OTX-DED (DEXAMETHASONE INTRACANALICULAR INSERT)

PHASE II TOPLINE RESULTS: INVESTOR CALL

DEC 6th, 2021

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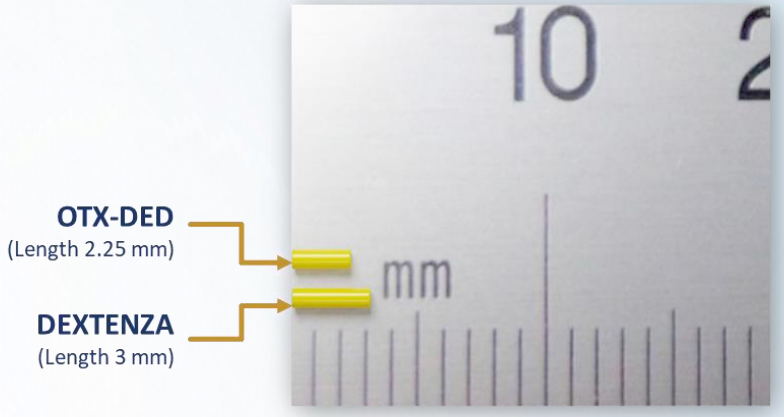
OTX-DED (DEXAMETHASONE INTRACANALICULAR INSERT)

OFF-LABEL STEROIDS ARE CURRENTLY USED TO TREAT EPISODIC DRY EYE

ISSUES WITH EXISTING TREATMENTS

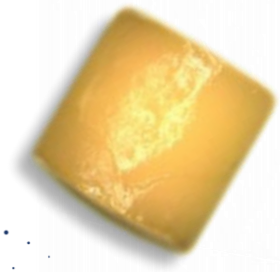
- Approved therapies for the chronic treatment of DED are known for slow onset of action & burning/stinging upon application
- All currently approved topical steroid eye drops in US have preservatives which have the potential to cause ocular surface toxicity



Rendering showing OTX-DED is shorter in length than DEXTENZA

KEY PRODUCT ATTRIBUTES

- Dexamethasone (0.2mg or 0.3 mg) loaded in hydrogel
- Preservative-free
- Occludes the canaliculus providing more rapid onset of action
- Fully biodegradable insert
- Leverages safety profile of DEXTENZA®



DEXTENZA [package insert]. Bedford, MA: Ocular Therapeutix Inc; 2021 https://www.dextenza.com/wp-content/uploads/DEXTENZA-Full-Prescribing-Information.pdf

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PHASE 2 STUDY OBJECTIVE AND DESIGN

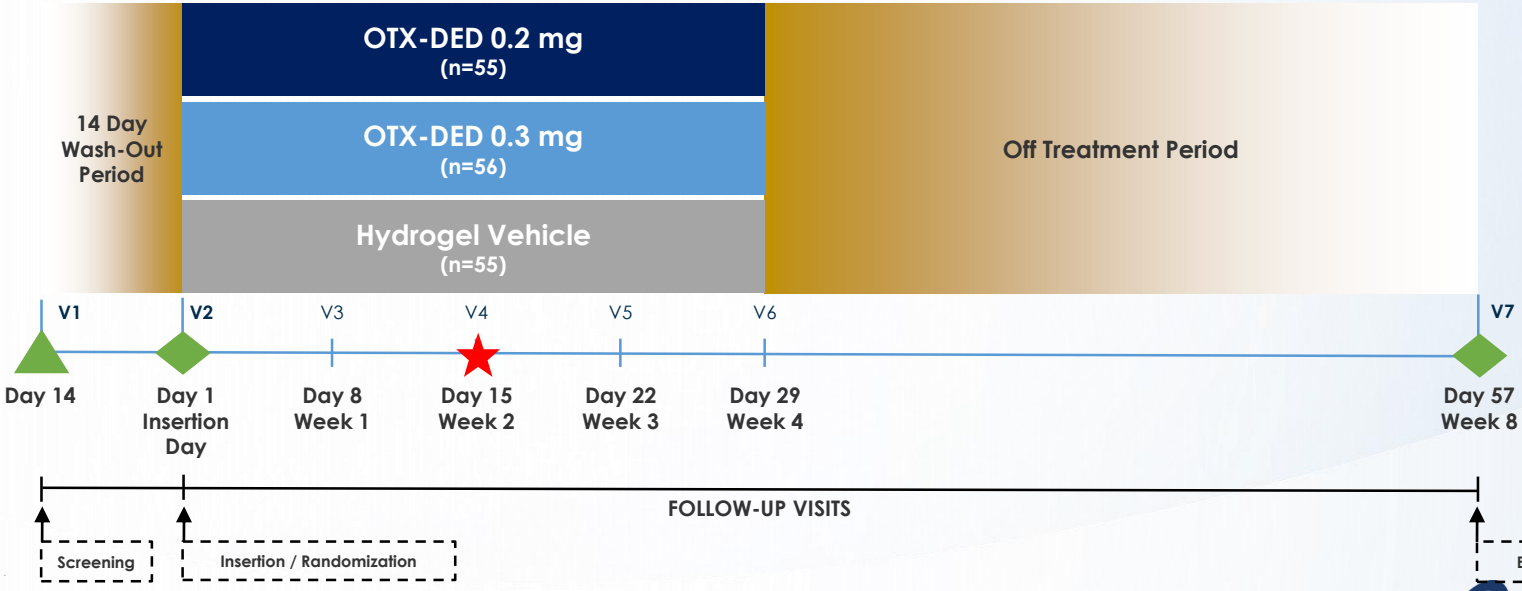
OBJECTIVE: EFFICACY AND SAFETY OF OTX-DED FOR THE SHORT-TERM TREATMENT OF SIGNS AND SYMPTOMS OF DRY EYE DISEASE

