Redefining the Management of Neovascular AMD

April 11, 2026

14th Annual Vit-Buckle Society Meeting | Las Vegas, NV

OCULAR THERAPEUTIX

Retina experience redefined™

Forward-Looking Statements

Any statements in this presentation about future expectations, plans, and prospects for the Company, including statements regarding the development and regulatory status of the Company's or its competitors' product candidates, including statements regarding the SOL-1 Phase 3 superiority trial being conducted under a Special Protocol Assessment (SPA) agreement with the U.S. FDA and aligned with FDA draft guidance for neovascular AMD drug development; the timing, design, enrollment, randomization, conduct and retention of subjects in the Company's clinical trials, including the Company's SOL-1 trial and its SOL-R Phase 3 non-inferiority trial of OTX-TKI for the treatment of wet age-related macular degeneration (wet AMD), also known as neovascular age-related macular degeneration (nAMD); statements regarding the potential utility or adoption of OTX-TKI or its competitors, if approved; statements regarding the Company's intention to submit a new drug application for OTX-TKI, based on data from the Company's SOL-1 trial in wet AMD, subject to planned formal discussions with the FDA; and other statements containing the words "anticipate", "become", "believe", "estimate", "expect", "intend", "designed", "goal", "may", "might", "plan", "position", "predict", "project", "target", "potential", "will", "would", "could", "should", "continue", and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors. Such forward-looking statements involve substantial risks and uncertainties that could cause the Company's development programs, future results, performance, or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the design, timing, conduct and outcomes of ongoing and planned clinical trials, including the SOL-R trial and the second year of the SOL-1 trial; the risk that the FDA will not agree with the Company's interpretation of the written agreements under the Special Protocol Assessments for OTX-TKI, including for the SOL-1 trial; uncertainty as to whether the FDA will accept a new drug application for OTX-TKI on the basis of a single pivotal clinical trial, namely SOL-1; uncertainty as to the minimum clinical data required to demonstrate the safety of a proposed product candidate such as OTX-TKI, even if the FDA recognizes that only one pivotal clinical trial may be required to demonstrate efficacy; the risk that even though the FDA has agreed with the overall design of the SOL-1 trial, the FDA may not find that the data generated by the trial and submitted by the Company are sufficient to demonstrate the safety and efficacy of OTX-TKI to the degree necessary to support marketing approval for wet AMD; uncertainty as to whether the Company will be able to timely satisfy the FDA's other requirements for regulatory approval of OTX-TKI, including the FDA's Chemistry, Manufacturing and Control's requirements, even if the Company can satisfy the FDA's clinical requirements to demonstrate safety and efficacy; uncertainty as to what restrictions, if any, may be imposed on the label for OTX-TKI, if approved, pending the receipt of additional clinical data or otherwise; the risk that the FDA might not agree to the Company's design, protocol, and statistical analysis plan of the SOL-R trial; the risk that the Company and the FDA may not agree on the registrational pathway for any of its product candidates, including OTX-TKI; uncertainty as to whether the data from earlier clinical trials will be predictive of the data of later clinical trials, particularly later clinical trials that have a different design or utilize a different formulation than the earlier trials; uncertainty as to whether preliminary or interim data from a clinical trial will be predictive of final data from such trial; uncertainties regarding the potential commercial advantages and/or position of the Company's product candidates; availability of data from clinical trials and expectations for regulatory submissions and approvals; the Company's scientific approach and general development progress; uncertainties inherent in translating, or in the applicability of, laboratory results to clinical applications; uncertainties inherent in estimating the Company's cash runway, future expenses and other financial results, including its ability to fund future operations, including clinical trials; and other factors discussed in the "Risk Factors" section contained in the Company's quarterly and annual reports on file with the Securities and Exchange Commission. In addition, the forward-looking statements included in this presentation represent the Company's views as of the date of this presentation. The Company anticipates that subsequent events and developments may cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so, whether as a result of new information, future events or otherwise, except as required by law. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this presentation.

Disclaimer

The following presentation discusses OTX-TKI - an investigational product candidate that has not been approved by the FDA or any other regulatory body; safety and effectiveness have not been established

Faculty

Jeffrey S. Heier, MD

Chief Scientific Officer,
Ocular Therapeutix, Inc.

Peter K. Kaiser, MD

Chief Development Officer,
Ocular Therapeutix, Inc.

Andrew A. Moshfeghi, MD

Vice Chair, Clinical Affairs,
Department of Ophthalmology,
Keck School of Medicine

OCULAR THERAPEUTIX Retina experience redefined™

Disclosures

Jeffrey S. Heier

- **Chief Scientific Officer for Ocular Therapeutix**
- **Consultant:** Aavantgarde, Abbvie/Regenxbio, Alzheon, Annexon, Astellas, Aviceda, Bayer, Beacon, Breye Therapeutics, Caeregen, Cogent, Cognition, Complement Therapeutics, Endogena, Focus Biosciences, Frontera, Galimedix, Inflammx, Kaigene, Kanghong, Lilly, Manistee, Nanoscope, Notal Vision, Novartis, Ocugen, Ocuphire, Ora, Inc., Osanni Bio, Perceive Biotherapeutics, Ray Therapeutics, Samsung Bioepis, Sanofi, Stealth Biotherapeutics, Laboratoires Thea, Vanotech, Visgenx
- **Research support:** 4DMT, Abbvie/Regenxbio, Annexon, Apellis, Astellas, Bayer, Beacon, Boehringer Ingleheim, Cognition Therapeutics, Curacle, Janssen R&D, Kodiak, Notal Vision, Novartis, Oculis, Perceive Bio, Sanofi, Skyline, Stealth Biotherapeutics, Vanotech
- **Stock/Stock options:** Adverum, Aldeyra, Alzheon, Aviceda, Caeregen, Inflammx, jCyte, Ocular Therapeutix, Osanni Bio, Ray Therapeutics, RevOpsis, Vinci, Visgenx, Vitranu

---

Peter K. Kaiser

- **Chief Development Officer for Ocular Therapeutix**
- **Consultant**: Abbvie, Alexion, Alkeus, Allgenesis, Alzheon, Amaros, Annexon Biosciences, Astellas, Augen Therapeutics, Aviceda, Bayer, Biogen Idec, Carl Zeiss Meditec, Celltrion Healthcare Co., Cognition Therapeutics, Complement Therapeutics, Eli Lilly, Endogena Therapeutics, Eyestem, Frontera Therapeutics, Galimedix, Innovent, Invirsa, iRenix, Isarna, Janssen, jCyte, Kanaph Therapeutics, Kanghong, Kera Therapeutics, Kriya Therapeutics, Movu/Santec, Nanoscope Therapeutics, Ocugenix, Oculis, Omeros, Ophthalmx, Osanni Bio, Panther Pharmaceuticals, Ray Therapeutics, RegenxBio, Resonance Medicine Inc., Restore Vision, Retinal Sciences, ReVana, RevOpsis, Roivant, Samsung Bioepis, Sandoz, SGN Nanopharma Inc., SmileBiotek Zhuhai Ltd, Stealth Biotherapeutics, Stuart, Sudo Biosciences, Sustained Nano Systems, Théa, Tilak, Vanotech, VisgenX
- **Stock/Stock Options**: AAVAntgarde Bio, Alzheon, Aviceda, Inflammx, jCyte, Ocular Therapeutix, Osanni Bio, Ray Therapeutics, RevOpsis, Vinci, Vitranu
- **Board of Directors:** AAVAntgarde Bio

Andrew A. Moshfeghi

- **Consultant:** Alcon, Annexon, Apellis, Astellas, Bausch + Lomb, Ocular Therapeutix, Pr3vent, Valitor, Regeneron
- **Stock/Stock options:** Ocular Therapeutix, Pr3vent, Valitor

Agenda

Science Behind the Therapy
Peter K. Kaiser, MD

SOL-1 Phase 3 Trial

- **SOL Program**
  Jeffrey S. Heier, MD
- **Results**
  Andrew A. Moshfeghi, MD

Translating SOL-1 Results
Peter K. Kaiser, MD

Clinical Evidence
Jeffrey S. Heier, MD

OCULAR THERAPEUTIX Retina experience redefined

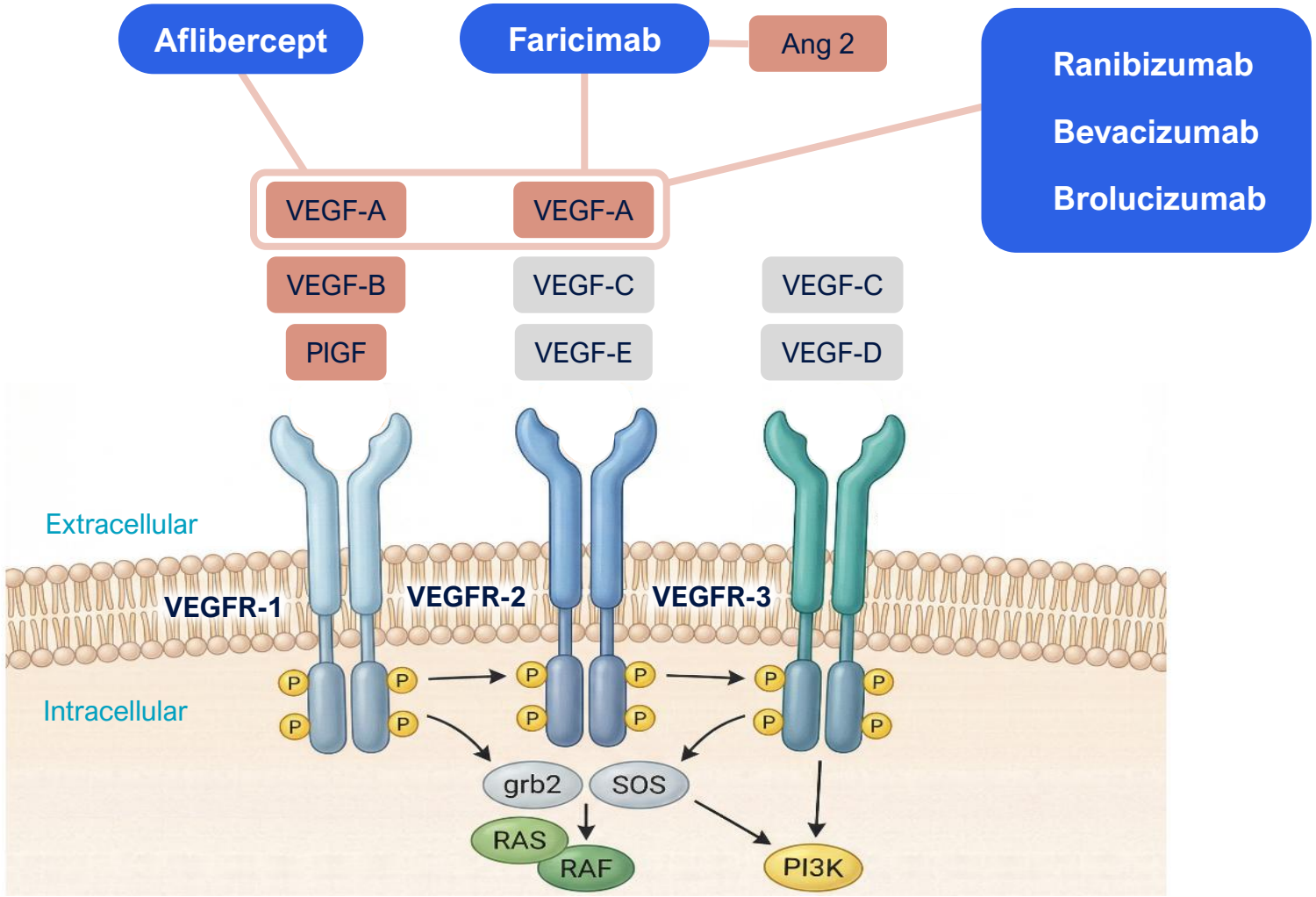
Science Behind the Therapy

Peter K. Kaiser, MD

OCULAR THERAPEUTIX Retina experience redefined

Current Anti-VEGF Therapies Selectively Target Only Extracellular VEGF

Current **Anti-VEGF** agents act **extracellularly by binding selective ligands**, like VEGF-A, preventing receptor binding and activation[1,2]



Select extracellular target binding of VEGF, PlGF and Ang-II to inhibit angiogenesis. Adapted from Zhao et al. 2015.[2-4]

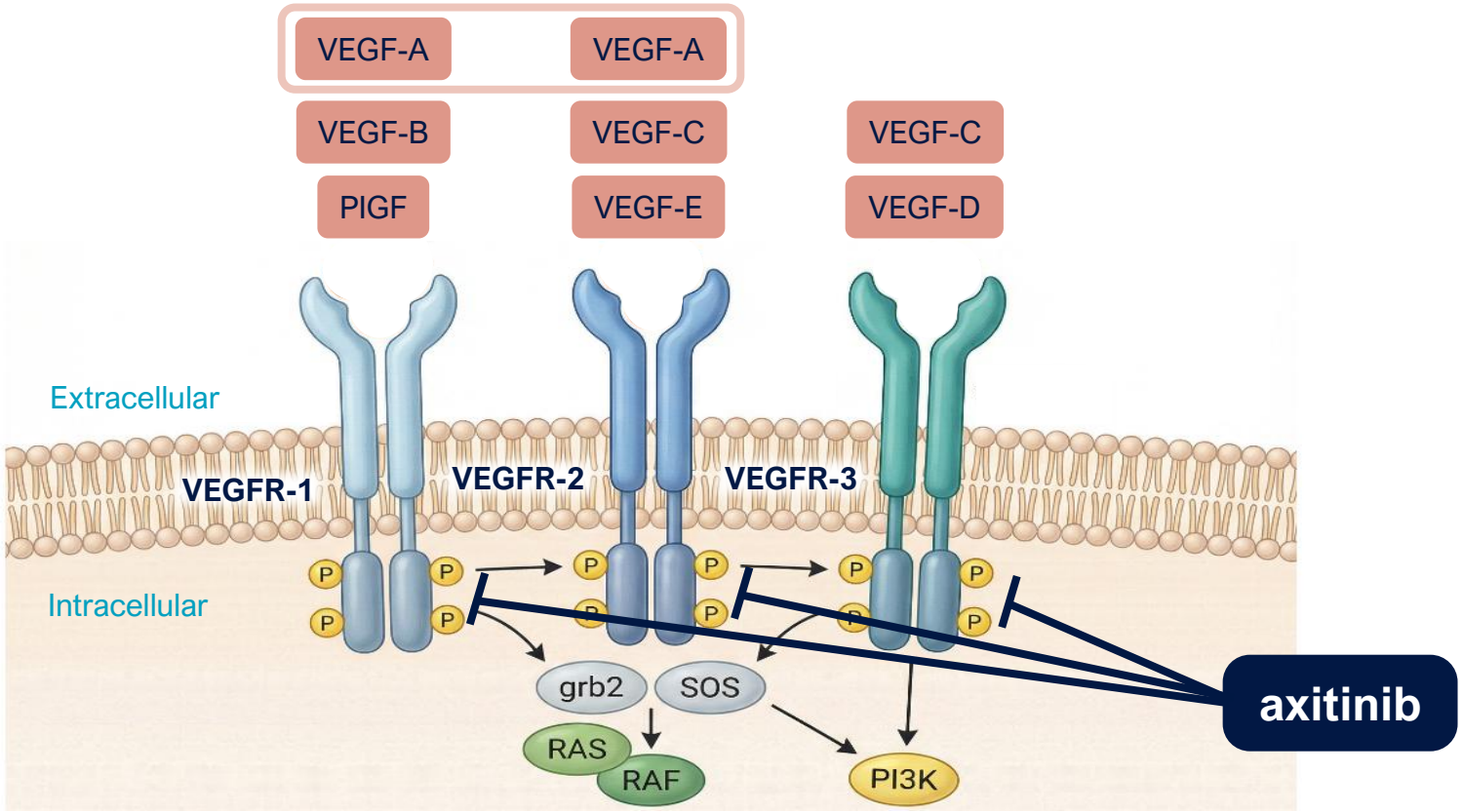
OCULAR THERAPEUTIX Retina experience redefined™

1. Hu-Lowe DD, et al. *Clin Cancer Res*. 2008;14(22):7272-7283. 2. Zhao Y, et al. *Oncologist*. 2015;20(6):660-673. 3. Tan CS, et al. *Clin Ophthalmol*. 2022;16:917-933. 4. Khachigian LM, et al. *J Transl Med*. 2023;21(1):133.

PlGF, placenta growth factor; VEGF(R), vascular endothelial growth factor (receptor); P, phosphate; grb2, growth factor receptor-bound protein 2; SOS, son of sevenless; RAS, rat sarcoma viral oncogene homolog; RAF, rapidly accelerated fibrosarcoma; PI3K, phosphatidylinositol 3-kinase; TKI, tyrosine kinase inhibitor; Ang 2, angiopoietin-2

Tyrosine Kinase Inhibitors Act Intracellularly to Inhibit Receptor Signaling

Tyrosine Kinase Inhibitors (TKI) bind at the **intracellular tyrosine kinase domains** of VEGF receptors, inhibiting ATP binding and preventing activation of pro-angiogenic signaling[1,2]



Select angiogenesis intracellular targets of inhibition for tyrosine kinase inhibitors. Adapted from Zhao et al. 2015.[2-4]

OCULAR THERAPEUTIX Retina experience redefined™

1. Hu-Lowe DD, et al. *Clin Cancer Res*. 2008;14(22):7272-7283. 2. Zhao Y, et al. *Oncologist*. 2015;20(6):660-673. 3. Tan CS, et al. *Clin Ophthalmol*. 2022;16:917-933. 4. Khachigian LM, et al. *J Transl Med*. 2023;21(1):133.

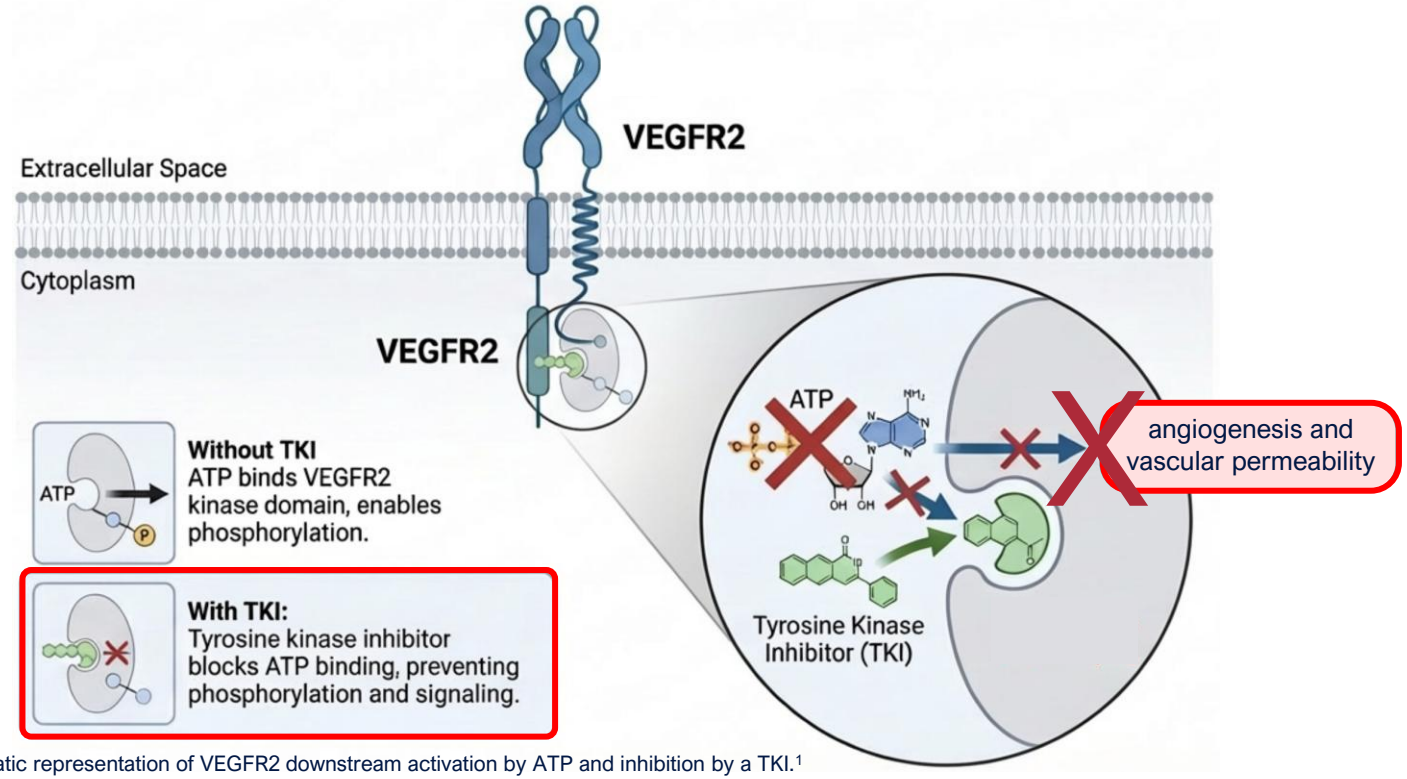
PlGF, placenta growth factor; VEGF(R), vascular endothelial growth factor (receptor); P, phosphate; grb2, growth factor receptor-bound protein 2; SOS, son of sevenless; RAS, rat sarcoma viral oncogene homolog; RAF, rapidly accelerated fibrosarcoma; PI3K, phosphatidylinositol 3-kinase; TKI, tyrosine kinase inhibitor.

Receptor Inhibition by Tyrosine Kinase Inhibitors

Critically important to understand testing conditions to interpret TKI inhibition

ATP competes with TKI drugs for receptor binding[1]

Receptor inhibition depends on ATP + drug concentrations[2]



Schematic representation of VEGFR2 downstream activation by ATP and inhibition by a TKI.[1]

1. Shaik F, et al. *Biomolecules.* 2020;10(12):1673. **2.** Activity-based Biochemical Kinase Panel Screening and Profiling Services. https://www.assayquant.com/kinsight-services/kinome-profiling/. Accessed February 23, 2026.

ATP, adenosine triphosphate; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor; VEGFR2, VEGF receptor 2

Receptor Inhibition by Tyrosine Kinase Inhibitors

Critically important to understand testing conditions to interpret TKI inhibition

ATP competes with TKI drugs for receptor binding[1]

Apparent % inhibition depends on ATP + drug concentration[2]

ATP Testing Levels

Low ATP levels reduce competition and increase % apparent inhibition[3]

Physiologic ATP levels (~1-4 mM)[4,5]

Local ATP elevated in retinal disease[6]

Drug Testing Levels

Supratherapeutic concentrations artificially increase % apparent inhibition[7]

TKIs are highly protein bound (eg. melanin)[8-10]

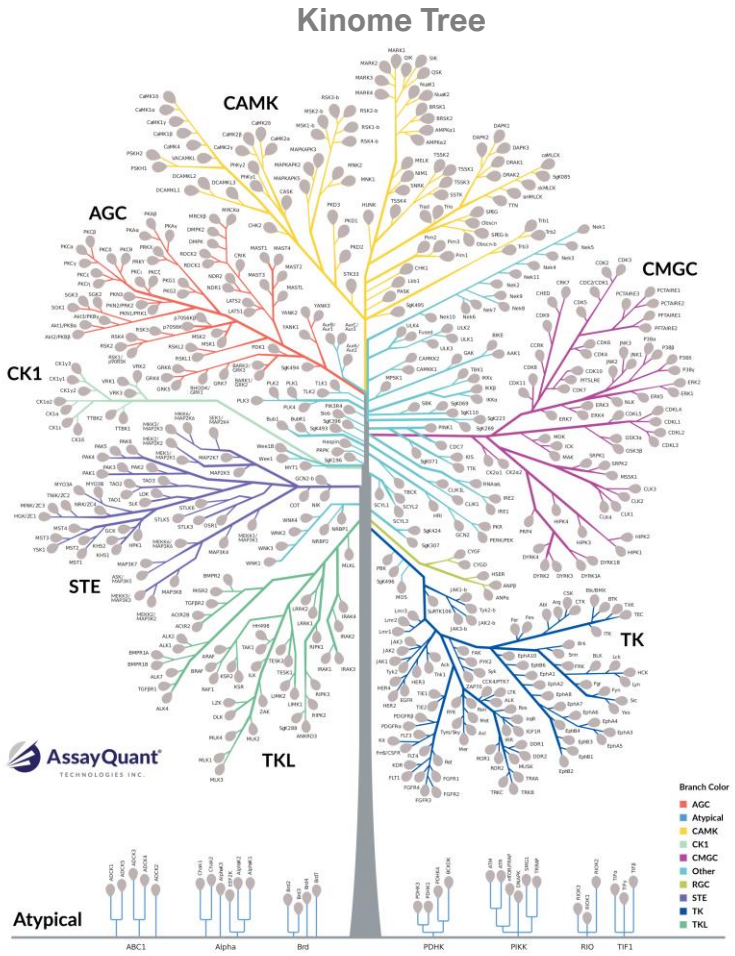
Testing should reflect unbound drug levels in the retina

OCULAR THERAPEUTIX Retina experience redefined™

1. Shaik F, et al. *Biomolecules*. 2020;10(12):1673. 2. Activity-based Biochemical Kinase Panel Screening and Profiling Services. https://www.assayquant.com/kinsight-services/kinome-profiling/. Accessed February 23, 2026. 3. Duong-Ly KC, et al. The human kinome and kinase inhibition. In: *Curr Protoc Pharmacol*. John Wiley & Sons, Inc.; 2013. 4. Greiner JV, et al. *Biology (Basel).* 2021;10(11):1166. 5. Patel C, et al. Target and Selectivity Profiling of Axitinib in Cell-Based and Biochemical Assays. Presented at the Association for Research in Vision and Ophthalmology. May 8, 2025, Salt Lake City, UT 6. Ye SS, et al. *Front Pharmacol*. 2021;12:654445. 7. Liu C, et al. *Cell Rep Med*. 2023;4(10):101227. 8. Hulin A, et al. *Clin J Am Soc Nephrol*. 2024;19(7):927-938. 9. Kadavil H, et al. *Expert Opin Drug Deliv*. 2025;22(9):1275-1301. 10. Marini J, et al. *J Hematol Oncol Pharm*. 2022;12(4):196-203.
ATP, adenosine triphosphate; TKI, tyrosine kinase inhibitor.

AssayQuant Kinome Tree

Independent, Quantifiable, Simultaneous Evaluation of Inhibition Activity of TKI drugs



Adapted from AssayQuant.[1]

AssayQuant Kinome tree is an independent, standardized visualization of kinase profiling data[1]

Each kinase receptor is a node with color intensity reflecting magnitude of inhibition[1,2]

OCULAR THERAPEUTIX Retina experience redefined™

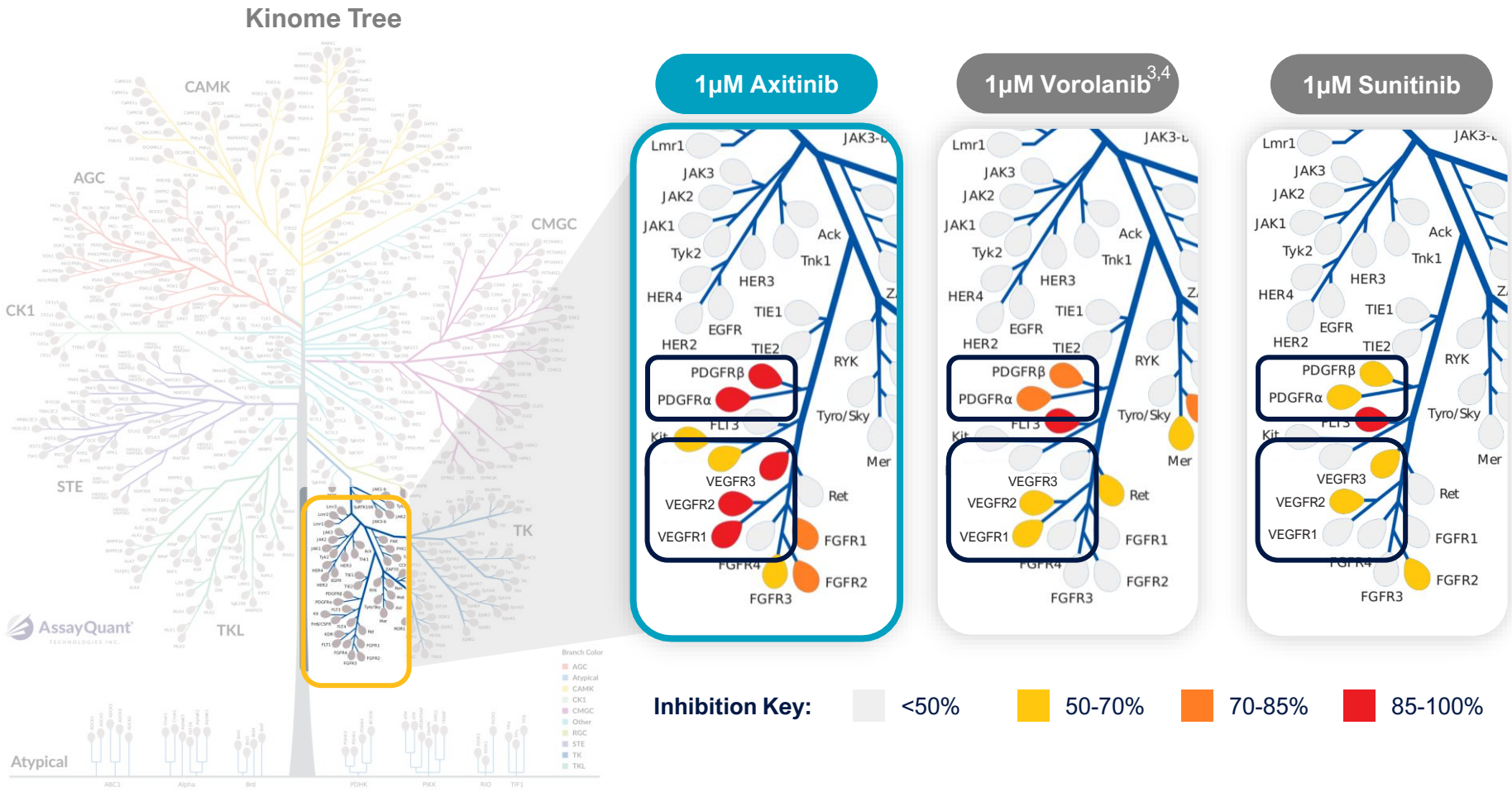
AssayQuant is an independent, standardized visualization of kinase profiling data.

1. Activity-based Biochemical Kinase Panel Screening and Profiling Services. https://www.assayquant.com/kinsight-services/kinome-profiling/. Accessed February 23, 2026. 2. González-Vera JA, et al. *Proteomes.* 2015;3(4):369-410.

TKI, tyrosine kinase inhibitor;

Axitinib: Highly Selective, Potent Pan-VEGFR Inhibitor

Independent AssayQuant Kinome Tree Analysis



Adapted from AssayQuant.[1]

At **physiologic** ATP concentrations (1mM) and **therapeutic** TKI (1μM) concentrations*, **axitinib***:

VEGFR 1/2/3:
>90% inhibition[1,2]

PDGFR α/β:
>85% inhibition[1]

*Kinome Tree inhibition analysis conducted in collaboration with AssayQuant; PhosphoSens® assay (AssayQuant®) conducted at 1mM ATP and 1μM drug concentrations.

1. Data on file, Ocular Therapeutix. 2. Patel C, et al. Target and Selectivity Profiling of Axitinib in Cell-Based and Biochemical Assays. Presented at the Association for Research in Vision and Ophthalmology. May 8, 2025, Salt Lake City, UT. 3. Singh RP, et al. A 12-Month, Ocular Pharmacokinetic Study of EYP-1901, a Sustained-release, Intravitreal Formulation of the Tyrosine Kinase Inhibitor Vorolanib. Presented at the American Society of Retina Specialists Annual Meeting; July 28–August 1, 2023; Seattle, WA; 4. Kupperman BD, et al. Poster B0301. Presented at ARVO 2024 Annual Meeting, May 5–9, 2024; Seattle, WA

TKI, tyrosine kinase inhibition; VEGFR, vascular endothelial growth factor receptor; ATP, adenosine triphosphate.

OCULAR THERAPEUTIX Retina experience redefined™

AssayQuant Independent Potency Comparison Among TKIs

Tyrosine Kinase Inhibitor Potency (% Inhibition)

*Evaluated at physiologic ATP levels (1mM) & Drug Concentrations (1μM)**

TK Receptors[1,2]	1μM Axitinib *Most Potent VEGFR, PDGFR TKI*	1μM Vorolanib[7-9] *Derivative of Sunitinib*	1μM Sunitinib
VEGF RECEPTORS			
VEGFR1	100%	32%	59%
VEGFR2	98%	53%	51%
VEGFR3	92%	51%	41%
OTHER RECEPTORS			
PDGFRα	94%	65%	70%
PDGFRβ	88%	64%	78%

Inhibition Key: <50% | 50-70% | 70-85% | 85-100%

FDA-APPROVED INDICATIONS	Renal cell carcinoma[3]	Not approved by FDA; X-82 approved in China in combination with everolimus for advanced renal cell carcinoma[4,9]	Renal cell carcinoma Gastrointestinal stromal tumors Pancreatic neuroendocrine tumors[5,6]

OCULAR THERAPEUTIX Retina experience redefined™

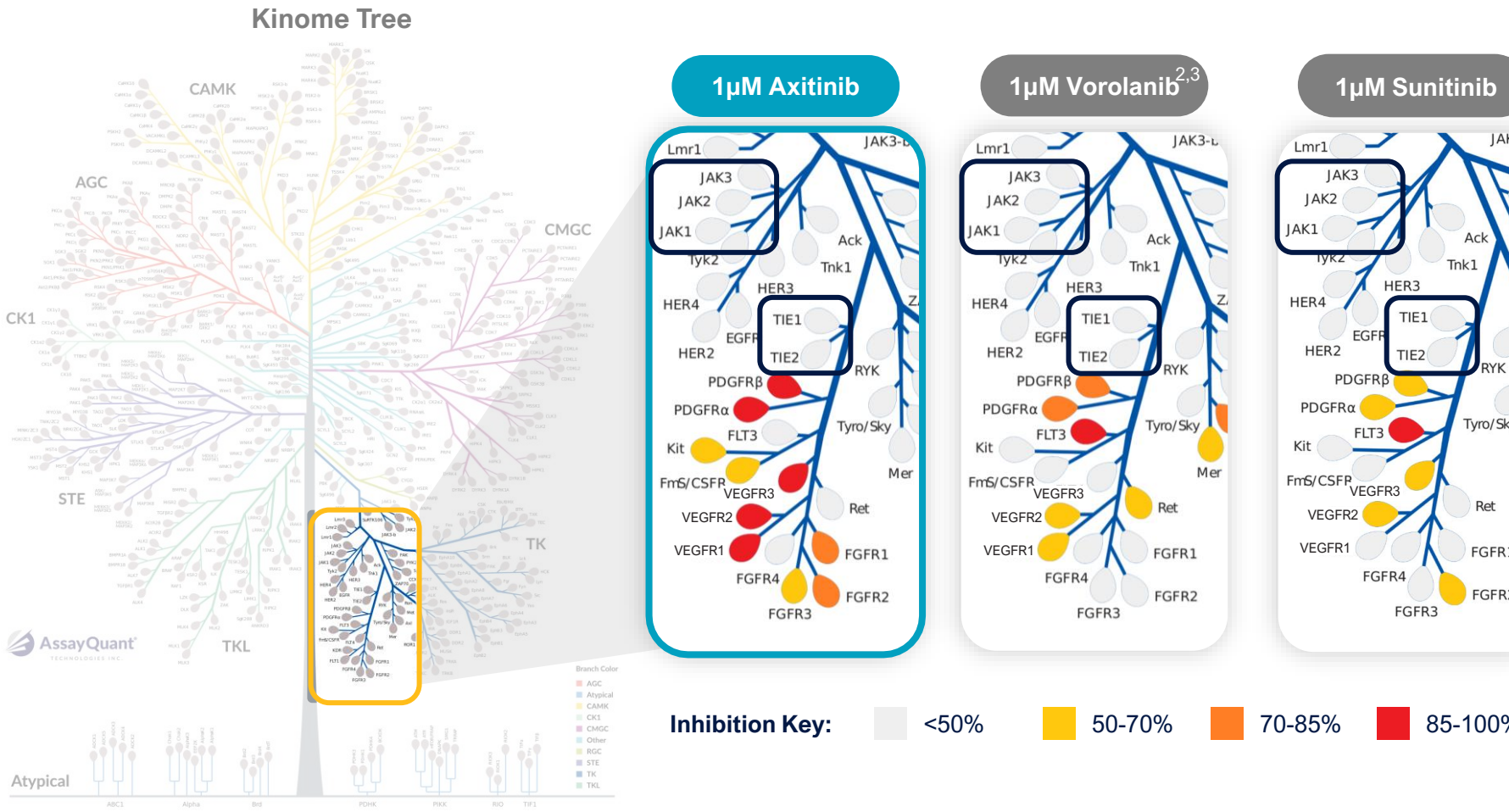
*Kinome Tree inhibition analysis conducted in collaboration with AssayQuant. PhosphoSens® assay (AssayQuant®) conducted at 1mM ATP and 1μM drug concentrations.

