



1

### Cecelia Koetting Financial Disclosures

"All relevant relationships have been mitigated."

- Orasis-C, S, R
- Trukera (B+L) -C
- PRN/EyePromise-C
- Tarsus-C,S,R
- Topcon-C
- Tenpoint-C
- Glaukos-C
- B +L- C, S, R
- Azura-C
- Dome-C,S,R
- Myze- C
- MOVU- C
- Vital Tears- C
- + SCOPE-C
- Viatris-C,R
- Allergan/Abbvie -C, R
- Alcon-C, S, R
- Harrow- C, S
- Blinkjoy-C
- Vicci- C

Intrepid

KOETTING

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## Continued growth

More options to better help our patients

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### FDA-Approved Myopia Management in the US

- **MySight 1 Day (CooperVision) — Dual-Focus Soft Contact Lens**
- FDA approved: November 2019
- Indication: Slowing myopia progression in children aged 8–12 years at initiation
- Mechanism: Dual-focus optics reduce peripheral hyperopic defocus
- Safety: No complications during monitoring over 6 years in children ages 8–12
- **Eyeglass Lenses: Essilor Stellest** lenses.
- FDA Approved in September 2025 for children aged 6 to 12
- specialized "lenslets" to create peripheral light defocus,
- Has been shown to reduce myopia progression by 71% on average

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### Low Dose Atropine CHAMP Study: U.S. Regulatory Data FDA did not approve in 2025

#### Study Design

- Phase 3 randomized controlled trial (NVK002) conducted across U.S. and European sites, comparing 0.01% and 0.02% atropine concentrations against placebo over 24 months.

#### Key Results

- 0.01% consistently slowed myopia progression with excellent safety profile. 0.02% showed mixed results with increased side effects, supporting lower concentration approach.

While the studies met their predefined statistical targets, regulators ruled the clinical impact on myopia was insufficient

Other studies:

LAMP: 0.05% concentration showed only 0.04mm additional axial length growth after cessation VS 1%

ATOM: 0.5% concentrations showed significant acceleration in myopia progression after cessation

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### Expansive Market of Presbyopes

If only 5% of presbyopes utilize presbyopia drops, the market is **~3 times larger** than the RX dry eye market

| Category   | Diagnosed                   | % Patients Rx-Treated | Total Patients |
|------------|-----------------------------|-----------------------|----------------|
| Dry Eye    | > 16.4 Million <sup>1</sup> | 10% <sup>2</sup>      | 1.64 Million   |
| Presbyopia | > 120 Million <sup>3</sup>  | 5%                    | 5+ Million     |

In a recent market research with over 400 Optometrists and Ophthalmologists, **70%** stated they expect to increase their use of presbyopia drops in the next three years.<sup>4</sup>

References: <sup>1</sup> Farnham et al. Prevalence of dry eye disease among adults in USA. AJO 2017;182:20-28  
<sup>2</sup> National Eye Survey. EyeNet 2022. Data on file. Novartis Pharmaceuticals Corp. May 2022  
<sup>3</sup> Poon et al. Global prevalence of presbyopia. Ophthalmology 2018;125:1460-1469  
<sup>4</sup> Market research - Nov 2022. Grass Pharmaceuticals. Data on file.

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**KC1** Finish fixing

Koetting, Cecelia, 2026-06-26T02:55:58.044

|                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                   |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>Pilocarpine 1.25%</li> <li>Brand Vuity</li> <li>Preserved with BAK</li> <li>Once daily dosing (approved for BID)</li> <li>Approx. 6 hour efficacy</li> <li>Strong clinical trial data for Presby correction, not so strong in practice</li> </ul> | <ul style="list-style-type: none"> <li>Pilocarpine 0.4%</li> <li>Brand Qlosi</li> <li>Preservative free formulation</li> <li>Contains HA and HPMC</li> <li>Better tolerated in OSD</li> <li>Up to BID dosing</li> <li>Approx 6-8 hour efficacy, some longer</li> </ul> | <ul style="list-style-type: none"> <li>Aceclidine 1.44%</li> <li>Brand Viziz</li> <li>Preservative free formulation</li> <li>Once day dosing</li> <li>Different receptor selectivity profile</li> <li>Reported Approx 10 hour efficacy</li> </ul> |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

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### Just to the Market

#### Carbachol 2.75% + Brimonidine 0.1% (Yuvezzi)- Tenpoint

#### Improving Near Vision Through Small Aperture Optics

**Carbachol**

Potent and durable pupil modulation<sup>2,3</sup>

Induces pupil constriction<sup>2,3</sup>

**Brimonidine Tartrate<sup>2,4,5</sup>**

Sympatholytic alpha-2 agonist<sup>2,4</sup>

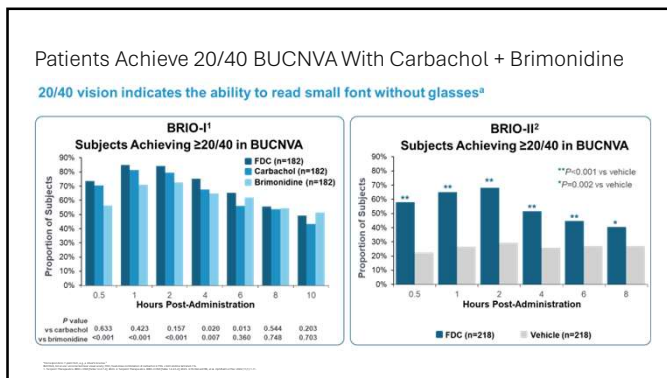
Inhibits pupil dilation<sup>2,4</sup>

Increases bioavailability of carbachol to prolong its effect<sup>2</sup>

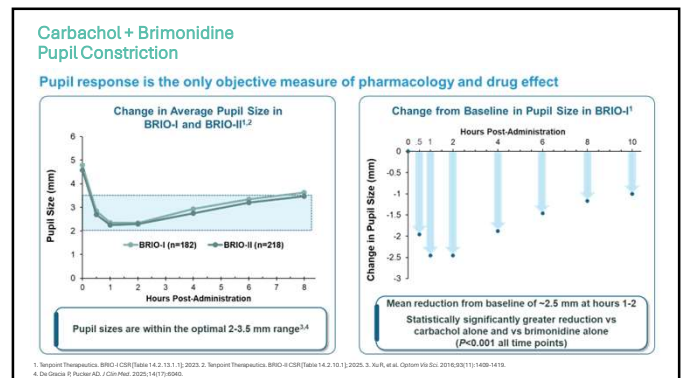
Relaxes tonic contraction of ciliary muscle, potentially mitigating side effects vs. carbachol alone<sup>6</sup>

© 2024 Tenpoint Therapeutics, Inc.  
1. Yuvezzi (Carbachol 2.75% + Brimonidine 0.1% Ophthalmic Solution) NDA 202-122-015, 2024. 2. Tenpoint Therapeutics, Inc. (2024) 3. Yuvezzi (Carbachol 2.75% + Brimonidine 0.1% Ophthalmic Solution) NDA 202-122-015, 2024. 4. Yuvezzi (Carbachol 2.75% + Brimonidine 0.1% Ophthalmic Solution) NDA 202-122-015, 2024. 5. Yuvezzi (Carbachol 2.75% + Brimonidine 0.1% Ophthalmic Solution) NDA 202-122-015, 2024. 6. Yuvezzi (Carbachol 2.75% + Brimonidine 0.1% Ophthalmic Solution) NDA 202-122-015, 2024.

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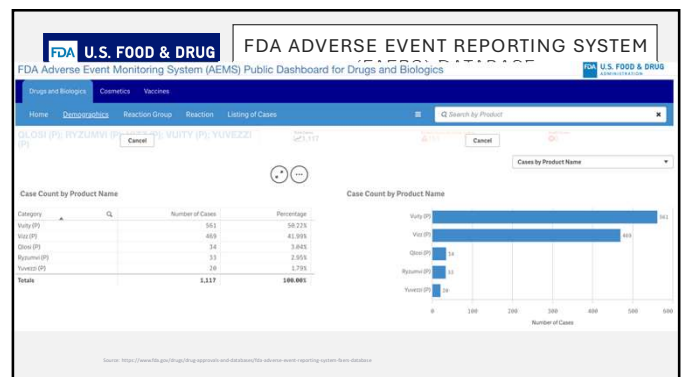
10

### Not Available . . . Yet..... Sort of

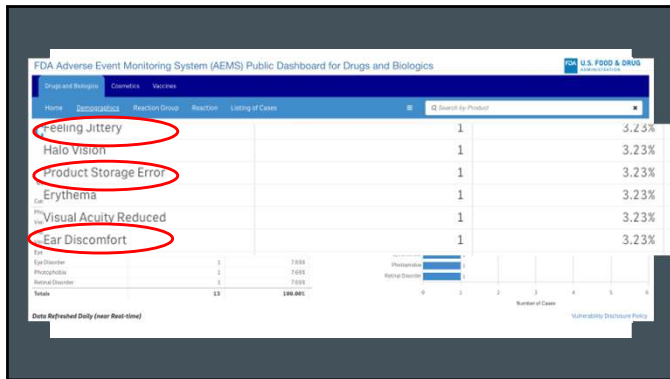
#### 0.75% phentolamine ophthalmic solution (Viatrix)

- Viatrix
  - 0.75% phentolamine
  - Nonselective alpha adrenergic antagonist that inhibits the contraction of smooth muscle of the iris, P
  - Ciliary Muscle sparing
- VEGA-3 Phase 3 Trial met primary endpoint 2025
  - Primary endpoints of 3 lines or more binocular NV gain with less than 5 letter loss at BCDVA at 12 hours on day 8 in 27.2% of patients vs 11.5% in placebo.
  - Minimal issues with Dim Light /low light environment
- Submission for FDA, filed with PDUFA date October 17, 2026
- Already FDA approved for mydriasis reversal.