DESIGN

- Prospective, Randomized, Double-Masked, Vehicle-controlled study
- Key Inclusion criteria:
  - DED diagnosis in both eyes for ≥6 months
  - Eye dryness severity score (VAS) ≥30
  - Bulbar conjunctival hyperemia grade ≥ 2 (CCLRU scale)

ENDPOINTS

- **Primary endpoint:** Bulbar conjunctival hyperemia- worst zone (Day 15), change from baseline
- **Secondary endpoints**
  - Bulbar conjunctival hyperemia- individual zones, total
  - Eye Dryness Score (visual analogue scale [VAS])
- **Safety:** Adverse Events (Ocular and Non-ocular)



OUTCOME MEASURES

EFFICACY ENDPOINTS

SIGNS:

- **Primary Endpoint:** Photographic assessment of bulbar conjunctival hyperemia change from baseline (CFB) at 15 days (evaluated via central reading center, CCLRU grading scale, 0-4 per region)- worst zone
- **Secondary Endpoint**: Bulbar conjunctival hyperemia using CCLRU grading score, CFB, individual zones and total

SYMPTOMS **Secondary Endpoint**

- Eye Dryness Score (visual analogue scale (VAS)), CFB and absolute values at each post baseline study visit

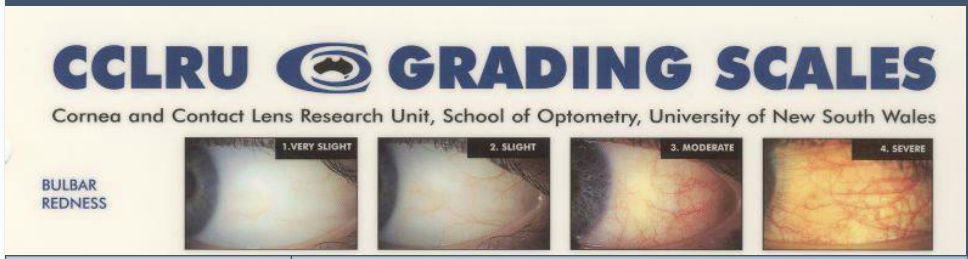
Visual Analogue Scale (VAS) for Eye Dryness

	No discomfort	Maximal (the most) discomfort
Eye Dryness Severity	0%	100%
Eye Dryness Frequency	0%	100%

SAFETY ENDPOINTS

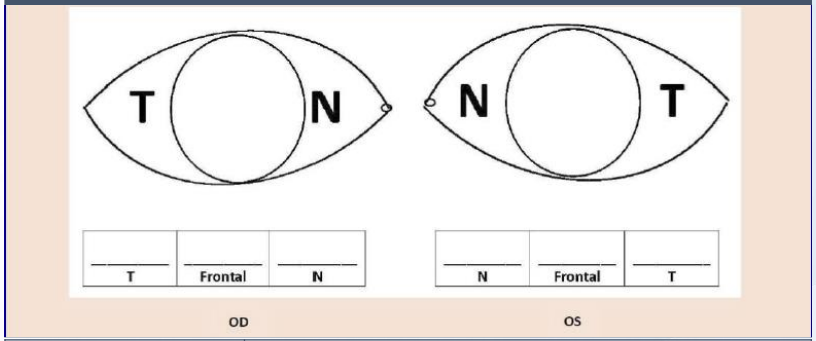
- Adverse events; Best-corrected visual acuity; Slit lamp examination; Intraocular pressure; Dilated fundus examination; Artificial tear use during the study

