Phase 1 First-In-Human Study of KSI-301: A Novel Anti-VEGF Antibody Biopolymer Conjugate With Extended Durability Following a Single Dose Administration (3670)

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Background

- Current anti-VEGF agents have limited durability resulting in narrow re-treatment windows, burdensome treatment regimens, repeated undertreatment, and poor real-world outcomes.
- KSI-301 is a novel Antibody Biopolymer Conjugate designed to solve this real-world problem.

ABC PLATFORM™

The science behind the ABC Platform and KSI-301’s design optimizes for durability and potency across molecular size (ocular PK), formulation strength (clinical dose) & ocular target tissue bioavailability

KSI-301 objective: to develop the next front line therapy for all patients with retinal vascular disease

- Clinically proven target: VEGF
- Antibody-based biologic
- Intravitreal injection
- Optically clear solution
- No ocular residue

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Methods

Open-label, single ascending dose study in subjects with DME. Study eye received one intravitreal injection of KSI-301 (1.25 mg, 2.5 mg, or 5 mg) and were then followed for 12 weeks. The primary endpoint was Week 2. Three subjects were enrolled in each dose cohort. Subjects in the 1st cohort were sequentially assessed with a waiting period of at least 24 hours. The waiting period between cohorts was 7 days. Dose escalation was based on OMAC safety review. The study was conducted at 5 US sites.

Design of Single Ascending Dose Study in Diabetic Macular Edema Patients

KSI-301 - Single Intravitreal Injection

Primary objective: 2-week safety

Extended follow-up

Median changes from baseline to week 12

-300 -200 -100 0 100 200 300

12.5 +12.5 +12.5

WEEK 12

Baseline

WEEK 6

Day 0

Day 1

Week 1

Week 2

Week 4

Week 8

Week 12

Single-Dose Bioactivity Observations

Purpose

This first-in-human study sought to explore initial safety and tolerability of KSI-301 and to establish a maximum tolerated dose. Bioactivity was evaluated by measuring visual function and retinal anatomy.

Phase 1 Single Dose Study - Summary

- Rapid high-magnitude and durable treatment responses were seen at all dose levels tested.
- Twelve weeks after a single dose, median BCVA improvement from baseline of +9 ETDRS chart letters and median improvement in retinal edema of -1.21 microns (OCT C3T) were observed.
- No dose-limiting toxicities, drug-related adverse events, or intracranial inflammation were observed through each patient’s last visit at 12 weeks.

Case Study 1

Resolution of chronic macular edema sustained through 12 weeks in patient with prior suboptimal response

Case Study 2

Resolution of subretinal fluid through 12 weeks in patient with chronic edema and extensive foveal lipid exudates

Conclusions

- A novel anti-VEGF antibody biopolymer conjugate showed safety and rapid-onset durable effects in a single ascending dose clinical study.
- A Phase 1b multiple dose study in 50+ patients with treatment naïve wet AMD, DME, and RVO is now ongoing (NCT03795832).
- A Phase 2 pivotal study of KSI-301.5 mg vs. bevacizumab in naïve wet AMD is being initiated, with all KSI-301 subjects on Q12W-Q20W dosing.

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