1. Data on file, Ocular Therapeutix. 2. Patel C, et al. Target and Selectivity Profiling of Axitinib in Cell-Based and Biochemical Assays. Presented at the Association for Research in Vision and Ophthalmology. May 8, 2025, Salt Lake City, UT. 3. INLYTA (axitinib) prescribing information. U.S. Food and Drug Administration; 2012. Accessed February 27, 2026. 4. Sheng X, et al. *EBioMedicine.* 2020;55:102755. 5. Blumenthal GM, et al. *Oncologist.* 2012;17(8):1108-1113. 6. SUTENT (sunitinib malate) prescribing information. U.S. Food and Drug Administration; 2006. Accessed February 27, 2026. 7. Singh RP, et al. A 12-Month, Ocular Pharmacokinetic Study of EYP-1901, a Sustained-release, Intravitreal Formulation of the Tyrosine Kinase Inhibitor Vorolanib. Presented at the American Society of Retina Specialists Annual Meeting; July 28–August 1, 2023; Seattle, WA. 8. Kupperman BD, et al. Poster B0301. Presented at ARVO 2024 Annual Meeting, May 5–9, 2024; Seattle, WA. 9. Xiu X, et al. *Organic Process Research & Development*. 2024;28(2):492-499.

TKI, tyrosine kinase inhibitor; ATP, adenosine triphosphate; VEGFR, vascular endothelial growth factor receptor; PDGFR, platelet-derived growth factor receptor; JAK, janus kinase.

Axitinib: Highly Selective, Potent Pan-VEGFR Inhibitor

Independent AssayQuant Kinome Tree Analysis



Adapted from AssayQuant.[1]

At **physiologic** ATP concentrations (1mM) and **therapeutic** TKI (1μM) concentrations **axitinib** *:

No meaningful JAK1 or TIE2 inhibition[1]

*Kinome Tree inhibition analysis conducted in collaboration with AssayQuant; PhosphoSens® assay (AssayQuant®) conducted at 1mM ATP and 1μM drug concentrations..

1. Data on file 041, Ocular Therapeutix. 2. Singh RP, et al. A 12-Month, Ocular Pharmacokinetic Study of EYP-1901, a Sustained-release, Intravitreal Formulation of the Tyrosine Kinase Inhibitor Vorolanib. Presented at the American Society of Retina Specialists Annual Meeting; July 28–August 1, 2023; Seattle, WA; 3. Kupperman BD, et al. Poster B0301. Presented at ARVO 2024 Annual Meeting, May 5–9, 2024; Seattle, WA

TKI, tyrosine kinase inhibition; VEGFR, vascular endothelial growth factor receptor; ATP, adenosine triphosphate; JAK, janus kinase; TIE2, tyrosine kinase with immunoglobulin-like and epidermal growth factor–like domains-2.

OCULAR THERAPEUTIX Retina experience redefined™

AssayQuant Independent Potency Comparison Among TKIs

Tyrosine Kinase Inhibitor Potency (% Inhibition)

*Evaluated at physiologic ATP levels (1mM) & Drug Concentrations (1μM)**

TK Receptors[1,2]	1μM Axitinib *Most Potent VEGFR, PDGFR TKI*	1μM Vorolanib[3-5] *Derivative of Sunitinib*	1μM Sunitinib
VEGF RECEPTORS			
VEGFR1	100%	32%	59%
VEGFR2	**98%**	**53%**	**51%**
VEGFR3	92%	51%	41%
OTHER RECEPTORS			
PDGFRα	94%	65%	70%
PDGFRβ	88%	64%	78%
JAK1	9%	15%	16%
JAK2	9%	16%	17%
JAK3	<0%	<0%	14%
TIE2	22%	<0%	19%

Inhibition Key: <50% | 50-70% | 70-85% | 85-100%

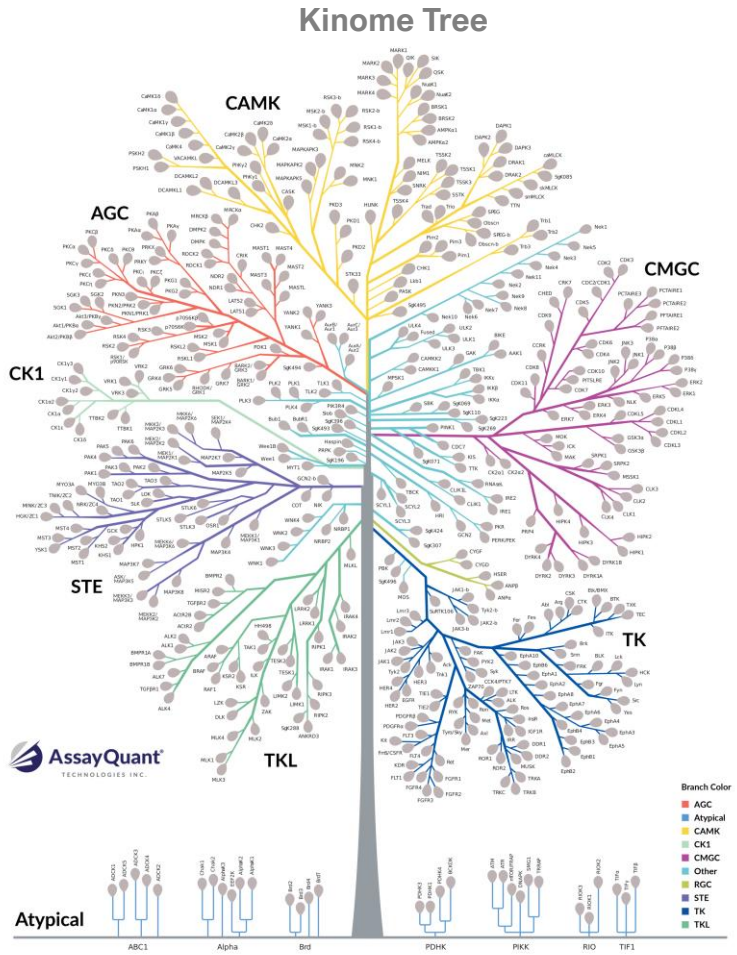
OCULAR THERAPEUTIX Retina experience redefined™

*Kinome Tree inhibition analysis conducted in collaboration with AssayQuant. PhosphoSens® assay (AssayQuant®) conducted at 1mM ATP and 1μM drug concentrations.

1. Data on file, Ocular Therapeutix. 2. Patel C, et al. Target and Selectivity Profiling of Axitinib in Cell-Based and Biochemical Assays. Presented at the Association for Research in Vision and Ophthalmology. May 8, 2025, Salt Lake City, UT. 3. Singh RP, et al. A 12-Month, Ocular Pharmacokinetic Study of EYP-1901, a Sustained-release, Intravitreal Formulation of the Tyrosine Kinase Inhibitor Vorolanib. Presented at the American Society of Retina Specialists Annual Meeting; July 28–August 1, 2023; Seattle, WA; 4. Kupperman BD, et al. Poster B0301. Presented at ARVO 2024 Annual Meeting, May 5–9, 2024; Seattle, WA; 5. Xiu X, et al. *Organic Process Research & Development*. 2024;28(2):492-499.; TKI, tyrosine kinase inhibitor; ATP, adenosine triphosphate; VEGFR, vascular endothelial growth factor receptor; PDGFR, platelet-derived growth factor receptor; JAK, janus kinase. TIE2, tyrosine kinase with immunoglobulin-like and epidermal growth factor–like domains-2.

Independent AssayQuant Kinome Tree

Always look for testing conditions when evaluating claims about receptor inhibition



Adapted from AssayQuant.[1]

AssayQuant Kinome tree is an independent, standardized visualization of kinase profiling data[1]

ATP Testing Levels

Low ATP levels reduce competition and increase % apparent inhibition[2]

Physiologic ATP levels (~1-4 mM)[3-4]

Local ATP elevated in retinal disease[5]

Drug Testing Levels

Supratherapeutic concentrations artificially increase % apparent inhibition[6]

TKIs are highly protein bound (eg. melanin)[7-10]

Testing should reflect unbound drug levels in the retina

There can be **different kinome trees** for the *same compound* depending on ATP and drug concentrations used in test

OCULAR THERAPEUTIX Retina experience redefined™

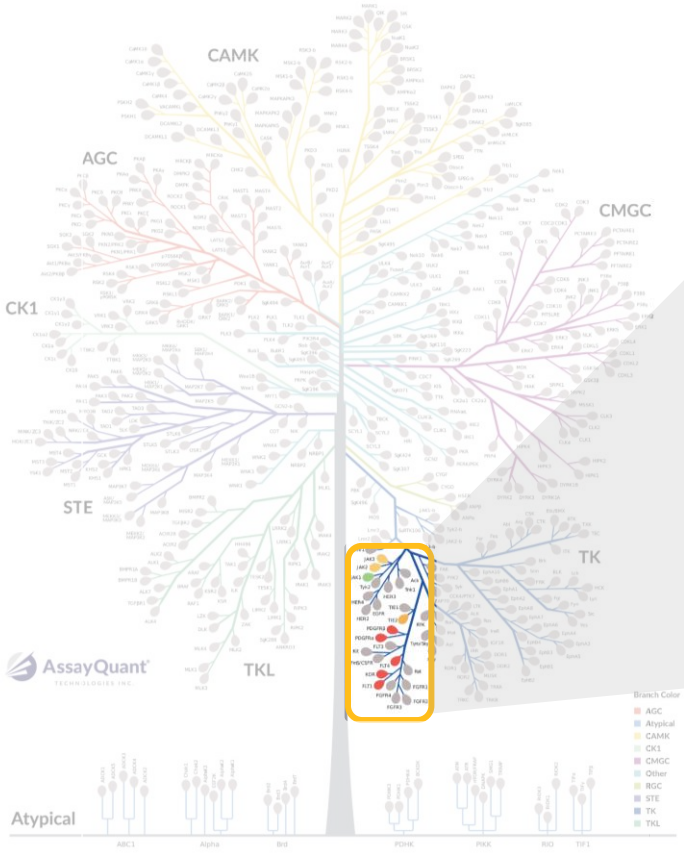
AssayQuant is an independent, standardized visualization of kinase profiling data.
1. Activity-based Biochemical Kinase Panel Screening and Profiling Services. https://www.assayquant.com/kinsight-services/kinome-profiling/. Accessed February 23, 2026. 2. Duong-Ly KC, et al. *Curr Protoc Pharmacol*. 2013;Chapter 2:Unit2.9. 3. Greiner JV, et al. *Biology (Basel).* 2021;10(11):1166. 4. Patel C, et al. Target and Selectivity Profiling of Axitinib in Cell-Based and Biochemical Assays. Presented at the Association for Research in Vision and Ophthalmology. May 8, 2025, Salt Lake City, UT 5. Ye SS, et al. *Front Pharmacol.* 2021;12:654445. 6. Liu C, et al. *Cell Rep Med*. 2023;4(10):101227. 7. Hulin A, et al. *Clin J Am Soc Nephrol.* 2024;19(7):927-938. 8. Kadavil Het al. *Expert Opin Drug Deliv*. 2025;22(9):1275-1301. 9. Marini J, et al. *J Hematol Oncol Pharm*. 2022;12(4):196-203.

ATP, adenosine triphosphate; TKI, tyrosine kinase inhibitor.

Non-Physiologic AssayQuant Potency Comparison

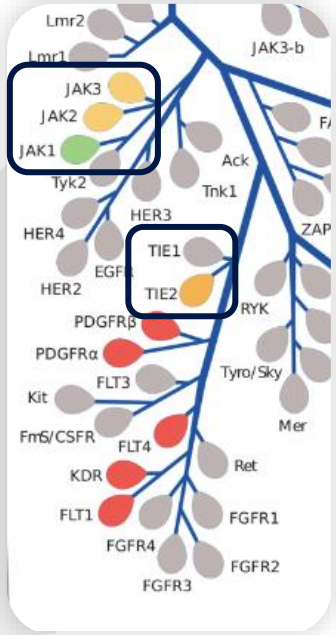
Independent AssayQuant Kinome Tree Analysis

Kinome Tree

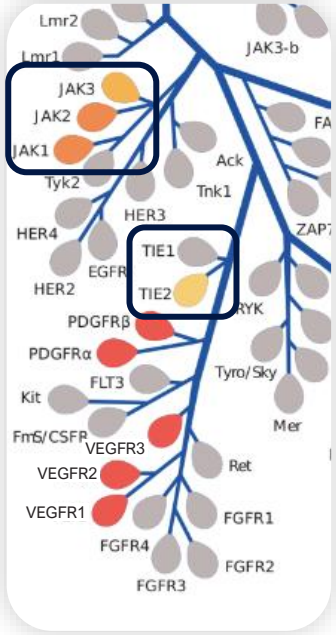


Non-physiologic Drug Levels

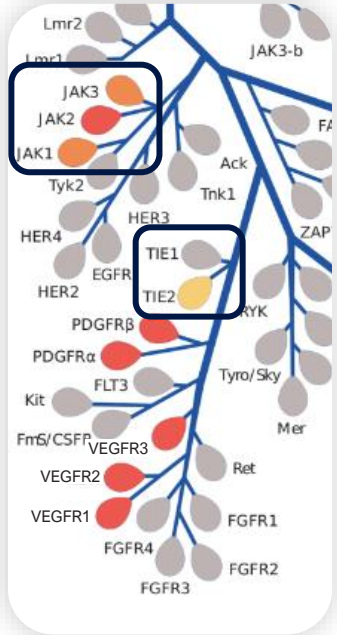
10μM Axitinib



10μM Vorolanib[1,2]



10μM Sunitinib



Inhibition Key: ≥90% | 70-90% | 50-70% | 30-50% | <30% | Not tested

At **too low** ATP concentrations (Km) and **unobtainable, high** TKI (10μM) concentrations **axitinib***:

— Artificial —
JAK1 and TIE2 inhibition

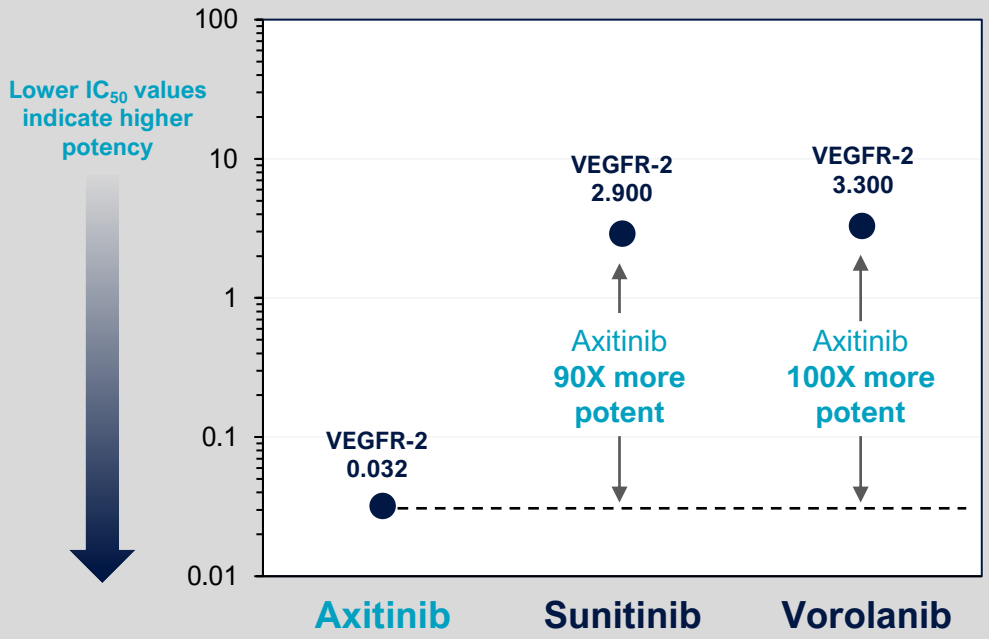
Adapted from AssayQuant.[1]

*Kinome Tree inhibition analysis conducted in collaboration with AssayQuant; PhosphoSens® assay (AssayQuant®) **conducted at Km (low) ATP, 10μM drug concentration (very high)**; eg. Axitinib has a maximum solubility of approximately 1μM in physiologically relevant conditions; To achieve a 10μM axitinib concentration DMSO must be used as a co-solvent; Data on file, Ocular Therapeutix. 1. Singh RP, et al. A 12-Month, Ocular Pharmacokinetic Study of EYP-1901, a Sustained-release, Intravitreal Formulation of the Tyrosine Kinase Inhibitor Vorolanib. Presented at the American Society of Retina Specialists Annual Meeting; July 28–August 1, 2023; Seattle, WA; 2. Kupperman BD, et al. Poster B0301. Presented at ARVO 2024 Annual Meeting, May 5–9, 2024; Seattle, WA; TKI, tyrosine kinase inhibition; VEGFR, vascular endothelial growth factor receptor; ATP, adenosine triphosphate; JAK, janus kinase; TIE2, tyrosine kinase with immunoglobulin-like and epidermal growth factor–like domains-2.

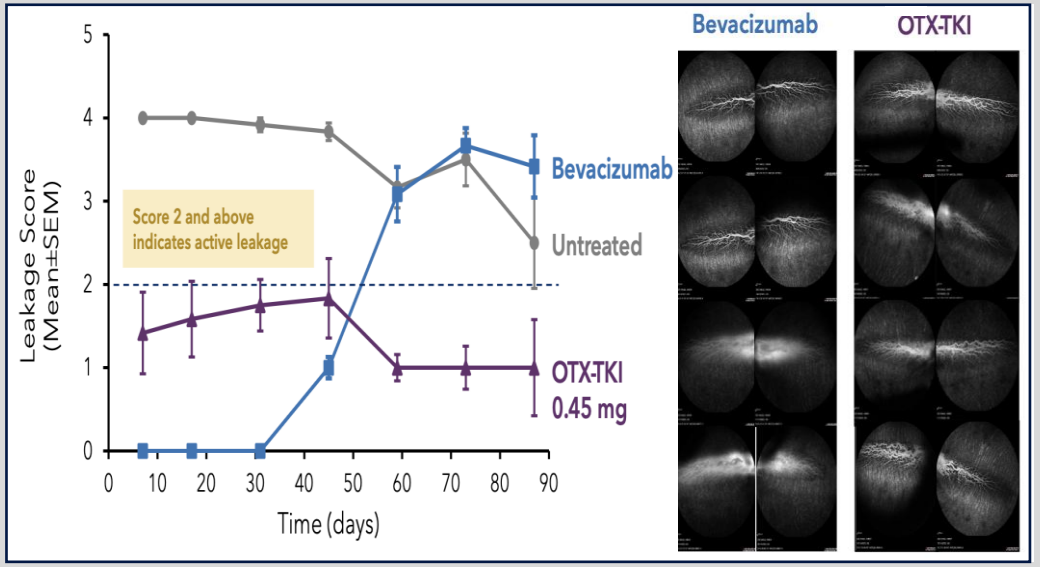
OCULAR THERAPEUTIX Retina experience redefined™

Axitinib: Highly Selective, Very Potent Pan-VEGFR Inhibitor

Independent IC_{50} Cell Phosphorylation (nM)[1,2,3]



VEGF Challenge Rabbit Model[2]



Highly selective for all VEGF receptors, ~100x more potent for VEGFR-2[1,2,3]

Sustained leakage control in repeat VEGF challenge animal model[2]

OCULAR THERAPEUTIX Retina experience redefined™

1. Patel C, et al. Target and Selectivity Profiling of Axitinib in Cell-Based and Biochemical Assays. Presented at Association in Vision and Ophthalmology. May 4, 2025. Salt Lake City, UT. **2.** Blizzard, C et al. Pharmacodynamic efficacy of optimized intravitreal axitinib implant (OTX-TKI) in a VEGF challenge rabbit model. Presented at the Association in Vision and Ophthalmology. May 9, 2024. Seattle, WA, US. **3.** Reaction Biology, Germany; Cellular Phosphorylation Assay Service. (https://www.reactionbiology.com) CHO Cellular assay data demonstrated no TIE2 inhibition within physiological drug solubility range at normal cellular ATP levels via the gold standard cell phosphorylation assay; Ocular Therapeutix. Data on File 042. 2026.

VEGFR, vascular endothelial growth factor receptor; IC50, inhibitory concentration 50%; SEM, standard error of mean

OTX-TKI: Axitinib via Hydrogel Allows for Tunable Sustained Release

AXITINIB

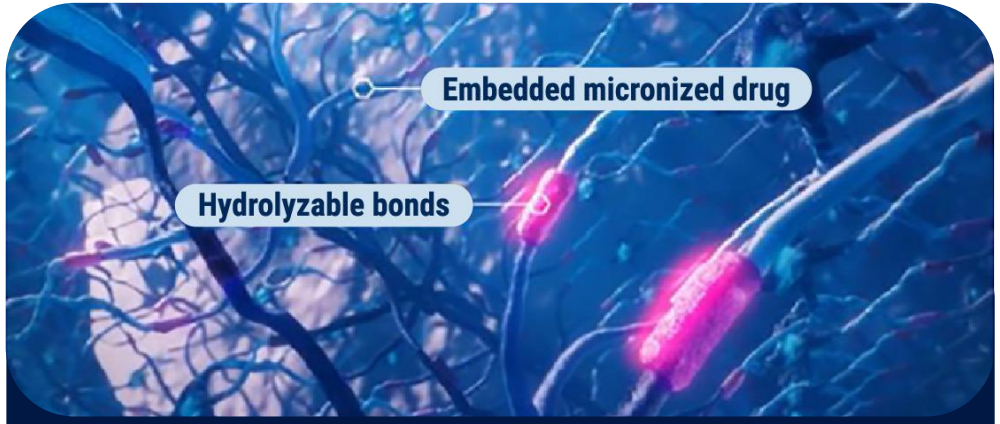
Multi-target Tyrosine Kinase Inhibitor (TKI)

Highly selective pan VEGF inhibitor[1]
Highly potent TKI[2]

+

ELUTYX™ TECHNOLOGY

Bioresorbable, Sustained Drug Delivery



Proprietary hydrogel
Versatile, biocompatible, tunable platform[3]

OTX-TKI

is being developed with the aim to provide:

A single injection, single hydrogel insert[3,4]

Continuous and consistent delivery up to 12 months[3,5]

Complete and predictable bioresorption[3,5]

OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined™

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. Blizzard CD, et al. Ocular Implant Containing a Tyrosine Kinase Inhibitor. US Patent 11,439,592 B2. September 13, 2022. 4. Tan CS, et al. *Clin Ophthalmol*. 2022;16:917-933. 5. Data on File 033. Ocular Therapeutix. 2026.
TKI, Tyrosine Kinase Inhibitor; VEGF, Vascular Endothelial Growth Factor

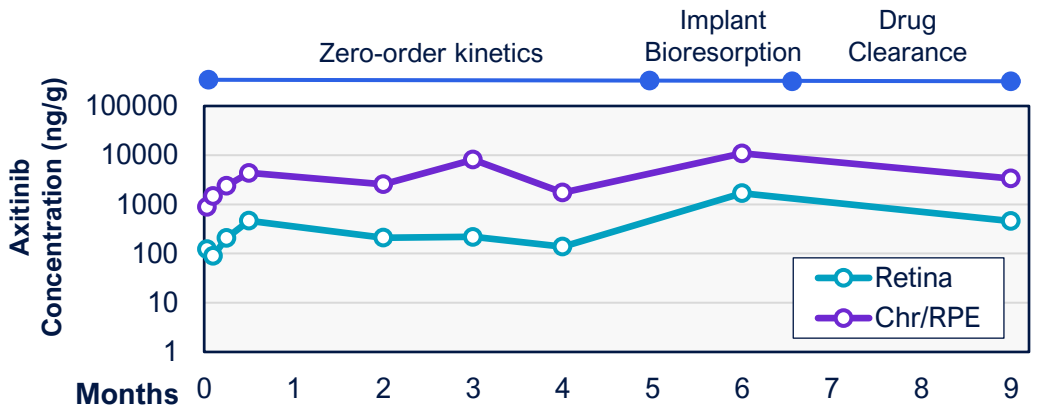
OTX-TKI is Designed to Release Axitinib and Maintain Intraocular Drug Over Time with Complete Bioresorption

OTX-TKI In Vivo Delivery Profile[1]

Rapid, continuous and consistent axitinib delivery

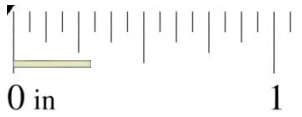
Targeted drug delivery to retina and choroid

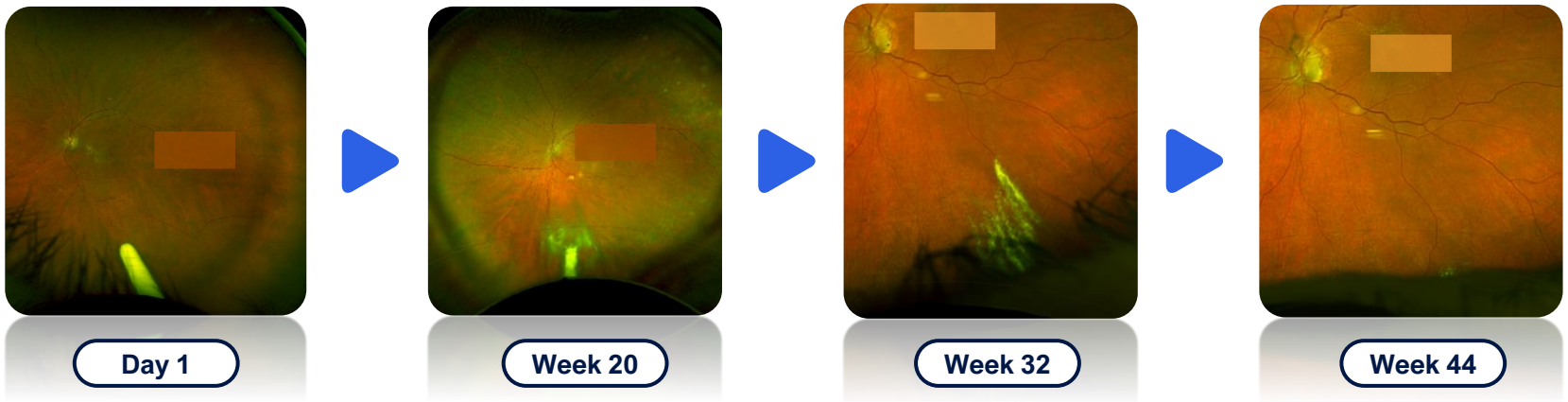
Axitinib concentrations following a single OTX-TKI in NHPs[1]



Hydrogel bioresorbs completely and predictably via hydrolysis for potential redosing[1-3]

Dry OTX-TKI Dimensions
7mm length, 0.4mm diameter





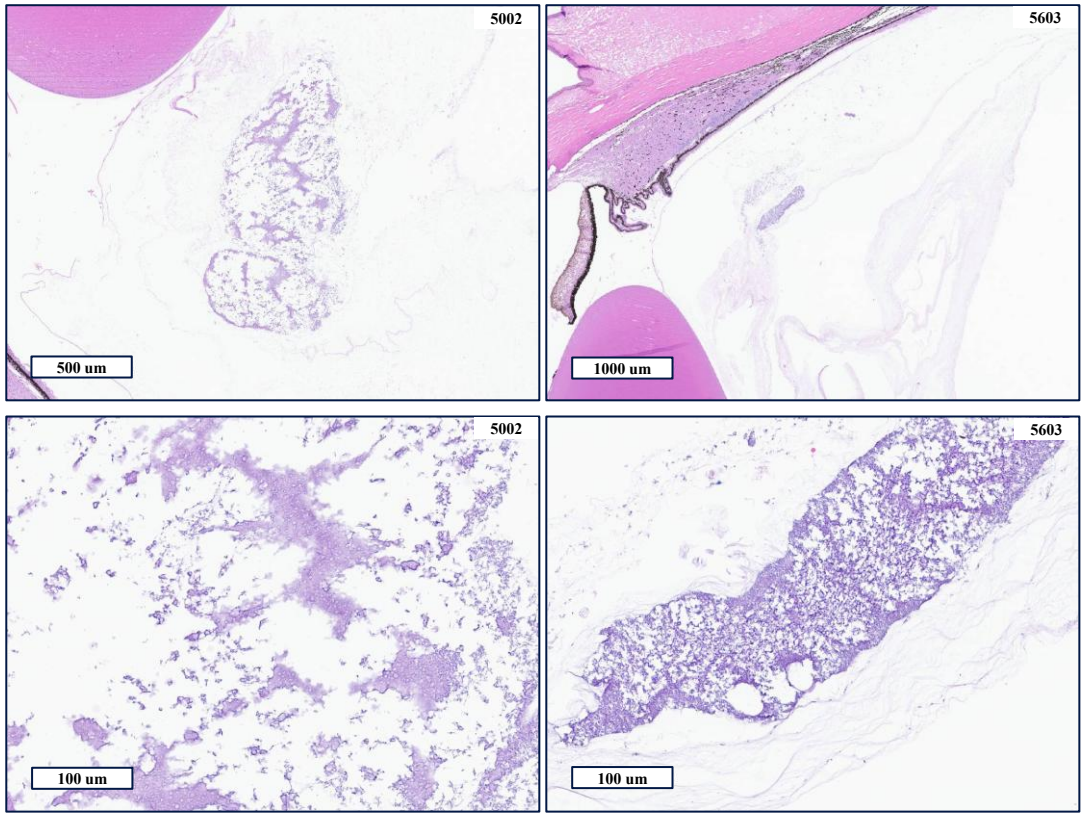
OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined™

1. Data on File 033. Ocular Therapeutix. 2. Li J, et al. *Nat Rev Mater.* 2016;1(12):16071. 3. Müller DA, et al. *J Orthop Surg Res*. 2016;11(1):111.
Chr, choroid; RPE, retinal pigment epithelium; NHP, non-human primate.

Histology of Ocular Tissues Demonstrates Axitinib Elution with No Inflammatory Cells

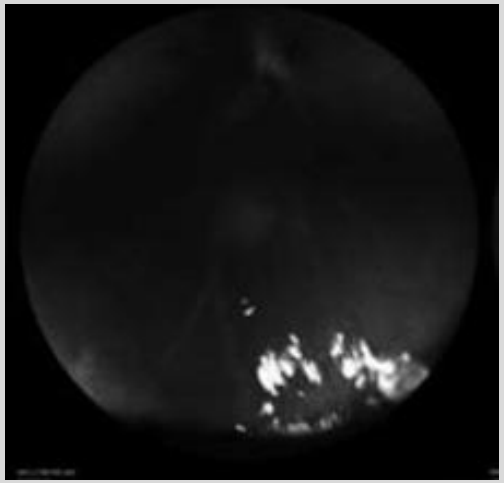
Histology of Ocular Tissues from 0.7 mg OTX-TKI in NHPs



Microscopic Findings

White, refractile, basophilic, granular axitinib in the vitreous

No inflammatory cells in vitreous, retina, or AC

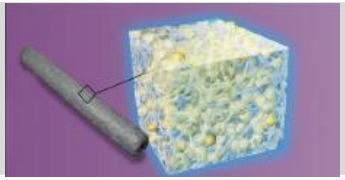
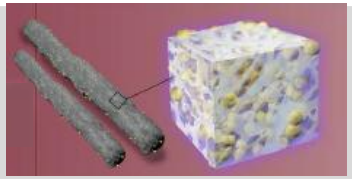
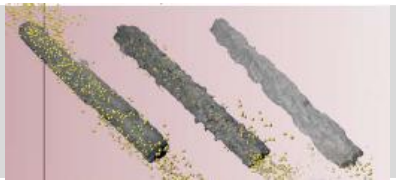
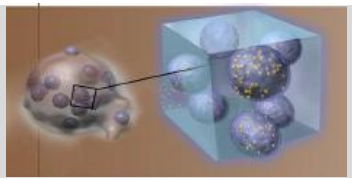
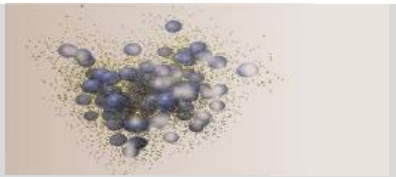
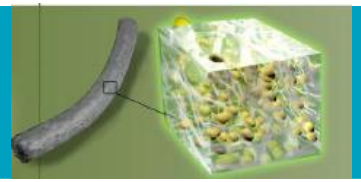


From NHP Toxicity Study, not human picture

OCULAR THERAPEUTIX Retina experience redefined™

Data on File 043. Ocular Therapeutix; 2026
AC, anterior chamber; NHP, non-human primates

Comparison of Hydrogel vs Other Retinal Polymer Implants

	Implant (Full View)	Implant Dimensions (Length x Diameter)	Needle Size	Matrix Degradation & Release^^	Polymer Byproduct	Implant Remnants at 12 Months
OZURDEX abbvie		6mm x 0.46mm*	22-gauge*		Lactic acid and glycolic acid†	**Remnant** lasts ~12 months‡
EYP-1901 EyePoint Pharmaceuticals		**Two implants** with length of 8mm each¶	22-gauge#		>75 KDa polyvinyl alcohol‖	**Two remnants** last 18-24 months**
GB-102 graybug		N/A	27-gauge††		Lactic acid and glycolic acid††	N/A
OTX-TKI OCULAR THERAPEUTIX		**7mm x 0.40mm^**	**25-gauge^**		**Inert hydrogel PEG chains^**	**No remnants^^**

OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

Schematic drawings, not drawn to scale or color, for illustrative purposes only; yellow or gray dots/spheres depict therapeutic agents released by implants

*. Li M, et al. *Heliyon.* 2022;8(12):e12219. †. Pellegrini GABP, et al. *Int J Retina Vitreous.* 2025;11(1):7. ‡. Kim JT, et al. *Retina*. 2020; 40(11):p 2226-2231. §. Schmit-Eilenberger VK. Clin *Ophthalmol.* 2015;9:801-811. ¶. Diameter of EYP-1901 unconfirmed; EyePoint Pharmaceuticals. Clinical Study Protocol. Protocol No. EYP-1901-201. Published January 25, 2024. ClinicalTrials.gov identifier: NCT05381948.. #. EyePoint Pharmaceuticals DAVIO2 Topline Results Conference Call, December 4, 2023. ‖. Wykoff CC, et al. *J Vitreoretin Dis*. 2024;8(5):577-586. **EyePoint Pharmaceuticals. TD Cowen 44th Annual Health Care Conference. March 5, 2024. https://investors.eyepointpharma.com/events-and-presentations. ††. Graybug Vision Inc. Clinical Study Protocol. Protocol No. GBV-102-002. Published September 8, 2020. ClinicalTrials.gov identifier: NCT03953079. ^. Blizzard CD, et al. Ocular Implant Containing a Tyrosine Kinase Inhibitor. US Patent 11,439,592 B2. September 13, 2022. ^^ Data on File 044. Ocular Therapeutix. 2026.
PEG, polyethylene glycol

OCULAR THERAPEUTIX Retina experience redefined™

OTX-TKI is Designed for Seamless, Immediate Adoption

Ideal Target Product Profile

Pan-VEGF and PDGF
inhibitory activity[1]

Axitinib has best-in-class (TKI) potency[1]

Extended durability
up to 12 months[2]

OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined™

1. Gross-Goupil M, et al. *Clin Med Insights Oncol*. 2013;7:269-277. 2. Eichenbaum, DA, et al. American Academy of Ophthalmology Annual Meeting; October 18-21, 2024; Chicago, IL. 3. Data on File 044. Ocular Therapeutix. 2026.. 4. Blizzard CD, et al. Ocular Implant Containing a Tyrosine Kinase Inhibitor. US Patent 11,439,592 B2. September 13, 2022. 5. Stuart M. Instylla: An easy, predictable, and simpler way to embolize tumors. MedTech Strategist. 2021.. 6. Almony A. *Am J Manag Care*. 2023;29(suppl 6):S81-S89 .
VEGF, vascular endothelial growth factor; PDGF, platelet-derived growth factor; IVT, intravitreal.

