Ocular Therapeutix 2026 Investor Day

June 17, 2026

OCULAR THERAPEUTIX

Retina experience redefined™

Forward Looking Statements and Disclaimers

Any statements in this presentation about future expectations, plans, and prospects for the Company, including the development of, regulatory status of, and regulatory submissions regarding the Company's product candidates, including the timing, design, enrollment, randomization, and conduct of the Company's ongoing Phase 3 clinical trials and long-term extension study of AXPAXLI (also called OTX-TKI) for the treatment of wet AMD and the Company's ongoing Phase 3 clinical trial for the treatment of non-proliferative diabetic retinopathy; the Company's plan and timing to submit a new drug application for AXPAXLI for the treatment of wet AMD utilizing the 505(b)(2) pathway based on Week 52 efficacy and safety data from the Company's SOL-1 clinical trial and Week 52 data from an interim safety analysis to be conducted in the Company's SOL-R clinical trial; the Company's trial designs for, and planned amendments to the clinical trial protocols of, the SOL-R clinical trial and the HELIOS-3 clinical trial; the timing of the availability of data from the SOL-R trial; the commercial potential and size of potential markets for AXPAXLI and the Company's commercialization, regulatory, and labeling strategies for AXPAXLI for the treatment of wet AMD, if approved; the potential utility of AXPAXLI; the sufficiency of the Company's cash resources; and other statements containing the words "anticipate", "believe", "designed", "estimate", "expect", "intend", "goal", "may", "might", "plan", "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, uncertainties regarding the design, timing, conduct and outcomes of the Company's ongoing clinical trials, including the Company's SOL-1 trial, SOL-R trial, HELIOS-3 trial, and SOL-X trial; the timing and costs involved in commercializing any product or product candidate that receives regulatory approval; the risk that the FDA will not agree with the Company's interpretation of the Special Protocol Assessment (SPA) for the SOL-1 trial; uncertainty as to whether the FDA will accept a new drug application for AXPAXLI on the basis of a single pivotal clinical trial, notwithstanding discussions the Company has had with the FDA regarding its planned NDA submission; uncertainty as to the minimum clinical data required to demonstrate the safety of a proposed product candidate such as AXPAXLI, 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 AXPAXLI to the degree necessary to support marketing approval for wet AMD; the risk that the FDA might not agree to the Company's design, protocol, and statistical analysis plan of any of its clinical trials for which the Company has not obtained an SPA, including the ongoing SOL-R and HELIOS-3 trials; the risk that the Company and the FDA may not agree on, or maintain agreement with respect to, the registrational pathway for any of its product candidates, including AXPAXLI; uncertainty as to whether the Company will be able to timely satisfy the FDA's other requirements for regulatory approval of AXPAXLI, 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 whether the Company's NDA will qualify for, or whether the FDA will agree to review the NDA, if accepted for filing, under the 505(b)(2) pathway, notwithstanding discussions the Company has had with the FDA regarding its planned regulatory pathway, and whether the 505(b)(2) pathway will provide any time-savings as compared to the traditional 505(b)(1) pathway; uncertainty regarding what restrictions, if any, may be imposed on the label for AXPAXLI, if approved, pending the receipt of additional clinical data or otherwise; 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, whether preliminary or interim data from a clinical trial will be predictive of final data from such trial, or whether data from a clinical trial assessing a product candidate for one indication will be predictive of results in other indications; uncertainty as to the Company's ability to retain regulatory approval of any product or product candidate that receives regulatory approval; uncertainty as to whether data from the Company's SOL-X clinical trial will demonstrate additional clinically meaningful, long-term benefits; uncertainties regarding the potential commercial advantages and/or position of the Company's product candidates; uncertainty regarding the implementation and impact of most-favored-nation and other reference pricing regimes on the commercial potential of AXPAXLI, especially in markets outside the United States; 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 estimating the Company's cash runway, future expenses, and other financial results, including its ability to fund future operations, including clinical trials; the Company's existing indebtedness and the ability of the Company's creditors to accelerate the maturity of such indebtedness upon the occurrence of certain events of default; 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.

This presentation discusses investigational product candidates in development. Their efficacy and safety profiles have not been established, and they have not been approved for marketing by the FDA or any other regulatory agency.

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Delivering Results to Better Serve Our Patients

