OTX-TKI From Phase 1 to Phase 3: SOL-1 and SOL-R Trials for Neovascular AMD

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On behalf of the clinical study investigators

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Disclosures

FINANCIAL DISCLOSURES

Research Grant: 4DMT, Adverum, Alexion, Annexon, Aviceda, Bayer, Boerhinger Ingelheim, Curacle, EyeBio, Eyepoint, Genentech, Gyroscope, IvericBio/Astellas, Kodiak, Novartis, Ocular Therapeutix, Oculis, Regeneron, RegenxBio, Rezolute, Roche, Stealth, Unity

Consultant: 4DMT, Abbvie, Adverum, Alimera, Galimedix, Genentech, Heidelberg, IvericBio/Astellas, Kodiak, Novartis, Ocular Therapeutix, Oculis, Regeneron, Regenxbio, Stealth

Speaker: Genentech, IvericBio/Astellas

STUDY AND PRODUCT DISCLOSURES

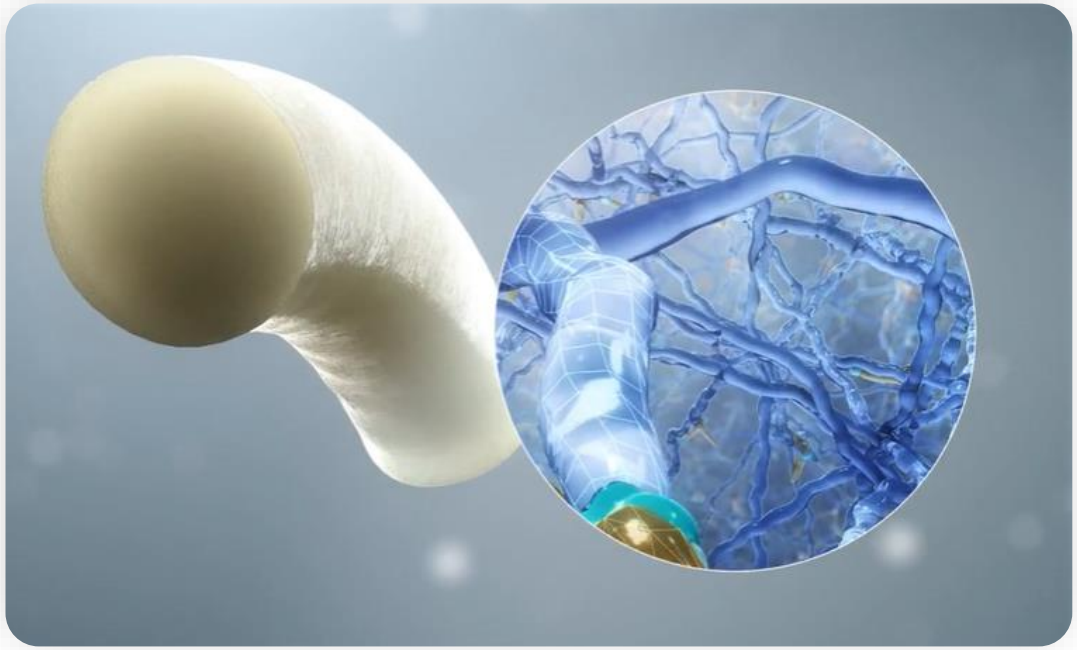
The following presentation discusses an investigational drug, OTX-TKI, in development. OTX-TKI's efficacy and safety profiles have not been established, and it has not been approved for marketing by the U.S. Food and Drug Administration (FDA) or any other health agency.

Ocular Therapeutix sponsored this clinical trial.

Sustained-release Axitinib Hydrogel Injection (OTX-TKI) for nAMD

OTX-TKI

- Delivers axitinib, a potent TKI
- Intravitreal administration with single-use applicator (25G needle)
- Steady-state axitinib release until hydrogel bioresorption
- Hydrogel bioresorbs at ~8-9 months



OTX-TKI PROGRAM STATUS

- Phase 3: nAMD[1,2]
- Phase 1: NPDR[3]