OTX-TKI is Designed for Seamless, Immediate Adoption

Ideal Target Product Profile

Pan-VEGF and PDGF inhibitory activity[1]

Axitinib has best-in-class (TKI) potency[1]

Extended durability up to 12 months[2]

Single Bioresorbable Hydrogel

No remnants[3]

Tunable hydrogel[4]

Hydrogel used in over 5 million patients[5]

OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined™

1. Gross-Goupil M, et al. *Clin Med Insights Oncol*. 2013;7:269-277. 2. Eichenbaum, DA, et al. American Academy of Ophthalmology Annual Meeting; October 18-21, 2024; Chicago, IL. 3. Data on File 044. Ocular Therapeutix. 2026.. 4. Blizzard CD, et al. Ocular Implant Containing a Tyrosine Kinase Inhibitor. US Patent 11,439,592 B2. September 13, 2022. 5. Stuart M. Instylla: An easy, predictable, and simpler way to embolize tumors. MedTech Strategist. 2021.. 6. Almony A. *Am J Manag Care*. 2023;29(suppl 6):S81-S89 .
VEGF, vascular endothelial growth factor; PDGF, platelet-derived growth factor; IVT, intravitreal.

OTX-TKI is Designed for Seamless, Immediate Adoption

Ideal Target Product Profile

Pan-VEGF and PDGF inhibitory activity[1]

Axitinib has best-in-class (TKI) potency[1]

Extended durability up to 12 months[2]

Single Bioresorbable Hydrogel

No remnants[3]

Tunable hydrogel[4]

Hydrogel used in over 5 million patients[5]

Optimizing for Retina Practices

Familiar IVT injection with **25g needle**[6]

Predictable schedule for patients[2]

Designed for **improved treatment adherence**[2]

OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined™

1. Gross-Goupil M, et al. *Clin Med Insights Oncol*. 2013;7:269-277. 2. Eichenbaum, DA, et al. American Academy of Ophthalmology Annual Meeting; October 18-21, 2024; Chicago, IL. 3. Data on File 044. Ocular Therapeutix. 2026.. 4. Blizzard CD, et al. Ocular Implant Containing a Tyrosine Kinase Inhibitor. US Patent 11,439,592 B2. September 13, 2022. 5. Stuart M. Instylla: An easy, predictable, and simpler way to embolize tumors. MedTech Strategist. 2021.. 6. Almony A. *Am J Manag Care*. 2023;29(suppl 6):S81-S89 .
VEGF, vascular endothelial growth factor; PDGF, platelet-derived growth factor; IVT, intravitreal.

SOL Program

Jeffrey S. Heier, MD

SOL: OTX-TKI Phase 3 Clinical Program in nAMD

Evaluating the efficacy, durability and safety of OTX-TKI in nAMD

Registrational Trials

SOL-1

Phase 3
Superiority Trial

Durability of a single OTX-TKI injection

SOL-R

Phase 3
Non-Inferiority Trial

Repeat dosing every 6 months

Complementary studies designed to provide a comprehensive characterization of OTX-TKI across patient populations

Extension Study

SOL-X

Open-Label Extension

Long-term safety and disease modifying potential of continuous VEGF suppression

Eligible patients who complete end of Year 2 visit in SOL-1 or SOL-R

OCULAR THERAPEUTIX Retina experience redefined

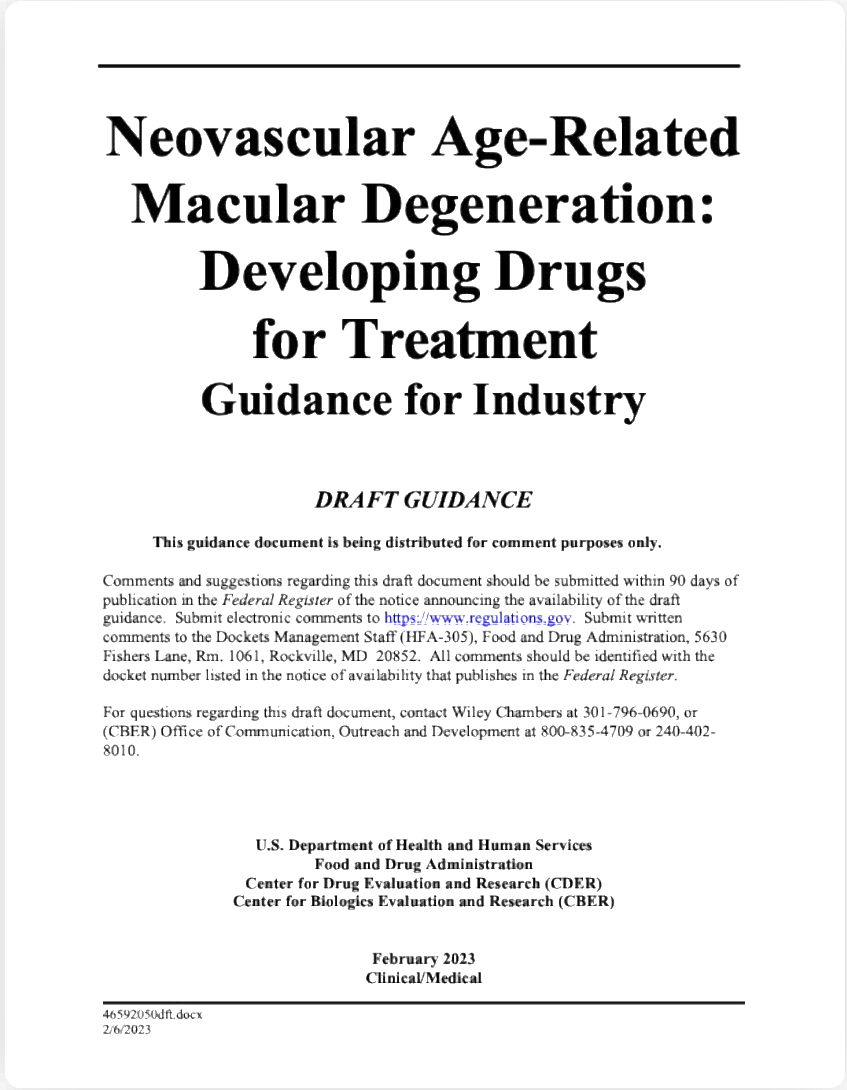
nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor

FDA Draft Guidance for Industry

2023

Q1

New FDA Drug Development Guidance released



Neovascular Age-Related Macular Degeneration: Developing Drugs for Treatment

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact Wiley Chambers at 301-796-0690, or (CBER) Office of Communication, Outreach and Development at 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

February 2023
Clinical/Medical

46592050dft.docx
2/6/2023

OCULAR THERAPEUTIX Retina experience redefined™

U.S. Food and Drug Administration. *Neovascular AMD: Developing Drugs for Treatment Guidance for Industry*. Updated February 2023. Accessed April 1, 2026. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/neovascular-age-related-macular-degeneration-developing-drugs-treatment

Q1, quarter 1

SOL-1 Trial is Designed to Align with FDA Guidance

FDA Guidance for Neovascular AMD Trials

One comparator arm should have the same dosing schedule as the investigational drug[1]

Sham injections are not recommended due to inadequate masking[2,3]

OCULAR THERAPEUTIX Retina experience redefined™

1. U.S. Food and Drug Administration. *Neovascular AMD: Developing Drugs for Treatment Guidance for Industry*. Updated February 2023. Accessed April 1, 2026. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/neovascular-age-related-macular-degeneration-developing-drugs-treatment. 2. Type C WRO [written response only] Aug 2024. **3.** Weiss J, Boyd B, Event: Q&A with FDA, at the American Academy of Ophthalmology Annual Meeting, October 20, 2024
Q1, quarter 1

SOL-1 Trial is Designed to Align with FDA Guidance

FDA Guidance for Neovascular AMD Trials	SOL-1 Trial Design
One comparator arm should have the same dosing schedule as the investigational drug[1]	✓ **Both study arms have the same dosing schedule**
Sham injections are not recommended due to inadequate masking[2,3]	✓ **No sham injections in either arm**

OCULAR THERAPEUTIX Retina experience redefined™

1. U.S. Food and Drug Administration. *Neovascular AMD: Developing Drugs for Treatment Guidance for Industry*. Updated February 2023. Accessed April 1, 2026. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/neovascular-age-related-macular-degeneration-developing-drugs-treatment. 2. Type C WRO [written response only] Aug 2024. **3.** Weiss J, Boyd B, Event: Q&A with FDA, at the American Academy of Ophthalmology Annual Meeting, October 20, 2024
Q1, quarter 1

SOL-1 Trial is Designed to Align with FDA Guidance

FDA Guidance for Neovascular AMD Trials	SOL-1 Trial Design
One comparator arm should have the same dosing schedule as the investigational drug[1]	✓ **Both study arms have the same dosing schedule**
Sham injections are not recommended due to inadequate masking[2,3]	✓ **No sham injections in either arm**

Given study adherence to the FDA Guidance,
SOL-1 is being conducted under a Special Protocol Assessment (SPA)

OCULAR THERAPEUTIX Retina experience redefined™

1. U.S. Food and Drug Administration. *Neovascular AMD: Developing Drugs for Treatment Guidance for Industry*. Updated February 2023. Accessed April 1, 2026. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/neovascular-age-related-macular-degeneration-developing-drugs-treatment. 2. Type C WRO [written response only] Aug 2024. **3.** Weiss J, Boyd B, Event: Q&A with FDA, at the American Academy of Ophthalmology Annual Meeting, October 20, 2024
Q1, quarter 1

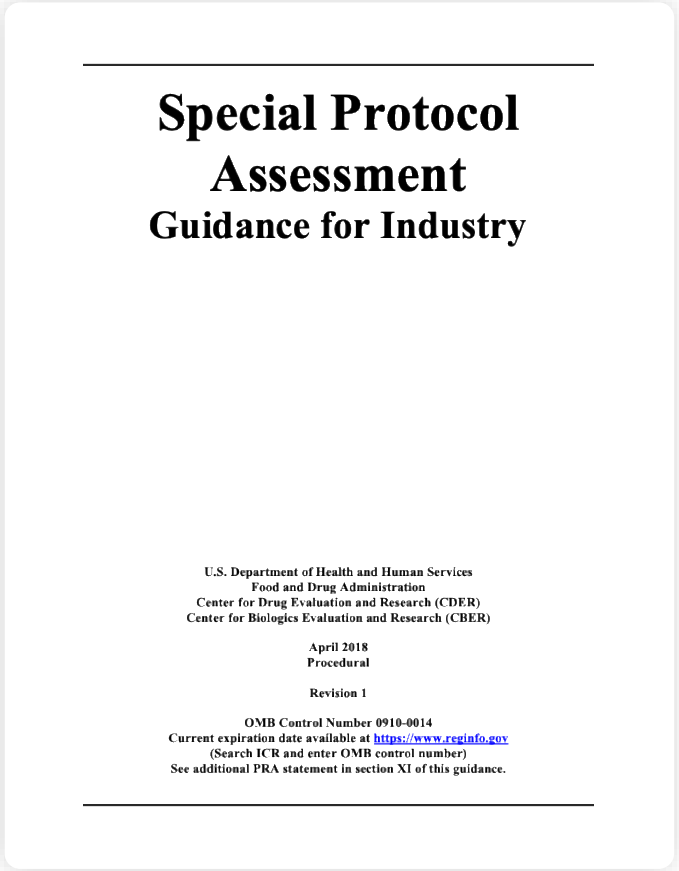
Special Protocol Assessment (SPA)

Agreement with FDA on critical design elements and statistical analysis plan (SAP) to support approval

With acceptance of SPA, study design, endpoints, and SAP cannot be changed

Adhering to protocol is critical to ensuring trial will be considered adequate and well-controlled

Conducting a trial under a SPA helps to derisk the regulatory process



Special Protocol Assessment

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

April 2018
Procedural

Revision 1

OMB Control Number 0910-0014
Current expiration date available at https://www.reginfo.gov
(Search ICR and enter OMB control number)
See additional PRA statement in section XI of this guidance.

OCULAR THERAPEUTIX Retina experience redefined™

U.S. Food and Drug Administration. *Special Protocol Assessment Guidance for Industry*. Updated April 2018. Accessed April 1, 2026. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/special-protocol-assessment-guidance-industry

FDA Recommendation for Endpoints to Demonstrate Superiority

≥15-Letter Decrease
Statistically significant **smaller** % of subjects with ≥15-letter decrease at 9 months or later

≥15-Letter Increase
Statistically significant **greater** % of subjects with ≥15-letter increase at 9 months or later

≥15-Letter Difference
Statistically significant **difference** between groups in mean BCVA of ≥15 letters at 9 months or later

SOL-1 Primary Endpoint: Proportion of subjects who maintained visual acuity, defined as <15 ETDRS letters of BCVA loss from baseline at Week 36

OCULAR THERAPEUTIX Retina experience redefined™

1. U.S. Food and Drug Administration. *Neovascular AMD: Developing Drugs for Treatment Guidance for Industry*. Updated February 2023. Accessed April 1, 2026. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/neovascular-age-related-macular-degeneration-developing-drugs-treatment.
BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study

OTX-TKI Evaluated in a Superiority Trial for nAMD

SOL-1

Compares a **Single OTX-TKI (0.45 mg) Dose** to a **Single Aflibercept (2 mg) Dose**

Multicenter, Double-Masked, Randomized Parallel-Group Trial

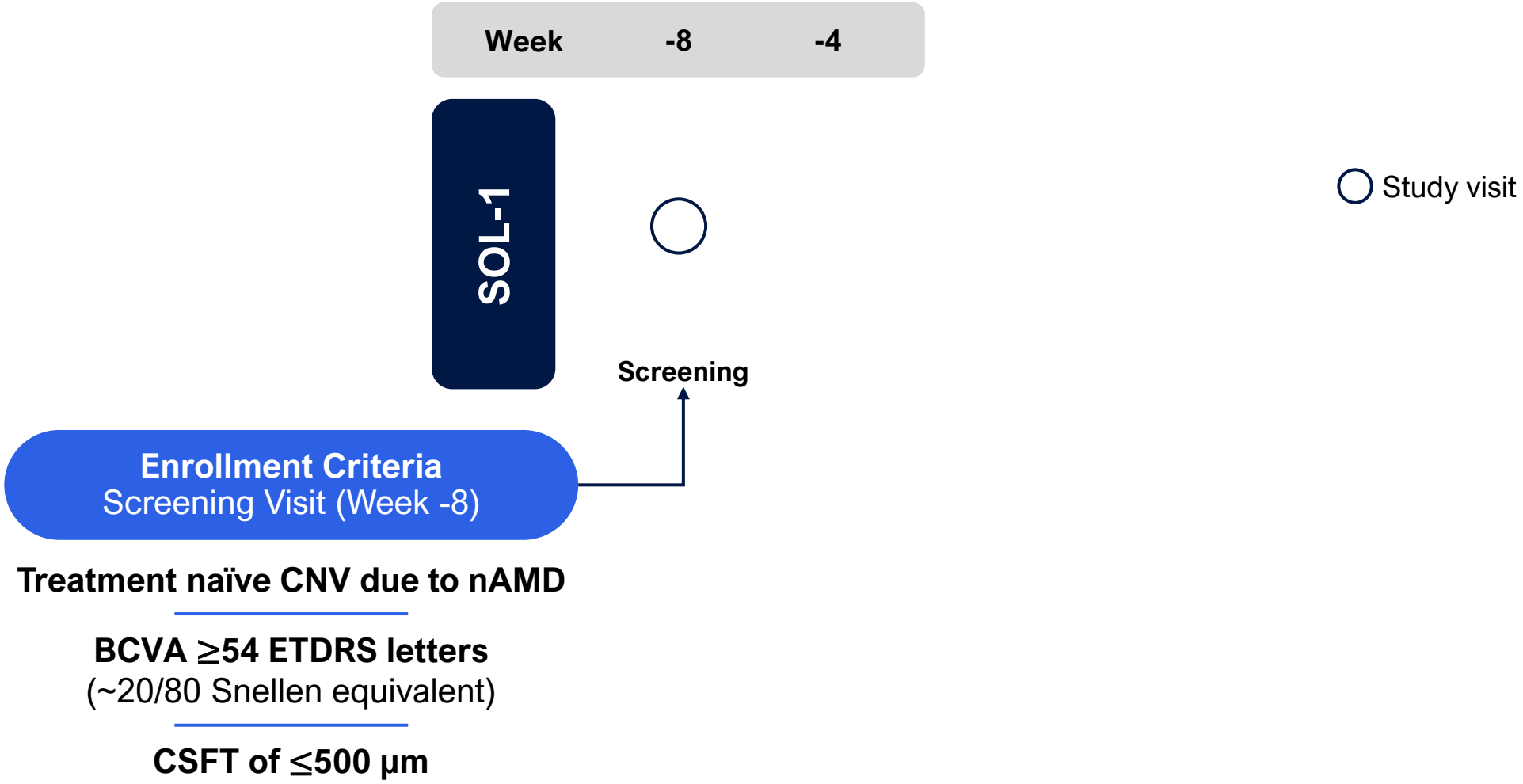
Designed to Assess Safety and Efficacy, including Durability, of OTX-TKI

OCULAR THERAPEUTIX Retina experience redefined™

ClinicalTrials.gov. identifier: NCT06223958
nAMD, neovascular age-related macular degeneration

Eligibility and Enrollment Criteria

Key Inclusion Criteria

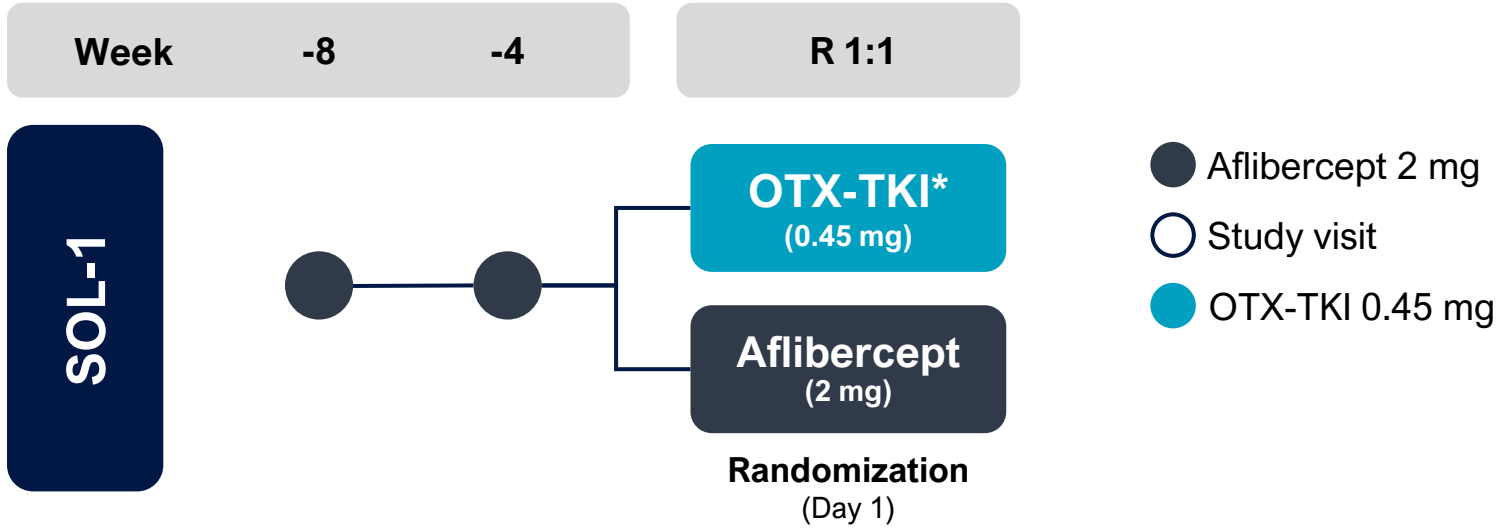


ClinicalTrials.gov. identifier: NCT06223958

CNV, choroidal neovascularization; nAMD, neovascular age-related macular degeneration; BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; CSFT; central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium

Eligibility and Enrollment Criteria

Key Inclusion Criteria



Enrollment Criteria
Screening Visit (Week -8)

Treatment naïve CNV due to nAMD

BCVA ≥54 ETDRS letters
(~20/80 Snellen equivalent)

CSFT of ≤500 µm

Randomization Criteria
Baseline Visit (Day 1)

BCVA gain ≥10 ETDRS letters

- OR -

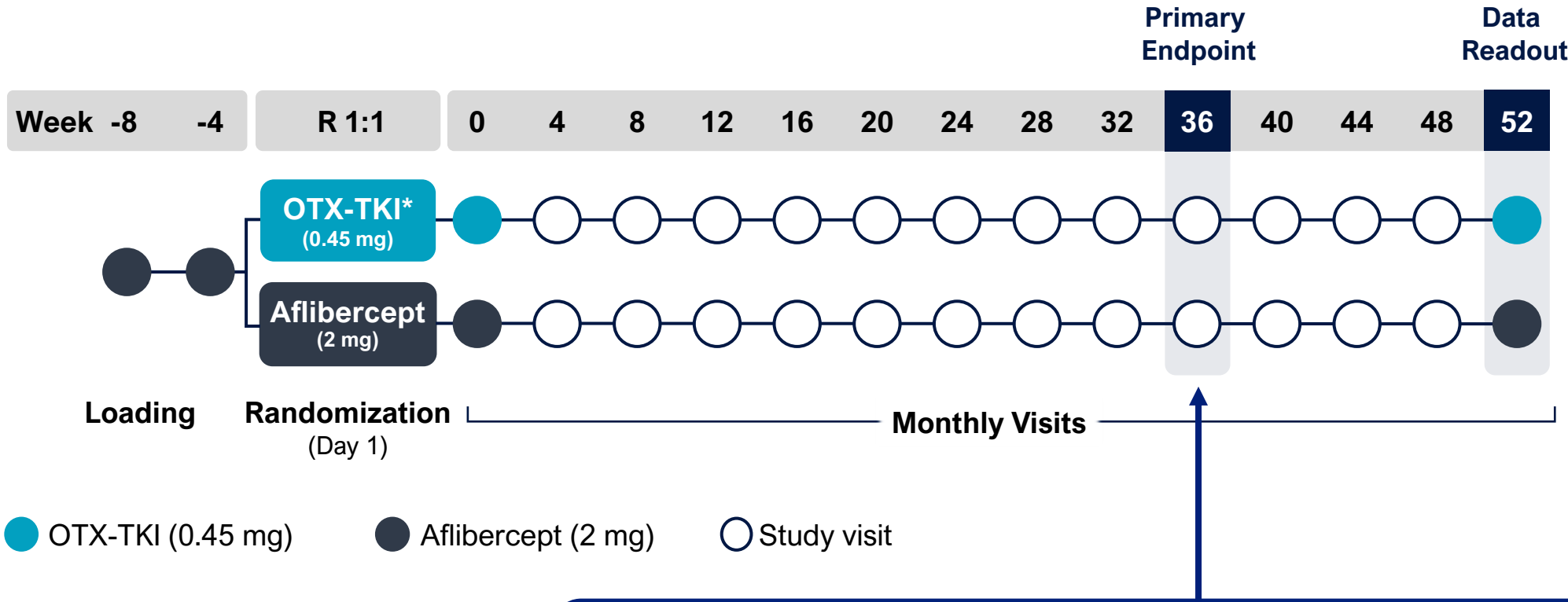
BCVA ≥84 ETDRS letters
(~20/20 Snellen equivalent)

CSFT of ≤350 µm

*No aflibercept injection is given at baseline
ClinicalTrials.gov. identifier: NCT06223958
CNV, choroidal neovascularization; nAMD, neovascular age-related macular degeneration; BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; CSFT; central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium

Direct Comparison: OTX-TKI and Aflibercept

SOL-1



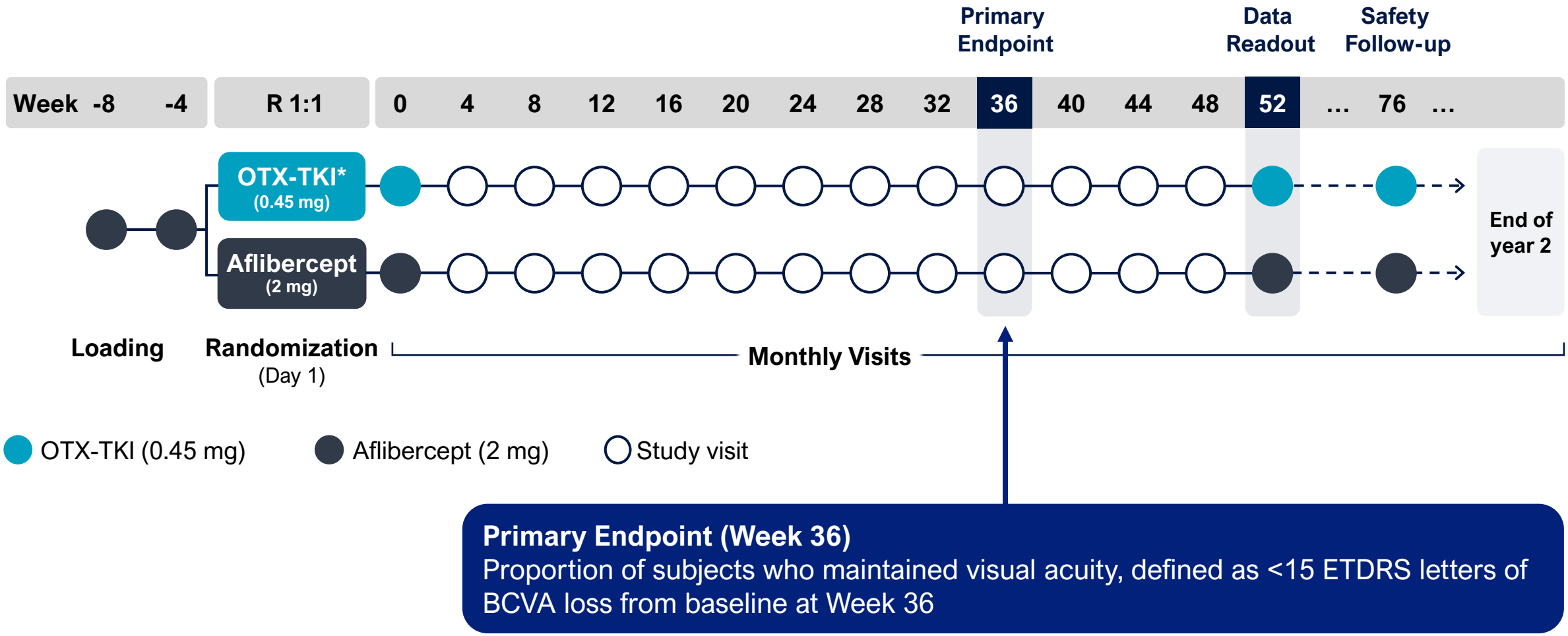
Primary Endpoint (Week 36)
Proportion of subjects who maintained visual acuity, defined as <15 ETDRS letters of BCVA loss from baseline at Week 36

OCULAR THERAPEUTIX Retina experience redefined™

*No aflibercept injection is given at baseline
ClinicalTrials.gov. identifier: NCT06223958
BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study

Direct Comparison: OTX-TKI and Aflibercept

SOL-1



Primary Endpoint (Week 36)
Proportion of subjects who maintained visual acuity, defined as <15 ETDRS letters of BCVA loss from baseline at Week 36

OCULAR THERAPEUTIX Retina experience redefined™

*No aflibercept injection is given at baseline
ClinicalTrials.gov. identifier: NCT06223958
BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study

Rescue Treatment Criteria and Execution

Rescue Treatment Criteria

BCVA loss ≥15 ETDRS letters from baseline due to nAMD

OR

New macular hemorrhage that would likely lead to irreversible vision loss if left untreated in the opinion of the investigator after discussion with Medical Monitor

ClinicalTrials.gov. identifier: NCT06223958
BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; nAMD, neovascular age-related macular degeneration

Rescue Treatment Criteria and Execution

Rescue Treatment Criteria

BCVA loss ≥15 ETDRS letters from baseline due to nAMD

OR

New macular hemorrhage that would likely lead to irreversible vision loss if left untreated in the opinion of the investigator after discussion with Medical Monitor

Trial Conduct

After the first rescue injection, rescue therapy can be provided at investigator discretion per their clinical judgement with aflibercept 2mg

Independent rescue monitor team of retina specialists were designated to provide consultation

ClinicalTrials.gov. identifier: NCT06223958
BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; nAMD, neovascular age-related macular degeneration

Clinical Trials: Evaluating Efficacy and Safety Intended for Regulatory Approval

Recent Non-inferiority Trial Designs

***Cannot claim superior durability**, only that a subgroup can mostly remain retreatment free for "x" amount of time*

- Investigational drug subgroup extended but not active control
- Can potentially result in "step therapy" for insurance coverage

OCULAR THERAPEUTIX Retina experience redefined™

U.S. Food and Drug Administration. *Neovascular AMD: Developing Drugs for Treatment Guidance for Industry*. 2023.

Clinical Trials: Evaluating Efficacy and Safety Intended for Regulatory Approval

Recent Non-inferiority Trial Designs

***Cannot claim superior durability**, only that a subgroup can mostly remain retreatment free for "x" amount of time*

- Investigational drug subgroup extended but not active control
- Can potentially result in "step therapy" for insurance coverage

Superiority Trial Design

***Only way to show superior durability** in a meaningful time frame and be compliant with FDA guidance*

- Proportion of 15-letter events (including rescue)
- Both arms treated identically (no sham; adequately masked)
- Potentially negates the requirement of step therapy

SOL-1

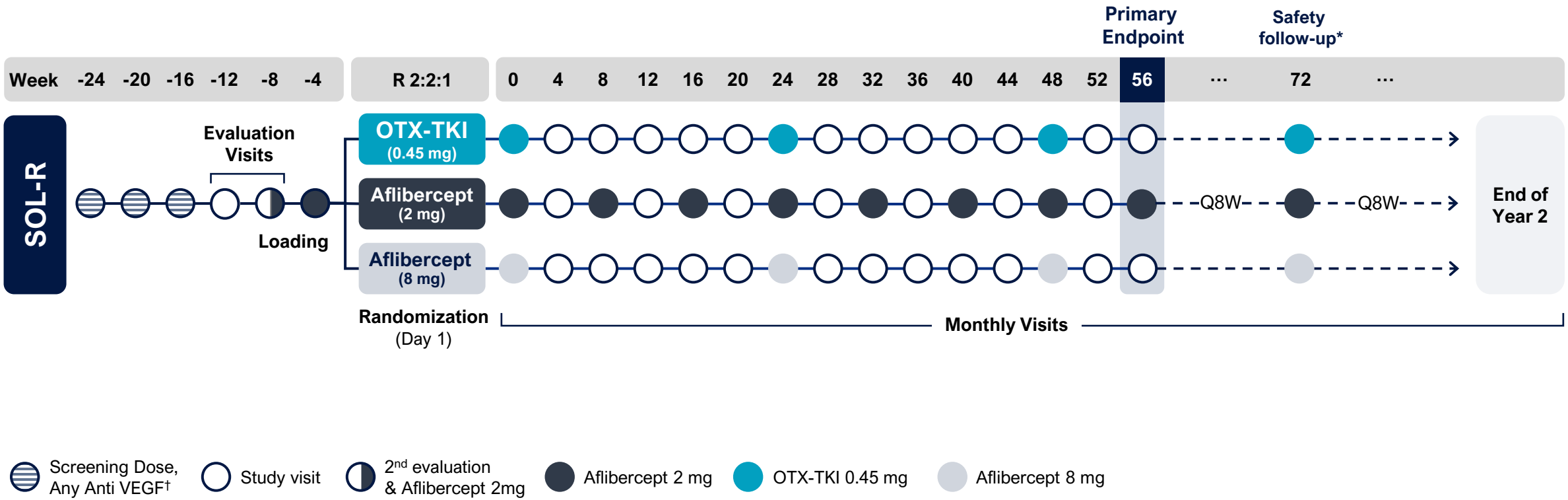
Trial design aligned with FDA under a Special Protocol Assessment agreement

OCULAR THERAPEUTIX Retina experience redefined™

U.S. Food and Drug Administration. *Neovascular AMD: Developing Drugs for Treatment Guidance for Industry*. 2023.

SOL-R: Phase 3 nAMD Study Design

Non-Inferiority Study Comparing OTX-TKI q24w to Aflibercept (2mg) q8w



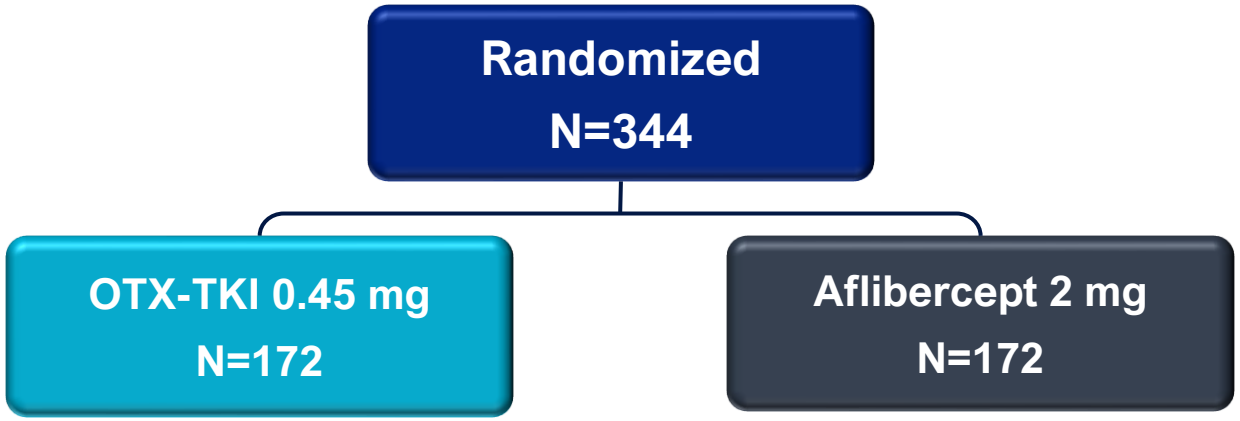
SOL-1

Results

Andrew A. Moshfeghi, MD

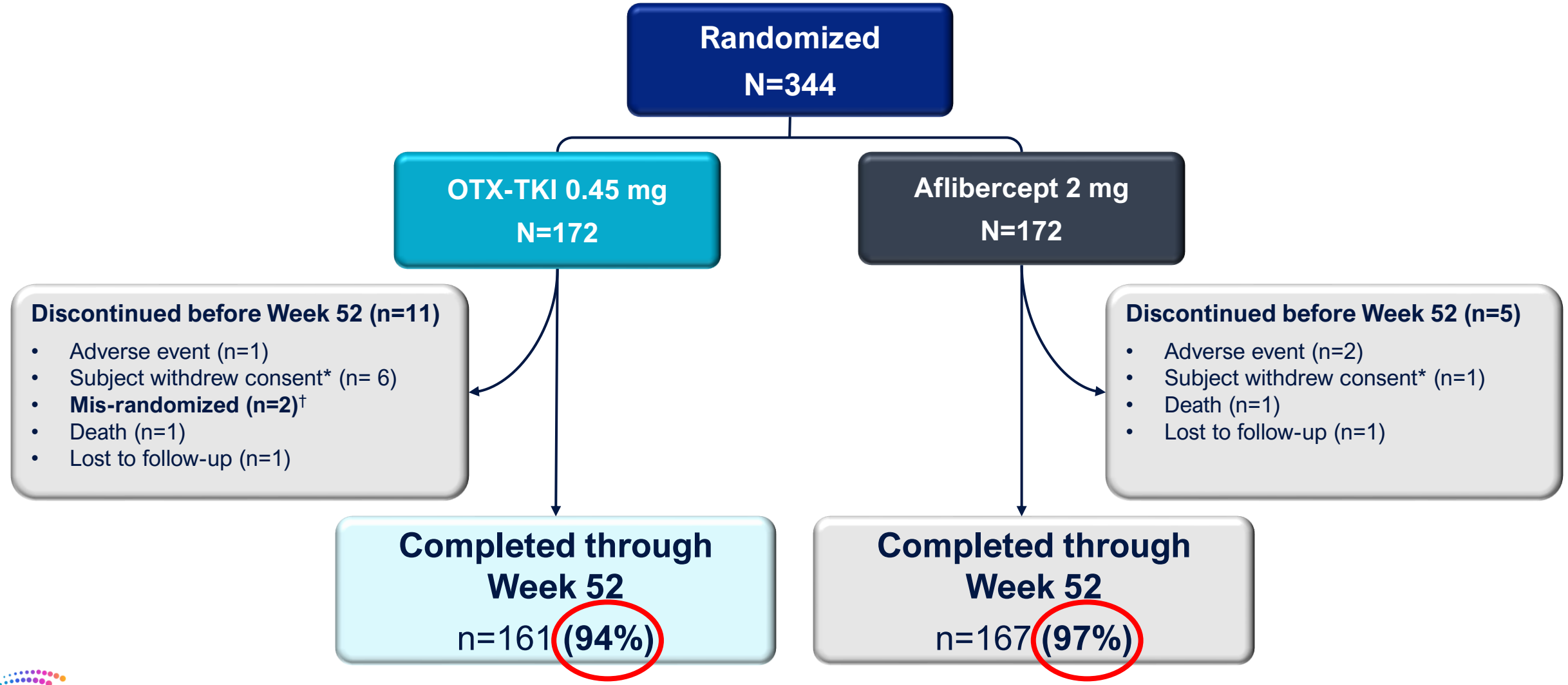
OCULAR THERAPEUTIX Retina experience redefined

Subject Disposition



Strong Subject Retention Maintained through Week 52

Subject Disposition



* Reasons included: personal reason, no reason, travel, offered another treatment at a different practice; only Day 1 completed, subject refused week 52 assessment
† Subjects did not receive study treatment and were not included in the full analysis set

Treatment Groups were Well Balanced

SOL-1

Baseline Demographics

Demographics	OTX-TKI 0.45 mg N = 172	Aflibercept 2 mg N = 172
Age, years, mean (SD)	75.7 (8.3)	76.3 (7.4)
Sex, n (%)		
Female	103 (59.9)	108 (62.8)
Ethnicity, n (%)		
Hispanic or Latino	33 (19.2)	47 (27.3)
Not Hispanic or Latino	139 (80.8)	125 (72.7)
Race, n (%)		
White	168 (97.7)	170 (98.8)
Asian	3 (1.7)	0
Native Hawaiian or Other Pacific Islander	1 (0.6)	0
American Indian or Alaska Native	1 (0.6)	2 (1.2)
Black or African American	0	1 (0.6)

SD, standard deviation

Excellent Vision at Baseline; Majority Demonstrated ≥10-letter Gain from Screening

SOL-1

Best-Corrected Visual Acuity

Screening Visit *(Week -8)*

Study Eye Characteristics	OTX-TKI 0.45 mg N = 172	Aflibercept 2 mg N = 172
BCVA, ETDRS letter score, mean (SD) Snellen Equivalent	70.9 (11.3) ~20/40	69.5 (10.8) ~20/40

Baseline *(Randomization)*

Study Eye Characteristics	OTX-TKI 0.45 mg N = 172	Aflibercept 2 mg N = 172
BCVA, ETDRS letter score, mean (SD) Snellen Equivalent	80.8 (7.6) ~20/25	79.2 (7.9) ~20/25
Change from Screening to Baseline, n (%) ≥ 10 ETDRS letter gain ≥84 ETDRS letters (~20/20)	 107 (62.9) 63 (37.1)	 114 (67.1) 56 (32.9)

OCULAR THERAPEUTIX Retina experience redefined™

BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; SD, standard deviation.

