First Clinical Data for X4P-001-RD Demonstrated Promising Activity in Patients with WHIM Syndrome, a Primary Immunodeficiency Disease

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Dose dependent increases in neutrophil and lymphocyte counts observed in all patients treated with X4P-001-RD

Preliminary results reported at ASH Annual Meeting from the open-label Phase 2 portion of the on-going Phase 2/3 study

CAMBRIDGE, Mass., December 11, 2017 – X4 Pharmaceuticals, a clinical stage biotechnology company developing novel CXCR4 inhibitor drugs to improve immune cell trafficking to treat cancer and rare disease, today announced the first clinical data from the open-label Phase 2 portion of an on-going Phase 2/3 study of X4P-001-RD, an investigational treatment for patients with WHIM syndrome, a primary immunodeficiency disease.

The objectives of the Phase 2 portion of the study is to evaluate the safety and efficacy of X4P-001-RD and to assess the dose required to achieve a consistent increase in circulating neutrophils and lymphocytes in patients with WHIM syndrome. The preliminary results from the study demonstrated promising activity with dose-dependent increases in neutrophil and lymphocyte counts in patients with WHIM syndrome. All patients enrolled in the study to date had meaningful increases in the levels of circulating white blood cells with daily oral administration of X4P-001-RD. X4P-001-RD was considered to be safe and well tolerated. Dose escalation continues to evaluate potential further increases in white blood cell counts. The data were presented at the 59th Annual Meeting of the American Society for Hematology (ASH) on December 9, 2017 in Orlando, Florida.

“Based upon the etiology of WHIM Syndrome, CXCR4 antagonism by X4P-001-RD should improve the primary pathophysiology underlying the disease,” said Dr. David C. Dale, MD, Professor of Medicine and former Dean of the School of Medicine at the University of Washington Medical Center and lead investigator of the study. “We are encouraged by the meaningful increases in white blood cell counts and look forward to observing how it correlates with other disease parameters in this severely immuno-deficient patient population.”

Results from the first 5 patients with genetically confirmed WHIM Syndrome who were enrolled in the dose escalation portion of the ongoing Phase 2/3 study (as of data cutoff date of October 16, 2017) were presented. Highlights of the poster presentation include:

- All patients demonstrated a dose-dependent increase in neutrophils and lymphocytes from screening values, with lymphocytes increasing in greater proportion than neutrophils
- X4P-001 drug exposure showed a dose-dependent increase correlated to the increases in neutrophils
- X4P-001 was well-tolerated, with no severe adverse events (AEs) observed
- Dose escalation is continuing in the Phase 2 portion of the study

“X4P-001-RD shows promising increases in white blood cell counts, a primary biomarker for response to therapy, in each of the WHIM patients we’ve studied to date,” said Sudha Parasuraman, MD, Chief Medical Officer of X4. “We look forward to sharing further data supporting our recommended Phase 3 dose and plans for further development in 2018 as we continue to advance this novel oral treatment for patients with WHIM.”

(https://clinicaltrials.gov/ct2/show/NCT03005327)

About WHIM Syndrome

WHIM syndrome is a primary immunodeficiency disease (“PID”) caused by genetic mutations in the CXCR4 receptor gene resulting in susceptibility to certain types of infections. WHIM is an abbreviation for the characteristic clinical symptoms of the syndrome: Warts, Hypogammaglobulinemia, Infections, and Myelokathexis. Within the overall category of primary immunodeficiencies, there are between 15,000 and 100,000 patients in the US that are classified with PID of unknown origin — of which WHIM is one.[1,2,3] WHIM syndrome is a rare disorder and the precise prevalence or incidence of patients that have the genetic mutation responsible for WHIM syndrome is unknown. Because patients are highly susceptible to infections, WHIM syndrome is associated with significant morbidity beginning in early childhood and continuing throughout life. Current therapy is limited to treatment of acute infections with antibiotics or prevention through the use of intravenous immunoglobulin or G-CSF. There is no approved therapy for the treatment of WHIM syndrome.

About X4P-001-RD for Primary Immunodeficiency Disease

X4P-001-RD, an oral, small molecule inhibitor of CXCR4, or C-X-C receptor type 4, is being developed for use as a life-long treatment for patients with WHIM syndrome and other primary genetic immunodeficiencies. X4P-001-RD is currently being studied in a Phase 2/3 trial in patients with WHIM syndrome. Within the bone marrow, a normally functioning CXCR4 receptor controls the release of neutrophils and leukocytes into the blood stream, thereby ensuring normal immune surveillance functions throughout the body. In patients with WHIM syndrome, mutations to the CXCR4 receptor cause aberrant signaling leading to retention of neutrophils and leukocytes in the bone marrow and inadequate immune surveillance and function.[4,5] X4P-001-RD is designed to normalize the signaling for the mutant CXCR4 receptor to promote the release of neutrophils and leukocytes, thereby restoring healthy immunity.

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.

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[3] Modell V, Gee B, et al. Global study of primary immunodeficiency diseases (PI) — diagnosis, treatment, and economic impact: an updated report from the Jeffrey Modell Foundation. *Immunol Res.* 2011;51:61–70.

[4] Hernandez PA, Gorlin RJ, Lukens JN, et al. Mutations in the chemokine receptor gene CXCR4 are associated with WHIM syndrome, a combined immunodeficiency disease. *Nature Genetics* 2003;34(1):70-74.

[5] Gulino AV, Moratto D, Sozzani S, et al. Altered leukocyte response to CXCL12 in patients with Warts Hypogammaglobulinemia, Infections, Myelokathexis (WHIM) syndrome. *Blood* 2004;104(2):444-452.