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

April 16, 2018

Clinical data demonstrate single agent X4P-001-IO increases immune cell infiltration and activation in the tumor microenvironment (TME)

Supportive preclinical data show robust anti-tumor activity of CXCR4 inhibition in aggressive murine model of melanoma

CAMBRIDGE, Mass., April 16, 2018 – X4 Pharmaceuticals, a clinical stage biotechnology company developing novel CXCR4 inhibitor drugs to improve immune cell trafficking to treat cancer and rare diseases, today highlighted data from a presentation at the 2018 American Association for Cancer Research (AACR) Annual Meeting. The data, generated from serial tumor biopsies and blood draws taken from melanoma patients, demonstrated dramatic infiltration and activation of cytotoxic CD8+ T cells and increased inflammatory status in the tumor microenvironment (TME) following once-daily oral administration of X4P-001-IO. X4P-001-IO is an investigational CXCR4 allosteric antagonist. Findings highlight single agent X4P-001-IO has the ability to help restore immunity within the TME and has the potential to enhance the anti-tumor activity of agents such as checkpoint inhibitors.

Results from the tumor biopsies taken from melanoma patients before and after receiving single agent X4P-001-IO treatment for 3 weeks, were analyzed and presented. Single agent X4P-001-IO showed evidence of enhanced immune cell infiltration and activation in the tumor microenvironment, including:

- Increases in proliferating CD8+ cells, indicative of cytotoxic T cell activation,
- Increases in Granzyme B, a marker of immune-mediated cell killing,
- Decreases in distance between CD8+ T cells and the nearest tumor cells, indicative of increased CD8+ T cell infiltration,
- Increases in antigen presentation/processing gene expression, suggesting enhanced antigen priming and activation, and
- Increases in the Tumor Inflammation Signature (TIS), indicative of increased inflammation status in the TME.

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. The combination of X4P-001-IO alone and in combination with Keytruda was well tolerated.

“These results demonstrate that CXCR4 inhibition substantially alters the tumor microenvironment in a way that is consistent with the emerging understanding of tumor immunity and inflammatory response,” said Robert Andtbacka, MD, CM, a surgeon and investigator with the Huntsman Cancer Institute of the University of Utah, Associate Professor in the Division of Surgical Oncology at the University of Utah School of Medicine, and Principle Investigator of the X4P-001-IO study in melanoma.

In a separate poster presentation, preclinical findings showed that CXCR4 inhibition increases CD8+ T cells in the tumor microenvironment and has potent anti-tumor activity in the syngenic B16-OVA murine melanoma model. The anti-tumor activities were associated with the increase in immunostimulatory CD8+/Perforin+ cells and the reduction of immunosuppressive myeloid derived suppressor cells (MDSCs) and Treg populations in the tumor microenvironment.

“Results from these posters demonstrate the unique mechanism of X4P-001-IO, as it impacts critical aspects of immune cell trafficking, infiltration and activation – playing a positive role in tumor immunity,” said Sudha Parasuraman, MD, X4’s Chief Medical Officer. “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 posters were presented in the Immune Response to Therapy Session at the 2018 American Association for Cancer Research (AACR) Annual Meeting, taking place April 14-18, 2018 in Chicago, IL.

About X4P-001-IO in Cancer

X4P-001-IO is an investigational selective, oral, small molecule inhibitor of CXCR4 (C-X-C receptor type 4) that regulates the tumor microenvironment thereby enhancing endogenous anti-tumor responses. CXCR4 is a chemokine receptor that modulates immune function and angiogenesis through the trafficking of key immune cells such as T- cells, dendritic cells, and myeloid derived suppressor cells. 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 is being investigated in three separate clinical studies in solid tumors.

About X4 Pharmaceuticals

X4 Pharmaceuticals is developing novel therapeutics designed to improve immune cell trafficking to treat cancer and rare diseases. The Company’s oral small molecule drug candidates inhibit the CXCR4 receptor, a pathway which plays a central role in immune surveillance. X4’s most advanced

product candidate, X4P-001-RD, is in a Phase 2/3 study in patients with WHIM syndrome, a rare genetic, primary immunodeficiency disease. X4P-001-IO is currently under investigation in multiple Phase 1/2 studies in refractory clear cell renal cell carcinoma (ccRCC) and melanoma. 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 please visit X4pharm.com.

Keytruda® is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.