Interim Safety and Efficacy Results From the Phase 1 HELIOS Trial of Sustained-Release Axitinib Implant (OTX-TKI) for NPDR

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On behalf of the HELIOS investigators

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Disclosures

FINANCIAL DISCLOSURES (DILSHER S. DHOOT)

Consultant/Advisor: Alcon Pharmaceuticals; Alimera Sciences, Inc.; Allergan; Annexon; Apellis Pharmaceuticals, Inc.; Bayer Healthcare Pharmaceuticals, Inc.; Biocryst; Coherus; EyePoint Pharmaceuticals; Genentech; IvericBio; Novartis; Ocular Therapeutix; Optos, Inc.; Outlook Therapeutics; Oxular; Regeneron; REGENXBIO; Roche; Santen, Inc.

Grant: Ocular Therapeutix, Inc.

STUDY AND PRODUCT DISCLOSURES

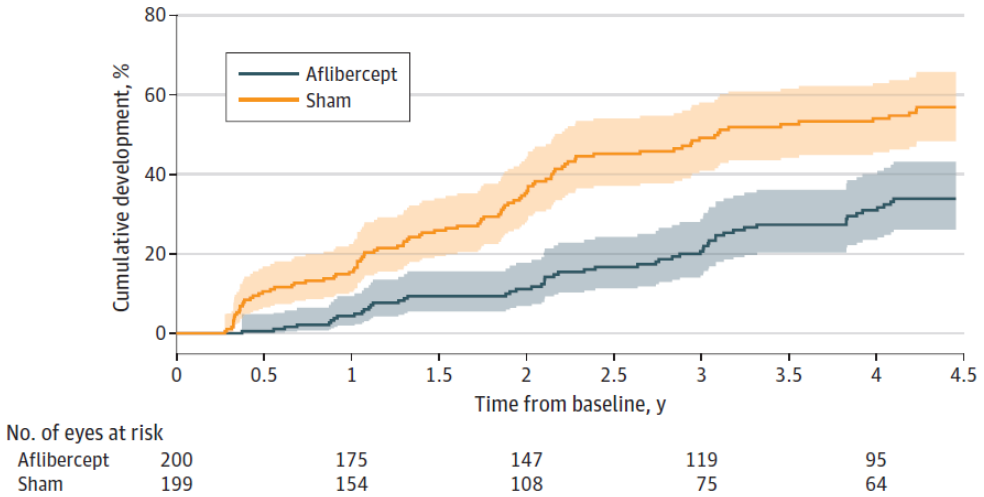
The following presentation discusses an investigational drug candidate, AXPAXLI™ (also referred to as OTX-TKI), in development. OTX-TKI's efficacy and safety profiles have not been established, and it has not been approved for marketing by the U.S. Food and Drug Administration (FDA) or any other health agency.

Ocular Therapeutix sponsored this clinical trial.

DR is Chronic, Progressive, and Burdensome With a Need for Earlier Treatment to Prevent Progression

- Efficacy of anti-VEGF therapy and **need for proactive treatment of NPDR established** in PANORAMA and Protocol W studies[1,2]
- Despite this, **<1% of NPDR patients are treated** with anti-VEGF therapy and majority of retina specialists (62.7%) **do not recommend treating NPDR** patients without DME[3-5]
- This may be due to the **unsustainable treatment burden** of frequent injections and **worse outcomes in eyes that had interrupted or reduced treatment** compared to those never treated at all[5]

Cumulative Development of PDR or CI-DME with Vision Loss[1]

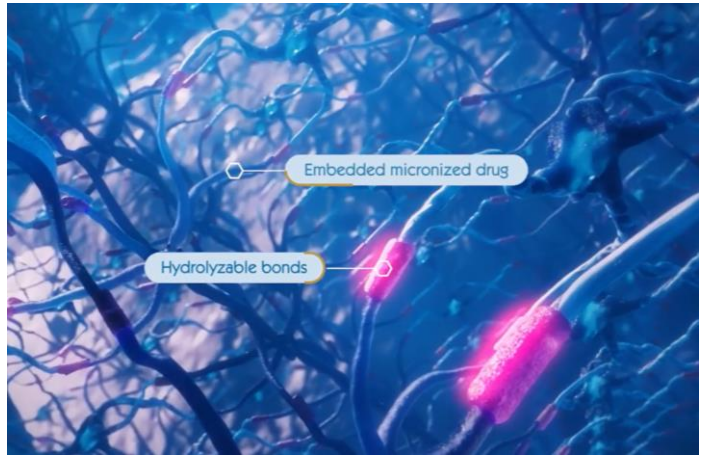


Early intervention with 3 aflibercept loading doses followed by Q16W, prevents progression to severe or vision-threatening disease