Anatomic Improvement Observed After Two Aflibercept Injections

SOL-1

Central Subfield Thickness

Screening Visit *(Week -8)*

Study Eye Characteristics	OTX-TKI 0.45 mg N = 172	Aflibercept 2 mg N = 172
BCVA, ETDRS letter score, mean (SD) Snellen Equivalent	70.9 (11.3) ~20/40	69.5 (10.8) ~20/40
CSFT, µm, mean (SD)	303.6 (72.5)	302.7 (78.3)

Baseline *(Randomization)*

Study Eye Characteristics	OTX-TKI 0.45 mg N = 172	Aflibercept 2 mg N = 172
BCVA, ETDRS letter score, mean (SD) Snellen Equivalent	80.8 (7.6) ~20/25	79.2 (7.9) ~20/25
CSFT, µm, mean (SD)	219.3 (37.1)	226.8 (42.1)

OCULAR THERAPEUTIX Retina experience redefined™

BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; CSFT, central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium; SD, standard deviation

SOL-1 Results Demonstrate Potential Treatment Benefit of OTX-TKI

Superiority Primary Endpoint Successfully Met

OTX-TKI Demonstrated Superior Maintenance of Vision

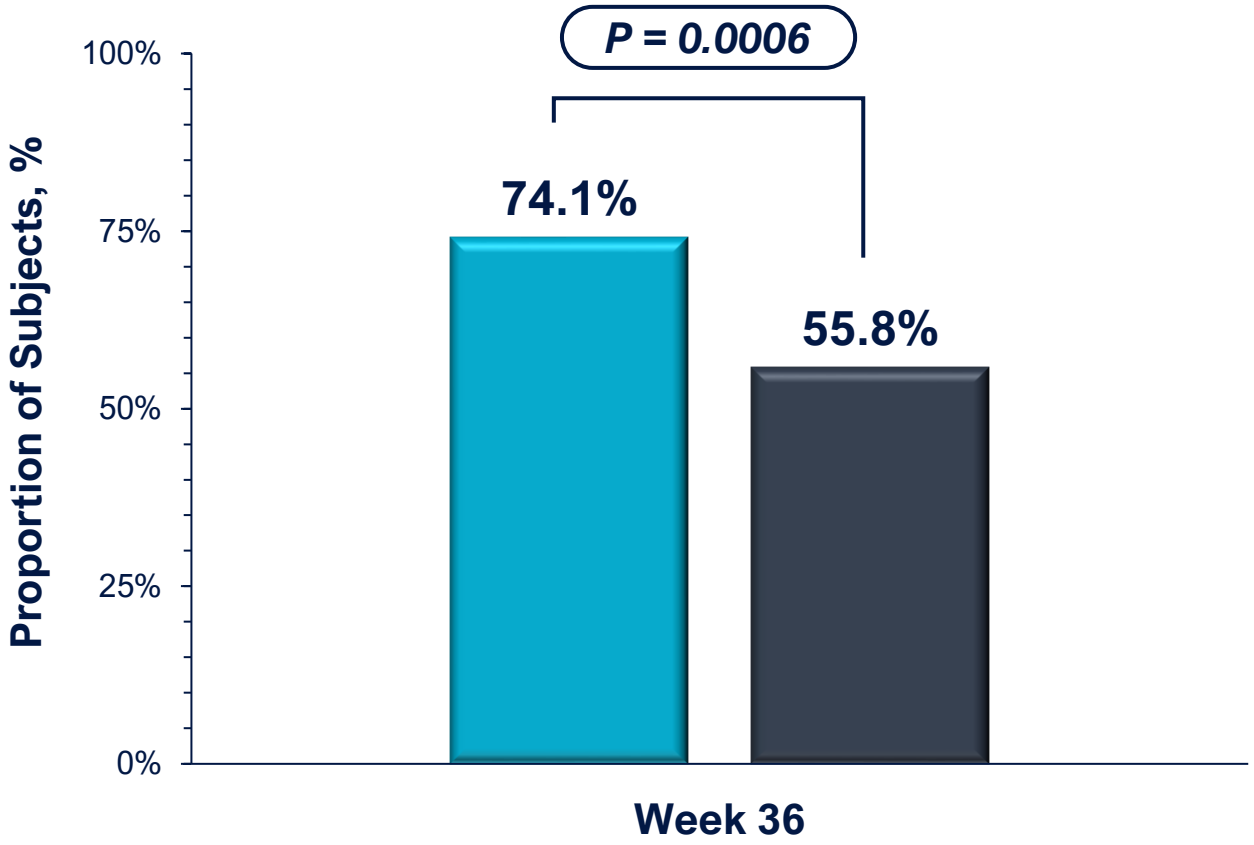
OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

Maintenance of vision defined as proportion of subjects who maintain visual acuity, a loss of <15 ETDRS letters of BCVA from baseline

Statistically Significant Higher Proportion of Subjects Maintained Visual Acuity* with OTX-TKI vs. Aflibercept 2 mg at Week 36

SOL-1

Primary Endpoint



	OTX-TKI (0.45 mg) n = 170	Aflibercept (2 mg) n = 172
Proportion of Subjects	**74.1%**	**55.8%**
Risk difference vs. aflibercept 2 mg 95% CI *P* value	17.5% (7.7, 27.4) ***0.0006***	
Observed difference vs. aflibercept 2 mg	18.3%	

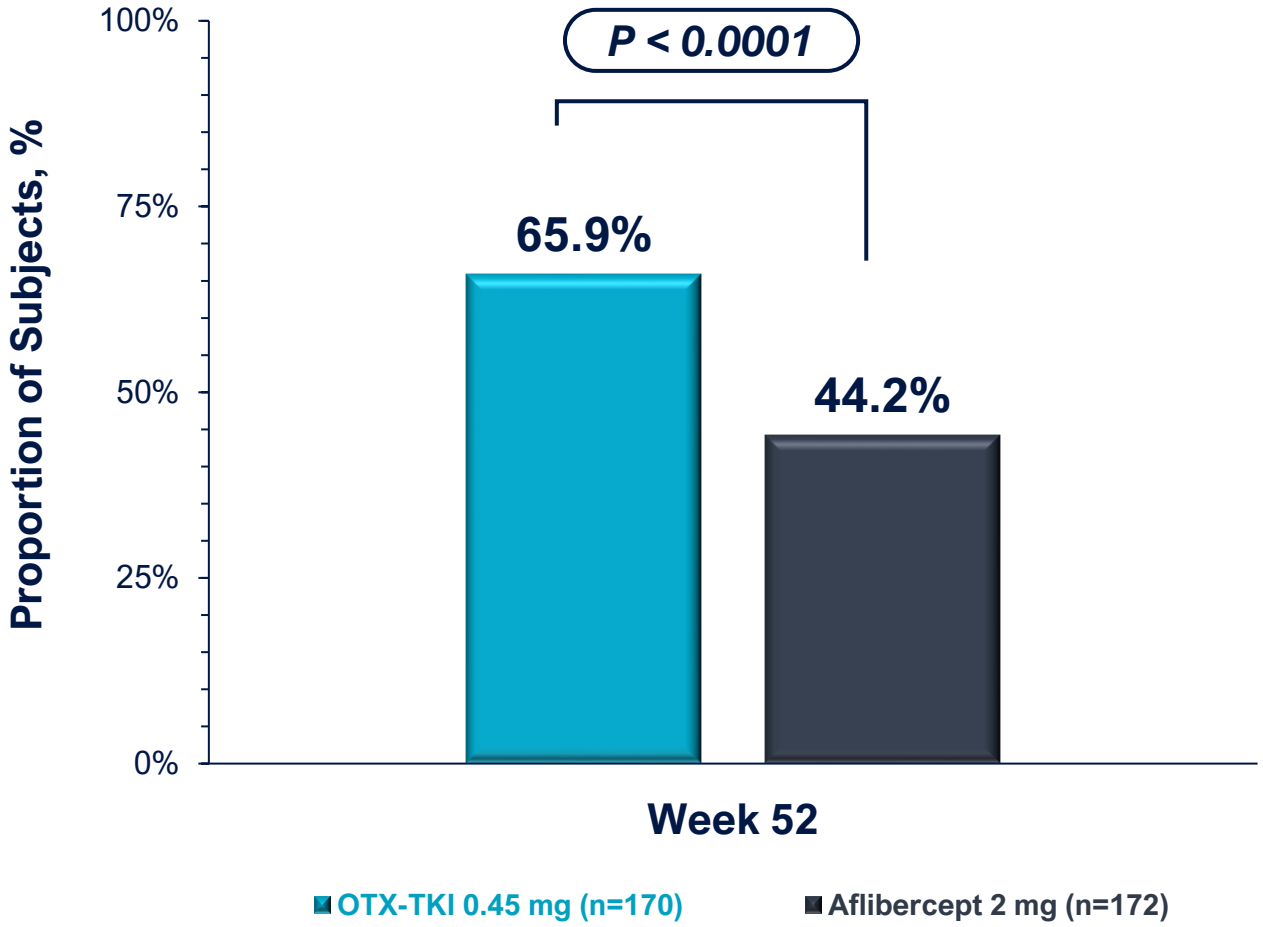
OCULAR THERAPEUTIX Retina experience redefined™

*Defined as proportion of subjects who maintain visual acuity, a loss of <15 ETDRS letters of BCVA from baseline, at Week 36
Predefined statistical rules were applied to adjust for treatment discontinuation or deviation as per the pre-specified statistical analysis plan. Full analysis set
BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; SD, standard deviation

OTX-TKI 0.45 mg (n=170)
Aflibercept 2 mg (n=172)

Treatment Benefit Continued through Week 52 with High Statistical Significance

Key Secondary Endpoint: Subjects Maintained Visual Acuity*



	OTX-TKI (0.45 mg) n = 170	Aflibercept (2 mg) n = 172
Proportion of Subjects	**65.9%**	**44.2%**
Risk difference vs. aflibercept 2 mg 95% CI *P* value	21.1% (10.8, 31.4) ***<0.0001***	
Observed difference vs. aflibercept 2 mg	21.7%	

*Defined as proportion of subjects who maintain visual acuity, a loss of <15 ETDRS letters of BCVA from baseline, at Week 52
Predefined statistical rules were applied to adjust for treatment discontinuation or deviation as per the pre-specified statistical analysis plan Full analysis set
ETDRS, Early Treatment Diabetic Retinopathy Study; BCVA, best-corrected visual acuity; CI, confidence interval.

Key Secondary and Secondary Efficacy Endpoints

SOL-1

Key Secondary Endpoints*

1	**Proportion of subjects who maintained visual acuity**** with one rescue injection or fewer at Week 52	✓
2	**Proportion of subjects who maintained visual acuity**** at Week 52	✓
3	**Proportion of subjects who maintained visual acuity**** with one rescue injection or fewer at Week 36	✓
4	**BCVA change from baseline** at Week 36	✗
5	**BCVA change from baseline** at Week 52	✗

Secondary Endpoints*

1	**CSFT changes from baseline** at Weeks 36	✓
2	**Proportion with no CSFT increase** (≤50 microns) at Weeks 36	✓
3	**Proportion CSFT ≤ 350 microns** at Weeks 36 and 52	✓
4	**Mean time to the first rescue injection**	✓
5	**Mean time to the second rescue injection**	✓
6	**Proportion of subjects who lose ≥ 10 letters** at Weeks 36 and 52	✓

OCULAR THERAPEUTIX Retina experience redefined™

*Superiority analysis per statistical analysis plan
**Maintained visual acuity defined as <15 ETDRS letters of BCVA loss.
BCVA, Best-corrected visual acuity; CSFT Central subfield thickness

✓ indicates endpoint met

SOL-1 Results Demonstrate Potential Treatment Benefit of OTX-TKI

SOL-1

Superiority Primary Endpoint Successfully Met

First trial to demonstrate durability ≥ 9 months

~75% of subjects treated with OTX-TKI did not receive rescue treatments by Week 36

Unmatched Durability

Visual and anatomic stability with OTX-TKI

On average, OTX-TKI subjects maintained visual and anatomical outcomes, with most remaining rescue-free

Sustained Disease Control

OTX-TKI demonstrated a well-tolerated safety profile through Week 52

There were no cases of endophthalmitis, occlusive or non-occlusive retinal vasculitis

Well-Tolerated

OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined™

Rescue-free subjects include those who did not require rescue injections as specified by the protocol

SOL-1 Results Demonstrate Potential Treatment Benefit of OTX-TKI

SOL-1

Superiority Primary Endpoint Successfully Met

Unmatched Durability

Sustained Disease Control

Well-Tolerated

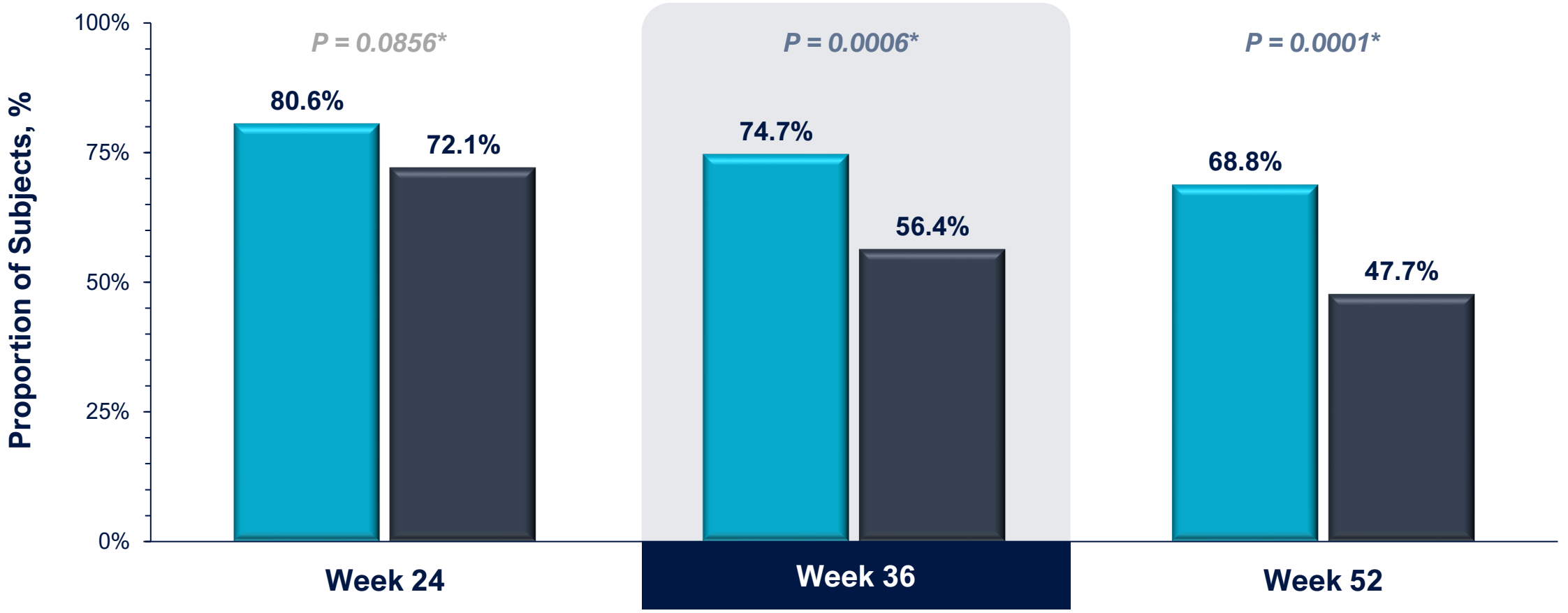
OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined™

Most Subjects (~75%) in the OTX-TKI Arm Did Not Receive Rescue Injections

SOL-1

Proportion of Rescue-Free Subjects



Post hoc analysis

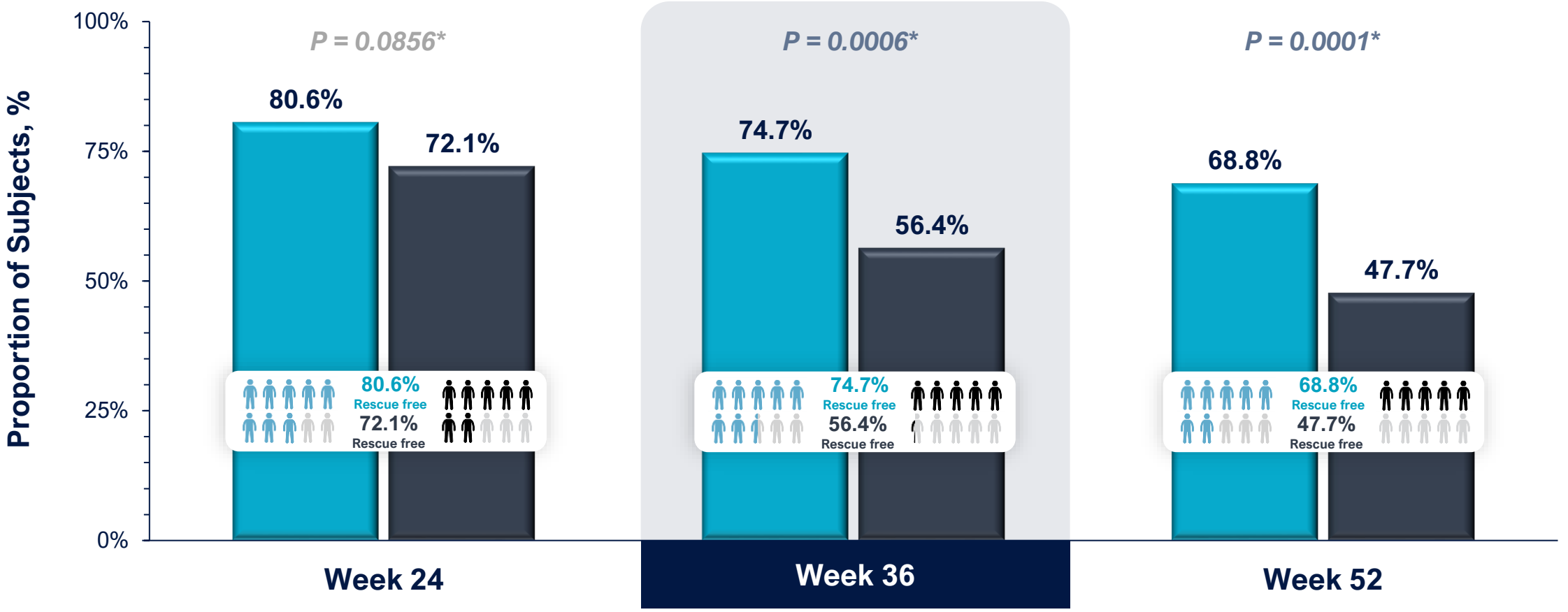
Rescue-free subjects include those who did not require rescue injections as specified by the protocol
Full analysis set; *Descriptive p-values

OCULAR THERAPEUTIX Retina experience redefined™

Most Subjects (~75%) in the OTX-TKI Arm Did Not Receive Rescue Injections

SOL-1

Proportion of Rescue-Free Subjects



OTX-TKI 0.45 mg (n=170)

Aflibercept 2 mg (n=172)

Post hoc analysis

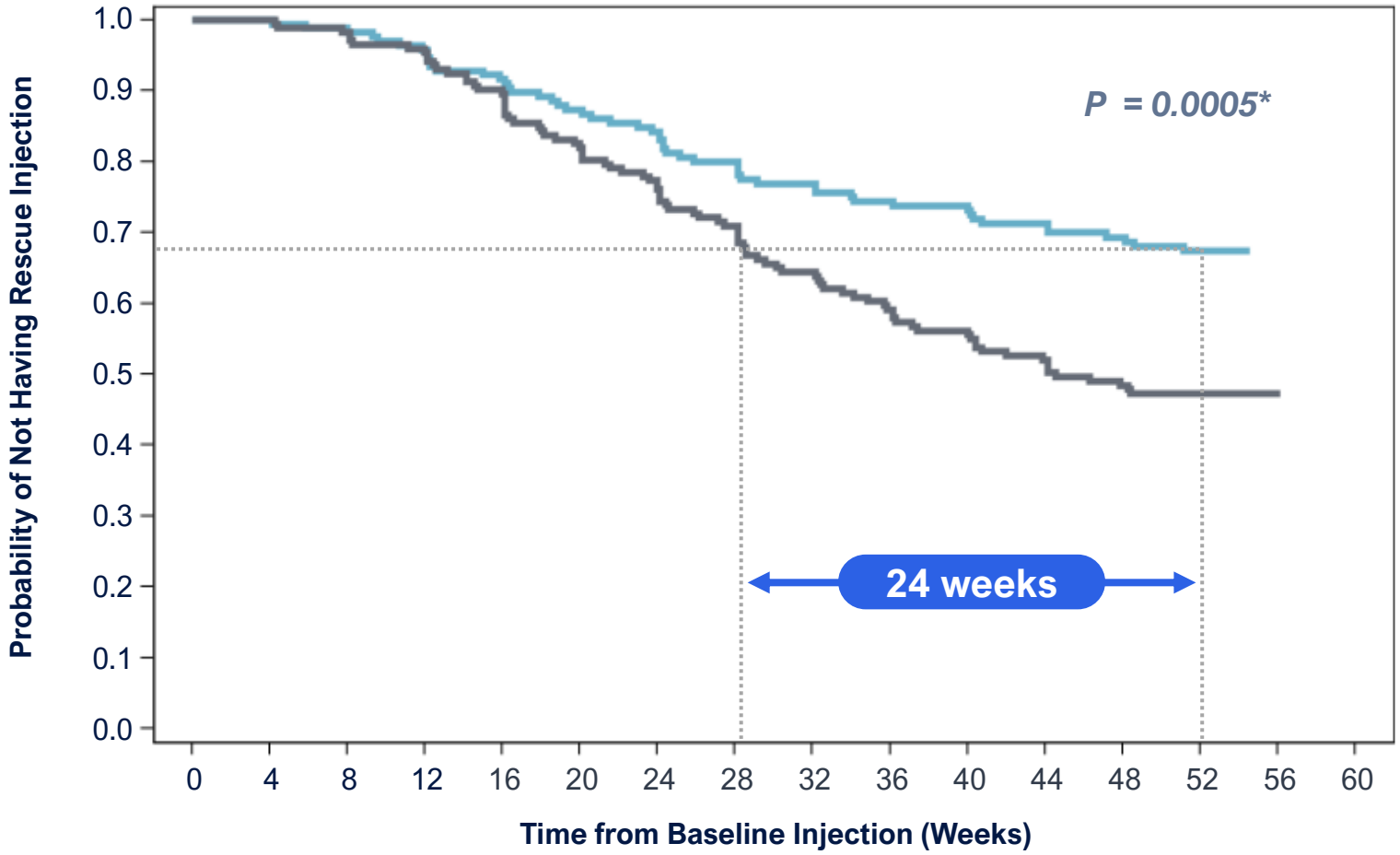
Rescue-free subjects include those who did not require rescue injections as specified by the protocol
Full analysis set; *Descriptive p-values

OCULAR THERAPEUTIX Retina experience redefined™

OTX-TKI Extended Durability, Significantly Delaying First Rescue Injection

SOL-1

Secondary Endpoint: Time to First Rescue Treatment



Rescue-free subjects include those who did not require rescue injections as specified by the protocol
*Nominal P value

OCULAR THERAPEUTIX Retina experience redefined™

SOL-1 Results Demonstrate Potential Treatment Benefit of OTX-TKI

SOL-1

Superiority Primary Endpoint Successfully Met

Unmatched Durability

Sustained Disease Control

Well-Tolerated

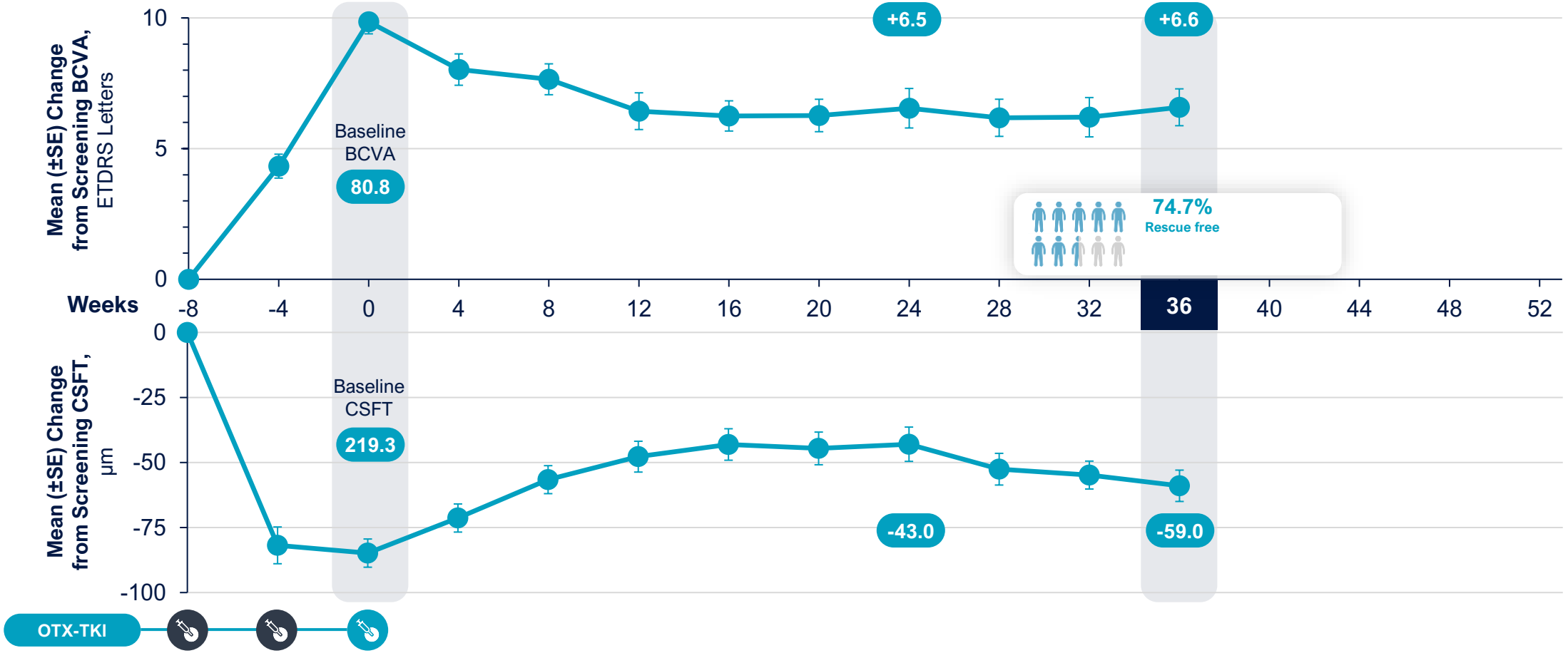
OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined™

On Average, OTX-TKI Subjects Maintained Vision and Anatomy, with Most Remaining Rescue-Free

SOL-1

Mean Change in BCVA and CSFT from Screening



OTX-TKI 0.45 mg (n=170)

Aflibercept 2 mg (n=172)

Post hoc analysis

Full analysis set. Only data up to Week 52 is included in the analyses

For subjects who received any rescue injections, their observed BCVA and CSFT values after the 1st rescue injection are set to missing. Baseline measurements are the last non-missing measurement prior to the study drug injection on Day 1

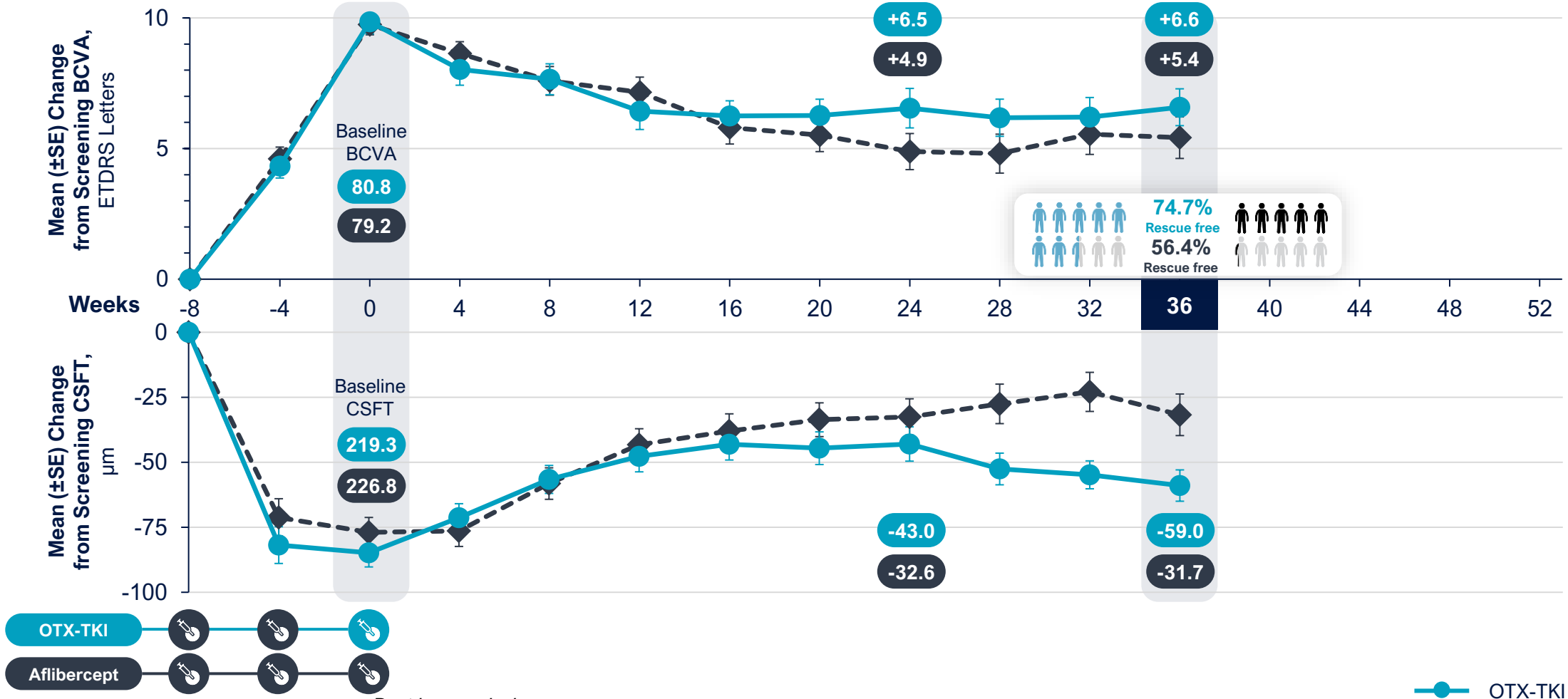
BCVA, best-corrected visual acuity; CSFT; central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium; ETDRS, Early Treatment Diabetic Retinopathy Study; SE, standard error

OCULAR THERAPEUTIX Retina experience redefined™

On Average, OTX-TKI Subjects Maintained Vision and Anatomy, with Most Remaining Rescue-Free

SOL-1

Mean Change in BCVA and CSFT from Screening



Post hoc analysis

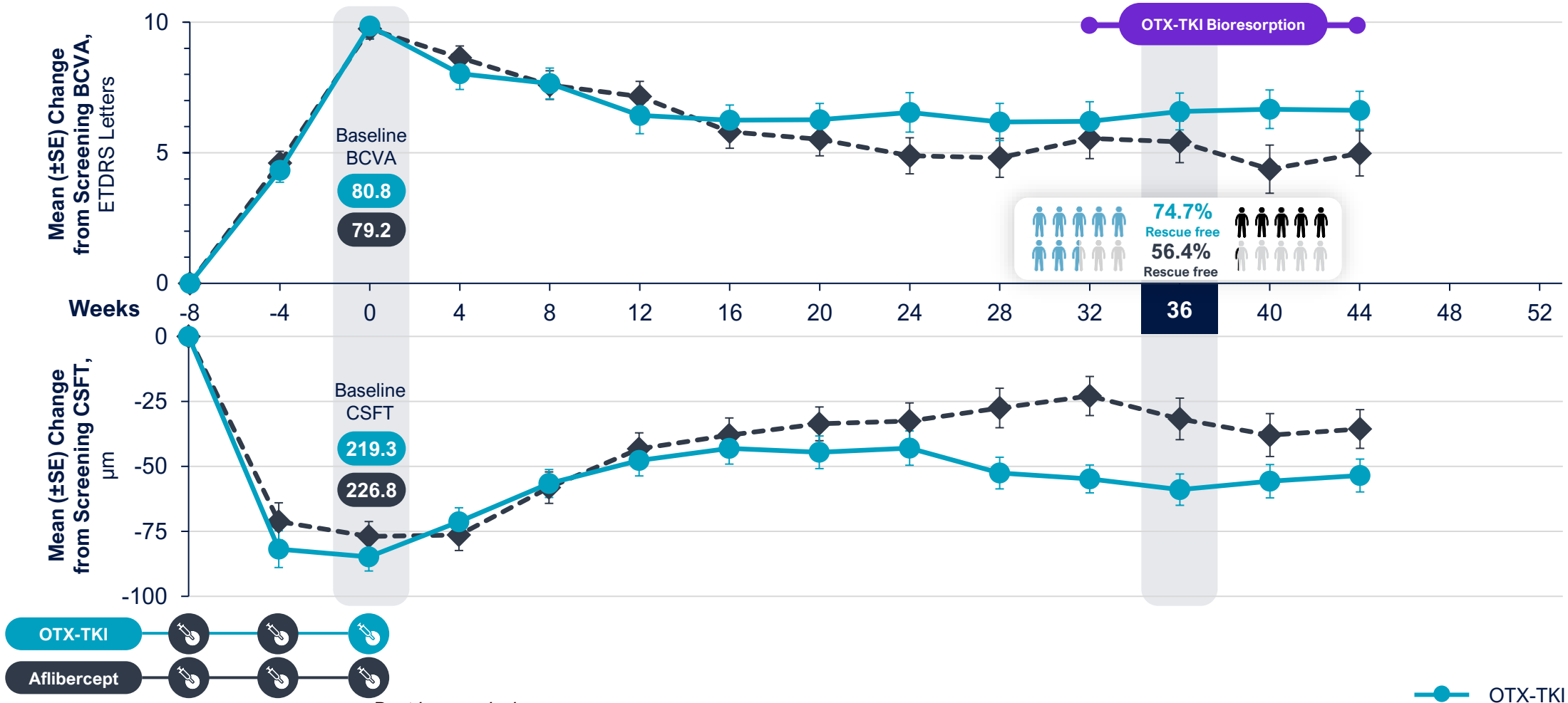
Full analysis set. Only data up to Week 52 is included in the analyses
For subjects who received any rescue injections, their observed BCVA and CSFT values after the 1st rescue injection are set to missing. Baseline measurements are the last non-missing measurement prior to the study drug injection on Day 1
BCVA, best-corrected visual acuity; CSFT; central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium; ETDRS, Early Treatment Diabetic Retinopathy Study; SE, standard error

