X4 Pharmaceuticals and Collaborators Present Data that WHIM Syndrome is Underdiagnosed and Patients are Impacted by Broad Spectrum of Medical Complications

October 15, 2018

Three poster presentations showcased at NORD Rare Disease Summit

Company continues to support genetic screening program to aid in diagnosis of patients with WHIM syndrome

CAMBRIDGE, Mass. October 15, 2018 – X4 Pharmaceuticals, a clinical stage biotechnology company developing novel *CXCR4* antagonist drugs, today announced that the company and its collaborators have had three poster presentations about WHIM syndrome, a rare, chronic and life-threatening primary immunodeficiency, accepted for presentation at the National Organization for Rare Disorders (NORD) Rare Disease and Orphan Products Breakthrough Summit. The summit is being held October 15-16 in Washington, D.C.

WHIM is an inherited disease caused by a mutation in a patient's *CXCR4* gene. X4 is currently developing X4P-001-RD, an investigational targeted, oral therapy for WHIM syndrome in a Phase 2/3 clinical trial. X4 is collaborating with patients, research institutions, advocacy organizations and medical specialists who focus on WHIM and primary immunodeficiencies to further elucidate the findings that WHIM is under-diagnosed and that patients experience a broad spectrum of medical complications that cause serious morbidity and mortality.

The poster presentations at the NORD Rare Disease Summit present summarized findings from patient interviews, as well as a review of published literature detailing over 100 patients with WHIM. Key findings from the poster presentations include:

- All four classic clinical characteristics of WHIM do not need to be present in a patient for a diagnosis. The variability of WHIM's clinical presentation has led to under-diagnosis and underappreciation of the condition among patients and physicians alike.
- Patients with WHIM syndrome appear to have increased risk for human papilloma virus, cervical carcinoma, lymphoproliferative disease/lymphoma, as well as various life-threatening infections.
- Survey research from patients suggests there are additional emotional and psychosocial manifestations of WHIM stemming from its broad spectrum of medical complications.

"Our new insights into WHIM are leading us on a path toward new solutions. It is encouraging to see global collaboration that is enabling us to gain a better understanding of the constellation of symptoms associated with WHIM and to uncover the impact of WHIM syndrome on the morbidity and mortality of patients," said Jean Donadieu, MD, Coordinator of Expert Centre and Lead Investigator of Registry Network at the Hôpital Trousseau in Paris.

In addition, collaborators in pediatric immunology and immunodeficiencies at leading academic institutions including University of South Florida at Johns Hopkins All Children's Hospital, St. Petersburg, FL, and Massachusetts General Hospital, Boston, MA, will present an overview on the first WHIM genetic screening study developed through a collaborative effort among academia, a patient foundation, and sponsors. This genetic screening study for WHIM syndrome is co-sponsored by the Jeffrey Modell Foundation, a non-profit organization for primary immunodeficiency diseases and X4; the screening is offered at no cost to patients or insurers. The establishment of this study illustrates how integrating research efforts and collaboration between funding entities can be a powerful way to improve a patient's care and can serve as a model for how open communication can best serve patients in the rare disease community.

"WHIM syndrome is a primary immunodeficiency disease that is probably much more common than is currently recognized. The emerging new understanding and awareness of WHIM syndrome can support the ability of the medical community to identify many potentially undiagnosed patients which will further build momentum for advancing new therapies for patients with WHIM," said Jolan Walter, MD, PhD, Division Chief and Robert A. Good Endowed Chair of Pediatric Allergy Immunology, University of South Florida at Johns Hopkins All Children's Hospital, and lead investigator of the WHIM Genetic Screening Study.

"X4 is pleased to be collaborating with leading clinicians, researchers and patient organizations as we aim to make progress for a better understanding of WHIM and improving treatment options for patients," said Tarek Ebrahim, MD, Vice President Medical Affairs, Rare Disease, of X4 Pharmaceuticals. "The findings we are presenting indicate that increased education and awareness can improve appropriate diagnosis of WHIM in the medical community, leading to improved recognition and treatment of the life-long impact resulting from this congenital immunodeficiency."

About WHIM Syndrome

WHIM syndrome is a primary immunodeficiency disease caused by genetic mutations in the CXCR4 receptor generesulting 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 U.S. that are classified with primary immunodeficiency disease 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. Individuals with WHIM syndrome are

more susceptible to potentially life-threatening bacterial **infections**[4]. Additionally, 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 X4 Pharmaceuticals

X4 Pharmaceuticals is developing novel therapeutics designed to improve immune cell trafficking to treat rare diseases and cancer. The Company's oral small molecule drug candidates antagonize the CXCR4 pathway, which plays a central role in immune surveillance. X4's most advanced product candidate is in a Phase 2/3 clinical trial in patients with WHIM syndrome, a rare genetic, primary immunodeficiency disease, and is currently under investigation in multiple clinical trials in solid tumors. 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. For more information, visit x4.theyatesnetwork.com.

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2. Gathmann B, Grimbacher B, et al. The European internet-based patient and research database for primary immunodeficiencies: results 2006–2008. Clin Exp Immunol. 2009 Sep;157 Suppl 1:3-11.
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. Primary Immunodeficiency Foundation: https://primaryimmune.org/disease/whim-syndrome

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