12-Month Update on Randomized, Controlled, Trial of OTX-TKI (Axitinib Intravitreal Implant) for the Treatment of Wet AMD

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Disclosures

Financial Disclosures (Arshad M. Khanani):

Consultant:
Abbvie**,** Adverum Biotechnologies, AGTC, Alimera Sciences, Allergan, Apellis Pharmaceuticals, Arrowhead, Pharmaceuticals, AsclepiX Therapeutics, Aviceda Therapeutics, Bausch & Lomb , BroadWing Bio, Cholgene Therapeutics, 4D Molecular Therapeutics, Eyepoint Pharmaceuticals, Fronterra Therapeutics, Gemini Pharmaceuticals, Genentech, Graybug Vision, Gyroscope Therapeutics, IVERIC bio, Janssen Pharmaceuticals, Kato Pharmaceuticals, Kartos Therapeutics, Kodiak Sciences, Kriya Therapeutics, Ocular Therapeutix, Oculis, Ocuterra, Opthea, Oxurion, Novartis, Perfuse, PolyPhotonix, Ray Therapeutics, Recens Medical, Regeneron Pharmaceuticals, REGENXBIO, Roche, Stealth Biotherapeutics Therapeutics, Thea Pharma, UNITY Biotechnology, Vanotech

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Adverum Biotechnologies, Annexon Biosciences, Apellis Pharmaceuticals, AsclepiX Therapeutics, 4D Molecular Therapeutics, Gemini Pharmaceuticals, Genentech, Graybug Vision, Gyroscope Therapeutics, IVERIC bio, Janssen Pharmaceuticals, Kodiak, Neurotech, NGM Biopharmaceuticals, Novartis, Ocular Therapeutix, Oculis, Ocuterra, Opthea, Oxurion, Recens Medical, REGENXBIO, Roche, UNITY Biotechnology

Speaker:
Abbvie, Apellis, Genentech, Novartis

Financial:
Aviceda Therapeutics, PolyPhotonix, Recens Medical

Study and Product Disclosures:

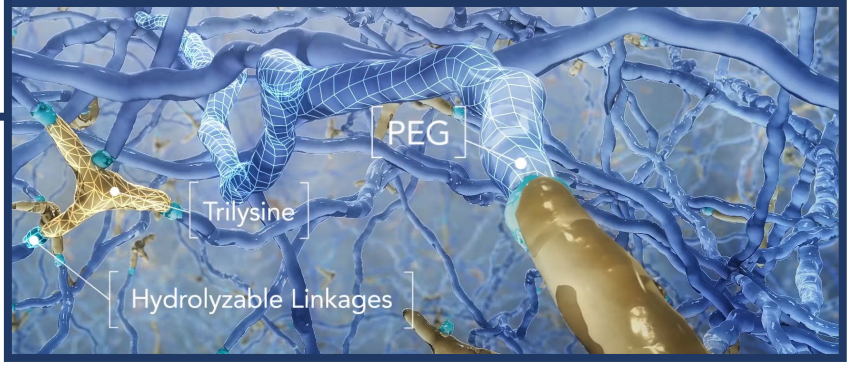
- The following presentation discusses an investigational drug, OTX-TKI, in development. OTX-TKI's efficacy and safety profiles have not been established, and it has not been approved for marketing by the U.S. Food and Drug Administration (FDA) or any other health agency
- Ocular Therapeutix sponsored this clinical trial

