X4 Pharmaceuticals Announces EMA Validation of Marketing Authorization Application (MAA) for Mavorixafor for the Treatment of WHIM Syndrome

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Submission supported by positive results from global, Phase 3 4WHIM clinical trial;

U.S. regulatory approval in WHIM syndrome granted in 2024

Decision on MAA expected in 1H 2026

BOSTON, Jan. 24, 2025 (GLOBE NEWSWIRE) -- **X4 Pharmaceuticals** (Nasdaq: XFOR), a company driven to improve the lives of people with rare diseases of the immune system, today announced that its Marketing Authorization Application (MAA) for mavorixafor for the treatment of WHIM syndrome (warts, hypogammaglobulinemia, infections and myelokathexis), a rare primary immunodeficiency, has been validated for review and is now under evaluation with the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP). The EMA previously granted orphan designation to mavorixafor in WHIM syndrome. In April 2024, mavorixafor received U.S. Food and Drug Administration approval as XOLREMDI®, an oral, once-daily treatment for use in patients 12 years of age and older with WHIM syndrome to increase the number of circulating mature neutrophils and lymphocytes.

"Making mavorixafor available to those in the European Union living with WHIM syndrome is a top priority for X4 and this submission demonstrates our continued ability to deliver on our key milestones and generate growth," said Paula Ragan, Ph.D., President and Chief Executive Officer of X4 Pharmaceuticals. "With our MAA now validated for review by the EMA, we expect to enable our recently announced European partner, Norgine, to provide this much-needed treatment to patients as rapidly as possible should it be approved. We look forward to working alongside the EMA as they assess our application."

Mavorixafor is a small-molecule antagonist of the CXCR4 receptor being developed as a once-daily oral therapy for people with rare primary immunodeficiencies, including WHIM syndrome. The global, pivotal, 4WHIM Phase 3 trial that X4 conducted met its primary endpoint, a key secondary endpoint, and was generally well tolerated in the trial, with no treatment-related serious adverse events reported and no discontinuations for safety events. Additionally, in the 4WHIM trial, once-daily oral mavorixafor resulted in reductions in the rate, severity, and duration of infections in participants with WHIM syndrome.

If approved by the EMA, mavorixafor would be the first drug indicated for patients with WHIM syndrome in Europe, a population estimated to be approximately 1,000 people. Earlier this month X4 announced an exclusive licensing and supply agreement with Norgine to commercialize mavorixafor in Europe, Australia, and New Zealand.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION
XOLREMDI is contraindicated with drugs highly dependent on CYP2D6 for clearance.

WARNINGS AND PRECAUTIONS
Embryo-Fetal Toxicity: Based on its mechanism of action, XOLREMDI is expected to cause fetal harm when administered to a pregnant woman. Verify pregnancy status of female patients of reproductive potential prior to starting XOLREMDI. Advise females of reproductive potential to use effective contraception during treatment with XOLREMDI and for three weeks after the final dose.

QTc Interval Prolongation: XOLREMDI causes concentration-dependent QTc prolongation. QTc prolongation may occur when XOLREMDI is taken with concomitant medications that increase XOLREMDI exposure and/or drug products with a known potential to prolong QTc. Correct any modifiable risk factors for QTc prolongation, assess QTc at baseline, and monitor QTc during treatment as clinically indicated in patients with risk factors for QTc prolongation or receiving concomitant medications that increase XOLREMDI exposure and/or drugs with a known potential to prolong the QTc interval. Dose reduction or discontinuation of XOLREMDI may be required.

ADVERSE REACTIONS
The most common adverse reactions (in ≥10% patients and more frequently reported than placebo) were thrombocytopenia, pityriasis, rash, rhinitis, epistaxis, vomiting, and dizziness.

DRUG-DRUG INTERACTIONS
Avoid co-administration of XOLREMDI and strong CYP3A4 inducers. Reduce XOLREMDI daily dosage when administered with strong CYP3A4 inhibitors. Monitor more frequently for adverse reactions associated with an increase in exposure of XOLREMDI when used concomitantly with moderate CYP3A4 inhibitors or P-gp inhibitors and reduce XOLREMDI daily dosage if necessary.

USE IN SPECIFIC POPULATIONS
Advise females that breastfeeding is not recommended during treatment with XOLREMDI and for three weeks after the final dose.

