Safety and Efficacy of a Novel Hydrogel-based Cyclosporine Intracanalicular Insert for the Treatment of Dry Eye Disease: A Phase 1 Study

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FINANCIAL DISCLOSURES

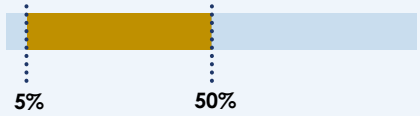
Shettle L was an investigator in this clinical trial.

Cheung M, Blender N, Vantipalli S, Metzinger JL, and Goldstein MH are employees of Ocular Therapeutix, Inc.

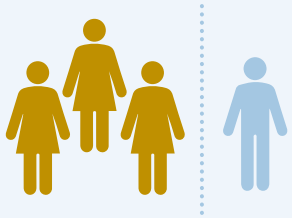
Clinical Trial Sponsor: Ocular Therapeutix, Inc.

Unmet Needs in Dry Eye Disease Therapy

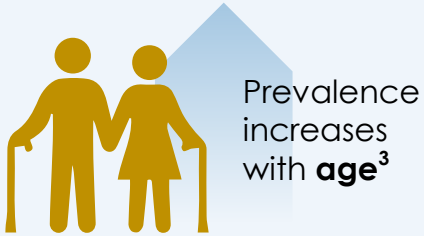
Dry eye disease (DED) is a multifactorial disorder of the tears and ocular surface and represents the most common reason for seeking medical eye care.[1,2]



Prevalence is estimated to be **5**% to **50**% of the global population[2]



Prevalence is 2-3 times higher in the **female** population compared to the male population[3]



Prevalence increases with **age**[3]

Cyclosporine is a potent immunomodulator that acts selectively and locally when administered to the ocular surface.[4,5]

- FDA-approved for treatment of dry eye disease signs and symptoms
- Demonstrated to decrease inflammatory mediators and increase tear fluid secretions

Challenges with existing treatments[6-10]:

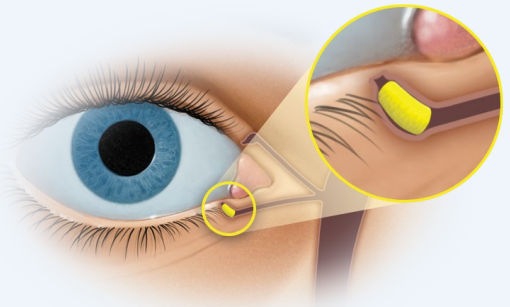
- Take weeks to months for therapeutic effect
- Tolerability issues (i.e., stinging, burning, ocular irritation and dysgeusia)
- Burden of patient administration

References: 1. Craig JP, et al. *Ocul Surf*. 2017 Jul;15(3):276-283. **2.** Stapleton F, et al. *Ocul Surf*. 2017;15(3):334-365. **3.** Dana R, et al. *Am J Ophthalmol*. 2019;202:47-54. **4.** Stevenson W, et al. *Arch Ophthalmol*. 2012;130(1):90-100. **5**. Turner K, et al. *Cornea*. 2000;19(4):492-496. **6.** RESTASIS [prescribing information]. Irvine, CA; Allergan, Inc; 2012. **7.** CEQUA [prescribing information]. Cranbery, NJ; Sun Pharmaceuticals; 2018. **8.** XIIDRA [prescribing information]. Lexington, MA; Shire US Inc.; 2016. **9.** Fraunfelder FT, et al. *J Ophthalmol*. 2012;2012:285851. **10.** Epstein SP, et al. *J Ocul Pharmacol Ther*. 2009;25(2):113-119.

