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VEGA-1 Phase 2 trial: Phentolamine Ophthalmic Solution Maintains Pupillary Reflex with Improved Distance-Corrected Near Vision in Presbyopes

(Poster ID 91213)

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Dr. Singh's financial disclosures:

- Ocuphire
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- B+L
- Alchemy Vision Project
- Eyepoint/ImprimisRxx
- Elios
- Visiox

POS and POS + Low Dose Pilocarpine Presbyopia Eye Drops

Differentiated MOA with Two Potential Product Labels for Functional Near Vision Improvement

0.75% POS

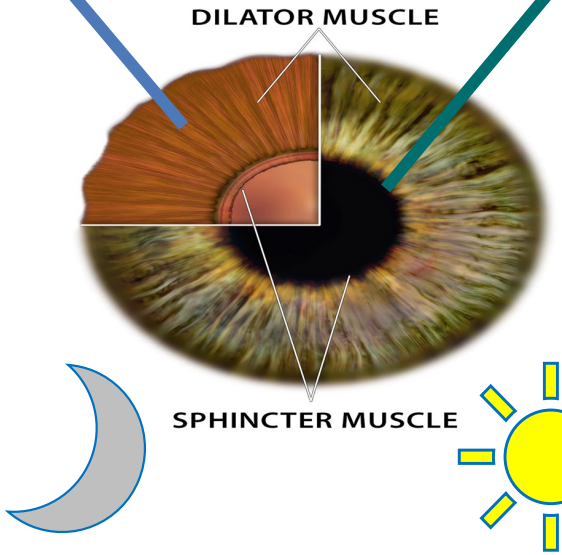
POS as a Single Agent for Presbyopia

Single Durable Drop

- Phentolamine α1/2 antagonist 505(b)(2)
- Novel MOA on iris dilator with 24 hr durability with moderate pupil reduction
- Well-tolerated with no systemic effects
- Stable, preservative-free, single-use vial