The safety and effectiveness of XOLREMDI have not been established in pediatric patients younger than 12 years of age.

XOLREMDI is not recommended in patients with severe renal impairment, end-stage renal disease, or moderate to severe hepatic impairment.

To report suspected adverse reactions, contact X4 Pharmaceuticals at 1-866-MED-X4MI (1-866-633-9464) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see the full Prescribing Information for XOLREMDI.

About WHIM Syndrome
WHIM syndrome is a rare, combined primary immunodeficiency and chronic neutropenic disorder caused by CXCR4 receptor dysfunction that results in impaired mobilization of white blood cells from the bone marrow into peripheral circulation. WHIM syndrome is named for its four classic manifestations: warts, hypogammaglobulinemia, infections, and myelokathexis, although only a minority of patients experience all four manifestations in the acronym. People with WHIM syndrome characteristically have low blood levels of neutrophils (neutropenia) and lymphocytes (lymphopenia), and as a result, experience serious and/or frequent infections. It is estimated that at least 1,000 people are currently diagnosed with WHIM syndrome in the U.S., with another 1,000 estimated in Europe.

About XOLREMDI® (mavorixafor)
XOLREMDI (mavorixafor) is a selective CXCR4 receptor antagonist approved in the U.S. as an oral, once-daily treatment for use in patients 12 years of age and older with WHIM syndrome to increase the number of circulating mature neutrophils and lymphocytes. CXCR4 receptor stimulation by its ligand, CXCL12, has been shown to play a key role in the movement of white blood cells (leukocytes) to and from the bone marrow compartment. Treatment with XOLREMDI results in increased mobilization of neutrophils and lymphocytes from the bone marrow into peripheral circulation.

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 expertise in CXCR4 and immune system biology, X4 has successfully developed mavorixafor, an orally available CXCR4 antagonist that is currently being marketed in the U.S. as XOLREMDI

in its first indication and being reviewed by the EMA for approval in the EU for the same indication. The company is also evaluating additional uses of mavorixafor and is conducting a global, pivotal Phase 3 clinical trial (4WARD) in people with certain chronic neutropenic disorders. X4 is headquartered in Boston, Massachusetts and operates a research center of excellence 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 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 X4’s expectations related to the EMA’s evaluation of mavorixafor for WHIM syndrome; the potential for MAA approval in the European Union; X4’s plans to work with its partner, Norgine, to broaden patient access; the initiation, timing, progress, and results of X4’s 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 X4’s research and development programs; the timing and anticipated interactions with regulatory authorities and any related approvals for mavorixafor in Europe, Australia, and New Zealand, including a marketing authorization application; the potential market opportunity for mavorixafor; the anticipated strategic benefits of X4’s exclusive licensing agreement with Norgine and of any current or future collaborations; and the mission and goals for X4’s 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: uncertainties inherent in the regulatory approval process could impact the timing, progress, and outcome of the EMA’s review; potential delays or difficulties in commercializing mavorixafor in Europe could occur even if regulatory approval is granted; there could be challenges in coordinating with external partners including Norgine; 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 or maintain orphan drug designation or exclusivity for X4’s drug candidates, which could limit the potential profitability of X4’s product candidates; 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 X4’s ongoing Phase 3 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 anticipated; X4 may be unable to obtain and maintain regulatory approvals, including the marketing authorization approval; uncertainties inherent in the initiation and completion of preclinical studies and clinical trials and clinical development; the regulatory review and approval processes of the FDA, EMA, and other comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable, and if X4 is ultimately unable to obtain regulatory approval for X4’s product candidates, including additional indications for mavorixafor, X4’s business will be substantially harmed; 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 neutropenia; adverse safety effects could arise from the testing or use of X4’s product and product candidates; the need to align with X4’s collaborators may hamper or delay X4’s development and commercialization efforts or increase X4’s costs; X4’s business may be adversely affected and costs may increase if any of X4’s key collaborators fails to perform its obligations or terminates the collaboration; the internal and external costs required for X4’s ongoing and planned activities, and the resulting impact on expense and use of cash, may be higher than expected, which may cause the company to use cash more quickly than expected or to change or curtail some of X4’s plans or both; and other risks and uncertainties, including those described in the section entitled “Risk Factors” in X4’s Quarterly Report on X4’s Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 13, 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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