



Targeting  
Dry Eye Disease  
&  
Neuropathic  
Corneal Pain



**Corporate Presentation**

**MAY 2024**

Nasdaq: OKYO

Non-Confidential

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# Dry Eye Disease: Overview



## Ocular Surface Damage

*Inadequate or unstable tears resulting in lack of moisture and progressive damage to the ocular surface*

## Inflammation & Pain: Key Symptoms of Dry Eye Disease

*Tear film instability triggers chronic inflammation which leads to symptoms of pain, itchiness, stinging, burning, and blurry vision*

**700,000,000\***  
*Worldwide patients*

**49,000,000\*\***  
*US patients*

**Up to 35%\*\*\***  
*+50 yrs old affected*

## Risk & Growth Factors

*Age 50 or older, Female, Wear contact lenses, Digital screen time*



# Limits of Current Standard of Care

6 FDA-Approved Drugs in the Market with Significant Limitations, Slow Onset of Action, and Numerous Side Effects

	API	Limitations*
<b>Restasis</b> Allergan	0.05% cyclosporine	Delayed response, up to 6 months to improve symptoms, burning sensation <b>70% patients do not refill Rx at Month 12**</b>
<b>Xiidra</b> Novartis (Bauch & Lomb)	5% LFA-1 antagonist	Eye irritation and burning sensation, change in taste <b>70% patients do not refill Rx at Month 12**</b>
<b>Cequa</b> Sun Pharma	0.09% cyclosporine	Burning, pain upon instillation, blurry vision, UTI (side effects on label)
<b>Eysuvis</b> Alcon	0.25% loteprednol	Short-term treatment only (maximum 2 weeks)
<b>Tyrvaya</b> Viatris	0.03 mg / inhalation Varenicline	Sneezing, cough & throat irritation (side effects on label)
<b>Meibo</b> Bausch & Lomb	Perfluorohexyloctane	Approved in May 2023, launched in second half of 2023

# Global DED Market Expected to Reach ~\$11 Billion by 2030\*



>> ~\$3.8 Billion Annual Healthcare Costs\*\*

>> ~\$50 Billion Annual Costs of Managing DED to US Economy\*\*

>> Current Treatment Options Inadequate;  
More Effective Treatment May Increase Market Size

>> Bausch & Lomb Recent Acquisition of Xiidra for \$2.5 Billion

# OK-101: A Lipid-Conjugated Chemerin Peptide

Drug candidate with anti-inflammatory and ocular pain reducing properties

Lipid conjugated peptide chemistry minimizes drug washout and enhances the potency

Preservative free, EDTA free

Simple, stable formulation

IND cleared by FDA	December 2022
240 patient trial initiated	May 2023
Top Line data released	Jan 8, 2024

## Chemerin Receptor

### Modulates

Inflammation

### Receptor localization

Monocytes, macrophage, dendritic cells, NK cells, Treg cells, spinal cord neurons

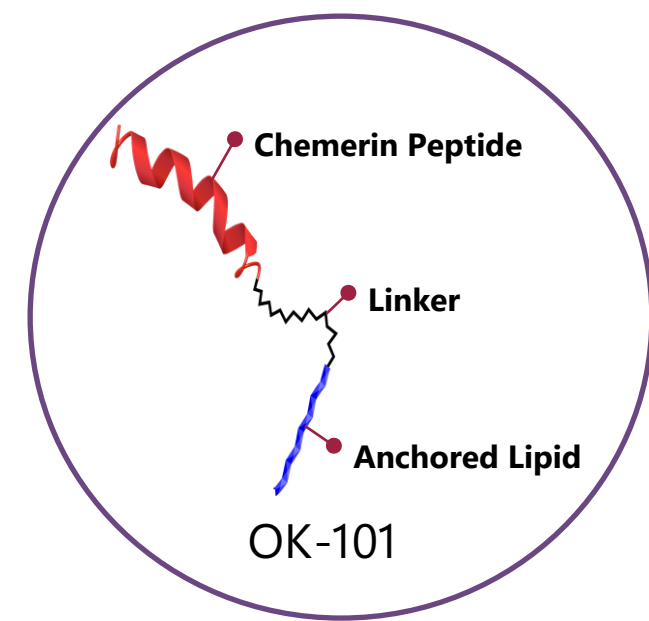
### Endogenous ligand

Chemerin: 136 aa peptide

Resolvin E1

### Therapeutic targets (based on resolvin E1 efficacy)

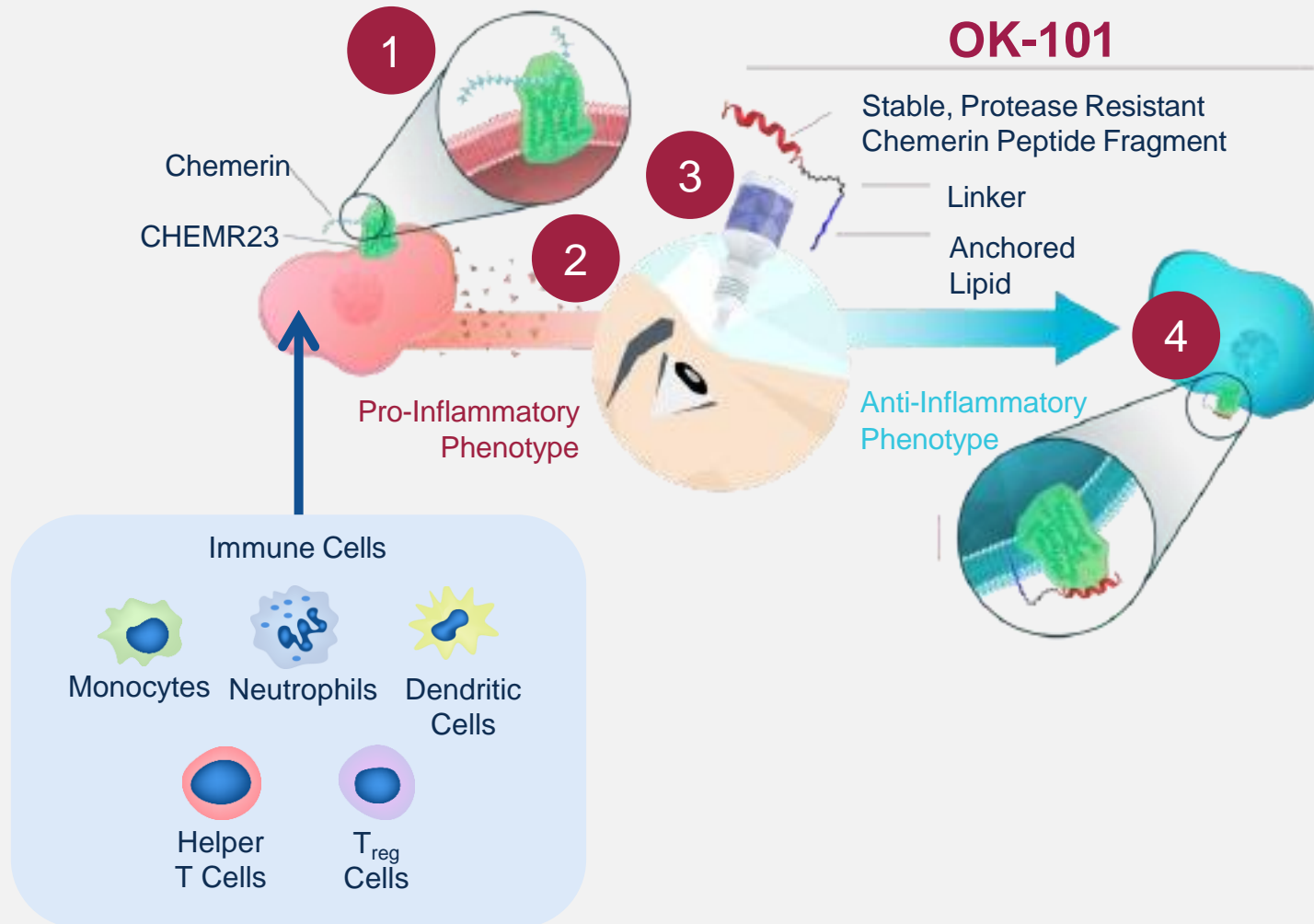
Dry eyes, neuropathic pain, asthma



# Pipeline Focus: OK-101 to Treat Ocular Diseases

	Indication	Pre-clinical	Phase 1	Phase 2	Phase 3
OK-101	Dry Eye Disease ("DED")	Phase 2 Trial Completed			
	Neuropathic Corneal Pain ("NCP")	Plan to open trial in Q2 2024			
	Allergic Conjunctivitis				
	Uveitis				

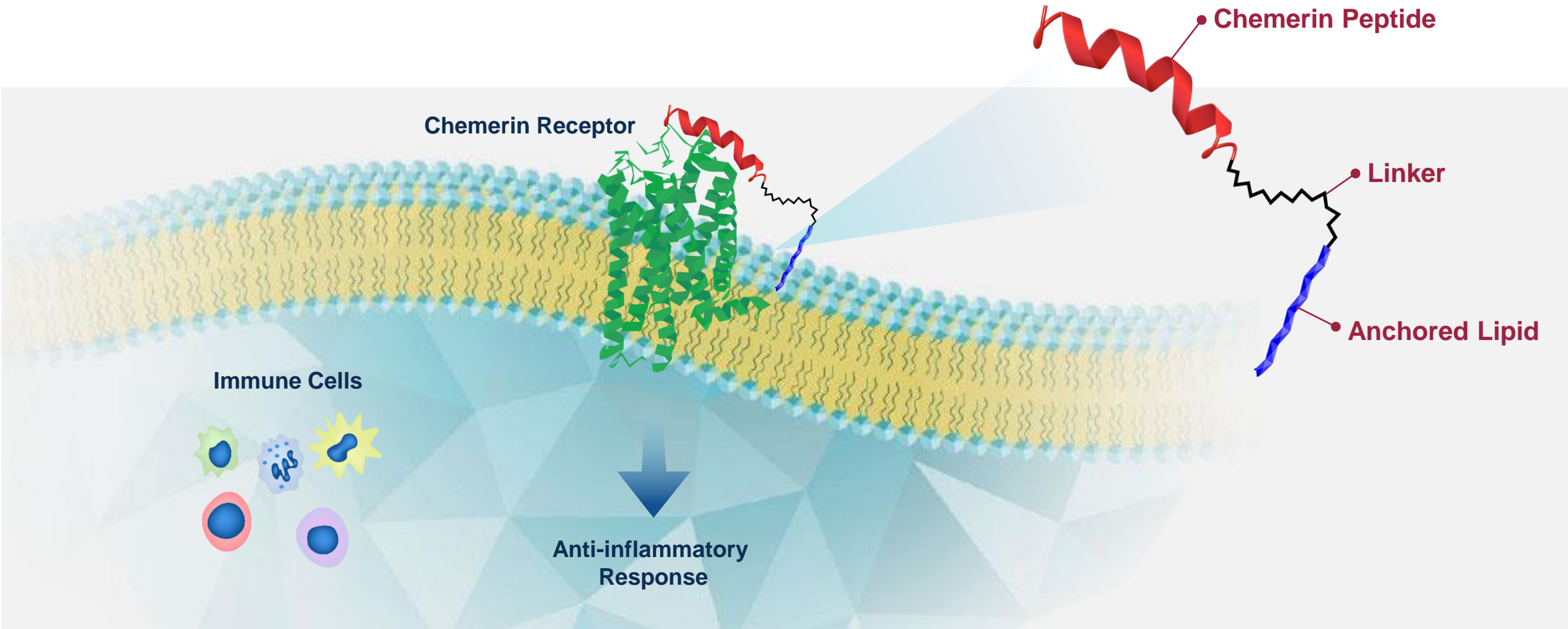
# Chemerin Derived Peptide: A Potential Regulator of Inflammation & Pain