OTX-TKI Implant: Axitinib Delivered Using Elutyx™ Technology

ELUTYX TECHNOLOGY

BIORESORBABLE, TARGETED, SUSTAINED DRUG DELIVERY

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



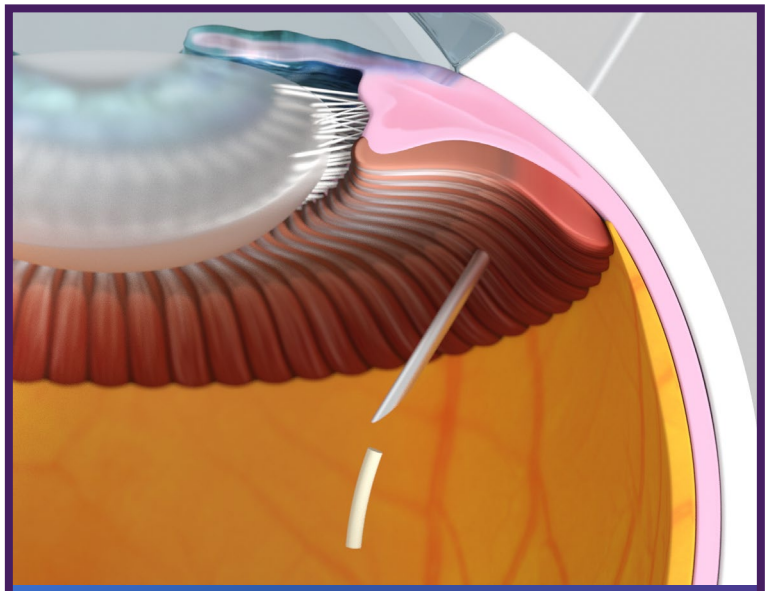
AXITINIB

MULTI-TARGET TYROSINE KINASE INHIBITOR FOR RETINAL VASCULAR DISEASES

Axitinib is a highly selective inhibitor of all VEGF and PDGF receptors with high affinity and low solubility compared to other ocular TKIs[1]

Drug	Inhibitory Concentrations for VEGFR2/KDR (IC_{50} in nM) (lower values indicate higher affinity)
Axitinib[2]	**0.2**
Sunitinib[3]	43
Vorolanib[3]	52

OTX-TKI INTRAVITREAL IMPLANT: AXITINIB DELIVERED USING ELUTYX TECHNOLOGY



- Single implant
- Administered by a 25G needle
- Target release for 9-12 months
- Completely bioresorbable

References: 1. Zhao Y, et al. *Oncologist*. 2015;20(6):660-673. **2.** Gross-Goupil M, et al. *Clin Med Insights Oncol*. 2013;7:269-277. **3.** Liang C, et al. *Mol Ther Oncolytics*. 2022;24:577-584.
KDR=kinase insert domain receptor; PDGF=platelet-derived growth factor; VEGF=vascular endothelial growth factor

OTX-TKI U.S.-based Wet AMD Clinical Trial Design

Multicenter, Randomized, Double-masked Trial

Screening

Key Inclusion Criteria

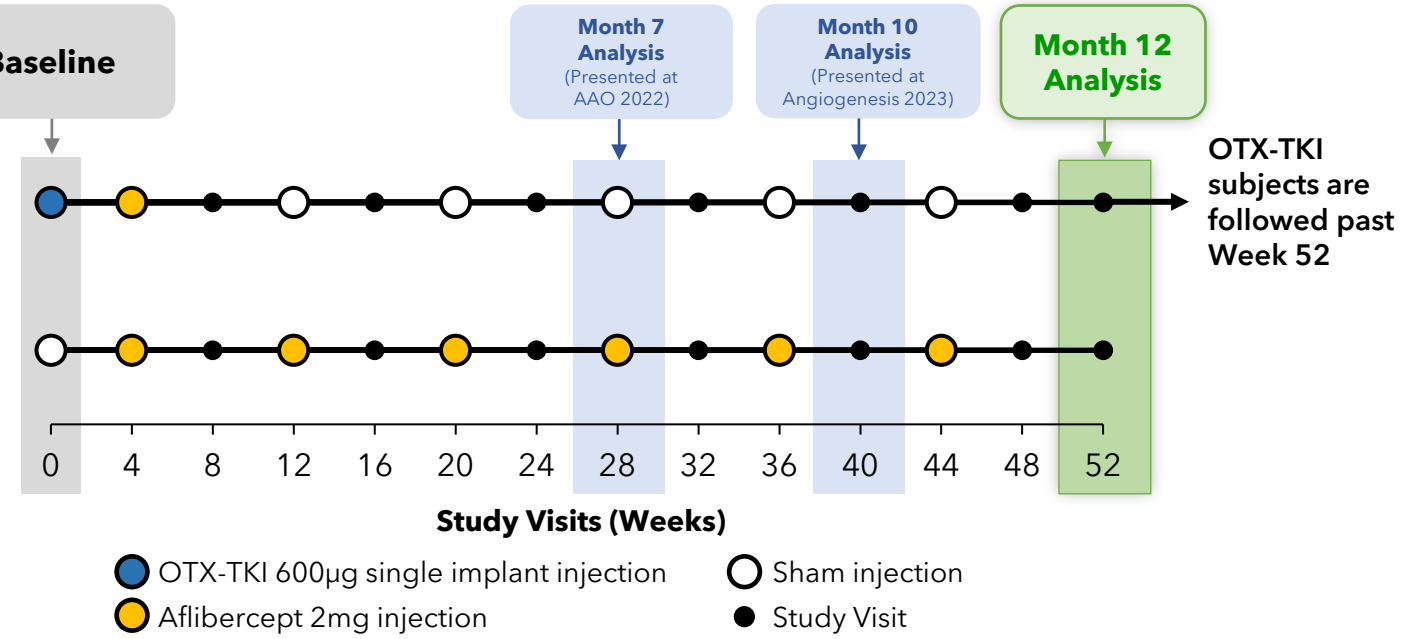
- Sub foveal neovascularization secondary to AMD
- **Controlled fluid**
- **Previously treated with anti-VEGF injections**

