Interim Safety and Efficacy Data from a Phase 1 Clinical Trial of Sustained-release Axitinib Hydrogel Implant (OTX-TKI) in Wet AMD Subjects: 7-month Analysis

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on behalf of the clinical study investigators: Stephen Couvillion, MD; David Eichenbaum, MD; Arshad Khanani, MD; Nathan Steinle, MD; Charles Wykoff, MD, PhD; Samantha Xavier, MD

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FINANCIAL DISCLOSURES

- **Presenter Disclosures (Dilsher S. Dhoot) :**
  - *Consultant/Advisor:* Alimera Sciences, Inc.; Allergan; Apellis Pharmaceuticals, Inc.; Bayer Healthcare Pharmaceuticals, Inc.; EyePoint Pharmaceuticals; Genentech; Novartis, Alcon Pharmaceuticals; Optos, Inc.; Regeneron; Santen, Inc.
  - *Grant:* Ocular Therapeutix, Inc.
- **Study Disclosures:** This clinical trial was sponsored by Ocular Therapeutix, Inc.

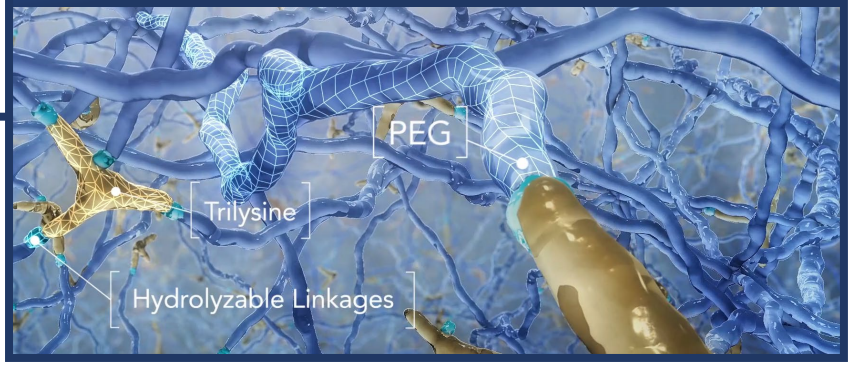
The following presentation discusses an investigational drug, OTX-TKI, in development. OTX-TKI's efficacy and safety profiles have not been established, and it has not been approved for marketing by the FDA.

OTX-TKI: HYDROGEL DELIVERY OF AXITINIB

HYDROGEL DELIVERY PLATFORM

BIORESORBABLE, TARGETED, SUSTAINED DRUG DELIVERY

OTX's proprietary bioresorbable polymer matrix, a polyethylene glycol (PEG) hydrogel is a versatile platform for localized sustained drug delivery



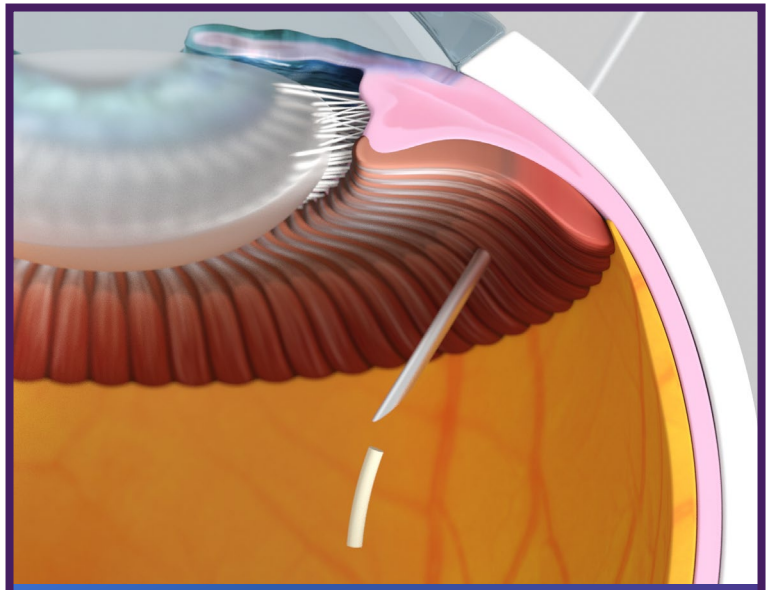
AXITINIB

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: AXITINIB IN A HYDROGEL INTRAVITREAL IMPLANT



- Single implant
- Completely bioresorbable
- Target release for 6-9 months
- Administered by a 25G or smaller needle

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.** Eyepoint Pharmaceuticals, Inc. Form 8-K. Published online September 15, 2020. Accessed August 24, 2022. https://sec.report/Document/0001564590-20-043596/
Abbreviations: KDR, kinase insert domain receptor; PDGF, platelet-derived growth factor; VEGF, vascular endothelial growth factor