1. Pro-inflammatory chemerin activates immune cells at the inflammation site
2. Peptides derived from chemerin physiologically inhibit the inflammatory response
3. The data suggests that topically administered OK-101 peptide can dramatically enhance the anti-inflammatory response
4. Proprietary MAP technology designed to enhance residence time of OK-101 on ocular surface



# OK-101: Targeting Chemerin Receptor

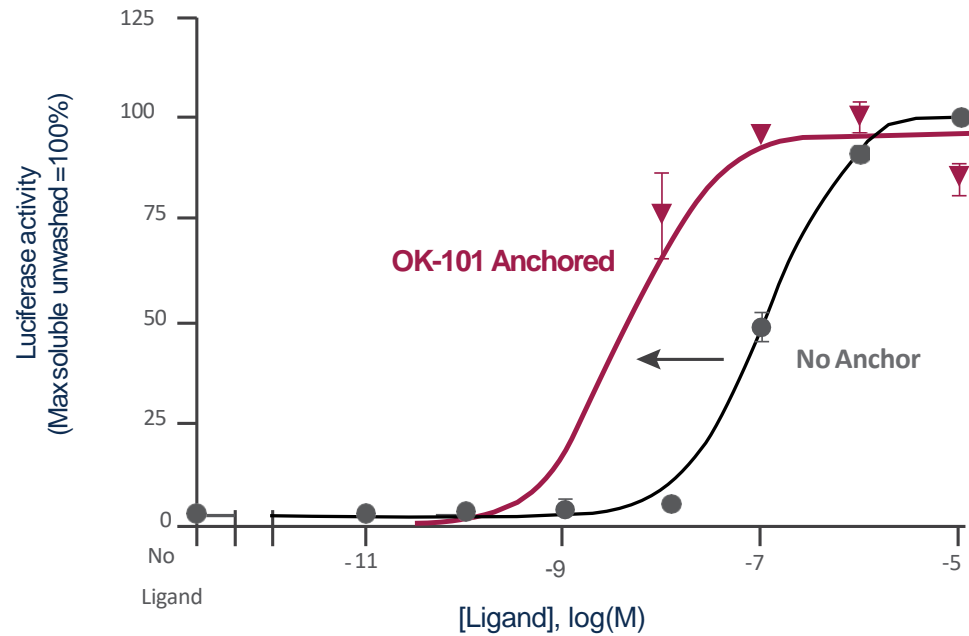


# Membrane Anchoring Improves Potency, Durability

\*In-vitro studies

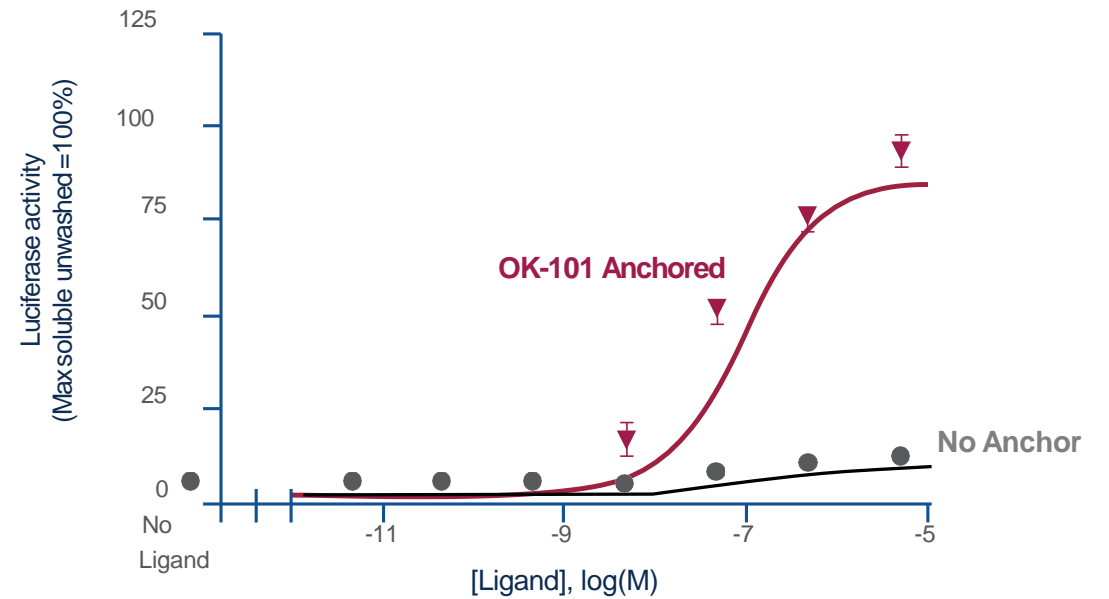
## Enhanced Potency

Human Chemerin Receptor

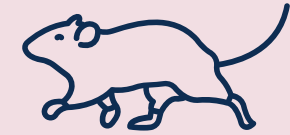
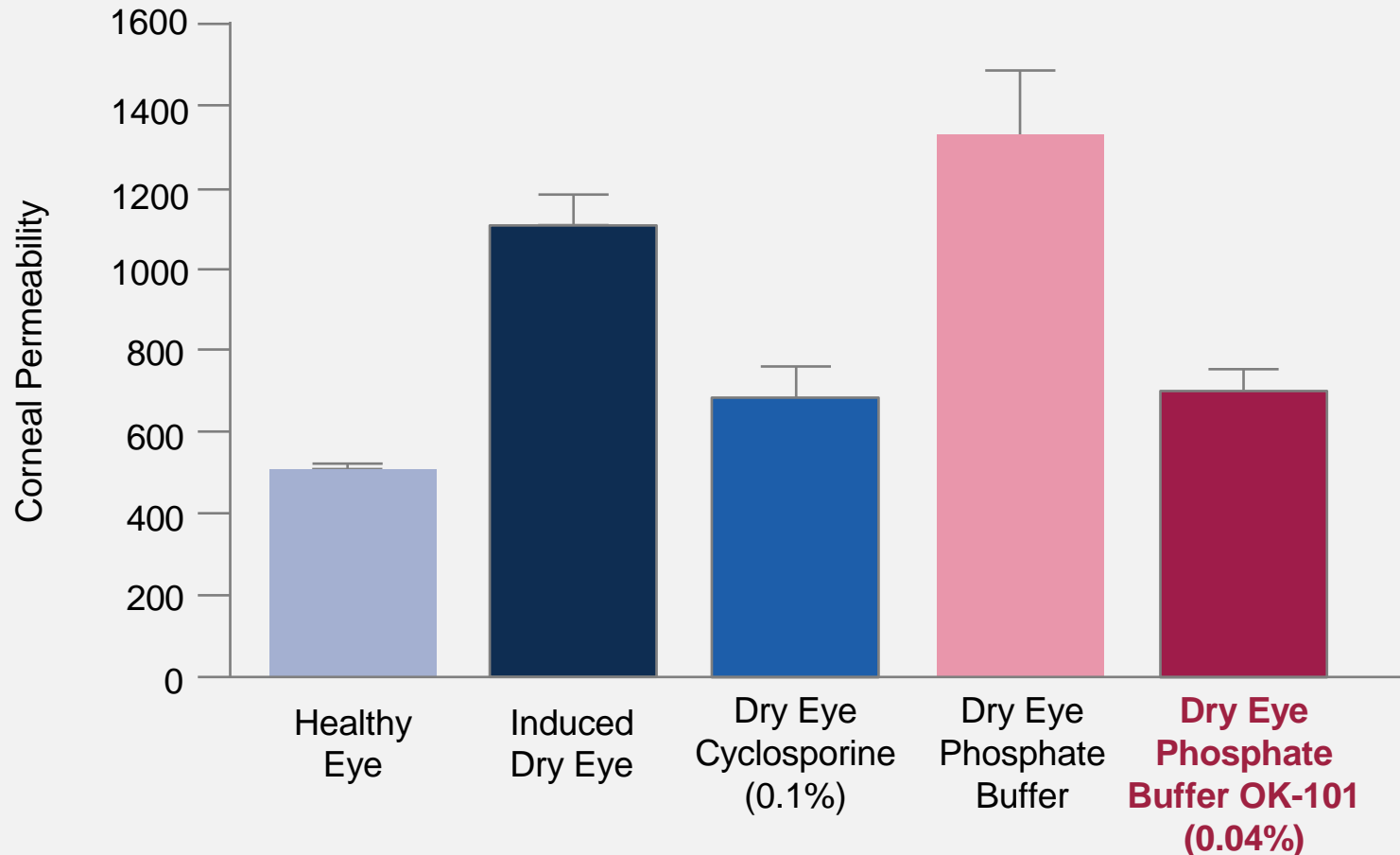


## Increased Durability

Human Chemerin Receptor (Wash Resistant)



# Validation: OK-101 Efficacy in Dry Eye Mouse Model



OK-101 and cyclosporine were administered topically twice a day

Corneal permeability significantly reduced with OK-101 vs phosphate buffer alone

Potency of OK-101 was comparable to cyclosporine, an active ingredient of Restasis (Allergan) & Cequa (Sun Pharma)