Pravin U. Dugel, MD
Executive Chairman, President & CEO

We Continue to Execute as Promised

Bear Narrative

1H 2024

SOL-1 trial will be impossible to enroll

OCULAR RESULTS

Outstanding enrollment rate

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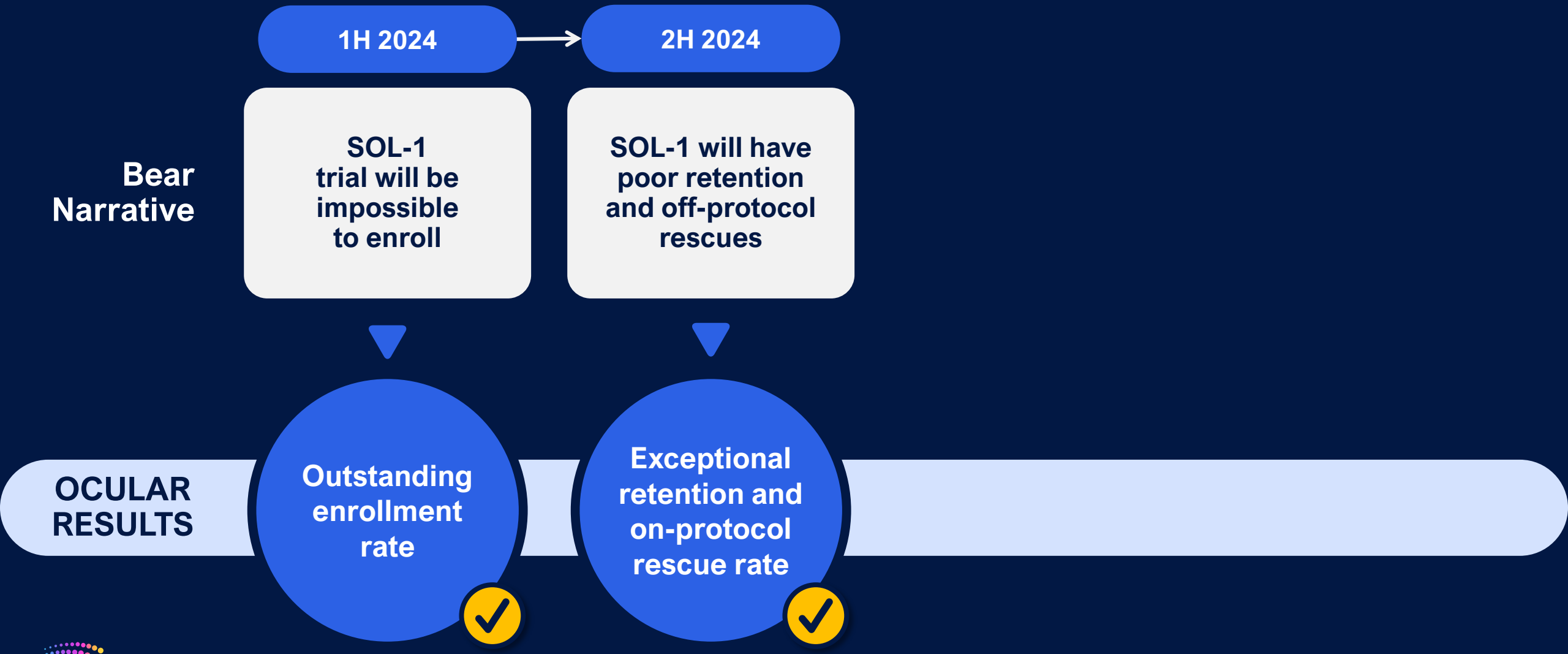
We Continue to Execute as Promised



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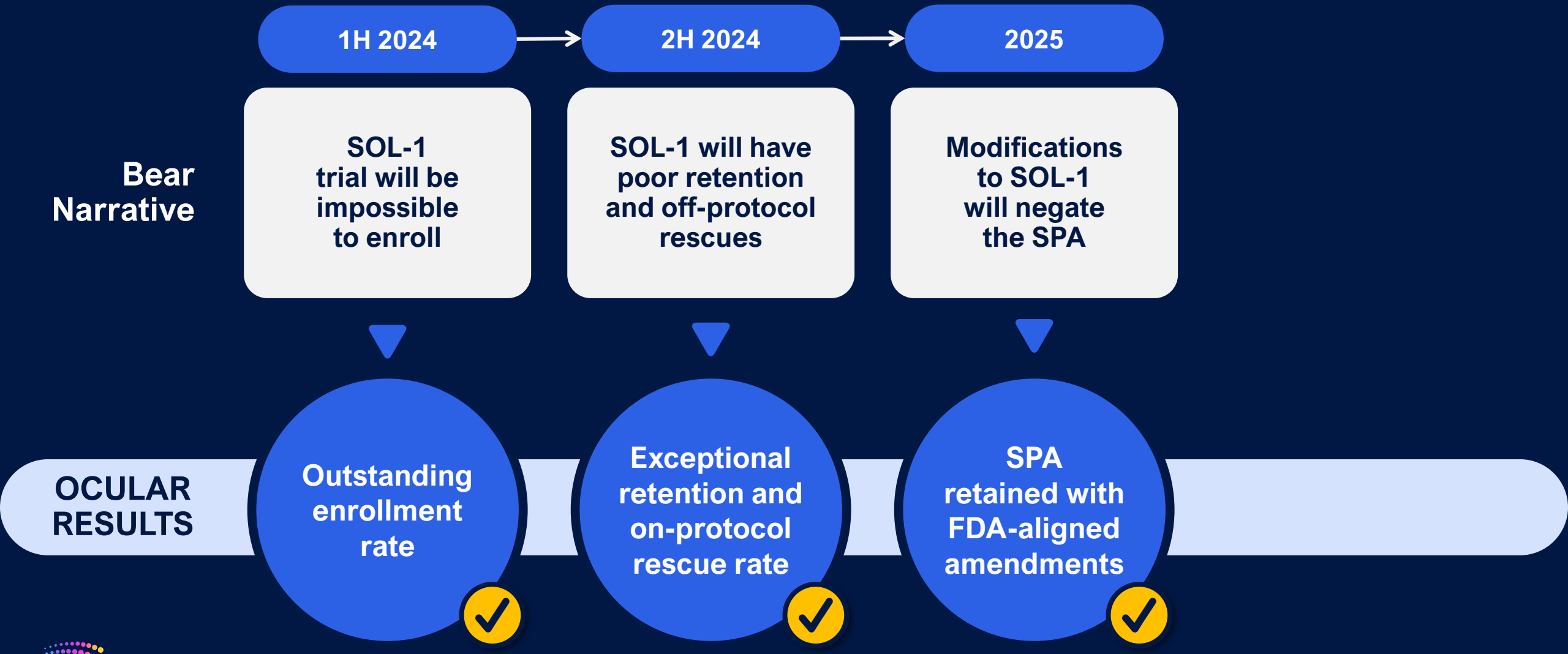
We Continue to Execute as Promised



