Efficacy and Safety Results of First-in-Human Phase 2 Trial of OK-101 in Dry Eye Patients

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BACKGROUND

Dry eye syndrome represents a major economic burden in public healthcare accounting to total annual cost for the management of disease including lost productivity due to symptoms to the US economy more than $50 billion annually. Symptoms of dry eye include constant discomfort and irritation accompanied by visual impairment and potential damage to ocular surface. The infiltration of T cells in the conjunctiva, loss of mucin secreting conjunctival goblet cells and increase in the levels of inflammatory cytokines in both conjunctiva and tears is known to cause the chronic inflammation associated with the DED. Therefore, development of new therapeutic agents that targets inflammatory pathways and restores goblet cells is crucial in improving symptoms in DED patients.

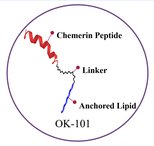
The chemerin receptor (CMKLR1 or ChemR23) is a chemokine like G protein-coupled receptor (GPCR) expressed on select populations of cells including inflammatory mediators as well as epithelial cells[1-3]. Activation of CMKLR1 has been shown to resolve the inflammation in animal models of asthma[4] and modulate the inflammation environment in autoimmune diseases by recruiting regulatory T cells (Tregs)[5]. In this Phase 2 clinical study, we assessed the efficacy and safety of OK-101 (an agonist of CMKLR1) ophthalmic solution compared with placebo in dry eye disease (DED) patients. We also evaluated ocular tolerance of OKYO-0101 following repeated ocular instillation in rabbits followed by clinical ophthalmic observations.

METHODS

The double-masked, randomized, placebo-controlled Phase 2 trial was conducted at 6 sites in the U.S. and enrolled 240 subjects with DED dosed twice-daily (BID). Patients were randomly divided into 3 cohorts, with one of the cohorts dosed with 0.05% OK-101 (n=81), a second with 0.1% OK-101 (n=80), and the third cohort with vehicle (n=79). The duration of a patient's treatment was 14 weeks, including a 2-week run-in period on placebo, to exclude placebo responders from the study, followed by 12 weeks in the randomized portion of the study. After enrollment (day 0), subjects were evaluated at days 15, 29, 57 and 85. Key objective (fluorescein and lissamine staining scores [Ora Calibra® scales], ocular discomfort score [Ora Calibra® scale] and 8-item visual analog scale measures were assessed at all visits. The primary objective efficacy measure (sign) was mean change from baseline inferior corneal staining score (ICSS) at day 85. The co-primary subjective efficacy measure (symptom) was mean change from baseline ocular discomfort score (ODS) at Day 85. Secondary measures included conjunctival lissamine staining scores using Ora Calibra® scales and 8-item visual analog scale scores at day 85.

OK-101

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

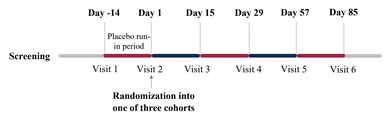
Receptor localization
Monocytes, macrophage, dendritic cells, NK cells, Treg cells, spinal cord neurons

Endogenous ligand
Chemerin: 136 aa peptide
Resolvin E1

Therapeutic targets (based on resolvin E1 efficacy)
Dry eyes, neuropathic pain, asthma

STUDY DESIGN AND SAFETY

OK-101 DED Phase 2 Trial Design



OK-101 (0.05%) n = 81	OK-101 (0.1%) n = 80	Placebo n = 79

Study Overview

Total Subjects: Enrolled = 384	Baseline characteristics were balanced amongst treatment groups
Screen Failures = 144	No drug-related SAEs, most AEs were mild stinging & burning
Randomized Subjects = 240	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

CRO Partner
Ora

OK-101 Phase 2 DED Study: Patient Demographics

Category	OK-101 (0.1%)	OK-101 (0.05%)	Placebo	All Subjects
Age (Years): n	80	81	79	240
Mean (SD)	66.2 (10.6)	63.6 (11.98)	64.4 (13.69)	64.7 (12.15)
Median	67.0	63.0	65.0	65.0
Min, Max	35, 85	20, 87	26, 94	20, 94
Sex				
Male: n (%)	30 (37.5)	20 (24.7)	17 (21.5)	67 (27.9)
Female: n (%)	50 (62.5)	61 (75.3)	62 (78.5)	173 (72.1)
Ethnicity				
Hispanic or Latino: n (%)	6 (7.5)	6 (7.4)	2 (2.5)	14 (5.8)
Not Hispanic or Latino: n (%)	74 (92.5)	75 (92.6)	77 (97.5)	226 (94.2)
Race				
American Indian or Alaska Native: n (%)	1 (1.3)	2 (2.5)	2 (2.5)	5 (2.1)
Asian: n (%)	7 (8.8)	9 (11.1)	6 (7.6)	22 (9.2)
Black or African American: n (%)	19 (23.8)	20 (24.7)	8 (10.1)	47 (19.6)
Native Hawaiian or Other Pacific Islander: n (%)	1 (1.3)	0	0	1 (0.4)
White: n (%)	52 (65.0)	50 (61.7)	63 (79.7)	165 (68.8)

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 Subjects Withdrawn Study Drug due to Ocular TEAE: n (%)	0	1 (1.2)	1 (1.3)
Number of Subjects with Ocular TEAEs (Severity)			
Mild: n (%)	5 (6.3)	14 (17.3)	4 (5.1)
Moderate: n (%)	0	1 (1.2)	0
Severe: n (%)	0	0	0
Number of Subjects with Ocular TEAEs by Relationship to Study Drug			
Definitely Related: n (%)	4 (5.0)	8 (9.9)	0
Possibly Related: n (%)	0	1 (1.2)	3 (3.8)
Not Related: n (%)	1 (1.3)	6 (7.4)	1 (1.3)

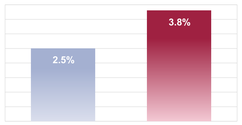
OK-101 Drop Comfort: 2 Minutes Post-Instillation Study Eye

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 Phase 2 Trial Highlights – Safety Outcome

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.