OTX-CSI, a Cyclosporine Intracanalicular Insert

A sustained-release, biodegradable, preservative-free cyclosporine insert designed to provide effective therapy for up 12 weeks

- Combines two DED treatment modalities into a single therapy: cyclosporine and punctal occlusion
- Inserted into the canaliculus and slowly releases cyclosporine to the ocular surface
- Contains 0.36 mg of cyclosporine in a polyethylene glycol (PEG) hydrogel rod



Rendering of placement of insert in the canaliculus

Preclinical Pharmacokinetics in Beagle Dogs

- Reduced tear fluid production (typically seen in dry eye disease) did not inhibit transport of cyclosporine from the insert to the tear fluid[1]
- Tear fluid drug levels were maintained above the target concentration required for T-cell immunomodulation for 12 weeks[2]

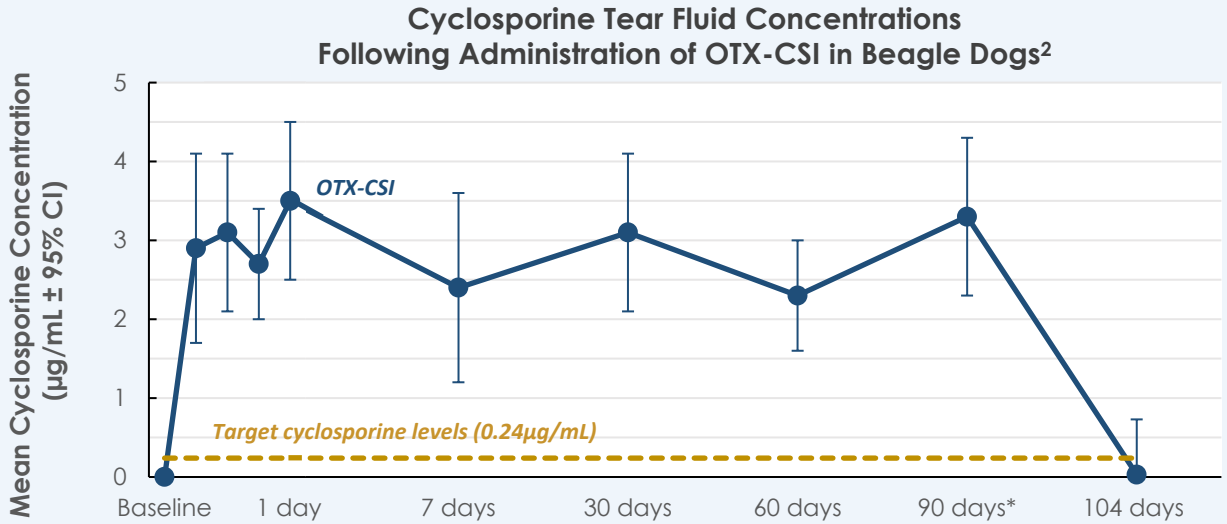
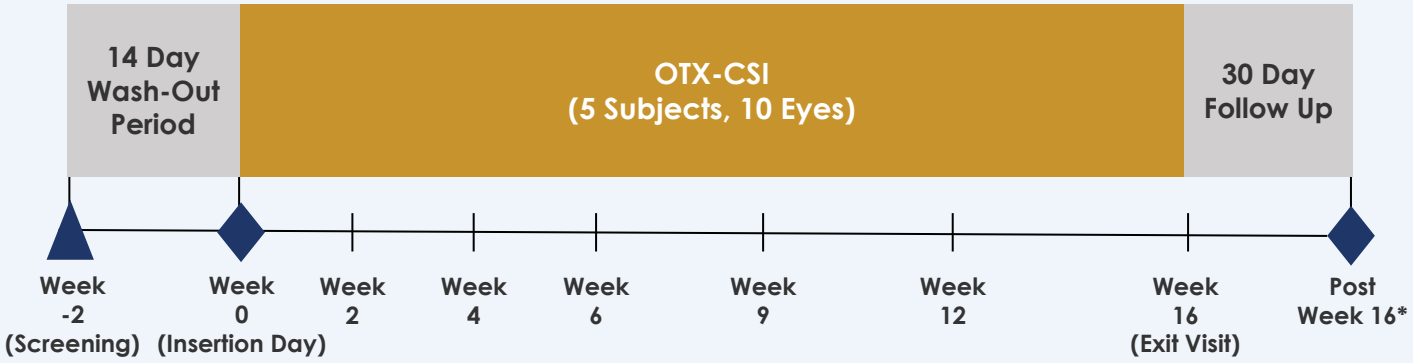


Image courtesy of Ocular Therapeutix, Inc.