R

Randomization 3:1
(OTX-TKI : Aflibercept)

OTX-TKI Arm

Aflibercept Arm



Rescue Anti-VEGF Injection Criteria:

- Loss of ≥10 letters from best previous BCVA with current BCVA worse than baseline, or
- Evidence of ≥75µm CSFT increase from previous best value and ≥5 letters loss from best previous BCVA, or
- New macular hemorrhage

AAO=American Academy of Ophthalmology; AMD=age-related macular degeneration; BCVA=best corrected visual acuity; BL=baseline; CSFT=central subfield thickness; AMD=age-related macular degeneration; VEGF=vascular endothelial growth factor

Baseline Characteristics

Baseline Characteristic	OTX-TKI (N=16)†	Aflibercept (N=5)
Mean (SD) Age, Years	76 (8)	84 (8)
Male, n (%) **Female, n (%)**	8 (50) 8 (50)	3 (60) 2 (40)
Mean (SD) Months since wet AMD diagnosis	18 (12)	18 (12)
Mean (SD) Number of anti-VEGF Injections within 12 Months Prior to baseline*	8 (3)	8 (4)
Mean (SD) BCVA in ETDRS Letters	70.9 (17.7)	73.8 (9.0)
Mean (SD) CSFT, µm	273.8 (43.0)	240.6 (29.6)

*Annualized data

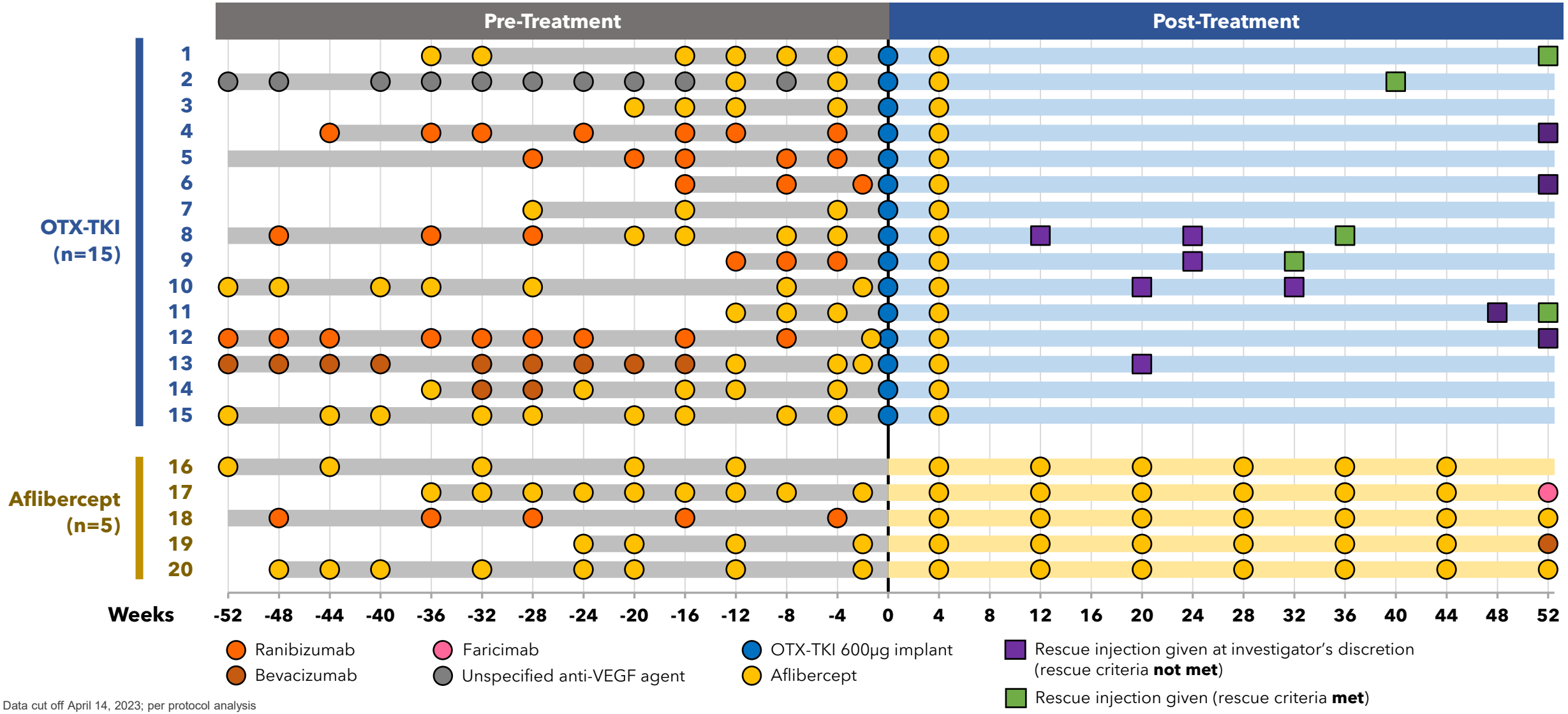
† Includes one subject not treated per protocol who has been removed from efficacy analysis as subject incorrectly received aflibercept instead of sham injection at Month 3 and 5 visits