OCULAR THERAPEUTIX Retina experience redefined™

On Average, OTX-TKI Subjects Maintained Vision and Anatomy, with Most Remaining Rescue-Free

SOL-1

Mean Change in BCVA and CSFT from Screening



Post hoc analysis

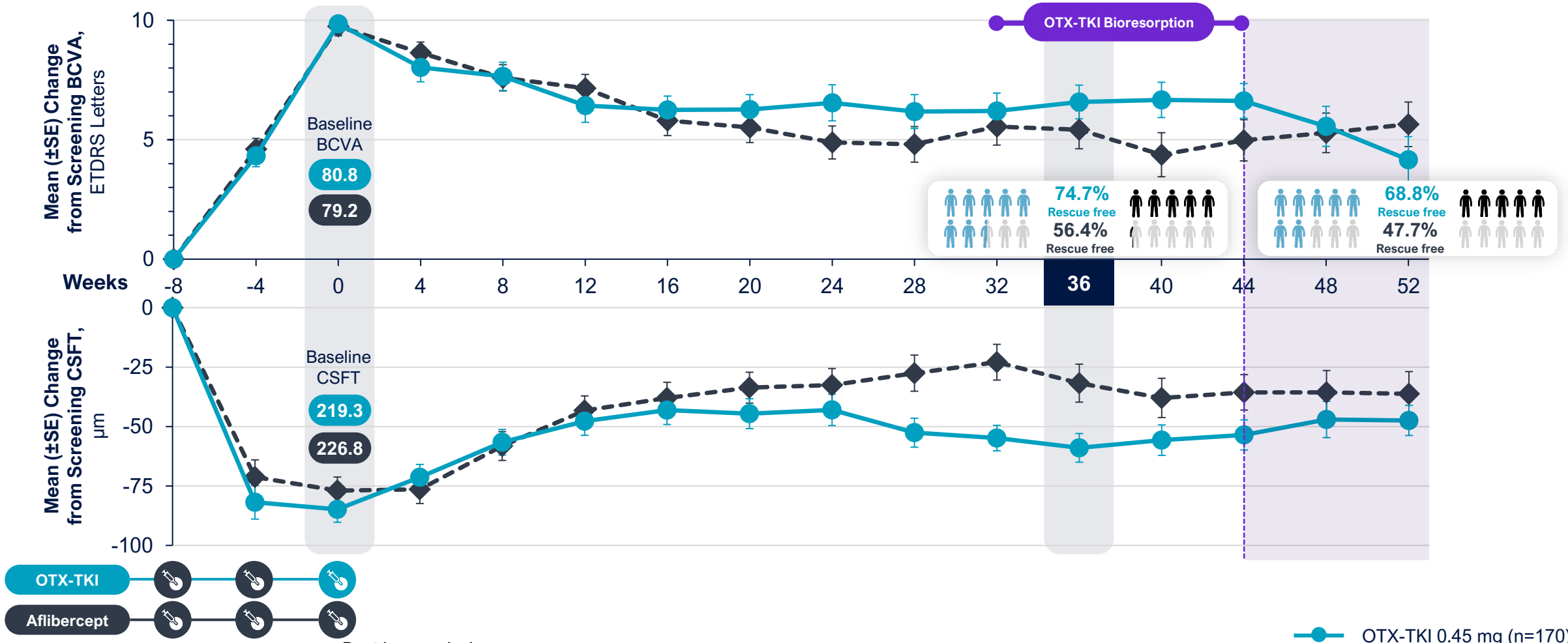
Full analysis set. Only data up to Week 52 is included in the analyses
For subjects who received any rescue injections, their observed BCVA and CSFT values after the 1st rescue injection are set to missing. Baseline measurements are the last non-missing measurement prior to the study drug injection on Day 1
BCVA, best-corrected visual acuity; CSFT; central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium; ETDRS, Early Treatment Diabetic Retinopathy Study; SE, standard error

OCULAR THERAPEUTIX Retina experience redefined™

On Average, OTX-TKI Subjects Maintained Vision and Anatomy, with Most Remaining Rescue-Free

SOL-1

Mean Change in BCVA and CSFT from Screening



Post hoc analysis

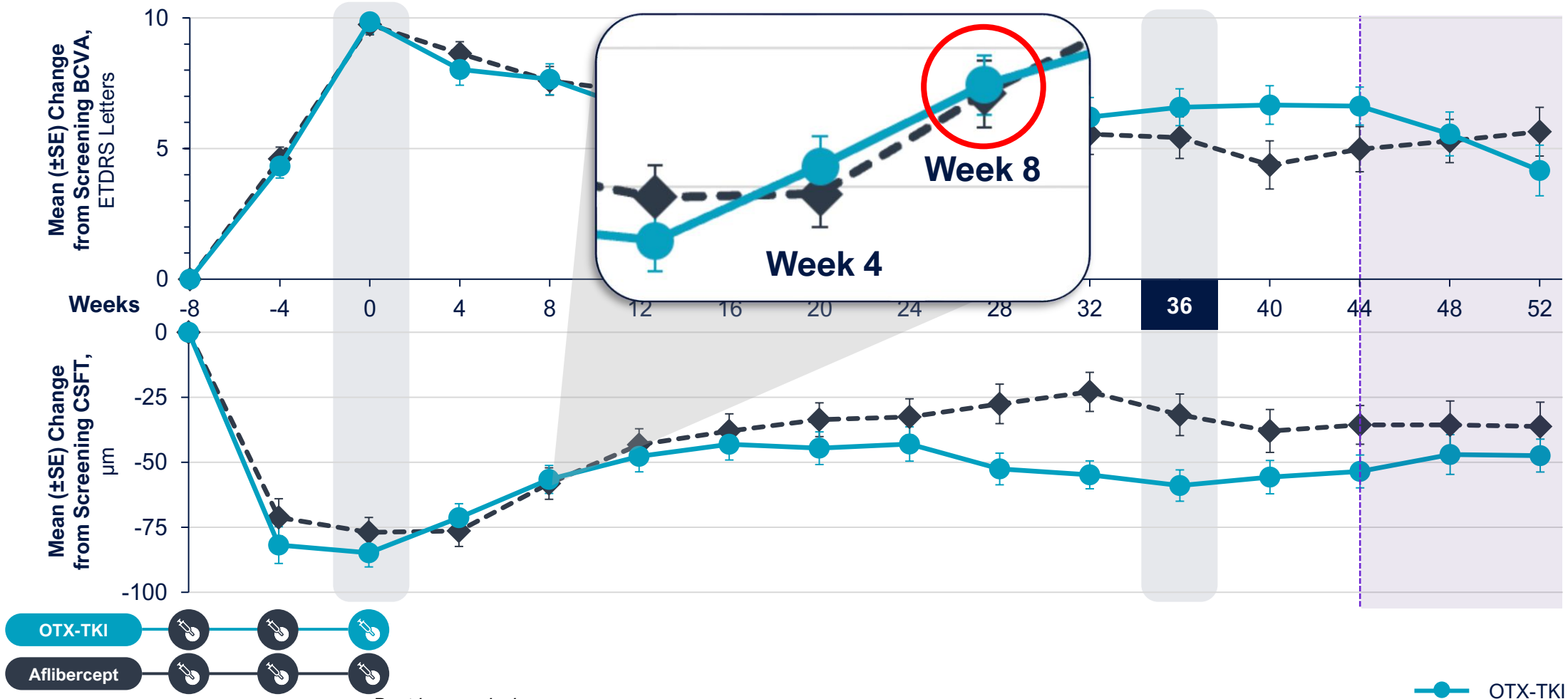
Full analysis set. Only data up to Week 52 is included in the analyses
For subjects who received any rescue injections, their observed BCVA and CSFT values after the 1st rescue injection are set to missing. Baseline measurements are the last non-missing measurement prior to the study drug injection on Day 1
BCVA, best-corrected visual acuity; CSFT; central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium; ETDRS, Early Treatment Diabetic Retinopathy Study; SE, standard error

OCULAR THERAPEUTIX Retina experience redefined™

On Average, OTX-TKI Subjects Maintained Vision and Anatomy, with Most Remaining Rescue-Free

SOL-1

Mean Change in BCVA and CSFT from Screening



Post hoc analysis

Full analysis set. Only data up to Week 52 is included in the analyses
For subjects who received any rescue injections, their observed BCVA and CSFT values after the 1st rescue injection are set to missing. Baseline measurements are the last non-missing measurement prior to the study drug injection on Day 1
BCVA, best-corrected visual acuity; CSFT; central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium; ETDRS, Early Treatment Diabetic Retinopathy Study; SE, standard error

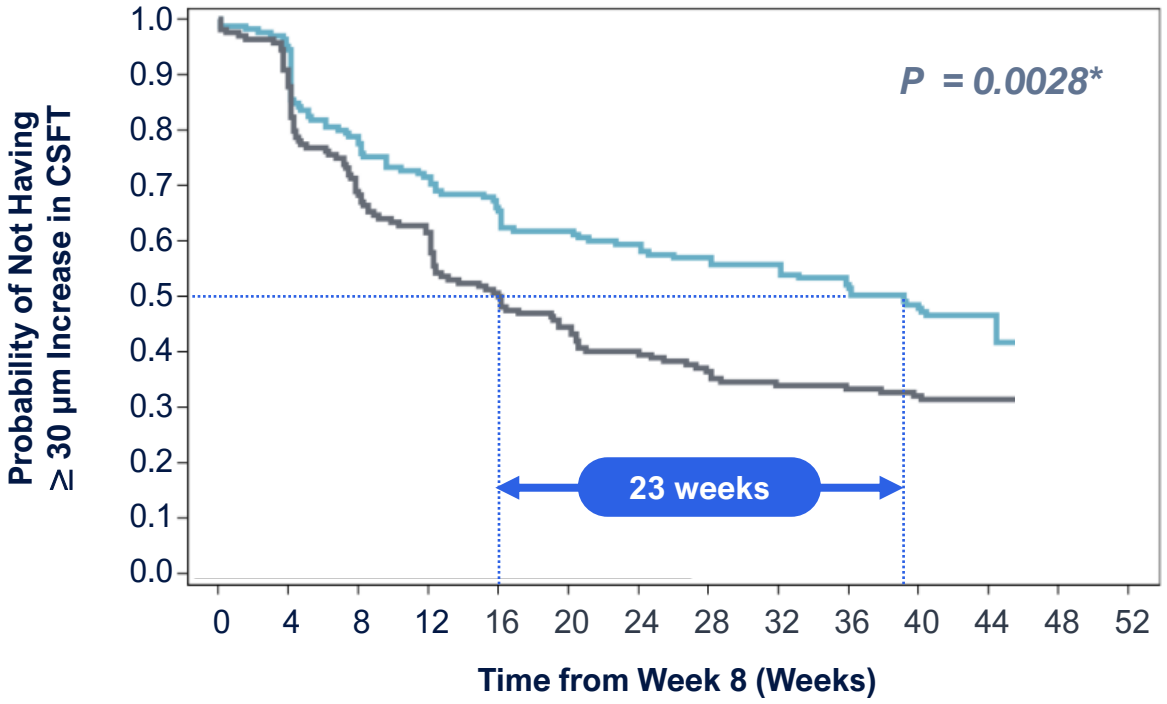
OCULAR THERAPEUTIX Retina experience redefined™

OTX-TKI was Associated with a Slower Increase in Anatomic Change

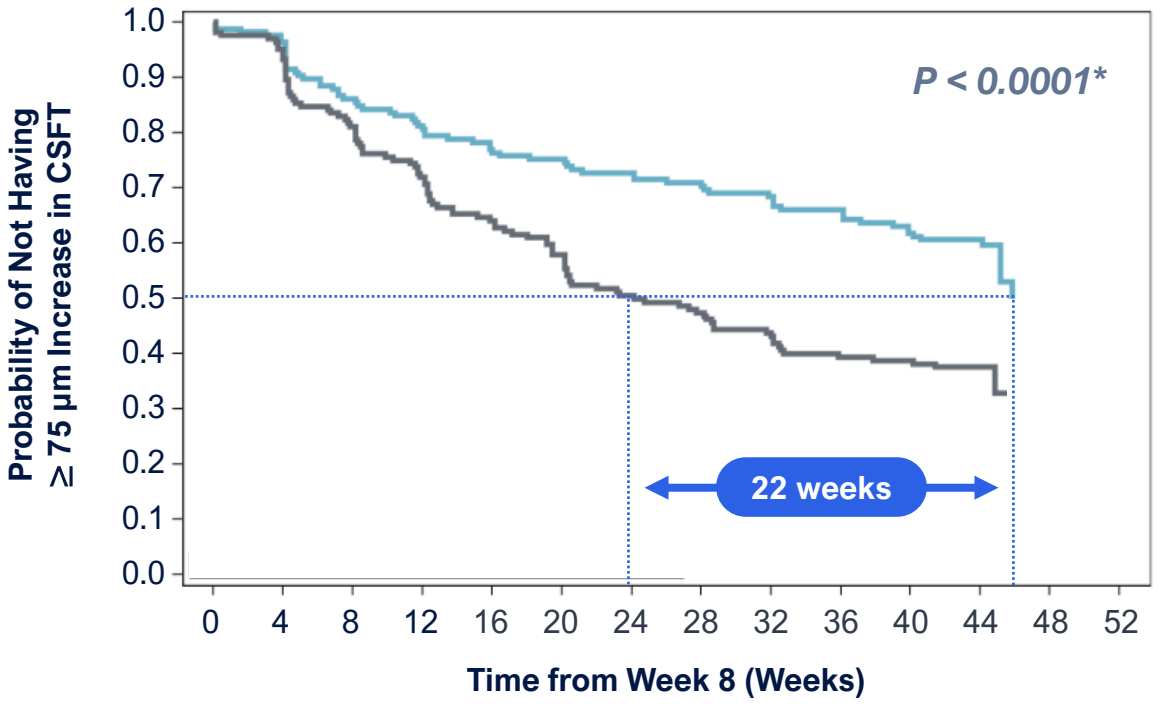
SOL-1

Time to CSFT Increase from Week 8

Time to ≥ 30 µm Increase in CSFT



Time to ≥ 75 µm Increase in CSFT



OTX-TKI 0.45 mg (n=165)

Aflibercept 2 mg (n=164)

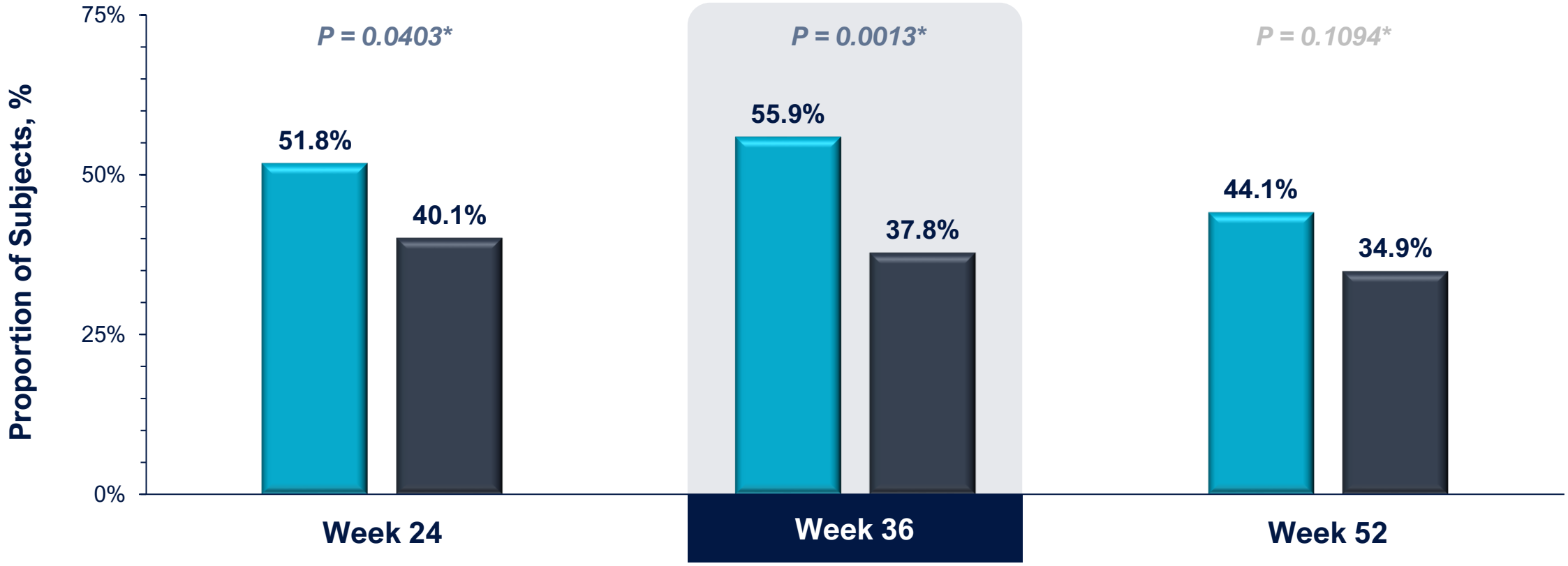
OCULAR THERAPEUTIX Retina experience redefined™

Post hoc analysis

Subjects with CSFT at Week 8 in Full Analysis Set; *Descriptive p-value
CSFT; central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium;

Anatomic Control in the OTX-TKI arm

Proportion of Subjects with ≤30 µm Increase in CSFT from Baseline



OCULAR THERAPEUTIX Retina experience redefined™

Post hoc analysis

Full analysis set. *Descriptive p-value

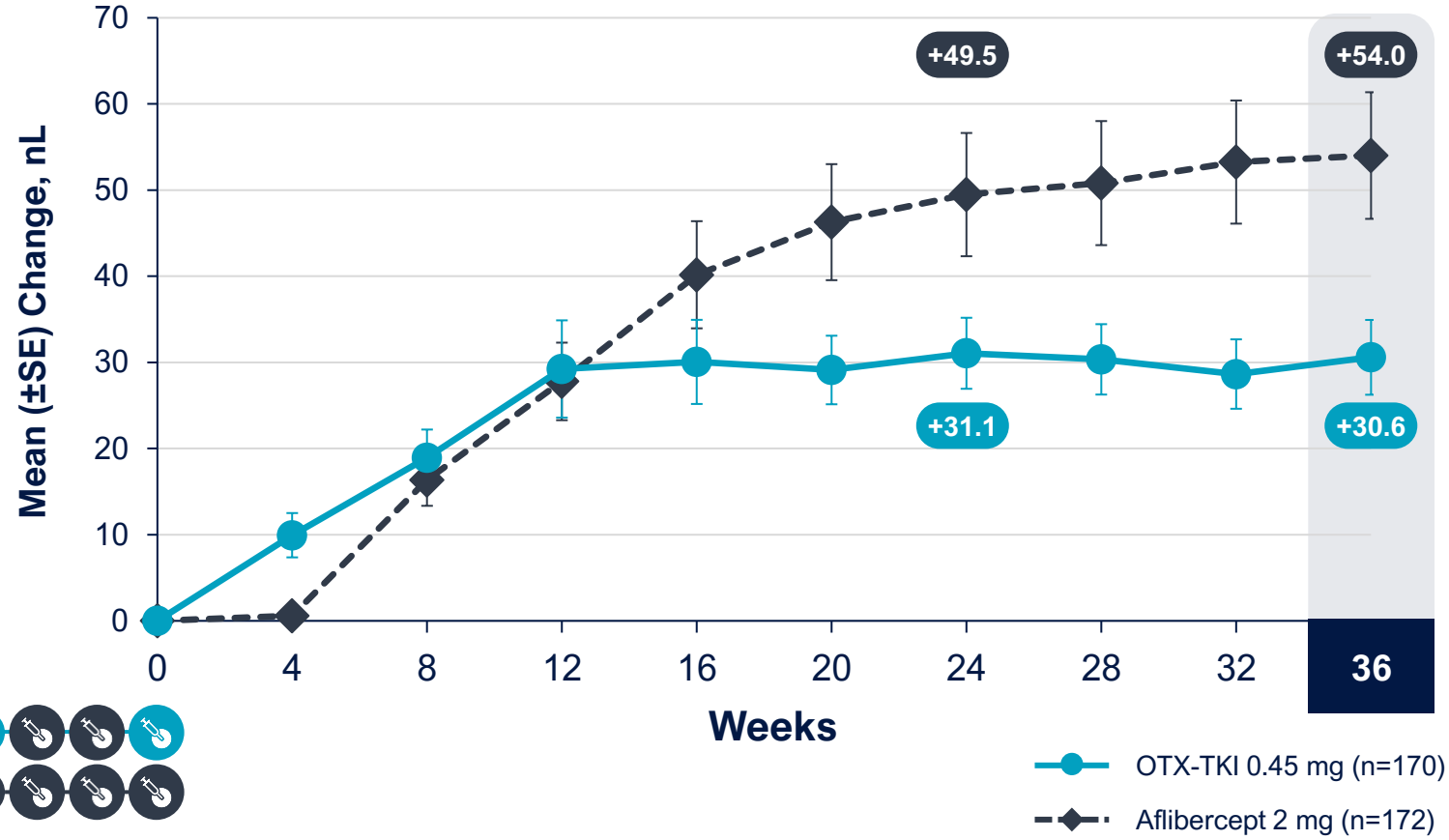
CSFT; central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium; CI, confidence interval

OTX-TKI 0.45 mg (n=170)

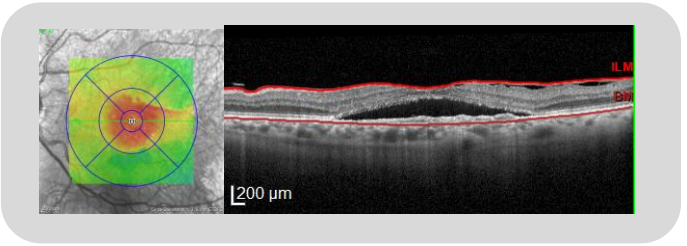
Aflibercept 2 mg (n=172)

OTX-TKI Delivered Sustained Fluid Control

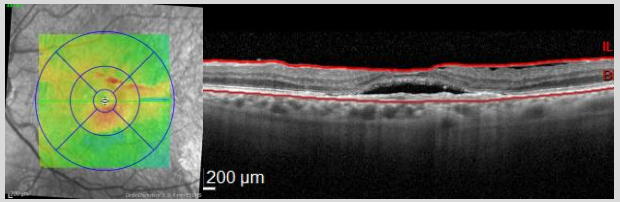
Mean Change in Intra-Retinal and Sub-Retinal Fluid Volume



Total Fluid Volume: 60 nL



Total Fluid Volume: 30 nL



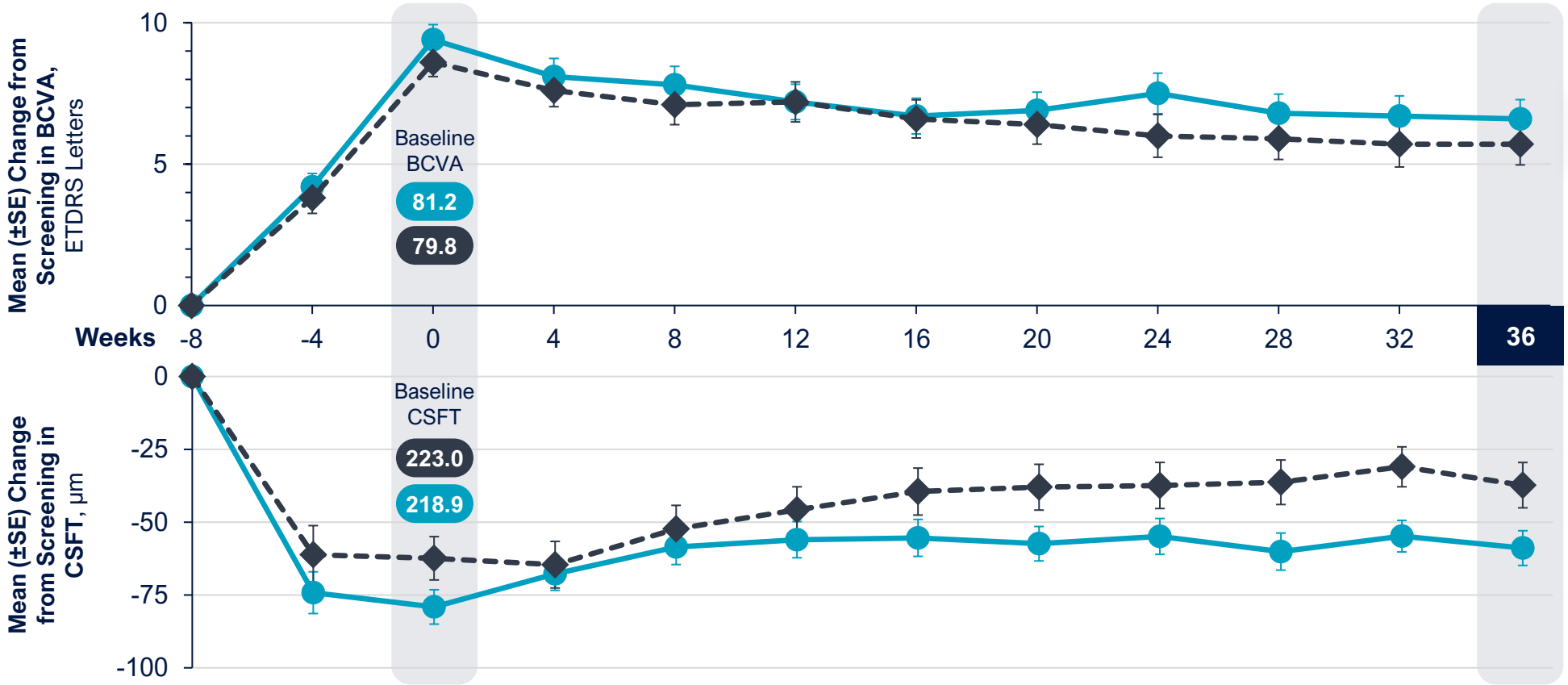
Pre-specified exploratory analysis

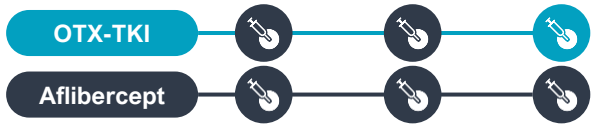
Full analysis set
SE, standard error

Subjects without Rescue Treatment Maintained Their Visual Gain and Demonstrated Better Disease Control

SOL-1

Mean Change in BCVA and CSFT in Rescue-Free Subjects





OCULAR THERAPEUTIX Retina experience redefined™

Post hoc analysis

Rescue-free subjects include those who did not require rescue injections as specified by the protocol

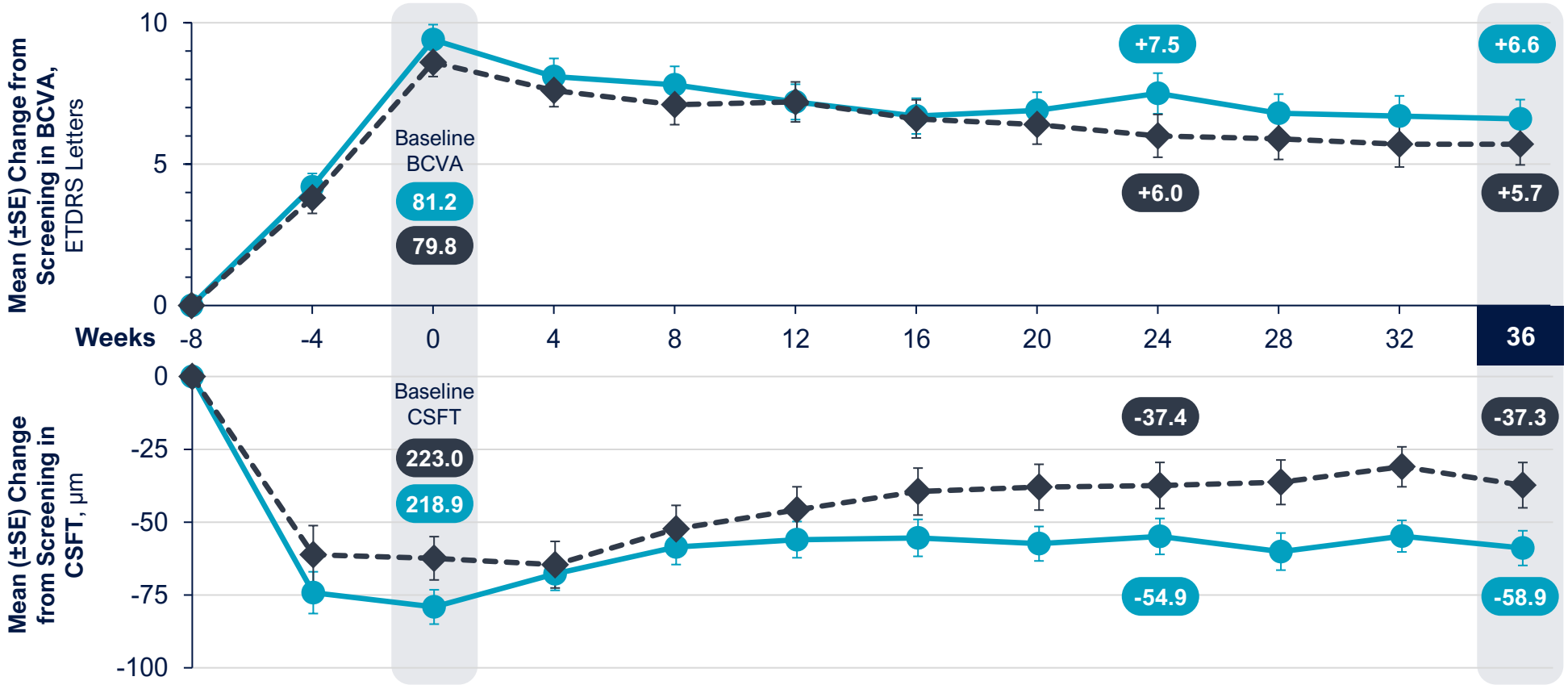
BCVA, best corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; CSFT; central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium; SE, standard errorl

OTX-TKI 0.45 mg (n=127)

Aflibercept 2 mg (n=97)

Subjects without Rescue Treatment Maintained Their Visual Gain and Demonstrated Better Disease Control

Mean Change in BCVA and CSFT in Rescue-Free Subjects



Observed Difference from BSL
(ETDRS Letters)

	OTX-TKI (0.45 mg)	Aflibercept (2 mg)
24w	-1.9	-2.6
36w	-2.8	-2.9

Post hoc analysis

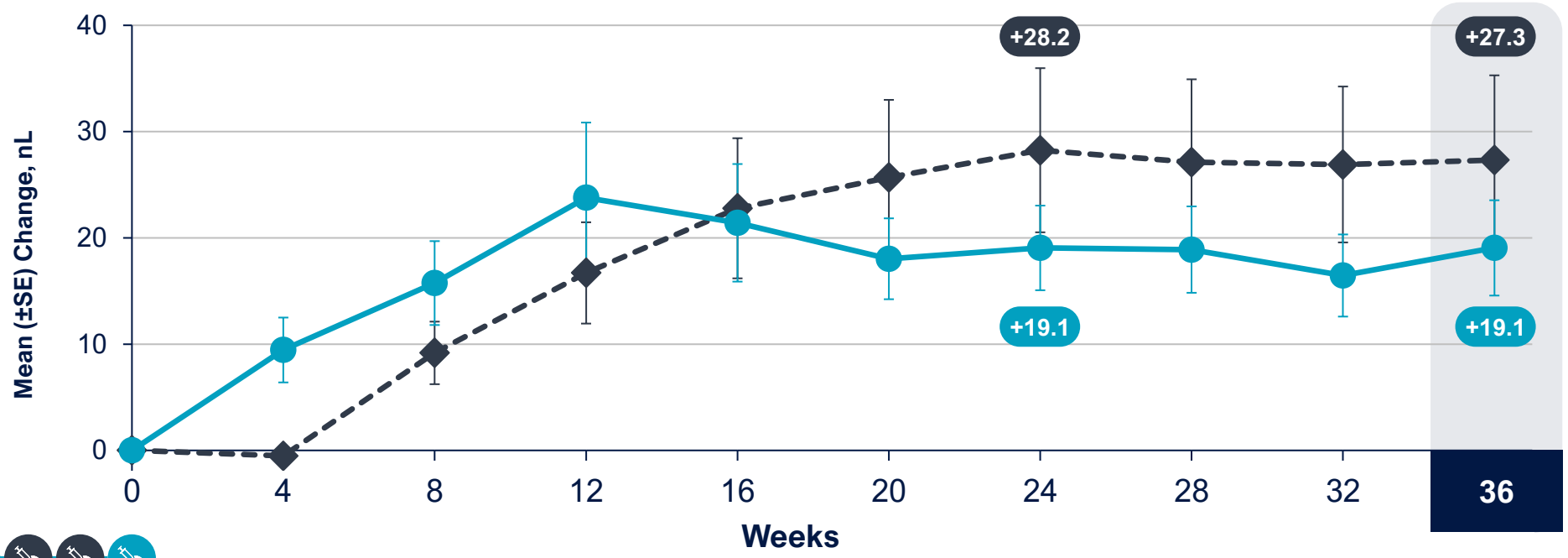
Rescue-free subjects include those who did not require rescue injections as specified by the protocol
BCVA, best corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; CSFT; central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium; SE, standard errorl

OTX-TKI 0.45 mg (n=127)
Aflibercept 2 mg (n=97)

Effective Control of Retinal Fluid Volume in OTK-TKI Subjects without Rescue Treatment

SOL-1

Mean Change in Total Intra-Retinal and Sub-Retinal Fluid Volume in Rescue-Free Subjects



Post hoc analysis

Rescue-free subjects include those who did not require rescue injections as specified by the protocol
SE, standard error

OCULAR THERAPEUTIX Retina experience redefined™

SOL-1 Results Demonstrate Potential Treatment Benefit of OTX-TKI

SOL-1

Superiority Primary Endpoint Successfully Met

Unmatched Durability

Sustained Disease Control

Well-Tolerated

OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined™

No Treatment or Procedure Related Systemic SAEs

SOL-1

Non-Ocular Events

Subjects with Non-Ocular AEs Through Week 52, n (%)	OTX-TKI 0.45 mg n = 170	Aflibercept 2 mg n = 172
Non-ocular AEs		
≥ 1 AE	84 (49.4)	73 (42.4)
≥ 1 SAE	19 (11.2)	21 (12.2)
≥ 1 treatment-related AE	0	0
≥ 1 treatment-related SAE	0	0
≥ 1 study procedure-related AE	1 (0.6)	0
≥ 1 study procedure-related SAE	0	0
AE leading to study discontinuation	3 (1.8)	3 (1.7)
AE leading to death*	2 (1.2)	1 (0.6)

OCULAR THERAPEUTIX Retina experience redefined™

*Stroke (day 103); worsening of metastatic melanoma (day 319); lung cancer metastatic (day 503)
AE, adverse event; SAE, serious AE

No Treatment or Procedure Related Ocular SAEs

Ocular Events in the Study Eye

Subjects with Ocular AEs Through Week 52, n (%)	OTX-TKI 0.45 mg n = 170	Aflibercept 2 mg n = 172
Ocular AEs in the study eye		
≥ 1 AE	90 (52.9)	58 (33.7)
≥ 1 SAE*	1 (0.6)	0
≥ 1 treatment-related AE	15 (8.8)	1 (0.6)
≥ 1 treatment-related SAE	0	0
≥ 1 study procedure-related AE	15 (8.8)	7 (4.1)
≥ 1 study procedure-related SAE	0	0
Ocular AE leading to study discontinuation	0	0

