X4 Pharmaceuticals Announces Rare Disease Research Collaboration with Yale University

August 2, 2017

Multi-Year Research Plan to Investigate Mechanisms of Aberrant Immune Function in a Genetic Model of WHIM Syndrome

CAMBRIDGE, Mass., August 2, 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 announced the initiation of a multi-year sponsored research program with Yale University to develop and study a genetic model of WHIM syndrome, a rare genetic immunodeficiency disease which currently has no approved treatments.

The multi-year research collaboration will investigate the fundamental mechanisms that result in chronic immune deficiency in a genetic preclinical model of WHIM syndrome. The research will be conducted with João Pedro Pereira, PhD, an Associate Professor of Immunobiology and a member of Yale's Stem Cell Center and Yale Cancer Center's Program in Cancer Immunology. Dr. Pereira's laboratory is focused on the study of the mechanisms of hematopoiesis, the fundamental and complex process that generates many different cell types including all immune cells, and its role in conferring immunity.

"The incorrect positioning of immune cells in primary and secondary immune organs due to CXCR4 mutations has been well documented," said Dr. Pereira. "This research will elucidate the fundamental mechanisms that lead to chronic impairment of the immune system, particularly of long-term immunity, as a result of aberrant immune cell positioning and trafficking. CXCR4 plays a fundamental role in immunity and we look forward to more deeply understanding its impact on the immune system."

"It is gratifying to work with a leading immunobiologist like Dr. Pereira, who has developed cutting edge technologies to study immune cell trafficking and function on a single cell level," said Sudha Parasuraman, MD, Chief Medical Officer of X4. "X4's research program with Yale offers the exciting possibility to gain mechanistic insights into WHIM syndrome and the role that CXCR4 plays broadly in immunity, so that we can further demonstrate the potential of our drug candidate, X4P-001-RD, to address the unmet need of patients with WHIM syndrome."

About WHIM Syndrome

WHIM syndrome is a primary genetic immunodeficiency disease caused by mutations in the CXCR4 receptor gene resulting susceptibility to certain infections. WHIM is an abbreviation for the characteristic 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 disease of unknown origin — of which WHIM is one of these diseases of unknown origin. The precise prevalence of patients that have the genetic mutation responsible for WHIM syndrome is unknown, but we estimate that several thousand patients worldwide suffer from WHIM syndrome. 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. There is no approved therapy for the treatment of WHIM syndrome.

About X4P-001-RD for Primary Genetic 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.[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 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.

[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.