Initial clinical evaluation of safety, tolerability and pharmacodynamics of the locally-acting ROCK inhibitor AMA0076

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Purpose: To evaluate the safety, tolerability and IOP-lowering potential of different topical ocular formulations of AMA0076 in humans.

Methods: A First-in-Human (FIH) study with an initial AMA0076 formulation and a subsequent Phase 1b study with optimized formulations were completed. The FIH study was a multicenter, randomized, double-masked, placebo-controlled dose-escalation study with AMA0076 (or matching placebo) applied topically for 28 days in 82 POAG/OHT patients aged 30-85. The Phase 1b study was a single center, randomized, double-masked, placebo-controlled, repeat-dose, 3 period cross over study in which 21 healthy male and female subjects aged 35-65 were randomized. Each treatment period in the Phase 1b study entailed 1 week of BID topical ocular administration (14 active: 7 placebo) with a washout period of 1 week between treatment periods. Safety evaluation in both studies included AE reporting, vital signs, ECG, laboratory, and visual acuity assessments. Both studies also included biomicroscopy, hyperemia grading (according to a standardized photographic scale), and IOP determinations obtained at baseline and end of treatment at the same diurnal timepoints (pre-dose, 2, 4, and 8 hours post-dosing).

Results: AMA0076 was safe and generally well tolerated in both studies. No SAEs were reported. There was no discernible difference in non-ocular AEs or other systemic assessments (vitals, ECG, laboratory) by treatment group in either study. All ocular AEs in both studies resolved without sequelae. At the optimal IOP-lowering dose in each study, all ocular AEs were rated as mild in intensity, with a rate of mild, transient hyperemia in the FIH study and the Phase 1b study of 0% and 28.6%, respectively. In these dose regimens, a decrease in mean diurnal IOP compared to placebo was achieved (p = 0.020 and p < 0.005, respectively).

Conclusions: The optimal dose of AMA0076 demonstrated IOP reduction without significant hyperemia in both clinical studies. No other ROCK inhibitor has demonstrated this finding in the clinic. Therefore, AMA0076, due to its Localized Drug Action, has the potential to optimize the use of ROCK inhibition to lower IOP in patients with glaucoma and ocular hypertension.