Data cut off April 14, 2023

BCVA=best corrected visual acuity; CSFT=central subfield thickness; ETDRS=Early Treatment Diabetic Retinopathy Study; AMD=age-related macular degeneration; SD=standard deviation; VEGF=vascular endothelial growth factor

Reduction in Anti-VEGF Injections Following OTX-TKI at 12 Months

89% reduction in treatment burden with OTX-TKI at 12 months

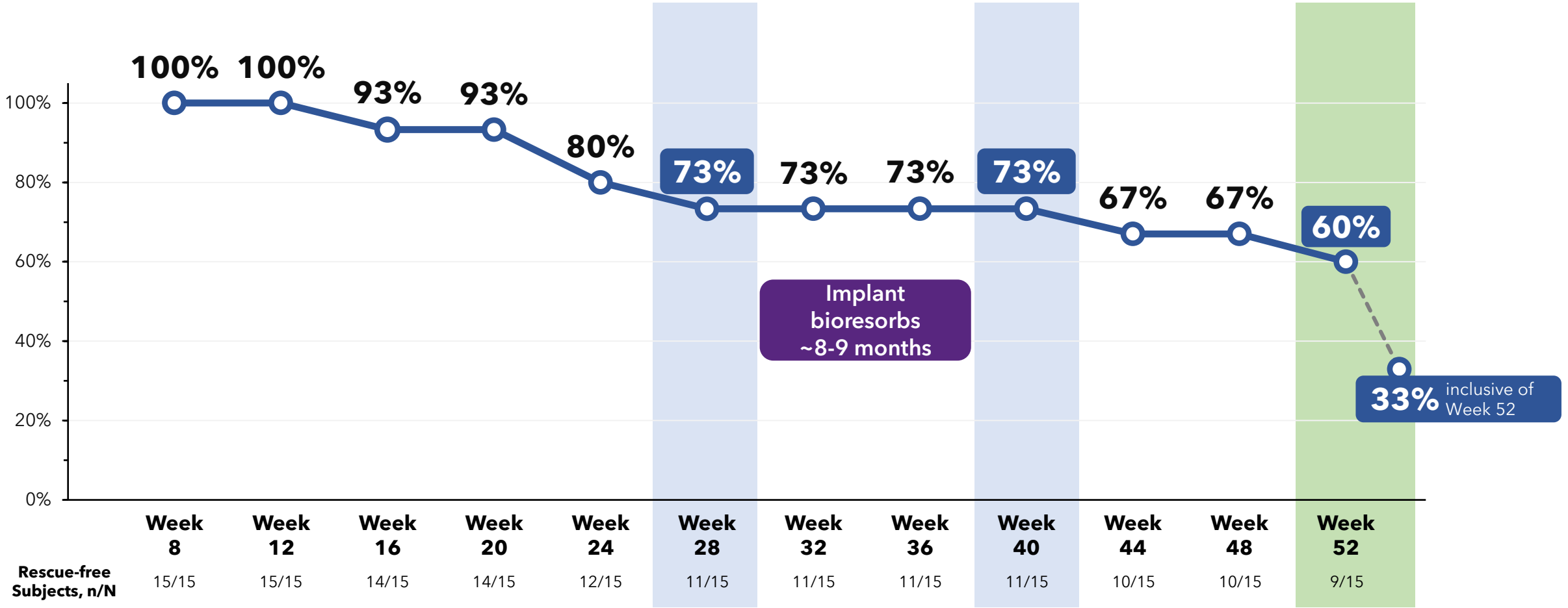


Data cut off April 14, 2023; per protocol analysis
Reduction in treatment burden calculation includes all rescue injections
Sham injection was given at Week 0 in the Aflibercept Arm and at Weeks 12, 20, 28, 36 and 44 in the OTX-TKI Arm (not shown). At Week 52, subjects in the aflibercept group were treated with wet AMD standard of care at the investigator's discretion.