*Severe vision loss due to 3+ PSC cataract, 78 ETDRS letters at baseline, recovered to 70 ETDRS letters after cataract surgery
AE, adverse event; SAE, serious AE; PSC, posterior subcapsular cataract; ETDRS, Early Treatment Diabetic Retinopathy Study

OTX-TKI was Generally Well Tolerated

Ocular Adverse Events in the Study Eye

Subjects with Ocular AEs (> 2%) Through Week 52, n (%)	OTX-TKI 0.45 mg n = 170	Aflibercept 2 mg n = 172
Vitreous floaters	21 (12.4)	2 (1.2)
Cataract	12 (7.1)	5 (2.9)
Conjunctival hemorrhage	11 (6.5)	5 (2.9)
Retinal hemorrhage	10 (5.9)	17 (9.9)
Dry eye	7 (4.1)	2 (1.2)
Vitreous detachment	7 (4.1)	3 (1.7)
Punctate keratitis	6 (3.5)	0
Vitreous opacities	6 (3.5)	0
Eye pain	5 (2.9)	1 (0.6)
Anterior chamber opacity	4 (2.4)	0
Posterior capsule opacification	4 (2.4)	6 (3.5)

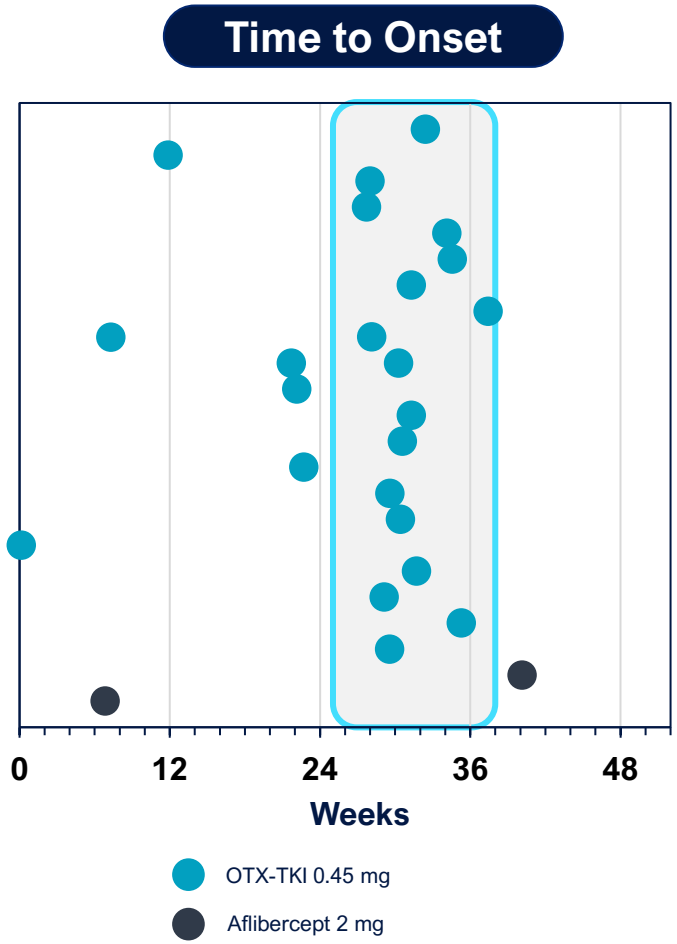
There were no cases of endophthalmitis, occlusive or non-occlusive retinal vasculitis

AE, adverse event

Appearance of Floaters May Correspond to Hydrogel Dissolution and Drug Elution

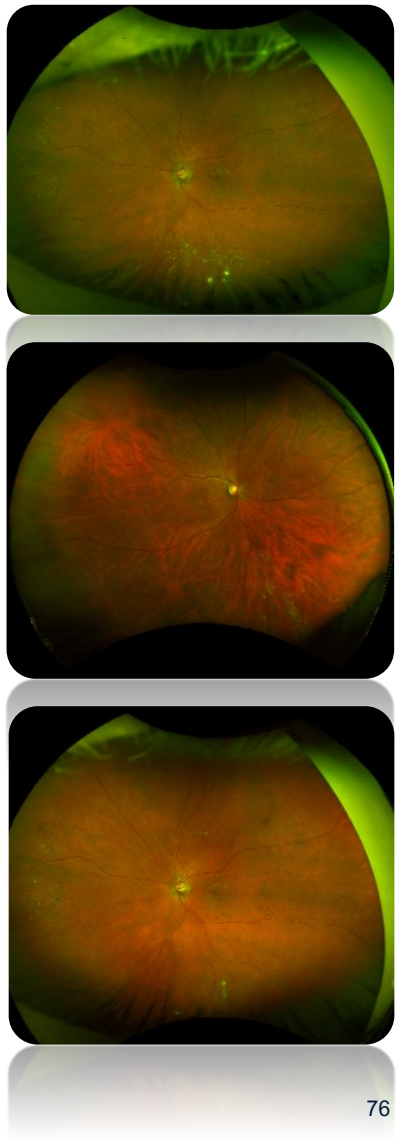
SOL-1

Evaluation of Vitreous Floaters



	OTX-TKI 0.45 mg n = 23*	Aflibercept 2 mg n = 2
Time to onset, days		
Mean (SD)	187.9 (64.0)	164.5 (164.8)
Median	207.0	164.5
BCVA change from prior visit before onset of floaters, ETDRS letters		
Mean change (SD)	-0.4 (5.0)	-5.5 (6.4)
Median change	0.0	-5.5

- All cases were mild to moderate in severity
- No evidence of IOI associated with floaters
- Onset of vitreous floaters AE coincides with drug elution stage of OTX-TKI implant bioresorption process
- **For all subjects** with vitreous floaters AE reported, **drug particles are no longer visible**
  - Mean time ~ 20 weeks



OCULAR THERAPEUTIX Retina experience redefined™

*23 events in the study eye, 21 subjects; No case observed to be associated with cataract formation
Optos images on day of onset of AE of vitreous floaters
OTK-TKI: Mean change from baseline (SD) in BCVA, -3.3 (8.2) ETDRS letters; median change from baseline, -1.0 ETDRS letters
Study is ongoing until Year 2
SD, standard deviation; BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; AE, adverse events; IOI, intraocular inflammation

Mild/Moderate IOI Resolved with Topical Treatment or Observation

Evaluation of Intraocular Inflammation

- Nine events observed in study eyes of 7 subjects in the OTX-TKI arm
- **All cases were mild or moderate** in severity and resolved

	MedRA Term	Eye	Severity	Medication
1	Iritis	Study eye	Mild	Topical corticosteroids
	Iritis	Study eye	Moderate	Topical corticosteroids
2	Iridocyclitis	Study eye	Mild	Topical corticosteroids
3	AC inflammation	Study eye	Moderate	Topical corticosteroids
4	Vitreal cells	Study eye	Mild	None
5	Iritis	Study eye	Mild	Topical corticosteroids
6	Eye inflammation	Study eye	Moderate	Topical corticosteroids
7	Iritis	Study eye	Mild	Topical corticosteroids
	Uveitis	Study Eye	Moderate	Topical corticosteroids
		Non-study eye	Mild	None

There were no cases of endophthalmitis, occlusive or non-occlusive retinal vasculitis, confirmed by wide-field fluorescein angiography when needed (by Duke Reading Center)

OCULAR THERAPEUTIX Retina experience redefined™

Subjects with ≥1 IOI event were counted once; subjects with multiple event types were categorized under one MedRA Preferred Term.
AC, anterior chamber; MedRA, Medical Dictionary for Regulatory Activities; IOI, intraocular inflammation

SOL-1 Results Demonstrate Potential Treatment Benefit of OTX-TKI

SOL-1

Superiority Primary Endpoint Successfully Met

First trial to demonstrate durability ≥ 9 months

~75% of subjects treated with OTX-TKI did not receive rescue treatments by Week 36

Unmatched Durability

Visual and anatomic stability with OTX-TKI

On average, OTX-TKI subjects maintained visual and anatomical outcomes, with most remaining rescue-free

Sustained Disease Control

OTX-TKI demonstrated a well-tolerated safety profile through Week 52

There were no cases of endophthalmitis, occlusive or non-occlusive retinal vasculitis

Well-Tolerated

OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined™

Maintenance of vision defined as proportion of subjects who maintain visual acuity, a loss of <15 ETDRS letters of BCVA from baseline
Rescue-free subjects include those who did not require rescue injections as specified by the protocol

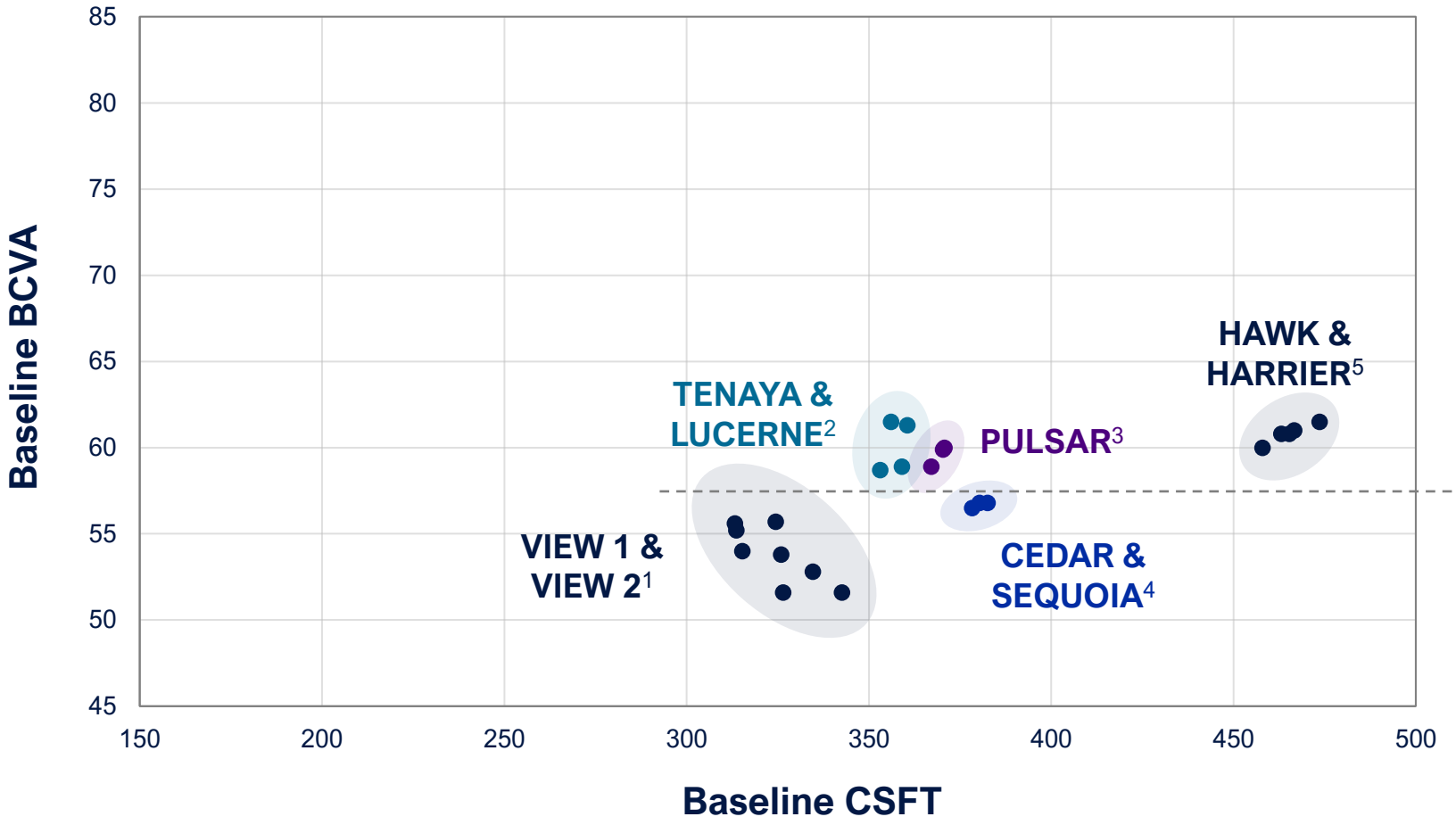
Translating SOL-1 Results

Peter K. Kaiser, MD

OCULAR THERAPEUTIX Retina experience redefined

SOL-1 Evaluates a Distinct nAMD Cohort with Excellent Baseline Vision

Baseline BCVA Across nAMD Trials



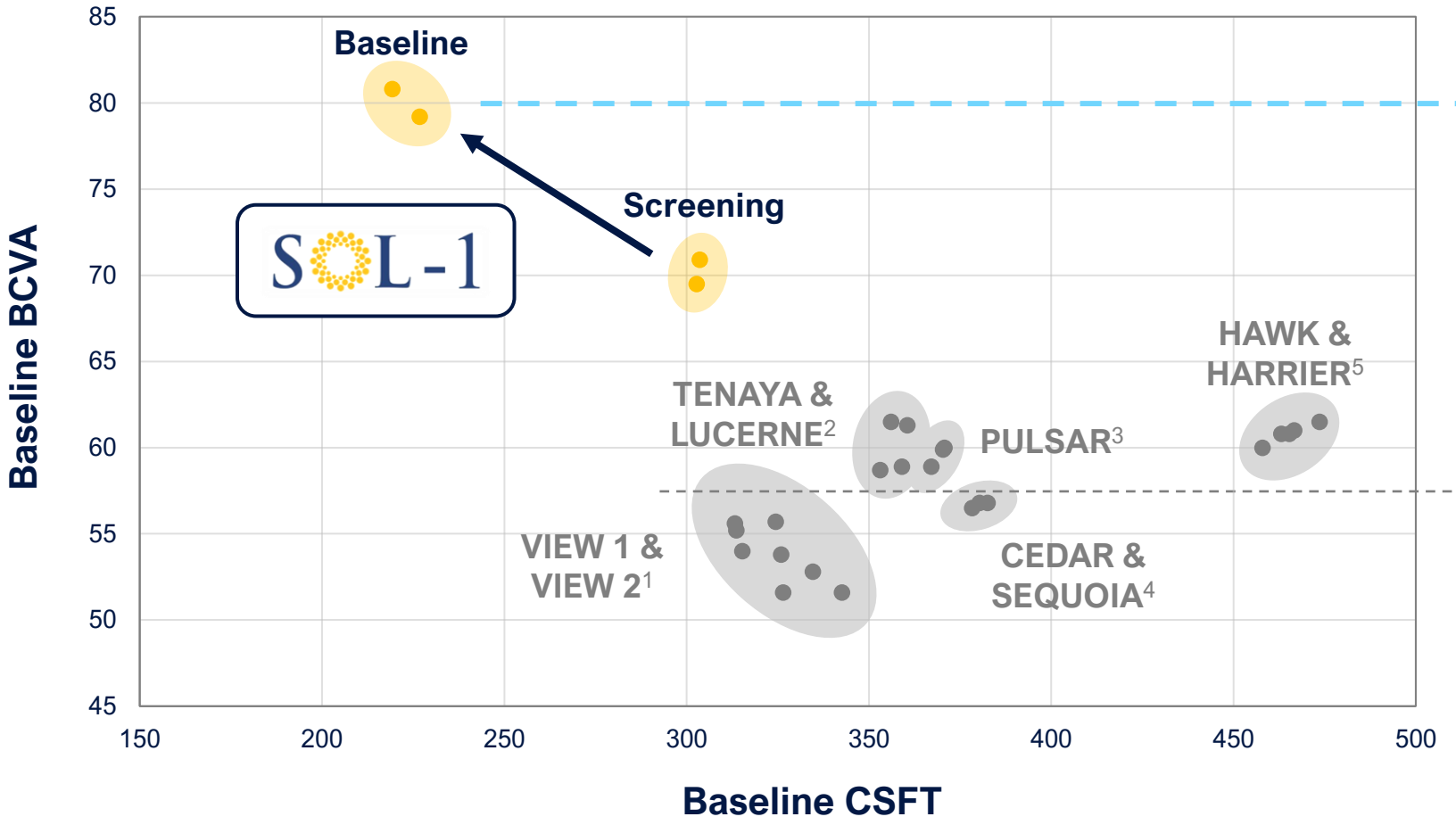
nAMD Trials
mean BCVA: **52 to 62 letters (~20/100 to 20/60)**

OCULAR THERAPEUTIX Retina experience redefined™

1. Heier JS, et al. *Ophthalmology*. 2012;119(12):2537-2548. 2. Heier JS, et al. *Lancet*. 2022;399(10326):729-740. 3. Lanzetta P, et al. *Lancet*. 2024;403(10432):1141-1152. 4. Kunimoto D, et al. *Ophthalmology*. 2020;127(10):1331-1344. 5. Dugel PU, et al. *Ophthalmology*. 2020;127(1):72-84.
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; nAMD, neovascular age-related macular degeneration

SOL-1 Evaluates a Distinct nAMD Cohort with Excellent Baseline Vision

Baseline BCVA Across nAMD Trials



SOL-1
mean BCVA: **81 letters (~20/25)**
mean CSFT: **219 µM**

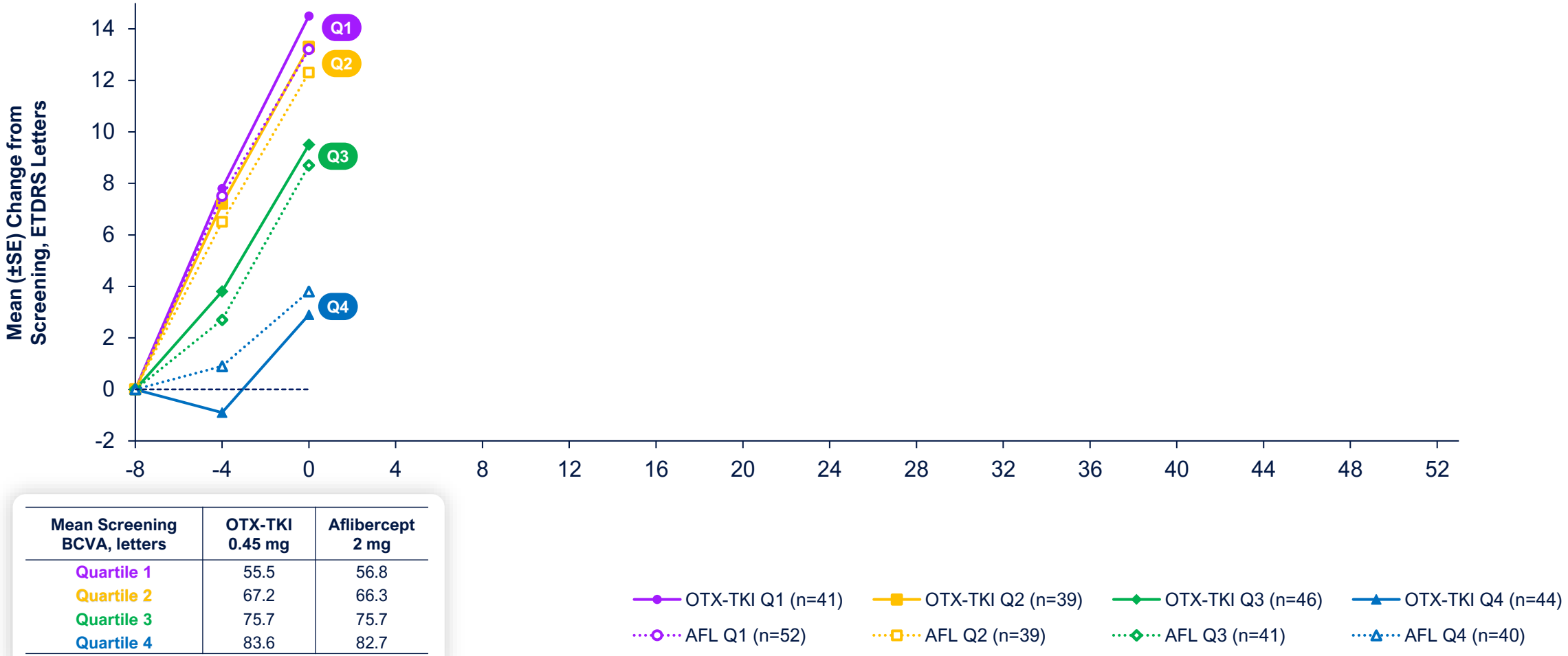
nAMD Trials
mean BCVA: **52 to 62 letters (~20/100 to 20/60)**

OCULAR THERAPEUTIX Retina experience redefined™

1. Heier JS, et al. *Ophthalmology*. 2012;119(12):2537-2548. 2. Heier JS, et al. *Lancet*. 2022;399(10326):729-740. 3. Lanzetta P, et al. *Lancet*. 2024;403(10432):1141-1152. 4. Kunimoto D, et al. *Ophthalmology*. 2020;127(10):1331-1344. 5. Dugel PU, et al. *Ophthalmology*. 2020;127(1):72-84.
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; nAMD, neovascular age-related macular degeneration

Initial Gains in Vision Depend on Screening BCVA

Mean Change in BCVA: By Screening BCVA

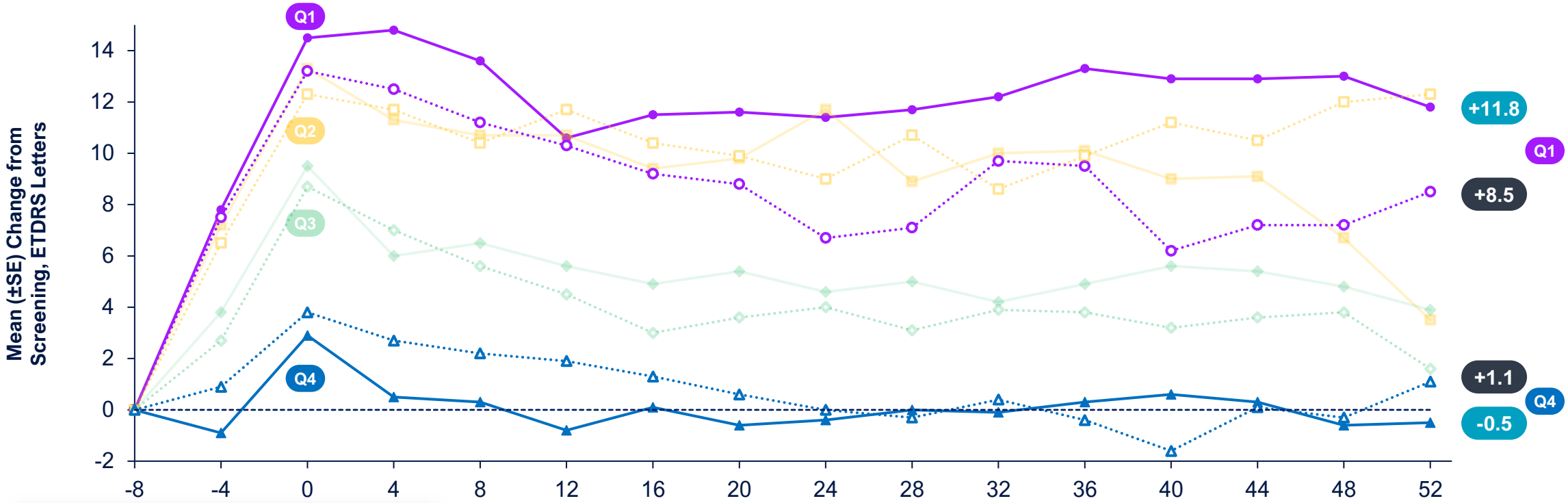


Mean Screening BCVA, letters	OTX-TKI 0.45 mg	Aflibercept 2 mg
Quartile 1	55.5	56.8
Quartile 2	67.2	66.3
Quartile 3	75.7	75.7
Quartile 4	83.6	82.7

Post hoc analysis
Full analysis set
AFL, aflibercept; BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study, Q, quartile

Subjects Generally Maintained Their Initial Vision Gains

Mean Change in BCVA: By Screening BCVA



Mean Screening BCVA, letters	OTX-TKI 0.45 mg	Aflibercept 2 mg
Quartile 1	55.5	56.8
Quartile 2	67.2	66.3
Quartile 3	75.7	75.7
Quartile 4	83.6	82.7

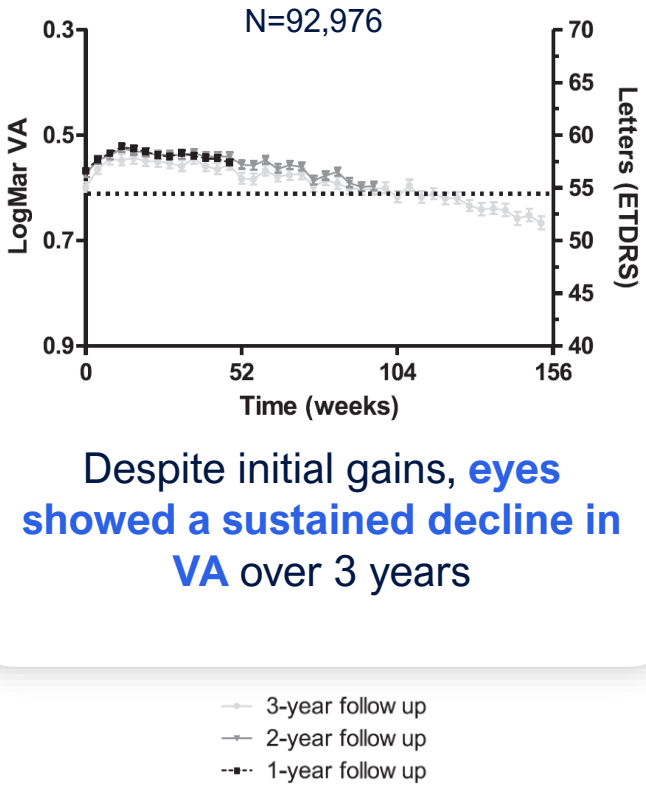
OTX-TKI
- OTX-TKI Q1 (n=41)
- OTX-TKI Q2 (n=39)
- OTX-TKI Q3 (n=46)
- OTX-TKI Q4 (n=44)

Aflibercept
- AFL Q1 (n=52)
- AFL Q2 (n=39)
- AFL Q3 (n=41)
- AFL Q4 (n=40)

Post hoc analysis
Full analysis set
AFL, aflibercept; BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study, Q, quartile

Eyes with Excellent Baseline Vision Decline on Average in Real-World Studies

Visual Acuity Over Time



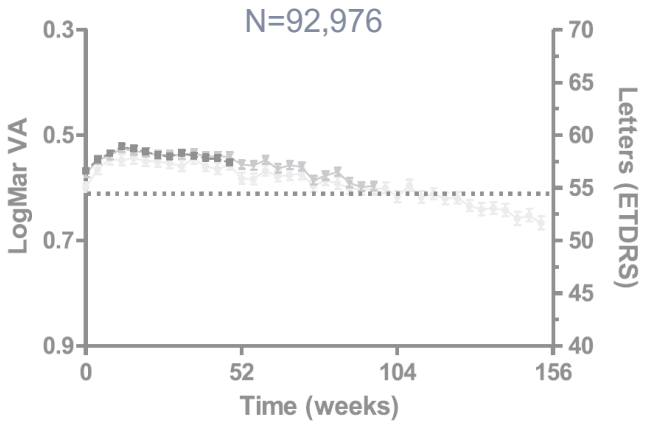
Despite initial gains, **eyes showed a sustained decline in VA** over 3 years

OCULAR THERAPEUTIX Retina experience redefined™

Writing Committee for the UK Age-Related Macular Degeneration EMR Users Group. The neovascular age-related macular degeneration database: multicenter study of 92 976 ranibizumab injections: report 1: visual acuity. *Ophthalmology*. 2014;121(5):1092-1101.
ETDRS, Early Treatment Diabetic Retinopathy Study; VA, visual acuity; RWE, real world evidence

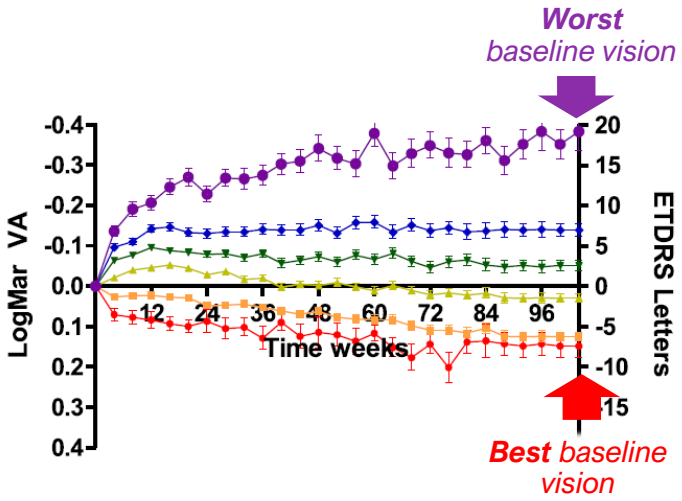
Eyes with Excellent Baseline Vision Decline on Average in Real-World Studies

Visual Acuity Over Time



Despite initial gains, **eyes showed a sustained decline in VA** over 3 years

Change in Vision
Stratified by Baseline VA



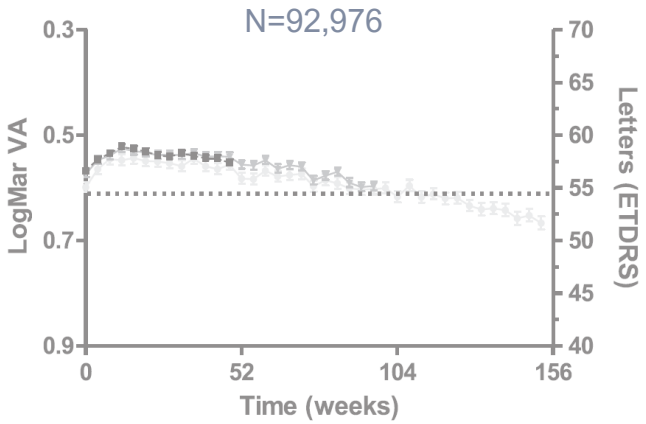
Change in vision is dependent on baseline status with **eyes starting with better vision showing greater decline**

OCULAR THERAPEUTIX Retina experience redefined™

Writing Committee for the UK Age-Related Macular Degeneration EMR Users Group. The neovascular age-related macular degeneration database: multicenter study of 92 976 ranibizumab injections: report 1: visual acuity. *Ophthalmology*. 2014;121(5):1092-1101.
ETDRS, Early Treatment Diabetic Retinopathy Study; VA, visual acuity; RWE, real world evidence

Actual Visual Acuity, NOT Change, is What is Meaningful to Patients

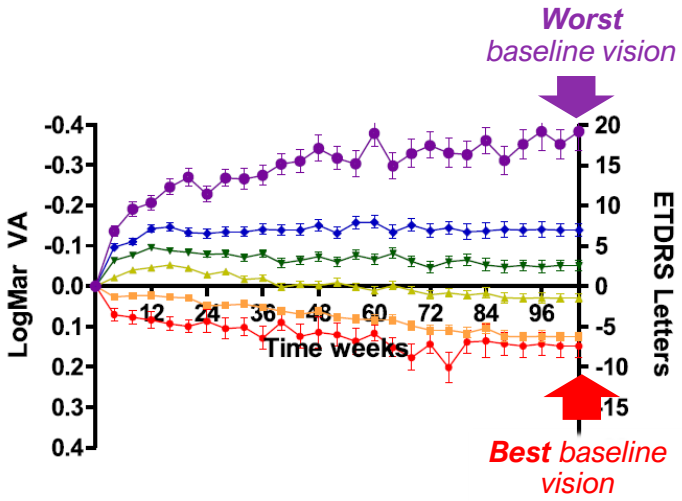
Visual Acuity Over Time



Despite initial gains, **eyes showed a sustained decline in VA** over 3 years

3-year follow up
2-year follow up
1-year follow up

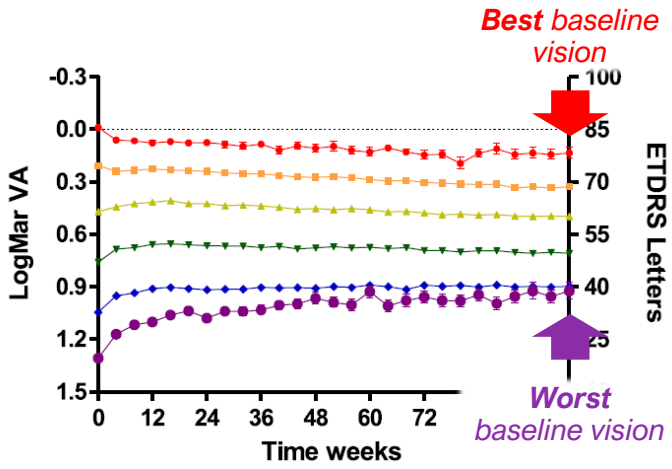
Change in Vision
Stratified by Baseline VA



Change in vision is dependent on baseline status with **eyes starting with better vision showing greater decline**

Baseline -0.29-0.00 (n=166)
Baseline 0.01-0.30 (n=2166)
Baseline 0.31-0.60 (n=3729)
Baseline 0.61-0.90 (n=2905)
Baseline 0.91-1.20 (n=1843)
Baseline 1.21-1.50 (n=411)

Mean Vision
Stratified by Baseline VA



Best baseline vision maintains the highest overall visual acuity

Baseline -0.29-0.00 (n=166)
Baseline 0.01-0.30 (n=2166)
Baseline 0.31-0.60 (n=3729)
Baseline 0.61-0.90 (n=2905)
Baseline 0.91-1.20 (n=1843)
Baseline 1.21-1.50 (n=411)

OCULAR THERAPEUTIX Retina experience redefined™

Writing Committee for the UK Age-Related Macular Degeneration EMR Users Group. The neovascular age-related macular degeneration database: multicenter study of 92 976 ranibizumab injections: report 1: visual acuity. *Ophthalmology*. 2014;121(5):1092-1101.
ETDRS, Early Treatment Diabetic Retinopathy Study; VA, visual acuity; RWE, real world evidence

Real-World Evidence Simulation (IRIS Registry): Patient Population

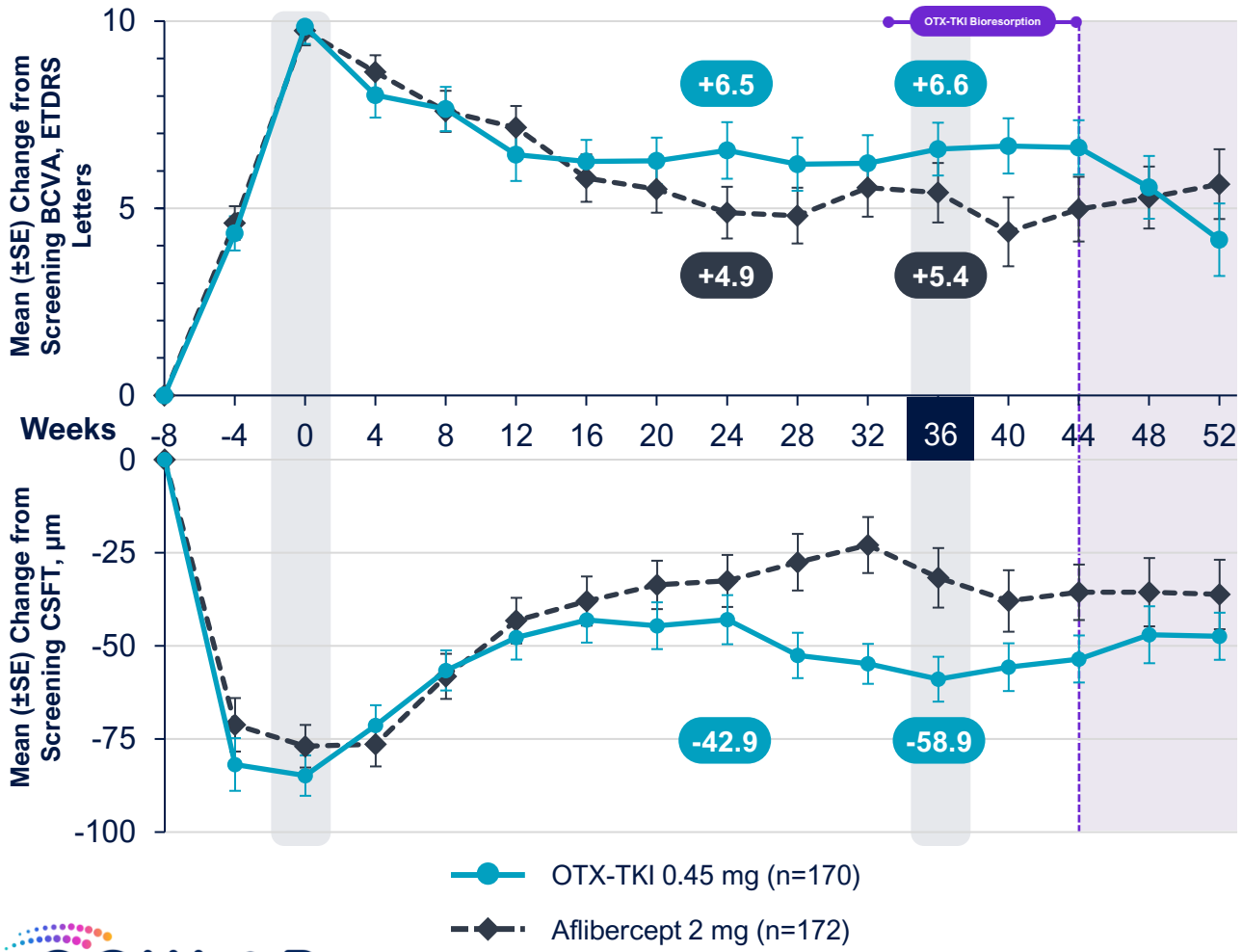
	SOL-1 Trial	IRIS Registry
	OTX-TKI N = 172	SOL-1 Emulated N = 6178
VA, ETDRS letters, mean (SD)		
Screening	70.9 (11.3)	68.4 (10.1)
Baseline	80.8 (7.6)	79.0 (6.1)
CSFT, µm, mean (SD)		
Screening	303.6 (72.5)	312.8 (71.3)
Baseline	219.3 (37.1)	257.4 (45.9)

OCULAR THERAPEUTIX Retina experience redefined™

Data on File, Ocular Therapeutix.
VA, visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; CSFT, central subfield thickness.

