X4 Pharmaceuticals Announces Positive Interim Clinical Data from Ongoing Six-Month Phase 2 Trial of Mavorixafor in Chronic Neutropenia (CN) and Initiation of Pivotal Phase 3 CN Trial

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100% of evaluable participants at Month 6 achieved target absolute neutrophil count (ANC) increase with once-daily, oral mavorixafor +/- stable-dose G-CSF as of the interim analysis data cut-off date

Durable mean ANC levels above the lower limit of normal for CN were achieved for participants on mavorixafor monotherapy at Months 3 and 6

Company webinar today at 8:00 am ET will detail the interim clinical results and feature clinical experts in the treatment of CN

BOSTON, June 27, 2024 (GLOBE NEWSWIRE) -- **X4 Pharmaceuticals** (Nasdaq: XFOR), a company driven to improve the lives of people with rare diseases of the immune system, today announced positive new clinical data from its ongoing Phase 2 clinical trial evaluating the safety and efficacy of mavorixafor, an oral CXCR4 antagonist, in the treatment of people with chronic neutropenia (CN). An interim analysis of data from the ongoing six-month study showed that once-daily oral mavorixafor was generally well tolerated and durably increased participants' absolute neutrophil counts (ANC) both as a monotherapy and in combination with stable doses of injectable granulocyte colony-stimulating factor (G-CSF), the only therapy approved in the U.S. for severe chronic neutropenia.

Today the company also announced that it is currently screening patients for enrollment into its global, pivotal Phase 3 clinical trial, the 4WARD study, evaluating the efficacy, safety, and tolerability of oral, once-daily mavorixafor (with or without stable doses of G-CSF) in people with congenital, acquired primary autoimmune, or idiopathic CN who are experiencing recurrent and/or serious infections. The 52-week trial is a randomized, double-blind, placebo-controlled, multicenter study aiming to enroll 150 participants.

"For the first time, we have demonstrated the ability of mavorixafor monotherapy to durably and meaningfully increase ANC in people living with chronic neutropenia," said Paula Ragan, Ph.D., President and Chief Executive Officer of X4 Pharmaceuticals. "In addition, we were pleased to see that once-daily mavorixafor used in combination with G-CSF also led to meaningful and sustained ANC increases and was generally well tolerated, further supporting the design of our newly initiated Phase 3 4WARD clinical trial, which will study the use of mavorixafor alone and with G-CSF in people with CN dealing with recurrent and/or serious infections. Today's exciting interim results build on the momentum we established in April with mavorixafor's first approval in the U.S., and we look forward to quickly advancing the 4WARD trial as we pursue a second indication to deliver for more patients in need."

Interim Analysis of Data from Phase 2 Clinical Study of Mavorixafor in CN
The Phase 2 study of mavorixafor is a six-month, open-label clinical trial that enrolled a total of 23 participants diagnosed with idiopathic, congenital, or cyclic CN. The interim analysis included results from the two treatment groups in the study (mavorixafor monotherapy and mavorixafor with stable-dose G-CSF) that most closely mirror the participant population of the newly initiated Phase 3 4WARD trial. Fifteen participants were enrolled across these two groups and, as of the May 14, 2024 interim analysis data cut-off date, seven had completed the study, and five remain ongoing. Data from a third treatment group of eight participants receiving mavorixafor and dose-adjusted G-CSF are expected to be presented later this year.

The mavorixafor monotherapy group included 10 participants and the mavorixafor with stable-dose G-CSF group included five participants. As of the data cut-off date, findings from the interim analysis show:

- 100% (6/6) of evaluable participants who had completed the six-month study achieved target ANC increase (ANC >500 cells/µL) at Months 3 and 6 on once-daily mavorixafor therapy with or without stable-dose G-CSF.
- Participants on mavorixafor monotherapy achieved mean ANC levels above the lower limit of normal for CN (≥1,500 cells/µL) at Month 3 (n=8) and Month 6 (n=3).
    - Mavorixafor monotherapy also durably increased ANC in participants with severe CN (ANC<500 cells/µL at baseline), achieving mean ANC of ~800-1,000 cells/µL (ANC range targeted by experts) at Months 1, 3, and 6 (n=5, 3, and 2, respectively).
- Participants on mavorixafor in combination with stable-dose G-CSF experienced increases in mean ANC of >1,000 cells/µL at Months 1, 3, and 6 (n=4, 4, and 3, respectively) versus baseline.

Across the 23 participants enrolled in the study, mavorixafor was generally well tolerated as a monotherapy and in combination with G-CSF, with no drug-related serious adverse events reported, as of the interim analysis data cut-off date. Of the 23 participants, three discontinued due to non-serious adverse events. The overall safety profile remains consistent with previous clinical studies.

Jean Donadieu, M.D., Ph.D., pediatrician in the hemato-oncology department of Trousseau Hospital in Paris, coordinator of the French registry for chronic neutropenia, and coordinator of the French chronic neutropenia reference center, commented on the results: "I am pleased to see that these interim data are consistent with the previous results of the Phase 1b study, but now with durability of effect and a good tolerability profile out to six

months of treatment. This patient group has only one currently approved treatment option – one that is injectable and that has dose-related, dose-limiting, and challenging side effects and risks. The results from this interim analysis offer a sound and compelling rationale for mavorixafor's evaluation in a Phase 3 trial, which is very good news for my patients with chronic neutropenia who, I believe, would benefit from an oral therapy to help reduce recurring or severe infections."