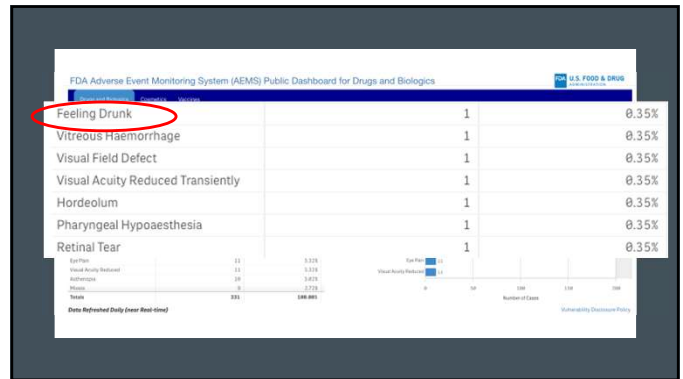
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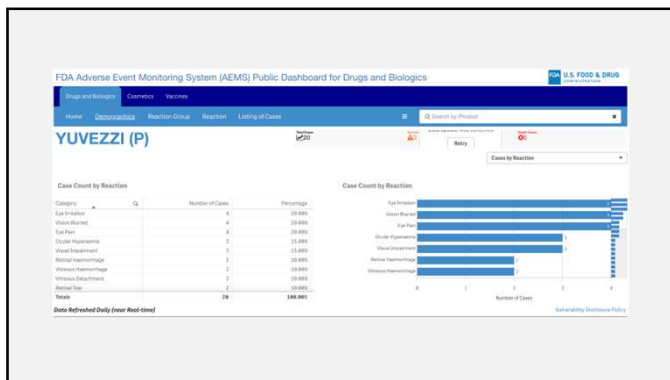
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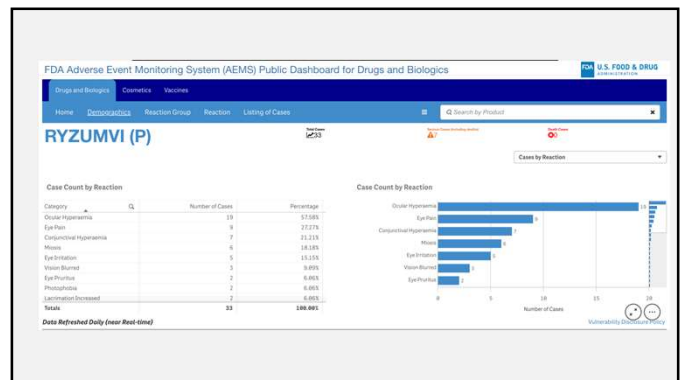
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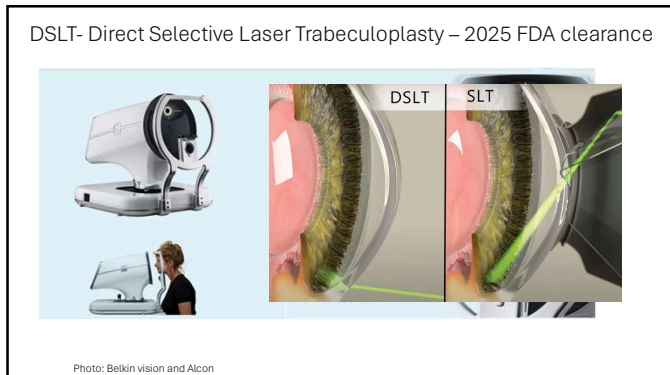
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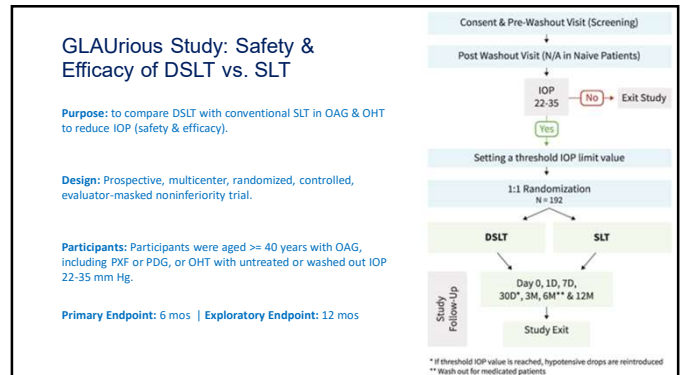
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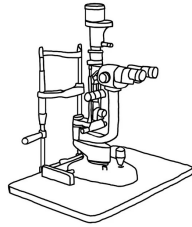
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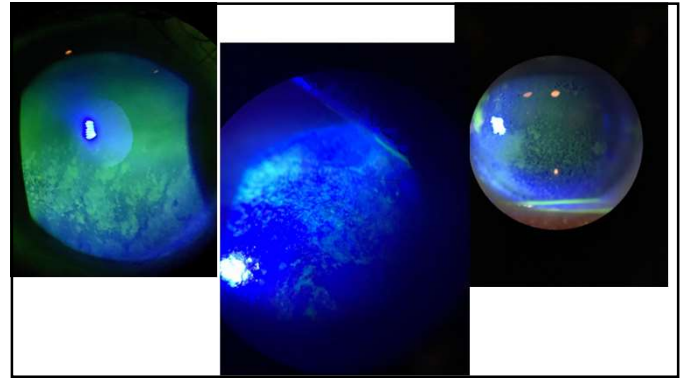
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## SLIT LAMP EXAM



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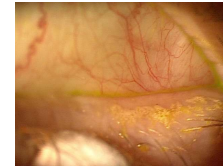
## Lid and Conjunctival Staining

- Lissamine Green
- Stains dead and degenerate cells
- Lid margin for lid wiper epitheliopathy
- Conjunctival staining

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## Express the Glands and Grade

- Express the Gland Using:
  - Cotton tip applicator
  - Your clean finger
  - Gland expressor
  - Meibomian gland evaluator
    - Just do it!
- Any pitting?
- Any capping?
- Any lid structure abnormality?



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## PRYSM iO from NuSkin

- Portable wellness device
- Designed to estimate antioxidant status using your fingertip
- You place your finger on the sensor
  - Device shines multiple wavelengths of light into the skin
- It analyzes light absorption patterns
  - AI/model compares this to a large database
- Outputs a score (the higher the better)
- Uses hyperspectral optical sensing (fancy spectroscopy-lite)
  - Tens of thousands to hundreds of thousands of measurements per scan

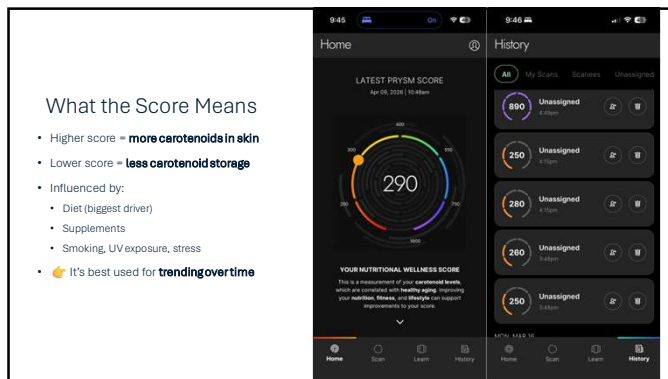


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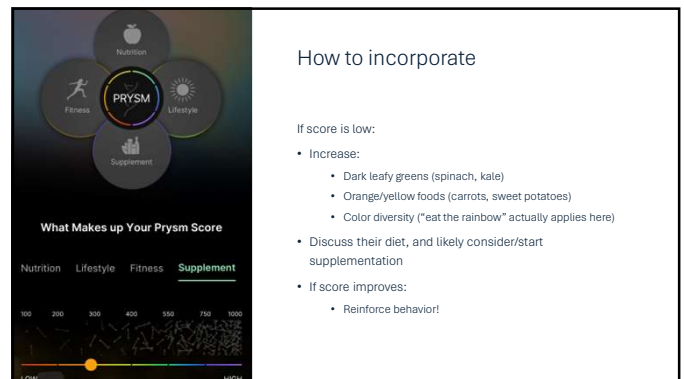
## Ok wait, what is it measuring?

- It does **NOT** measure antioxidants directly in blood
- It estimates **skin carotenoid levels**
- **What's legit**
  - Skin carotenoid measurement via spectroscopy **is real science**
  - Has been used in research settings
  - Correlates reasonably with serum carotenoids (not perfectly)
- Why carotenoids?
  - Found in fruits/veggies (beta-carotene, lutein, etc.)
  - Stored in skin
  - Correlate with diet quality and antioxidant intake
- 🍌 So it's basically a **proxy marker for diet**
- Use the Prysm iO score like:
  - A **nutrition** Fitbit
  - A **behavior** feedback loop
  - A **motivational** tool

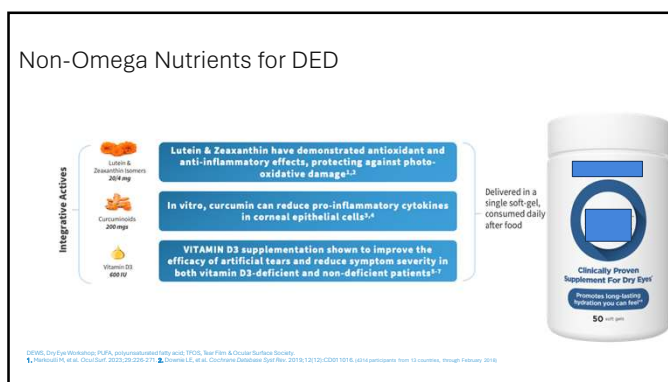
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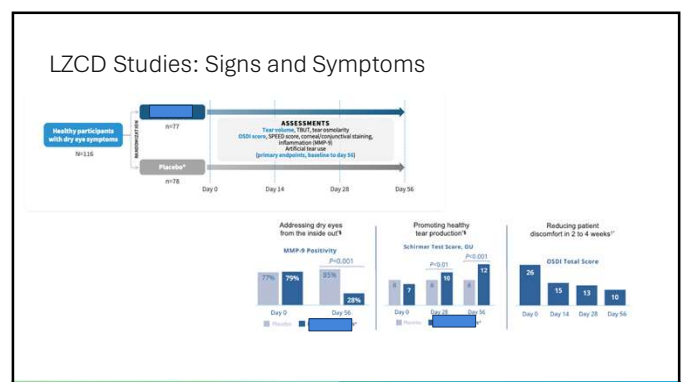
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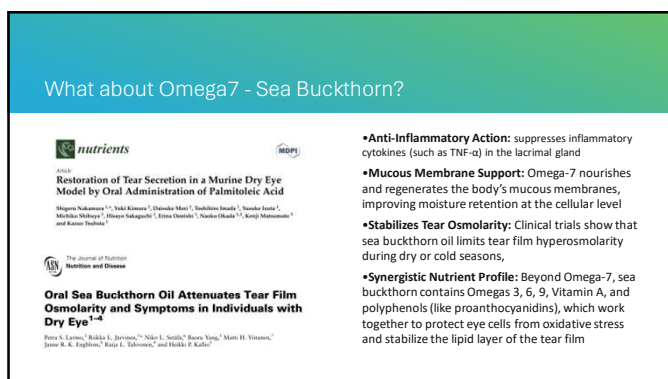
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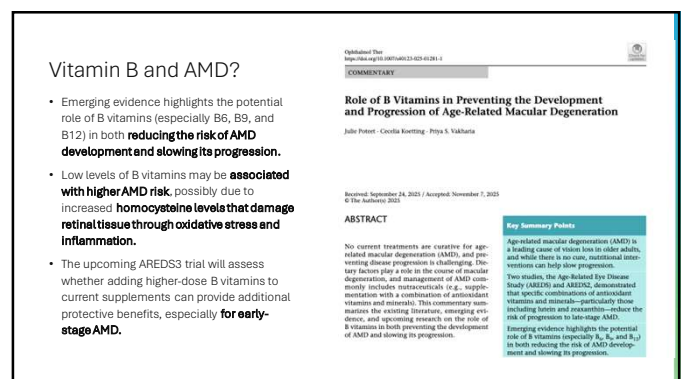
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## Demodex Blepharitis