Iris Dilator Muscle **Inhibition**

Iris Sphincter and Ciliary Muscles **Activation**



Evening drop ***Daytime drop***

Optimal Pupil Size is 2-3 mm

0.4% LDP

POS with LDP as Adjunctive Therapy for Presbyopia

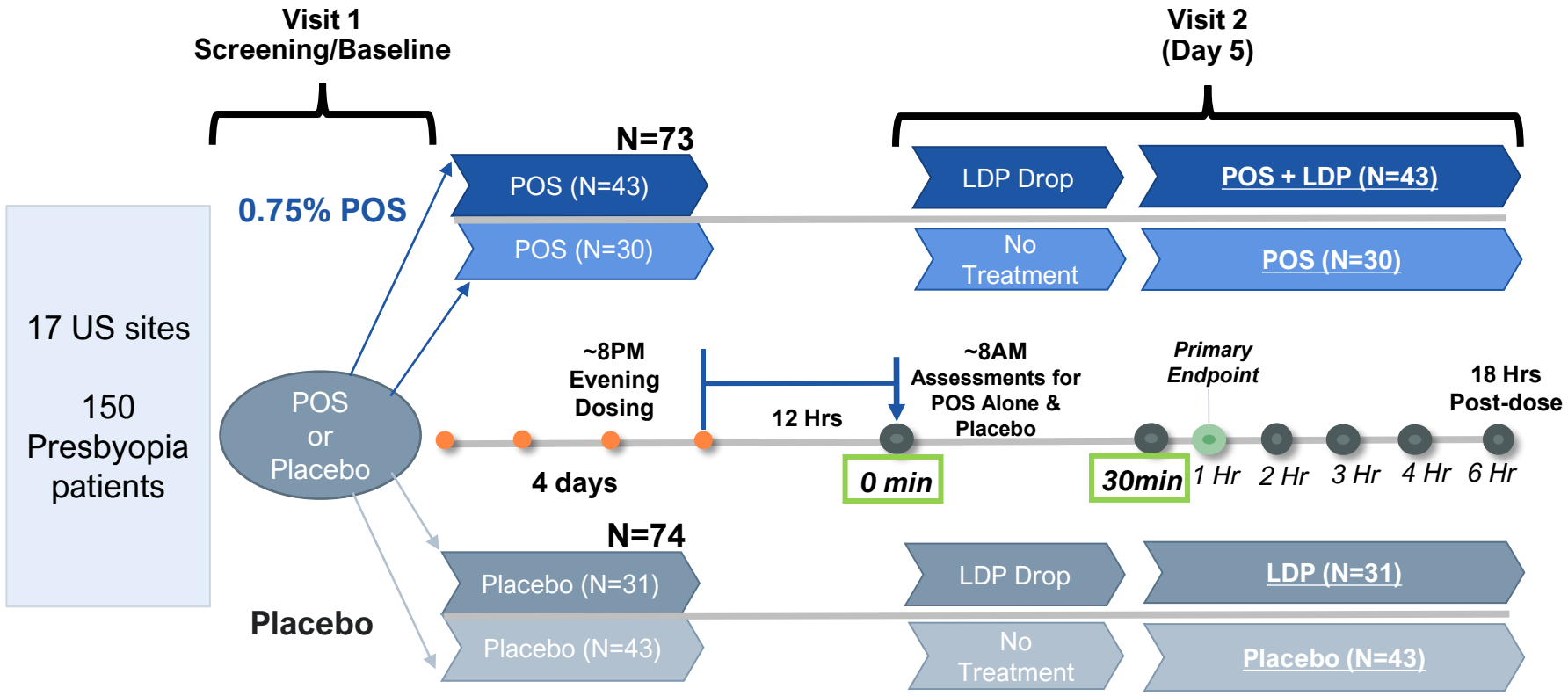
Two Drops Tunable Option

- Cholinergic agonist 505(b)(2)
- Known MOA on sphincter with potent miotic effects at approved doses (1%, 2%, 4%)
- Low concentration avoids tolerability issues
- Preserved, multi-use vial

Source: POS® data from 12 completed trials; Pilocarpine product label and literature

Presbyopia VEGA-1 Phase 2 Design

Randomized, Double-Masked, Placebo-Controlled Multi-Center One-Week Trial



Endpoints

Primary: % of subjects with ≥ 3 lines of improvement in distance-corrected near visual acuity comparing POS + LDP vs placebo alone at 1 hour

Secondary:

- % of subjects with ≥ 2 and ≥ 3 lines gained at time points from 30 min to 6 hours in photopic and mesopic lighting comparing POS + LDP vs placebo, POS alone, and LDP alone
- No loss of distance vision
- Pupil diameter at time points
- Safety and tolerability (redness)

Eligibility Criteria

- Males or females ≥ 40 and ≤ 64years of age
- BCDVA of 0.0 LogMAR(20/20 Snellen equivalent) or better in each eye under photopic conditions
- DCNVA of 0.4 LogMAR (20/50 Snellen equivalent) or worse under photopic conditions in each eye & binocularly

Clinical trial NCT#04675151

Source: VEGA-1 Study Design; *3-4 daily evening doses and then visit 2 on Day 5

VEGA-1: Demographics and Baseline Characteristics

Treatment and Placebo Arms Were Balanced

	Placebo Alone N=43	POS Alone N=30	LDP Alone N=31	POS+LDP N=43	Total N=147
Age (years): Median (Range)	52 (42-62)	54 (41-60)	52 (44-64)	53 (43-63)	53 (41-64)
Sex: Male n (%) **Female** n (%)	15 (35%) 28 (65%)	7 (23%) 23 (77%)	13 (42%) 18 (58%)	5 (12%) 38 (88%)	40 (27%) 107 (73%)
Race: White n (%) **Other*** n (%)	37 (86%) 6 (14%)	26 (87%) 1 (3%)	28 (90%) 3 (10%)	40 (93%) 3 (7%)	131 (89%) 15 (11%)
Dark Iris Color: n (%)	18 (42%)	12 (40%)	12 (39%)	18 (42%)	60 (41%)
Light Iris Color: n (%)	25 (58%)	18 (60%)	19 (61%)	25.1 (58%)	87 (59%)
Photopic DCNVA Mean Letters read-Binocular *(Snellen Equiv.)* *70 letters = 20/20*	46 (20/63)	45 (20/63)	48 (20/63)	46 (20/63)	46 (20/63)
Photopic BCDVA Mean Letters read-Binocular *(Snellen Equiv.)* *55 letters = 20/20*	62 (20/15)	61 (20/15)	60 (20/15)	61 (20/15)	61 (20/15)
Photopic Pupil Diameter Mean (mm)	4.3	4.5	4.3	4.3	4.3
Mesopic Pupil Diameter Mean (mm)	5.1	5.0	5.0	5.1	5.1
IOP (mmHg)	13.5	14.8	13.9	14.4	14.1

