Phentolamine Mesylate
Topical Treatment for Night Vision Disturbances
Results from a Phase 2 Clinical Study

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Financial Disclosure

- I have the following financial interests or relationships to disclose:
  - Abbott Medical Optics: C;
  - AcuFocus, Inc.: C,O;
  - Alcon Laboratories, Inc.: C;
  - ArcScan: C,O;
  - Carl Zeiss Inc: C;
  - Clerio Vision: C,O;
  - Oculus, Inc.: C;
  - OcuPhire: C,O;
  - RX Vision: C,O;
  - M & S Technologies: C;
  - Visiometrics: C,O;
4 Million People in the US Suffer from NVDs

*No Approved Solution Yet*
Phentolamine Mesylate Eye Drop
A Non-Selective Alpha Antagonist

Mechanism of Action: Pupil Reduction and Vasodilation

Normal Eye

Phentolamine Treatment

α1 receptors
Dilator Muscles

α1 agonists
α1 antagonists

Dilated Artery
Normal Artery
Constricted Artery
Phentolamine Mesylate NVD Phase 2 Trial Design

\[ n = 120 \text{ eyes (60 subjects)} \]
Endpoints

**Primary Efficacy Endpoint**
- Percent of eyes with at least 50% (0.3 log) mesopic Contrast Sensitivity Function (CSF) improvement with glare at 2 or more frequencies (1.5, 3, 6, 12, 18 cpd)

**Secondary Endpoints**
- Pupil Diameter
- Mesopic Distance HCVA
- Mesopic Distance LCVA

**Safety Endpoints**
- Intraocular pressure (IOP)
- Eye redness
- Subjective comfort
- Heart rate and blood pressure
- Biomicroscopic and ophthalmoscopic examination
## Demographics

<table>
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<th>Trait</th>
<th>1.00%</th>
<th>0.50%</th>
<th>Placebo</th>
<th>Overall</th>
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<td><strong>Central Corneal Thickness Right Eye (microm)</strong></td>
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<td>Mean</td>
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</table>
Phentolamine Mesylate Clinical Efficacy: Pupil Size

*Treatment Induces Meaningful Pupil Size Reduction*

Pre-dose Pupil Diameter

Average Pupil Size (mm)±SE

- **1%**
- **Placebo**

† = p<0.001

*(Day 32 1.0% compared to Day 15 Placebo)*
Phentolamine Mesylate Clinical Efficacy: Contrast Sensitivity

CSF Improvements Seen at Two or More Frequencies in >30% of Eyes

Pre-Dose Contrast Sensitivity

Percent of Eyes with 0.3 log increase in CSF - Predose

Days

0 5 10 15 20 25 30 35 40

p=0.027  p=0.06  p=0.014

1% (n=40)

Placebo (n=38)

*(Day 32 1.0% compared to Day 15 Placebo)
Phentolamine Mesylate Clinical Efficacy: Duration of Effect

Pupil Size Reduction and CSF Improvements Lasts > 24 hours

Half-life of Effect = 2.0 days

\[ y = 1.585e^{-0.342t} \]

\[ R^2 = 0.9914 \]
Phentolamine Mesylate Clinical Efficacy: Visual Acuity

*2 Line Improvement in Mesopic Low Contrast VA in > 40% of Eyes*

Percent of Eyes with Improvement in Mesopic Low Contrast Visual Acuity

- One Line: p = 0.041*
- Two Lines: p = 0.028*
- Three Lines: p = 0.155

ETDRS Lines of Improvement

- 1% Day 32
- Placebo Day 15
Phentolamine Mesylate 1% Ophthalmic Solution

- Reduces pupil size by 15% in mesopic conditions
- Improves CSF for more than 24 hours in those with night vision disturbances who would benefit from a smaller pupil (i.e., night myopes, keratoconus, LASIK/PRK, IOLs, other non-cataractous causes)
- Improves mesopic low letter contrast visual acuity
- Causes mild, transient (6-8 hours) topical eye redness
- Has No Serious topical or systemic safety concerns
- Decreases IOP by 15% in normotensive subjects

The 2 day efficacy half-life of phentolamine mesylate allows 24 hour coverage without daytime redness with a once daily bedtime dose
Thank You!