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### Demodex Blepharitis is a *Large* Issue

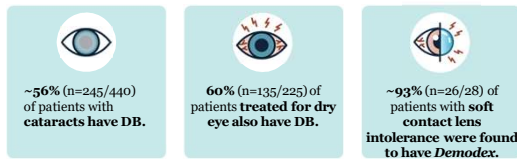
- ~45 million unique adult eye care professional visits/year
- ~20 million with blepharitis  
45% with *Demodex* infestation
- 2.1 million blepharitis ICD-10-CM diagnoses/year

Wilson FA et al. J Ophthalmol. 2015;2015:435606. Schaumborg DA et al. Invest Ophthalmol Vis Sci. 2011;52(4):1994-2005. American Optometric Association. Accessed September 15, 2025. <https://www.aao.org/AAO/Documents/Advocacy/HP/Treatment/200Options%20Blepharitis.pdf>. Primary Care Optometry News. Updated February 1, 1997. Accessed September 15, 2025. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4010000/>. Quiroz-Mercado H et al. Invest Ophthalmol Vis Sci. 2020;61(7):2984. Zhao Y-E et al. Ophthalmic Epidemiol. 2012;19(2):95-102. Symphony Claims Data Analysis.

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### Demodex Blepharitis (DB) is Highly Prevalent But Underdiagnosed

DB affects ~58% of eye care patients in the US  
That's approximately 25 million patients



Trautler W et al. Clin Ophthalmol. 2022;16:1153-1164. O'Dell L et al. Clin Ophthalmol. 2022;16:2979-2987. Tarkowski W et al. Biomed Res Int. 2015;2015:259109.

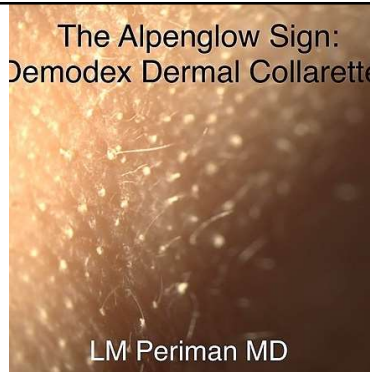
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**DON'T FORGET THE FACE: ALPENGLOW SIGN**

The Alpenglow Sign:  
Demodex Dermal Collarette



LM Periman MD

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### Start with the basics.... Eyelid hygiene!

- Few things actually work on Demodex
  - Antibiotics don't
  - Alcohol doesn't
  - Betadine doesn't
  - Baby shampoo for sure doesn't
  - HOCL doesn't
- BUT lid hygiene products with
  - Tea tree oil does
  - Okra extract does
  - Manuka honey does

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### Mānuka Honey

- Natural honey is well known for its anti-inflammatory and antimicrobial properties<sup>1,2</sup>
- Theory is because it has low pH, high osmolarity, hydrogen peroxide content, as well as non-peroxide constituents, including methylglyoxal<sup>2</sup>
- In recent years, New Zealand native Mānuka honey (*Leptospermum scoparium*) has received particular interest as a potential treatment for demodex blepharitis<sup>1</sup>
- Has higher concentration of methylglyoxal than other honeys<sup>1</sup>



Source: <https://www.gettyimages.com/detail/photo/bee-royalty-free-image/512586241?fromopenview=true>

1. Leung A, et al. *Innate Immun*. 2012;18:459-466. 2. Crisp JP, et al. *BMJ Open Ophthalmol*. 2017;1:e000065.

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## TRUSTED OPTIONS FROM TRUSTED BRANDS



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### Anti-demodectic effects of okra eyelid patch in *Demodex* blepharitis compared with tea tree oil

WENTING LI<sup>1,2</sup> and LAN QING<sup>1,2</sup>

<sup>1</sup>Department of Ophthalmology and Vision Science, The Eye, Ear, Nose and Throat Hospital of Fudan University; <sup>2</sup>NHC Key Laboratory of Myopia, Laboratory of Myopia, Chinese Academy of Medical Sciences, Fudan University, Shanghai 200031, P.R. China

Received January 7, 2020; Accepted January 16, 2021

DOI: 10.1093/eye/eyz379

- Patients were randomized → okra eyelid patch treatment or TTO eye care patch treatment for 3 months

- Demodex* count, the OSDI score, MG expressibility and meibum quality, Schirmer I test, TBUT, and CFS
  - Determined prior to treatment and after 1 and 3 months of treatment

- The average survival time
  - Okra group was  $115.25 \pm 11.87$  minutes
  - Control group was  $378.75 \pm 37.94$  minutes ( $P < .01$ )
- After 3 months of okra eyelid patch treatment
  - Demodex* count was significantly reduced from  $10.15 \pm 4.53$  to  $1.30 \pm 1.41$  ( $P < .01$ )
  - OSDI score of the patients was reduced by  $16.84 \pm 10.17$  ( $P < .01$ )
- No significant difference
  - In the *Demodex* count ( $P = .716$ ) and OSDI ( $P = .873$ ) between the treatment and control groups
- Okra eyelid patch treatment significantly eradicate ocular *Demodex* as well as markedly alleviate ocular symptoms
- Due to causing less irritation than TTO, the okra eyelid patch may be more suitable for sensitive patients with *Demodex* blepharitis

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Cleaning may help control recurrence but Rx needs help!

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## 2025 DEPTH Expert Consensus on Treatment for Demodex Blepharitis

Clinical Ophthalmology

Dovepress

### The Demodex Expert Panel on Treatment and Eyelid Health (DEPTH) Consensus Regarding the Preferred Treatment for Demodex Blepharitis

Eric Dornfeld<sup>1</sup>, Kelly K. Nichols<sup>2</sup>, Brandon D. Agnew<sup>3</sup>, Marjan Farid<sup>4</sup>, Preema K. Gupta<sup>5,6</sup>, Richard Lyndon Linker<sup>7</sup>, Stephen Pflugfelder<sup>8</sup>, Christopher E. Sloan<sup>9</sup>, Nandini Venkateswarar<sup>10</sup>, Ian Benjamin Goldberg<sup>11</sup>, Paul H. Karpman<sup>12</sup>, Caroline Koenig<sup>13</sup>, Jaime McGee<sup>14</sup>, Laure H. Periman<sup>15</sup>, Elizabeth Yu<sup>16</sup>

- Experts achieved consensus on the use of lotilaner ophthalmic solution, 0.25% as the **first-line treatment** for patients with DB.
- Panelists also agreed that blepharoxfoliation or IPL therapy could serve supplementally to lotilaner ophthalmic solution, 0.25%, if needed.

47 Dornfeld, Eric, et al. "The Demodex Expert Panel on Treatment and Eyelid Health (DEPTH) Consensus Regarding the Preferred Treatment for Demodex Blepharitis." *Clinical Ophthalmology* (2025): 1893-1904.

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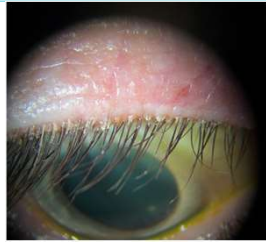
## Mechanism of Action: Lotilaner Ophthalmic Solution 0.25%

- Lotilaner is a gamma-aminobutyric acid (GABA)-gated chloride channel inhibitor selective for mites. Inhibition of these GABA chloride channels causes a paralytic action in the target invertebrate organism, leading to its death.
  - Works only on hatched ADULT demodex, not the eggs
  - So must finish the course- 6 weeks, 2 life cycles
- The lipophilic nature of the drop may promote its uptake in the oily sebum of the eyelash follicles where the mites reside.

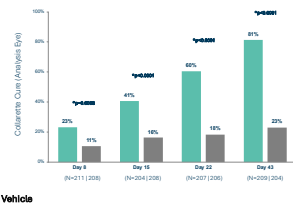
Lotilaner. Tarsus; 2023. Accessed September 15, 2025. <https://tarsusrx.com/wp-content/uploads/XDEMY-Precribing-Information-24JUL23.pdf>  
Gonzalez-Salinas R, et al. *J Ocul Pharmacol Ther*. 2021;37(8):479-484. You E, et al. *Cornea*. 2023;42(4):435-443.  
Toulain CE, et al. *Parasit Vectors*. 2017;10(1):522.

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## Clinically Meaningful Collarette Cure



Clinically Meaningful Collarette Cure  
Grade 0-1 (no more than 10 collarettes)



Average baseline collarette grade = 2.8 in both TP-03 and vehicle groups

## MG Atrophy in Patients With Demodex Blepharitis

### Purpose

MG atrophy and Demodex blepharitis are both common in the cataract-aged population; however, the relationship between the 2 conditions was not previously studied. The purpose of this study was to explore the characteristics of MG atrophy in the presence and absence of collarettes, the pathognomonic sign of Demodex blepharitis, in patients with cataract comorbidity.