CCLRU Conjunctival Hyperemia Grading Scale



Grade	Scale
0	None
1	Very Slight
2	Slight
3	Moderate
4	Severe

Regions for Conjunctival Hyperemia Grading



Worst Zone	Scale (0-4)
Nasal (N)	Scale (0-4)
Temporal (T)	Scale (0-4)
Frontal	Scale (0-4)
Total	Scale (0-12)

CCLRU: Cornea and Contact Lens Research Unit; NEI: National Eye Institute

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DEMOGRAPHICS AND BASELINE MEASUREMENTS

	OTX-DED (0.2 mg)	OTX-DED (0.3 mg)	OTX-DED Total	Vehicle Hydrogel	TOTAL
Modified Intent to Treat (mITT)	**55**	**56**	**111**	**55**	**166**
Age, mean	63.7	65.4	64.6	63.8	64.3
Female, %	74.5	69.6	72.1	74.5	72.9
Race, %					
Caucasian	70.9	67.9	69.4	74.5	71.1
African American	20.0	25.0	22.5	14.5	19.9
Asian	9.1	7.1	8.1	10.9	9.0
BASELINE CHARACTERISTICS (STUDY EYE)					
Mean Conjunctival Hyperemia					
Worst Zone (Scale 0-4)	1.95	1.98	1.96	2.02	1.98
Nasal (Scale 0-4)	1.80	1.88	1.84	1.93	1.87
Temporal (Scale 0-4)	1.67	1.84	1.76	1.89	1.8
Frontal (Scale 0-4)	1.58	1.79	1.68	1.76	1.71
Total (Scale 0-12)	5.05	5.50	5.28	5.58	5.38
Mean Eye Dryness Severity Score (0-100 scale)	72.8	70.0	71.4	72.4	71.7
Mean Eye Dryness Frequency Score (0-100 scale)	73.3	74.5	73.9	74.5	74.1

Total # of screen failures: 52 of 224 screened

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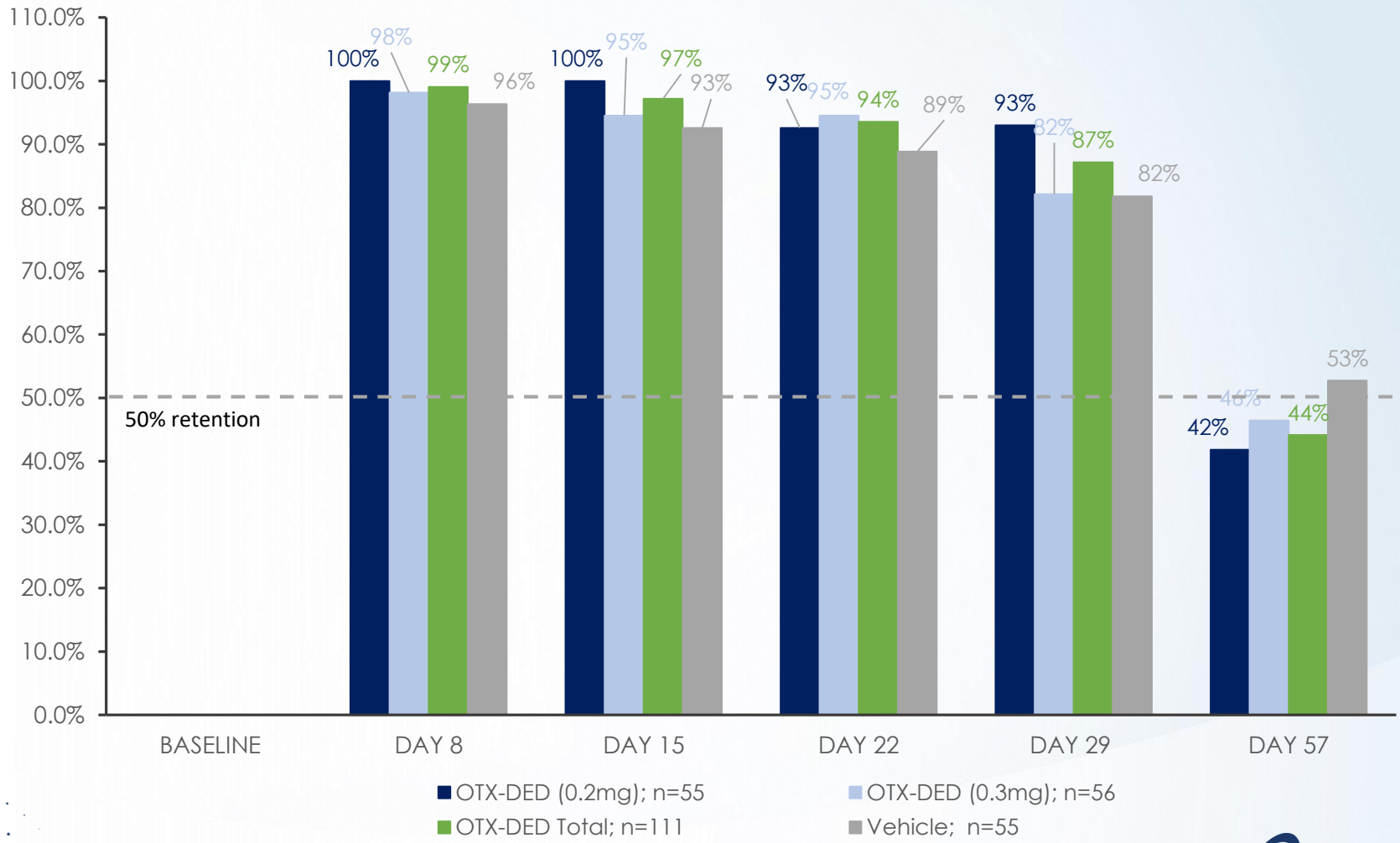
OTX-DED RETENTION RATE
INSERT PRESENCE VISUALIZATION

