Data reported in the poster are from preclinical studies in both mouse and non-human primate (NHP) models, including comparisons between XTX202 and XTX200, a non-masked, parent version of XTX202, as well as aldesleukin, a synthetic form of IL-2 approved for certain cancer indications by the U.S. Food and Drug Administration. Key data include:

- XTX202, in its masked form, did not bind to IL-2 receptors, and matrix metalloproteinase (MMP) activation of XTX202 restored full binding to IL-2 receptor beta that is found on immune activating CD8 T cells and natural killer cells, illustrating the tight, protease-dependent control of IL-2 activity conferred by XTX202.

- XTX202 was engineered to eliminate binding to IL-2Rα in order to enhance immune activation by CD8 T cells and NK cells, and to minimize immune suppression by regulatory T cells. No binding to IL-2Rα was detectable even after MMP-dependent activation of XTX202.
- XTX202 inhibited tumor growth in syngeneic mouse models as a single agent with no evidence of toxicity or peripheral immune activation, thus demonstrating tumor selective activity.
- XTX202 matched the tumor growth inhibition activity of aldesleukin and the non-masked control XTX200, without activation of immune response outside the TME, thereby avoiding the body weight loss in mice that was associated with doses of XTX200 or aldesleukin required for tumor growth inhibition.
- XTX202 was well-tolerated in repeat dose studies in NHPs at doses up to 30 mg/kg.
- XTX202 is estimated to have a greater than 100-fold improvement in therapeutic index compared to aldesleukin.

About Xilio Therapeutics

Xilio Therapeutics is a privately-held biotechnology company that uses its proprietary technology to engineer potent cancer immunotherapies that have the potential to unleash the power of the immune system selectively at the site of the tumor. Xilio has designed its investigational therapies with the goal of maximizing efficacy and overcoming the significant toxicities associated with certain clinically validated immuno-oncology therapies, positioning them as potential treatments for a significant number of patients. The company's proprietary pipeline includes XTX202, a tumor-selective modified form of IL-2, and XTX101, a tumor-selective anti-CTLA-4 monoclonal antibody (mAb), as well as tumor-selective IL-12 and IL-15 research programs. Xilio was founded in 2016 and is headquartered in Waltham, Mass. For more information, please visit www.xiliotx.com.

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