References: 1. Vanslette A, Blizzard CD, Driscoll A, et al. Pharmacokinetics of OTX-CSI, a cyclosporine intracanalicular insert, in surgically induced dry eye beagle dogs . Presented at the Association for Research in Vision and Ophthalmology Annual Meeting. Virtual. May 2021. **2.** Vanslette A, Haberman P, Blizzard C, et al. Evaluating Safety and Pharmacokinetics of OTX-CSI, a Sustained Cyclosporine Releasing Intracanalicular Insert in Beagles. Presented at the Association for Research in Vision and Ophthalmology Annual Meeting. Virtual. May 2020.

Clinical Study Design and Baseline Demographics

A Phase 1, Open-label Study in Subjects with DED



*Subject remains in study until insert is no longer visible and no evidence of biological activity

Key Inclusion Criteria

- DED in both eyes for ≥ 6 months
- VAS eye dryness severity score ≥30 in the study eye
- Total Corneal Fluorescein Staining Score (NEI scale) ≥6 and <15
- Schirmer score (unanesthetized) >0mm and ≤10mm at 5 minutes

Endpoints

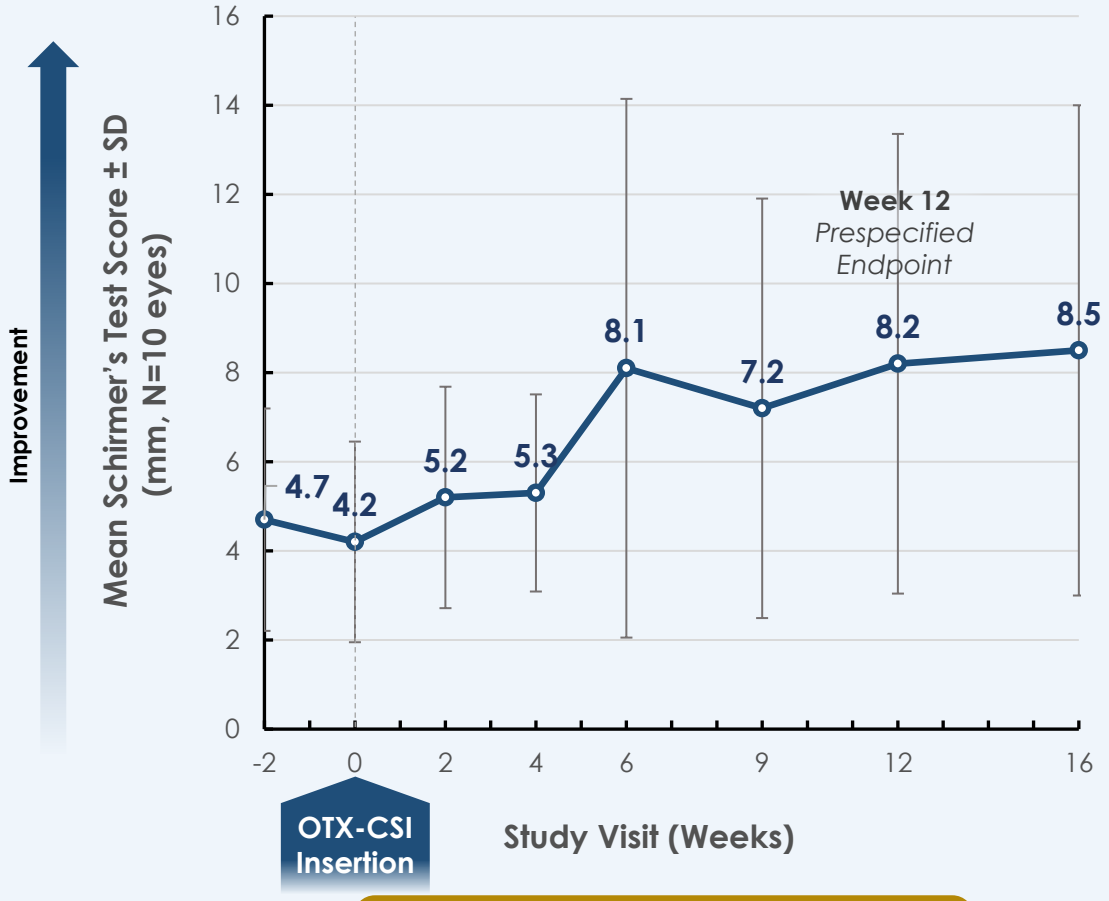
- Safety (adverse events collection)
- Schirmer's Test (without anesthesia) at Week 12
- Eye Dryness Score Severity and Frequency
- Total Corneal Fluorescein Staining (NEI scale)
- Ocular Surface Disease Index (OSDI)