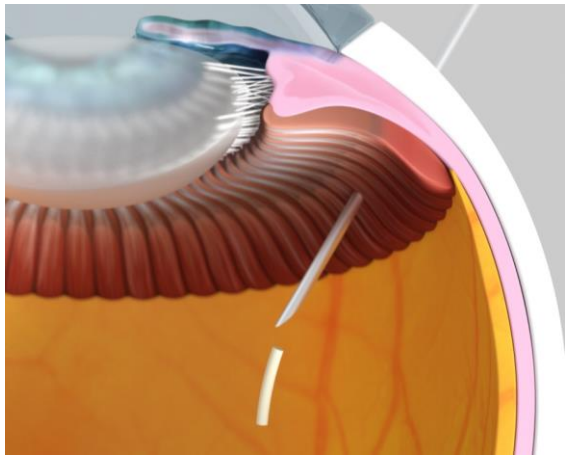
There is an unmet need for early intervention with longer lasting treatment options

1. Maturi RK, et al. *JAMA*. 2023;329(5):376-385. **2.** Brown DM, Wykoff CC, Boyer D, et al. *JAMA Ophthalmol*. 2021;139(9):946-955. **3.** Market Scope. 2022 Retinal Pharmaceuticals Market Report: Global Analysis for 2021 to 2027. Published August 2022. **4.** Market Scope. US Retina Quarterly Update: O2 2022 Analysis of Historical Trends and Latest Developments. Published August 2022 **5.** Hahn P, Garg SJ, eds. 2023 Global Trends in Retina Survey. Chicago, IL. American Society of Retina Specialists; 2023. **6**. Goldberg RA, Hill L, Davis T, et al. *BMJ Open Ophthalmol*. 2022;7(1):e001007.

OTX-TKI: Sustained-release Axitinib in Hydrogel



Drug	Inhibitory Concentrations for VEGFR2/KDR (nM) (lower IC-50 values indicate higher affinity)
Axitinib[5]	**0.2**
Sunitinib[6]	40
Vorolanib[6]	64



ELUTYX TECHNOLOGY

Bioresorbable, Targeted, Sustained Drug Delivery

- OTX's proprietary bioresorbable polymer matrix is a hydrogel-based, versatile, biocompatible platform for localized sustained drug delivery

AXITINIB

Multi-target Tyrosine Kinase Inhibitor

- High affinity for VEGFR-2 compared to sunitinib and vorolanib[1-3]
- Highly selective for all VEGF receptors[4-6] with no TIE2 inhibition at physiologic tissue concentrations[1]

OTX-TKI

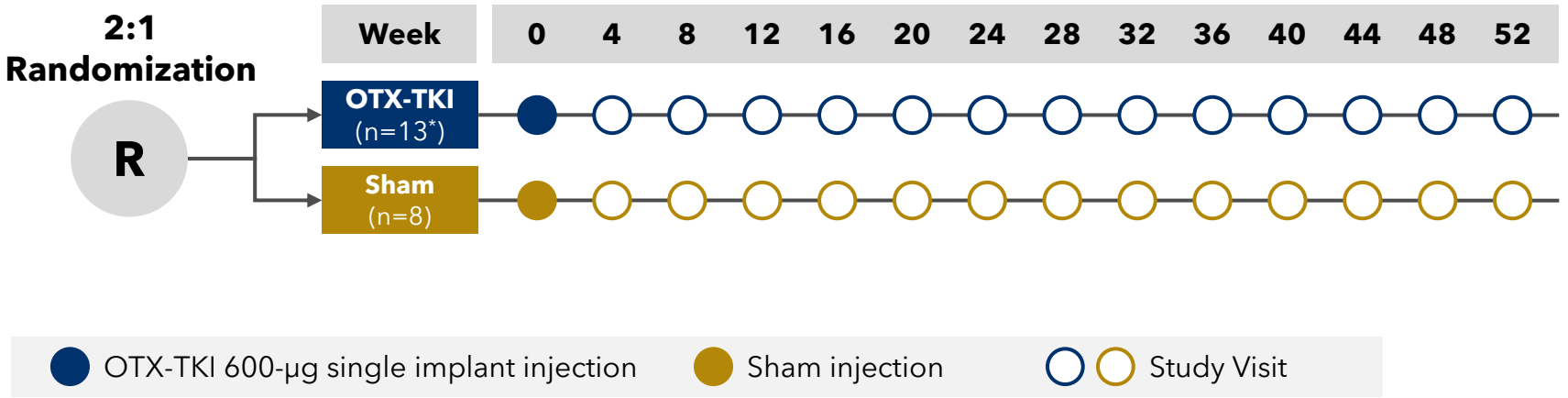
Single Intravitreal Bioresorbable Implant