How does SOL-1 data align with real world outcomes?

SOL-1 Clinical Trial



SOL-1 Emulated Population

IRIS Registry

Subjects (N=6178)

OCULAR THERAPEUTIX Retina experience redefined™

Post hoc analysis

Data on File, Ocular Therapeutix.

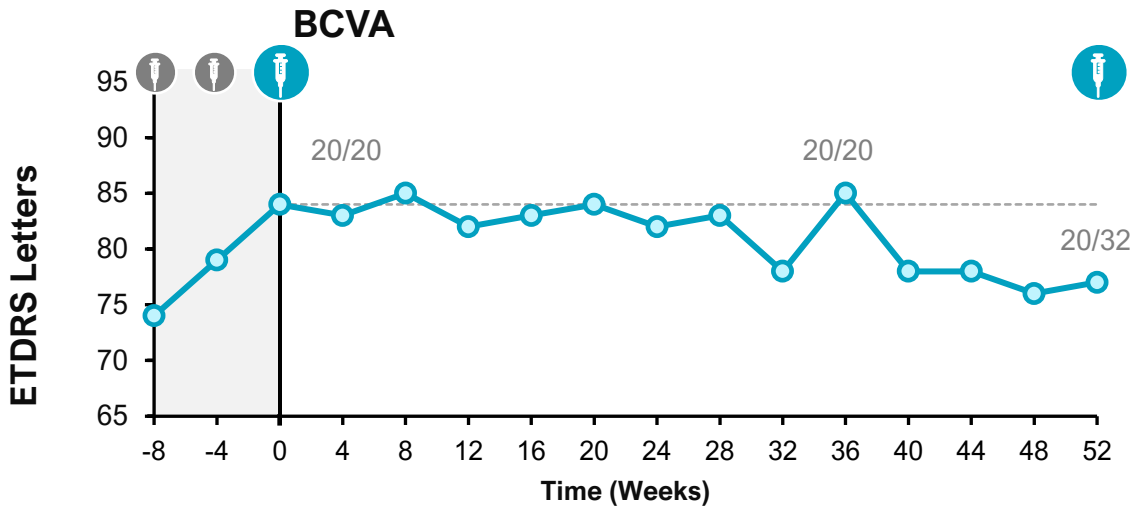
SOL-1

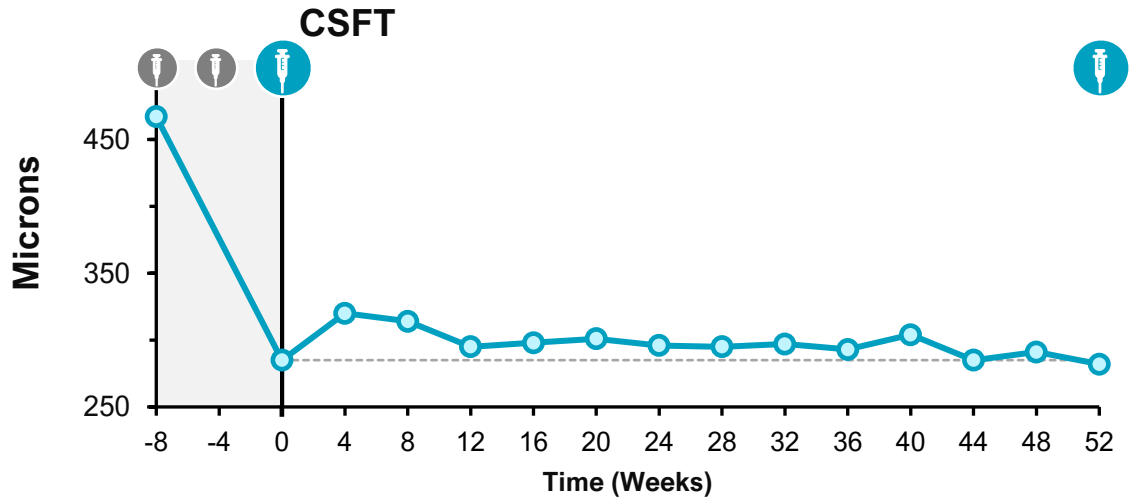
Clinical Evidence

Jeffrey Heier, MD

OCULAR THERAPEUTIX Retina experience redefined

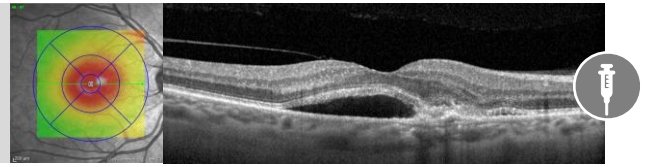
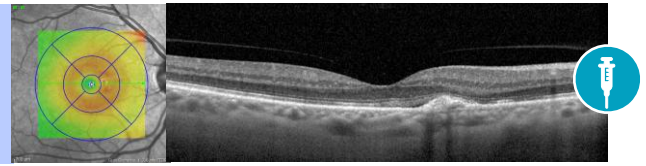
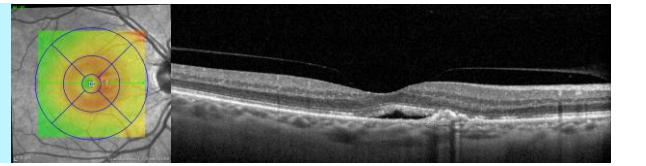
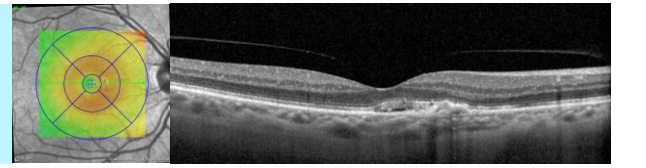
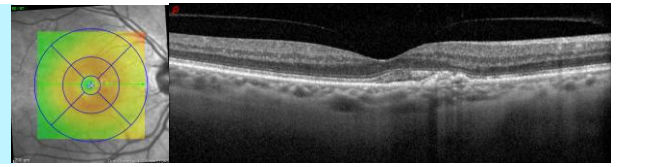
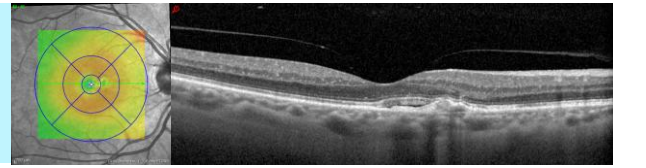
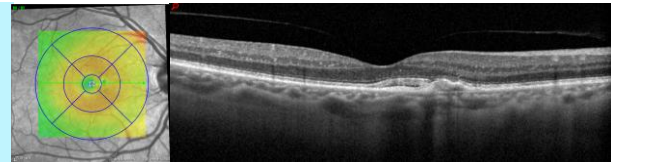
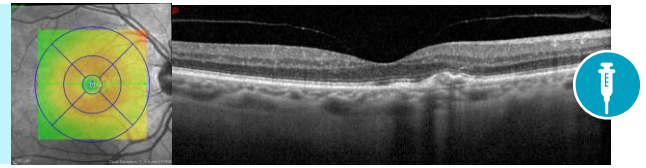
OTX-TKI Case 1





Screening Aflibercept (2mg)

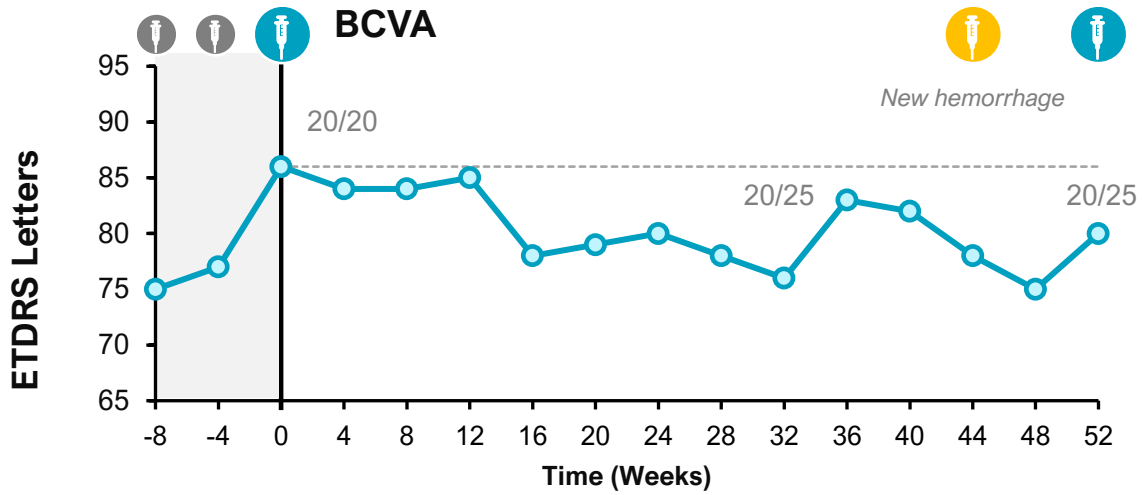
OTX-TKI (0.45mg)

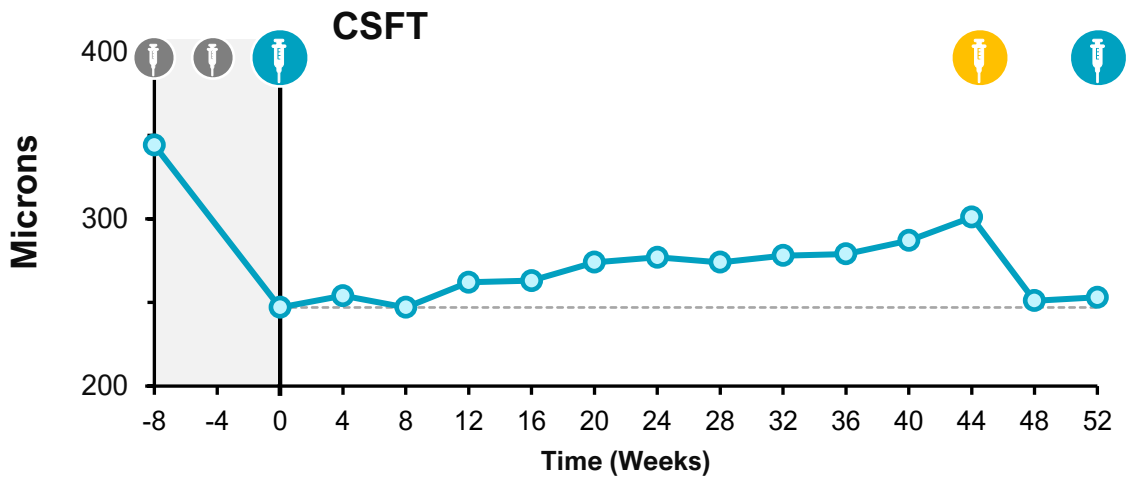
-8 Weeks	**BCVA:** 74 Ltrs (-10) **CSFT:** 467 µm	
Baseline	**BCVA:** 84 Ltrs *Snellen: 20/20* **CSFT:** 285 µm	
Week 4	**BCVA (Δ):** 83 (-1) Ltrs **CSFT (Δ):** 320 (+35) µm	
Week 12	**BCVA (Δ):** 82 (-2) Ltrs **CSFT (Δ):** 295 (+10) µm	
Week 24	**BCVA (Δ):** 82 (-2) Ltrs **CSFT (Δ):** 296 (+11) µm	
Week 36	**BCVA (Δ):** 85 (+1) Ltrs *Snellen: 20/20* **CSFT (Δ):** 293 (+8) µm	
Week 44	**BCVA (Δ):** 78 (-6) Ltrs **CSFT (Δ):** 285 (0) µm	
Week 52	**BCVA (Δ):** 77 (-7) Ltrs *Snellen: 20/32* **CSFT (Δ):** 282 (-3) µm	

OCULAR THERAPEUTIX Retina experience redefined™

Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

OTX-TKI Case 2

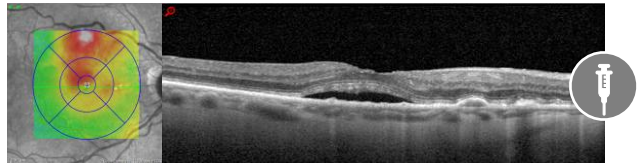
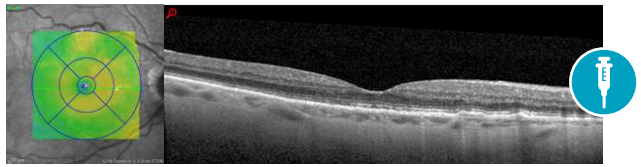
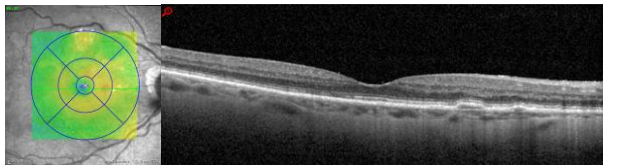
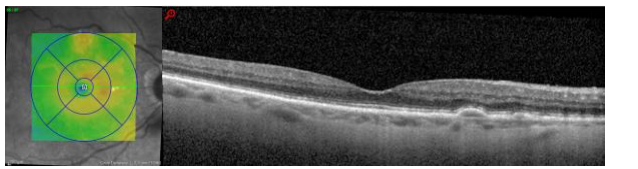
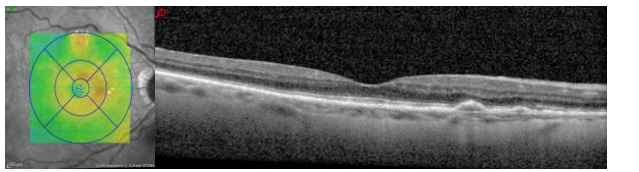
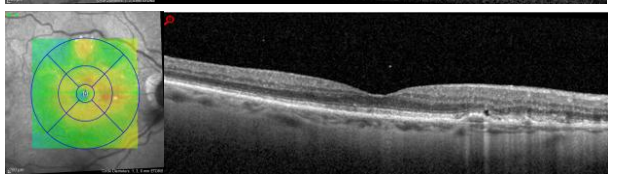
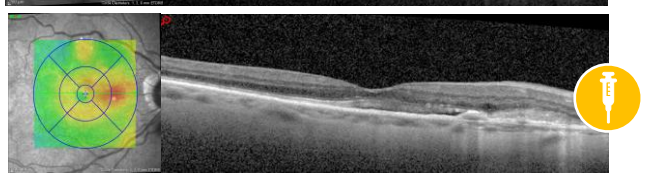
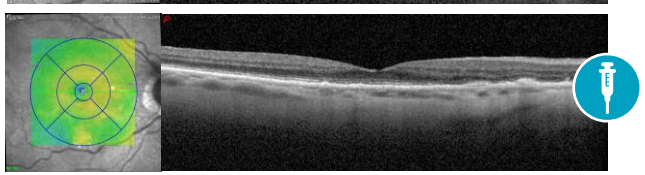




Screening Aflibercept (2mg)

OTX-TKI (0.45mg)

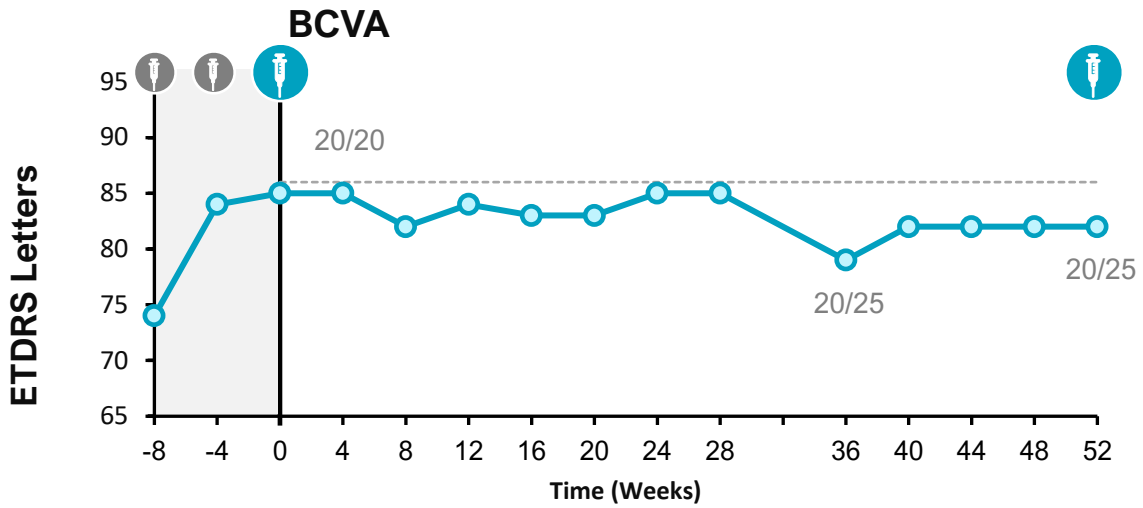
Per-Protocol Rescue Aflibercept (2mg)

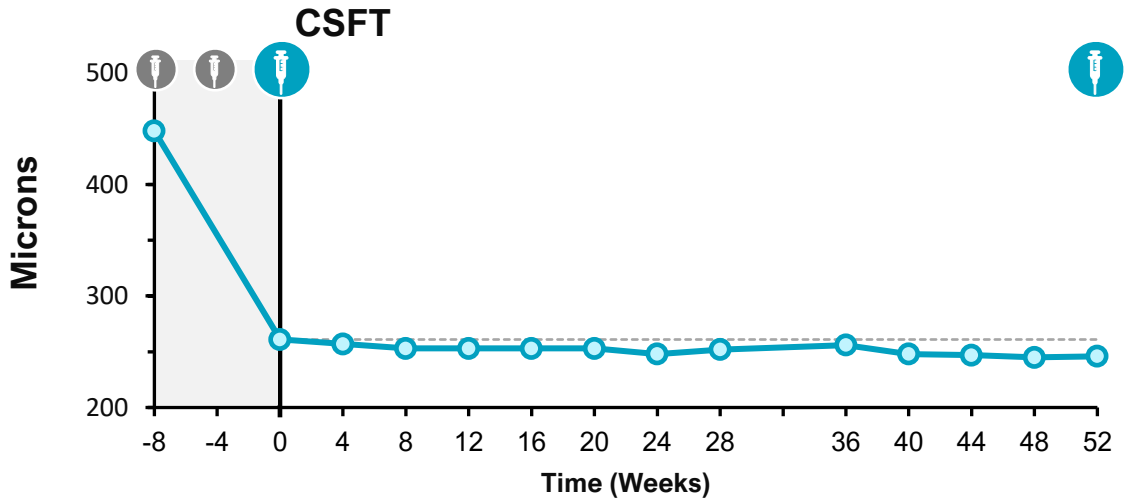
-8 Weeks	**BCVA:** 75 Ltrs **CSFT:** 344 µm	
Baseline	**BCVA:** 86 Ltrs *Snellen: 20/20* **CSFT:** 247 µm	
Week 4	**BCVA (Δ):** 84 (-2) Ltrs **CSFT (Δ):** 254 (+7) µm	
Week 12	**BCVA (Δ):** 85 (-1) Ltrs **CSFT (Δ):** 262 (+15) µm	
Week 24	**BCVA (Δ):** 80 (-6) Ltrs **CSFT (Δ):** 277 (+30) µm	
Week 36	**BCVA (Δ):** 83 (-3) Ltrs *Snellen: 20/25* **CSFT (Δ):** 279 (+32) µm	
Week 44	**BCVA (Δ):** 78 (-8) Ltrs **CSFT (Δ):** 301 (+54) µm	
Week 52	**BCVA (Δ):** 80 (-6) Ltrs *Snellen: 20/25* **CSFT (Δ):** 253 (+6) µm	

OCULAR THERAPEUTIX Retina experience redefined™

Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

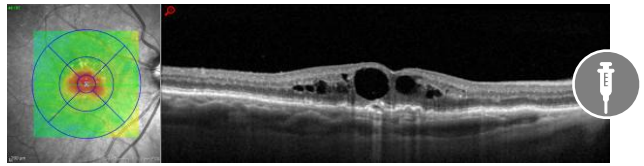
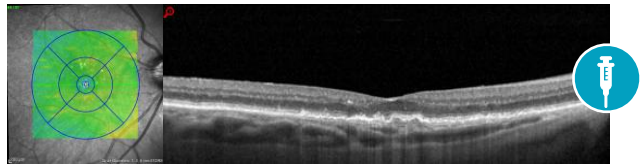
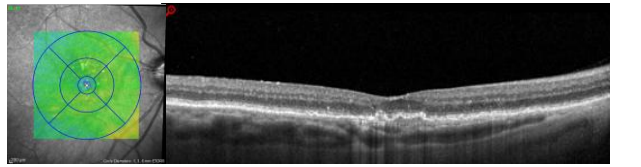
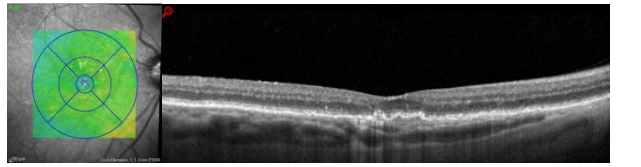
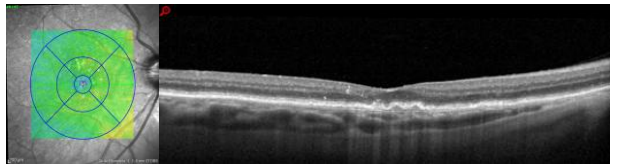
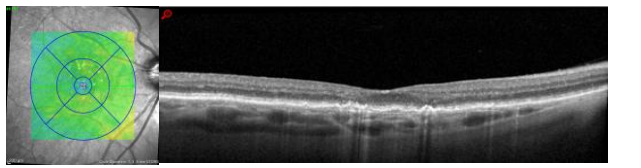
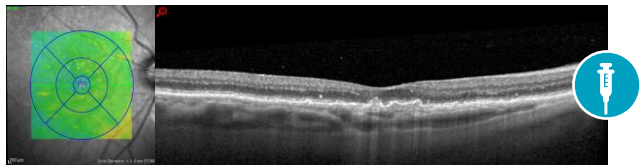
OTX-TKI Case 3





Screening
Aflibercept (2mg)

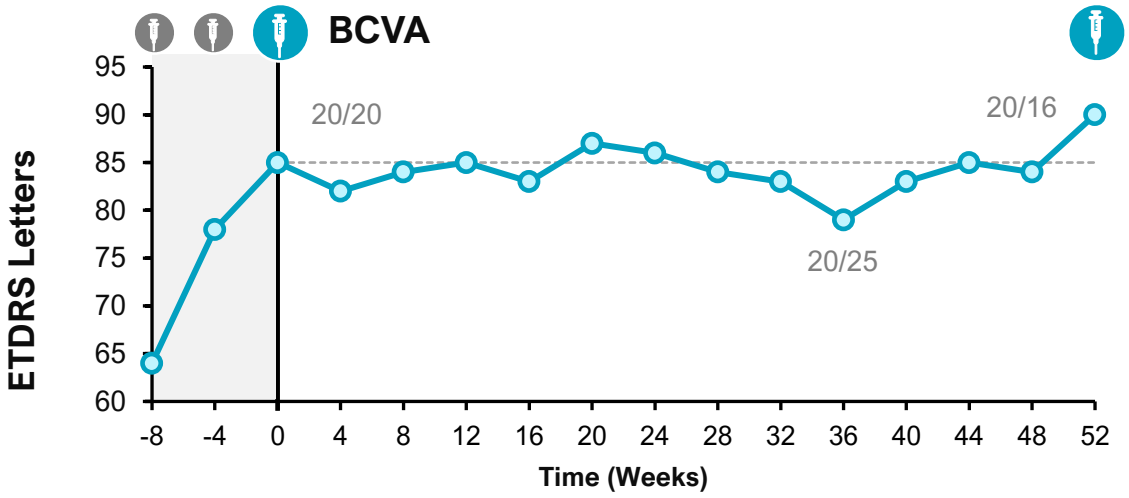
OTX-TKI
(0.45mg)

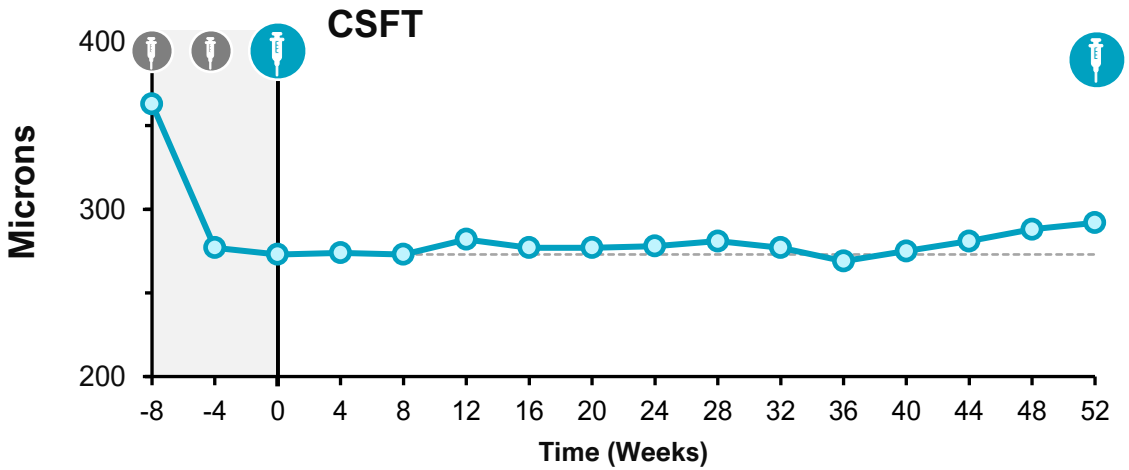
-8 Weeks	**BCVA:** 74 Ltrs **CSFT:** 448 µm	
Baseline	**BCVA:** 85 Ltrs *Snellen: 20/20* **CSFT:** 261 µm	
Week 4	**BCVA (Δ):** 85 (0) Ltrs **CSFT (Δ):** 257 (-4) µm	
Week 12	**BCVA (Δ):** 84 (-1) Ltrs **CSFT (Δ):** 253 (-8) µm	
Week 24	**BCVA (Δ):** 85 (0) Ltrs **CSFT (Δ):** 248 (-13) µm	
Week 36	**BCVA (Δ):** 79 (-6) Ltrs *Snellen: 20/25* **CSFT (Δ):** 256 (-5) µm	
Week 52	**BCVA (Δ):** 82 (-3) Ltrs *Snellen: 20/25* **CSFT (Δ):** 246 (-15) µm	

OCULAR THERAPEUTIX Retina experience redefined™

Subject missed Week 32 visit
Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

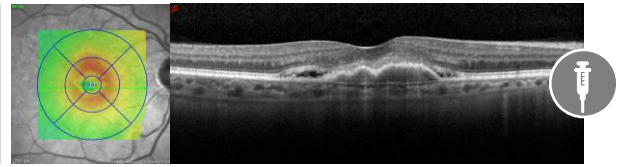
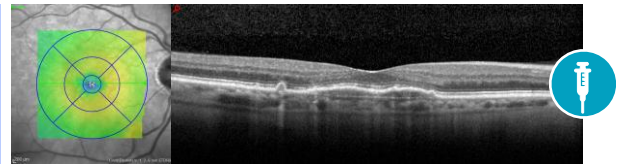
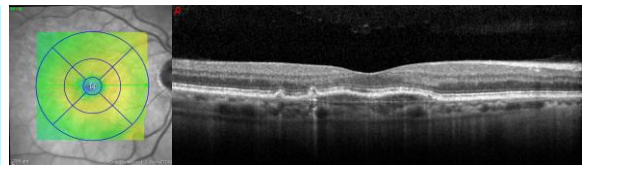
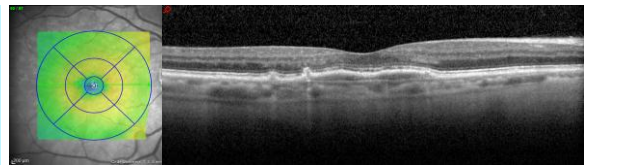
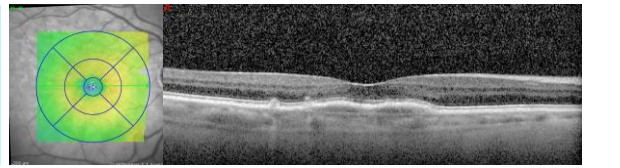
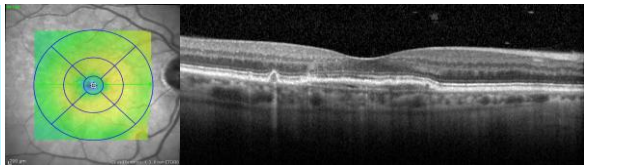
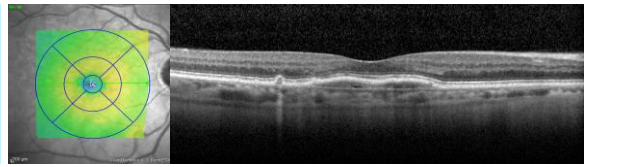
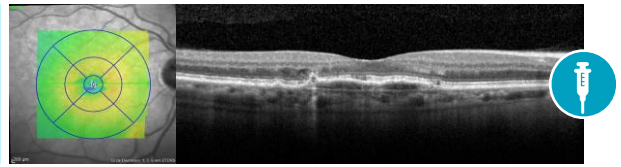
OTX-TKI Case 4





Screening
Aflibercept (2mg)

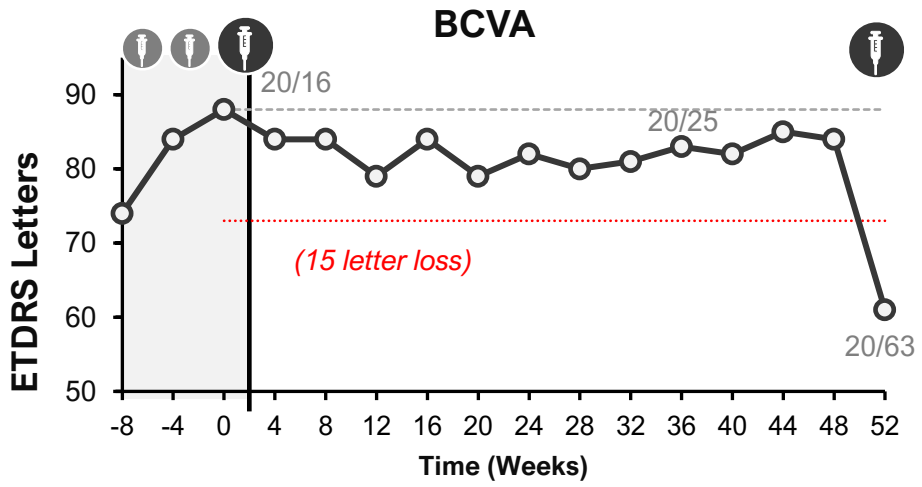
OTX-TKI
(0.45mg)

-8 Weeks	**BCVA:** 64 Ltrs **CSFT:** 363 µm	
Baseline	**BCVA:** 85 Ltrs *Snellen: 20/20* **CSFT:** 273 µm	
Week 4	**BCVA (Δ):** 82 (-3) Ltrs **CSFT (Δ):** 274 (+1) µm	
Week 16	**BCVA (Δ):** 83 (-2) Ltrs **CSFT (Δ):** 277 (+4) µm	
Week 24	**BCVA (Δ):** 86 (+1) Ltrs **CSFT (Δ):** 278 (+5) µm	
Week 36	**BCVA (Δ):** 79 (-6) Ltrs *Snellen: 20/26* **CSFT (Δ):** 269 (-4) µm	
Week 44	**BCVA (Δ):** 85 (0) Ltrs **CSFT (Δ):** 281 (+8) µm	
Week 52	**BCVA (Δ):** 90 (+5) Ltrs *Snellen: 20/16* **CSFT (Δ):** 292 (+19) µm	

OCULAR THERAPEUTIX Retina experience redefined™

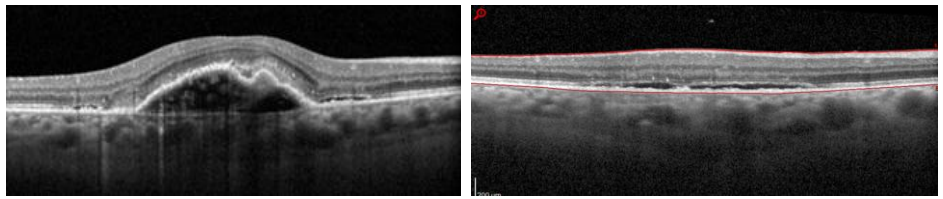
Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

Aflibercept Case 1



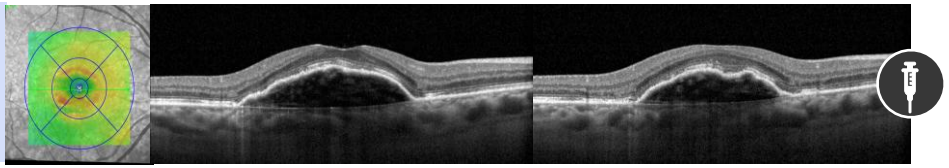
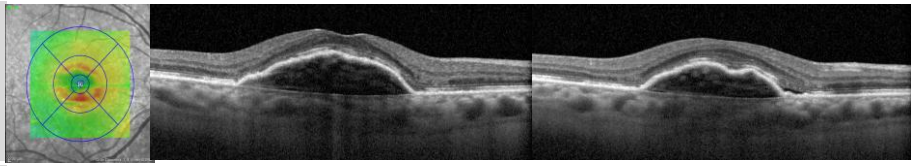
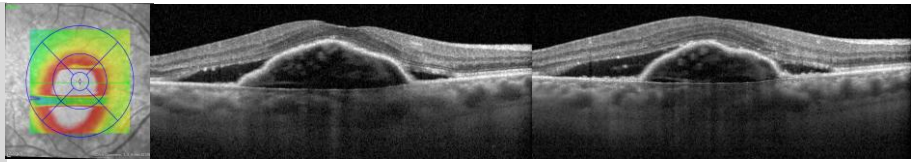
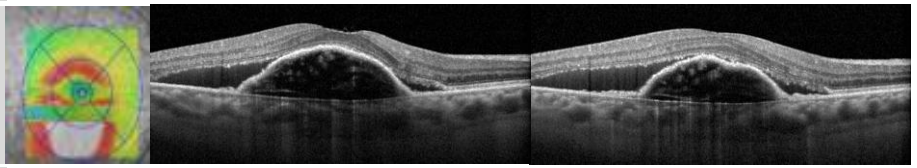
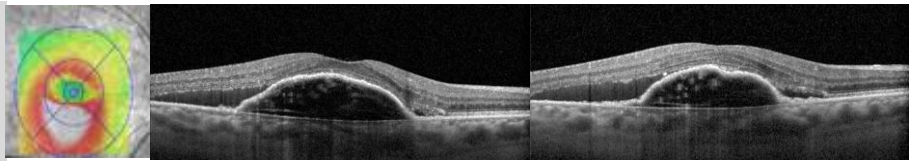
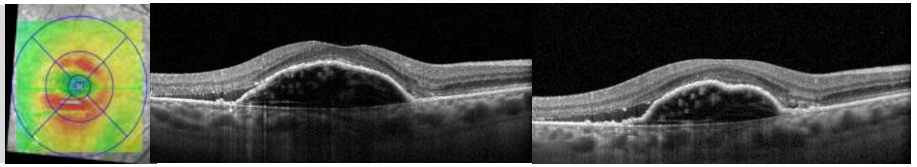
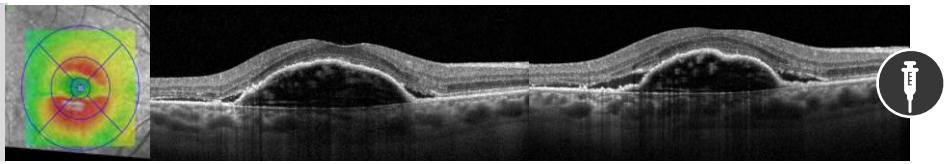
-8 Weeks