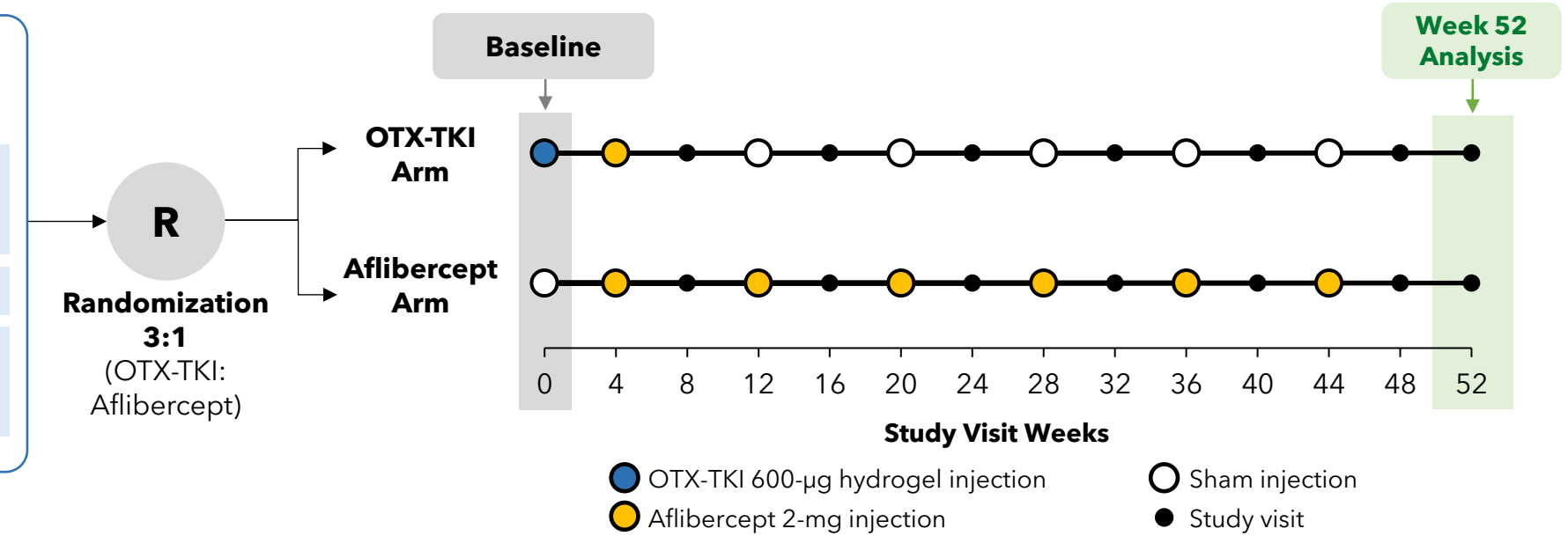
nAMD (Neovascular age-related macular degeneration); NPDR (Non-proliferative diabetic retinopathy); TKI (Tyrosine kinase inhibitor).
Image shown is for illustrative purposes only.
1. NCT06223958. 2. NCT06495918 3. NCT05695417.

Phase 1 US-based Clinical Trial Design of OTX-TKI in nAMD

MULTICENTER, RANDOMIZED, DOUBLE-MASKED TRIAL

KEY INCLUSION CRITERIA

- Subfoveal neovascularization secondary to AMD
- Controlled fluid
- Previously treated with anti-VEGF injections



