About the 4WHIM Trial

We are investigating the safety and efficacy of mavorixafor, a small-molecule, non-competitive, allosteric antagonist of *CXCR4* for patients who have been genetically confirmed to have WHIM.

Patients who meet the entry criteria will be enrolled in the Randomized Period for a trial duration of 52 weeks. In the Open-Label Period, patients may receive mavorixafor until commercial availability or trial termination by the Sponsor.

The 4WHIM trial is now enrolling males and females ≥12 years of age, diagnosed with WHIM (Warts, Hypogammaglobulinemia, Infections, and Myelokathexis) syndrome.

If you have patients interested in participating, please contact us. We are available to discuss any concerns or answer any questions you may have.

4WHIM

For more information about this trial, visit **4WHIM.com** or search **NCT03995108** on **clinicaltrials.gov**.

X4 PHARMACEUTICALS

Do you have a patient with these symptoms?

- ✓ Low white blood cell count
- ✓ Frequent infections
- ✓ Treatment-refractory warts

These may be signs of WHIM (Warts, Hypogammaglobulinemia, Infections, and Myelokathexis) syndrome.

4WHIM is a randomized, double-blind, multicenter, parallel, placebo-controlled Phase 3 trial in patients with WHIM with open-label extension investigating the efficacy and safety of mavorixafor.

Now enrolling patients (≥12 years of age) genetically confirmed to have WHIM syndrome

Protocol number: X4P-001-103

4WHIM

WHIM Syndrome

WHIM syndrome is a rare, autosomal dominant primary immunodeficiency disease caused by mutations in the *CXCR4* gene leading to abnormal immune cell trafficking.

Patients affected by WHIM may present with warts, hypogammaglobulinemia, infections, and myelokathexis. In addition, patients with WHIM may experience frequent upper respiratory tract and systemic infections, often beginning in infancy and possibly leading to life-threatening complications. Potentially fatal infections, such as meningitis and sepsis have been reported.

Some patients with WHIM are at a higher risk for EBV-associated T and B cell lymphoproliferative disease and lymphoma. In addition, patients with WHIM have an increased risk of malignancy due to human papillomavirus (HPV) transformation, leading to carcinoma. WHIM is caused by mutations in the *CXCR4* gene.

Genetic testing is available to confirm the diagnosis of WHIM.

Participation Requirements for the 4WHIM Phase 3 Clinical Trial

Patients who meet the following criteria may be eligible to participate:

- Male and female subjects who are at least 12 years of age and Tanner stage ≥3
- Have a genotype-confirmed mutation of *CXCR4* consistent with WHIM phenotype
- Have a confirmed ANC ≤400 cells/μL during screening. Baseline must be obtained while patient has no clinical evidence of infection. If the ANC value reflects subclinical infection, it may be repeated prior to randomization
- Subjects or their legal guardian must sign and date a written, Informed Consent form and any required authorization prior to initiation of any trial procedures
- Patients are required to agree to use a highly effective form of contraception
- Patients must be willing and able to comply with the protocol

Trial Arms

All patients eligible for the trial will undergo random allocation 1:1 to mavorixafor 400 mg daily QD or matching placebo and stratified by prophylactic Ig use. This trial comprises 2 phases:

Randomized Period

- The primary objective of this period is to demonstrate the efficacy of mavorixafor in patients with WHIM as assessed by increasing levels of circulating neutrophils compared with placebo, and relative to a clinically meaningful threshold
- Comprises a 52-week randomized period
- During the overnight baseline visit, all patients eligible for the trial will undergo 1:1 randomization to mavorixafor 400 mg QD or matching placebo
- At weeks 1 and 4, patients will have a telephone call from the investigator or designee to evaluate safety and discuss the diary before continuing on a schedule of overnight visits every 13 weeks (at weeks 13, 26, 39, and 52)

Open-Label Period

- The primary objective of this period is to evaluate the safety and tolerability of mavorixafor in patients with WHIM
- Lasts until mavorixafor becomes commercially available or until trial ends
- All patients eligible for this part of the trial will receive mavorixafor 400 mg QD
- From Year 2 onward, patients will attend office visits every 6 months (Weeks 26 and 52) with phone contact between office visits (i.e., at Weeks 13 and 39)

End-of-Study (EOS) Visit

- An EOS visit will be conducted at 30 days (±5 days) post-treatment

Number of Patients

- The planned enrollment in the Randomized Period is up to 28 patients (≥12 years of age and Tanner stage ≥3). The stratum of patients using prophylactic Ig within 5 months of trial entry is capped at 30% of the overall patient count
- Only patients who participate in the Randomized Period are eligible for the Open-Label Period
- After the LSLV (last subject, last visit) at week 52, data lock and data analysis will be performed according to a pre-specified statistical analysis plan (SAP)

Additional Trial Information

- All interested patients who decide to participate will be required to sign an Informed Consent form (ICF)
- Participants are required to attend a screening visit to determine if they meet the eligibility requirements
- Both the subjects and the trial staff are blinded during the randomized period. The investigator can lift the blind if the subject's safety is determined to be at risk