### Methods

- Records of consecutive patients presenting for cataract surgery from December 2021–July 2022 were reviewed retrospectively.
- The presence and severity of collarettes, MG atrophy on meibography (LipScan), meibum quality, meibum expressibility, and telangiectasia were evaluated and graded using clinical grading scales (Table 1).
- LipScan grading was performed blindly and independently by 2 investigating clinicians.
- Descriptive analyses were performed with additional analyses controlling for age and sex of subjects.

Table 1. Grading scales of collarettes and different parameters in evaluating MG structure

| Clinical parameter                   | Grading scale                                                                                                                                                                                         |
|--------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1. Collarette (scale 0–4)            | 0 = 0–2 lashes have collarettes<br>1 = 3–10 lashes have collarettes<br>2 = > 10 but < 1/3 lashes have collarettes<br>3 = ≥ 2/3 but < 1/2 lashes have collarettes<br>4 = ≥ 2/3 lashes have collarettes |
| 2. Amount of atrophy (scale 0–3)     | 0 = no atrophy<br>1 = 1%–33% atrophy<br>2 = 34%–66% atrophy<br>3 = > 66% atrophy                                                                                                                      |
| 3. Meibum quality (scale 1–4)        | 1 = olive oil (clear liquid)<br>2 = cloudy<br>3 = cloudy with debris<br>4 = toothpaste-like                                                                                                           |
| 4. Meibum expressibility (scale 1–3) | 1 = easy<br>2 = moderate<br>3 = difficult                                                                                                                                                             |
| 5. Telangiectasia score (scale 0–4)  | 0 = no findings<br>1 = mild telangiectasia<br>2 = moderate telangiectasia<br>3 = severe telangiectasia<br>4 = florid telangiectasia                                                                   |

### Results

- A total of 420 patients with mean age 67.6 ± 9.6 years and 65% female were included.
- Eyes with collarettes had significantly higher amount of MG atrophy (1.744 ± 1.01) than eyes without collarettes (1.46 ± 0.94,  $P = .002$ ) and more telangiectasia ( $P < .001$ ) (Figure 2).
- Eyes with clinical meaningful sign of Demodex blepharitis (> 10 lashes with collarettes, or grade 2–4) had significantly more MG atrophy ( $P < .001$ ), and poorer meibum quality ( $P = .031$ ) than eyes without collarettes (Figure 3).
- No difference in meibum expressibility was observed in eyes with or without collarettes.
- Analyses controlling for age and sex yielded similar results.

Koetting C, Yeu E. Meibomian gland atrophy in patients with Demodex blepharitis. Poster presented at: American Academy of Ophthalmology 2022; October 28–29, 2022, San Diego, CA.

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## MG Atrophy in Patients With Demodex Blepharitis (continued)

Figure 1. Proportions of patients in collarette grades of 0–4 (N = 420)

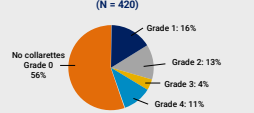


Table 2. Summary of mean (± SD) values of clinical parameters of MG structure at collarette grades of 0–4

| Collarette grade (0–4) | Telangiectasia score (0–4) | Meibum scale (1–4) | Meibum expressibility (1–3) | LipScan atrophy (0–4) |
|------------------------|----------------------------|--------------------|-----------------------------|-----------------------|
| 0                      | 0.95 (± 0.95)              | 2.12 (± 0.82)      | 2.02 (± 0.53)               | 1.46 (± 0.94)         |
| 1                      | 1.13 (± 0.84)              | 2.18 (± 0.79)      | 1.90 (± 0.59)               | 1.63 (± 1.05)         |
| 2                      | 1.28 (± 0.97)              | 2.29 (± 0.65)      | 2.10 (± 0.59)               | 1.61 (± 0.91)         |
| 3                      | 1.78 (± 0.94)              | 2.59 (± 0.71)      | 2.18 (± 0.53)               | 1.94 (± 1.08)         |
| 4                      | 1.79 (± 0.95)              | 2.37 (± 0.75)      | 2.05 (± 0.57)               | 1.98 (± 1.08)         |

Figure 2. Analyses results in eyes with or without collarettes

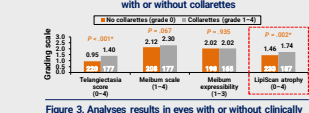
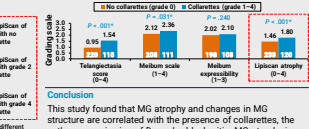


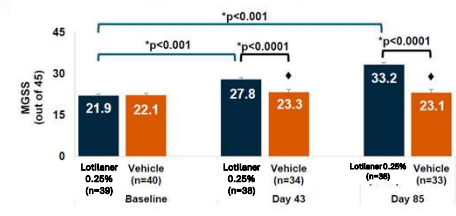
Figure 3. Analyses results in eyes with or without clinically meaningful sign of Demodex blepharitis (collarettes grade 2–4)



**Conclusion**  
This study found that MG atrophy and changes in MG structure are correlated with the presence of collarettes, the pathognomonic sign of Demodex blepharitis. MG atrophy is the leading cause of MG.

## NEW: ERSA and RHEA: MGSS score

Figure 3. Meibomian Gland Secretion Score (MGSS)

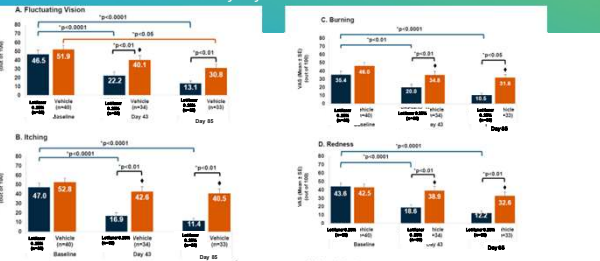


\*p<0.1 compared to baseline

Gaddie IB et al. American Academy of Ophthalmology, November 6–8, 2024; Indianapolis, IN, Poster #197.

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## NEW: ERSA and RHEA: Dry Eye on VAS



Gaddie IB et al. American Academy of Ophthalmology, November 6–8, 2024; Indianapolis, IN, Poster #197.

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## Systematic Review of Bacterial and Fungal Co-Infection in Patients with Demodex Blepharitis

Presenting Author: Cecelia Koetting, OD, FAAO<sup>1</sup>

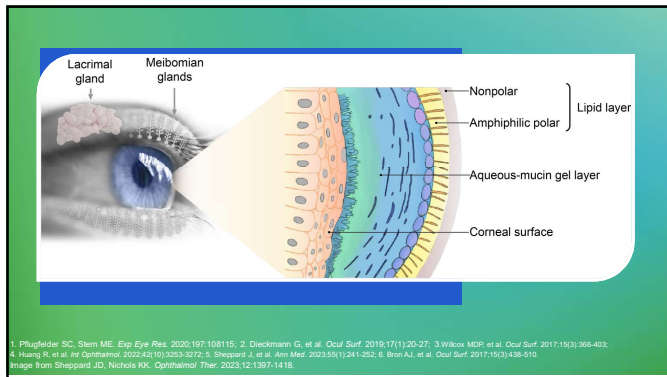
Coauthors: Eric Rosenberg, DO<sup>2</sup>; Nicole Fram, MD<sup>3</sup>; James Mun, PhD<sup>4</sup>

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### Lacrimal Functional Unit (LFU)

- Basal tear film production is regulated by the lacrimal functional unit (LFU), which is comprised of:
  - Lacrimal Glands
  - Meibomian glands
  - Goblet cells
- BUT ALSO
  - Cornea
  - Conjunctiva
  - Neural Network
- LFU innervated by the trigeminal nerve

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### WHO RUNS THE LFU SHOW? CORNEAL AND NASAL NERVES

- Trigeminal nerve CNV: sensory sensory sensory with a little motor
- Has 3 branches
  - V1, V2, V3
  - V2 supplies sensory function to the forehead, cornea AND nasal
- CNV is accessible within the nasal cavity
  - Parasympathetic stimulation of the LFU activates basal tear production
  - 34% of basal tear production is due to inhaling air through the nose.

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### Corneal Sensory Nerves

**Cold thermoreceptors monitor for changes to the tear film and regulate basal tear production<sup>1,3</sup>**

**Polymodal nociceptors detect and warn of irritating and harmful stimuli and produce reflex tears<sup>4-8</sup>**

1. Wang, J. et al. *Invest Ophthalmol Vis Sci.* 2010;51(10):3969-3976. 2. Belmonte C et al. *Invest Ophthalmol Vis Sci.* 2011;52(6):3888-3892. 3. Parra A et al. *Air Med.* 2010;16(12):1396-1399. 4. Quillo T et al. *Air Commun.* 2015;6:7150.

64

### Corneal Sensory: Reflex Tear vs Basal Tear

**Noxious Heat<sup>1</sup>**

TRPV1, TRPA1

**Polymodal Nociceptor<sup>1</sup>**

Detect: Noxious chemical, thermal, and mechanical stimuli

**Response: Irritation and pain, reflex tearing<sup>5-7</sup>**

**Cool/Cold<sup>2</sup>**

TRPM8

**Cold Thermoreceptor<sup>1</sup>**

Stimuli: Evaporative cooling, increasing osmolarity<sup>5,2,8</sup>

**Response: Cool/cold sensation, basal tear production<sup>1,3</sup>**

TRPA1, nociceptive receptor potential ankyrin 1; TRPV1, nociceptive receptor potential vanilloid 1; TRPM8, nociceptive receptor potential melastatin 8. 1. Belmonte C et al. *Invest Ophthalmol Vis Sci.* 2011;52(6):3888-3892. 2. Belmonte C et al. *Invest Ophthalmol Vis Sci.* 2011;52(6):3888-3892. 3. Parra A et al. *Air Med.* 2010;16(12):1396-1399. 4. Quillo T et al. *Air Commun.* 2015;6:7150. 5. Wang, J. et al. *Invest Ophthalmol Vis Sci.* 2010;51(10):3969-3976. 6. Belmonte C et al. *Invest Ophthalmol Vis Sci.* 2011;52(6):3888-3892. 7. Parra A et al. *Air Med.* 2010;16(12):1396-1399. 8. Quillo T et al. *Air Commun.* 2015;6:7150.

