X4 Pharmaceuticals announces new data for lead candidate X4P-001 in renal cell carcinoma at EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium

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Preclinical data demonstrate mechanism of X4P-001 in renal cell carcinoma combination regimen

CAMBRIDGE, Mass., November 30, 2016 – X4 Pharmaceuticals, a clinical stage biotechnology company developing novel CXCR4 inhibitor drugs to improve immune cell trafficking and increase the ability for T-cells to track and destroy cancer, today announced the presentation of preclinical data for X4P-001, the Company's lead drug candidate, at the EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium, held November 29 – December 2 in Munich, Germany. The findings in preclinical models of renal cell carcinoma (RCC) elucidate the molecular mechanism that directs the trafficking of key immune cells in the tumor microenvironment that result in synergistic anti-tumor effect of X4P-001 and axitinib, a tyrosine kinase inhibitor approved for use as a targeted therapy for RCC. The data also showed that X4P-001 blocks the critical escape mechanism that leads to resistance to treatment with axitinib, a vascular endothelial growth factor receptor (VEGF-R) antagonist cancer therapy.

"While treatment with VEGF-R antagonists is first line therapy, it can be hindered by acquired resistance," said James W. Mier, M.D., Associate Professor of Medicine at the Beth Israel Deaconess Medical Center and senior author of the poster presentation. "These data show clear evidence that by inhibiting CXCR4, X4P-001 blocks a critical mechanism of this resistance, resulting in a synergistic anti-tumor effect which may ultimately lead to improved patient outcomes."

The poster, entitled "MDSC trafficking and function in RCC by CXCR4 in the presence of a VEGF-R antagonist is dependent on HIF-2a expression," shows that CXCR4 inhibition with X4P-001 blocks the primary pathway that leads to resistance to VEGF-R cancer therapies in renal cell carcinoma. Acquired resistance of tumors to VEGF-R antagonists is dependent on HIF-2a, CXCR4/CXCL12, and the infiltration of myeloid derived suppressor cells (MDSCs), into the tumor. CXCR4 inhibition with X4P-001 blocks communication between the tumor and MDSCs, suppresses HIF-2a expression, reduces MDSC tumor infiltration, and improves anti-tumor effect.

"These data demonstrate the potential of X4P-001 in combination with approved therapies as a potential new treatment approach to achieve impactful clinical responses for patients with advanced ccRCC, a cancer with serious unmet needs," said Paula Ragan, PhD, Founder, President and CEO of X4. "The data provide additional compelling rationale for our ongoing Phase 1/2 clinical study evaluating the combination of X4P-001 and axitinib in patients with advanced ccRCC."

About X4P-001 in Cancer
X4P-001 is an oral, small molecule inhibitor of CXCR4, or C-X-C receptor type 4, the receptor for the chemokine CXCL12 (also known as stromal derived factor-1, or SDF-1). Recent studies demonstrate that CXCR4/CXCL12 is a primary receptor-ligand pair that cancer cells and surrounding stromal cells express and use to block normal immune function and promote angiogenesis through the trafficking of T-effector and T-regulatory cells, as well as myeloid derived suppressor cells (MDSCs), in the tumor microenvironment.[1, 2] Pre-clinical studies have demonstrated X4P-001 activity alone and in combination with approved cancer therapies resulted in an increased tumor-specific immune response and significant inhibition of tumor growth. X4P-001 has been tested in over 70 subjects in four clinical trials in healthy volunteers and HIV-infected patients to date and was shown to be well tolerated.

About Renal Cell Carcinoma
Kidney cancer is among the ten most common cancers in both men and women with more than 60,000 new diagnoses each year in the United States.[3] Clear cell renal cell carcinoma (ccRCC) is the most common form of kidney cancer, and advanced ccRCC accounts for approximately 20% of the patient population. Therapies for advanced ccRCC include immunotherapies, mammalian target of rapamycin (mTOR) kinase inhibitors, and angiogenesis inhibitors, such as vascular endothelial growth factor (VEGF) inhibitors.[4] There continue to be unmet medical needs with advanced ccRCC because durable responses remain a serious clinical challenge for patients with advanced disease.

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. X4P-001, the company's lead program, is in Phase 1/2 testing in refractory clear cell renal cell carcinoma (ccRCC) and other solid tumor indications. The company's second program, X4P-002, is in pre-clinical development for oncology applications. 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.

[1] Feig C., et. al., "Targeting CXCL12 from FAP-expressing carcinoma-associated fibroblasts synergizes with anti-PD-L1 immunotherapy in pancreatic cancer," *PNAS*, Oct. 31, 2013.

[2] Guo F., et. al., "CXCL12/CXCR4: a symbiotic bridge linking cancer cells and their stromal neighbors to oncogenic communication networks," *Oncogene*, May 11, 2015.

[3] National Cancer Institute, “Surveillance, Epidemiology, and End Results Program,” http://seer.cancer.gov/statfacts/html/kidrp.html

[4] Kidney Cancer Association, “Therapies for Advanced Kidney Cancer,” http://www.kidneycancer.org/knowledge/learn/therapies-for-advanced-kidney-cancer/