X4 Pharmaceuticals Announces Positive Phase 3 Results Showing Mavorixafor Reduced the Rate, Severity, and Duration of Infections vs. Placebo in Participants Diagnosed with WHIM Syndrome

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~60% reduction in annualized infection rate seen in the mavorixafor arm vs. placebo (p<0.01)

>75% reduction in the percentage of individuals experiencing severe infections (Grade 3 or higher) in the mavorixafor group vs. placebo group

>70% reduction in mean total days with infections (2 weeks on mavorixafor treatment vs. 7 weeks on placebo)

Company on track to submit NDA for mavorixafor early in 2H 2023 following completion of pre-NDA meeting with FDA

X4 webinar today at 4 pm ET to include live Q&A with clinical experts

BOSTON, May 16, 2023 (GLOBE NEWSWIRE) -- **X4 Pharmaceuticals, Inc.** (Nasdaq: XFOR), a leader in the discovery and development of novel small molecule therapeutics to benefit patients with rare diseases of the immune system, is hosting a webinar today highlighting new data from its global, pivotal, 4WHIM Phase 3 clinical trial of once-daily, oral mavorixafor in individuals with WHIM syndrome. Following the **announcement** of positive top-line data from the 4WHIM trial in November 2022, today's event focuses on the impact of mavorixafor on the rate, severity, and duration of infections in trial participants.

"Today, we're announcing that mavorixafor treatment demonstrated statistically significant and clinically meaningful improvements across a number of key infection metrics versus placebo in our pivotal, Phase 3 trial in those diagnosed with WHIM Syndrome," said Paula Ragan, Ph.D., President and Chief Executive Officer of X4 Pharmaceuticals. "Given that frequent, severe, and long-lasting infections remain the most challenging burden for individuals with WHIM syndrome, we believe that demonstration of these clinical benefits in the 4WHIM trial are an important step in delivering a much-needed breakthrough for patients and their caregivers. We look forward to these data being presented at the upcoming annual meetings of the Clinical Immunology Society (CIS) and the European Hematology Association (EHA)." Dr. Ragan added, "We recently completed our pre-NDA meeting with the FDA and remain on track to submit for U.S. approval of mavorixafor for WHIM syndrome early in the second half of 2023."

Dr. Ragan concluded: "While we remain committed to delivering for the WHIM community, these meaningful results from the 4WHIM trial further bolster our commitment to advancing mavorixafor as quickly as possible as a potential treatment for the estimated 50,000 patients in the U.S. diagnosed with idiopathic, cyclic, and congenital chronic neutropenia (CN). We continue to look forward to delivering on our key CN milestones in the second or third quarter of 2023."

Key highlights from today's event include:

- **Rate of Infections**: In the trial, mavorixafor treatment resulted in a statistically significant reduction (~60%) in annualized infection rate versus placebo (p<0.01). In addition, the data showed that the reduction was greater with time on treatment, with participants on mavorixafor experiencing less than one infection per year versus 4.5 for those on placebo; during the second 6 months of the trial, the difference also achieved statistical significance (p<0.005).
- **Severity of Infections:** During the trial, 29% (5 of 17) of those on placebo experienced Grade 3 or higher infections, whereas only 7%, (1 of 14) of those on mavorixafor experienced a Grade 3 or higher infection, equating to a 75% reduction in the number of individuals experiencing severe infections. Importantly, the single Grade 3 infection in the mavorixafor treatment arm occurred during the first 3 months of the trial; after 3 months of treatment, there were no serious infections in the mavorixafor-arm, whereas the frequency of severe infections in those on placebo remained unchanged over the 52-week trial period.
- **Duration of Infections:** In the trial, mavorixafor treatment reduced the total duration (in days) of infections by more than 70% as compared to placebo, with those on placebo experiencing a mean of 7 weeks (49.1 days) with infections over the 52-week trial period versus a mean of only 2 weeks (14.1 days) with infections for those treated with mavorixafor.
- **Other Infection Metrics:** Mavorixafor treatment resulted in a 40% lower total infection score, a metric that combines infection number and severity (LS mean [95% CI]: mavorixafor, 7.41 [1.64–13.19]; placebo, 12.27 [7.24–17.30]). Treatment with mavorixafor also resulted in reductions in upper and lower respiratory tract and skin infections compared with those on placebo; participants on placebo required greater medical intervention, with 10 of the 17 participants on placebo requiring treatment with antibiotics over the course of the study, versus 3 of the 14 receiving mavorixafor; and slight improvements in

warts were demonstrated both in the mavorixafor and placebo arms (no difference between arms).
- **Safety and Tolerability:** As reported previously, mavorixafor was generally well tolerated in the 4WHIM trial, with no drug-related serious adverse events, no treatment limiting toxicities, and no discontinuations due to safety. Approximately 90% of participants in the trial continued on to receive mavorixafor treatment in the ongoing open-label extension study.

A late-breaking abstract of these data was accepted for oral presentation at the annual meeting of the Clinical Immunology Society (CIS) taking place May 18-21, 2023 in St. Louis, MO. Dr. Raffaele Badolato, Professor of Pediatrics at the University of Brescia (Italy) and an investigator in the 4WHIM clinical trial, will present at 11:30 am CT on Sunday, May 21st. Although the session is only accessible live to conference attendees, the company will post the presentation slides to its website concurrent with the presentation.