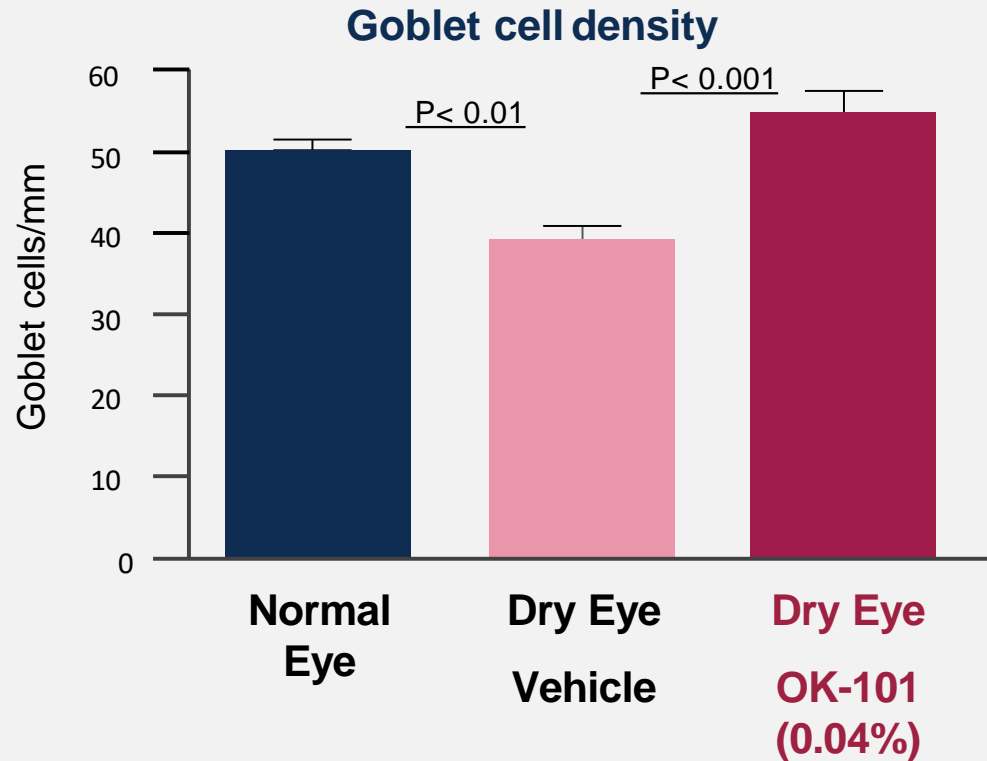
**Reducing corneal permeability with OK-101 improves corneal integrity in dry eye mouse model**

\*Patil et al. (2019) 14th Congress on Ocular Pharmacology and Therapeutics, New Orleans, LA

# OK-101 Normalized Goblet Cells & Reduced Inflammatory CD4 T Cells\* Enucleated Mouse Eyes from Scopolamine-Treated Dry-Eye Mouse Study

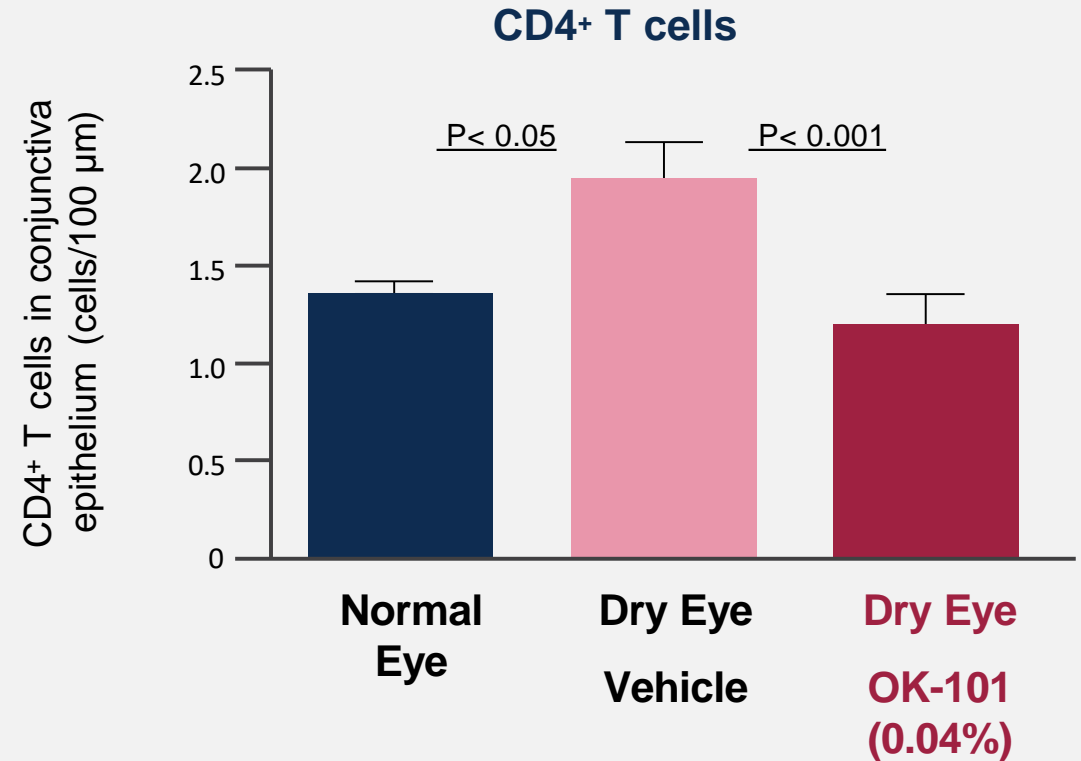
## Increased Mucin-Secreting Goblet Cells\*

### OK-101 normalized goblet cell density



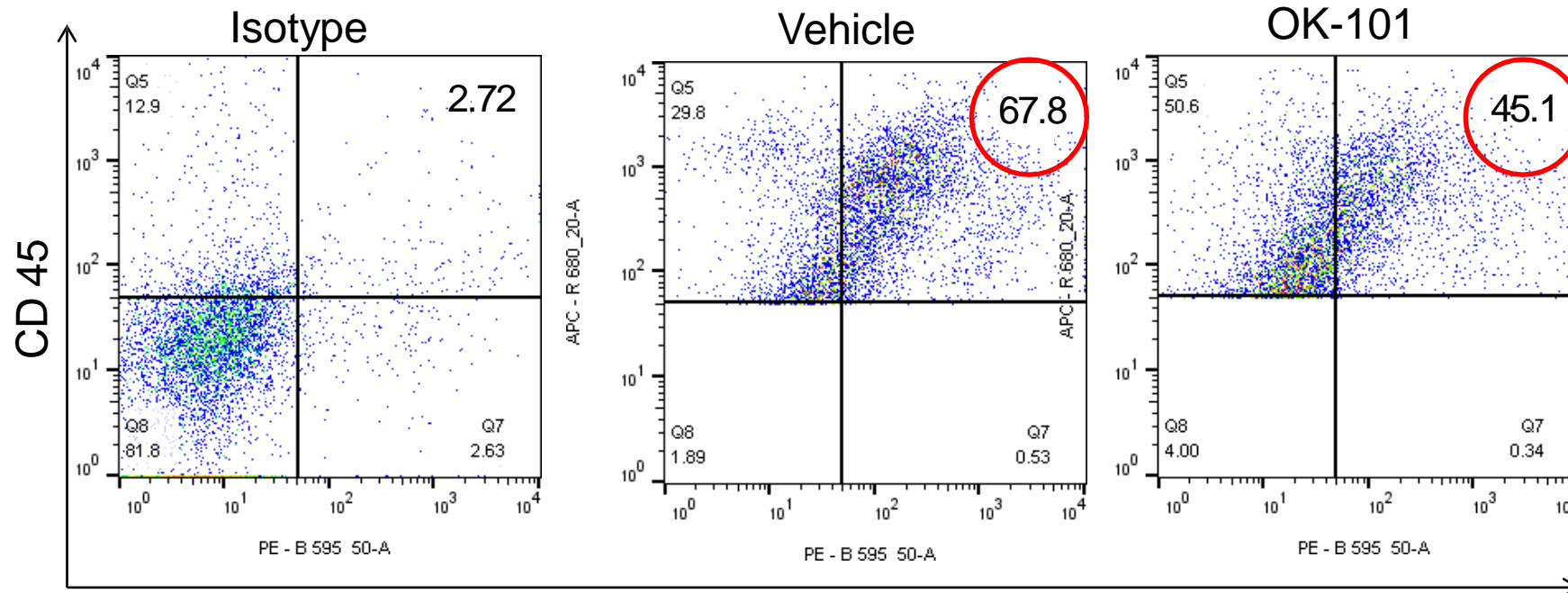
## Reduced Inflammatory Biomarkers\*

### OK-101 reduced count of CD4+ T cells



# OK-101 Decreased Activated Immune MHCII<sup>+</sup> Cells in Draining Lymph Nodes of DED Mice

Flow cytometry of draining lymph nodes gated on CD45

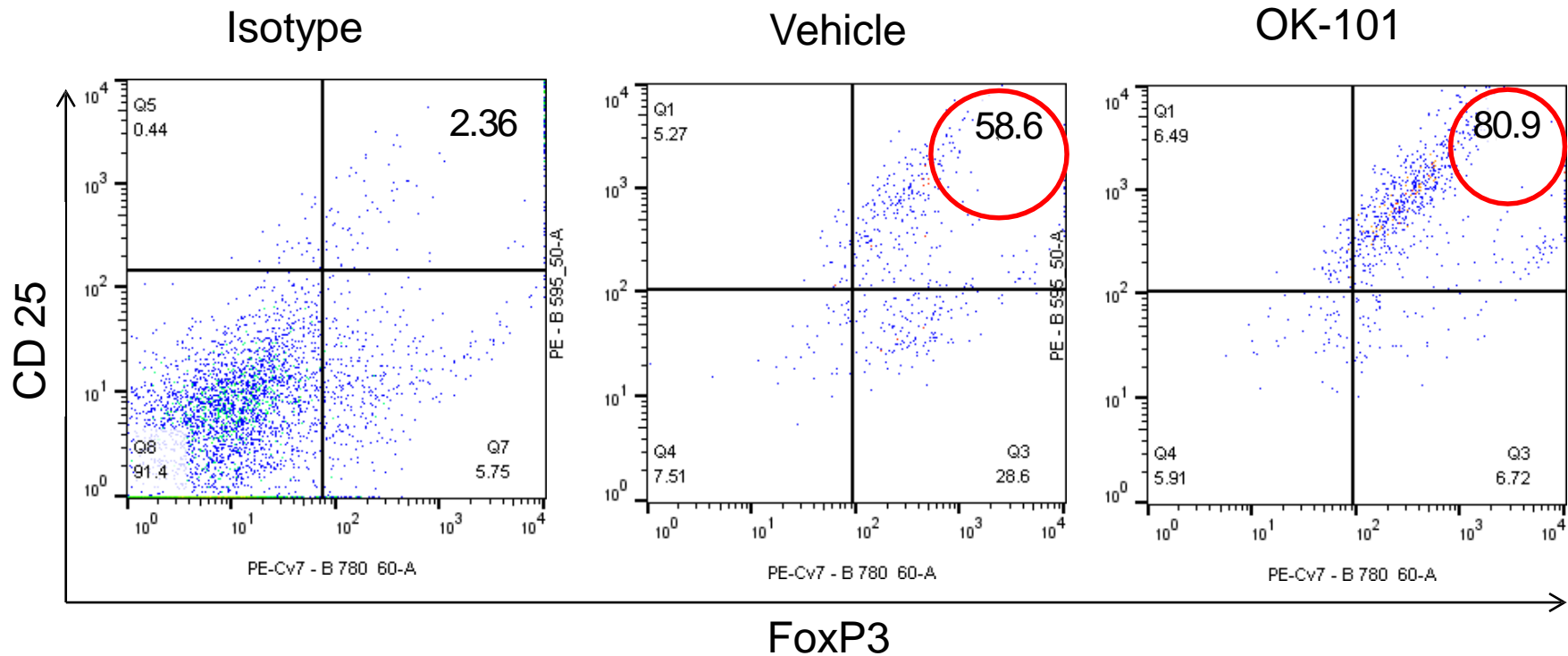


(MHC) class II cell surface receptors involved in antigen presentation are increased in DED