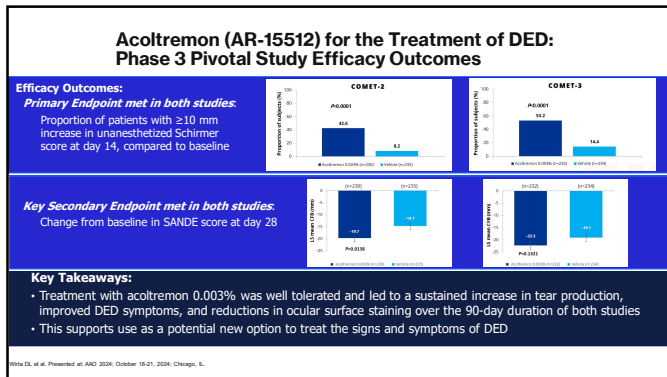
65

### FDA Approved June 2025: Acoltremon (AR-15512) Ophthalmic Solution 0.003%

- Transient receptor potential melastatin 8 (TRPM8) receptors are expressed on trigeminal sensory nerve terminals in corneal epithelium
- TRPM8 receptors are stimulated by ocular surface cooling and increased tear osmolarity associated with tear evaporation to regulate basal tear production<sup>1-4</sup>

1. Hirata H et al. *Invest Ophthalmol Vis Sci.* 2010;51(10):3969-3976. 2. Belmonte C et al. *Invest Ophthalmol Vis Sci.* 2011;52(6):3888-3892. 3. Parra A et al. *Air Med.* 2010;16(12):1396-1399. 4. Quillo T et al. *Air Commun.* 2015;6:7150.

66



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### Compounding Benefits

- Preservative free options
- Or less preservatives\*\*
- Differing concentrations
- Medications that wouldn't otherwise be formulated for the eye
- Sometimes cheaper than traditional Rx
- Decreased treatment burden

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Not your mama's compounding pharmacy

|                                       |                               |                                      |
|---------------------------------------|-------------------------------|--------------------------------------|
| Post-operative medications            | Glaucoma medications          | Myopia management and dilation drops |
| Preservative free compounded steroids | Topical compounded tacrolimus | Compounded losartan                  |
| Compounded insulin                    | Compounded cyclosporine       | Compounded antibiotics               |
| Compounded Antifungals                | Mitomycin-C                   |                                      |

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### Autologous Serum is a biologic

**PLATELET RICH PLASMA**

**PLATELET POOR PLASMA**

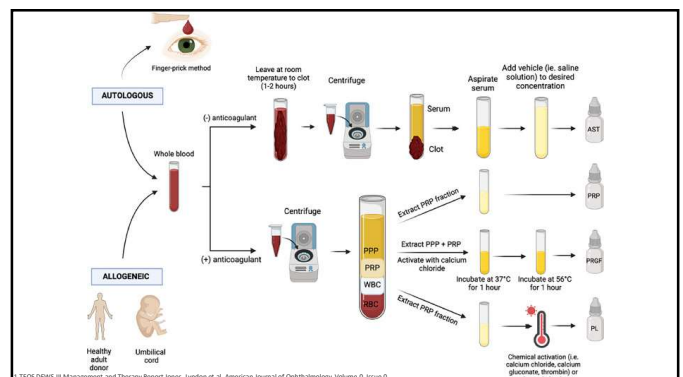
**RED BLOOD CELLS**

70

### BENEFITS OF BIOLOGICS

- Neurosensory Repair = Growth factors (Epitheliotropic)
- Anti-inflammatory = Cytokines
- Prevent Infections = Immunoglobulins/Proteins
- Repair Osmolarity = Dilute proinflammatory mediators
- Natural Analgesic Actions = Reduces pain
- Resembles biological tears = pH/osmolarity
- No preservatives/stabilizers
- No side effects = No burning or stinging

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## ASED VS PRP?

### ASED

- Does NOT contain platelets
- Less concentration of GF/Plasma factors
- Serum is not plasma
- Has inflammatory cytokines
- Contains high amounts of TGF-Beta – suppress wound healing
- Diluted with saline (20-50%) to reduce inflammatory cytokines (further dilutes GF)

### PRP

- PRP contains Platelets
- Contains higher concentration of growth factors
- GF released in a biologically relevant ratio
- Does not contain inflammatory cytokines
- Not diluted with saline
- Dispensed 100%
- PRP is used in medicine and dentistry

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## ASED VS PRP VS PRGF

| Feature / Property              | ASED (Autologous Serum Eye Drops)                                          | PRP (Platelet-Rich Plasma)                                                 | PRGF (Plasma Rich in Growth Factors)                                                                       |
|---------------------------------|----------------------------------------------------------------------------|----------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|
| <b>Source</b>                   | Patient's whole blood, serum isolated after clotting                       | Patient's blood, centrifuged to concentrate platelets (not activated)      | Patient's blood, centrifuged and processed to release growth factors (activated platelets, fibrin removed) |
| <b>Cellular Components</b>      | Cell-free serum (no platelets, no leukocytes)                              | Contains platelets (may release growth factors over time)                  | Platelet-derived growth factors, minimal leukocytes/fibrin (cleaner prep)                                  |
| <b>Growth Factor Profile</b>    | Baseline serum levels (EGF, TGF-β, fibronectin, vitronectin, IgG, albumin) | Higher levels of PDGF, VEGF, TGF-β, bFGF from platelets                    | Optimized mix of platelet-derived growth factors, more consistent concentrations                           |
| <b>Biological Activity</b>      | Mimics natural tear composition, supports epithelial healing               | Stronger wound healing and anti-inflammatory effect, but less standardized | Potent epithelial and stromal healing activity, standardized prep increases reproducibility                |
| <b>Stability (Frozen)</b>       | Stable up to 6 months (-20 °C) or longer at -80 °C                         | Stable up to ~12 months (-20 °C)                                           | Stable up to 9-12 months (-20 °C), retains potency and stability                                           |
| <b>Stability (Refrigerated)</b> | Discard after 7-10 days due to stability concerns                          | Some studies: up to 4 weeks, but not widely accepted clinically            | Demonstrated stability up to 7 days in-use, research suggests up to several days at room temp              |
| <b>Main Clinical Uses</b>       | Severe dry eye, neurotrophic keratitis, ocular surface disease             | Corneal ulcers, epithelial defects, severe dry eye, post surgical healing  | Similar to PRP but marketed as more standardized: epithelial defects, ulcers, keratoconjunctivitis sicca   |
| <b>Advantages</b>               | Most studied, mimics tear composition, safe                                | Rich in platelets → more growth factors, enhanced healing                  | More controlled prep, reduced fibrin/leukocytes, reproducible growth factor concentration                  |
| <b>Limitations</b>              | Lower concentration of growth factors vs platelet prep                     | Variability in prep methods, platelet degradation risk                     | Proprietary systems required, higher cost                                                                  |

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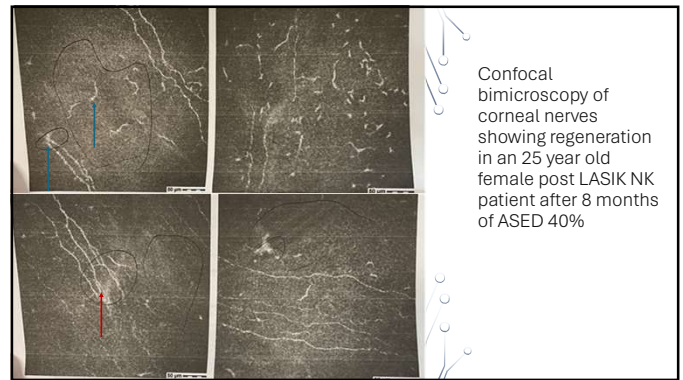
## AUTOLOGOUS SERUM TEARS FOR NK

Matsumoto et al 2004

Complete healing of all the 14 eyes with NK treated with autologous serum drops and an increase in corneal sensitivity in 64.2% of cases

The study demonstrated that serum harbors neurotrophins and growth factors to the ocular surface.

More recent studies confirmed that autologous serum eye drops allowed high rates of corneal healing, and also the improvement of corneal nerve morphology with increased number, length, width, and density



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## Acanthamoeba May 2024- 15 YOA female

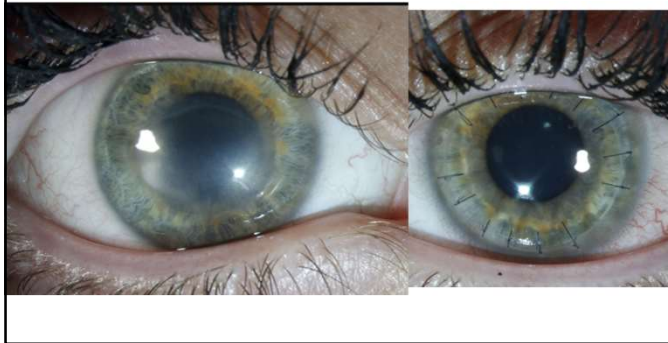
- Presents for initial evaluation to my OSD clinic
- History:
  - Acanthamoeba bilateral infection May 2024, Hot tub Contact lenses.
  - S/p corneal biopsy with AMT OS- 7/26/2024
  - S/p Penetrating keratoplasty, OS- 10/30/2024
- Patient reports vision stable, currently using scleral CL in the right eye fit recently
- Left eye with clear graft on exam no signs of infection or rejection - few loose sutures



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## 4 months Compounded Topical Losartan



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### Topical Compounded Losartan

- An angiotensin II receptor blocker (ARB)
  - Typically for high blood pressure, reduce the risk of stroke in patients with an enlarged heart, and protect the kidneys in people with type 2 diabetes
- Compounded topical losartan exerts its antifibrotic effect in corneal scarring
- Acts as a **surrogate for the epithelial basement membrane** suppressing TGF-β-directed scarring until the EBM regenerates and re-establishes its own control over TGF-β passage into the stroma
  - Phase 1 — Myofibroblast elimination (days to ~2 weeks)**
  - Phase 2 — Stromal remodeling (weeks to months)**

