Phentolamine Ophthalmic Solution Rapidly Reverses Pharmacologically-Induced Mydriasis in 2 Pivotal Phase 3 Trials

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INTRODUCTION

- Pharmacologically-induced mydriasis (dilation) typically lasts 6 to 24 hours, during which time patients commonly experience ocular discomfort, impaired vision, and difficulty in daily tasks
- The MIRA-2 and MIRA-3 Phase 3 pivotal clinical trials assessed the efficacy and safety of 0.75% phentolamine ophthalmic solution (POS) to accelerate the reversal of mydriasis

METHODS

- Randomized, double-masked, placebo-controlled, multi-center Phase 3 trials in healthy subjects randomized to POS or placebo (two drops in the study eye, and one drop in the fellow eye) dosed one hour after dilation mydriatic agents with 2.5% phenylephrine, 1% tropicamide, or Paremyd® (3:1:1)
- 553 subjects (MIRA-2 n=185 and MIRA-3 n=368)
- Photopic pupil diameter was measured using the Neuroptics 300 VIP Pupilometer; Visual acuity was measured using ETDRS charts
- Primary endpoint: % of study eyes returning to ≤ 0.2 mm from baseline pupil diameter (PD) at 90 min post-treatment (POS vs placebo)
- Secondary endpoints included mean time to return to baseline PD overall, by study eyes and fellow eyes, by each mydriatic agent and by light and dark irides

DEMOGRAPHIC AND BASELINE CHARACTERISTICS

	POS (n=338)	Placebo (n=215)	Total (n=553)
Age, years, Mean (SD)	34 (12-80)	34 (12-80)	34 (12-80)
Female Sex, % (n)	62% (210)	56% (120)	60% (330)
White Race, % (n)	75% (252)	78% (167)	76% (419)
African American, % (n)	16% (55)	17% (37)	17% (92)
Hispanic/Latino Ethnicity, % (n)	7% (25)	8% (17)	8% (42)
Dark Irides, % (n)	53% (180)	52% (112)	53% (292)
Mean PD (-1 hr.) in study eye, mm	5.1	5.0	5.1
Max PD (0 min) in study eye, mm	7.2	7.1	7.2

Across the 2 pivotal Phase 3 trials, POS statistically significantly demonstrated a faster mean time to return to ≤ 0.2 mm from baseline PD compared with placebo, with a time savings of ~ 4 hrs. POS was effective across common mydriatic agents, iris colors, and age, providing a potential treatment to reverse pharmacologically induced mydriasis.

Figure 1: Summary of MIRA Pivotal Phase 3 Trial Designs

	MIRA-2 1st Phase 3	MIRA-3 2nd Phase 3
US Sites	12	16
Subjects Enrolled	185	368
Eligibility	Healthy ≥ 12 years old	Healthy ≥ 12 years old
Randomization	1:1	2:1
Mydriatic Agents	2.5% Phenylephrine, 1% Tropicamide and Paremyd®	2.5% Phenylephrine, 1% Tropicamide and Paremyd®
Positive Data Readout	1Q 2021	1Q 2022
Primary Endpoint	• % of subjects (study eye; 2 drops) returning to baseline (within 0.2 mm) pupil diameter (PD) at 90 min	
Secondary Endpoints	• % return to baseline PD at 0min to 24h (overall, by mydriatic, by iris color) • Mean time to return to baseline PD • Mean change in pupil diameter at all timepoints • Distance-corrected near vision • Accommodation (Tropicamide/Paremyd) • Safety and tolerability	

Figure 2A: Time (hrs) to Return to ≤ 0.2 mm of Baseline Pupil Diameter (Study Eye and Fellow Eye)