- Sustained axitinib release allowing a redosing interval for 6-12 months
- Administered by a 25G needle
- Covered by patents expiring through 2044[7]

TIE2 (Tyrosine kinase with immunoglobulin-like and EGF-like domains-2); TKI (Tyrosine kinase inhibitor); VEGF (Vascular endothelial growth factor [receptor]).

1. Unpublished data; Data on File. **2.** Hu-Lowe DD, et al. Clin Cancer Res. 2008;14(22):7272-7283. **3.** McTigue M, et al. Proc Natl Acad Sci U S A. 2012;109(45):18281-18289. **4.** Zhao Y, et al. Oncologist. 2015;20(6):660-673. **5.** Gross-Goupil M, et al. Clin Med Insights Oncol. 2013;7:269-277. **6.** Liang C, et al. Mol Ther Oncolytics. 2022;24:577-584. **7.** Blizzard CD, et al. US Patent: Ocular implant containing a tyrosine kinase inhibitor. Published online September 13, 2022. Accessed September 26, 2022.

HELIOS Phase 1 Study of OTX-TKI in NPDR



Multicenter, double-masked, randomized, parallel group study of OTX-TKI in patients with moderately severe to severe NPDR without CI-DME

STUDY OUTCOMES

PRIMARY: Safety and tolerability of OTX-TKI

SECONDARY: DRSS changes, rescue therapy, BCVA and CST changes

*14 patients enrolled in OTX-TKI treatment arm, with 1 patient death unrelated to treatment.
BCVA (Best-corrected visual acuity); CI-DME (Center-involved diabetic macular edema); CST (Central subfield thickness); DRSS (Diabetic retinopathy severity scale); NPDR (Non-proliferative diabetic retinopathy).

HELIOS Safety Overview at Week 48

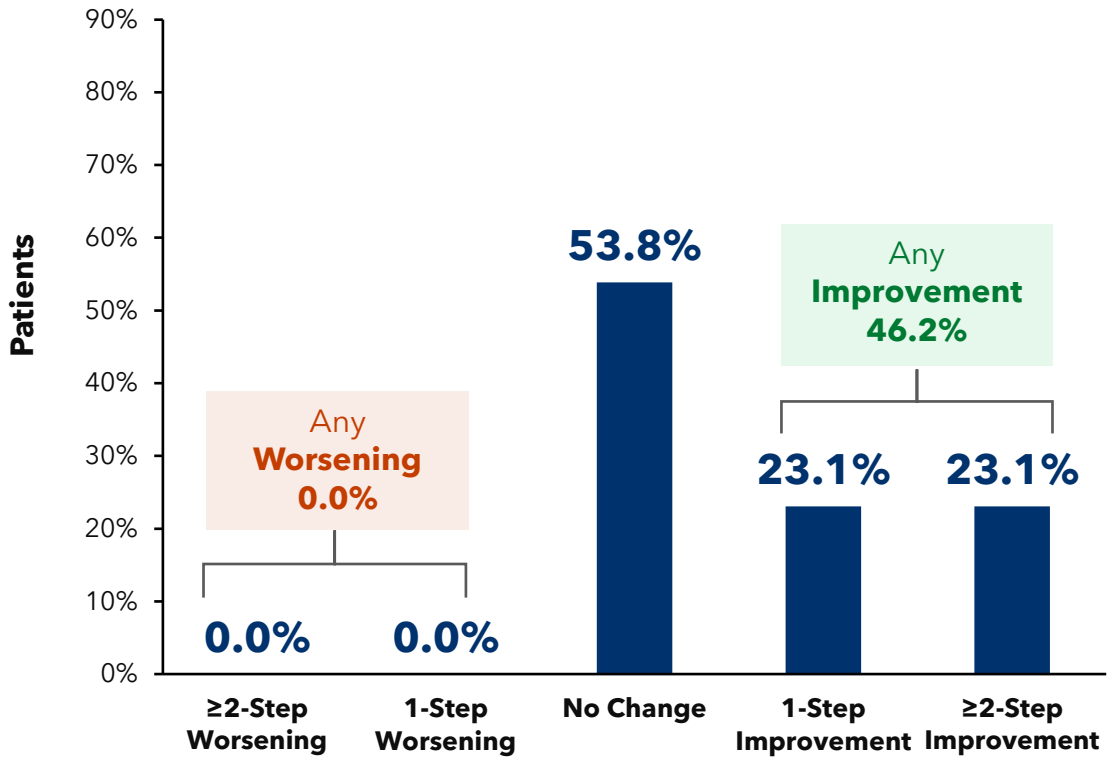
OTX-TKI was generally well tolerated, with no ocular SAEs reported