Source: VEGA-1 Results

VEGA-1: Planned P3 Efficacy Endpoint Met by POS and POS+LDP

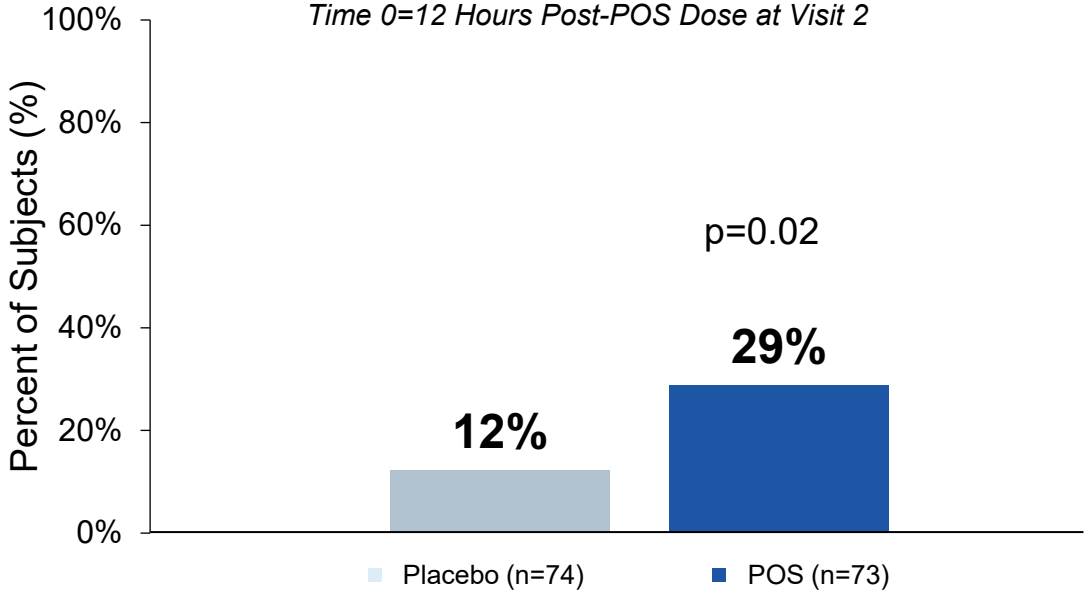
POS Single Drop and LDP Combination Provide Statistically Significant Near Vision Gain

1 **POS as a Single Drop for Presbyopia**

2 **POS with LDP Adjunctive Therapy**

Percent of Subjects with **≥ 15 Letter Gain In Near & < 5 Letters Loss In Distance Vision** in Photopic Binocular DCNVA

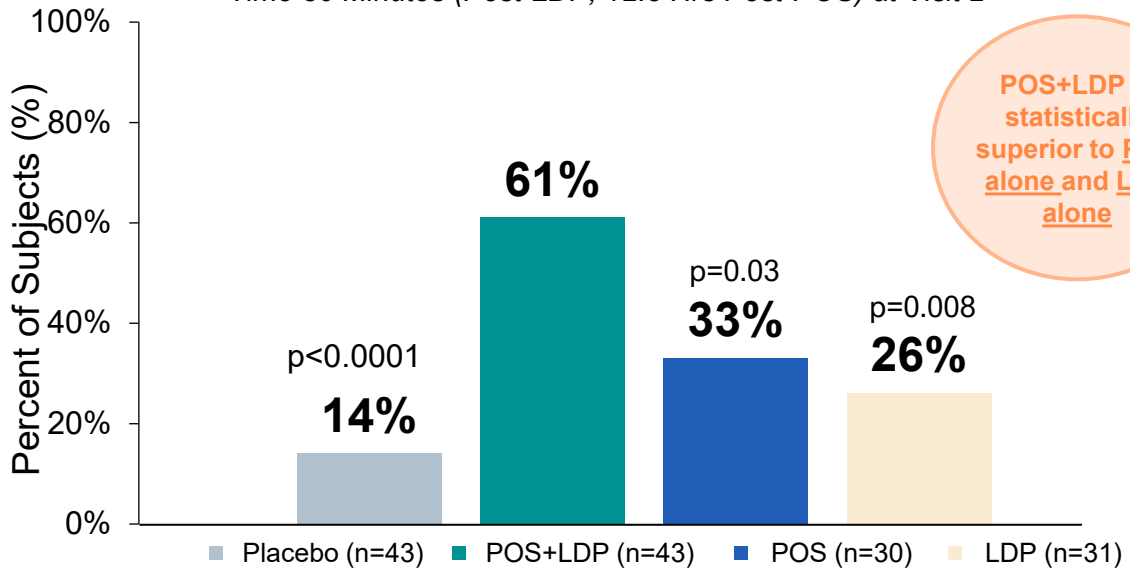
Time 0=12 Hours Post-POS Dose at Visit 2