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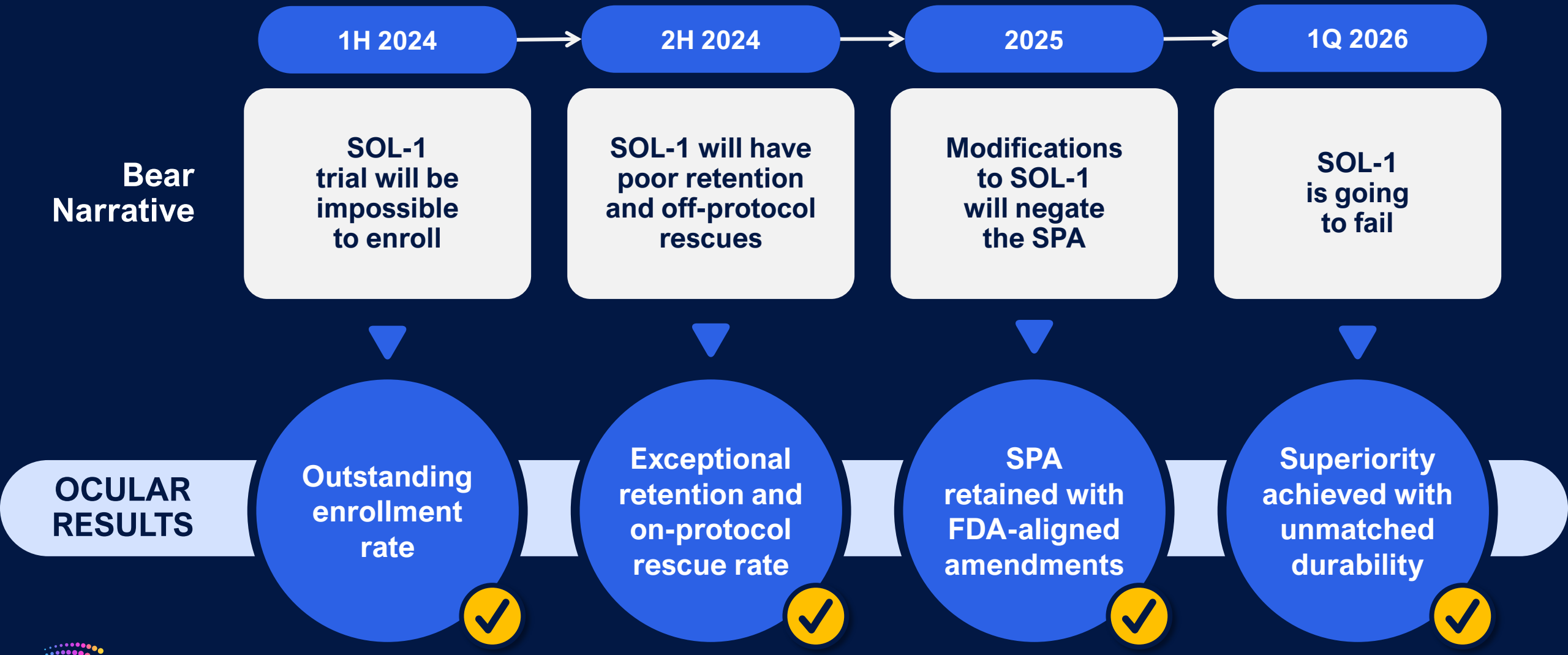
SPA, Special Protocol Assessment

We Continue to Execute as Promised



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SPA, Special Protocol Assessment

We Continue to Execute as Promised

Bear Narrative

TODAY

FDA will not accept a single trial for NDA submission

OCULAR RESULTS

Per Type C meeting minutes, will submit NDA on a single trial

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NDA, New Drug Application

We Continue to Execute as Promised

Bear Narrative

TODAY

FDA will not accept a single trial for NDA submission

OCULAR RESULTS

Per Type C meeting minutes, will submit NDA on a single trial

2025 CDER Single Trial Approvals[1]

28
Single Trial Approvals

61%
of Evaluable Approvals

48%
of Non-Orphan Approvals

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1. OCUL internal analysis of CDER's novel drugs approvals for 2025
NDA, New Drug Application; CDER, Center for Drug Evaluation and Research

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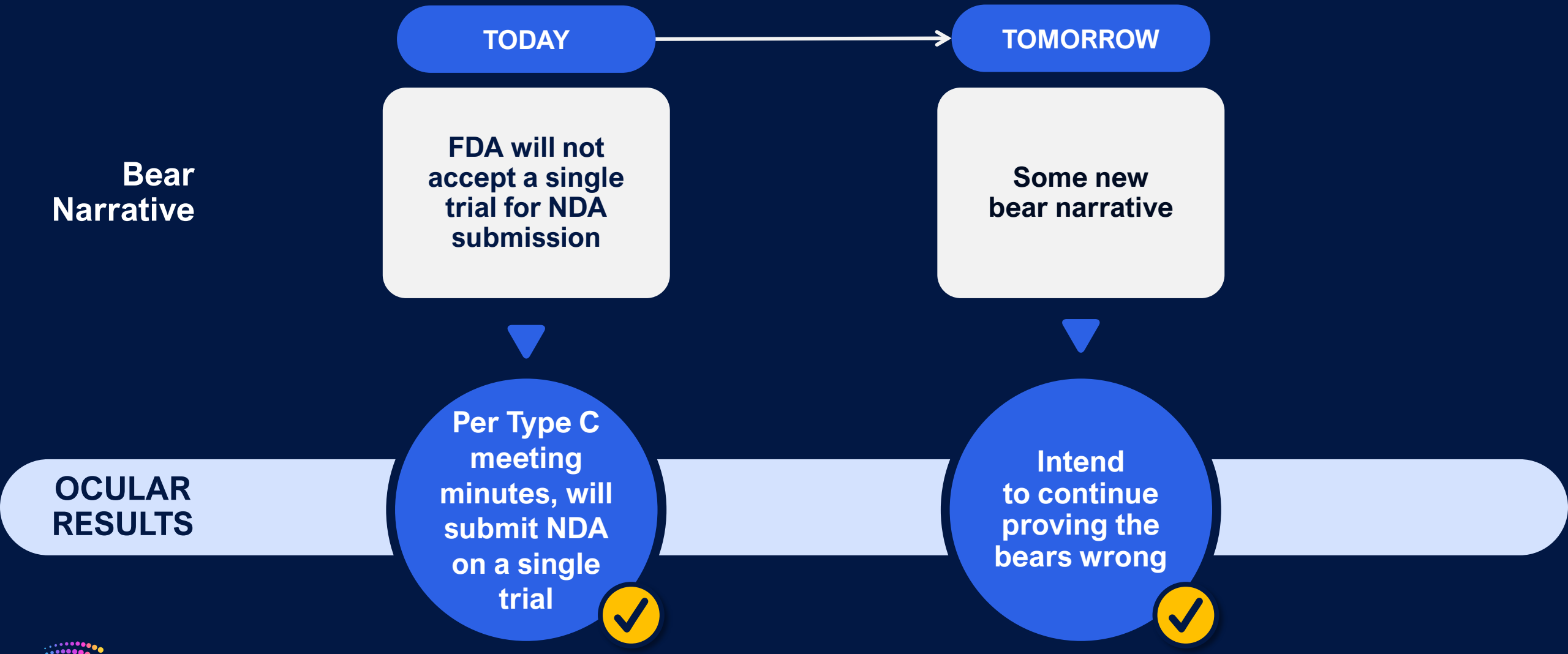