OTX-TKI Demonstrated Extended Duration of Action

60% were rescue-free up to 12 months with 4 additional subjects rescued at 12 months

Percentage of OTX-TKI Subjects Rescue-Free Up to Each Visit (n=15)

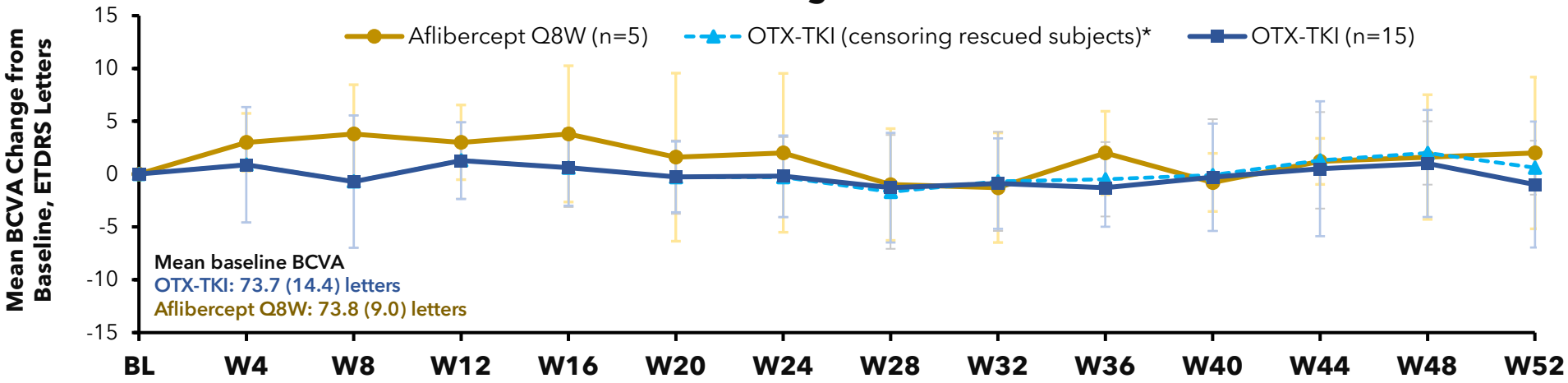


	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32	Week 36	Week 40	Week 44	Week 48	Week 52
Rescue-free Subjects, n/N	15/15	15/15	14/15	14/15	12/15	11/15	11/15	11/15	11/15	10/15	10/15	9/15

Data cut off April 14, 2023
Rescue-free rate calculations: If subjects received rescue anti-VEGF therapy at a study visit, those were reflected to count at the following study visit in the graph above
Percentages presented in the graph above represent rescue-free rates up to each study visit, except for the 33% at Week 52 which includes rescue injections given at the Week 52 study visit

Vision and CSFT with OTX-TKI were Comparable to Aflibercept Q8W

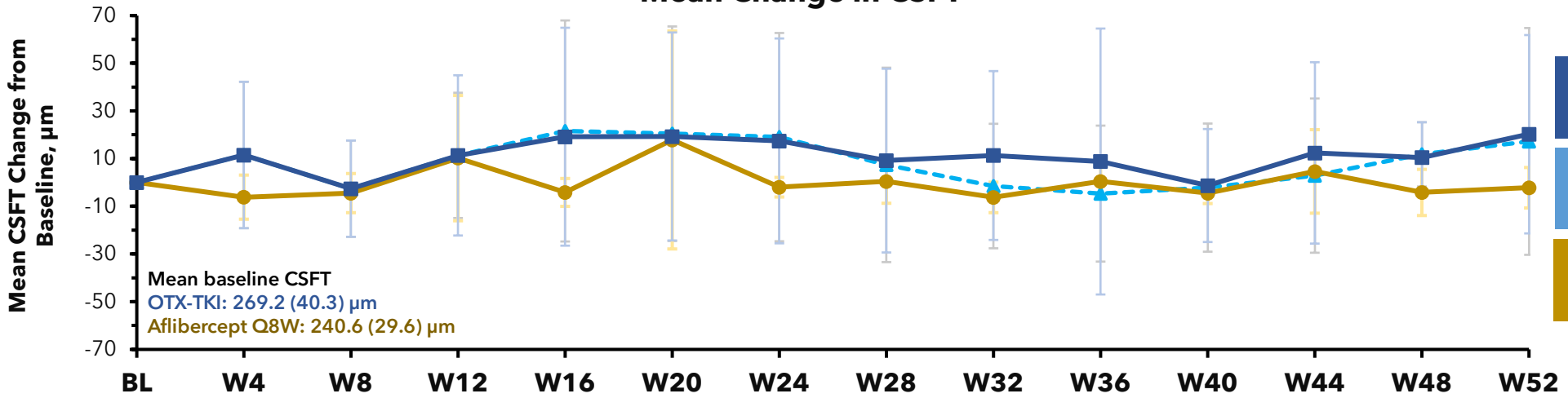
Mean Change in BCVA



Mean (SD) change in BCVA from baseline to Week 52:

