X4 Pharmaceuticals Presents Clinical Data Demonstrating Immune Activation Through CXCR4 Pathway with X4P-001-IO

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Combination of X4P-001-IO and Keytruda® (pemrbolizumab) further enhanced immune activation and lymphocyte infiltration into tumors

Supportive preclinical data show substantial single agent activity of CXCR4 inhibition in aggressive model of melanoma

CAMBRIDGE, Mass., November 10, 2017 – 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 multiple presentations at the Society for Immunotherapy of Cancer (SITC) Annual Meeting. The data, primarily generated from biopsies of tumors from melanoma patients, demonstrated important changes in the tumor microenvironment and the activation of tumor-specific immune cell responses following oral administration of X4P-001-IO, an investigational CXCR4 antagonist. These data underscore the ability of X4P-001-IO to enhance immune surveillance, memory and activation through adaptive immune pathways (e.g., T-cells).

Preliminary results from evaluable tumor biopsies of melanoma patients who received treatment with X4P-001-IO at 400 mg daily for 21 days were presented, and highlights of the poster presentation were as follows:

- X4P-001-IO showed preliminary evidence of enhanced immune cell infiltration and activation in the tumor microenvironment as a single agent, including:
    - Increases in cytotoxic CD8+ T cells
    - Increases in Granzyme B, a marker of immune-mediated cell killing
    - Increased IFN-gamma signature and PD-L1 levels supporting the use of X4P-001-IO in combination with anti-PD-1 checkpoint inhibitor therapy
- Immune related activity by X4P-001-IO was further enhanced when combined with Keytruda, an approved anti-PD-1 immune checkpoint inhibitor
- The combination of X4P-001-IO was generally safe and well tolerated

In a separate poster presentation, preclinical findings demonstrated compelling single agent anti-tumor activity from CXCR4 inhibition in the syngeneic B16-OVA melanoma model. The addition of checkpoint inhibitors further enhanced anti-tumor efficacy in this model. The anti-tumor activity of single agent X4P-001-IO was associated with increased tumor infiltrating CD8+ T-cells. The combination treatment with checkpoint inhibitors further decreased immunosuppressive myeloid derived stem cells (MDSCs) and T-regulatory (Tregs) cells.

“We are pleased to have further validated the potential mechanisms of CXCR4 inhibition in modulating the immune response to tumors,” 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-IO study in melanoma. “Within three weeks on therapy, we can visually see an influx of CD8+ T-cells, increases in immune signatures such as interferon-gamma, and measure substantial priming of the tumors which is an important factor in response to existing treatment with checkpoint inhibitors.”

“Results from these clinical and preclinical studies contribute to our growing understanding of the role that X4P-001-IO plays in modulating the immune response to tumors. These important findings will play a critical role in defining future rational combination strategies and indications for X4P-001-IO, “said Sudha Parasuraman, MD, Chief Medical Officer of X4.

Both posters were presented in the Immune Modulation, Cytokines, and Antibodies Session at the Society for Immunotherapy of Cancer (SITC) Annual Meeting on November 8-12 in National Harbor, MD.

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 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.[1] 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%.[2] Adjuvant therapies for patients with resectable stage III melanoma include immunomodulating drugs, such as high dose interferon-α therapy and anti-CTLA-4 or PD-1 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. 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.

1. National Cancer Institute, "SEER Stat Fact Sheets: Melanoma of the Skin," http://seer.cancer.gov/statfacts/html/melan.html
2. 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