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NDA, New Drug Application

What You Will Hear Today About AXPAXLI

AXPAXLI:
Positioned to Redefine Retina

Unmatched Durability with Sustained Disease Control in SOL-1

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AXPAXLI:
Positioned to Redefine Retina

Groundbreaking Profile

Unmatched Durability with Sustained Disease Control in SOL-1

Clear Path to Market

FDA Aligned on NDA Submission in 4Q 2026

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NDA, New Drug Application

AXPAXLI:
Positioned to Redefine Retina

Unmatched Durability with Sustained Disease Control in SOL-1

FDA Aligned on NDA Submission in 4Q 2026

Why haven't we submitted the NDA yet?

- **Goal:** Fastest path to FDA approval with least regulatory risk
- Adhering to FDA guidance by including >300 subjects

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NDA, New Drug Application

AXPAXLI:
Positioned to Redefine Retina

Groundbreaking Profile

Unmatched Durability with Sustained Disease Control in SOL-1

Clear Path to Market

FDA Aligned on NDA Submission in 4Q 2026

- **Aligned w/ FDA on AXPAXLI NDA submission plan**
- **NDA to be based on SOL-1 efficacy & safety data plus interim SOL-R safety data**
- **Goal: Fastest path to FDA approval with least regulatory risk**

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NDA, New Drug Application

AXPAXLI:
Positioned to Redefine Retina

Groundbreaking Profile

Unmatched Durability with Sustained Disease Control in SOL-1

Clear Path to Market

FDA Aligned on NDA Submission in 4Q 2026

Focused on Commercial Success

Preparing to Meet Immediate Demand (if Approved)

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NDA, New Drug Application

AXPAXLI:
Positioned to Redefine Retina

- SOL-R efficacy data no longer part of NDA submission
- Will now evaluate superiority vs aflibercept (8mg) Q6M at Week 96 as a key secondary endpoint in SOL-R
- **Goal:** Best-in-disease product

Focused on Commercial Success

Preparing to Meet Immediate Demand (if Approved)

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NDA, New Drug Application; Q6M, every 6 months

AXPAXLI:
Positioned to Redefine Retina

Groundbreaking Profile

Unmatched Durability with Sustained Disease Control in SOL-1

Clear Path to Market

FDA Aligned on NDA Submission in 4Q 2026

Focused on Commercial Success

Preparing to Meet Immediate Demand (if Approved)

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NDA, New Drug Application

Renowned Retina Leaders Will Provide Unique Perspectives

Arshad M. Khanani, MD, MA, FASRS

Sierra Eye Associates
Reno, Nevada

Lejla Vajzovic, MD, FASRS

Duke University
Durham, North Carolina

Darius M. Moshfeghi, MD

Stanford University
Stanford, California

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Ocular Therapeutix 2026 Investor Day Agenda