Baseline Demographics and Measurements

	All Subjects (N=5 subjects)
Age, mean (range)	73.0 (63-82)
Female, n (%)	5 (100%)
Race, n (%)	
White	5 (100%)
Mean Schirmer's Test Score without anesthesia (SD, mm)	4.2 (2.3)
Mean Total Corneal Fluorescein Staining Score (SD, NEI scale)	6.7 (0.5)
Mean Eye Dryness Severity Score (SD, 0-100 scale)	51 (10.6)
Mean Eye Dryness Frequency Score (SD, 0-100 scale)	51 (14.4)
Mean Ocular Surface Disease Index (SD, 0-100 scale)	45.7 (17.8)

Following OTX-CSI Insertion, DED Signs Improved at Week 16 Compared to Baseline

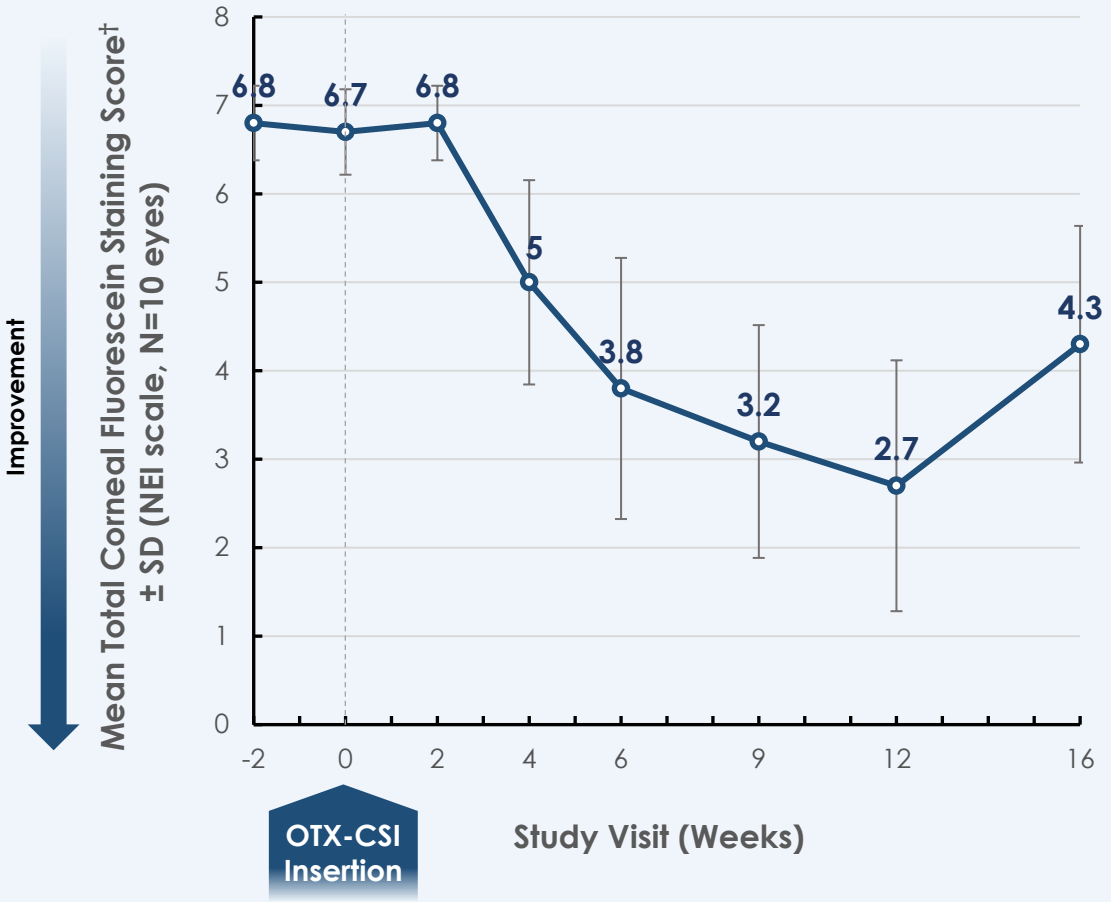
SCHIRMER'S TEST SCORES (UNANESTHETIZED)