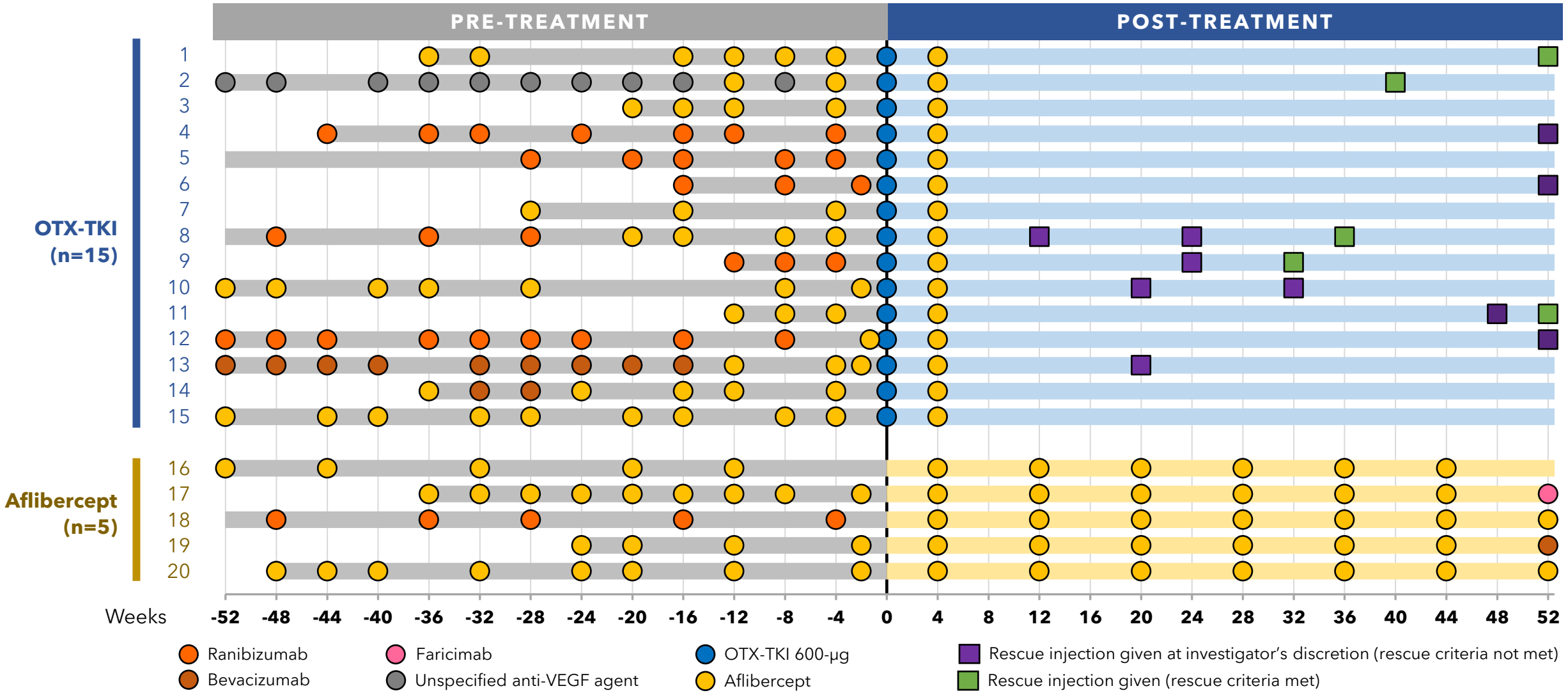
RESCUE ANTI-VEGF INJECTION CRITERIA

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

BCVA (Best corrected visual acuity); CSFT (Central subfield thickness); nAMD (Neovascular age-related macular degeneration); VEGF (Vascular endothelial growth factor).

Moshfeghi AA, et al. *Invest Ophthalmol Vis Sci.* 2023;64(8):936.

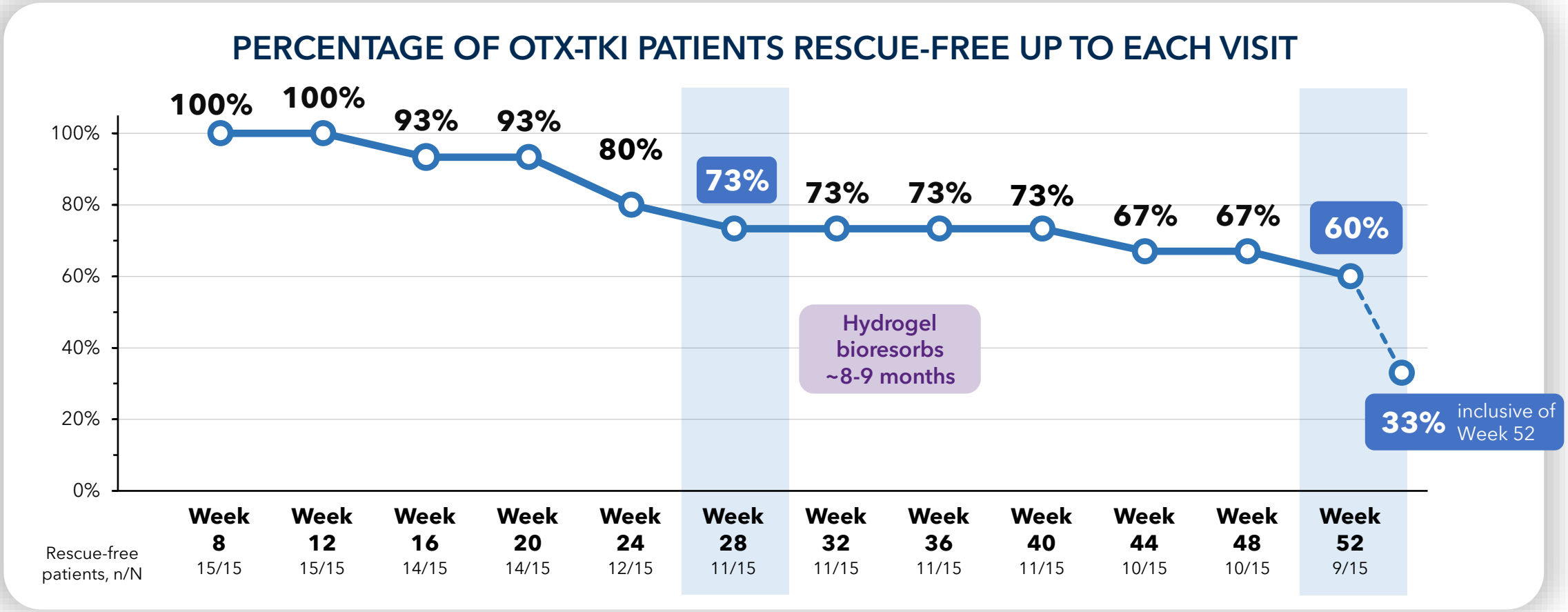
89% Reduction in Anti-VEGF Treatment Burden at Week 52 With OTX-TKI Treatment