Investor Webinar Details:
X4 will host an investor webinar to present and discuss the new data today at 8:00 am ET. To register for the event, click here. A live Q&A will follow the formal presentation. Following the conclusion of the live webcast, a replay of the event and the presented slides will be available within the investors' section of the X4 Pharmaceuticals website at www.x4pharma.com.

About Chronic Neutropenia and Mavorixafor
Chronic neutropenia is a rare blood condition lasting more than three months, persistently or intermittently, and characterized by increased risk of infections and reduced quality of life due to abnormally low levels of neutrophils circulating in the blood. Neutrophils are retained in the bone marrow by the CXCR4/CXCL12 axis, creating a reserve of cells. Downregulation of the CXCR4 receptor by mavorixafor, an orally active CXCR4 antagonist, has been shown to mobilize neutrophils from the bone marrow into the peripheral blood across multiple disease states. The level of circulating neutrophils is typically measured by drawing blood to determine the absolute neutrophil count (ANC).

About the Phase 1b/Phase 2 Chronic Neutropenia Trial
The Phase 1b/Phase 2 clinical trial (NCT04154488) is a proof-of-concept, open-label, multicenter study designed to assess the safety and tolerability of oral mavorixafor, with or without injectable G-CSF, in participants with chronic neutropenic disorders, including idiopathic, cyclic, and congenital neutropenia. In the Phase 1b portion of the study, participants received one dose of oral mavorixafor and were assessed for magnitude of absolute neutrophil count (ANC) response and tolerability. In this initial portion of the study, 100% of participants (n=25) responded to treatment and mavorixafor was generally well tolerated alone or dosed concurrently with G-CSF. The ongoing Phase 2 portion of the trial (n=23 fully enrolled) is assessing the safety, tolerability, and the impact on participants' neutropenia of oral, once-daily mavorixafor with and without concurrent injectable G-CSF therapy over a six-month period.

About the 4WARD Global, Pivotal, Phase 3 Clinical Trial
The 4WARD trial is a global, pivotal Phase 3 clinical trial (NCT06056297) evaluating the efficacy, safety, and tolerability of oral, once-daily mavorixafor (with or without G-CSF) in people with congenital, acquired primary autoimmune, or idiopathic chronic neutropenia who are experiencing recurrent and/or serious infections. The 52-week trial is a randomized, double-blind, placebo-controlled, multicenter study aiming to enroll 150 participants with confirmed trough ANC levels less than 1,500 cells per microliter at baseline screening and histories of two or more serious and/or recurrent infections in the prior year. The primary endpoint of the trial is based on two outcome measures: annualized infection rate and positive ANC response.

About X4 Pharmaceuticals
X4 is delivering progress for patients by developing and commercializing innovative therapies for those with rare diseases of the immune system and significant unmet needs. Leveraging our expertise in CXCR4 and immune system biology, we have successfully developed mavorixafor, which has received U.S. approval as XOLREMDI™ (mavorixafor) capsules in its first indication. We are also evaluating the use of mavorixafor in additional potential indications. X4 corporate headquarters are in Boston, Massachusetts and our research center of excellence is 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, implied or express statements regarding the potential therapeutic benefit of mavorixafor; the initiation, timing, progress, and results of our current and future studies and clinical trials, including the Phase 2 clinical trial in chronic neutropenia and the Phase 3 4WARD clinical trial and related preparatory work and the period during which the results of the trials will become available; and the mission and goals for our business. Any forward-looking statements in this press release are based on management's current expectations and beliefs. These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond X4's control, which could cause actual results to differ materially from those contemplated in these forward-looking statements, including the risks that: we may encounter adverse events for mavorixafor at any stage that negatively impact development and/or commercialization; the expected availability, content, and timing of clinical data from our ongoing clinical trials of mavorixafor may be delayed or unavailable, including clinical results from our ongoing Phase 2 clinical trial and the announced Phase 3 4WARD trial; the trials and studies may not have satisfactory outcomes; the outcomes of preclinical studies or earlier clinical trials will not be predictive of later clinical trial results; the design and rate of enrollment for clinical trials, including the current design of our Phase 3 clinical trial evaluating mavorixafor in certain chronic neutropenic disorders may not enable successful completion of the trial(s); we may be unable to obtain and maintain regulatory approvals; uncertainties inherent in the initiation and completion of preclinical studies and clinical trials and clinical development; 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 safety effects arising from the testing or use of our product and product candidates may negatively impact development and/or commercialization; there will be changes in expected or existing competition; there will be changes in the regulatory environment; our business may be adversely affected and our costs may increase if any of our key collaborators fails to perform its obligations or terminates our collaboration; the internal and external costs required for our ongoing and planned activities, and the resulting impact on expense and use of cash, may be higher than expected which may cause us to use cash more quickly than we expect or to change or curtail some of our plans or both; and other risks and uncertainties, including those described in the section entitled "Risk Factors" in X4's Annual Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on May 7, 2024, 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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