Preliminary Findings from a Phase 1 Trial Evaluating the Safety, Tolerability and Biological Activity of OTX-TKI, a Hydrogel-Based, Sustained-Release Intravitreal Axitinib Implant, in Subjects with Neovascular Age-Related Macular Degeneration (nAMD)

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Purpose:
OTX-TKI (axitinib intravitreal implant) is a resorbable implant delivering small-molecule tyrosine kinase inhibitor, axitinib, in a sustained-release formulation to the vitreous. Here we evaluate preliminary findings regarding the safety, tolerability and biological activity of OTX-TKI in subjects with neovascular age-related macular degeneration (nAMD).

Methods:
Prospective, multi-center, open-label, dose escalation Phase 1 trial is ongoing. Subjects with nAMD (treatment-naïve and with a history of anti-VEGF therapy) were eligible to receive intravitreal placement of OTX-TKI. Two dosing cohorts are being evaluated: 200 µg (n=6) and 400 µg (n=6). Assessments include: Spectral-domain optical coherence tomography (SD-OCT) imaging to assess central subfield thickness (CSFT), best-corrected visual acuity (BCVA), slit lamp biomicroscopy, tonometry, indirect and direct ophthalmoscopy, and adverse event collection, performed at baseline, day 0 (injection), days 3, 7, 14, and with continued monthly visits until implants no longer visible.

Results:
No serious ocular adverse events have been reported to date (200 µg: 9-10.5 months; 400 µg: 6 months ongoing follow-up). Most common adverse events observed in the study eye included tiny pigmented keratic precipitates (3/12), subretinal hemorrhage (2/12), subconjunctival hemorrhage (3/12) and pain (2/12) following OTX-TKI injection. Implants exhibited little movement in the vitreous and were no longer visible after 9 - 10.5 months in the 200 µg group. No consistent CSFT change was noted in the 200 µg group through the study period. In the 400 µg group, some subjects showed a decrease in CSFT and demonstrated a clinically meaningful reduction in intraretinal and/or subretinal fluid by 2 months, maintained for up to 6 months (first 2 subjects to hit the 6 month timepoint).

Conclusions:
OTX-TKI appears to be generally well-tolerated to date with a favorable safety profile. To date, minimal movement and consistent resorption of implants has been observed. Preliminary signs of biological activity, as evidenced by a decrease in CSFT in the 400 µg group, has been observed in some subjects with durability up to 6 months. Additional follow-up of current dose groups and assessments of higher doses of OTX-TKI (600 µg) and combination therapy with a single anti-VEGF injection at the time of OTX-TKI placement is ongoing.