U.S. PHASE 1 STUDY DESIGN

Multicenter, Randomized, Double-masked Trial

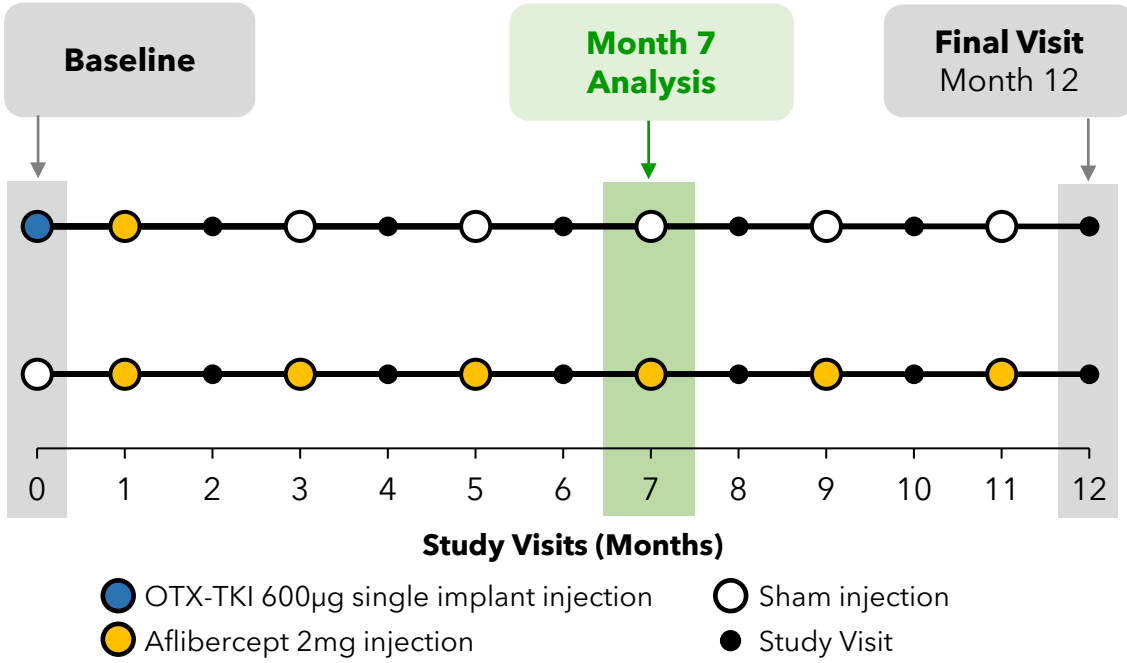
Screening

Key Inclusion Criteria

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

Randomization 3:1
OTX-TKI:Aflibercept

- **OTX-TKI Arm**
- **Aflibercept Arm**



Rescue Anti-VEGF Injection Criteria:

- Loss of ≥10 letters from best previous BCVA due to AMD 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

Abbreviations: AMD, age-related macular degeneration; BCVA, best corrected visual acuity; BL, baseline; CSFT, central subfield thickness; nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor

BASELINE CHARACTERISTICS

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

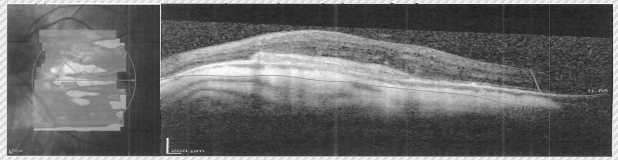
*Annualized data
† Includes one subject not treated per protocol

Interim review: data cut off August 24, 2022
Abbreviations: BCVA, best corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; nAMD, neovascular age-related macular degeneration; SD, standard deviation; VEGF, vascular endothelial growth factor

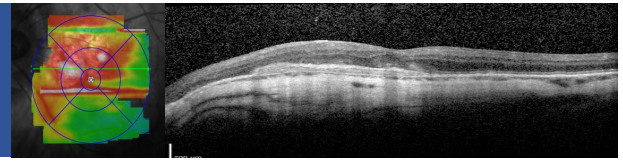
ONE OTX-TKI PATIENT REMOVED FROM EFFICACY ANALYSIS

Subject incorrectly received aflibercept instead of sham injection at Month 3 and 5 visits