# OK-101 Increased Tregs in the Draining Lymph Nodes of DED Mice

Flow cytometry of draining lymph nodes gated on CD45+ CD3+ and CD4+ T cells



Inflammation in DED is mainly mediated by Th17 resulting in decreased Tregs cells

# Corneal Neuropathic Pain in Dry Eye Disease (DED)



DED patients suffer from corneal neuropathic pain, making their condition more resistant to anti-inflammatory drugs

No Current FDA approved topical treatment for ocular pain

ChemR23 receptor on leukocytes targeted by OK-101 is **also** expressed on neurons and glial cells in the dorsal root ganglion and spinal cord

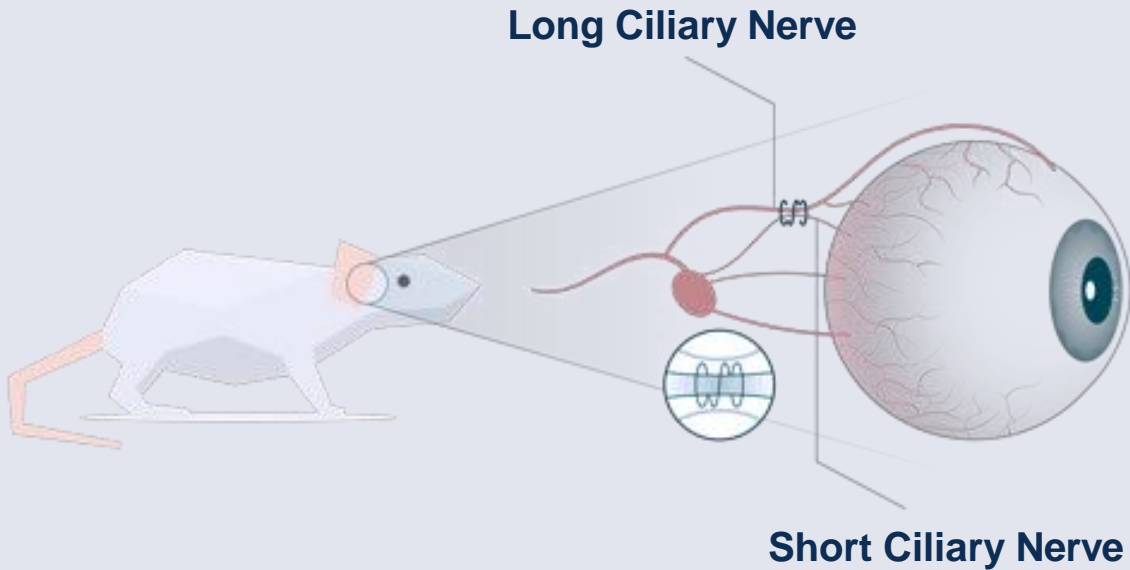
DED patients would benefit from a drug that comprises anti-inflammatory and neuropathic pain reducing characteristics

**OK-101: a potentially promising candidate for the treatment of both inflammation and pain**

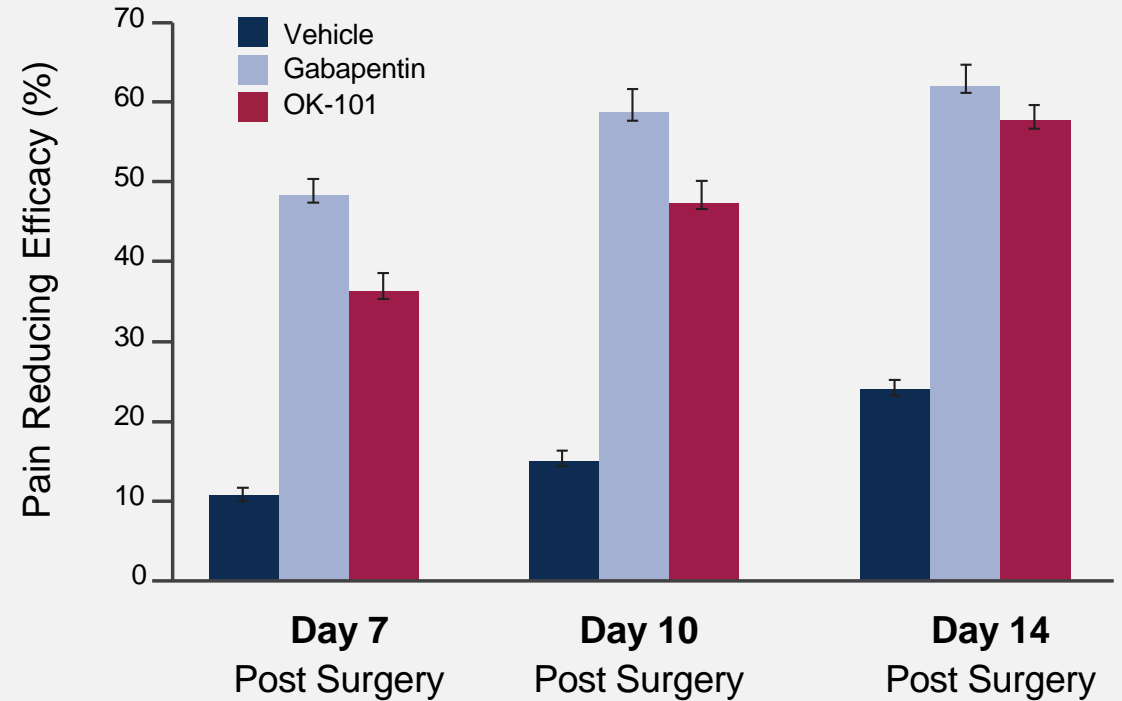
# OK-101 Reduced Neuropathic Corneal Pain ("NCP") in Mouse Model

## Ciliary Ligation Model\* Illustrates OK-101 Potential to Reduce Ocular Pain

Ciliary nerve ligation surgery to create the corneal neuropathic pain (CNP) model



## OK-101\*\* Reduced Corneal Pain Response Comparable to Gabapentin\*\*\* (GBP)



\* Collaboration with Dr. Pedram Hamrah, Tufts Medical Center, Boston (Kenyon B, ARVO Abstract 4085, 2020)

\*\* Topical administration (0.04%)

\*\*\* Administered by intraperitoneal injection, 100 mg/kg once at Day 4, 7, 10, and 14

# OK-101 Addresses Inflammation and Pain Components of Dry Eye in Mouse Models

## Extrinsic Factors:

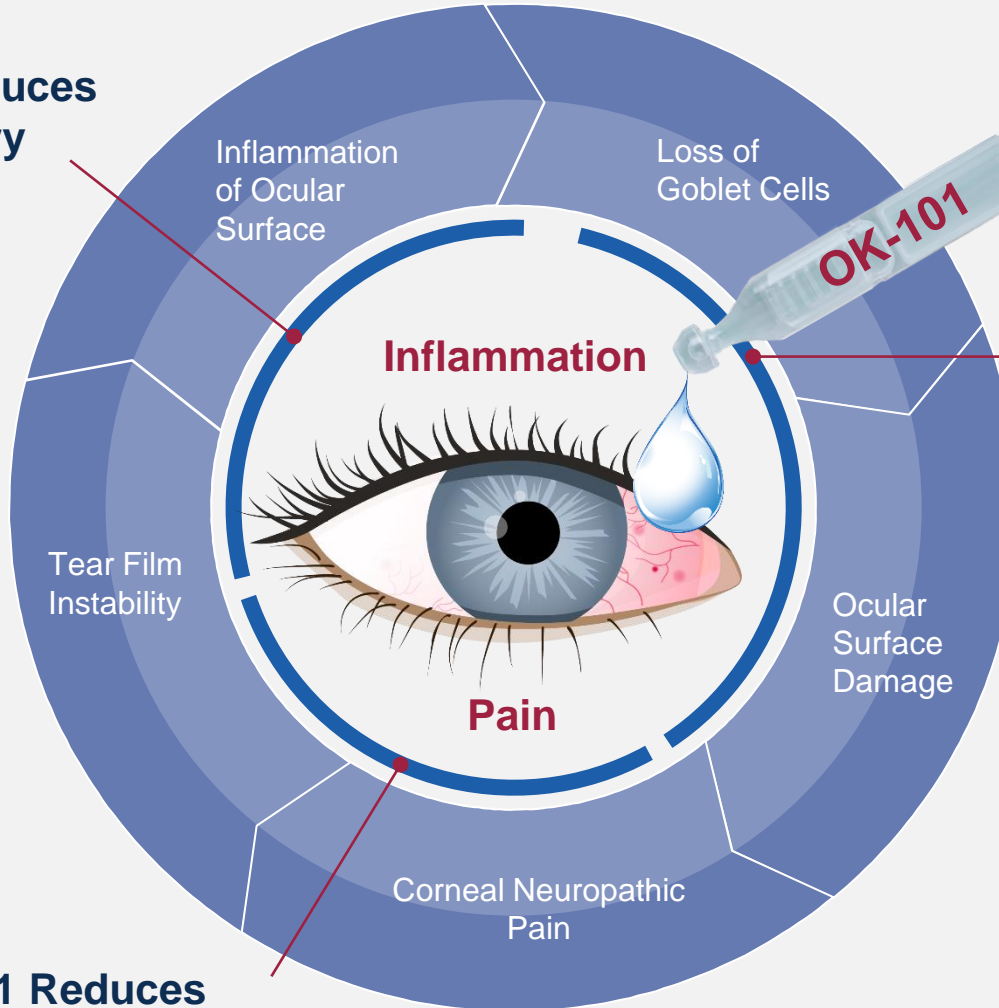
- Contact lens
- Digital screen time
- Allergies
- Surgery
- Blepharitis C