RETENTION WAS HIGH THROUGH THE 30-DAY PERIOD



Modified Intent to Treat Population with Observed Data (N=166)

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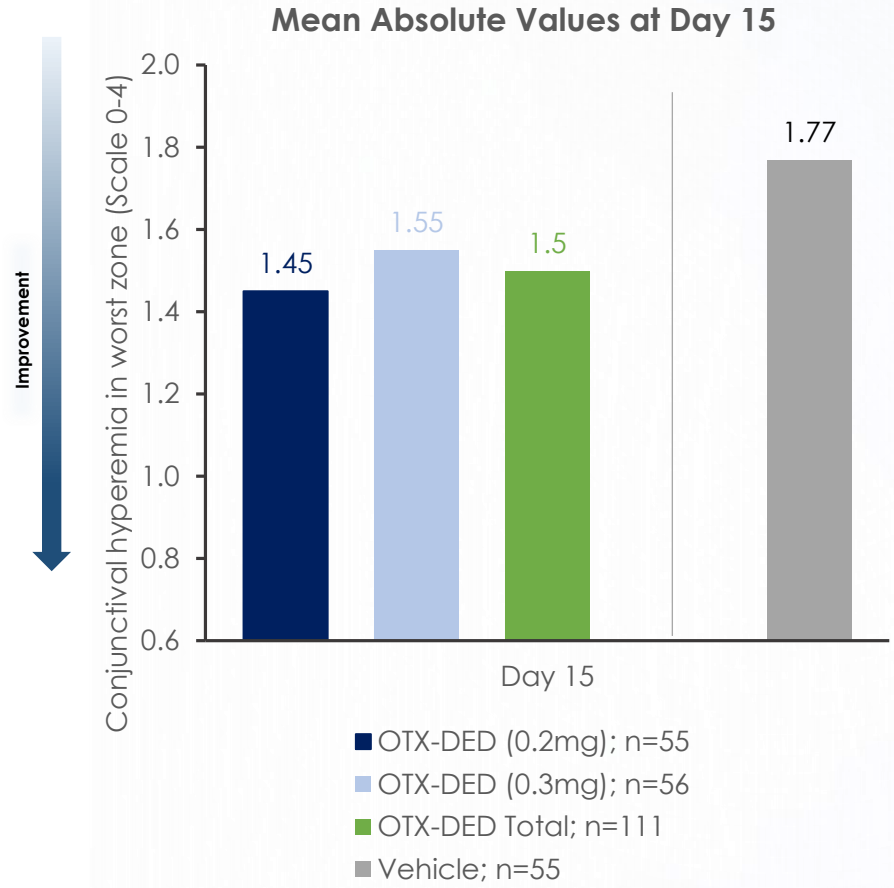
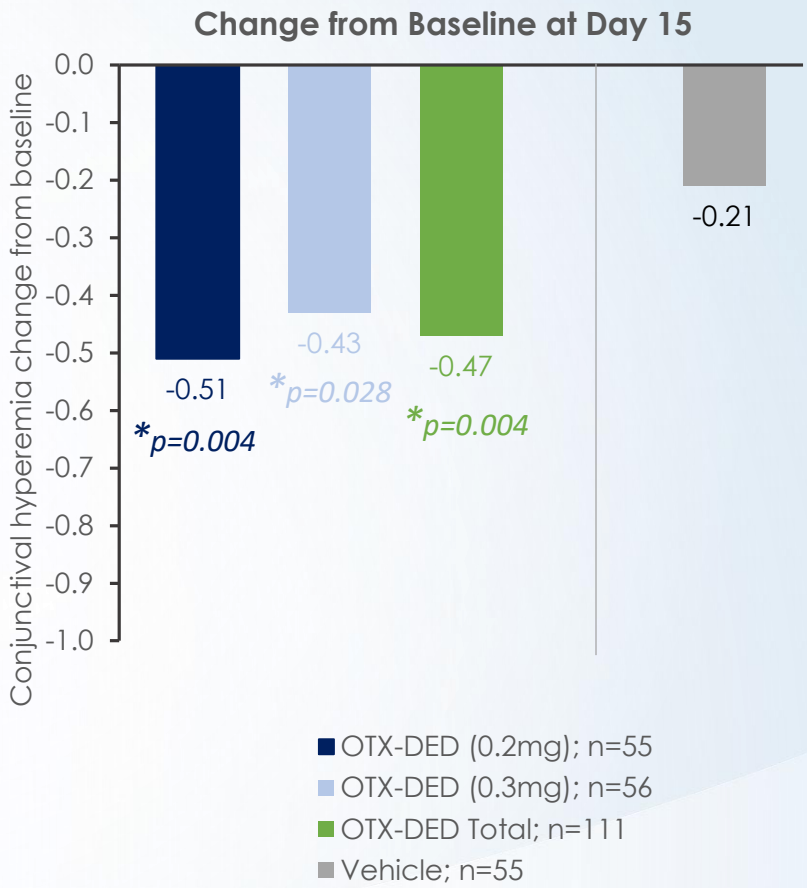
PRIMARY EFFICACY ENDPOINT
CONJUNCTIVAL HYPEREMIA, WORST ZONE AT DAY 15

STATISTICALLY SIGNIFICANT IMPROVEMENT IN PRIMARY ENDPOINT (CONJUNCTIVAL HYPEREMIA IN THE WORST ZONE) FOR OTX-DED RELATIVE TO VEHICLE HYDROGEL FOR 0.2 AND 0.3 MG GROUPS





Sensitivity analysis (MCMC, LOCF, FCS) shows similar results as expected due to minimal data missing (only about 3%)

Modified Intent to Treat Population with Observed Data (N=166); Least Squares Means (LS Means) for change from baseline
*Statistically significant compared to vehicle - p<0.05, Trial not powered to show statistical significance;
MCMC: Markov chain Monte Carlo method; LOCF: Last observation carried forward; FCS: Fully Conditional Specification method

