Background

WHIM (Warts, Hypogammaglobulinemia, Infections, Myelokathexis) Syndrome:
- Ultra-rare, autosomal dominant, immunodeficiency disease caused by mutations in the CXCR4 chemokine receptor gene
- CXCR4 mutations cause receptor hyporesponsiveness and leukocyte retention in patient bone marrow, resulting in severe chronic pancytopenia, including neutropenia and lymphopenia
- There are no approved therapies for WHIM syndrome; immunoglobulins (Ig) and granulocyte colony stimulating factor (G-CSF) are used to treat clinical symptoms of the disease
- CXCR4 antagonists are being investigated as a treatment for these patients

X4P-001:
- Selective, allometric, small molecule antagonist of CXCR4
- Orally bioavailable with a long half-life (~3-24 hours), allowing once-daily dosing
- Inhibition of CXCR4 hyperactivation is predicted to increase the mobilization of white blood cells, including neutrophils and lymphocytes, into circulation, resulting in improvement in clinical symptoms

Phase 2 Study of X4P-001: A Targeted Oral Therapy for Patients with WHIM Syndrome

Study Design

X4P-001 MKK:
- This is an interim report from the Phase 2 part of an ongoing Phase 2/3 study of X4P-001 for treating patients with WHIM syndrome
- As of 20 March 2018, 8 patients have been enrolled

Primary Objectives:
- Evaluate safety and tolerability of X4P-001 in patients with WHIM syndrome
- Determine the dose required to achieve a consistent increase in absolute neutrophil count (ANC) and absolute lymphocyte count (ALC)

X4P-001 Induces Dose-Dependent Increases in ANC/ALC and Serum Drug Concentration

- No changes in Ig levels or vaccine titers have been observed up to 4 weeks on treatment

Patient Demographics and Characteristics

Baseline Blood Count and Immunoglobulin Parameters

Pharmacokinetics and PK/PD Relationship

Safety

X4P-001 was well-tolerated with no serious adverse events (AEs) reported at the doses tested

- Treatment emergent AEs (events that began or worsened after administration of the first dose of X4P-001 that occurred in more than 1 patient were: sinusitis, dry mouth, and nausea (2 each)
- X4P-001 related AEs were nausea (2 each), dry eye, dry mouth, nasal dryness, dyspnea, conjunctivitis, and rash (1 each); all related AEs were grade 1

Conclusions

X4P-001 is safe and well tolerated at doses up to 400 mg for durations up to 400 days

- X4P-001 drug exposure shows a dose-dependent increase which is correlated with AUC0-24 of absolute neutrophil counts
- In the absence of any safety issues, the recommended dose for future studies is the highest dose tested; the recommended Phase 3 dose of X4P-001 is therefore 400 mg QD

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