Historical OCT
(~19 months prior to baseline)
CSFT: 508 µm

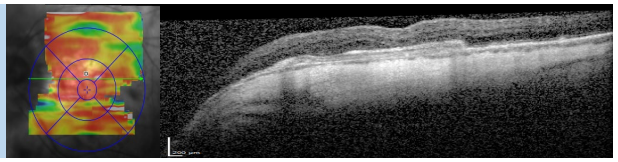


Baseline
CSFT: 343 µm
BCVA: 30 letters

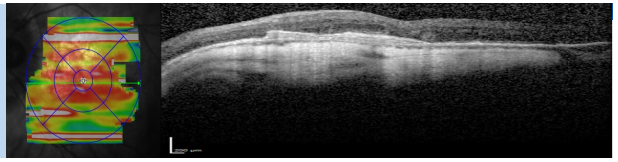


Mandated aflibercept

Month 1
CSFT change: 0 µm
BCVA change: +14 letters

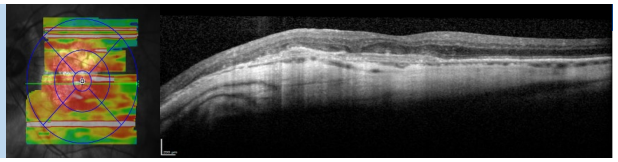


Month 2
CSFT change: -9 µm
BCVA change: +15 letters

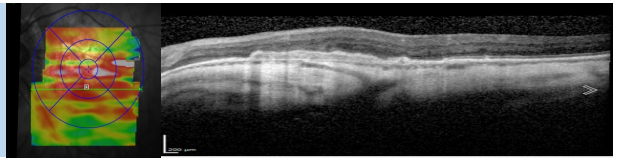


Misdosed aflibercept

Month 3
CSFT change: -19 µm
BCVA change: +22 letters

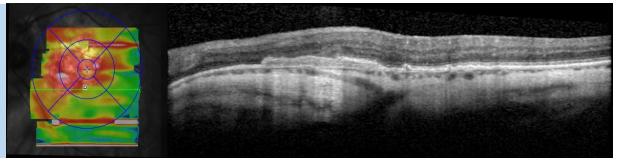


Month 4
CSFT change: -7 µm
BCVA change: +25 letters

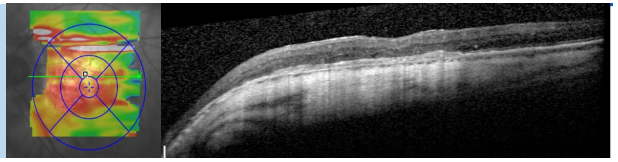


Misdosed aflibercept

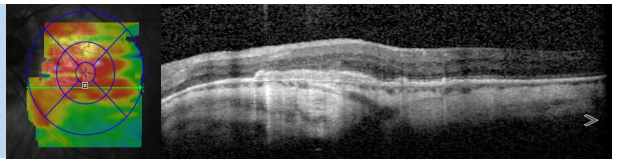
Month 5
CSFT change: -17 µm
BCVA change: +23 letters