20% (1/5) of subjects showed ≥10mm increase from baseline*

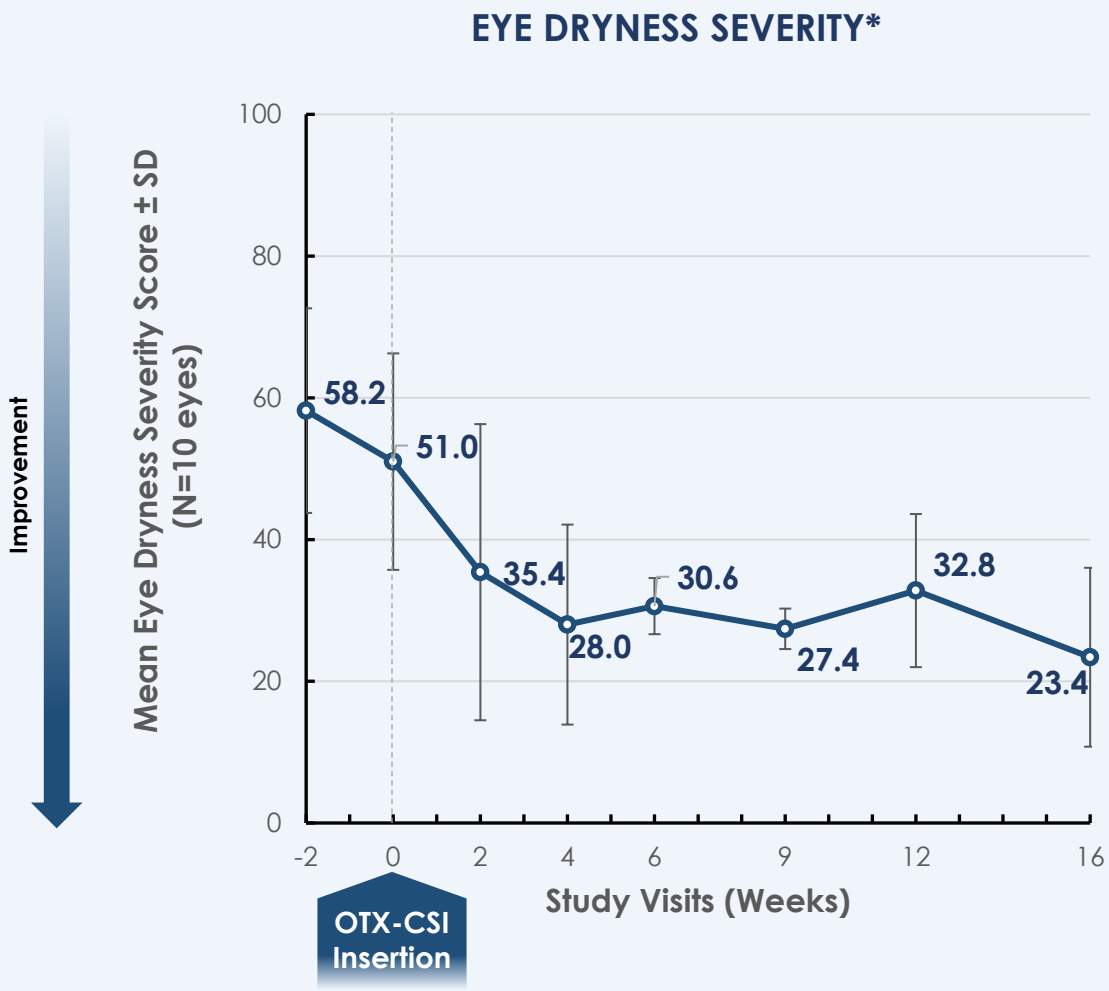
* One of 10 eyes (10%) showed ≥10mm increase from baseline at Week 12