In addition, X4 is also announcing today that its submitted abstract of these data was accepted for oral presentation at the annual meeting of the European Hematology Association (EHA), taking place June 8-15, 2023 in Frankfurt, Germany. Dr. Jean Donadieu, Pediatrician in the Hemato Oncologic Department of Trousseau Hospital (Paris), Coordinator of the French Histiocytosis Registry, Coordinator of the pediatric branch of the French Histiocytosis Reference Center, and also an investigator in the 4WHIM clinical trial, will be delivering an encore oral presentation of the results being presented at CIS.

Investor Event Details:
The X4 live-event webcast presentation and the accompanying slides are now accessible on the investor relations section of the X4 website at www.x4pharma.com. Following the completion of the event, a replay will be available on the website.

About Mavorixafor and WHIM Syndrome
WHIM (warts, hypogammaglobulinemia, infections, and myelokathexis) syndrome is a rare, inherited, combined immunodeficiency disease caused by reduced mobilization and trafficking of white blood cells from the bone marrow due to over-signaling of the CXCR4/CXCL12 pathway. People with WHIM syndrome characteristically have very low blood levels of neutrophils (neutropenia) and lymphocytes (lymphopenia), and as a result, experience frequent, recurrent infections with a high risk of lung disease, refractory warts from underlying human papillomavirus (HPV) infection, limited antibody production due to low levels of immunoglobulin, and an increased risk of developing certain types of cancer. Mavorixafor is an investigational small-molecule antagonist of CXCR4 being developed as a once-daily oral therapy to correct the dysfunction resulting from the underlying causes of WHIM. For the WHIM indication, mavorixafor has been granted Breakthrough Therapy Designation, Fast Track Designation, and Rare Pediatric Designation in the U.S., and Orphan Drug Status in both the U.S. and European Union. Should mavorixafor be approved in the U.S. for the indication of WHIM syndrome, X4 could be eligible to receive a Priority Review Voucher (PRV).

About the 4WHIM Phase 3 Clinical Trial
The 4WHIM Phase 3 clinical trial was a global, randomized, double-blind, placebo-controlled, multicenter study designed to evaluate the efficacy and safety of oral, once-daily mavorixafor in people with genetically confirmed WHIM syndrome. Originally designed to enroll 18-28 patients, the trial enrolled 31 patients aged 12 and older who received either 400 mg mavorixafor (n=14) or placebo (n=17) orally once daily for 52 weeks. An open-label extension phase of the clinical trial is ongoing.

About X4 Pharmaceuticals
X4 Pharmaceuticals is a late-stage clinical biopharmaceutical company focused on the discovery and development of novel therapies for people with rare diseases of the immune system. Our lead clinical candidate is mavorixafor, a small molecule antagonist of chemokine receptor CXCR4 that is being developed as an oral, once-daily therapy. Due to its ability to increase the mobilization of mature, functional white blood cells from the bone marrow into the bloodstream, we believe that mavorixafor has the potential to provide therapeutic benefit across a variety of chronic neutropenic disorders, including WHIM (Warts, Hypogammaglobulinemia, Infections, and Myelokathexis) syndrome, a rare, primary immunodeficiency. Following announcement of positive top-line data from our global, pivotal, 4WHIM Phase 3 clinical trial, we are currently preparing a U.S. regulatory submission seeking approval of oral, once-daily mavorixafor in the treatment of people aged 12 years and older with WHIM syndrome. We are also currently evaluating mavorixafor in a Phase 2 clinical trial in people with certain chronic neutropenic disorders following positive results from a Phase 1b clinical trial of mavorixafor in people with congenital, idiopathic, or cyclic neutropenia. We continue to leverage our insights into CXCR4 and immune system biology at our corporate headquarters in Boston, Massachusetts and at our research center of excellence in Vienna, Austria. For more information, please visit our website at www.x4pharma.com.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of applicable securities laws, including 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, without limitation, statements regarding the clinical progress of X4’s pipeline development programs, including the anticipated New Drug Application submission for mavorixafor for the treatment of WHIM syndrome and the timing thereof. Any forward-looking statements in this press release are based on management's current expectations and beliefs. Actual events or results may differ materially from those expressed or implied by any forward-looking statements contained herein, including, without limitation, on account of uncertainties inherent in the initiation and completion of clinical trials and clinical development; the risk that trials and studies may not have satisfactory outcomes; the risk that the outcomes of preclinical studies or earlier clinical trials will not be predictive of later clinical trial results; the risk that initial or interim results from a clinical trial may not be predictive of the final results of the trial or the results of future trials; the potential adverse effects arising from the testing or use of mavorixafor or other product candidates; the risk that the U.S. Food and Drug Administration (FDA) may not accept a regulatory submission for mavorixafor; the risk that the FDA may not approve mavorixafor for WHIM syndrome; the risks related to X4’s ability to raise additional capital; the impacts of general macroeconomic and geopolitical conditions, rising inflation, and uncertain credit and financial markets on X4’s business, clinical trials, and financial position; and other risks and uncertainties, including those described in the section entitled “Risk Factors” in X4’s Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on May 4, 2023, 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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