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, patients in the aflibercept group were treated with wet AMD standard of care at the investigator's discretion. VEGF (Vascular endothelial growth factor).

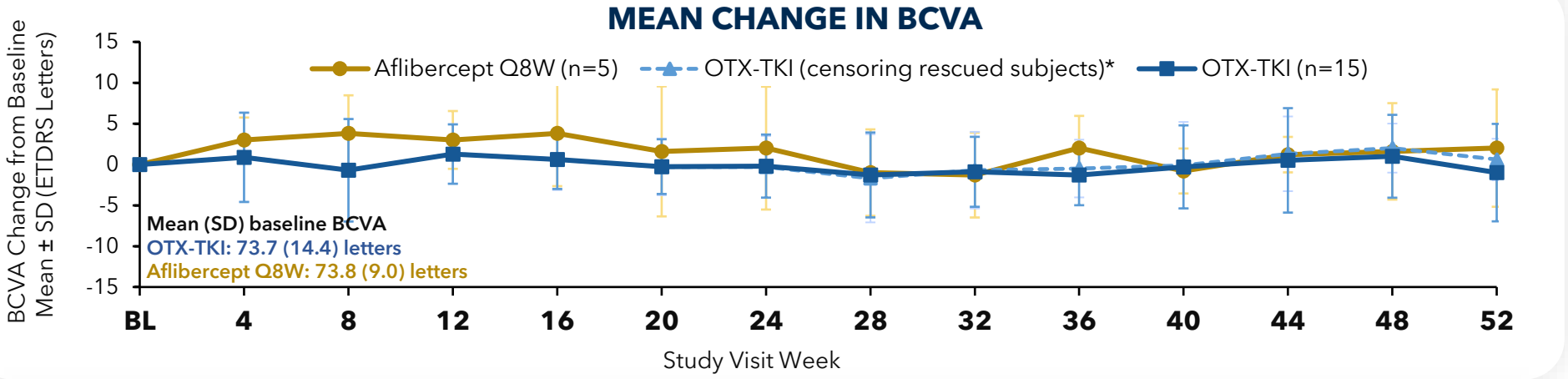
OTX-TKI Demonstrated Extended Duration of Action

73% of OTX-TKI–treated patients were rescue-free up to 28 weeks, 60% up to 52 weeks



Data cut off April 14, 2023. Rescue-free rate calculations: If patients received rescue anti-VEGF therapy at a study visit, those were reflected 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.
VEGF (Vascular endothelial growth factor).

Mean BCVA and CSFT with OTX-TKI were Comparable to Standard-of-care Aflibercept 2mg Q8W