## Intrinsic Factors:

- Aging
- Sex steroid imbalance
- Autoimmune diseases

## Dry Eye Cycle

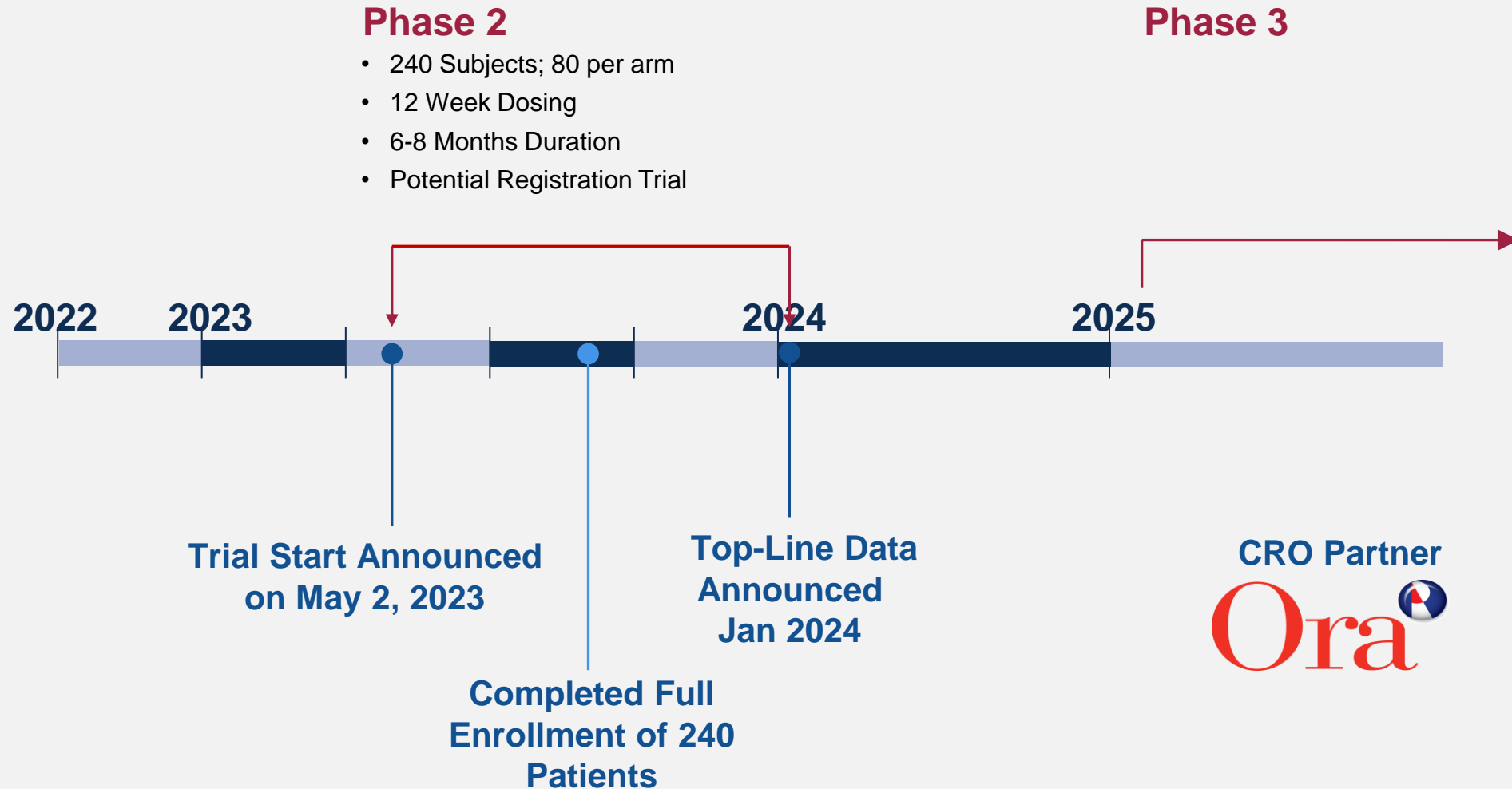
**OK-101 Reduces Inflammatory Markers**



**OK-101 Normalizes Goblet Cell Loss**

**OK-101 Reduces Corneal Neuropathic Pain**

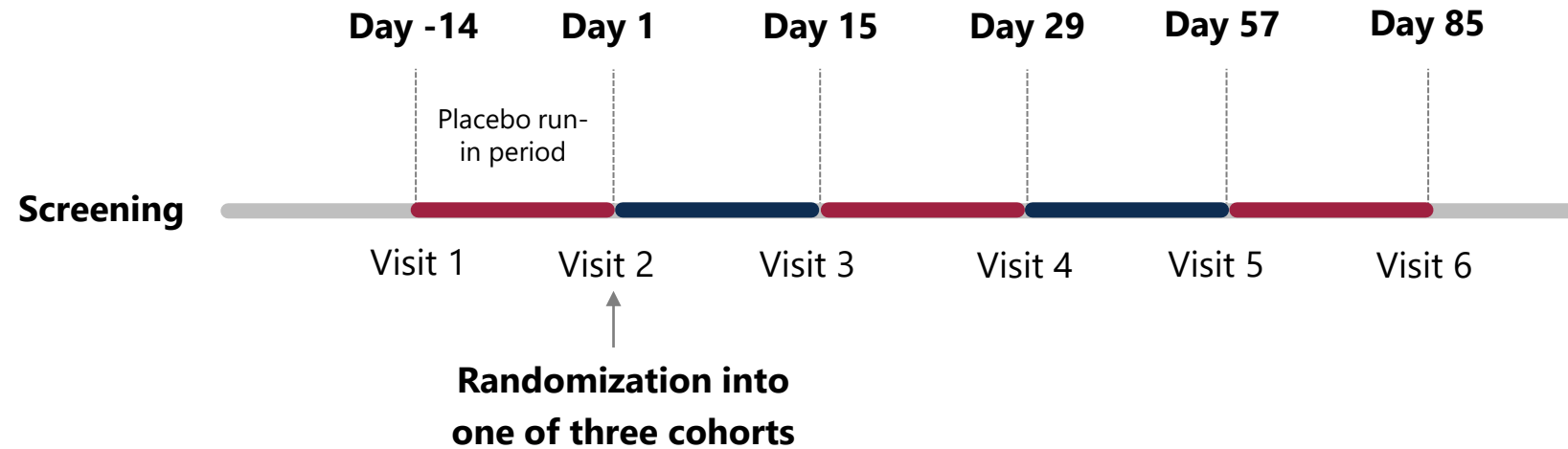
# OK-101 DED Development Timeline





# OK-101 DED Phase 2 Trial Design

**Note: First Human Trial of OK-101**



OK-101 (0.05%) n = 81

OK-101 (0.1%) n = 80

Placebo n = 79

## Study Overview

Total Subjects: Enrolled = 384

Screen Failures = 144

Randomized Subjects = 240

Baseline characteristics were balanced amongst treatment groups

No drug-related SAEs, most AEs were mild stinging & burning

1 discontinuation for iritis in 0.05% OK-101 group

## ENDPOINTS

### Primary Endpoints

(through Day 85)

Inferior Corneal Staining (Sign)

Ocular Discomfort Score (Symptom)

### Secondary Endpoints

Total Conjunctival Staining (sign)

Tear Film Break-up Time (TFBUT) (sign)

Blurred Vision

Burning/Stinging

Pain

Daily Symptom Diary

# CHEMISTRY OF OK-101

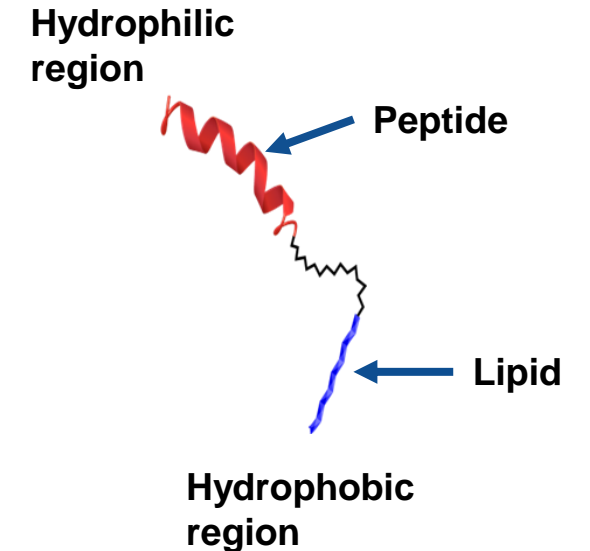
## OK-101 -- A LIPIDATED PEPTIDE

- AMPHIPATHIC MOLECULE (both hydrophilic and hydrophobic)
- POTENTIAL TO FORM MICELLES
- MOUSE DRY EYE STUDY ONLY USED 0.04% OK-101

**HUMAN TRIAL PERFORMED AT 0.05% AND 0.10% OK-101**

**ONLY SHOWING 0.05% DATA – FDA looks for lowest dose with excellent efficacy which is what we are seeing with 0.05%**

OK-101 being explored using dynamic light scattering studies to explore potential to form micelles at 0.10% concentrations



# US Regulatory Requirements for Dry Eye Disease

## Dry Eye: Developing Drugs for Treatment Guidance for Industry

### Requirements

- ✓ **Sign and Symptoms** (co-primaries,  $p < 0.05$ , no unit difference required) – can be achieved in separate studies if necessary
- ✓ **Sign Only** (e.g., Schirmer's Responder Rate  $\geq 10$  mm, clearing of corneal staining)
- ✓ **Symptom Only** (not allowed)

### Acceptable Signs and Symptoms of Dry Eye

- ✓ **Signs:** corneal staining, conjunctival staining, TFBUT, Schirmer's
- ✓ **Symptoms:** Eye dryness score, burning/stinging (ocular irritation), blurred vision, light sensitivity, sandy or gritty feeling, ocular pain or discomfort