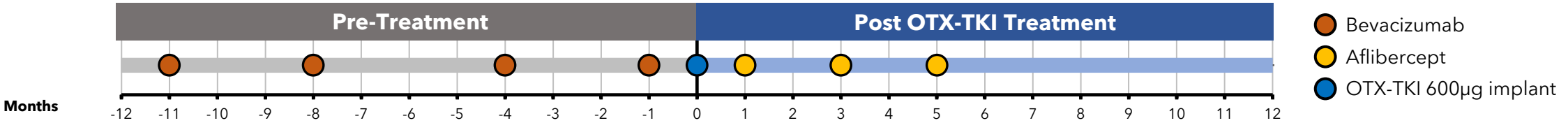


Month 7
CSFT change: -37 µm
BCVA change: +24 letters



Month 12
CSFT change: -27 µm
BCVA change: +15 letters

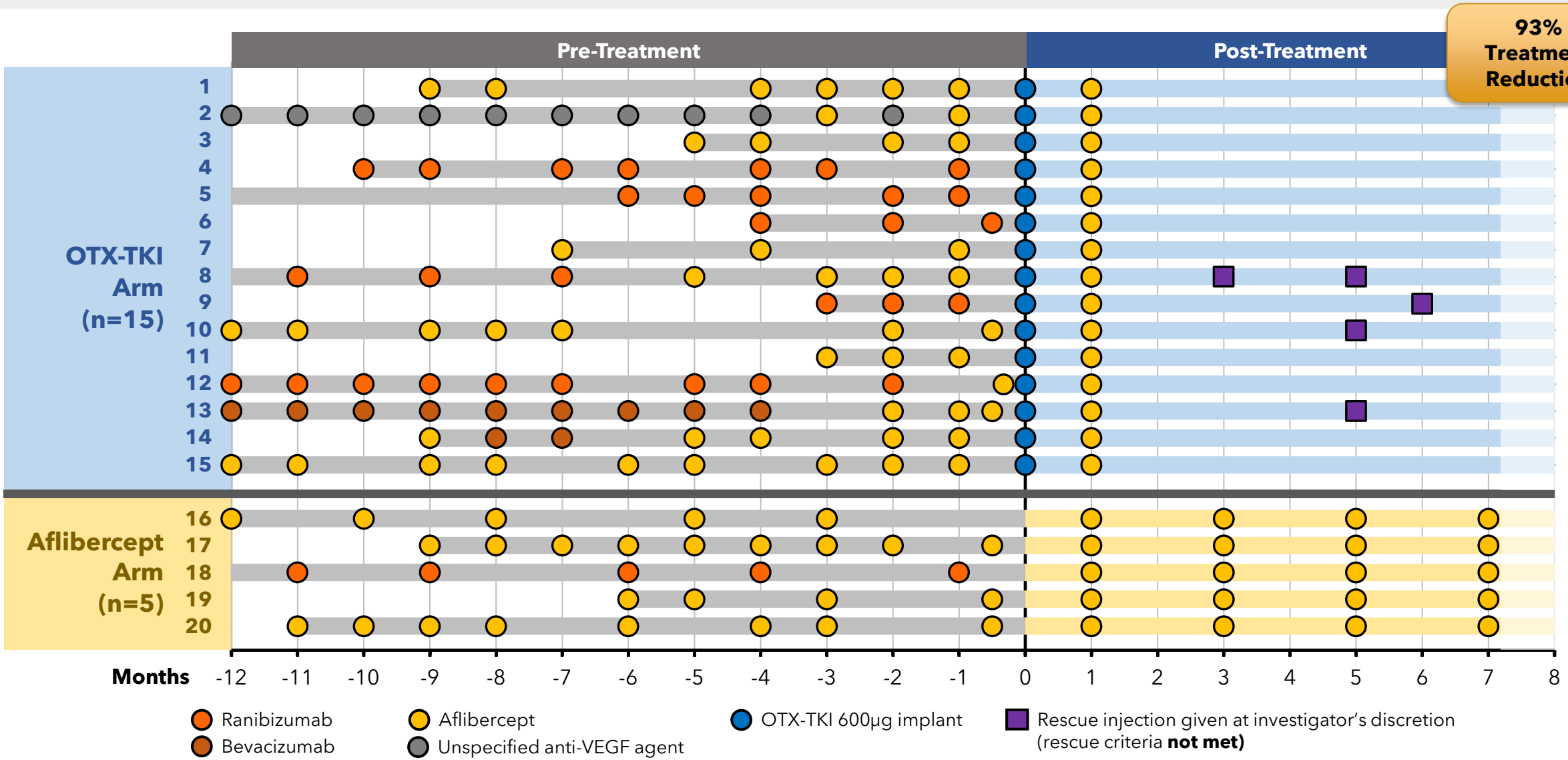




Subject incorrectly received aflibercept instead of sham injection at Month 3 and 5 visits by investigator
All changes in CSFT and BCVA are relative to baseline visit