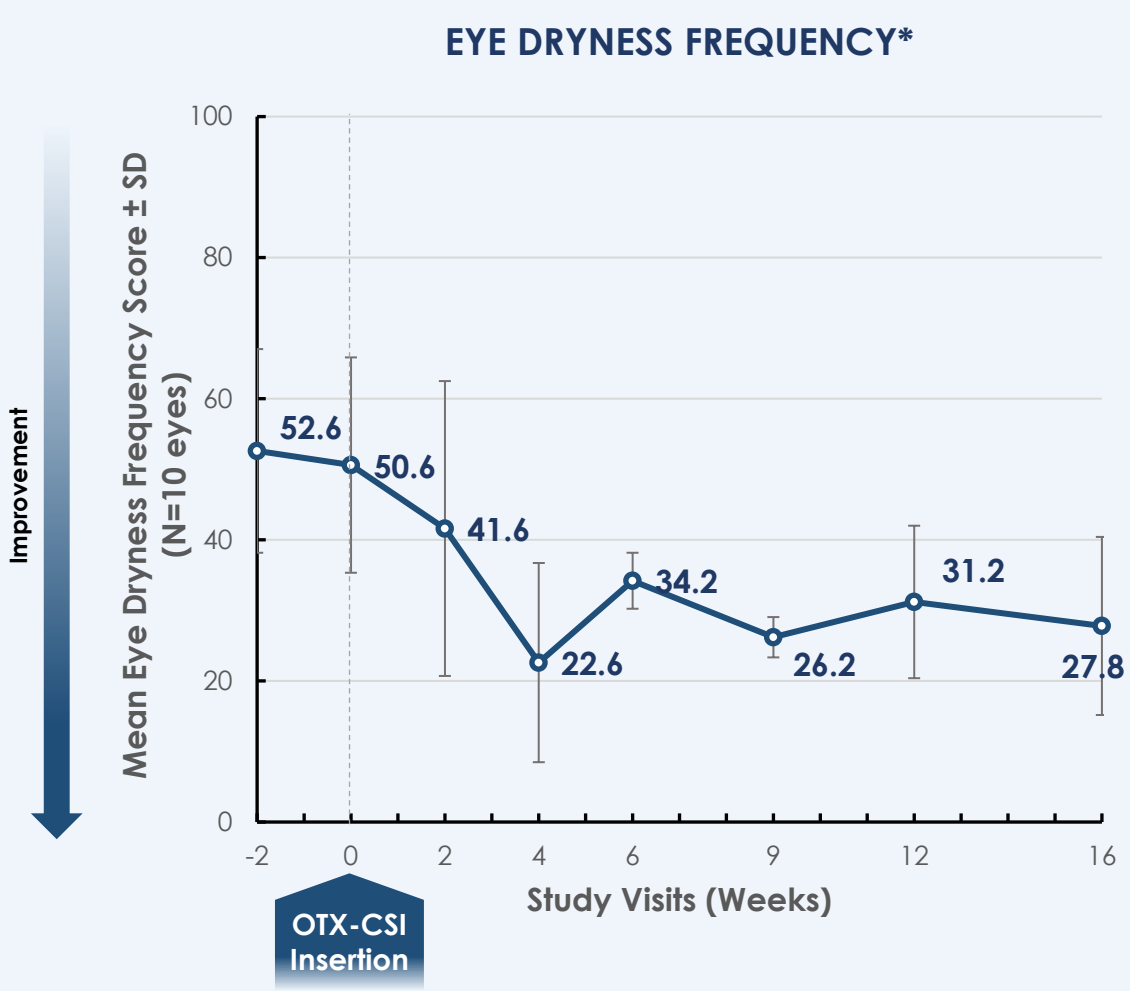
TOTAL CORNEAL FLUORESCEIN STAINING



†Staining was graded for five regions of the cornea and measured using the NEI 0-3 scoring scale. Total Corneal Fluorescein Staining is the sum of staining grades for five regions (0-15 scale)