Intro & Overview
Pravin U. Dugel, MD

SOL-1 Data & AXPAXLI Clinical Program Review
Nadia K. Waheed, MD, MPH

U.S. Regulatory Strategy in Wet AMD
Peter K. Kaiser, MD

Discussion: AXPAXLI NDA Submission Strategy
Moderator: Peter K. Kaiser, MD

Ocular Panelist: Arthur Ciociola, PhD

Preparing for a Successful Launch
David Robinson

SOL-R: Defining Non-Inferiority Success
Jeffrey S. Heier, MD

KOL Perspectives: Potential to Redefine Retina
Moderator: Jeffrey S. Heier, MD

KOLs: Arshad Khanani, MD; Lejla Vajzovic, MD; Darius Moshfeghi, MD

Summary & Takeaways
Pravin U. Dugel, MD

Audience Q&A
All

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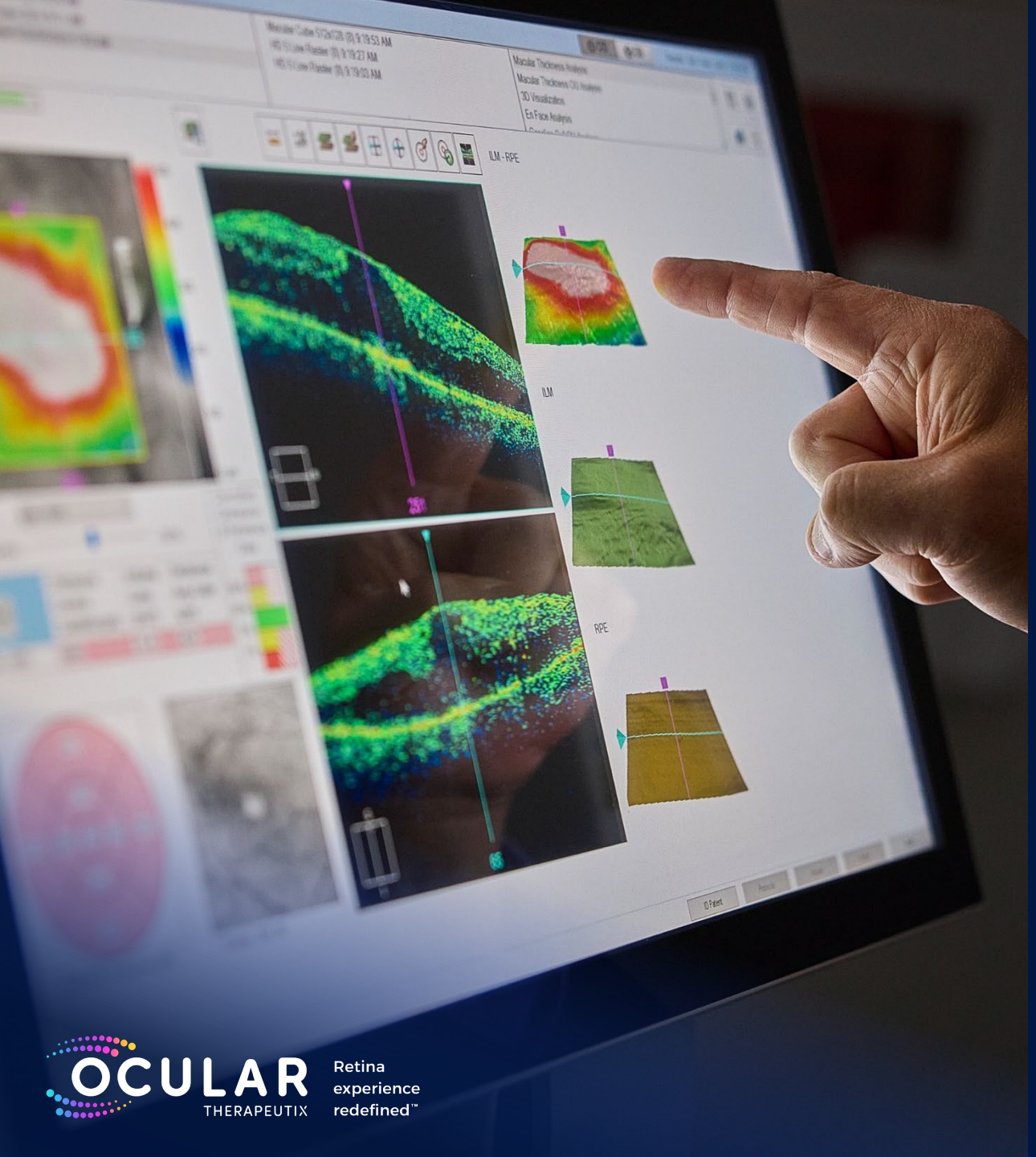

SOL-1 Data & AXPAXLI Clinical Program Review

Nadia K. Waheed, MD, MPH
Chief Medical Officer

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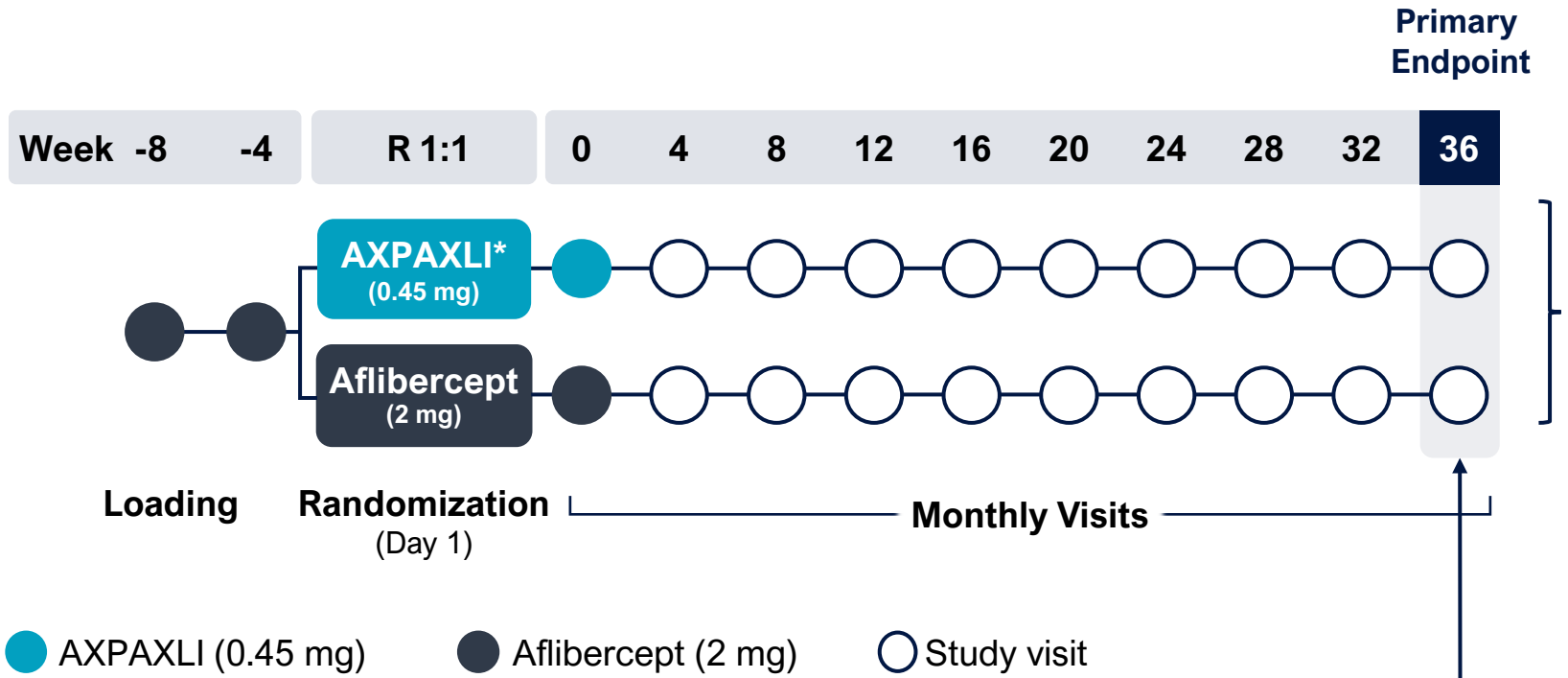
SOL-1: Superiority Trial Evaluated the Head-to-Head Durability of AXPAXLI vs Aflibercept (2 mg)