Journal of Clinical and Experimental Ophthalmology 2023;203:505-508  
https://doi.org/10.1093/oxfordjournals/jceoph.a012104

**REVIEW ARTICLE**

#### Topical losartan ophthalmic drops – a review of corneal wound healing and topical losartan for managing corneal haze and potential future indications

Mariam Abdelghaffar<sup>1</sup>, José Luis Güell<sup>2,3</sup>, Nuno Moura Coelho<sup>4,5</sup>

Received: 27 July 2024 / Revised: 2 December 2024 / Accepted: 7 December 2024 / Published online: 12 December 2024  
© The Author(s), under exclusive license to Springer Verlag GmbH Germany, part of Springer Nature 2024

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## Meibomian Gland Dysfunction and Evaporative DED

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### Compounded Vitamin D

- 2024, 56 patients
- Double arm randomized vitamin D drops vs placebo 8 weeks
- All enrolled had MGD, evaluated OSDI, corneal and conjunctival staining, Schirmer, TBUT and MGYS
- Statistically significant improvement in all but conj staining
- Utilized 1000 IU/ml (25ug/mL)

Journal of Clinical and Experimental Ophthalmology

#### Safety and Efficacy of Topical Vitamin D in the Management of Dry Eye Disease Associated With Meibomian Gland Dysfunction: A Placebo-Controlled Double-Blind Randomized Controlled Trial

Kamal Hassanpour, MD, MPH<sup>1,2</sup>, Farid Langer, MD<sup>3</sup>, Amir Rezaei Akbari, PhD<sup>4</sup>, Farid Karimian, MD, MPH<sup>5</sup>, Hamid Javadi, MD<sup>6</sup>, and Mohammad-Mehdi Shamschi, MD<sup>7</sup>

**Purpose:** The aim of this study was to evaluate the safety and efficacy of topical vitamin D in the management of dry eye disease associated with meibomian gland dysfunction (MGD).

**Methods:** In this randomized, controlled, double-blind, placebo-controlled trial, 56 patients with MGD were divided into two groups: vitamin D (1000 IU/mL) and placebo. The primary endpoint was the change in the OSDI score at 8 weeks. Secondary endpoints included changes in corneal and conjunctival staining, Schirmer, TBUT, and MGYS.

**Results:** The study included 56 patients (28 in each group). The OSDI score significantly improved in the vitamin D group compared to the placebo group at 8 weeks. There were no significant differences in the other endpoints.

**Conclusion:** Topical vitamin D (1000 IU/mL) is safe and effective in the management of dry eye disease associated with MGD.

**Keywords:** dry eye disease, meibomian gland dysfunction, vitamin D, OSDI, Schirmer, TBUT, MGYS.

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### What about hydrocortisone?

- Currently used outside US as ophthalmic drop
- Mild non-infectious allergic or inflammatory conjunctival diseases.
- Low intraocular penetration (1.5-3%),
- Low systemic penetration (<2% of applied dose)
- No significant risk of a rise in intraocular pressure (IOP).
- Phase 4 2021 study completed looking at use for MGD
- Phase 4 2025 study completed looking at use for MGD
- No current commercially available product OTC or Rx

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### 100% Perfluor For treatment of symptoms associated with MGD

#### Perioperative Use of Perfluorohexyloctane Ophthalmic Solution in Patients With Dry Eye Disease Undergoing Cataract Surgery

Journal of Clinical and Experimental Ophthalmology 2023;203:505-508

**INTRODUCTION**

Dry eye disease (DED) is a common condition characterized by insufficient tear production and/or excessive tear evaporation, leading to ocular discomfort and visual impairment. In patients undergoing cataract surgery, DED can exacerbate postoperative inflammation and delay healing. Perfluorohexyloctane (PFHO) is a novel ophthalmic solution that has been shown to improve tear film stability and reduce inflammation in patients with DED.

**OBJECTIVES**

The purpose of this study was to evaluate the safety and efficacy of PFHO in patients with DED undergoing cataract surgery. The primary endpoint was the change in the OSDI score at 4 weeks. Secondary endpoints included changes in corneal and conjunctival staining, Schirmer, TBUT, and MGYS.

**RESULTS**

The study included 100 patients (50 in each group). The OSDI score significantly improved in the PFHO group compared to the placebo group at 4 weeks. There were no significant differences in the other endpoints.

**CONCLUSIONS**

Perfluorohexyloctane (PFHO) is safe and effective in the management of dry eye disease associated with MGD.

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## What are Keratolytics?

Agents that soften and shed the skin epithelium or horny outer layer of skin through the process of breaking down keratin



Similar to the lid margin, secretory gland hyperkeratinization plays an important role in various skin disorders

Comedonal lesions in acne are inspissated hair follicles, filled with corneocytes, sebum, and other debris

Keratolytic treatments are used to shed dead corneocytes, loosen the sebum plug, and prevent the formation of inflammatory papules and pustules

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## AZR-MD-001 (SELENIUM SULFIDE) Triple MOA for the treatment of MGD

A potent keratolytic, with a unique MoA compared to traditional keratolytic agents, such as urea, AHA and BHA

**Keratostatic**  
Slows down both the rate of keratinocyte proliferation and keratin production<sup>1</sup>



**Keratolytic**  
Softens keratin plug by breaking down disulfide (S-S) bonds, alleviating hyperkeratinization that leads to blockage of Meibomian glands<sup>1</sup>



**Lipogenesis**  
Stimulates lipogenesis to increase the quantity of lipids produced by the Meibomian glands<sup>2</sup>



### AZR-MD-001 TRIPLE MOA

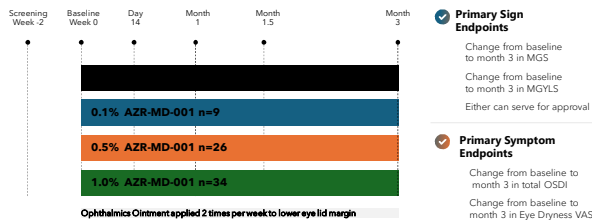
Decrease meibomian gland hyperkeratinization of ducts and orifices, loosen meibomian gland blockages, and increase secretion of meibomian gland lipids

<sup>1</sup>Data on file, Azura Ophthalmics. <sup>2</sup>Data on file, Azura Ophthalmics.

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## AZR-MD-001 Phase 2 program—Study design and overview

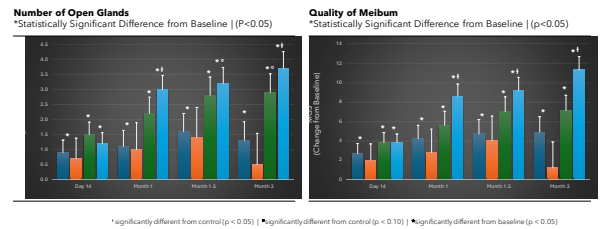
- Multicentre, randomized, double masked vehicle controlled clinical trial to evaluate safety and efficacy of signs and symptoms of meibomian gland dysfunction



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## Statistically significant improvement in signs

- Meibomian Gland Yielding Liquid Secretion (MGYS) and Meibomian Gland Score (MGS) – change from baseline



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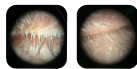
## NuLid Pro



NuLids PRO is a patented, automated device that operates by oscillation to professionally clean eyelids while massaging meibomian glands. A technician applies the single use tip onto the closed eyelids for 3 minutes.



NuLids PRO uniquely enables fast, effective, comfortable and affordable preventative care which is greatly needed for all but previously unavailable to practices.



Representative before and after results of a single NuLids PRO treatment. Exceptional eyelid and eyelash cleaning including complete elimination of collarettes.

82% more glands yielding clear liquid secretions after a 30 day course of home therapy.

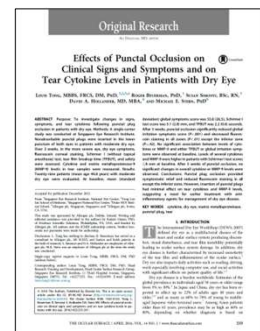
- In theory meibum is a non-Newtonian fluid which liquify quickly in the presence of increased shear forces
- Because NuLids applies sub-sonic vibration at a rate of 200Hz, it is ideal for transmitting vibrational energy through the closed eyelids through the MG's.