Improvements in Dry Eye Severity and Frequency from Baseline were Sustained to Week 16

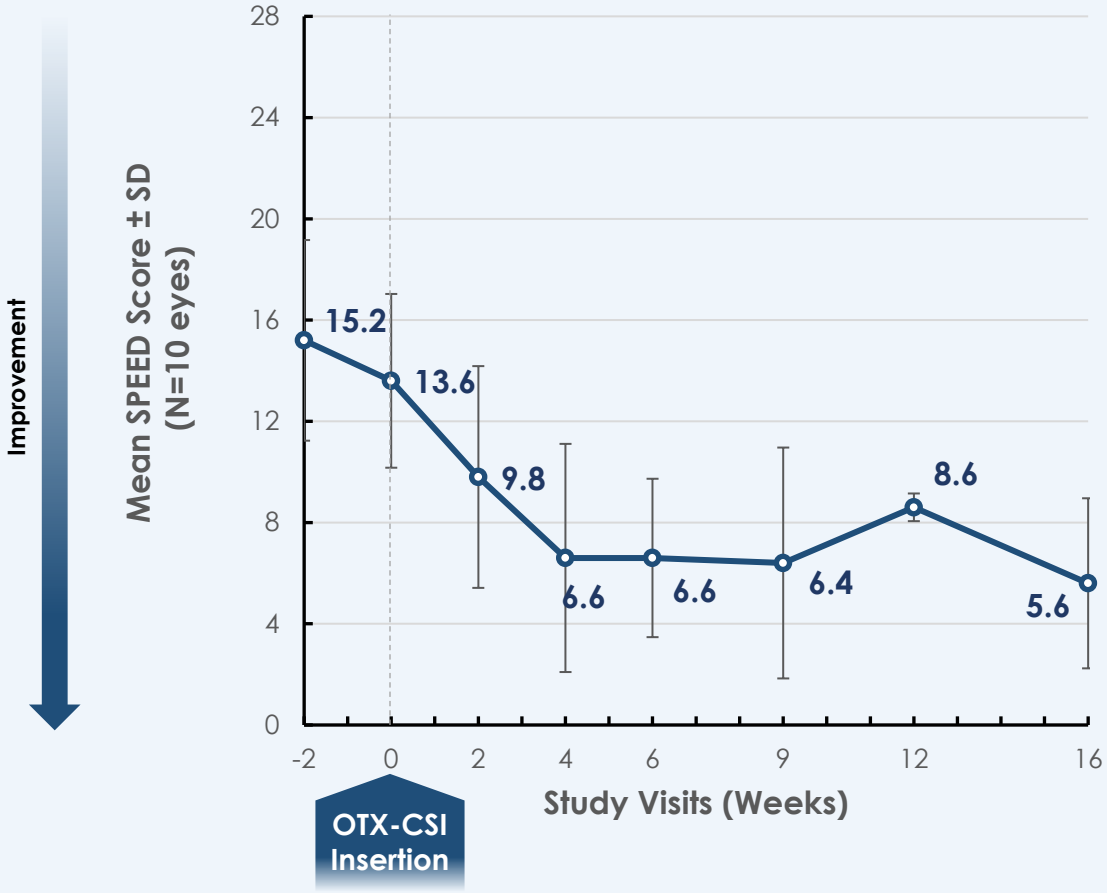




*Subjects rated the severity (level of discomfort) and frequency of the symptom eye dryness on a visual analog scale (0-100); 0 corresponds to "no discomfort" and 100 corresponds to "maximal discomfort"