- OTX-TKI was generally well tolerated
- All AEs were mild and balanced across the two arms, with no moderate or severe AEs reported in either arm
- No ocular SAEs reported in either arm
- No intraocular inflammation, iritis, vitritis, or vasculitis reported
- No subjects in either arm received rescue medication

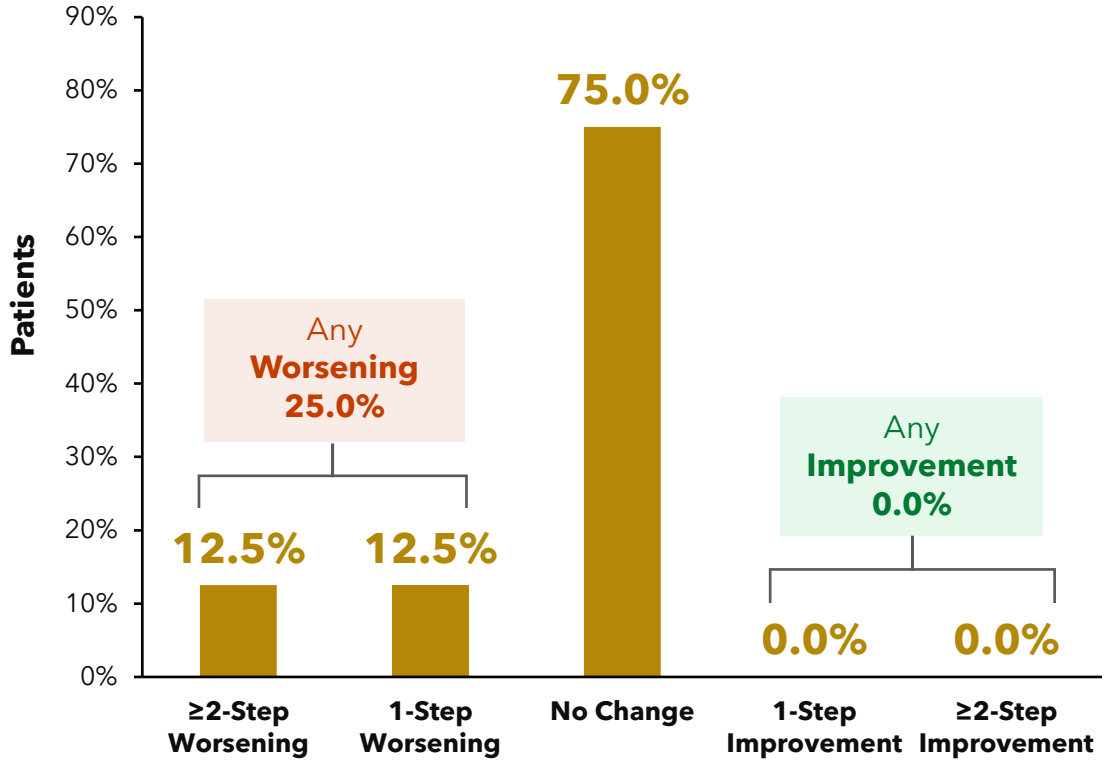
(S)AE ([Serious] adverse event).
Ocular Therapeutix data on file.