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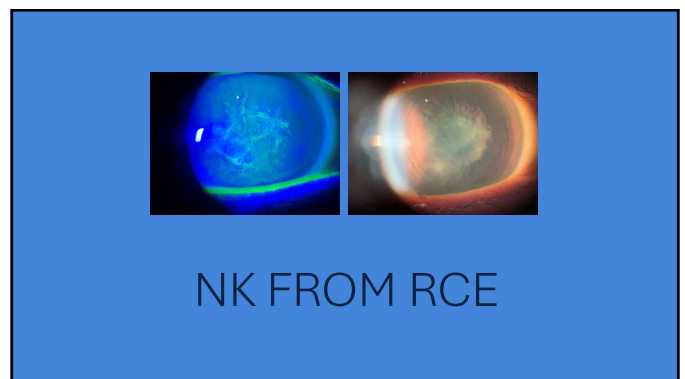
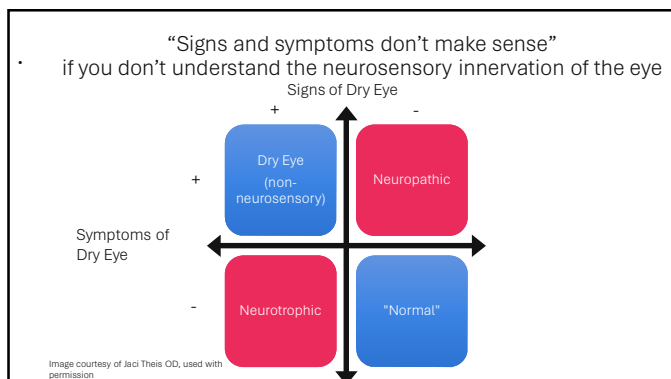
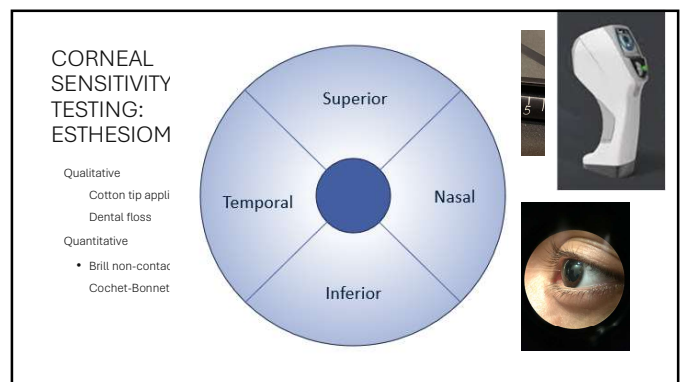
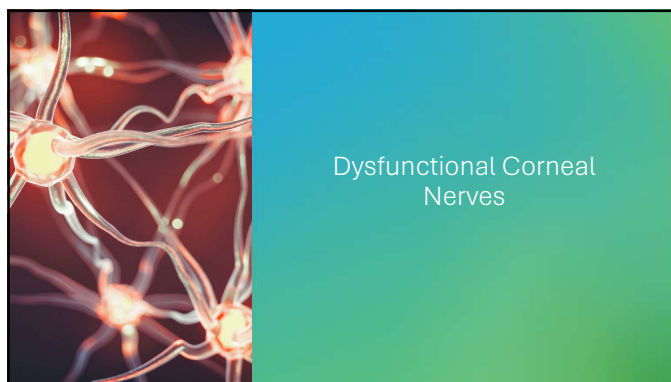
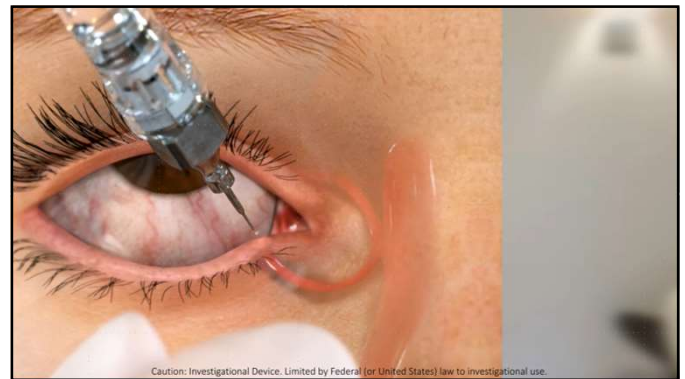
I was wrong. . . .Plugs don't worsen inflammation

After 3 weeks, punctal occlusion significantly reduced global irritation symptoms score ( $P < 0.001$ ) and decreased fluorescein staining in all zones ( $P < 0.01$ ) except the inferior zone ( $P = 0.42$ ).

After 3 weeks of punctal occlusion, no significant changes in overall cytokine or MMP-9 levels were observed.



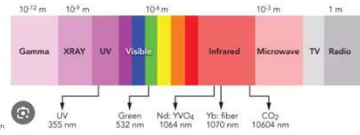
90





## Photobiomodulation (PBMT)

- Photobiology
  - Scientific discipline that studies the effects of light on living organisms and their biologic process
  - Phototherapy utilizes light waves lengths between 390-1100nm
  - May be pulsed or continuous waves
- Utilizing exposure of nonthermal red and infrared light for therapeutic benefits and functions by stimulating, healing, regenerating and protecting organizations at risk of injury degradation or death.
- Last 2 decades gained recognitions and increased use
  - Non-invasive physical therapy method
  - Pain relief
  - Anti-inflammatory response
  - Tissue regeneration



Markouli, M., Chandrasekhar, N., & Pappas, E. S. (2021). Photobiomodulation Overview Light. [https://doi.org/10.1007/978-1-4939-9888-8\\_1](https://doi.org/10.1007/978-1-4939-9888-8_1)

Paul, V., Kim, H., Kim, S., Cho, H. Effect of low-level light therapy in patients with dry eye: a prospective, randomized, observer-masked trial. *Sci Rep*. 2022 Mar 4;12(1):3275. doi: 10.1038/s41598-022-07427-0. PMID: 35260200. PMCID: PMC8881665

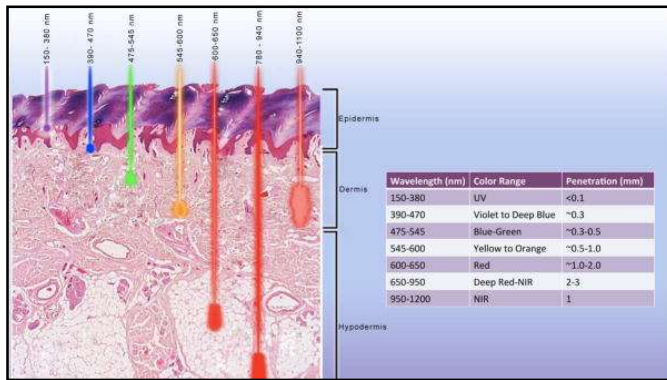
103

## DEVICES FOR LLLT/RED LIGHT THERAPY



- Well, go back to the Wild Wild West. . . . But here are a few things to give direction
- What are we looking for:
  - Good quality LEDs are quasimonochromatic with 98% of photons at the rated wavelength
  - Ensures all photons are travelling in approximately the same direction
- In Office
  - Optometric Aesthetics Ilight LLLT Pro
  - Essilor Marco Equinox LM LLLT
    - Essilor epi-c plus OPE IPL platform + Equinox
  - BioPhotus Celluma LLLT
  - MDElite Infinity Pro
    - Don't forget to use Ceramic goggles
- At Home devices
  - So many. . . . .

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## PHOTOBIMODULATION TREATMENT- VALEDA (LUMITHERA) FDA APPROVAL NOV 2024

- Treatment for vision loss in patients with intermediate dry AMD
- Low level light therapy
  - Targeted wavelength NIR 500-1000nm from light emitting diodes or laser
  - Creates chemical reaction at cellular level in electron transport channel- specifically enzyme cytochrome c oxidase within Complex IV
  - Increases mitochondrial activity in cells in retinal layers (RPE, ganglion cell nuclei, IPN, OPN) -> promotes ATP production
  - Also decreases NO activity increasing complex IV activity, creating PR improved function



Boyer D, Hu A, Wainrow D, Xavier S, Gonzalez V, Lad E, Rosen RB, Do D, Schneiderman Y, Ho A, Munk MR, Jaffe G, Tedford SE, Croissant CL, Walker M, Ruckert M, et al. CE. LIGHTSITE III: 12-Month Efficacy and Safety Evaluation of Multiwavelength Photobiomodulation in Nonexudative (Dry) Age-Related Macular Degeneration Using the Lumithera Valeda Light Delivery System. *Retina*. 2024 Mar 1;44(3):487-497. doi: 10.1097/AEE.0000000000003980. PMID: 37972955. PMCID: PMC7328355.

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## RETINAL PHOTOBIMODULATION

- Treatment indications:
  - Intermediate dry AMD with:
    - Visual acuity between 20/32-20/70
    - at least 3 medium drusen {> 63 µm and ≤ 125 µm in diameter), or large drusen {> 125µm in diameter)
  - The absence of neovascular maculopathy or center-involving geographic atrophy

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## RETINAL PHOTOBIMODULATION - LUMITHERA TRIALS

### LIGHTSITE III

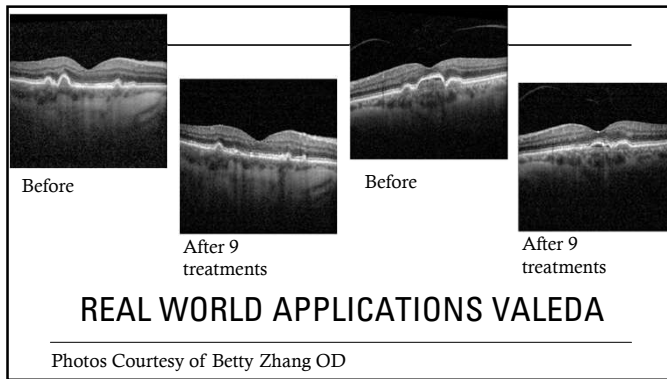
Double-masked, randomized, sham-controlled, parallel group, multi-center trial to assess the safety and efficacy of photobiomodulation (PBM) treatment with Valeda in subjects with dry age-related macular degeneration (AMD)

- Notable outcomes:
  - BCVA improvement
  - Decreased Drusen volume
  - Decreased incident GA

### BCVA Letter Gain Distribution at Month 21\*



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**Revakinagene taroretcel-lwey – Encapsulated implant (Encelto™)**

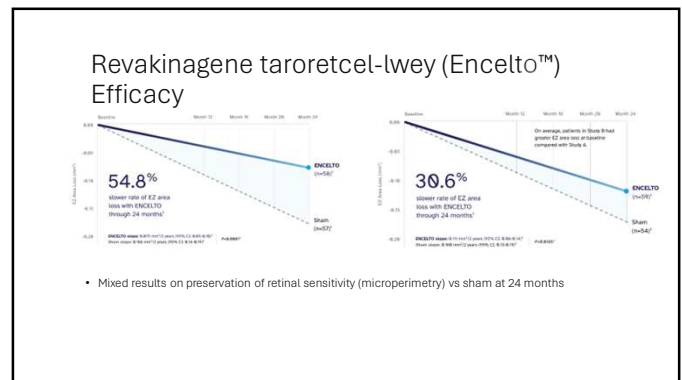
- A novel treatment for macular telangiectasia type 2 (MacTel type 2)
- MacTel Type 2 Pathophysiology review:
  - Acquired and bilateral
  - Chronic neurodegenerative process
    - loss of the outer nuclear layer and the ellipsoid zone
    - later formation of cyst-like cavitations
  - CNVM can be secondary complication