OTX-TKI DEMONSTRATED REDUCTION IN TREATMENT BURDEN

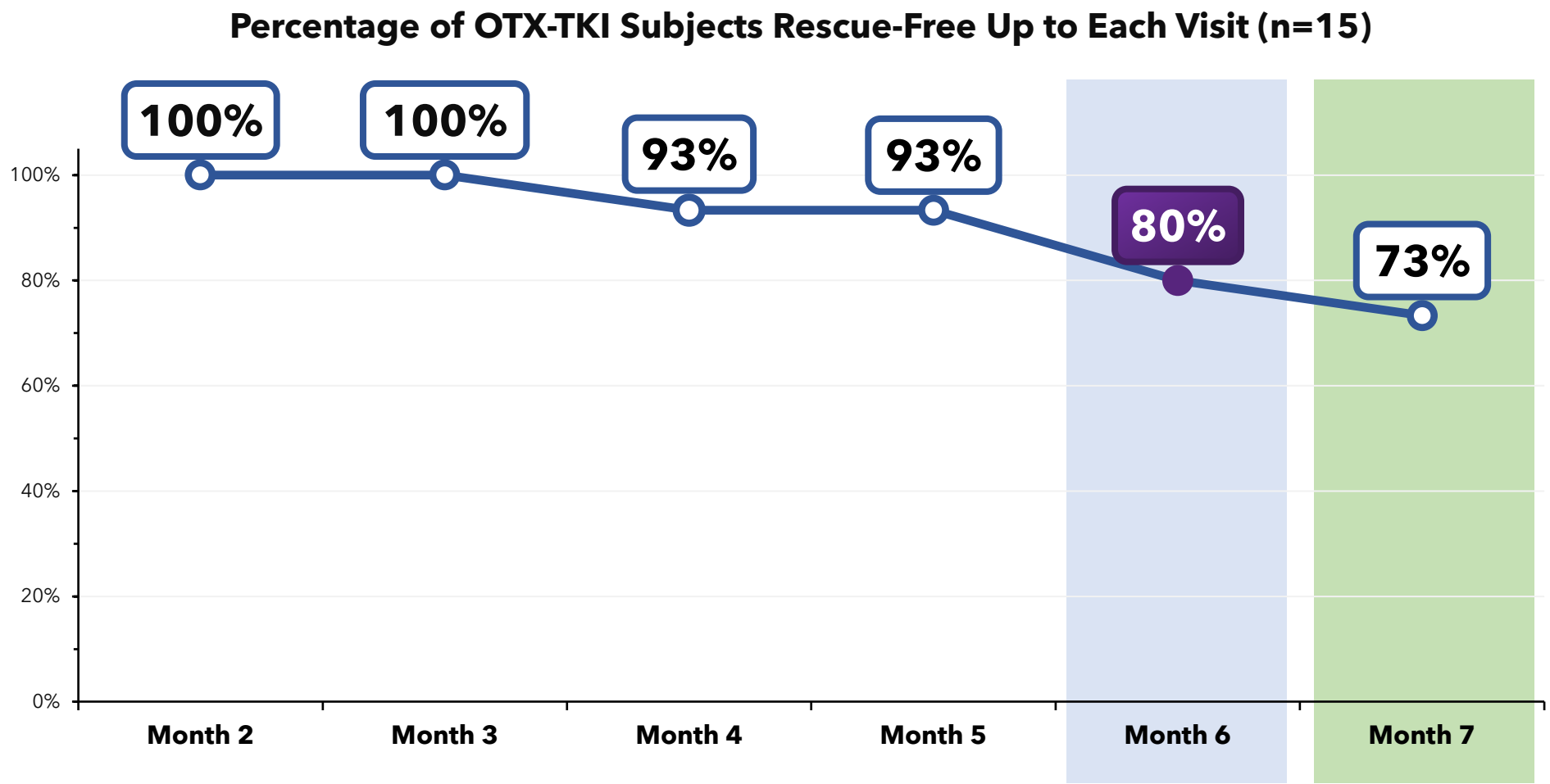
Clinically meaningful reduction in treatment burden and all rescues were given at investigator's discretion



Sham injection was given at Month 0 in the Aflibercept Arm and at Month 3, 5 & 7 in the OTX-TKI Arm (not shown). Interim review: data cut off August 24, 2022; per protocol analysis
Acute endophthalmitis was reported in Subject 8 who was rescued twice

OTX-TKI DEMONSTRATED EXTENDED DURATION OF ACTION

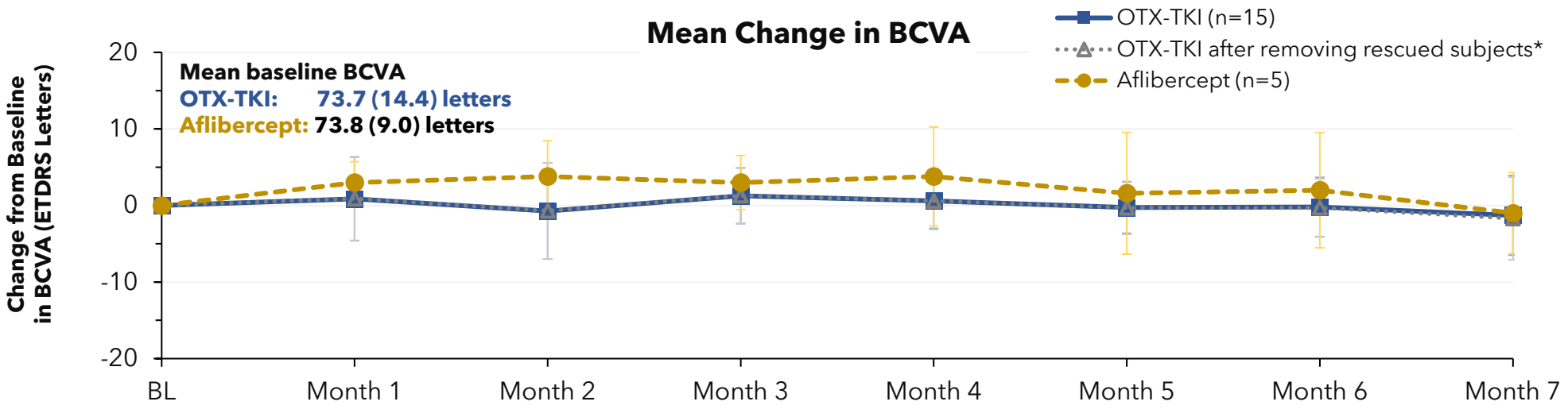
80% of subjects were rescue-free up to 6 months and 73% of subjects were rescue-free up to 7 months