BCVA: 74 Ltrs **CSFT:** 227 µm



Screening Aflibercept (2mg)

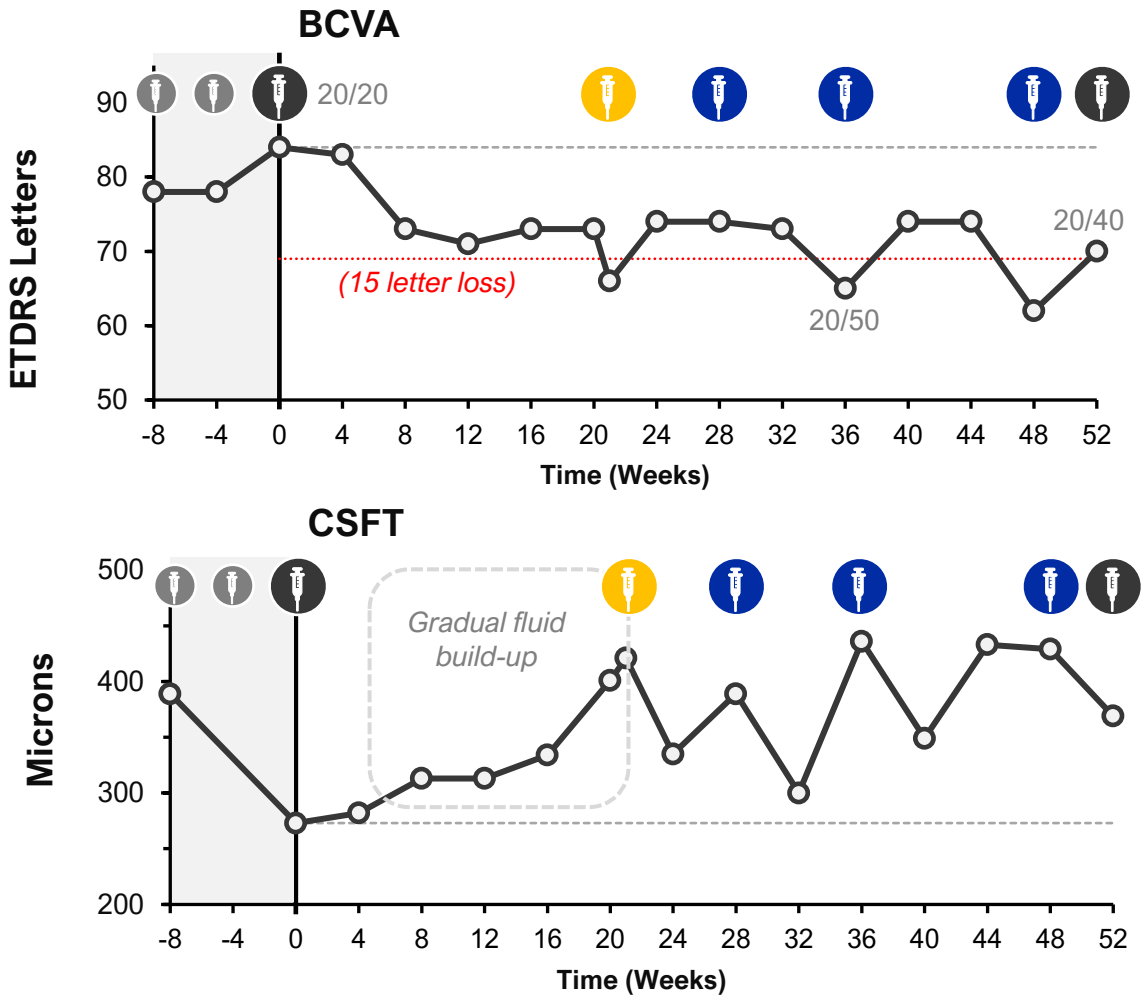
Study Aflibercept (2 mg)

Baseline	**BCVA:** 88 Ltrs *Snellen: 20/16* **CSFT:** 210 µm	
Week 4	**BCVA (Δ):** 84 (-4) Ltrs **CSFT (Δ):** 213 (+3) µm	
Week 12	**BCVA (Δ):** 79 (-9) Ltrs **CSFT (Δ):** 208 (-2) µm	
Week 24	**BCVA (Δ):** 82 (-6) Ltrs **CSFT (Δ):** 209 (-1) µm	
Week 36	**BCVA (Δ):** 83 (-5) Ltrs *Snellen: 20/25* **CSFT (Δ):** 207 (-3) µm	
Week 48	**BCVA (Δ):** 84 (-4) Ltrs **CSFT (Δ):** 203 (-7) µm	
Week 52	**BCVA (Δ):** 61 (-27) Ltrs *Snellen: 20/63* **CSFT (Δ):** 204 (-6) µm	

OCULAR THERAPEUTIX Retina experience redefined™

Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

Aflibercept Case 2

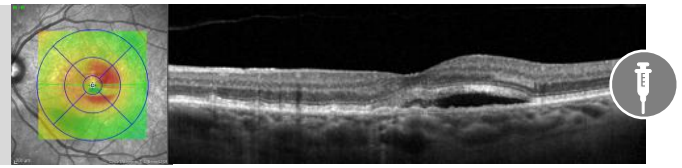
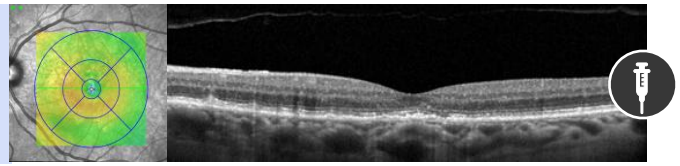
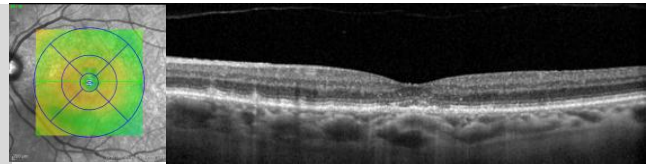
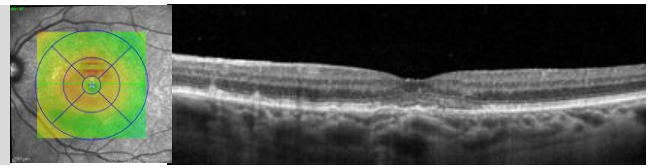
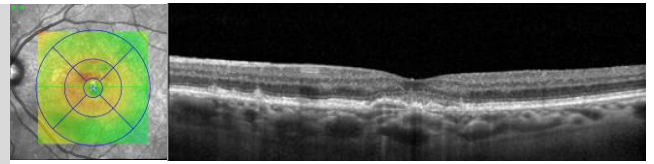
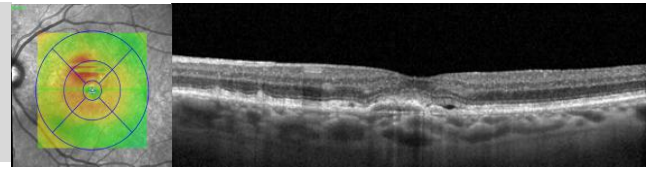
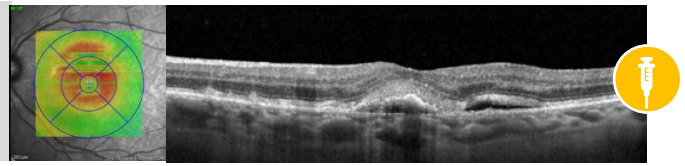


Screening Aflibercept (2mg)

Study Aflibercept (2 mg)

Per-Protocol Rescue Aflibercept (2mg)

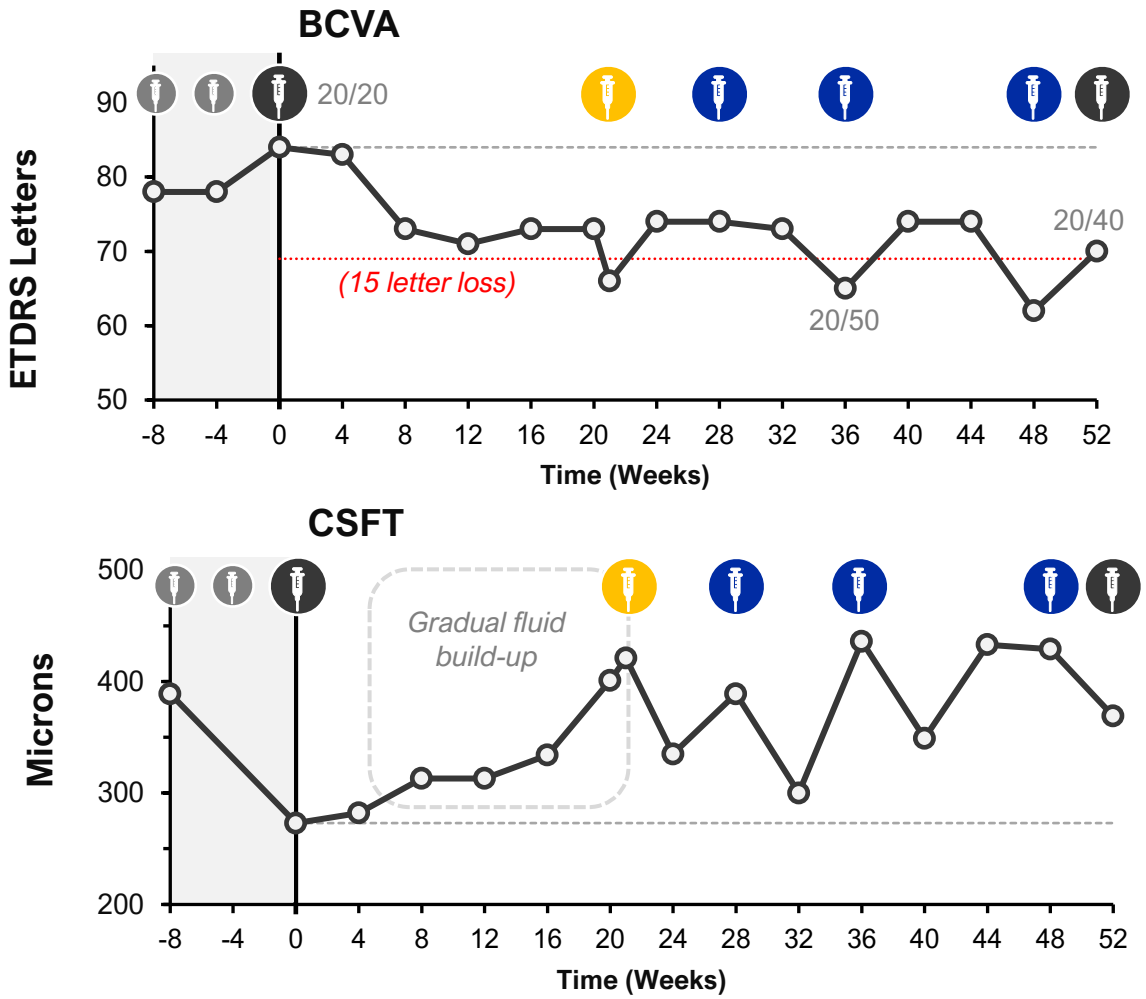
Investigator Discretion Rescue

-8 Weeks	**BCVA:** 78 Ltrs **CSFT:** 389 µm	
Baseline	**BCVA:** 84 Ltrs *Snellen: 20/20* **CSFT:** 273 µm	
Week 4	**BCVA (Δ):** 83 (-1) Ltrs **CSFT (Δ):** 282 (+9) µm	
Week 8	**BCVA (Δ):** 73 (-11) Ltrs **CSFT (Δ):** 313 (+40) µm	
Week 12	**BCVA (Δ):** 71 (-13) Ltrs **CSFT (Δ):** 313 (+40) µm	
Week 16	**BCVA (Δ):** 73 (-11) Ltrs **CSFT (Δ):** 334 (+61) µm	
Week 21 *unscheduled*	**BCVA (Δ):** 66 (-18) Ltrs **CSFT (Δ):** 421 (+148) µm	

OCULAR THERAPEUTIX Retina experience redefined™

Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

Aflibercept Case 2

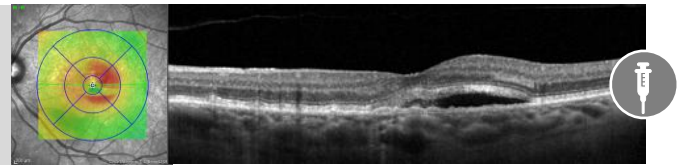
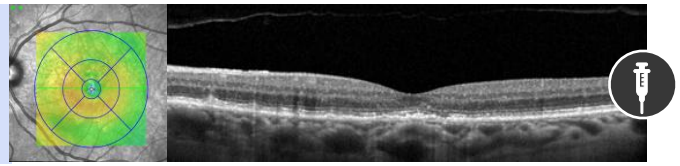
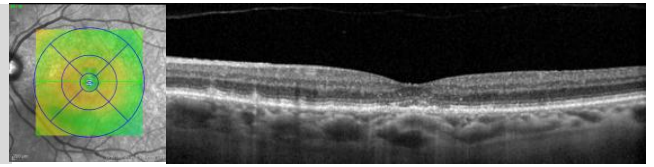
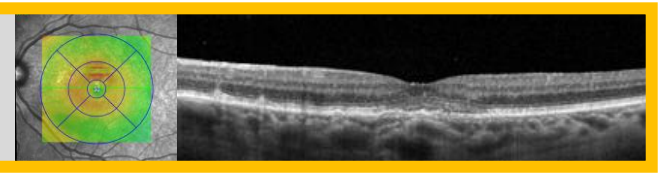
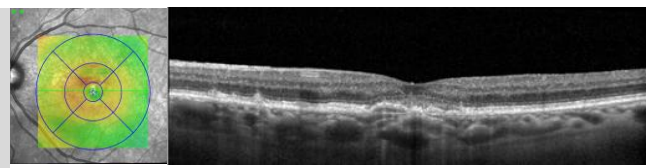
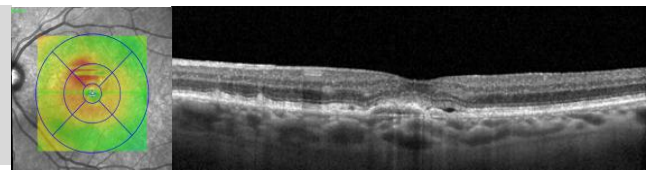
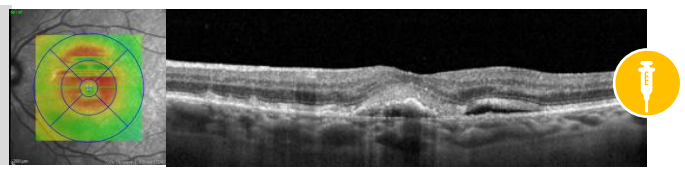


Screening Aflibercept (2mg)

Study Aflibercept (2 mg)

Per-Protocol Rescue Aflibercept (2mg)

Investigator Discretion Rescue

-8 Weeks	**BCVA:** 78 Ltrs **CSFT:** 389 µm	
Baseline	**BCVA:** 84 Ltrs *Snellen: 20/20* **CSFT:** 273 µm	
Week 4	**BCVA (Δ):** 83 (-1) Ltrs **CSFT (Δ):** 282 (+9) µm	
Week 8	**BCVA (Δ):** 73 (-11) Ltrs **CSFT (Δ):** 313 (+40) µm	
Week 12	**BCVA (Δ):** 71 (-13) Ltrs **CSFT (Δ):** 313 (+40) µm	
Week 16	**BCVA (Δ):** 73 (-11) Ltrs **CSFT (Δ):** 334 (+61) µm	
Week 21 *unscheduled*	**BCVA (Δ):** 66 (-18) Ltrs **CSFT (Δ):** 421 (+148) µm	

OCULAR THERAPEUTIX Retina experience redefined™

Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

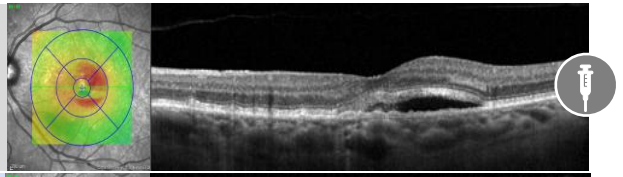
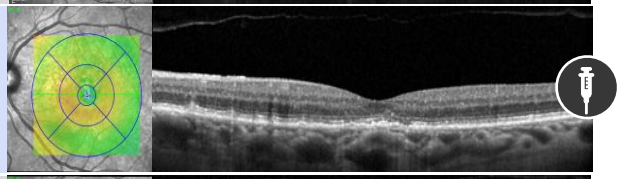
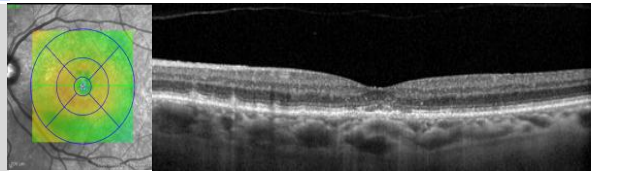
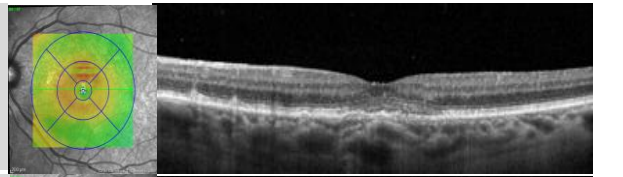
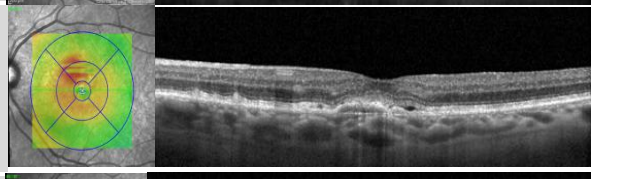
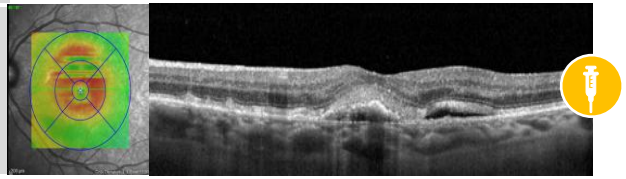
Aflibercept Case 2

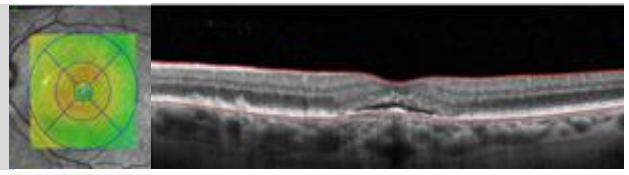
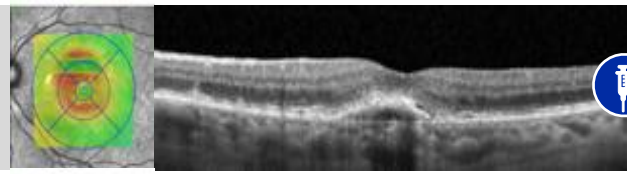
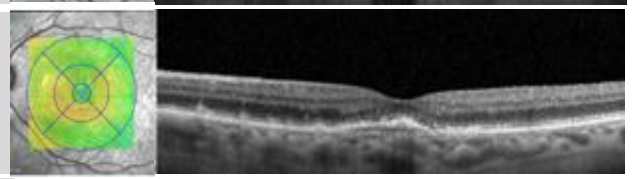
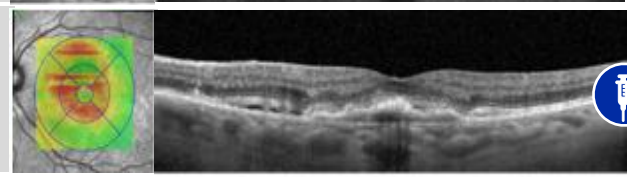
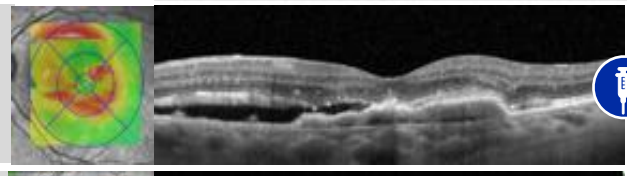
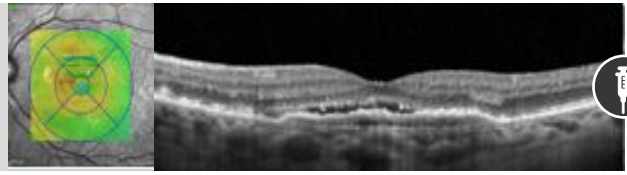
Screening Aflibercept (2mg)

Study Aflibercept (2 mg)

Per-Protocol Rescue Aflibercept (2mg)

Investigator Discretion Rescue

-8 Weeks	**BCVA:** 78 Ltrs **CSFT:** 389 µm	
Baseline	**BCVA:** 84 Ltrs *Snellen: 20/20* **CSFT:** 273 µm	
Week 4	**BCVA (Δ):** 83 (-1) Ltrs **CSFT (Δ):** 282 (+9) µm	
Week 8	**BCVA (Δ):** 73 (-11) Ltrs **CSFT (Δ):** 313 (+40) µm	
Week 16	**BCVA (Δ):** 73 (-11) Ltrs **CSFT (Δ):** 334 (+61) µm	
Week 21 *unscheduled*	**BCVA (Δ):** 66 (-18) Ltrs **CSFT (Δ):** 421 (+148) µm	

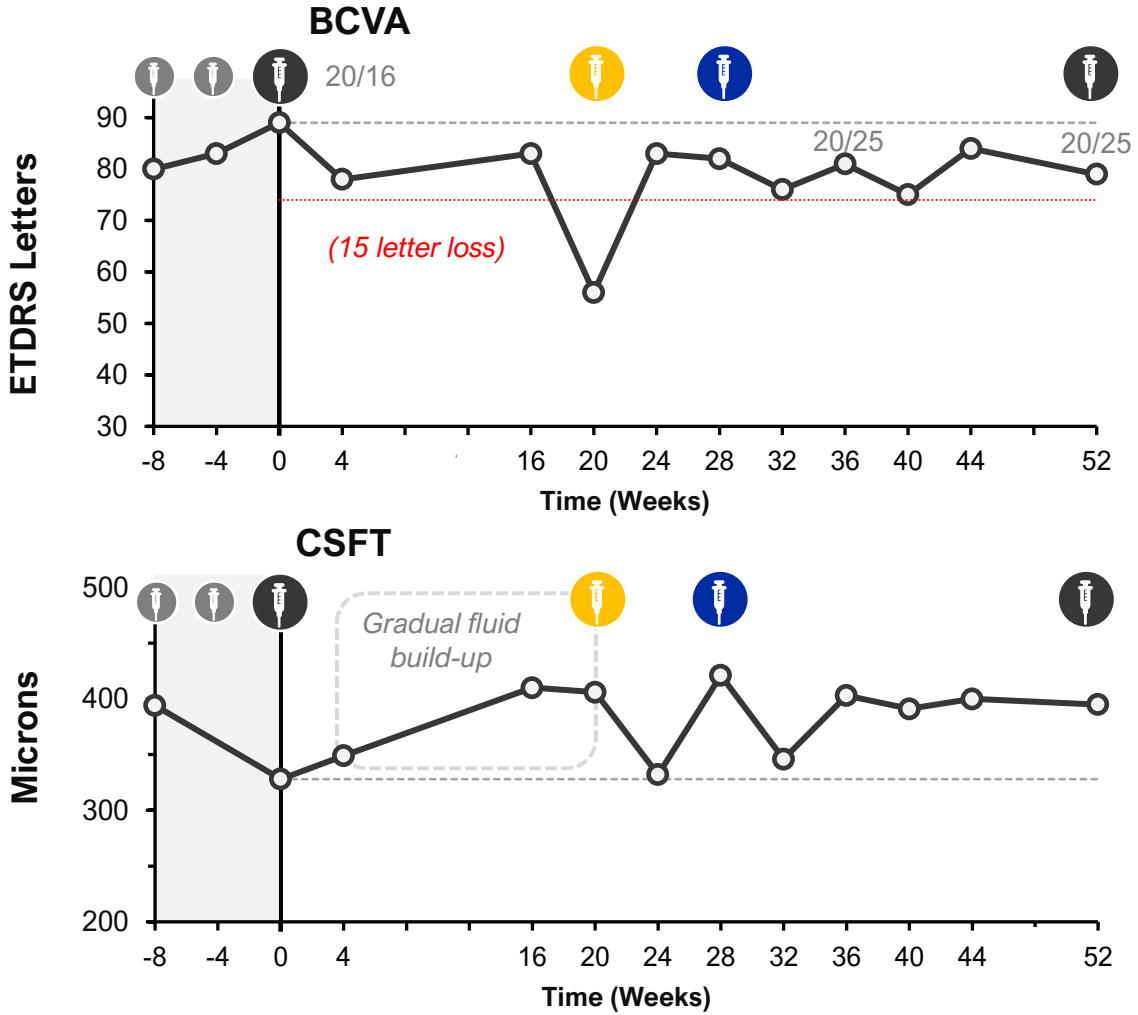
Week 24	**BCVA (Δ):** 74 (-10) Ltrs **CSFT (Δ):** 335 (+62) µm	
Week 28	**BCVA (Δ):** 74 (-10) Ltrs **CSFT (Δ):** 389 (+116) µm	
Week 32	**BCVA (Δ):** 73 (-11) Ltrs **CSFT (Δ):** 300 (+27) µm	
Week 36	**BCVA (Δ):** 65 (-19) Ltrs *Snellen: 20/50* **CSFT (Δ):** 436 (+163) µm	
Week 48	**BCVA (Δ):** 62 (-22) Ltrs **CSFT (Δ):** 429 (+156) µm	
Week 52	**BCVA (Δ):** 70 (-14) Ltrs *Snellen: 20/40* **CSFT (Δ):** 369 (+96) µm	

OCULAR THERAPEUTIX Retina experience redefined™

Case study of one subject; individual results may vary

BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

Aflibercept Case 3

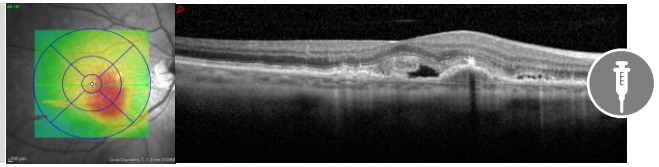
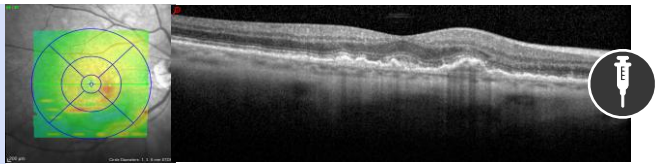
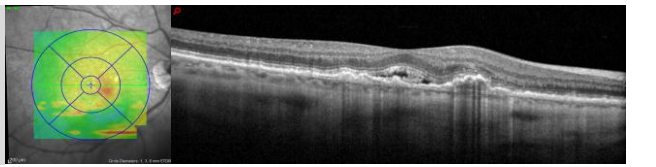
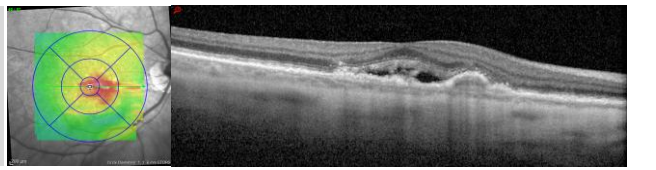
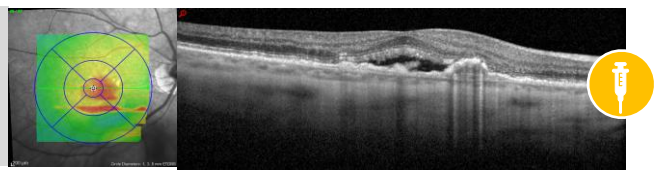
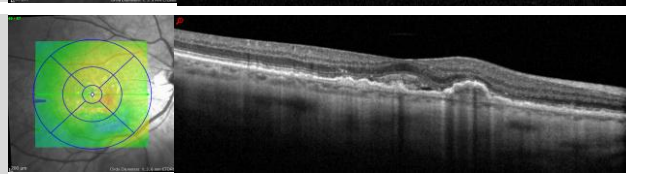
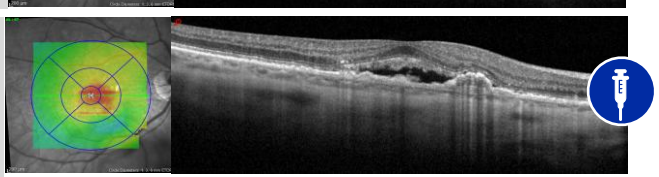
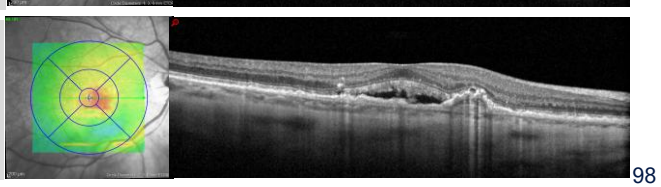


Screening Aflibercept (2mg)

Study Aflibercept (2 mg)

Per-Protocol Rescue Aflibercept (2mg)

Investigator Discretion Rescue

-8 Weeks	**BCVA:** 80 Ltrs **CSFT:** 394 µm	
Baseline	**BCVA:** 89 Ltrs *Snellen: 20/16* **CSFT:** 328 µm	
Week 4	**BCVA (Δ):** 78 (-11) Ltrs **CSFT (Δ):** 349 (+21) µm	
Week 16	**BCVA (Δ):** 83 (-6) Ltrs **CSFT (Δ):** 410 (+82) µm	
Week 20	**BCVA (Δ):** 56 **(-33)** Ltrs **CSFT (Δ):** 406 (+78) µm	
Week 24	**BCVA (Δ):** 83 (-6) Ltrs **CSFT (Δ):** 332 (+4) µm	
Week 28	**BCVA (Δ):** 82 (-7) Ltrs **CSFT (Δ):** 421 (+93) µm	
Week 36	**BCVA (Δ):** 81(-8) Ltrs *Snellen: 20/25* **CSFT (Δ):** 403 (+75) µm	

OCULAR THERAPEUTIX Retina experience redefined™

Subject missed W8/W12/W48 Visits
Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

Aflibercept Case 3

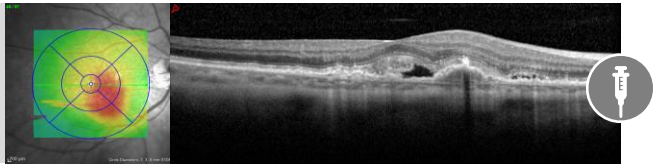
Screening Aflibercept (2mg) injection

Study Aflibercept (2 mg) administration

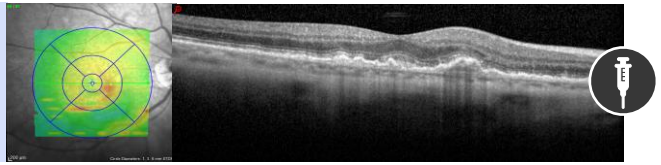
Per-Protocol Rescue Aflibercept (2mg)

Investigator Discretion Rescue

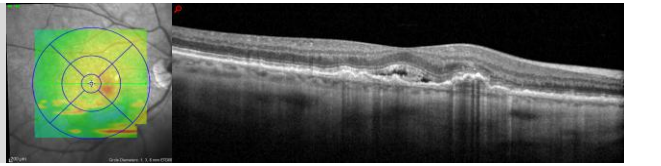
-8 Weeks
BCVA: 80 Ltrs
CSFT: 394 µm



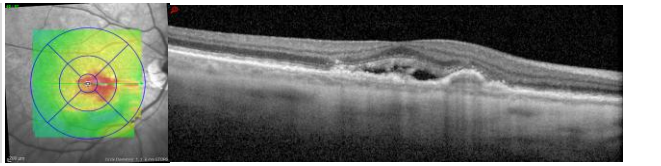
Baseline
BCVA: 89 Ltrs
Snellen: 20/16
CSFT: 328 µm



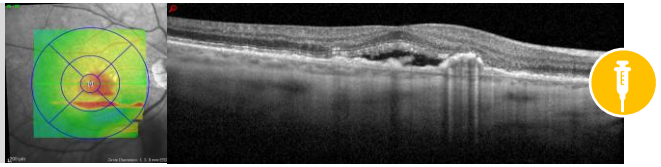
Week 4
BCVA (Δ): 78 (-11) Ltrs
CSFT (Δ): 349 (+21) µm



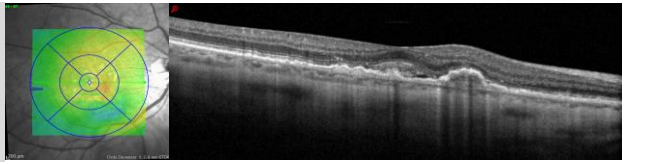
Week 16
BCVA (Δ): 83 (-6) Ltrs
CSFT (Δ): 410 (+82) µm



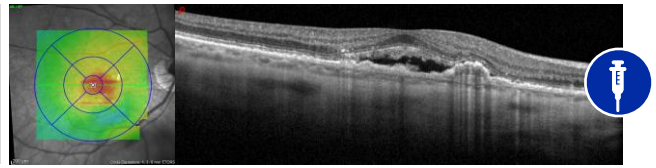
Week 20
BCVA (Δ): 56 (-33) Ltrs
CSFT (Δ): 406 (+78) µm



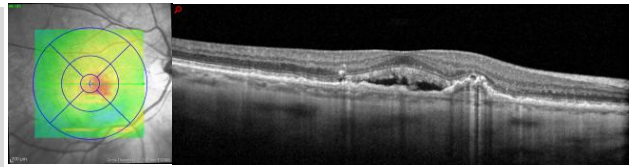
Week 24
BCVA (Δ): 83 (-6) Ltrs
CSFT (Δ): 332 (+4) µm



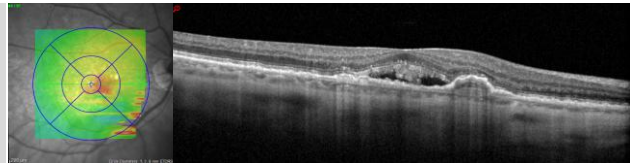
Week 28
BCVA (Δ): 82 (-7) Ltrs
CSFT (Δ): 421 (+93) µm



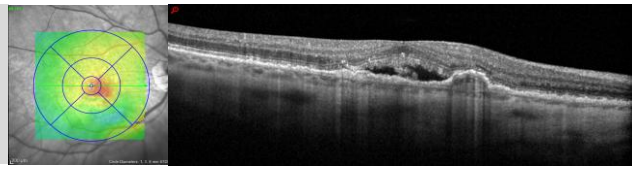
Week 36
BCVA (Δ): 81(-8) Ltrs
Snellen: 20/25
CSFT (Δ): 403 (+75) µm



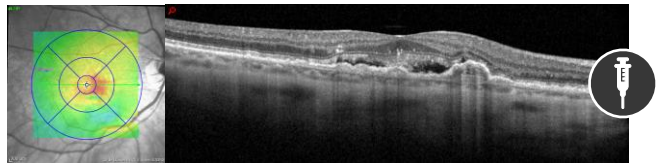
Week 40
BCVA (Δ): 75 (-14) Ltrs
CSFT (Δ): 391 (+63) µm



Week 44
BCVA (Δ): 84 (-5) Ltrs
CSFT (Δ): 400 (+72) µm



Week 52
BCVA (Δ): 79 (-10) Ltrs
Snellen: 20/25
CSFT (Δ): 395 (+67) µm



OCULAR THERAPEUTIX Retina experience redefined™

Subject missed W8/W12/W48 Visits
Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

Redefining the Management of Neovascular AMD

April 11, 2026

14th Annual Vit-Buckle Society Meeting | Las Vegas, NV

OCULAR THERAPEUTIX

Retina experience redefined™

MC-US-OTX-0218