SOL-1



Head-To-Head Comparison
Single injection of AXPAXLI vs single injection of Aflibercept (2 mg)

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

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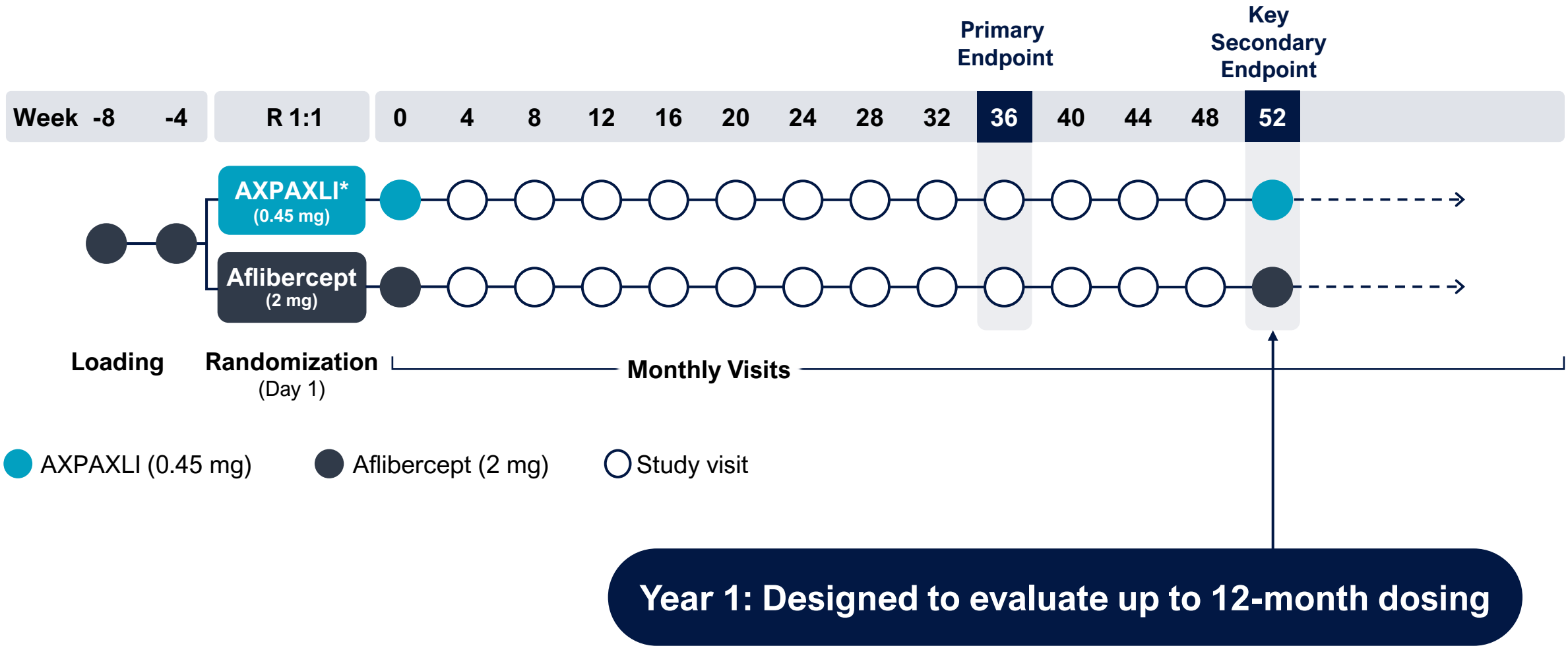
*No aflibercept injection is given at baseline; Trial subjects and designated personnel will remain masked through end of year 2
ClinicalTrials.gov identifier: NCT06223958
ETDRS, early treatment diabetic retinopathy

SOL-1: Superiority Trial Evaluated the Head-to-Head Durability of AXPAXLI vs Aflibercept (2 mg)