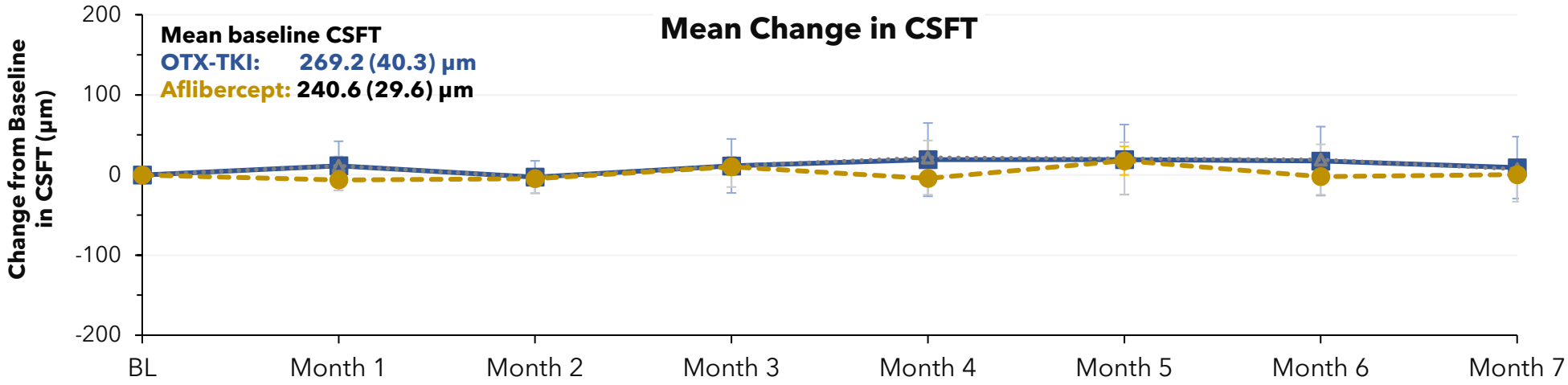
Interim review: data cut off August 24, 2022
Rescue-free rate calculations: If subjects received rescue anti-VEGF therapy at a study visit, they were counted as rescued at the following study visit in the graph above.

EFFECT OF OTX-TKI ON BCVA AND CSFT FOR 7 MONTHS

Sustained and stable effect with a single OTX-TKI implant comparable to aflibercept Q8W



Mean change in BCVA from baseline to Month 7:
OTX-TKI: -1.3 (5.2) letters
OTX-TKI: -1.7 (5.4) letters
(after removing rescue subjects)
Aflibercept: -1.0 (5.3) letters

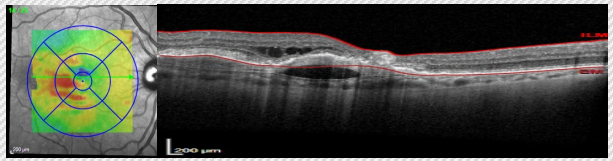


Mean change in CSFT from baseline to Month 7:
OTX-TKI: +9.2 (38.6) µm
OTX-TKI: +7.3 (40.8) µm
(after removing rescue subjects)
Aflibercept: +0.4 (9.1) µm

Interim review: data cut off August 24, 2022
Error bars represent standard deviation; n=14 in OTX-TKI arm at Months 2 and 7 due to missed visits
*Sample size for OTX-TKI after removing rescued subjects: n=15 at Baseline and Months 1 and 3; n=14 at Month 2 (missed visit) and Months 4 and 5; n=12 at Month 6 and n=11 at Month 7
Abbreviations: BCVA, best corrected visual acuity; BL, baseline; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study

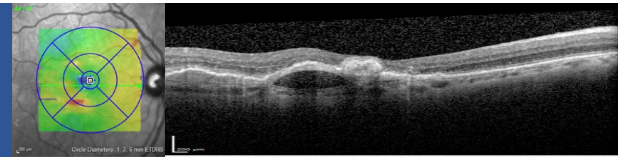
INDIVIDUAL CASE: OTX-TKI PATIENT 12

Historical OCT
(~1 month prior to baseline)
CSFT: 277 µm



Patient received SOC wet AMD therapy prior to enrollment in the study

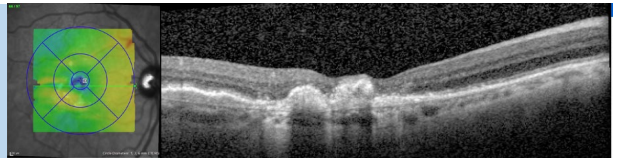
Baseline
CSFT: 278 µm
BCVA: 54 letters



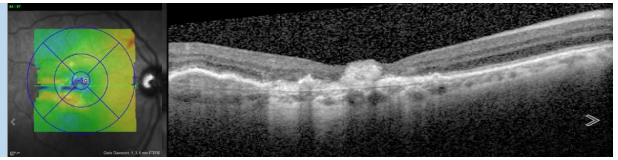
Month 2

Missed Visit

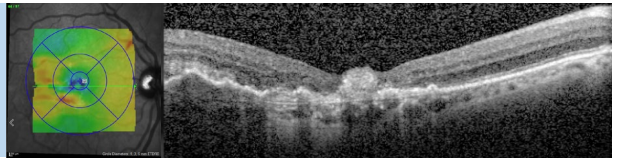
Month 3
CSFT change: -72 µm
BCVA change: +4 letters