# Approved DED Drugs

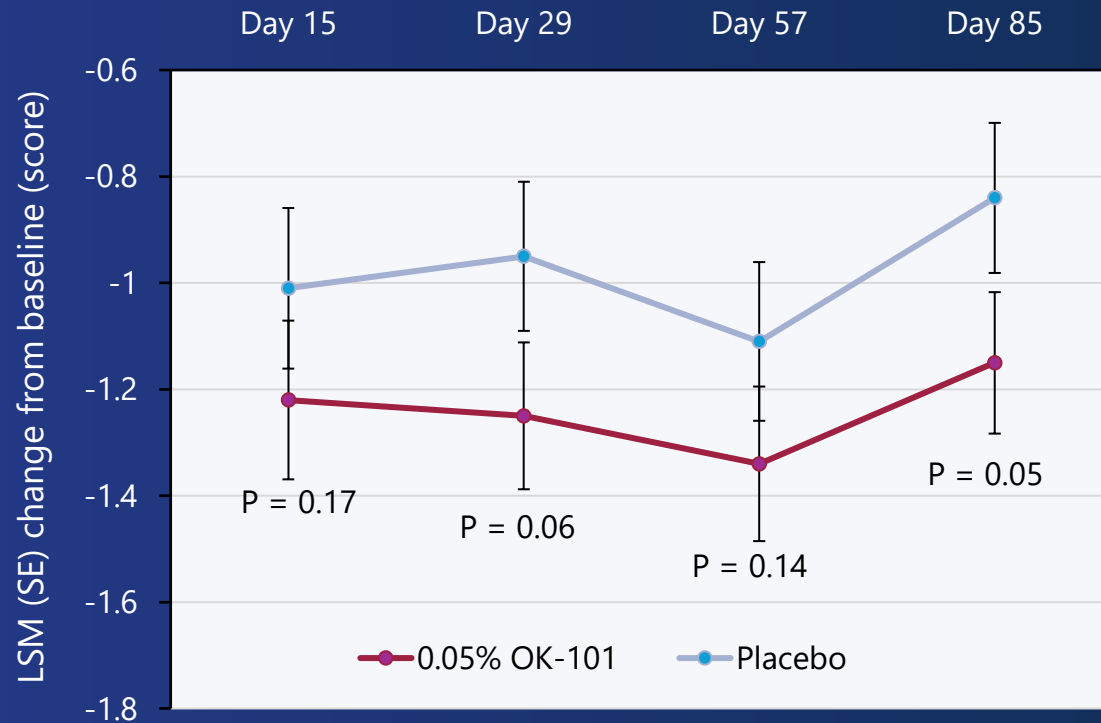
Drug Name	Company (Year approved)	Labelled indication	Onset of Action	Primary Endpoint (Sign)	Secondary Endpoint (Symptom)	Most common Adverse Effects
Restasis; Cyclosporine 0.05%	Allergan (2003)	Sign; BID	up to 6 months	<b>Tear production</b>	<b>N/A</b>	Ocular burning (17%)
Xiidra Lifitegrast 5%	Bausch & Lomb (2016)	Signs and symptoms BID	6-12 weeks	<b>Inferior Corneal Staining Score (ICCS)</b>	<b>Eye dryness score (EDS)</b>	Burning (15%), instillation site reaction (13.2%), dysgeusia (16%) and reduced visual acuity (11.4%).
Cequa Cyclosporine 0.09%	Sun Pharma (2018)	Sign; BID	2 weeks	<b>Tear production</b>	<b>N/A</b>	Pain on instillation of drops (22%) and conjunctival hyperemia (6%).
Eysuvis loteprednol 0.25%	Alcon (2020)	Signs and symptoms <b>QID</b>	4 days	<b>Conjunctival hyperaemia</b>	<b>Ocular discomfort</b>	Instillation site pain (5%)
Tyvaya; Varenicline 0.3mg	Oyster Point/ Viatis (2021)	Signs and symptoms BID	1-4 weeks	<b>Tear production</b>	<b>Eye dryness score (EDS)</b>	Sneezing (82%), cough (16%), throat irritation (13%), and instillation-site (nose) irritation (8%).
Meibo; Perfluorohexyloctane	Bausch & Lomb (2023)	Signs and symptoms <b>QID</b>	2 weeks	<b>Total corneal fluorescein staining</b>	<b>Eye dryness score (EDS)</b>	Blurred vision and conjunctival redness (1-3%)
Veveye; Cyclosporine 0.1%.	Novaliq/ Harrow (2023)	Signs and symptoms BID	2 weeks	<b>Tear production</b>	<b>N/A</b>	Instillation site reactions (8%) and temporary decreases in visual acuity (3%).

# Improvement in Conjunctival Sum Staining (Sign)

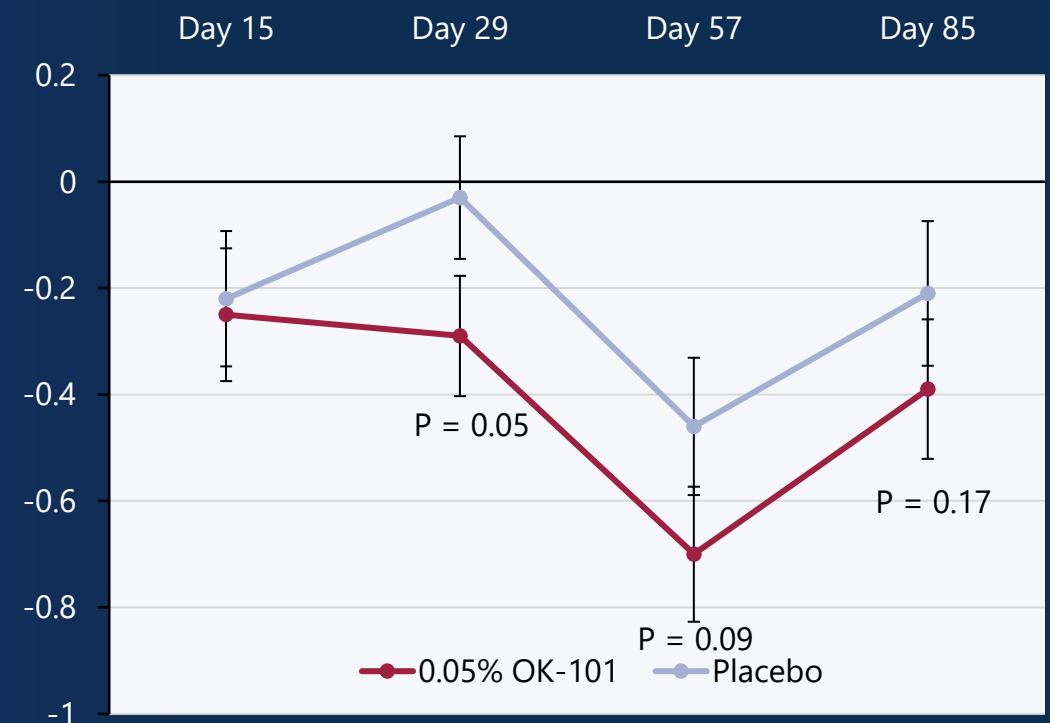
Data shown is change from baseline in Intent-to-Treat Population

P values are vs placebo based on Wilcoxon rank sum test

## Lissamine Green Staining



## Fluorescein Staining





# Significant Improvement in Tear Film Break Up Time (Sign)

Data shown is change from baseline in Intent-To-Treat Population

P values are vs placebo based on Wilcoxon rank sum test



## Significant Improvement in Pain (Symptom)

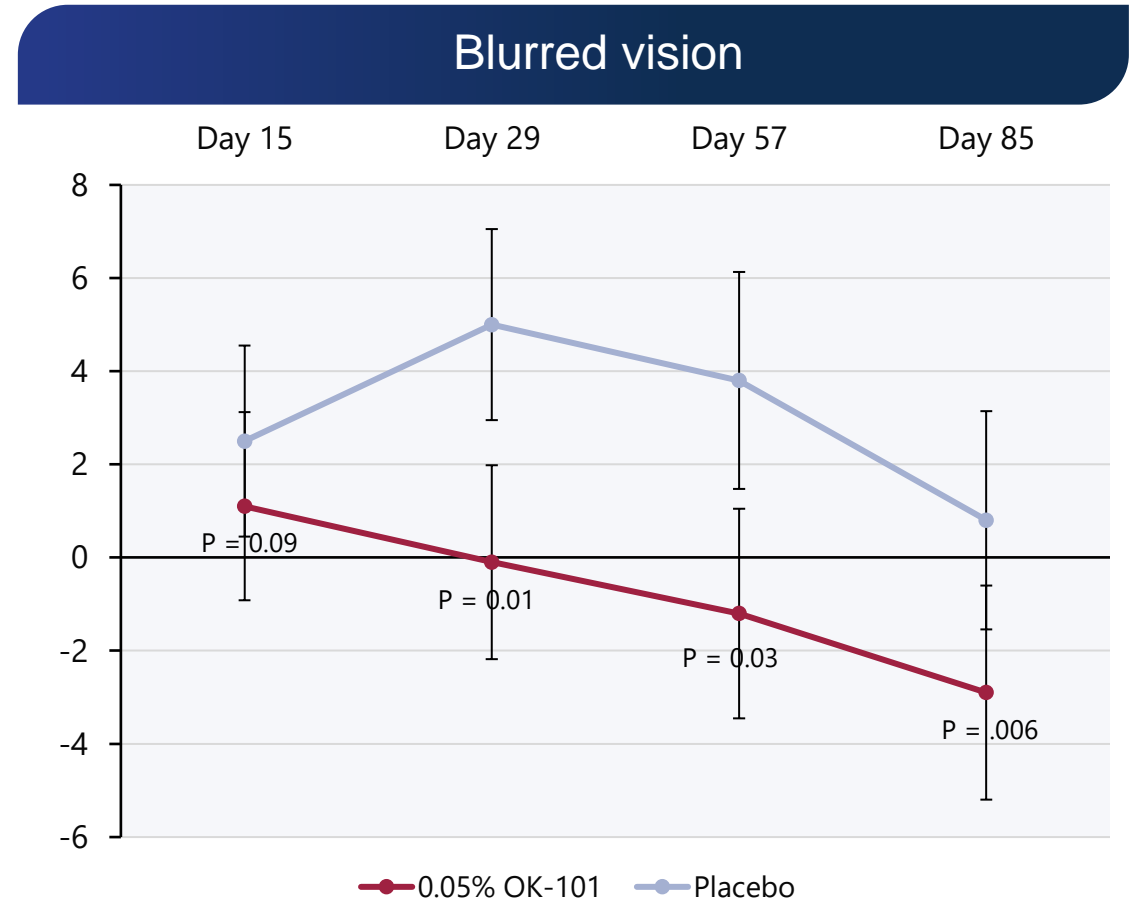
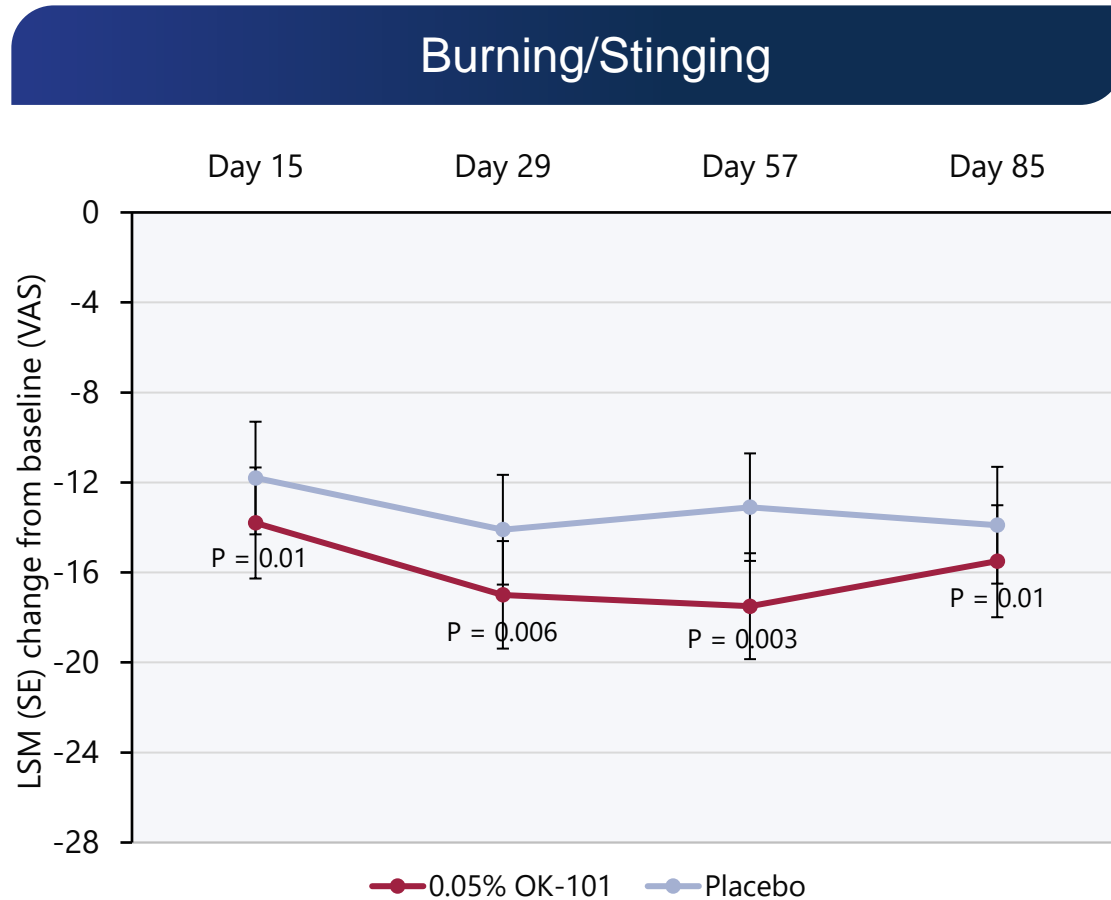
Data shown is change from baseline in Intent-To-Treat Population  
P values are vs placebo based on Wilcoxon rank sum test