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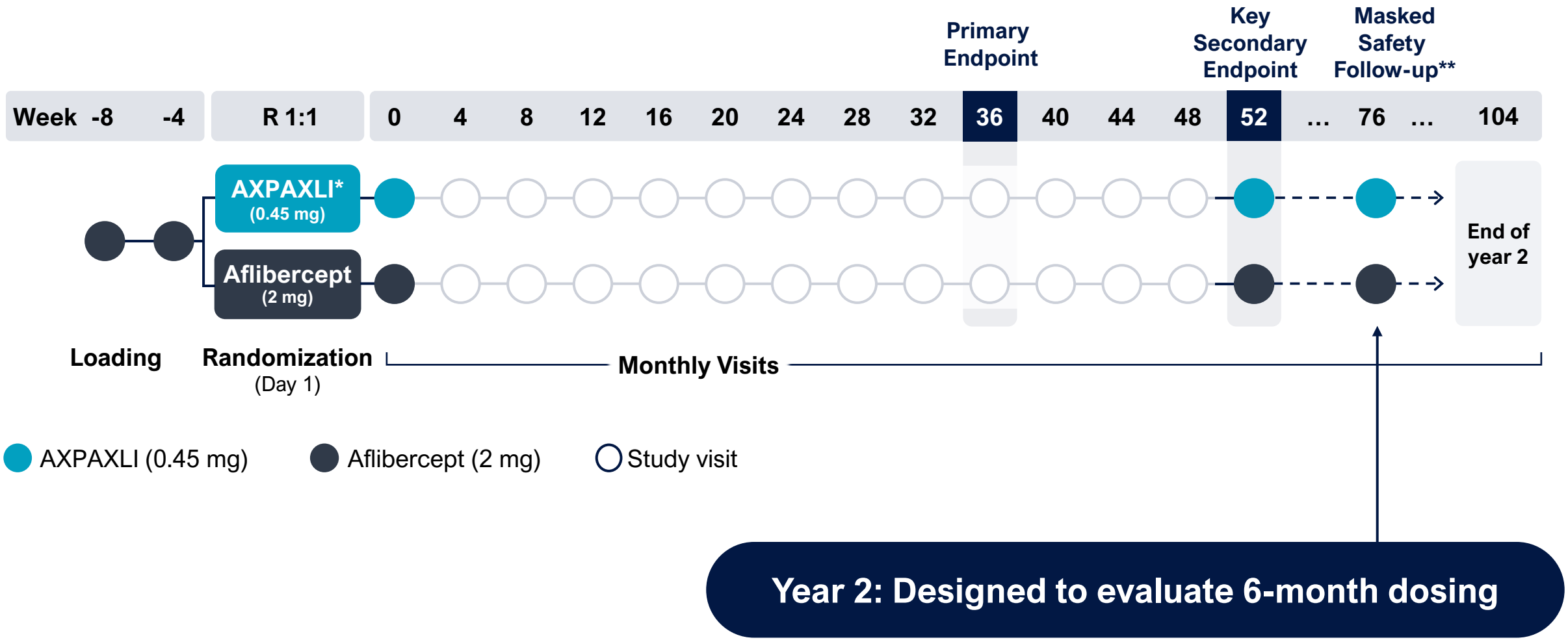

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*No aflibercept injection is given at baseline; **Trial subjects and designated personnel will remain masked through end of year 2
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SOL-1 Results Highlight AXPAXLI's Groundbreaking Product Profile

SOL-1

First Successful Superiority Trial of Novel Agent vs Approved anti-VEGF

Unmatched Durability

Sustained Disease Control

Well-Tolerated

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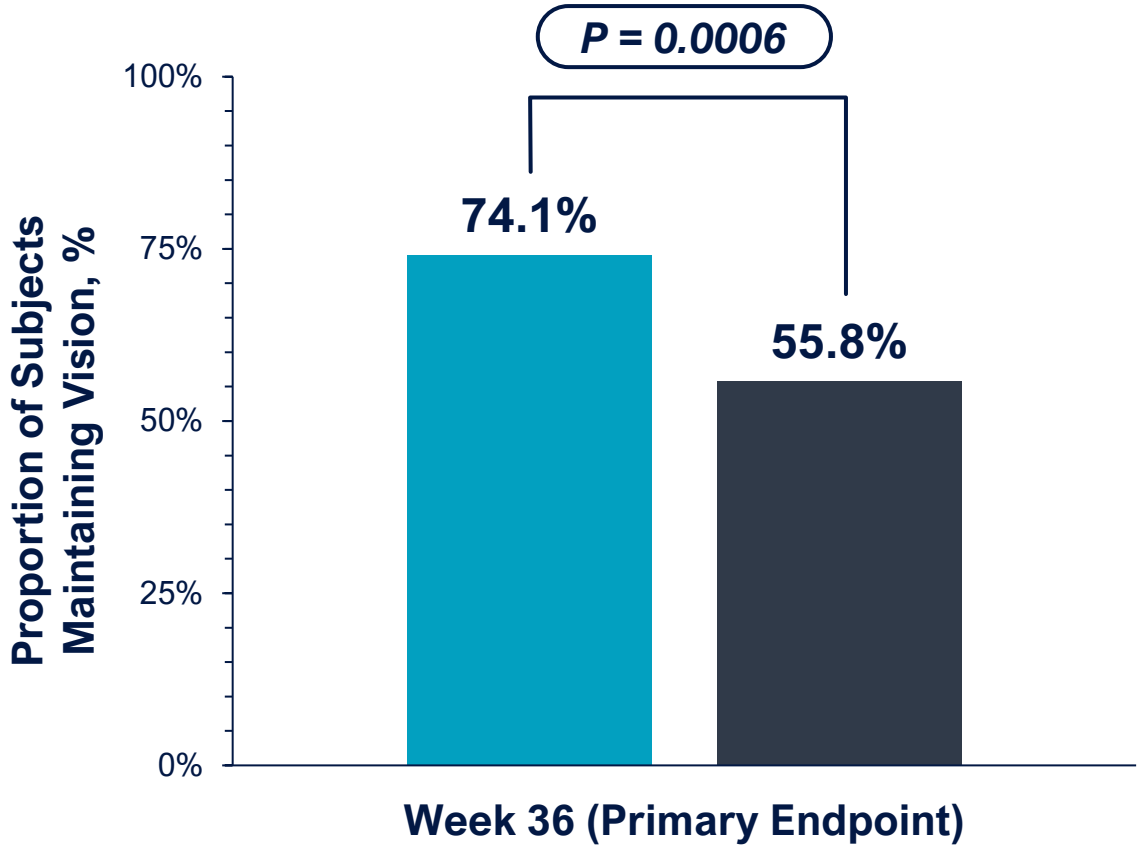
VEGF, vascular endothelial growth factor