DRSS at Week 48:
23.1% in OTX-TKI arm had a ≥2-step DRSS improvement vs 0% in sham

OTX-TKI (n=13)
Change in DRSS From Baseline to Week 48

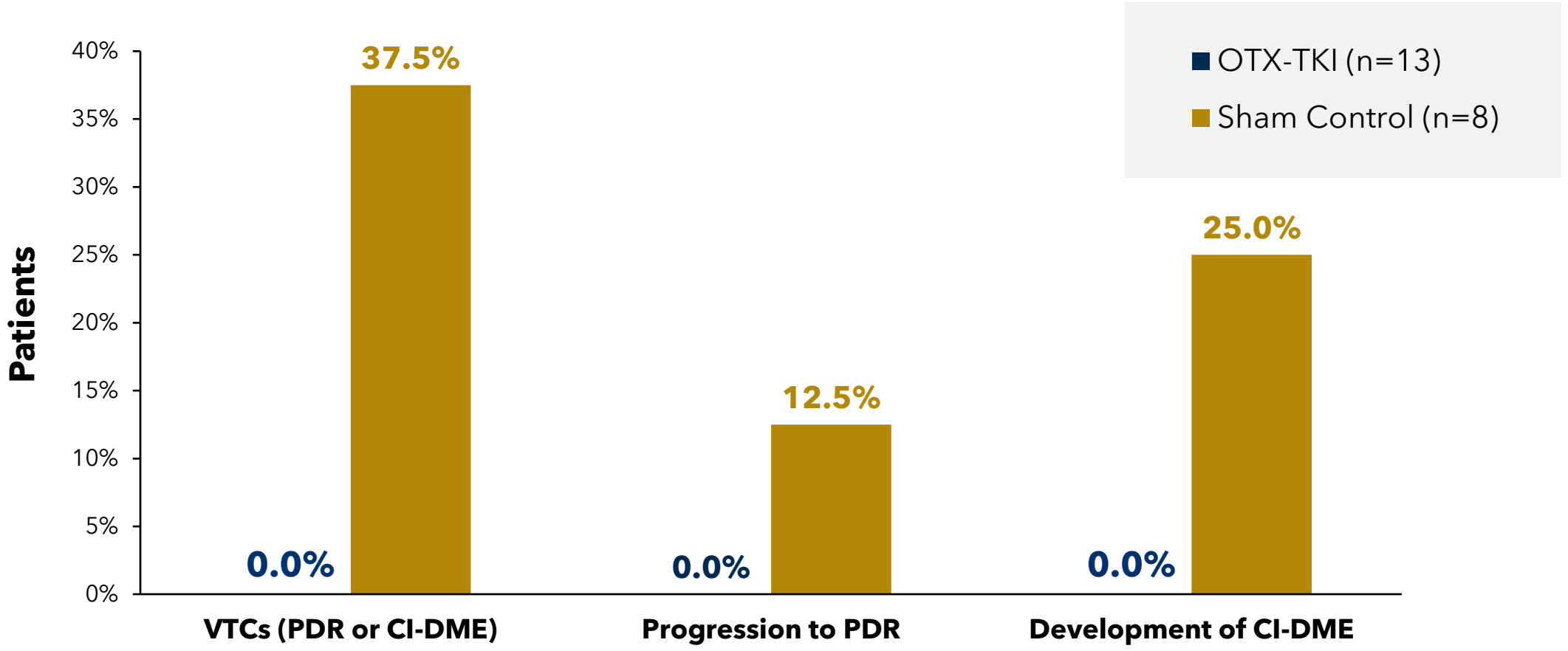


SHAM CONTROL (n=8)
Change in DRSS From Baseline to Week 48



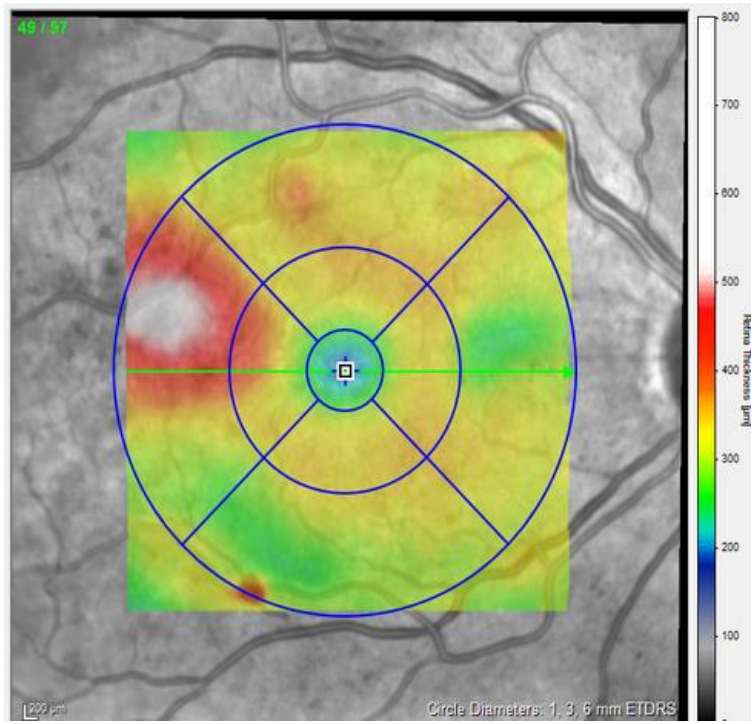
DRSS (Diabetic retinopathy severity scale).
Ocular Therapeutix data on file.