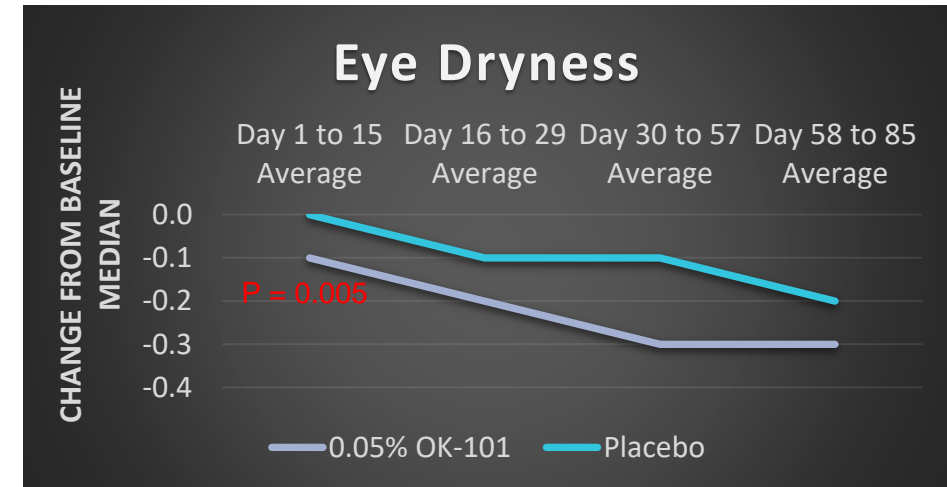
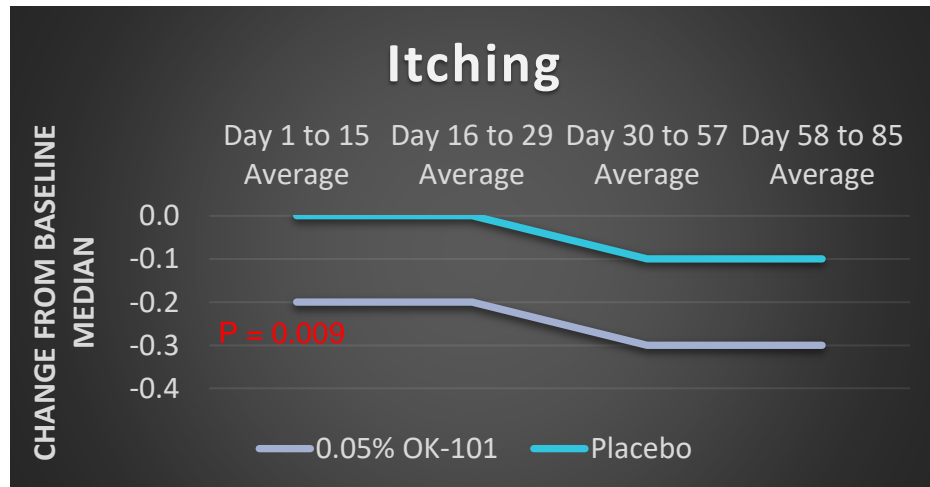
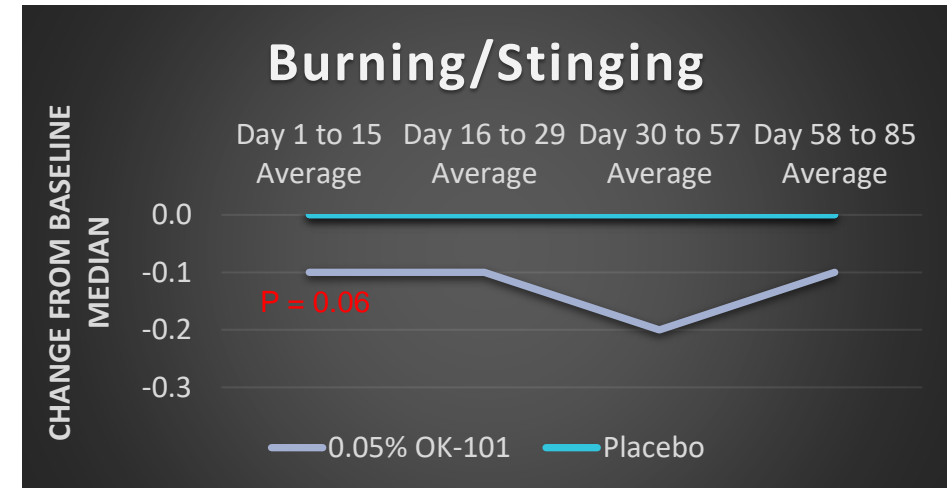
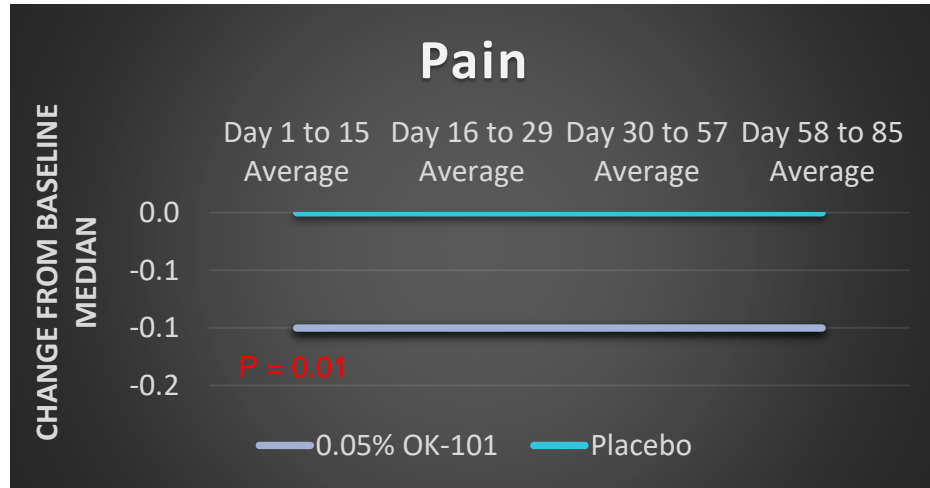
# Significant Improvement in Burning/Stinging & Blurred Vision (Symptoms)

Data shown is change from baseline in Intent-To-Treat Population

P values are vs placebo based on Wilcoxon rank sum test



# Significant Improvement in Symptoms by Patient Reported Daily Diary Within First Two Weeks

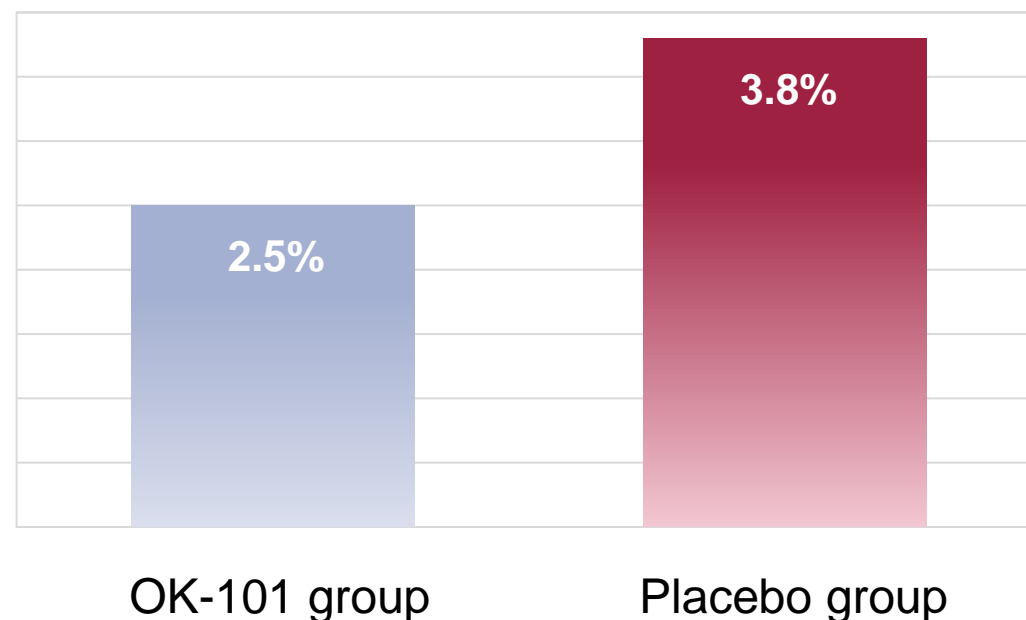


## Diary Symptoms Improvement Sustained Throughout the Trial

## OK-101 Phase 2 Trial Highlights - Safety

Treatment emergent adverse events (TEAEs) were observed to be similar to the placebo-treated group.

No severe drug related ocular TEAEs were seen. Possible drug-related TEAEs were observed in one patient in the OK-101 0.05% treatment group and 3 patients in the placebo-treated group, again highlighting the favorable safety profile of OK-101.



Additionally, fewer subjects in the OK-101 treated arm discontinued study medication (2.5%) compared to discontinuations in the placebo treated patients (3.8%).