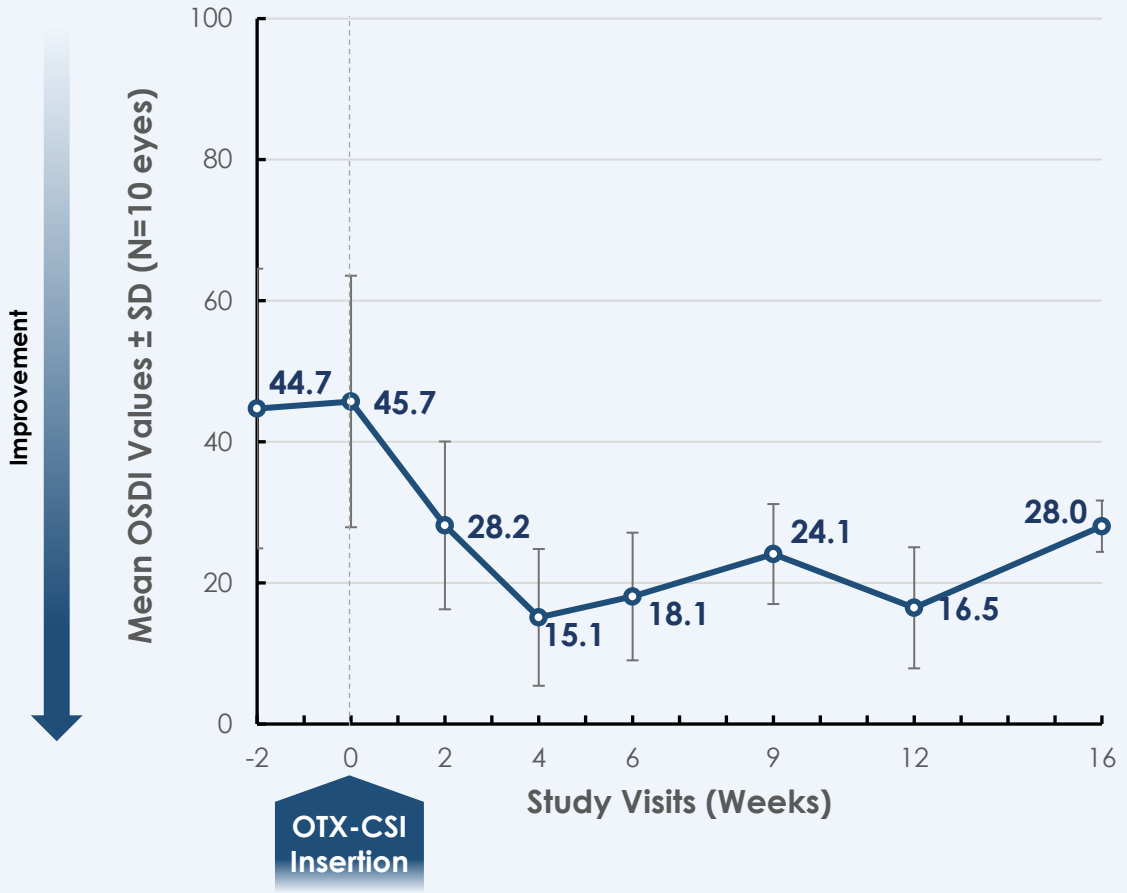
Subjects Reported Lower DED Symptom Questionnaire Scores Following OTX-CSI Insertion

SPEED QUESTIONNAIRE



SPEED, Standard Patient Evaluation of Eye Dryness (0-28 scale)

OCULAR SURFACE DISEASE INDEX



OSDI, Ocular Surface Disease Index (0-100 scale)

OTX-CSI was Generally Well-tolerated with a Favorable Safety Profile

No serious AEs reported

No treatment-related AEs reported

No AEs of stinging, burning or dysgeusia reported

Conclusions

Phase 1 Study Evaluating Safety and Efficacy of OTX-CSI in Subjects with DED

OTX-CSI improved signs and symptoms of DED as measured by change from baseline in Schirmer's Test, corneal staining, eye dryness severity/frequency, and DED symptom questionnaires

Improvements began as early as two weeks and lasted up to 16 weeks for Schirmer's Test and DED symptoms assessments

OTX-CSI was generally safe and well tolerated with no reported adverse events including stinging, burning, irritation, tearing, or blurred vision

A randomized, vehicle-controlled Phase 2 study evaluating the efficacy and safety of OTX-CSI for the treatment of dry eye disease is currently ongoing