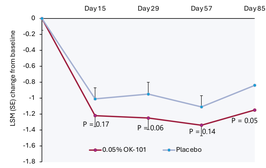


Additionally, fewer subjects in the OK-101 treated arm discontinued study medication (2.5%) compared to discontinuations in the placebo treated patients (3.8%).

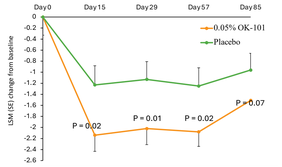
RESULTS: EFFICACY ANALYSIS

Improvement in Conjunctival Sum Lissamine Green Staining* (Sign)

Data shown is change from baseline using 0-8 scale in Intent-to-Treat and Above Median Population
P values are vs placebo based on ANCOVA Model



OK-101 (n = 81), Placebo (n = 79)



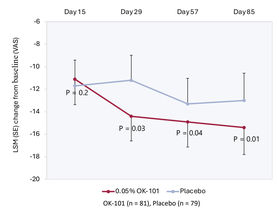
% Change from baseline (5.5)

Group	Day 15	Day 29	Day 57	Day 85
OK-101 (n = 26)	38.9	36.7	37.8	27.4
Placebo (n =28)	22.3	20.5	22.7	17.4
Change	16.6	16.2	15.1	10

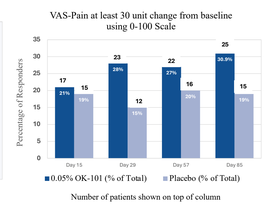
*Ora Calibra Scale 0-8

Significant Improvement in Pain[1] (Symptom)

Data shown is change from baseline using 0-100 Visual Analog Scale in Intent-To-Treat Population
P values are vs placebo based on Wilcoxon rank sum test



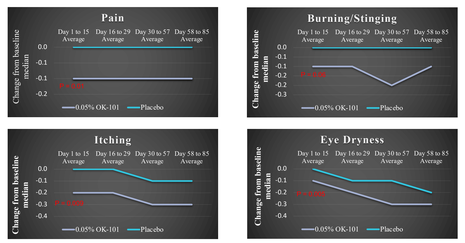
OK-101 (n = 81), Placebo (n = 79)



Number of patients shown on top of column

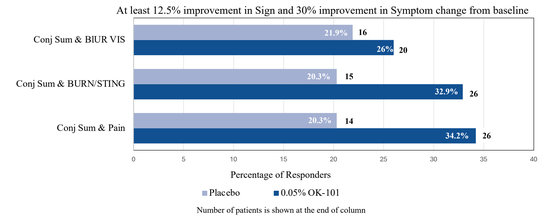
[1]Visual Analog Scale 0-100

Significant Improvement in Symptoms by Patient Reported Daily Diary



Diary Symptoms Improvement Sustained Throughout the Trial

Responders With Improvement in Both Signs*[1] and Symptoms[2] at Day 85 ITT Population

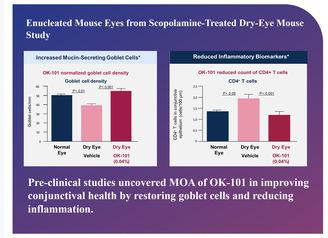


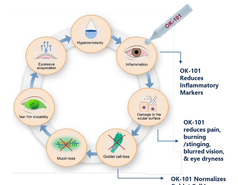
Number of patients is shown at the end of column

*Ora Calibra Scale, 0-8 scale, [1]Lissamine Green Staining [2]Visual Analog Scale (VAS) 0-100;

MECHANISM

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





* Patil et al. (2018) 14th Congress on Ocular Pharmacology and Therapeutics, New Orleans, LA

CONCLUSIONS

- OK-101 appears to act quickly, displaying rapid reduction of ocular DED symptoms. These clinical benefits combined with OK-101's exceptional tolerability profile make OK-101 a novel and promising therapeutic agent with the potential for a market leading position in DED.
- OK-101 demonstrated statistically significant and durable improvements in conjunctival staining, ocular pain and burning/stinging. Responder rate analysis involving the combination of conjunctival staining (sign) and ocular pain (symptom) endpoints indicates this combination as the primary endpoints for next clinical trial.
- While study didn't meet the primary endpoints, the totality of the data support advancing forward with a new study design that leverages our learnings of the novel mechanism of action of OK-101.
- The totality of the data that we are seeing, including the improvement in conjunctival integrity, positive increase in tear-film breakup time, and improvements in multiple symptom endpoints, all supporting the proposed MOA that we uncovered in preclinical animal models.

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