X4 Pharmaceuticals Initiates Pivotal Phase 3 Clinical Trial of Mavorixafor for the Treatment of WHIM Syndrome

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Global 4WHIM trial marks first-ever Phase 3 study in patients with WHIM syndrome

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 26, 2019--

X4 Pharmaceuticals, Inc. (Nasdaq:XFOR), a clinical-stage biopharmaceutical company focused on the development of novel therapeutics for the treatment of rare diseases, today announced the initiation of 4WHIM, a pivotal Phase 3 global clinical trial of mavorixafor (X4P-001) for the treatment of WHIM (**W**arts, **H**ypogammaglobulinemia, **I**nfections, and **M**yelokathexis) syndrome, a rare, inherited, primary immunodeficiency disease.

The global 4WHIM trial is a 52-week, randomized, double-blind, placebo-controlled, multicenter study designed to evaluate the safety and efficacy of mavorixafor in genetically confirmed WHIM patients. The trial is designed to enroll up to 28 subjects in approximately 20 countries, followed by an open-label extension trial.

The primary efficacy endpoint for the trial will compare the level of circulating neutrophils relative to a clinically meaningful threshold (500 cells/µL), in response to mavorixafor versus placebo measured during multiple 24-hour periods over the course of 52 weeks. Secondary endpoints include infection rates, wart burden, and assessments of immune system function and quality of life.

Mavorixafor is a potentially first-in-class, once-daily, oral, small molecule antagonist of chemokine receptor CXCR4. Proof of concept in WHIM patients has been demonstrated with meaningful increases in neutrophil and lymphocyte counts, both important biomarkers of CXCR4 signaling and immune function. Mavorixafor has been well tolerated in prior early phase clinical studies.

“We are very excited to initiate our global Phase 3 4WHIM trial as we seek to confirm mavorixafor’s transformative potential as a novel therapy for patients with WHIM,” said Lynne Kelley, M.D., FACS, Chief Medical Officer of X4 Pharmaceuticals. “Despite the severity of the disease and its significant burden on patients’ long-term health and daily quality of life, WHIM is often overlooked and misdiagnosed. As the first-ever late-stage clinical trial for the treatment of WHIM syndrome, initiation of this study is a critical step in bringing a new treatment option to this underserved patient population.”

“This marks an important milestone for X4 as we advance our lead drug candidate into the company’s first pivotal Phase 3 clinical trial,” commented Paula Ragan, Ph.D., President and Chief Executive Officer of X4 Pharmaceuticals. “Following on the success of our Phase 2 clinical trial, we are excited to build on our progress and commitment to innovate for patients throughout the world suffering from rare diseases such as WHIM.”

Recently, X4 announced a partnership with Invitae Corporation to support confirmation of a WHIM diagnosis, among other inherited primary immunodeficiencies. Through the collaborative PATH4WARD program, X4 and Invitae will provide genetic testing at no charge to patients to help clinicians expedite the diagnosis of these disorders.

For more information on the 4WHIM Phase 3 trial (NCT 03995108), please visit www.clinicaltrials.gov.

About WHIM Syndrome

WHIM syndrome is a rare, primary immunodeficiency disease caused by genetic mutations in the CXCR4 receptor gene and is named for the characteristic clinical symptoms of the syndrome – **W**arts, **H**ypogammaglobulinemia, **I**nfections, and **M**yelokathexis.[1] Patients with WHIM may experience significant morbidity beginning in early childhood and continuing throughout life with an increased likelihood of various recurrent, potentially life-threatening infections, and may also be susceptible to malignancies such as HPV-related cervical cancer and lymphomas.[1,2,3] The overall cancer risk in patients with WHIM is estimated to be 30 percent by 40 years of age.[4] There are no approved therapies for WHIM, and current standards of care are limited to treatment of acute infections with antibiotics or prevention of infections mainly through immunoglobulin substitution or G-CSF.[5] The exact prevalence of WHIM is unknown, however, in the U.S. alone there are between 15,000 and 100,000 patients classified as having a primary immunodeficiency disease of unknown origin – of which WHIM is one.[6,7,8]

About Mavorixafor

X4 Pharmaceutical’s lead product candidate, mavorixafor (X4P-001), is a potentially first-in-class, once-daily, oral inhibitor of CXCR4, currently in Phase 3 development for the treatment of WHIM syndrome, a rare, inherited, primary immunodeficiency disease caused by genetic mutations in the CXCR4 receptor gene. Mavorixafor has demonstrated proof of concept in WHIM in a Phase 2 trial, including clinically meaningful increases in neutrophil and lymphocyte biomarker counts, as well as a trend of reduction in infection rates and wart burden, and a favorable safety profile. Mavorixafor was designated orphan drug status by the U.S. Food and Drug Administration in 2018 for the treatment of WHIM and is also in development for Severe Congenital Neutropenia (SCN), Waldenström’s macroglobulinemia (WM), and clear cell renal cell carcinoma (ccRCC).

About X4 Pharmaceuticals

X4 Pharmaceuticals is developing novel therapeutics designed to improve immune cell trafficking to treat rare diseases, including primary immunodeficiencies and certain cancers. 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, mavorixafor (X4P-001), is in a global Phase 3 pivotal trial in patients with WHIM syndrome, a rare, inherited, primary immunodeficiency disease, and is currently also under investigation in combination with axitinib in the Phase 2a portion of an open-label Phase 1/2 clinical trial in clear cell renal cell carcinoma (ccRCC). X4 is also planning to commence clinical trials of mavorixafor in Severe Congenital Neutropenia (SCN) and Waldenström's macroglobulinemia (WM) in 2019. The company was founded and is led by a team with extensive biopharmaceutical product development and commercialization expertise and is committed to advancing the development of innovative medicines on behalf of patients with limited treatment options. X4 is a global company that is headquartered in Cambridge, Massachusetts with research offices based in Vienna, Austria. For more information, please visit www.x4pharma.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements include statements regarding plans for, or progress, scope, cost, duration or results or timing for the initiation, completion or availability of results of development of mavorixafor (X4P-001) or any of our other product candidates or programs, including regarding the Phase 3 clinical trial of mavorixafor for the treatment of patients with WHIM syndrome, the Phase 2a portion of the Phase 1/2 clinical trial of mavorixafor in combination with axitinib in ccRCC, or plans to commence clinical trials of mavorixafor in SCN and WM, the target indication(s) for development, the size, design, population, location, conduct, objective, duration or endpoints of any clinical trial, or the timing for initiation or completion of or reporting of results from any clinical trial, the potential benefits of mavorixafor, or any other product candidate or program or the commercial opportunity in any target indication as well as the expected offerings and benefits of the PATH4WARD program and X4's relationship with Invitae. These statements are subject to various risks and uncertainties, actual results could differ materially from those projected and X4 cautions investors not to place undue reliance on the forward-looking statements in this press release. These risks and uncertainties include, without limitation, the risk that trials and studies may be delayed and may not have satisfactory outcomes, potential adverse effects arising from the testing or use of mavorixafor or other product candidates, the risk that costs required to develop mavorixafor or other product candidates or to expand our operations will be higher than anticipated and the risk that the PATH4WARD program and X4's relationship with Invitae will not be successful. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, the risks and uncertainties described in the section entitled "Risk Factors" in X4's most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC), as updated by X4's Current Report on Form 8-K filed with the SEC on April 11, 2019, and in other filings X4 makes with the SEC from time to time. X4 undertakes no obligation to update the information contained in this press release to reflect subsequently occurring events or circumstances.

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[1]Primary Immunodeficiency Foundation: https://primaryimmune.org/disease/whim-syndrome

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