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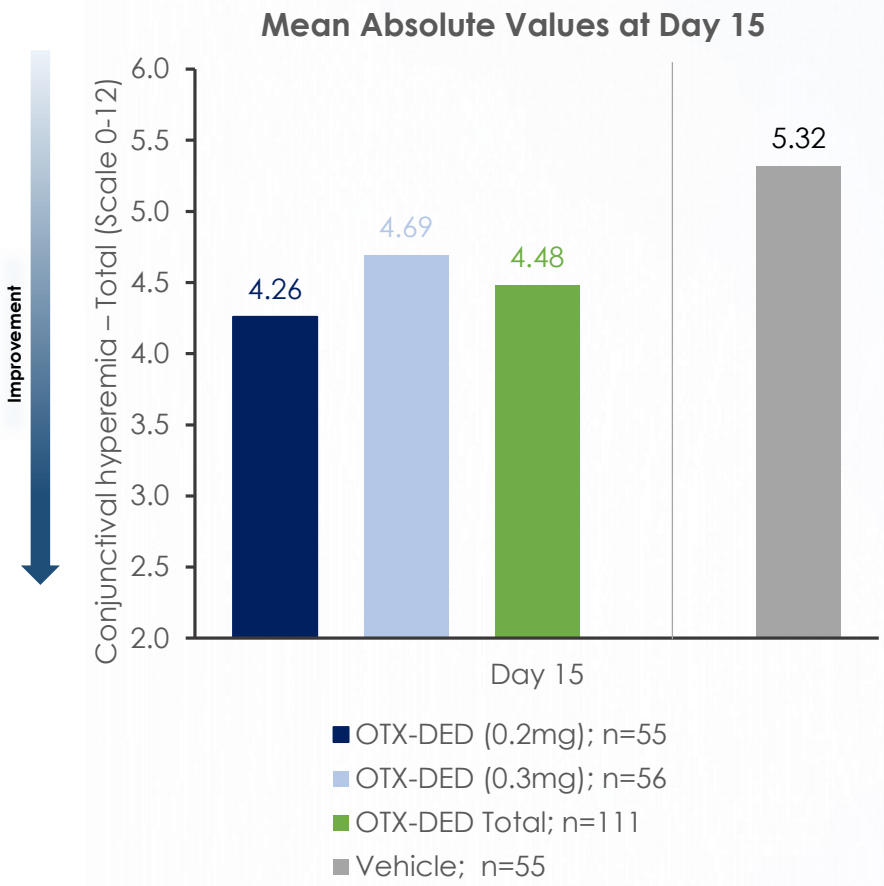
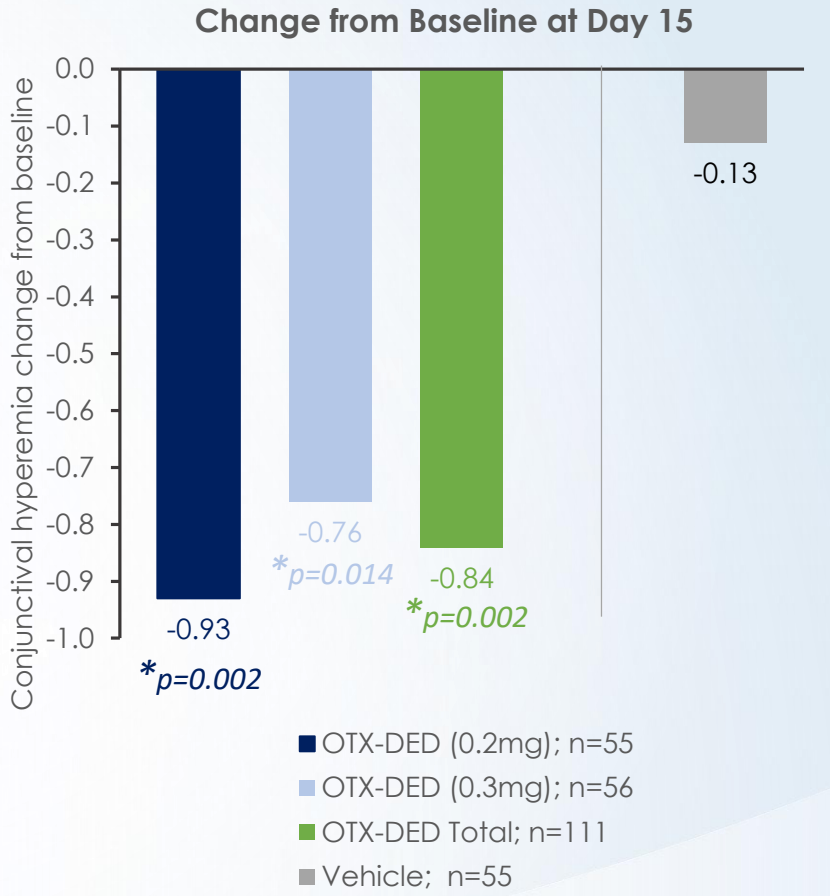
SECONDARY EFFICACY ENDPOINT
CONJUNCTIVAL HYPEREMIA, TOTAL AT DAY 15





Modified Intent to Treat Population with Observed Data (N=166); Least Squares Means (LS Means) for change from baseline
*Statistically significant compared to vehicle - p<0.05, Trial not powered to show statistical significance

