Two Phase 3 studies of the efficacy and safety of AR-13324 Ophthalmic Solution 0.02%: in Patients with Open Angle Glaucoma and Ocular Hypertension

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Purpose: We compared the ocular hypotensive efficacy and safety of AR-13324 Ophthalmic Solution 0.02% to timolol ophthalmic solution 0.5% BID in patients with elevated intraocular pressure (IOP) (open angle glaucoma and ocular hypertension) in two Phase 3 studies Rocket 1 and Rocket 2 (R1, R2). AR-13324 inhibits both Rho kinase and the norepinephrine transporter and increases trabecular outflow, reduces aqueous humor formation, and decreases episcleral venous pressure in preclinical models.

Methods: Subjects with baseline IOP >20 and <27 mmHg (in R1), and >20 and <25 mm Hg (in R2), were included in the primary efficacy analysis. In R1, patients were randomized to receive either AR-13324 0.2% QD (PM) or timolol 0.5% BID for 3 months, R2 was a 12 month study where AR-13324 0.2% was dosed QD and BID. In both studies, the efficacy endpoint was mean IOP at 8:00, 10:00, and 16:00 hours at Weeks 2, 6, and Month 3.

Results: A total of 411 subjects in R1 and 756 subjects in R2 were randomized. While AR-13324 0.2% QD did not meet the criteria for non-inferiority to timolol 0.5% BID in subjects with baseline IOP <27 mmHg in R1, it was non-inferior to timolol 0.5% BID in a pre-specified analysis of subjects with baseline IOPs of ≤23 mmHg and in a post hoc analysis of subjects with baseline IOP <25 mmHg. In Rocket 2, both regimens of AR-13324 0.2% were non-inferior to timolol 0.5% BID in the primary population (baseline IOP < 25 mmHg). The most common safety finding was conjunctival hyperemia, which was of mild severity in a majority of subjects. The BID dosing regimen of AR-

13324 resulted in more ocular adverse events and treatment discontinuations than QD dosing.

Conclusions:AR-13324 0.2%, dosed QD and BID, was non-inferior to timolol 0.5% BID in subjects with baseline pressures below 25 mmHg, with a better safety and tolerability profile with QD dosing.

Layman Abstract (optional): Provide a 50-200 word description of your work that non-scientists can understand. Describe the big picture and the implications of your findings, not the study itself and the associated details.: In these two large controlled studies, AR-13324, a new topical ocular solution working through several mechanisms. lowered intraocular pressure in patients with glaucoma and ocular hypertension, with relatively few safety issues.