Vision-Threatening Complications (VTCs) at Week 48:
0% in OTX-TKI arm developed PDR or CI-DME vs 37.5% in sham

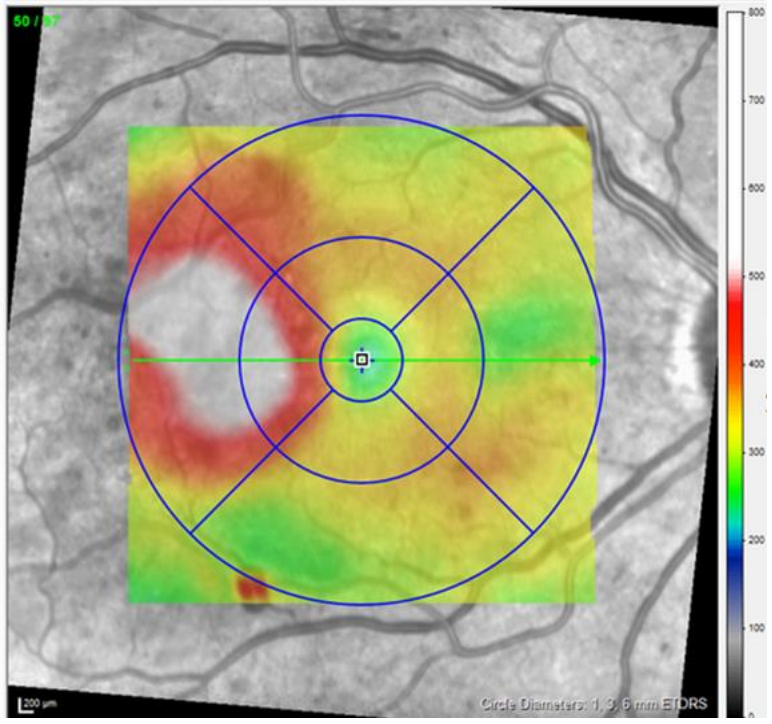


CI-DME (Center-involved diabetic macular edema); PDR (Proliferative diabetic retinopathy); VTC (vision-threatening complications [includes PDR or CI-DME])
Ocular Therapeutix data on file.