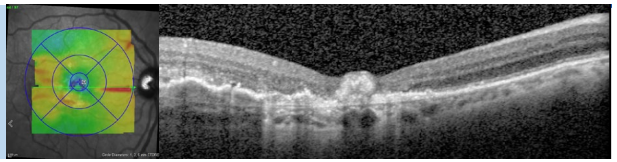
Month 4
CSFT change: -68 µm
BCVA change: +5 letters



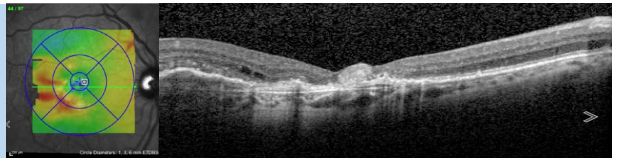
Month 5
CSFT change: -66 µm
BCVA change: +5 letters

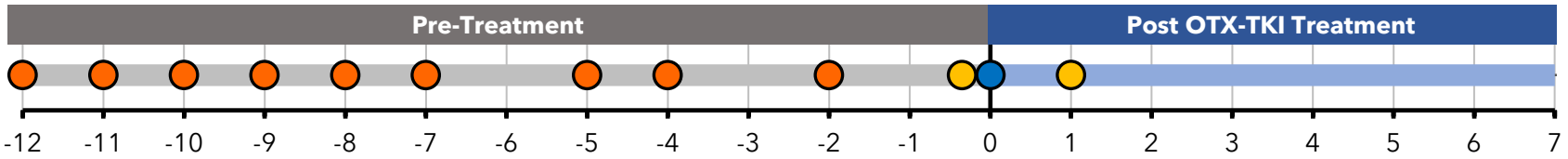


Month 6
CSFT change: -55 µm
BCVA change: +3 letters



Month 7
CSFT change: -54 µm
BCVA change: +4 letters



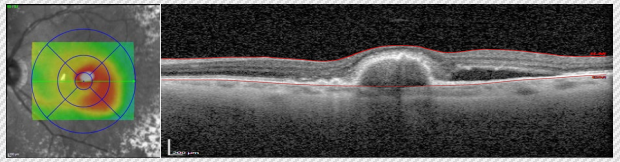


- Ranibizumab
- Aflibercept
- OTX-TKI 600µg implant
- Rescue injection – Rescue criteria **not met (investigator discretion)**

Patient received study-mandated aflibercept injection at Month 1; All changes in CSFT and BCVA are relative to baseline visit

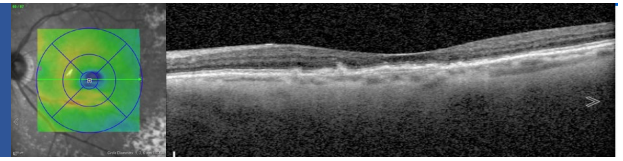
INDIVIDUAL CASE: OTX-TKI PATIENT 15

Historical OCT
(~21 months prior to baseline)
CSFT: 456 µm

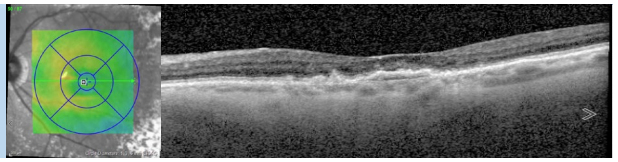


Patient received SOC wet AMD therapy prior to enrollment in the study

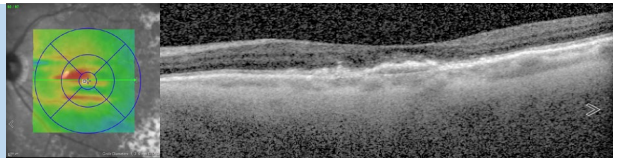
Baseline
CSFT: 183 µm
BCVA: 59 letters



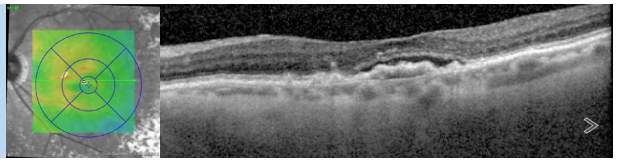
Month 2
CSFT change: +54 µm
BCVA change: +1 letter