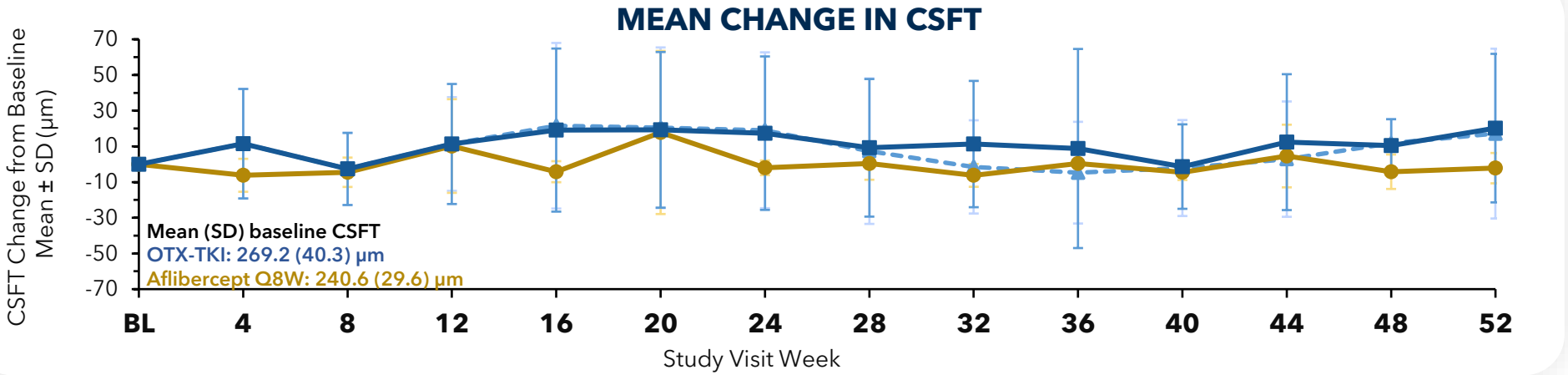


Mean (SD) change in BCVA from baseline to Week 52:

OTX-TKI: -1.0 (6.0) letters

OTX-TKI: +0.6 (2.6) letters (censoring rescued patients)

Aflibercept 2mg Q8W: +2.0 (7.2) letters



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 patients)

Aflibercept 2mg Q8W: -2.2 (8.5) µm

Data cut off April 14, 2023. n=14 in OTX-TKI arm at Weeks 8, 28, 40, and 48 due to missed visits.
*Sample size for OTX-TKI (censoring rescued patients): 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).

Retinal Thickness Variability

OTX-TKI CSFT variations by quartile appear comparable to variations observed in the brolucizumab Phase 3 trials HAWK & HARRIER, supporting OTX-TKI stability in reduced CSFT variability over time.

CSFT Standard Deviations (µm)

Quartile	HAWK & HARRIER[1] (N=1752) Week 12 (post loading doses) to Week 96	OTX-TKI (N=15) (Baseline to Week 52)
Q1	<8	<9
Q2	8-18	9-17
Q3	18-39	17-33
Q4	>39	>33

Reference: 1. Dugel PU, Jhaveri CD, Chakravarthy U, et al. Effect of retinal thickness variability on visual outcomes and fluid persistence in neovascular age-related macular degeneration: a post hoc analysis of the HAWK and HARRIER studies. *Retina*. 2022;42(3):511-518.

Safety Data

No reports of drug-related ocular or systemic SAEs in either arm

One event of acute endophthalmitis in the OTX-TKI arm that occurred following mandated aflibercept injection at Month 1

- Reported as moderate
- Injection procedure related, unrelated to study drug
- Resolved after IVT 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
Patients With AEs in the Study Eye, n (%)		
Elevated IOP	2 (12.5)	1 (20.0)[b]
Retinal detachment	0	0
Retinal vasculitis	0	0
Implant migration into the anterior chamber	0	N/A
Acute endophthalmitis	1 (6.25)[a]	0
Patients With Ocular AEs 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)[a]	1 (20.0)[b]
Severe	0	0
SAEs	1 (6.25)[a]	0

[a]Moderate and serious ocular AE in OTX-TKI arm was acute endophthalmitis 6 days after mandated aflibercept injection at Month 1.
[b]Moderate AE in aflibercept arm was elevated IOP.

Data cut off April 14, 2023.
AE (Adverse event); IOP (Intraocular pressure); IVT (Intravitreal); SAE (Serious adverse event).

US Phase 1 Study Showed Durability and Biological Activity of OTX-TKI for nAMD

- Changes in BCVA and CSFT were comparable to the standard-of-care, aflibercept 2mg Q8W
- OTX-TKI provided an 89% reduction in anti-VEGF treatment burden for treated patients at 52 weeks
- 60% of OTX-TKI–treated patients were rescue-free up to Week 52
- No drug-related ocular or systemic SAEs reported
- Pharmacodynamic effects observed in this trial support the characteristics of a potential treatment for nAMD with durability between 9-12 months with a single OTX-TKI injection

SOL-1 Phase 3 trial is fully enrolled and SOL-R Phase 3 trial is currently enrolling

Data cut off April 14, 2023; conclusions based on a limited number of patients OTX-TKI: N=16 and aflibercept: N=5.
BCVA (Best corrected visual acuity); CSFT (Central subfield thickness); nAMD (Neovascular age-related macular degeneration); SAE (Serious adverse event); VEGF (Vascular endothelial growth factor).