53% of subjects achieved ≥ 10 letter improvement in DCNVA at 12 hours (p=0.005 vs placebo) and a similar trend at other time points

Percent of Subjects with **≥ 15 Letter Gain In Near & < 5 Letters Loss In Distance Vision** in Photopic Binocular DCNVA

Time 30 Minutes (Post-LDP; 12.5 Hrs Post-POS) at Visit 2



POS+LDP is statistically superior to POS alone and LDP alone

79% of subjects achieved ≥10 letter improvement in DCNVA at 1 Hour (p=0.005 vs placebo) and a similar trend at other time points

Source: VEGA-1 Results

VEGA-1: Safety Findings Across All Arms

POS and POS+LDP Combination were Well-Tolerated with a Favorable Safety Profile

- No serious AEs, no deaths
- Most AEs were mild
  - No systemic AEs were observed in >5% subjects
  - No headaches, no brow aches, and no blurry vision AEs reported
  - Only mild, transient conjunctival hyperemia observed in <5% of subjects
- No significant loss in distance vision loss (≥5 letters):
  - In photopic lighting (160 cd/m^2): 0% placebo, 3% POS, 0% POS+LDP and 7% LDP
  - In mesopic lighting (3 cd/m^2): 7% placebo, 0% POS, 5% POS+LDP and 7% LDP
- No change in IOP

Source: VEGA-1 Results

Clinical Significance of Maintaining a Dynamic Pupil

An Important Factor to Consider in Developing Topical Solutions for Presbyopia Treatment

- **Dynamic pupillary response** is the ability of the pupil to constrict and dilate in response to changes in light, accommodative effort and other stimuli
- **Benefit of maintaining eye's natural ability** to adjust to different lighting conditions, reducing glare in bright light while optimizing retinal illuminance and neural contrast in low-light conditions