- **OTX-TKI: -1.0 (6.0) letters**
- **OTX-TKI: +0.6 (2.6) letters** (censoring rescued subjects)
- **Aflibercept Q8W: +2.0 (7.2) letters**

Mean Change in CSFT



Mean (SD) change in CSFT from baseline to Week 52:

- **OTX-TKI: +20.2 (41.6) µm**
- **OTX-TKI: +17.2 (47.6) µm** (censoring rescued subjects)
- **Aflibercept Q8W: -2.2 (8.5) µm**

Data cut off April 14, 2023
Error bars represent standard deviation; n=14 in OTX-TKI arm at Weeks 8, 28, 40 and 48 due to missed visits
*Sample size for OTX-TKI (censoring rescued subjects): n=15 at Baseline and Weeks 4 and 12; n=14 at Week 8 (missed visit) and Weeks 16 and 20; n=12 at Week 24 and n=11 at Weeks 28, 32, 36 and 40; n=10 at Week 44; n=9 at Weeks 48 and 52
BCVA=best corrected visual acuity; BL=baseline; CSFT=central subfield thickness; ETDRS=Early Treatment Diabetic Retinopathy Study; W, week

Safety Summary

- No reports of drug-related ocular or systemic SAEs in either arm
- One event of acute endophthalmitis in OTX-TKI arm which occurred following mandated aflibercept injection at Month 1
  - Reported as moderate
  - Injection procedure related
  - Unrelated to the study drug
  - Resolved after intravitreal antibiotic injection, with vision returning to baseline
- All events were mild except
  - Acute endophthalmitis SAE (moderate and resolved) and worsening of cataract (moderate) in OTX-TKI arm
  - Elevated IOP in aflibercept arm (moderate and resolved)

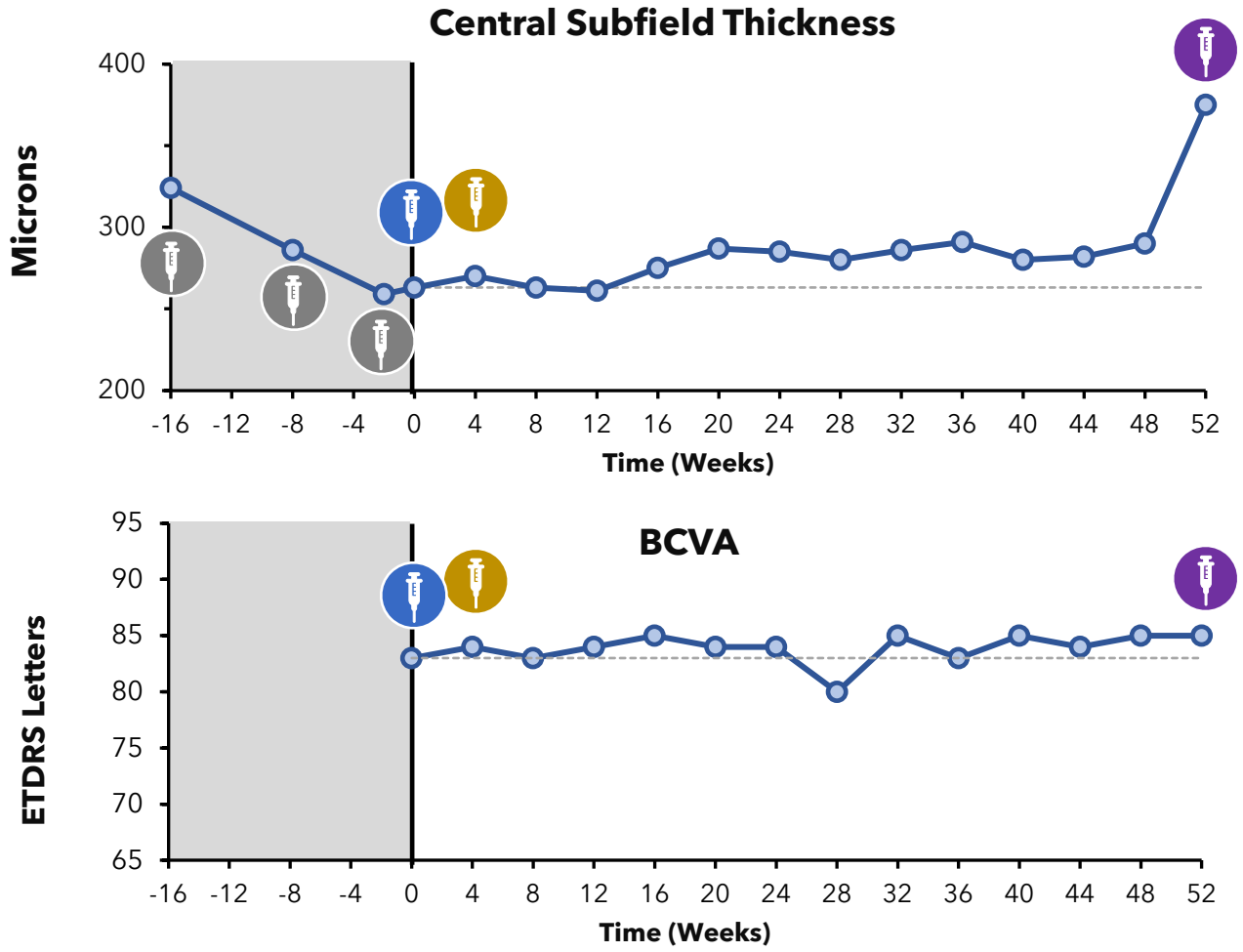
	OTX-TKI n=16	Aflibercept n=5
Subjects with Adverse Events in the Study Eye, n (%)		
Elevated IOP	2 (12.5)	1 (20.0)**
Retinal detachment	0	0
Retinal vasculitis	0	0
Implant migration into the anterior chamber	0	NA
Acute endophthalmitis	1 (6.25)*	0
Subjects with Ocular Adverse Events in the Study Eye Reported by Severity, n (%)		
Ocular AEs	16 (100.0)	3 (60.0)
Mild	14 (87.5)	2 (40.0)
Moderate	2 (12.5)*	1 (20.0)**
Severe	0	0
Serious AEs	1 (12.5)*	0

