X4 Pharmaceuticals Announces Initiation of a Phase 2/3 Clinical Study of X4P-001-RD in Patients with WHIM Syndrome, a Rare Genetic Primary Immunodeficiency Disease

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CAMBRIDGE, Mass., January 30, 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 initiation of a Phase 2/3 study with the first patient dosed with X4P-001-RD for the treatment of WHIM syndrome, a sub-type of a primary immunodeficiency disease characterized by warts, hypogammaglobulinemia, infections, and myelokathexis or "WHIM." The company is developing X4P-001-RD, a lower dosage form than X4P-001-IO that is currently in clinical development for the treatment of certain cancers, for use as a chronic treatment for patients with WHIM Syndrome.

"We are very pleased with the rapid progress across clinical, regulatory and formulation development that has resulted in X4 initiating this clinical study to evaluate the potential for our CXCR4 drug candidate to treat WHIM syndrome," said Paula Ragan, PhD, President and CEO of X4. "The initiation of this Phase 2/3 study is a critical milestone in developing a potentially life-changing therapeutic for WHIM patients who otherwise have no therapeutic options."

WHIM is a genetic primary immunodeficiency disease caused by the aberrant trafficking of specific immune cells that are critical for proper immune system functions. Mutations in the CXCR4 receptor gene have been identified as an underlying cause of WHIM, based on sequencing and linkage studies conducted over the past 10 years. These mutations result in suppression of the immune system and lead to increased rates of severe health complications, including infections such as pneumonias, cellulitis, meningitis, deep soft tissue abscesses, and skin infections. Infections begin in early childhood and recur throughout life. Patients with WHIM also characteristically have numerous warts on their hands, feet, trunk and various mucosal surfaces that in some cases progress to cancer[3]. By blocking the binding of CXCL12 ligand to the CXCR4 receptor, X4P-001-RD is designed to normalize the signaling from the mutant CXCR4 receptor to promote normal release of neutrophils and leukocytes, thereby restoring immune surveillance and normal immune function.

About X4P-001-RD for Primary Immunodeficiency Disease

X4P-001-RD, X4 Pharmaceutical's most advanced product candidate, is an oral, small molecule inhibitor of CXCR4, or C-X-C receptor type 4. 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.[1, 2] X4P-001-RD is designed to normalize the signaling for the mutant CXCR4 receptor to promote the release of neutrophils and leukocytes, thereby restoring immune surveillance. The molecule has been previously tested in more than 70 subjects in four clinical trials in healthy volunteers and HIV-infected patients, and was shown to be generally safe and well tolerated in these studies.

About WHIM

WHIM is an abbreviation for the characteristic symptoms of the syndrome: Warts, Hypogammaglobulinemia, Infections, and Myelokathexis. WHIM syndrome is a rare primary immunodeficiency with an estimated incidence of 0.23 per million births.[4] The exact prevalence of the disease is not known. Because patients are highly susceptible to infections, WHIM syndrome is associated with significant morbidity. Current therapy is limited to treatment of acute infections with antibiotics or prevention through the use of intravenous immunoglobulins. There is no approved therapy for the treatment of WHIM syndrome.

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 lead drug candidate, X4P-001-RD is currently in Phase 2/3 clinical development for the treatment of patients with a rare, genetic primary immunodeficiency disease, WHIM syndrome, and is in Phase 1/2 clinical development as a potential cancer therapy, for the treatment of patients with refractory clear cell renal cell carcinoma (ccRCC) and other solid tumor indications. 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] 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.

[2] 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.

[3] Kawai T and Malech, HL. WHIM Syndrome: Congenital Immune Deficiency Disease. Curr Opin Hematol. 2009; 16(1): 20–26.

[4] Beaussant-Cohen S, Fenneteau O, Plouvier E, et al. Description and outcome of a cohort of 8 patients with WHIM syndrome from the French Severe

Chronic Neutropenia Registry. Orphanet J Rare Dis. 2012;7:71.