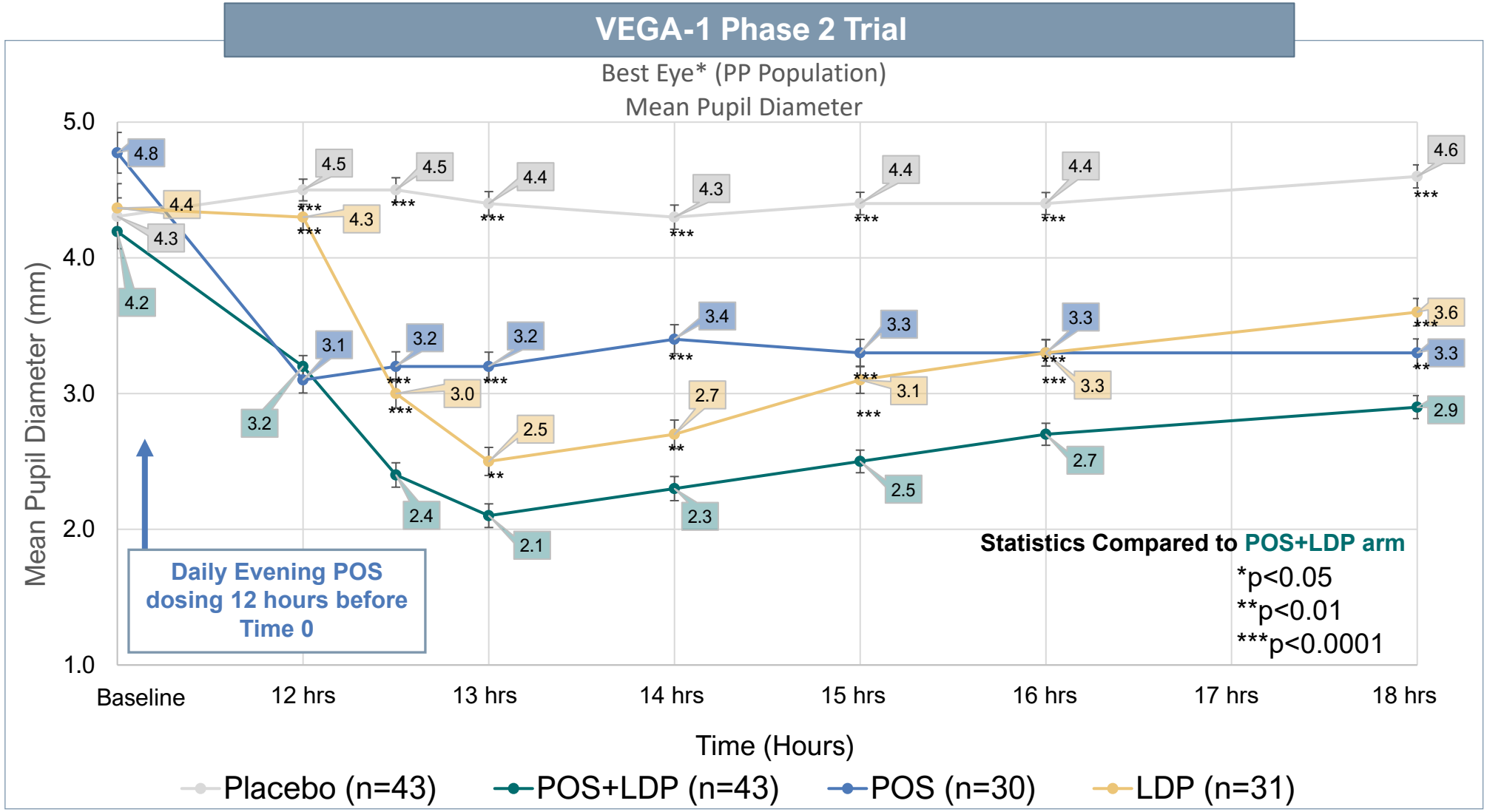
Approved **cholinergic agonists** (e.g., 1%-4% pilocarpine) powerfully reducing size of the pupil tend to **limit dynamic pupillary response**

Whereas **α1/2 antagonists** (e.g., 0.75% POS) **maintain dynamic pupillary response,** optimizing image contrast while also improving near vision, making it an ideal treatment for presbyopia

Source: VEGA-1 Results

VEGA-1: Mean Pupil Diameter Over Time

POS+LDP Reduced Pupil Diameter to 2-3 mm, Consistent With Improvement in Near Vision