*Moderate and serious ocular AE in OTX-TKI arm was Acute Endophthalmitis 6 days after mandated aflibercept injection at Month 1
**Moderate AE in Aflibercept arm was Elevated Intraocular pressure

Data cut off April 14, 2023
IOP=intraocular pressure; SAE=serious adverse event

OTX-TKI-Treated Subject 6

81-year-old female with anti-VEGF Q8W prior to study and rescue-free up to 1 year



anti-VEGF injection

OTX-TKI administration

study-mandated aflibercept

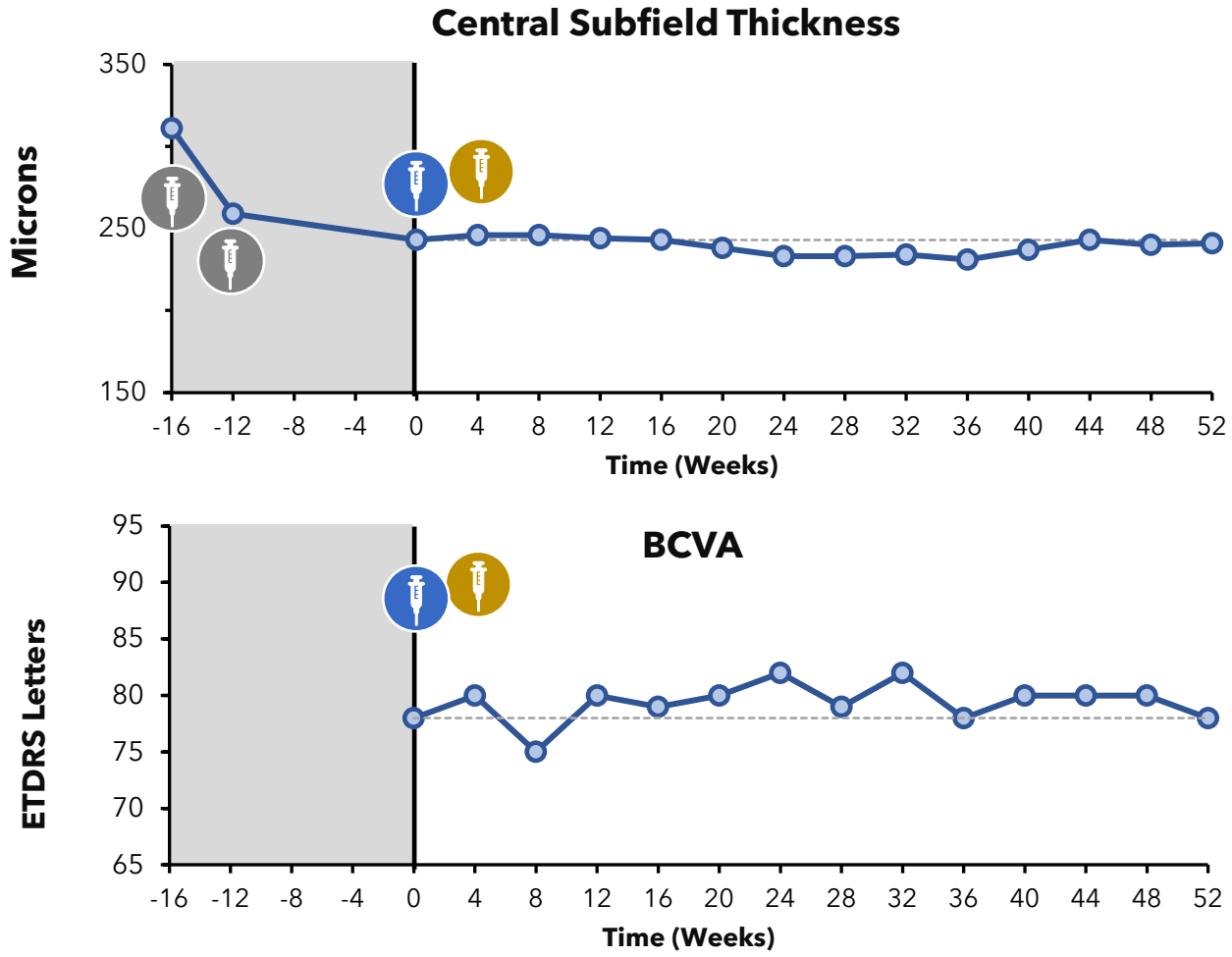
rescue injection given at investigator's discretion