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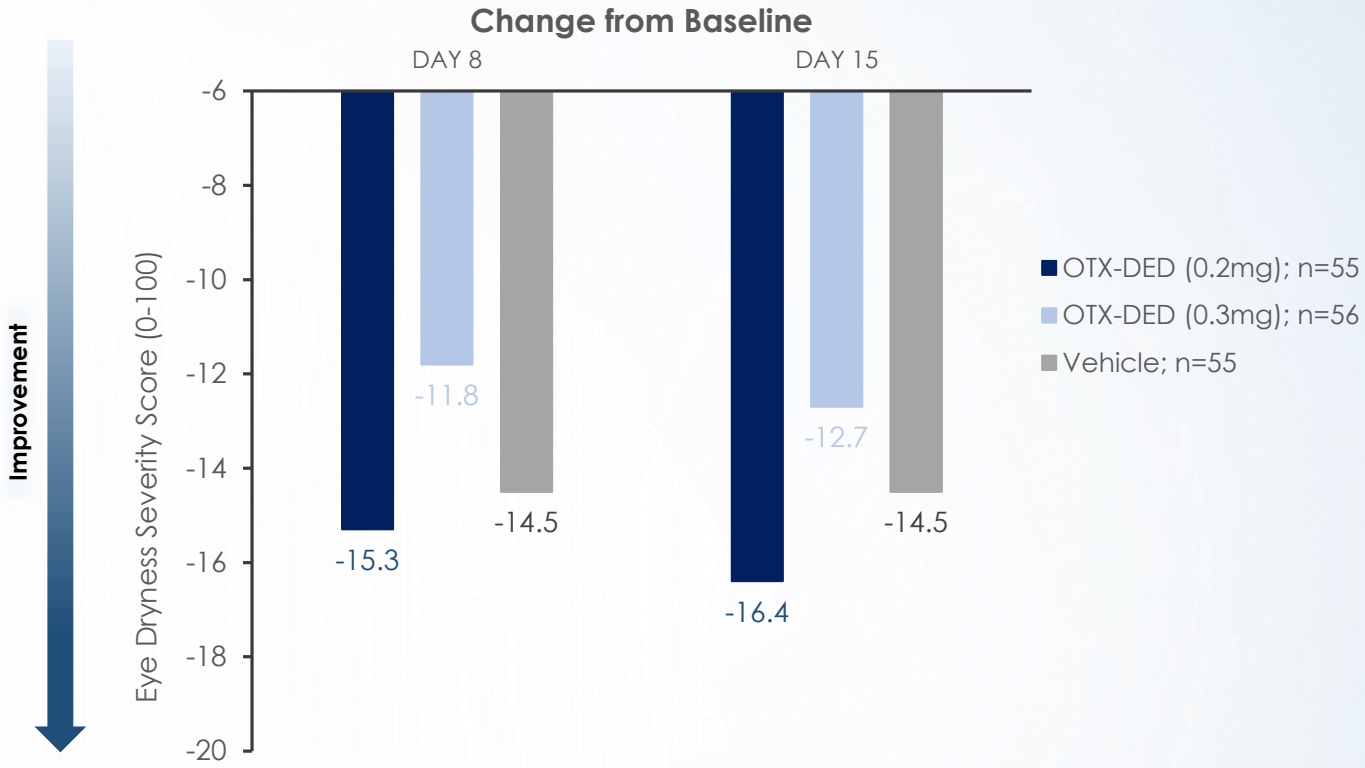
SECONDARY EFFICACY ENDPOINT

CONJUNCTIVAL HYPEREMIA NASAL, TEMPORAL & FRONTAL AT DAY 15

Modified Intent to Treat Population with Observed Data (N=166); Least Squares Means (LS Means) for change from baseline
*Statistically significant compared to vehicle - p<0.05, Trial not powered to show statistical significance;
Nasal, Temporal and Frontal: Scale 0-4

SECONDARY EFFICACY ENDPOINT: SYMPTOM
EYE DRYNESS SCORE (VAS): SEVERITY

EYE DRYNESS SEVERITY SYMPTOMS SCORES IMPROVED FROM BASELINE IN 0.2 & 0.3 MG GROUPS, WITH LITTLE SEPARATION BETWEEN ACTIVE GROUPS AND VEHICLE



BASELINE SCORES	OTX-DED (0.2 mg) n=55	OTX-DED (0.3 mg) n=56	Vehicle Hydrogel n=55
Mean Eye Dryness Severity Score (0-100 scale)	72.8	70.0	72.4