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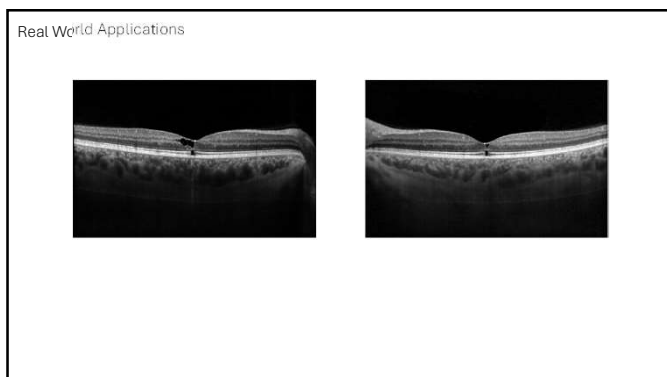
**Revakinagene taroretcel-lwey – Encapsulated implant (Encelto™)**

- **The Implant:** A specialized semi-permeable capsule, roughly the size of a grain of rice, is surgically implanted into the eye's vitreous cavity.
- **Genetically Modified Cells:** The capsule contains over 200,000 living, genetically engineered RPE cells
- **Continuous Protein Delivery:** These enclosed cells continuously produce and release a protein called recombinant human ciliary neurotrophic factor (rhCNTF).
- **Cell Protection:** The CNTF targets cells in the retina—particularly Müller glia—triggering a signaling cascade that protects light-sensing photoreceptors from dying off.
- The specialized capsule acts as a shield, allowing the therapeutic protein to pass through while keeping the living cells safe from the patient's immune system

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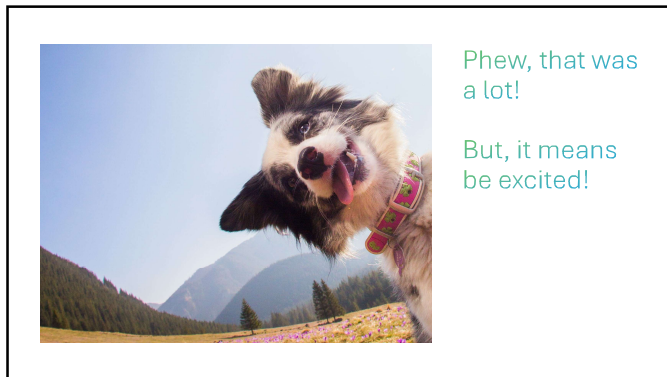


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**2025**  
**Ranibizumab**  
**100mg/mL**  
**implant**  
**FDA approval**

- Previously approved intravitreal injection anti-VEGF for nAMD, DME, and DR
- Now available as an IMPLANT
- Indication for for nAMD, Diabetic macular edema and Diabetic retinopathy
- Refillable
- Continuous release
- Fewer injection reduction of patient burden

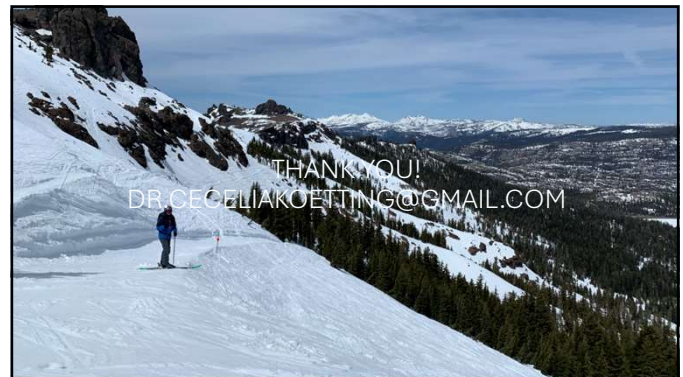
114



Phew, that was a lot!

But, it means be excited!

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### Ocular complications of GLP-1 agonists

- Non-insulin therapy for treatment of diabetes
- FDA-approved for weight
- Mechanism:
  - Increase insulin production
  - glucagon production
  - Delay stomach emptying



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### Ocular complications of GLP-1 agonists

- Blurred vision due to lenticular changes
- Typically resolves after 3-4 months
- Small percentage of users show worsening diabetic retinopathy and macular edema
- Mechanism not well understood
- Possible association with NAION
- Confounding variables and conflicting study results

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## RASP (Reactive Aldehyde Species)

### Pre-cytokine systems-based mediators of inflammation

- Covalently bind to cellular biomolecules on receptors and kinases

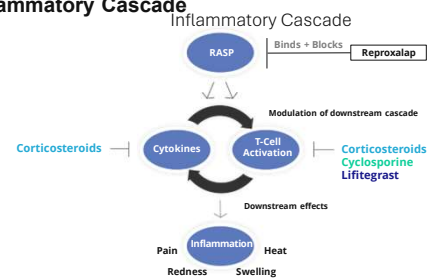
RASP type malondialdehyde (MDA) is believed to be associated with inflammatory ocular diseases

- This includes autoimmune diseases, allergic conjunctivitis, and dry eye disease

Eschenauer H et al. Chemistry and biochemistry of 4-hydroxymethyl, malondialdehyde and related aldehydes. Free Radic Biol Med. 1991;11(1):81-128.  
Raghu A et al. Cell signaling by reactive oxygen species: mechanisms and molecular mechanisms. Biochem J. 2012;442(2):403-416.  
Clark D et al. A Randomized Clinical Trial of the Efficacy and Safety of Topical Ocular Regeneration, a Novel RASP Inhibitor, in Dry Eye Disease. J Ocul Pharmacol Ther. 2021;37:160-166.  
Clark D et al. Early Clinical and Biomarker Activity of Regeneration in a Randomized, Double-Masked, Vehicle-Controlled Phase 2b Trial in Dry Eye Disease. Am J Ophthalmol. 2021;226:23-31.

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## Inflammatory Cascade



Sources: Lee S et al. HNE-induced S-LD expression is regulated by NF-κB and TGF-β1/Smad3 pathways via EGF receptor in murine macrophages. Cardiovasc Res. 2010;88(2):352-9. Chappell et al. Role of 4-hydroxy-2-nonenal in the pathogenesis of Fuchs' Dystrophy. Retina. 2003;23(1):4:229-36. Nishigaki et al. The advanced glycation end product precursor malondialdehyde induces S-LD expression and downregulates TGF-β1 in retinal cells. Cell Mol Biol Lett. 2010;20(4):847-82. Raghu A et al. Proinflammatory effects of malondialdehyde in lymphocytes. J Leukoc Biol. 2012;92(5):1055-67. Sharmagun H et al. Proinflammatory effects of advanced glycation end product malondialdehyde on macrophages. Diabetes. 2008;57(6):879-86.

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**FDA Candidate : Reproxalap 0.25% Topical Ocular**

**Aldeyra Therapeutics Announces PDUFA Extension of the New Drug Application for Reproxalap for the Treatment of Dry Eye Disease**

**FDA Rejected PDUFA March 2026**

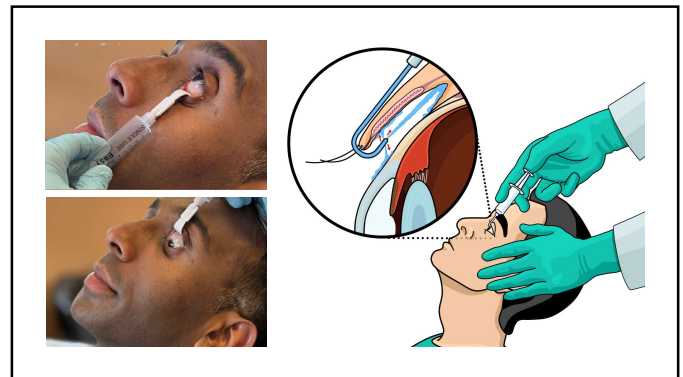
December 15, 2025

LEXINGTON, Mass. (BUSINESS WIRE)—Dec. 15, 2025—Aldeyra Therapeutics, Inc. (Nasdaq: ALDX) (Aldeyra), a biotechnology company devoted to discovering and developing innovative therapies designed to treat immune-mediated diseases, today announced that the U.S. Food and Drug Administration (FDA) has extended the Prescription Drug User Fee Act (PDUFA) target action date for the reproxalap New Drug Application (NDA) for the treatment of dry eye disease. The extended PDUFA target action date is March 16, 2026.

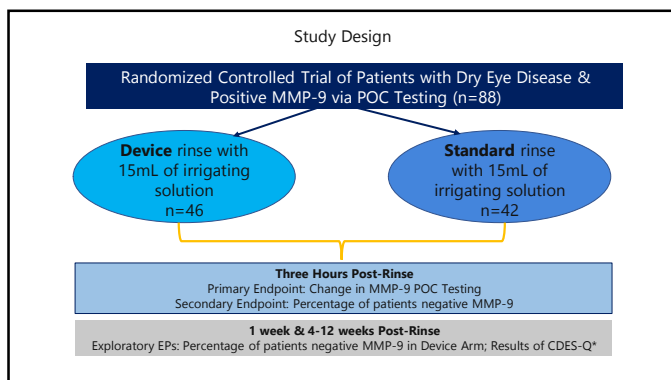
**inflammation in several animal models**

Source: Clark D et al. A Randomized Double-Masked Phase 2a Trial to Evaluate Activity and Safety of Topical Ocular Reproxalap, a Novel RARP Inhibitor, in Dry Eye Disease. J Ocul Pharmacol Ther. 2021;37(1):59-68. Clark D et al. Early Clinical and Biomarker Activity of Reproxalap in a Randomized, Double-Masked, Vehicle-Controlled Phase 2a Trial in Dry Eye Disease. Am J Ophthalmol. 2021;228:22-31.

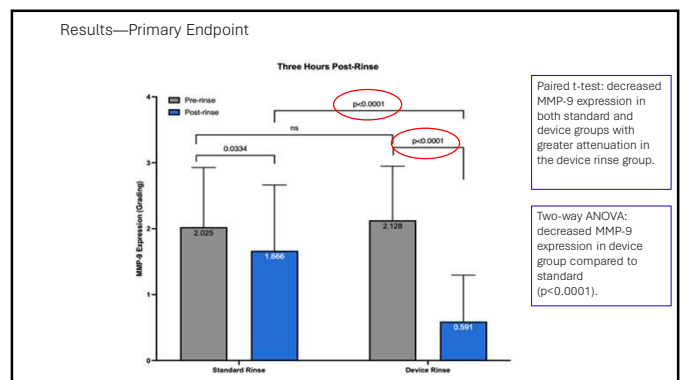
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