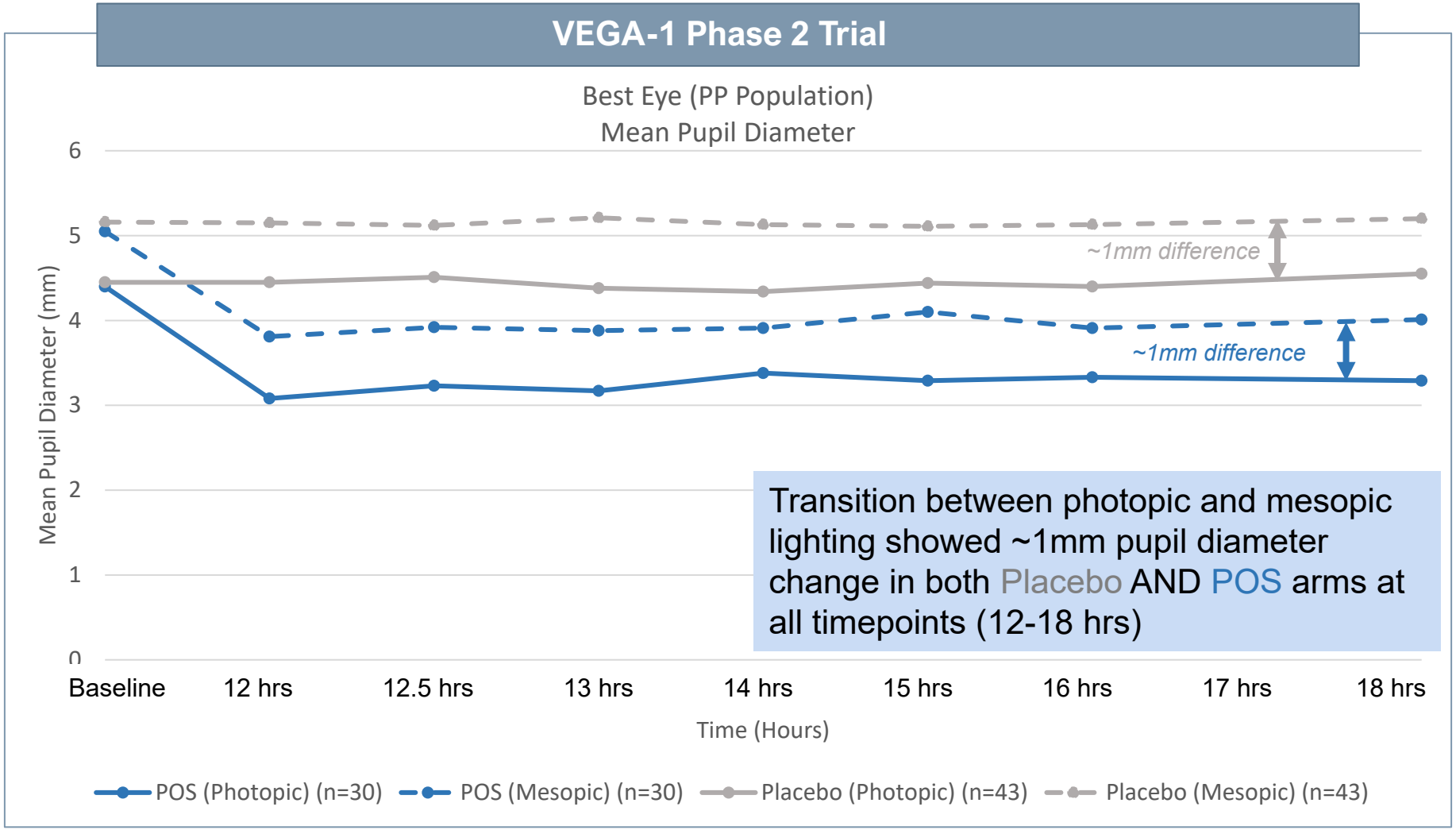
Note: PP population differs from mITT by only one subject; results were essentially identical.

Source: VEGA-1 Results

*Defined as eye tested with greatest reduction in diameter between Study Eye and Fellow Eye

