X4 Pharmaceuticals Announces Positive Results from Completed Six-Month Phase 2 Trial of Mavorixafor in Chronic Neutropenia (CN)

November 13, 2024

Mavorixafor durably and meaningfully elevated participants' mean absolute neutrophil counts (ANC)

Mavorixafor enabled substantial reductions in G-CSF dosing while maintaining mean ANC at normal levels

Phase 2 study results and new analysis confirming functionality of neutrophils in sub-study participants bolster confidence in achieving success in Phase 3 4WARD trial

Company conference call and webcast today at 8:00 am ET

BOSTON, Nov. 13, 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 now completed Phase 2 clinical trial evaluating mavorixafor, an oral CXCR4 antagonist, in the treatment of people with chronic neutropenia (CN). An analysis of final data from the six-month study showed that once-daily oral mavorixafor durably and meaningfully increased participants' mean absolute neutrophil counts (ANC). In addition, when tested in combination with injectable granulocyte colony-stimulating factor (G-CSF), mavorixafor treatment enabled clinicians to substantially reduce G-CSF dosing while maintaining normal mean ANC levels.

"Since the U.S. approval of G-CSF to treat severe chronic neutropenia, there has remained a significant unmet need for an optimal treatment in terms of long-term efficacy, safety, and route of administration," said Teresa Tarrant, M.D., Associate Professor of Medicine, Rheumatology, and Immunology at Duke University School of Medicine. "I am encouraged by these Phase 2 results showing that mavorixafor not only increased circulating neutrophils across study participants, but also that these neutrophils were functional in a sub-study population. The larger Phase 3 mavorixafor CN trial will expand on these data, and I remain optimistic about this potential much-needed innovation for patients with chronic neutropenia."

"We could not be more pleased with the results from the six-month Phase 2 study of mavorixafor in CN, which are consistent with our earlier findings that mavorixafor durably and meaningfully increased ANC in this population," said Paula Ragan, Ph.D., President and Chief Executive Officer of X4 Pharmaceuticals. "Importantly, we gained insights into the potential real-world use of mavorixafor in CN, should we ultimately obtain approval. These data not only confirm our interim findings, but also increase our confidence in a positive outcome for our ongoing pivotal Phase 3 4WARD trial and the potential of mavorixafor to help people living with chronic neutropenia."

Results from Completed Phase 2 Study of Mavorixafor in CN
The Phase 2 study of mavorixafor was a six-month, open-label clinical trial that enrolled a total of 23 participants diagnosed with idiopathic, congenital, or cyclic chronic neutropenia. The analysis presented today includes results from the two study treatment groups: mavorixafor monotherapy (n = 10 at baseline) and mavorixafor in combination with G-CSF (n=13 at baseline).

Mavorixafor monotherapy:

- Consistent with previously presented analyses, results from participants receiving mavorixafor monotherapy showed that **mavorixafor durably increased mean ANC from baseline, with mean ANC reaching normal levels** at Month 3 (n=9) and Month 6 (n=8).
    - Further analysis showed that **those with severe CN achieved greater than two-fold increases in mean ANC levels** out to six months (n=4), reaching levels typically targeted by physicians for patients with severe CN.

Mavorixafor in combination with injectable G-CSF:

- **New results** presented today demonstrated that physicians chose to **reduce G-CSF dosing in nine of 12 eligible participants**. Of those nine, eight had G-CSF reduced at the earliest timepoint permitted and three were taken completely off of G-CSF prior to their Month 6 visit.
    - Mean **reductions in G-CSF were 52% at Month 3 (n=8) and 70% at Month 6 (n=9)**, while mean ANC levels remained in the normal range.
- The three participants receiving mavorixafor who remained on stable doses of G-CSF maintained mean ANC levels in the normal range at all timepoints.

Neutrophil functionality assessment sub-study

- X4 also announced **new findings** from a sub-study comparing the mean percentage of functional neutrophils in samples

from healthy donors (n=5) to participants from the Phase 2 CN study (n=9) using two common study methods. These results demonstrated that the mean percentage of **functional circulating neutrophils in CN participants in this sub-study was comparable to that of healthy donors** after six months of mavorixafor dosing.

- The subset of participants with congenital neutropenia (n=4 of 9) also had mean percentage of functional neutrophils comparable to those of healthy donors.
- This is the first clinical demonstration of the functionality of neutrophils mobilized by mavorixafor, and further increases the company's confidence in achieving success in the ongoing pivotal Phase 3 4WARD clinical trial.

Safety summary

- Mavorixafor was generally well tolerated as a monotherapy and in combination with G-CSF, with no drug-related serious adverse events reported, consistent with previous clinical studies.

Investor Event Details:
The company will host a conference call and webcast today at 8:00 a.m. ET. The conference call can be accessed by dialing 1-800-267-6316 from the United States or 1-203-518-9783 internationally, followed by the conference ID: X4PHARMA. The live webcast and accompanying slide presentation will be accessible through the investor relations section of X4 Pharmaceuticals' website at www.x4pharma.com. A live Q&A will follow the formal presentation. Following the conclusion of the call and webcast, a replay will be available on the company's website.

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 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 Phase 2 portion of the trial (n=23) assessed 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 initiation, timing, progress, and results of our current and future preclinical studies and clinical trials and related preparatory work and the period during which the results of trials will become available, as well as our research and development programs; 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: X4 may have difficulty establishing and maintaining an effective sales and marketing organization or suitable third-party alternatives for any approved products; X4 may not be able to obtain regulatory approval for, or successfully commercialize, mavorixafor or any other product candidate for other chronic neutropenic disorders or any other potential indication; the expected availability, content, and timing of clinical data from X4's ongoing clinical trials of mavorixafor may be delayed or unavailable, including our ongoing Phase 3 clinical trial; the risk that trials and studies may be delayed and may not have satisfactory outcomes, including clinical results from our completed Phase 2 clinical trial; the outcomes of preclinical studies or earlier clinical trials will not be predictive of later clinical trial results, including clinical results from our completed Phase 2 clinical trial; the design and rate of enrollment for clinical trials, including the current design of a Phase 3 clinical trial evaluating mavorixafor in certain chronic neutropenic disorders may not enable successful completion of the trial(s); the commercial opportunity for mavorixafor in chronic neutropenic disorders may be smaller than we anticipate; X4 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, including assessing the ability of mavorixafor monotherapy to durably increase absolute neutrophil count in patients with chronic neutropenic; adverse safety effects arise from the testing or use of our product and product candidates; the need to align with our collaborators may hamper or delay our development and commercialization efforts or increase our costs; 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 Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 8, 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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Source: X4 Pharmaceuticals