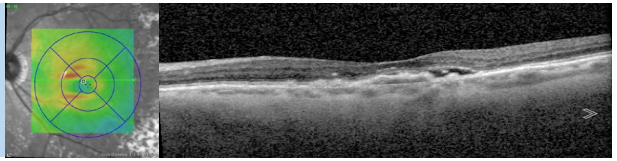
Month 3
CSFT change: +47 µm
BCVA change: -4 letters



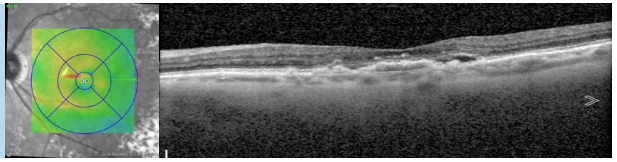
Month 4
CSFT change: +82 µm
BCVA change: +2 letters



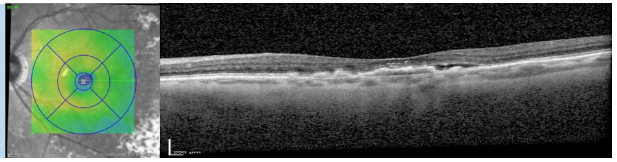
Month 5
CSFT change: +62 µm
BCVA change: -3 letters

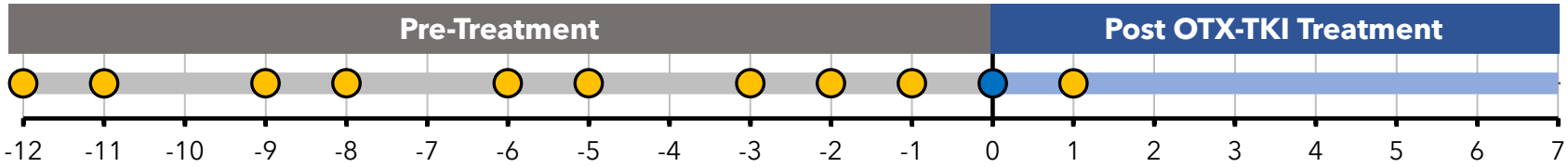


Month 6
CSFT change: +60 µm
BCVA change: -1 letter



Month 7
CSFT change: +9 µm
BCVA change: -2 letters





Aflibercept
OTX-TKI 600µg implant
Rescue injection – Rescue criteria **not met (investigator discretion)**

Patient received study-mandated aflibercept injection at Month 1; All changes in CSFT and BCVA are relative to baseline visit

SAFETY EVENTS

OTK-TKI was generally well tolerated with a favorable safety profile

- 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
  - Endophthalmitis in OTX-TKI arm (moderate and resolved)
  - Elevated IOP in Aflibercept arm (moderate and resolved)

Adverse Events in the Study Eye	OTX-TKI n=16	Aflibercept n=5
Elevated IOP	0	1**
Retinal detachment	0	0
Retinal vasculitis	0	0
Implant migration into the anterior chamber	0	NA
Acute Endophthalmitis	1*	0
Ocular Adverse Events Reported by Severity		
Ocular AEs	10	3
Mild	9	2
Moderate	1*	1**
Severe	0	0
Serious AEs	1*	0

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

Interim review: data cut off August 24, 2022
Abbreviations: IOP, intraocular pressure; SAE, serious adverse event

SUMMARY OF INTERIM DATA FROM OTX-TKI PHASE 1 CLINICAL TRIAL

Phase 1 randomized, controlled US clinical trial in previously treated patients with wet AMD with a single OTX-TKI implant showed safety, tolerability, and biological activity comparable to aflibercept administered every 2 months in this 7-month interim analysis

Safety

- OTK-TKI was generally well tolerated with a favorable safety profile
- No reports of drug-related ocular or systemic SAEs in either arm
- No reported adverse events such as elevated IOP, retinal detachment, retinal vasculitis, or implant migration into the anterior chamber in the OTX-TKI arm
- No subject drop-outs to date in either arm

Efficacy

- 80% of subjects were rescue-free up to 6 months & 73% of subjects were rescue-free up to 7 months following a single OTX-TKI implant injection
- Stable and sustained BCVA (-1.3 letter) and CSFT (+9.2 µm) with OTX-TKI at 7 months comparable to the Q8W aflibercept arm (-1 letter; +0.4 µm)
- Clinically meaningful reduction in treatment burden at 6- and 7-months post-treatment with OTX-TKI

Study is ongoing and will continue to follow-up until month 12

Interim review: data cut off August 24, 2022; Conclusions based on limited number of subjects OTX-TKI: n=16 and Aflibercept: n=5

ACKNOWLEDGEMENTS

Thank you to the investigators, study team and patients for their participation in the clinical study:

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