Worsening of DME in Sham Control Patient



BASELINE
CST = 237 µm

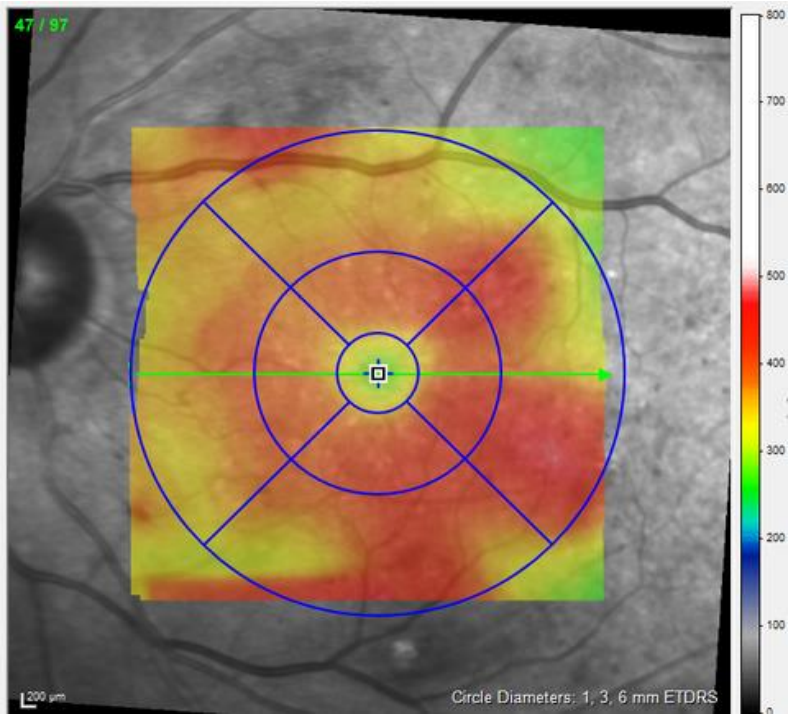


WEEK 48
CST = 285 µm

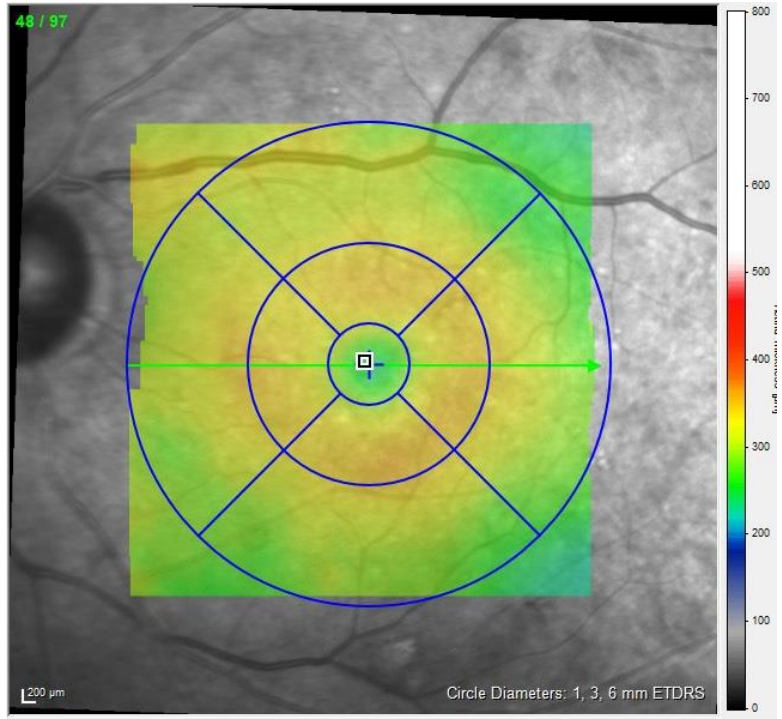
Sham Control: Patient 11-002 Developed CI-DME

DME (Diabetic macular edema); CST (Central subfield thickness); CI-DME (Center-involved diabetic macular edema).
Ocular Therapeutix data on file as of May 22, 2024.

Improvement in DME in Patient Receiving OTX-TKI



BASELINE
CST = 320 µm

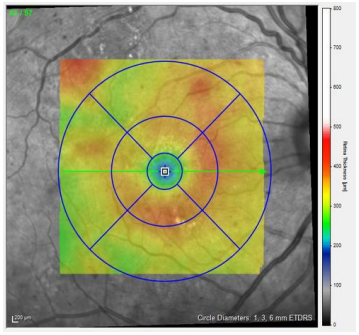
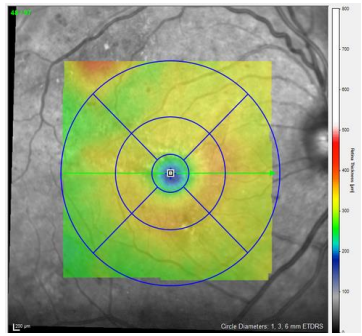
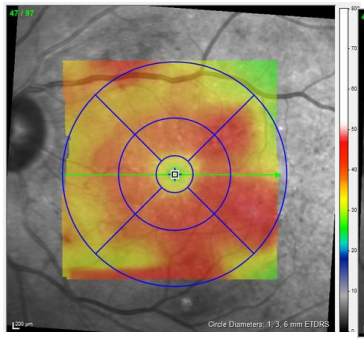
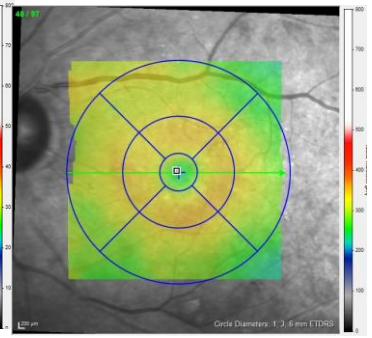
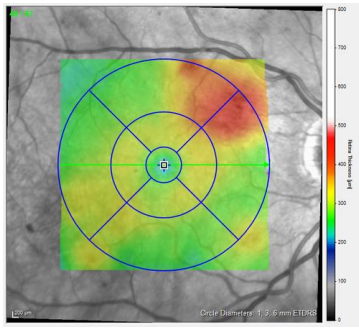
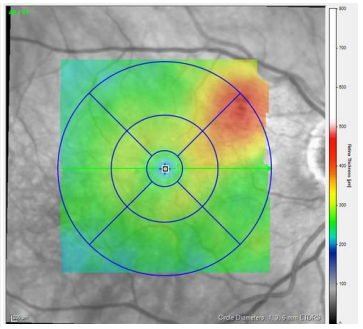