Modified Intent to Treat Population with Observed Data (N=166); Least Squares Means (LS Means) for change from baseline

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SAFETY: TREATMENT EMERGENT ADVERSE EVENTS

	OTX-DED (0.2 mg) n=55	OTX-DED (0.3 mg) n=56	OTX-DED Total n=111	Vehicle Hydrogel n=55	Total N=166
Subjects with at least 1 TEAE	12	13	25	11	36
%	21.8%	23.2%	22.5%	20.0%	21.7%
Subjects with at least 1 Ocular TEAE	7	12	19	7	26
%	12.7%	21.4%	17.1%	12.7%	15.7%
Subjects with at least 1 non-ocular TEAE	5	2	7	4	11
%	9.1%	3.6%	6.3%	7.3%	6.6%
Serious Adverse Events (SAE's)	0	0	0	2	2†
Ocular SAE's	0	0	0	0	0

†Serious Adverse Events were Cellulitis and COVID Pneumonia both in the vehicle group
Severe Adverse Events were Epiphora in 0.2 mg OTX-DED group & Cellulitis and COVID Pneumonia in the vehicle group

Modified Intent to Treat Population with Observed Data (N=166)

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OCULAR TREATMENT EMERGENT ADVERSE EVENTS

MOST COMMON ADVERSE EVENTS IN OTX-DED TREATED GROUPS - EPIPHORA (LACRIMATION INCREASE) (8.1%), IOP ELEVATION (3.6%)

	OTX-DED (0.2 mg) n=55	OTX-DED (0.3 mg) n=56	OTX-DED Total n=111	Vehicle Hydrogel n=55	Total N=166
Subjects with any Ocular TEAEs	7	12	19	7	26
%	12.7%	21.4%	17.1%	12.7%	15.7%
MOST COMMON OCULAR AEs					
Eye Pruritus	1		1	2	3
%	1.8%	0.0%	0.9%	3.6%	1.8%
Lacrimation Increase	2	7	9	2	11
%	3.6%	12.5%	8.1%	3.6%	6.6%
IOP Elevation	2	2	4	0	4
%	3.6%	3.6%	3.6%	0.0%	2.4%

- No Ocular Serious Adverse Events
- No cases of Dacryocanaliculitis

Modified Intent to Treat Population with Observed Data (N=166)

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SYSTEMIC ADVERSE EVENTS

	OTX-DED (0.2 mg) n=55	OTX-DED (0.3 mg) n=56	OTX-DED Total n=111	Vehicle Hydrogel n=55	Total (N=166)
Subjects with any Non-Ocular TEAEs	5	2	7	4	11
%	9.1%	3.6%	6.3%	7.3%	6.6%
COVID 19	1	0	1	0	1
%	1.8%	0	0.9%	0	0.6%
Arthralgia	1	1	2	0	2
%	1.8%	1.8%	1.8%	0.0%	1.2%

†Serious Adverse Events were Cellulitis and COVID Pneumonia both in the vehicle group

Modified Intent to Treat Population with Observed Data (N=166)

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CONCLUSIONS

Phase II Study Evaluating Safety and Efficacy of OTX-DED in Subjects with DED

- **Statistically significant improvement in the primary endpoint (bulbar conjunctival hyperemia in the worst zone) for OTX-DED relative to vehicle hydrogel for 0.2 and 0.3 mg groups**
  - Trial not powered for statistical significance
  - Data for secondary endpoints of conjunctival hyperemia scores best for Total = Nasal >Temporal >Frontal
    - All statistically significant except for Frontal (OTX-DED 0.3 mg group)
  - Sensitivity analysis (MCMC, LOCF, FCS) shows similar results as expected due to minimal data missing (only about 3%)
- Both doses seem to perform well with no dose response seen
- Symptoms (eye dryness score) improved from baseline in all three groups, with no separation between active groups and vehicle
  - Preliminary outlier analysis and post-hoc analysis show potential opportunities to differentiate between OTX-DED and vehicle hydrogel groups
- Observed to have a favorable safety profile and were generally well tolerated, with low rates of ocular pain/discomfort/irritation
  - Most common adverse events in OTX-DED treated groups (0.2 & 0.3 mg) - epiphora (lacrimation increase) (8.1%), IOP elevation (3.6%)
  - No ocular serious adverse events (SAE's)

MCMC: Markov chain Monte Carlo method; LOCF: Last observation carried forward; FCS: Fully Conditional Specification method