X4 Pharmaceuticals Announces Initiation of Phase 1b Study of X4P-001 in Patients with Resectable Stage III and Stage IV Melanoma

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Innovative biomarker study designed to study the trafficking of cancer-fighting immune cells into the tumor microenvironment

CAMBRIDGE, Mass., September 27, 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 dosing of the first patient in its Phase 1b study of X4P-001 in patients with resectable Stage III and Stage IV melanoma. X4P-001 is the Company's lead CXCR4 inhibitor drug candidate, and is also in clinical development for clear cell renal cell carcinoma (ccRCC).

This Phase 1b multi-center study in patients with resectable Stage III and Stage IV melanoma will evaluate the safety and tolerability of X4P-001 alone and in combination with the immuno-oncology therapy Keytruda®(pembrolizumab), an approved PD-1 inhibitor for patients with advanced melanoma and certain other cancers. In addition, the study will include analyses of participants' tumor biopsies to assess changes in the tumor microenvironment. Preliminary results from the study are expected in 2017.

"Immuno-oncology therapies have been a breakthrough for some melanoma patients. However, not all patients respond to the existing immuno-oncology approaches, and we believe that characteristics of the tumor microenvironment may be an important factor in response to treatment," said Robert Andtbacka, MD, 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 study in melanoma. "This study will allow us to evaluate how inhibition of CXCR4 may alter the landscape of the microenvironment providing insights into improving immune surveillance and tumor response in melanoma."

"We are excited to be working with leading researchers in melanoma and immuno-oncology, led by Dr. Andtbacka, to undertake this innovative protocol to study changes in the tumor microenvironment with administration of X4P-001 and its potential benefit to patients with advanced melanoma," said Paula Ragan, PhD, President and CEO of X4. "Results from this study will allow us to assess the utility of X4P-001 alone and in combination with checkpoint modulators, opening the possibility to study X4P-001 in additional tumor types. X4 aims to further understand the mechanism and activity of X4P-001 in the hopes of advancing new therapies that substantially increase durable long term responses and overall survival in melanoma and other advanced cancers."

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 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 Melanoma
Cutaneous malignant melanoma is the fifth most common cancer in men and the sixth most common cancer in women in the United States. When discovered early, melanoma is highly curable with 10-year overall survival rates approaching 95% for stage I melanoma and 45-77% for stage II melanoma[3]. However, patients with stage III and IV melanoma, the prognosis is much worse. The 10-year survival rate for stage IV melanoma is 10-15%[4]. Adjuvant therapies for patients with resectable stage III melanoma include immunomodulating drugs, such as high dose interferon-α therapy and anti-CTLA-4 antibody therapy. Unmet needs remain to establish and improve overall survival in patients with advanced resectable melanoma, as well as improving objective response rates in patients who do not respond to existing treatments.

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, "SEER Stat Fact Sheets: Melanoma of the Skin," http://seer.cancer.gov/statfacts/html/melan.html

[4] National Cancer Institute, "What are the survival rates for melanoma skin cancer, by stage?," http://www.cancer.org/cancer/skincancer-melanoma/detailedguide/melanoma-skin-cancer-survival-rates

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