X4 Pharmaceuticals Receives Breakthrough Therapy Designation from the FDA for Mavorixafor for the Treatment of WHIM Syndrome

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CAMBRIDGE, Mass.--(BUSINESS WIRE)--Nov. 12, 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 that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation for mavorixafor (X4P-001) for the treatment of adult patients with WHIM (**W**arts, **H**ypogammaglobulinemia, **I**nfections, and **M**yelokathexis) syndrome, a rare, inherited, primary immunodeficiency disease caused by genetic mutations in the CXCR4 receptor gene.

Mavorixafor is a potential first-in-class, once-daily, oral, small molecule antagonist of chemokine receptor CXCR4, and is currently being investigated in a pivotal Phase 3 global clinical trial, 4WHIM, for the treatment of WHIM syndrome. The Breakthrough Therapy Designation granted to mavorixafor is based on data from X4's Phase 2 open-label, multi-center trial of mavorixafor in adult patients with WHIM syndrome. In this trial, proof of concept was established based on clinically meaningful increases in absolute neutrophil counts (ANCs), absolute lymphocyte counts (ALCs), evidence indicating reductions in infection rates and wart burden, and a safety profile showing that mavorixafor is well-tolerated.

"Rare diseases such as WHIM don't often receive the attention and research that patients and their families deserve. The FDA's decision to grant Breakthrough Therapy Designation to mavorixafor for the treatment of adults with WHIM syndrome represents a significant milestone for patients and X4 alike, helping to further highlight the severity of this underdiagnosed disease and the importance of offering a potential novel, disease-modifying therapeutic option to this underserved patient population," said Paula Ragan, Ph.D., President and Chief Executive Officer of X4 Pharmaceuticals. "We are excited to continue to advance our ongoing global Phase 3 pivotal trial and look forward to working closely with the FDA to bring this potential first-in-class treatment option to patients with WHIM syndrome as quickly as possible through this expedited regulatory pathway."

A Breakthrough Therapy Designation may be granted to expedite the development and regulatory review of an investigational new drug that is intended to treat a serious or life-threatening condition where there is an unmet need. The criteria for Breakthrough Therapy Designation require preliminary clinical evidence that demonstrates that the drug may provide substantial improvements over any available therapy on at least one clinically significant endpoint.

Mavorixafor was granted orphan drug status by the FDA in 2018 and by the European Commission in 2019 for the treatment of WHIM syndrome. X4 is also developing the drug for the treatment of Severe Congenital Neutropenia (SCN), Waldenström's macroglobulinemia (WM), and clear cell renal cell carcinoma (ccRCC).

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 Pharmaceuticals' lead product candidate, mavorixafor (X4P-001), is a potential first-in-class, once-daily, oral inhibitor of CXCR4, currently in a Phase 3 clinical trial 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 syndrome in a Phase 2 clinical 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 granted orphan drug status by the U.S. Food and Drug Administration in 2018 and by the European Commission in 2019 for the treatment of WHIM syndrome, and is also being developed by X4 to treat 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 an open-label Phase 1/2 clinical trial in clear cell renal cell carcinoma (ccRCC), with several patients remaining on therapy over 12 months beyond the primary

endpoint. X4 is further investigating mavorixafor in a Phase 1b clinical trial for the treatment of Severe Congenital Neutropenia (SCN). X4 is also planning to commence a clinical trial of mavorixafor with ibrutinib for the treatment of Waldenström's macroglobulinemia (WM) in 2019. X4 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. These statements may be identified by the words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" or other similar terms or expressions that concern X4's expectations, strategy, plans or intentions. Forward-looking statements include, but are not limited to, statements regarding the clinical development of mavorixafor (X4P-001) or any of X4's other product candidates or programs. 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 X4's operations will be higher than anticipated, and the risk that despite the breakthrough therapy designation, the development and regulatory review will not be expedited. 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 new events or circumstances, except as required by law.

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