



X4 Pharmaceuticals Announces FDA Approval of XOLREMDI™ (mavorixafor) Capsules, First Drug Indicated in Patients with WHIM Syndrome

April 29, 2024

XOLREMDI targets CXCR4 pathway dysfunction, the underlying cause of WHIM syndrome

Breakthrough Therapy approval follows Priority Review of 4WHIM Phase 3 clinical trial data

X4 granted Rare Pediatric Disease Priority Review Voucher (PRV) concurrent with approval

Conference call and webcast to be hosted today at 8:30 am ET

BOSTON, April 29, 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 that the U.S. Food and Drug Administration (FDA) has approved [XOLREMDI™ \(mavorixafor\)](#) capsules for use in patients 12 years of age and older with WHIM syndrome (warts, hypogammaglobulinemia, infections and myelokathexis) to increase the number of circulating mature neutrophils and lymphocytes.

XOLREMDI, a selective CXC chemokine receptor 4 (CXCR4) antagonist, is the first therapy specifically indicated in patients with WHIM syndrome, a rare, combined primary immunodeficiency and chronic neutropenic disorder caused by CXCR4 pathway dysfunction. People with WHIM syndrome characteristically have low blood levels of neutrophils (neutropenia) and lymphocytes (lymphopenia) and experience serious and/or frequent infections. The FDA granted Breakthrough Therapy Designation to mavorixafor in WHIM syndrome and evaluated the New Drug Application (NDA) under Priority Review, a designation for therapies that have the potential to provide significant improvement in the treatment, diagnosis, or prevention of serious conditions.

“The approval of XOLREMDI is a transformational milestone both for X4 and, more importantly, for the WHIM syndrome community,” said Paula Ragan, Ph.D., President and Chief Executive Officer of X4 Pharmaceuticals. “We are incredibly grateful to the people living with WHIM syndrome, their families, and the investigators who took part in our clinical program, to U.S. regulators for their continued focus on rare-disease treatment development, and to our dedicated employees for making this targeted breakthrough therapy a reality.”

“Effective and innovative treatments are critical for those diagnosed with a primary immunodeficiency. The approval of XOLREMDI marks an important advancement for people living with WHIM syndrome, who are susceptible to serious and frequent infections,” said Jorey Berry, President and Chief Executive Officer of the Immune Deficiency Foundation (IDF). “We are very pleased to have been a partner to X4 in their journey to bring this much-needed treatment to this underserved rare disease community.”

Teresa K. 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 news: “Until now, supportive care for people with WHIM syndrome has focused on symptom management and not the underlying cause of disease — the dysfunction of the CXCR4 pathway. I am thrilled that with the approval of XOLREMDI, a therapy designed to address dysregulated CXCR4 pathway signaling, we now have a targeted treatment that has demonstrated the ability to elevate absolute neutrophil and lymphocyte counts, increasing WHIM patients’ ability to fight infections.”

The FDA approval of XOLREMDI was based on results of the pivotal, 4WHIM Phase 3 clinical trial, a global, randomized, double-blind, placebo-controlled, 52-week multicenter study that evaluated the efficacy and safety of XOLREMDI in 31 people aged 12 years and older diagnosed with WHIM syndrome. The efficacy of XOLREMDI was determined by improvement in absolute neutrophil counts (ANC), improvement in absolute lymphocyte counts (ALC), and a reduction in infections. In the 4WHIM trial, XOLREMDI treatment demonstrated increased time above threshold (≥ 500 cells/microliter) for absolute neutrophil count (TAT-ANC) vs. placebo ($p < 0.0001$) and increased time above threshold (≥ 1000 cells/microliter) for absolute lymphocyte count (TAT-ALC) v. placebo ($p < 0.0001$). The efficacy of XOLREMDI was further assessed in a composite endpoint consisting of total infection score and total wart change score using a Win-Ratio method. Analyses of the individual components of this composite endpoint showed an approximate 40% reduction in total infection score, weighted by infection severity, in XOLREMDI-treated patients compared with placebo-treated patients. There was no difference in total wart change scores between the XOLREMDI and placebo treatment arms over the 52-week period. Treatment with XOLREMDI also resulted in a 60% reduction in the annualized infection rate compared with placebo-treated patients. The most common adverse reactions reported in the 4WHIM trial ($\geq 10\%$ and more frequently reported than placebo) were: thrombocytopenia, pityriasis, rash, rhinitis, epistaxis, vomiting, and dizziness.

With the FDA approval of XOLREMDI, X4 has received a Rare Pediatric Disease Priority Review Voucher that can be used to obtain priority review for a subsequent application or sold to another drug sponsor.

X4Connect™ Offers Disease and Treatment-Related Support

X4 is committed to helping people with WHIM syndrome access XOLREMDI and announced today the launch of X4Connect, offering eligible U.S. patients dedicated support throughout their XOLREMDI treatment journey, including disease and treatment-related resources, help navigating insurance coverage, and copay assistance. For additional information about X4Connect, call 1-844-X4CNNCT (844-942-6628), Monday-Friday, 8am-8pm ET or visit <https://www.xolremdihcp.com/access-and-support>.

XOLREMDI will be commercially available in the U.S. through X4's specialty pharmacy partner PANTHERx[®] Rare.

Conference Call and Webcast

The company will host a conference call and webcast today at 8:30 am ET. The conference call can be accessed by dialing 1-877-451-6152 from the United States or 1-201-389-0879 internationally, followed by the conference ID: 13746357. The live webcast will be accessible through the investor relations section of X4 Pharmaceuticals' website at www.x4pharma.com. Following the completion of the call, a webcast replay will be available on the website.

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. 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. 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 $\geq 10\%$ 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.

About XOLREMDI™ (mavorixafor)

XOLREMDI (mavorixafor) is a selective CXCR4 receptor antagonist approved in the U.S. 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 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 X4's expectations as to the timing of commencement of planned launch, availability, and commercialization of XOLREMDI, which is approved in the U.S. for use in patients 12 years of age and older with WHIM syndrome to increase the number of circulating mature neutrophils and lymphocytes; X4's plans

for commercial launch of XOLREMDI in this indication, including its planned commercial launch in the U.S. through PANTHERx Rare; X4's belief in its readiness for commercial launch of XOLREMDI; the potential benefit of XOLREMDI in the indicated patient population; the potential number of patients with WHIM syndrome and the potential market for XOLREMDI; the anticipated timing for completion of commercial drug product manufacturing; 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's launch and commercialization efforts in the U.S. with respect to XOLREMDI may not be successful, and X4 may be unable to generate revenues at the levels or on the timing we expect or at levels or on the timing necessary to support our goals; the number of patients with WHIM syndrome, the unmet need for additional treatment options, and the potential market for XOLREMDI may be significantly smaller than we expect; XOLREMDI may not achieve the clinical benefit, clinical use, or market acceptance we expect or we may encounter reimbursement-related or other market-related issues that impact the success of our commercialization efforts; we may encounter adverse events for XOLREMDI at any stage that negatively impact commercialization; 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 Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on March 21, 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.

Investor Contact:

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

Media Contact:

Kit Rodophele
Account Director, Ten Bridge Communications
krodophele@tenbridgecommunications.com



Source: X4 Pharmaceuticals