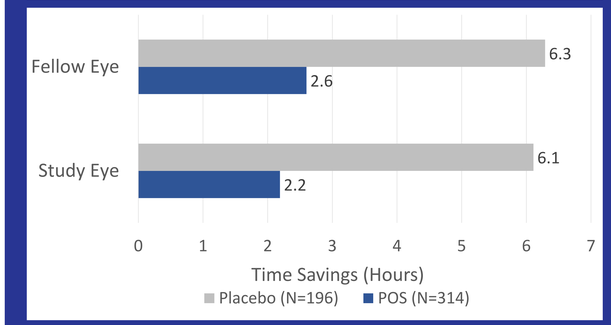

Figure 2B: Time (hrs) to Return to ≤ 0.2 mm of Baseline Pupil Diameter (Mydriatic Agent and Light/Dark Irides)

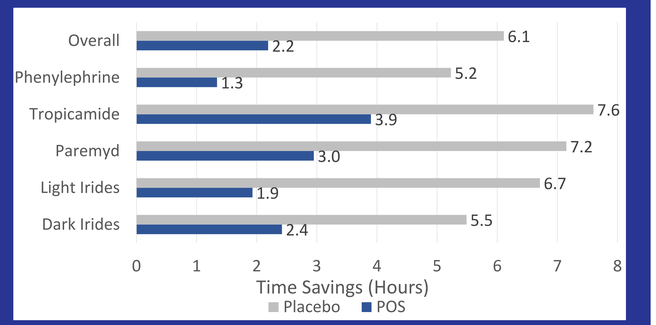

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Figure 3: Percent of Subjects With Study Eye Returning to ≤0.2 mm From Baseline Pupil Diameter by Time Point

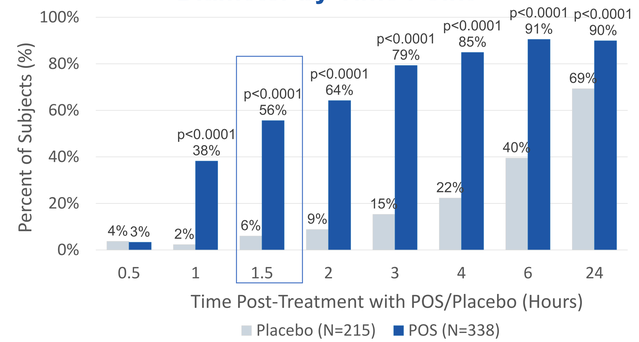

Figure 4: Percent of Subjects With Unchanged Accommodation From Baseline (-1 Hr) in Study Eye by Time Point

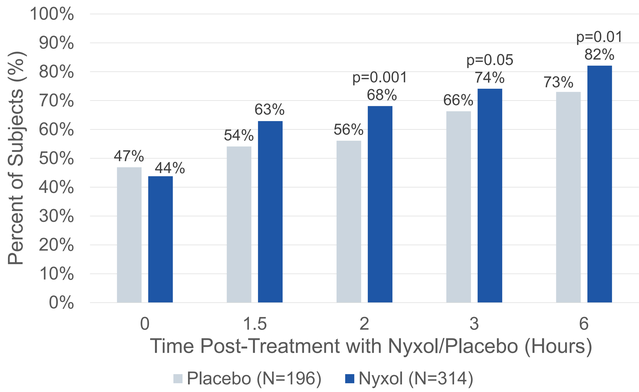

Figure 5: POS Additional Secondary Endpoints

Mydriatic Agent
Efficacy across all 3 mydriatic agents – phenylephrine, tropicamide, and Paremyd®

Irides Color
Efficacy was seen in both light and dark eyes

1 v. 2 Drops
Similar efficacy was seen with 1 drop (fellow eyes) and 2 drops (study eyes)

Accommodation
Over 60% subjects returned to baseline accommodation at 2-3 hours

Near Visual Acuity
Accelerated return to normal distance-corrected near visual acuity

Disclosures

Each author is a medical advisor (JP), consultant (LH, MB), or employee (MS, AK, AL, DC) of the study sponsor, Ocuphire Pharma, Inc. (Farmington Hills, MI)

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