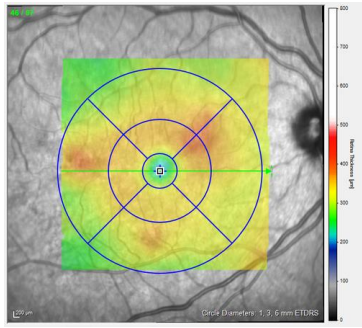
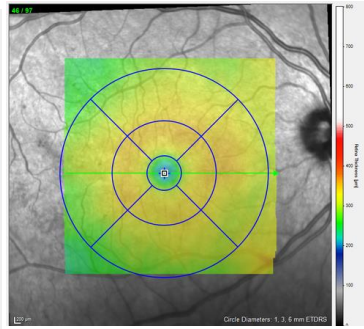
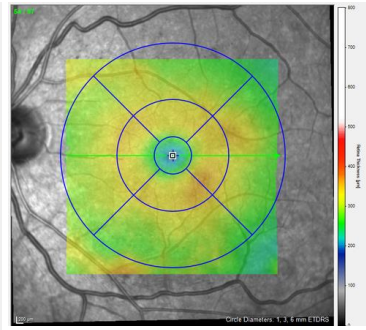
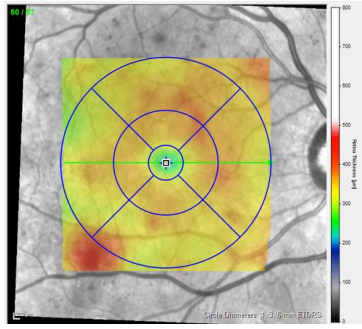
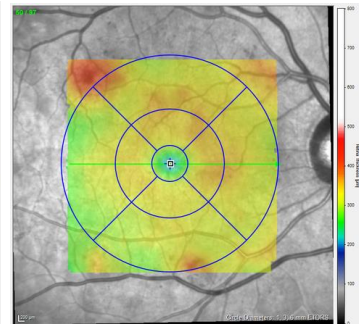
WEEK 48
CST = 289 µm

OTX-TKI Treatment: Patient 11-008

DME (Diabetic macular edema); CST (Central subfield thickness).
Ocular Therapeutix data on file as of May 22, 2024

Improvement in DME in Patients Receiving OTX-TKI

	BASELINE	WEEK 48
Patient 11-007		
Patient 11-008		
Patient 13-001		

	BASELINE	WEEK 48
Patient 15-004		
Patient 16-005		
Patient 16-006		

DME (Diabetic macular edema).
Ocular Therapeutix data on file as of May 22, 2024.

HELIOS Phase 1 Summary

OTX-TKI demonstrated DRSS stability or improvement with durability through 48 weeks

23.1% of patients in the OTX-TKI arm demonstrated a ≥2-step DRSS improvement, and 46.2% of patients demonstrated a 1- or ≥2-step DRSS improvement at 48 weeks

No patients in the OTX-TKI arm experienced worsening in DRSS at 48 weeks

No OTX-TKI patients developed PDR or CI-DME through Week 48

37.5% in the sham control arm developed PDR or CI-DME through Week 48

OTX-TKI was generally well tolerated with no reported incidence of intraocular inflammation, iritis, vitritis, or vasculitis

DRSS (Diabetic retinopathy severity scale); PDR (Proliferative diabetic retinopathy); CI-DME (Center-involved diabetic macular edema).

THANK YOU TO THE INVESTIGATORS IN THE HELIOS TRIAL

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