-16 Weeks	**CSFT:** 324 µm **BCVA:** Not available	
-8 Weeks	**CSFT:** 286 µm **BCVA:** Not available	
Baseline	**CSFT:** 263 µm **BCVA:** 83 letters	
Week 4	**CSFT Δ:** +7 µm **BCVA Δ:** +1 letter	
Week 8	**CSFT Δ:** 0 µm **BCVA Δ:** 0 letters	
Week 24	**CSFT Δ:** +22 µm **BCVA Δ:** +1 letter	
Week 48	**CSFT Δ:** +27 µm **BCVA Δ:** +2 letters	
Week 52	**CSFT Δ:** +112 µm **BCVA Δ:** +2 letters	

Data cut off April 14, 2023

OTX-TKI-Treated Subject 14

65-year-old female with anti-VEGF Q4-8W prior to study and rescue-free through 1 year



anti-VEGF injection

OTX-TKI administration

study-mandated aflibercept

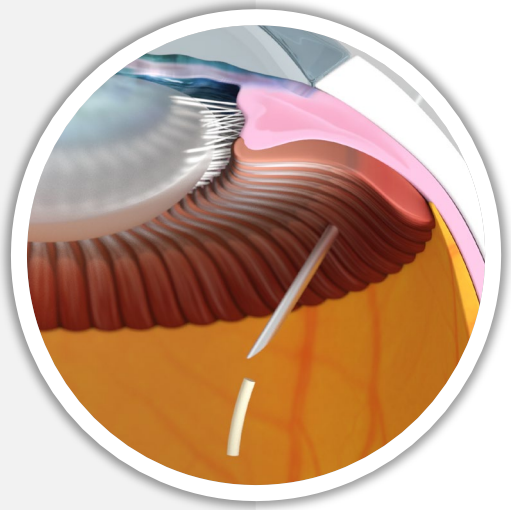
rescue injection given at investigator's discretion

-16 Weeks	**CSFT:** 311 µm **BCVA:** Not available	
-12 Weeks	**CSFT:** 259 µm **BCVA:** Not available	
Baseline	**CSFT:** 243 µm **BCVA:** 78 letters	
Week 4	**CSFT Δ:** +3 µm **BCVA Δ:** +2 letters	
Week 8	**CSFT Δ:** +3 µm **BCVA Δ:** -3 letters	
Week 24	**CSFT Δ:** -10 µm **BCVA Δ:** +4 letters	
Week 48	**CSFT Δ:** -3 µm **BCVA Δ:** +2 letters	
Week 52	**CSFT Δ:** -2 µm **BCVA Δ:** 0 letters	

Data cut off April 14, 2023

12 Month Results Support the Advancement of OTX-TKI to Pivotal Trials in Wet AMD

- OTX-TKI maintained vision and CSFT comparable to aflibercept Q8W with 89% reduction in treatment burden over a 12-month period
- Safety data showed OTX-TKI was generally well-tolerated
- Implant bioresorption and axitinib elution were consistent with previous clinical data, potentially allowing a window for redosing
- Pharmacodynamic effects observed in this trial support the characteristics of a potential treatment for wet AMD with durability between 9-12 months with a single injection



Next Steps: OTX-TKI Pivotal Trials in Wet AMD Prepared to Initiate as Early as Q3 2023*

*Subject to obtaining necessary financing
Data cut off April 14, 2023; Conclusions based on limited number of subjects OTX-TKI: n=16 and Aflibercept: n=5

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