X4 Pharmaceuticals Presents Clinical Data Demonstrating Single Agent X4P-001-IO Enhances Tumor Immunity through CXCR4 Antagonism

November 6, 2018

Clinical data demonstrate single agent X4P-001-IO modulated the immune cell profile in the tumor microenvironment and increased CD8+ T cell infiltration

Data presented at the Society for Immunotherapy of Cancer's (SITC) 33 rd Annual Meeting

CAMBRIDGE, Mass., November 6, 2018 – X4 Pharmaceuticals, a clinical-stage biotechnology company developing novel CXCR4 allosteric antagonist drug candidates designed to improve immune cell trafficking to treat rare diseases and cancer, today highlighted data from a poster presentation of a clinical study with X4P-001-IO, an investigational CXCR4 allosteric antagonist, at the Society for Immunotherapy of Cancer's (SITC) 33rd Annual Meeting, being held November 7-11, 2018, in Washington, D.C.

The data, generated from serial tumor biopsies and blood draws taken from patients with melanomas, demonstrated that single agent X4P-001-IO has the ability to help restore immunity within the tumor microenvironment (TME), based on infiltration and activation of cytotoxic CD8+ T cells and increased inflammatory status in the TME, following once-daily, oral administration of X4P-001-IO. The results also highlighted that X4P-001-IO and has the potential to enhance the anti-tumor activity of agents, such as checkpoint inhibitors.

"These results further validate the potential mechanisms of CXCR4 inhibition to substantially alter the tumor microenvironment and to favorably modulate the immune response to tumors," said Robert Andtbacka, MD, CM, lead investigator of the study during his time with the Huntsman Cancer Institute of the University of Utah as Professor in the Department of Surgery at the University of Utah School of Medicine. "These findings contribute to our growing understanding of the role that CXCR4 inhibition plays in modulating the immune response to tumors and help define rational for further study of X4P-001-IO in a broad set of tumor types."

As of October 3, 2018, 16 patients have been enrolled in the study; biopsies from 13 patients have been analyzed, and nine patient biopsies had both baseline (pre-dose) and post-X4P-001-IO treatment-evaluable biopsies. Results from the tumor biopsies taken from melanoma patients, before and after receiving single agent X4P-001-IO treatment for three weeks, were analyzed and presented. Analyses showed three weeks of single agent X4P-001-IO monotherapy enhanced tumor immunity. X4 expanded past analyses with the incorporation of additional patient data, where enhanced immunity was indicated by:

- increased proliferating CD8+ cells, indicative of cytotoxic T cell activation;
- increased IFN-gamma gene expression signature score, suggesting enhanced antigen priming and activation;
- increased Tumor Inflammation Signature (TIS), indicative of increased inflammation status in the TME.

Additionally, newly-reported analyses showed:

- increased CD8+ T cell density at the tumor interface, with the total density of CD8+ cells inside the tumor boundary area increased four-fold compared with baseline;
- increased numbers of cells expressing CD3 antigens, a pan T-cell marker, within tumor borders, and decreased expression of VISTA, a checkpoint molecule that inhibits T-cell activation and proliferation;
- increases in multiple chemoattractant factors in serum, consistent with increased trafficking of immune cells post CXCR4 inhibition.

After single agent X4P-001-IO treatment, patients received X4P 001-IO in combination with Keytruda® (pembrolizumab) for an additional 6 weeks. Continued signs of positive immune cell changes in the tumor microenvironment were seen. Treatment of additional patients in the study showed that X4P-001-IO as a single agent, and in combination with Keytruda® (pembrolizumab), continued to be well-tolerated in the study.

"We are excited by these results demonstrating X4P-001-IO's impact on tumor immunity through critical aspects of immune cell trafficking, infiltration and activation," said Ken Gorelick, MD, Chief Medical Officer of X4 Pharmaceuticals. "These data, together with X4P-001-IO's favorable safety and tolerability profile, support the potential for X4P-001-IO to improve outcomes for patients with tumors that are less responsive to checkpoint inhibitors."

The details of the poster presentation at SITC are as follows:

Title: X4P-001, an orally bioavailable CXCR4 antagonist, increases immune cell infiltration and tumor inflammatory status in the microenvironment of melanoma

Dates & Times: Friday, Nov. 9, from 8 a.m. – 8 p.m. ET

Saturday, Nov. 10, from 8 a.m. – 8:30 p.m. ET

Location: Hall E

Poster #: P53

About X4P-001-IO in Cancer
X4P-001-IO is an investigational selective, oral, small molecule antagonist of C-X-C receptor type 4 (CXCR4). CXCR4 is a chemokine receptor present in abundance on certain immune cells and cancer cells and it plays a critical role in immune cell trafficking, infiltration and activation in the tumor microenvironment. CXCR4 signaling is disrupted in a broad range of cancers, facilitating tumor growth by allowing cancer cells to evade immune detection and creating a pro-tumor microenvironment. X4P-001-IO has the ability to help restore immunity within the tumor microenvironment and has the potential to enhance the anti-tumor activity of approved and emerging oncology agents, such as checkpoint inhibitors and targeted therapies. X4P-001-IO is being investigated in several clinical studies in solid tumors.

About X4 Pharmaceuticals
X4 Pharmaceuticals is developing novel therapeutics designed to improve immune cell trafficking to treat rare diseases and cancer. The Company's oral small molecule drug candidates antagonize the CXCR4 pathway, which plays a central role in immune surveillance. X4's most advanced product candidate is in a Phase 2/3 clinical trial in patients with WHIM syndrome, a rare genetic, primary immunodeficiency disease, and is currently under investigation in multiple clinical trials in solid tumors. X4 was founded and is led by a team with deep product development and commercialization expertise, including several former members of the Genzyme leadership team, and is located in Cambridge, MA. For more information, visit x4.theyatesnetwork.com.

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