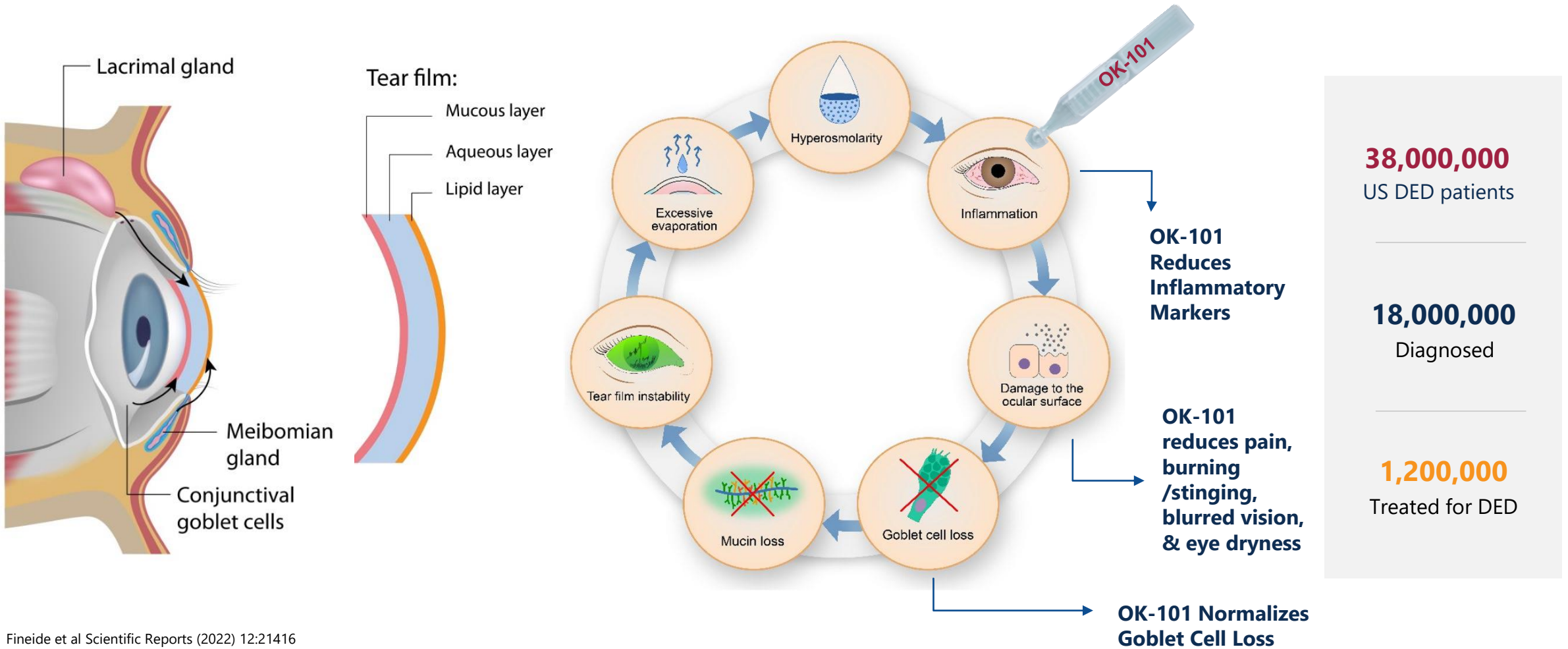
## OK-101 Phase 2 DED Study: Ocular Adverse Events

Category	OK-101 (0.1%) (N = 80)	OK-101 (0.05%) (N = 81)	Placebo (N = 79)
Number of Ocular AEs	7	19	7
Number of Ocular TEAEs	6	16	6
Number of Ocular SAEs	0	0	0
Number of Ocular TE-SAEs	0	0	0
<b>Number of Subjects Withdrawn Study Drug due to Ocular TEAE: n (%)</b>	<b>0</b>	<b>1 (1.2)</b>	<b>1 (1.3)</b>
<b>Number of Subjects with Ocular TEAEs (Severity)</b>			
Mild: n (%)	5 (6.3)	14 (17.3)	4 (5.1)
Moderate: n (%)	0	1 (1.2)	0
Severe: n (%)	0	0	0
<b>Number of Subjects with Ocular TEAEs by Relationship to Study Drug</b>			
Definitely Related: n (%)	4 (5.0)	8 (9.9)	0
Probably Related: n (%)	0	0	0
Possibly Related: n (%)	0	1 (1.2)	3 (3.8)
Not Related: n (%)	1 (1.3)	6 (7.4)	1 (1.3)

## OK-101 Drop Comfort: 2 Minutes Post-Instillation Study Eye

Drop Comfort	OK-101 0.1% (n=79)	OK-101 0.05% (n=77)	Placebo (n=76)
Mean Score (SD)	2.5 (2.32)	2.3 (2.32)	1.8 (1.73)
Median	2.0	1.0	1.5

# OK-101 Disrupts Dry Eye Cycle by Targeting Inflammation, Improving Tear Film Stability and by Ameliorating Multiple Symptoms



Fineide et al Scientific Reports (2022) 12:21416

# OK-101 to Treat Neuropathic Corneal Pain (NCP)

## July 28, 2023 – Announced Plans for OK-101 to Treat NCP\*

» Announced Clinical Trial Agreement with Tufts Medical Center for Trial on NCP

» NCP Trial to be conducted by Pedram Hamrah, MD, Professor, at Tufts Medical Center

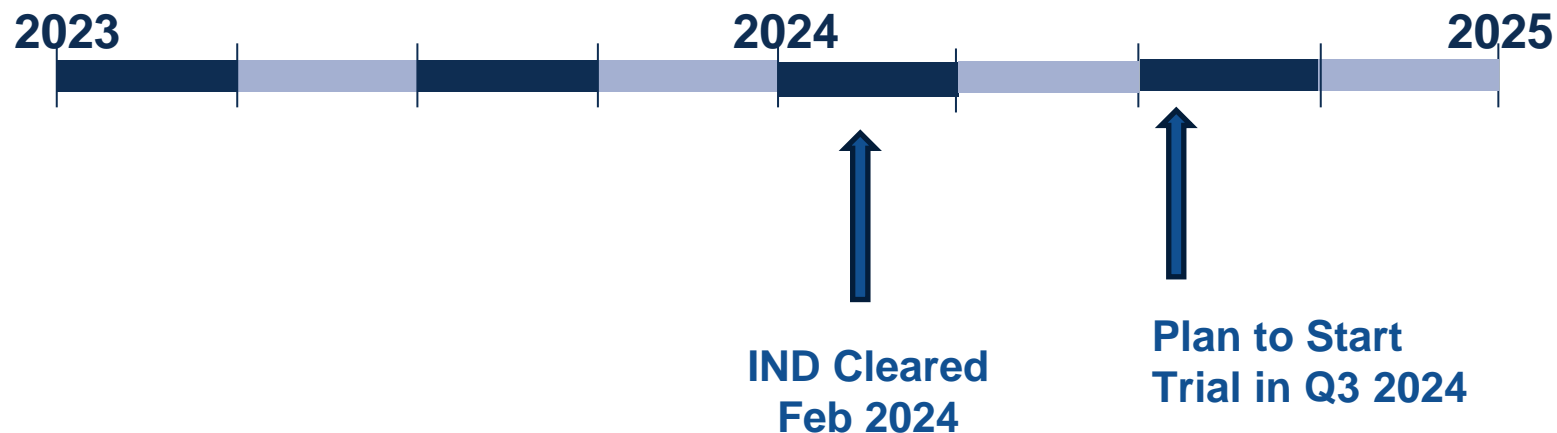
» IND filed with FDA for OK-101 to Treat NCP announced on Oct. 9, 2023

» Open Label Trial Planned to be Initiated in Q3 2024

# Plan to Start Phase 2 Trial for OK-101 to Treat Neuropathic Corneal Pain (NCP)

## Phase 2, Randomized, Double masked, Placebo-Controlled Study Assessing Safety and Efficacy of OK-101 in Subjects with NCP

- 48 subjects to be enrolled
- Three arms, 0.05% OK-101, 0.1% OK-101 and Placebo, (16 per arms)
- Four visits over the course of 16 weeks
- Study duration: 6-9 months
- Pedram Hamrah, MD, Principal Investigator, Tufts Medical Center



# Patent Protection through at least 2039

## OK-101 Technology:

Composition of Matter: US 10,233,219

Issued in US to 2034 with potential patent term extension up to 2039

### Dry Eye

- Method of Use: US 11,197,906
- Issued in US to 2037 with potential patent term extension up to 2042

### Neuropathic Pain

- Method of Use: US11,254,720
- Issued in US to 2034 (+187 days of \*PTA)

## OK-201 Technology:

Composition of Matter: US 10,899,796

Issued in US to 2036 (+70 days of \*PTA) with potential patent term extension up to 2042

### Dry Eye, Pain, Inflammation

- Method of Use: US 10,899,796
- Issued in US to 2036 (+70 days of \*PTA) with potential patent term extension up to 2042
- Issued European Patent on Comp. of Matter and Use for neuropathic pain, ocular pain, ocular inflammation, or dry eye: EP3373947

# Experienced Team With Considerable Drug Development Expertise

## Management

### Gary S. Jacob, PhD

#### Chief Executive Officer and Director

Co-inventor and developer of Synergy's FDA-approved drug Trulance, currently marketed by Bausch Health, Inc. 35 years of experience in the pharmaceutical and biotechnology industries.



### Raj Patil, PhD

#### Chief Scientific Officer

30 years of academic/pharmaceutical R&D experience and leadership experience at Alcon, Novartis and Ora, all leaders in Ophthalmology.



### William Clementi, PhD

#### Chief Operating Officer

Prior to launching his own regulatory consulting company, Clementi & Associates, Ltd., he held positions at Synthelabo's U.S. affiliate, Lorex Pharmaceuticals where he directed and designed pivotal studies in cardiovascular drug development and was Worldwide Director of Market Development industries.



### Keeren Shah

#### Chief Financial Officer

20 years of experience in controllership, financial planning and analysis, IPO offering and variety of finance positions at Visa Inc, Arthur Andersen, BBC Worldwide, Tiziana Life Sciences and Accustem Inc.



## Board

### Gabriele Cerrone Chairman, Founder

Extensive experience founding, financing, restructuring, and listing multiple micro-cap biotechnology companies in oncology, infectious diseases, and molecular diagnostics.



### Gary S. Jacob, PhD

#### Chief Executive Officer and Director

35 years of experience in the pharmaceutical and biotechnology industries, R&D, operations, business development and capital financing activities.

### Willy Simon

#### Non-Executive Director

International banking experience gained in senior leadership positions at multiple financial institutions.



### Bernard Denoyer

#### Non-Executive Director

Extensive financial management experience as Senior Vice President of Synergy Pharmaceuticals, Inc. Also served as CFO and Senior Vice President of META Group, Inc.



### John Brancaccio

#### Non-Executive Director

Financial executive with extensive international and domestic experience in pharmaceutical and biotechnology companies





# Key Takeaways



Significant drug effects were observed in multiple signs (conjunctival staining, TFBUT) and symptoms (ocular pain, burning/stinging and blurred vision) of DED as early as the 15-days after dosing.



Drug effect was durable throughout the trial for a number of endpoints.



Significant improvements were observed across multiple symptoms as measured in a daily symptom diary including pain, eye dryness and itching within the first two weeks of treatment.



OK-101 exhibited excellent drop comfort, comparable to that of artificial tear, with a favorable adverse event profile and no drug-related serious adverse events.



These observed endpoints support the proposed mechanism-of-action of restoring goblet cell loss by OK-101 as demonstrated in preclinical animal models.

The background is a complex, abstract composition. It features a central, dark, circular void that is surrounded by a dense field of fine, wavy lines. These lines are colored in a gradient from deep blue and purple at the top to bright orange and red at the bottom. Interspersed among these lines are numerous small, multi-colored dots (red, blue, yellow, green) that create a bokeh or starburst effect. The overall impression is one of dynamic energy and digital connectivity.

**Thank you**