X4 Pharmaceuticals announces data presentation for lead candidate X4P-001 at AACR Annual Meeting

April 19, 2016

Preclinical data demonstrated synergistic anti-tumor activity of X4P-001 in combination with VEGF inhibitor in preclinical models of renal cell carcinoma

CAMBRIDGE, Mass., April 19, 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, its lead drug candidate in development for the treatment of clear cell renal cell carcinoma (ccRCC) at the American Association of Cancer Research (AACR) Annual Meeting, held April 16-20 in New Orleans. The data demonstrated synergistic anti-tumor effects of CXCR4 inhibition in combination with axitinib, a tyrosine kinase inhibitor approved for use as a targeted therapy for renal cell carcinoma (RCC), in animal models of RCC. The data also showed that X4P-001 suppressed the increased MDSC tumor infiltration caused by axitinib treatment.

"We are excited to share these early findings with clinicians who know the challenges of treating patients with RCC," said James W. Mier, M.D., Associate Professor of Medicine at the Beth Israel Deaconess Medical Center and senior author of the poster presentation. "We believe there are opportunities to improve outcomes beyond the available targeted therapies, such as kinase inhibitors, which can be hindered by resistance. By inhibiting CXCR4, X4P-001 offers an approach to target a key mechanism of resistance and address unmet needs for cancer patients."

Acquired resistance of tumors to certain anti-cancer therapies has been associated with increased trafficking of key immune cells, such as T-regulatory cells and myeloid derived suppressor cells (MDSCs), in and around the tumor. Trafficking of these cells is controlled by chemokines such as CXCL-12 and its receptor, CXCR4. CXCR4 inhibition blocks the infiltration of these cells and neutralizes the immunosuppressive microenvironment, enabling the cancer-fighting T-cells to reach the tumor.

"These data confirm our belief that CXCR4 inhibition can play an important therapeutic role in immune cell trafficking with the potential to improve treatment outcomes for patients," said Robert Arbeit, M.D., Sr. Vice President of Clinical Development and Translational Research for X4 Pharmaceuticals and an author of the poster presentation. "The data also provide a strong rationale for our upcoming clinical study evaluating the combination of X4P-001 and axitinib in patients with advanced ccRCC."

The poster entitled "Regulation of MDSC trafficking and function in RCC by CXCR4 in the presence of a VEGF-R antagonist" will be presented on Tuesday, April 19th (Abstract number: 4155; 1-5pm). The reported findings include:

- X4P-001 in combination with axitinib demonstrated synergistic anti-tumor activity in two renal xenograft models; tumor regression was observed
- X4P-001 suppressed the increased MDSC tumor infiltration caused by axitinib treatment

About X4P-001

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 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 including tyrosine kinase inhibitors and checkpoint inhibitors resulting in an increased tumor-specific immune response and significant delays in tumor growth. X4P-001 was previously tested in over 70 subjects in four prior clinical trials in healthy volunteers and HIV-infected patients and was shown to be safe and 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 rapaymcin (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 and increase the ability for T-cells to track and destroy cancer cells. The company's oral small molecule drug candidates inhibit the CXCR4 receptor, a pathway which plays a central role in promoting the immunosuppressive and pro-angiogenic microenvironment of many cancers. X4P-001, the company's lead program, is expected to

enter Phase 1/2 testing in refractory clear cell renal cell carcinoma (ccRCC) and other solid tumor indications, and its 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/