X4 Pharmaceuticals Announces Positive Top-Line Results from 4WHIM Global, Pivotal Phase 3 Trial of Once-Daily, Oral Mavorixafor in WHIM Syndrome

November 29, 2022

4WHIM trial meets primary endpoint and first key secondary endpoint, with mavorixafor achieving statistically significant and clinically relevant longer times above threshold levels for both absolute neutrophil (P <0.0001) and absolute lymphocyte counts (P<0.0001) versus placebo

Mavorixafor was generally well tolerated in the trial

Company to host a conference call and webcast today at 4:30 p.m. ET

BOSTON, Nov. 29, 2022 (GLOBE NEWSWIRE) -- **X4 Pharmaceuticals** (Nasdaq: XFOR), a leader in the discovery and development of novel small-molecule therapeutics to benefit people with diseases of the immune system, today announced positive top-line results from the global, pivotal Phase 3 clinical trial (4WHIM) of its lead investigational therapy, mavorixafor, a novel CXCR4 antagonist, in people with WHIM syndrome.

Key Top-Line 4WHIM Trial Results:

- 4WHIM met its primary endpoint, with mavorixafor achieving clinical and statistical superiority over placebo when measuring TAT_{ANC}, or the length of time that participants' absolute neutrophil counts (ANC) remained above a clinically meaningful threshold of 500 cells per microliter (severe neutropenia), over 24-hour periods at 4 time points throughout the 52-week trial. Mean TAT_{ANC}, was 15.04 hours in the treatment group versus 2.75 hours in the placebo group (P<0.0001).
- 4WHIM also met a key secondary endpoint, with mavorixafor achieving clinical and statistical superiority over placebo when measuring TAT_{ALC}, or the length of time that participants' absolute lymphocyte counts (ALC) remained above a clinically meaningful threshold of 1,000 cells per microliter (lymphopenia), over 24-hour periods at 4 time points throughout the 52-week trial. Mean TAT_{ALC} was 15.80 hours in the treatment group versus 4.55 hours in the placebo group (P<0.0001).
- Increases in both TAT_{ANC} and TAT_{ALC} were maintained versus placebo and baseline across 52 weeks, demonstrating durability of treatment effect during the trial.
- Mavorixafor was generally well tolerated in the trial, with no treatment-related serious adverse events reported and no discontinuations for safety events.
- Following completion of the placebo-controlled portion of the trial, more than 90% of the eligible participants opted to receive treatment with mavorixafor in the open-label trial extension.
- Additional data review and analysis of the secondary and exploratory endpoints of the 4WHIM trial are ongoing, with plans to present detailed results at a future medical meeting.

"Mavorixafor is the first and only oral investigational therapy to demonstrate durable improvements in severe chronic neutropenia and lymphopenia, the hallmarks of WHIM syndrome," said Murray Stewart, DM FRCP, X4's interim Chief Medical Officer. "Following achievement of these key trial endpoints, we are now preparing to meet with U.S. regulatory authorities in the first half of 2023 to discuss next steps in advancing mavorixafor further towards a submission for regulatory approval and commercialization as the potential first treatment for people with WHIM syndrome."

Teresa Tarrant, M.D., Associate Professor of Medicine, Rheumatology, and Immunology at Duke University School of Medicine and a principal investigator in the 4WHIM trial, commented on the results: "WHIM syndrome is a combined immunodeficiency where patients experience chronically low blood levels of neutrophils and lymphocytes, leaving them susceptible to increased infection risk and risk of certain cancers. I am encouraged by these results for mavorixafor and look forward to the continued advancement of this potential new therapy for my patients with WHIM syndrome."

"Needless to say, we are thrilled with these positive results, only made possible through the commitment of the study participants who put their trust in us, through the dedication of physicians and healthcare professionals at participating clinical trial sites, and through the unabated years of effort by our X4 employees," said Paula Ragan, Ph.D., President, and Chief Executive Officer of X4. "These data not only give us strong confidence in the potential of mavorixafor to make a difference in the lives of those with WHIM syndrome and their families, but also strengthen our resolve to further evaluate mavorixafor in people living with chronic neutropenic disorders beyond those with WHIM."

Conference Call and Webcast
X4 will host a conference call and webcast today at 4:30 pm ET to discuss results from the company's Phase 3 trial of its lead candidate, mavorixafor, in the treatment of WHIM syndrome. The conference call can be accessed by dialing 1-877-451-6152 within the United States or 1-201-389-0879 internationally, followed by the conference ID: 13734531. The live webcast can be accessed on the investor relations section of X4 Pharmaceuticals' website at www.x4pharma.com. Following the completion of the call, a webcast replay of the conference call 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 genetic 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.

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.

About X4 Pharmaceuticals
X4 Pharmaceuticals is a late-stage clinical biopharmaceutical company leading the discovery and development of novel therapies for people with 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 mavorixafor's ability to antagonize CXCR4 and improve the mobilization of white blood cells, we believe that mavorixafor has the potential to provide therapeutic benefit across a variety of immune system diseases, including a range of chronic neutropenic disorders, including WHIM syndrome, a rare, primary immunodeficiency. Following announcement of positive top-line data from our global, pivotal, 4WHIM Phase 3 clinical trial, we are 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 advancing mavorixafor into a Phase 2 clinical trial in people with chronic neutropenic disorders, following positive results from a Phase 1b clinical trial of mavorixafor in people with congenital, idiopathic, and 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 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, express or implied statements regarding the clinical development and therapeutic potential of mavorixafor in WHIM syndrome; the anticipated reporting of data and future development plans of mavorixafor in WHIM syndrome; interactions with regulators and the timing thereof, including anticipated timing of submission for U.S. regulatory approval of mavorixafor in WHIM; expectations regarding the potential efficacy and commercial potential of mavorixafor; and management's ability to achieve its goals. 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 FDA may not support and accept a regulatory submission for mavorixafor, and X4's interactions with the FDA may not have satisfactory outcomes; the risks related to X4's ability to raise additional capital; and other risks and uncertainties, including those described in the section entitled "Risk Factors" in X4's Quarterly Report on Form 10-Q for the quarter ended September 30, 2022 filed with the Securities and Exchange Commission (SEC) on November 3, 2022, 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.

Contacts:
Daniel Ferry (investors)
Managing Director, LifeSci Advisors
daniel@lifesciadvisors.com
(617) 430-7576

Cherilyn Cecchini, M.D. (media)
LifeSci Communications
ccecchini@lifescicomms.com

Source: X4 Pharmaceuticals