VEGA-1: Pupillary Light Reflex in POS vs. Placebo

POS-Treated Eyes Demonstrated Normal Pupillary Response at All Timepoints

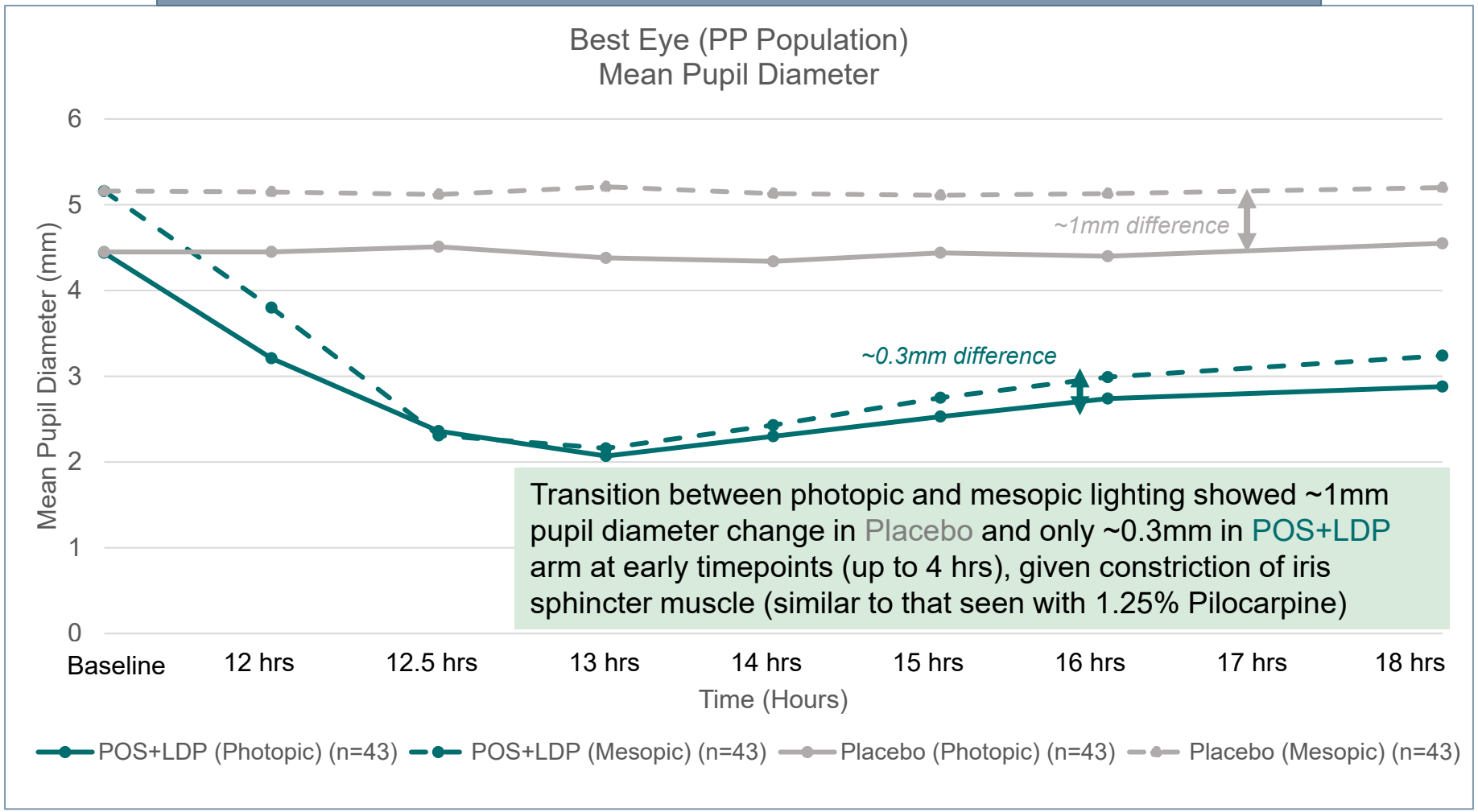


Note: PP population differs from mITT by only one subject; results were essentially identical.
Source: VEGA-1 Results

VEGA-1: Pupillary Light Reflex in POS+LDP

Addition of LDP to POS Diminished Pupillary Light Reflex

VEGA-1 Phase 2 Trial



Note: PP population differs from mITT by only one subject; results were essentially identical.

Source: VEGA-1 Results, Gemini-1 Results

Key Takeaways

- POS alone met planned P3 endpoint at 12 hours post-POS dose (29%; p=0.02), with at least 18 hours of sustained PD reduction
- POS+LDP Combination met planned P3 endpoint at 30 minutes post-LDP dose (or 12.5 hours post-POS dose) (61%; p<0.0001), with at least 18 hours of sustained PD reduction
- Favorable safety profile for POS Alone and POS + LDP Combination treatment
- POS alone allowed normal pupillary light reflex of ~1 mm change in mean pupil diameter when transitioning from photopic to mesopic conditions at all timepoints
- In comparison to POS alone treatment, pupillary light reflexes were diminished in combination arm due to the addition of 0.4% pilocarpine (LDP) that constricts iris sphincter muscle
  - This reduced pupillary light reflex is similarly seen in 1.25% pilocarpine presbyopia trials
  - These findings are clinically intuitive, as LDP's cholinergic mechanism causes strong constriction of the sphincter muscle, which is responsible for controlling the dynamic pupillary response
- These positive Phase 2 results in VEGA-1 allowed advancement into Phase 3 Program for two labels (POS and POS+LDP) with recruitment for VEGA-2 presbyopia trial ongoing

We thank all the VEGA-1 study participants, investigators and their staff !!!

Dr. Inder Paul Singh

VEGA-1 Clinical Trial Sponsor is Ocuphire Pharma

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