AXPAXLI Successfully Met Superiority Primary Endpoint

Vision Maintenance* with a Single Injection of AXPAXLI at Week 36



18.3%
Observed difference

Clear benefit† with AXPAXLI vs Aflibercept 2 mg

0.0006
P value

Exceptionally high statistical significance bolsters confidence in results

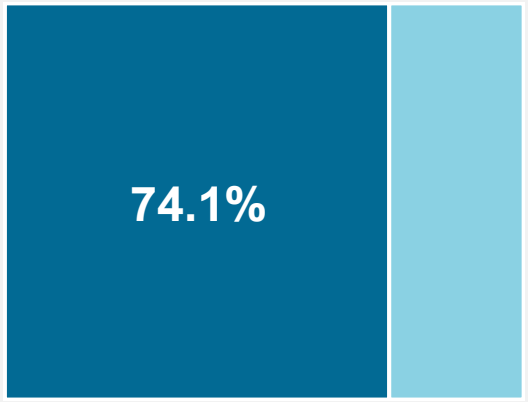
*Vision maintenance defined as <15 ETDRS letters of loss.
† 18.3% observed difference of vision maintainers at week 36 in AXPAXLI vs Aflibercept arm, 17.5% risk difference
ETDRS, early treatment diabetic retinopathy study

AXPAXLI Demonstrated Strong Potential for Annual Dosing

SOL-1

Month 9 Results

~3 of 4 AXPAXLI subjects maintained vision* with a single injection



P = 0.0006

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*Maintained vision defined as <15 ETDRS letters of loss.
ETDRS, early treatment diabetic retinopathy

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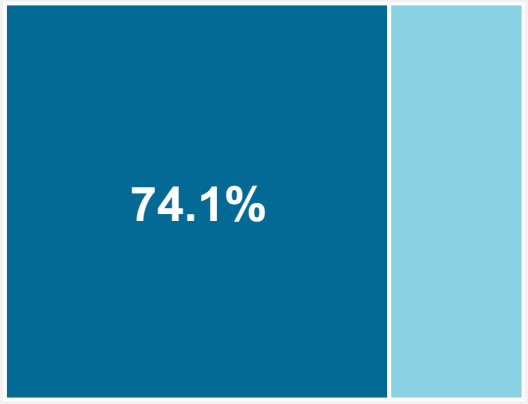
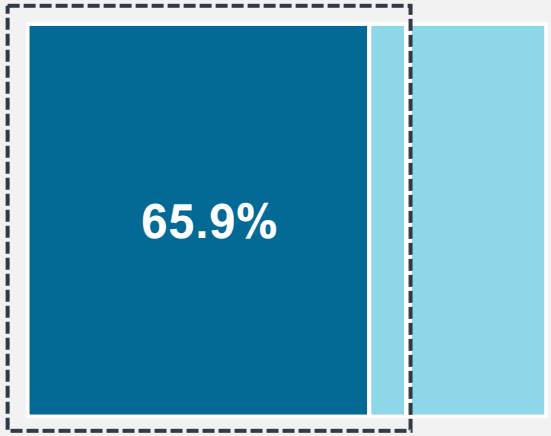


P = 0.0006

Month 12 Results

~2 of 3 AXPAXLI subjects maintained vision* with a single injection



P < 0.0001

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*Maintained vision defined as <15 ETDRS letters of loss.
ETDRS, early treatment diabetic retinopathy

AXPAXLI Demonstrated Strong Potential for Annual Dosing

SOL-1

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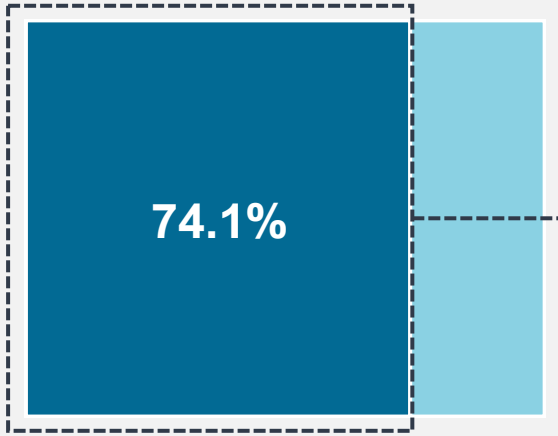

P = 0.0006

Month 12 Results

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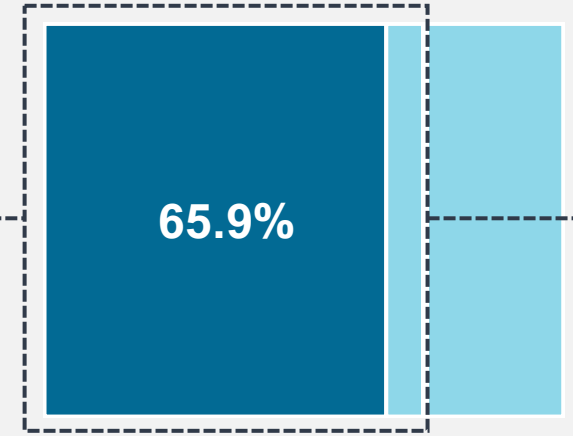
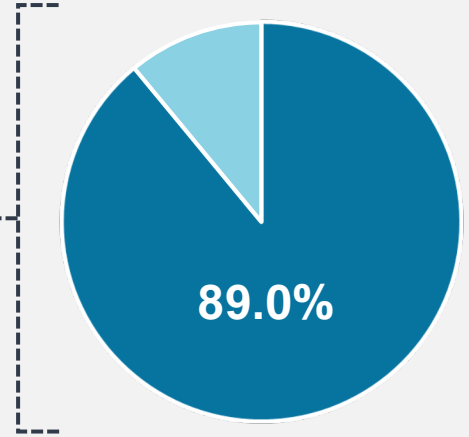


P < 0.0001

Continued Response

Of subjects that maintained vision at Month 9, **~90%** maintained vision **at Month 12**



Unmatched Durability Observed with AXPAXLI in SOL-1

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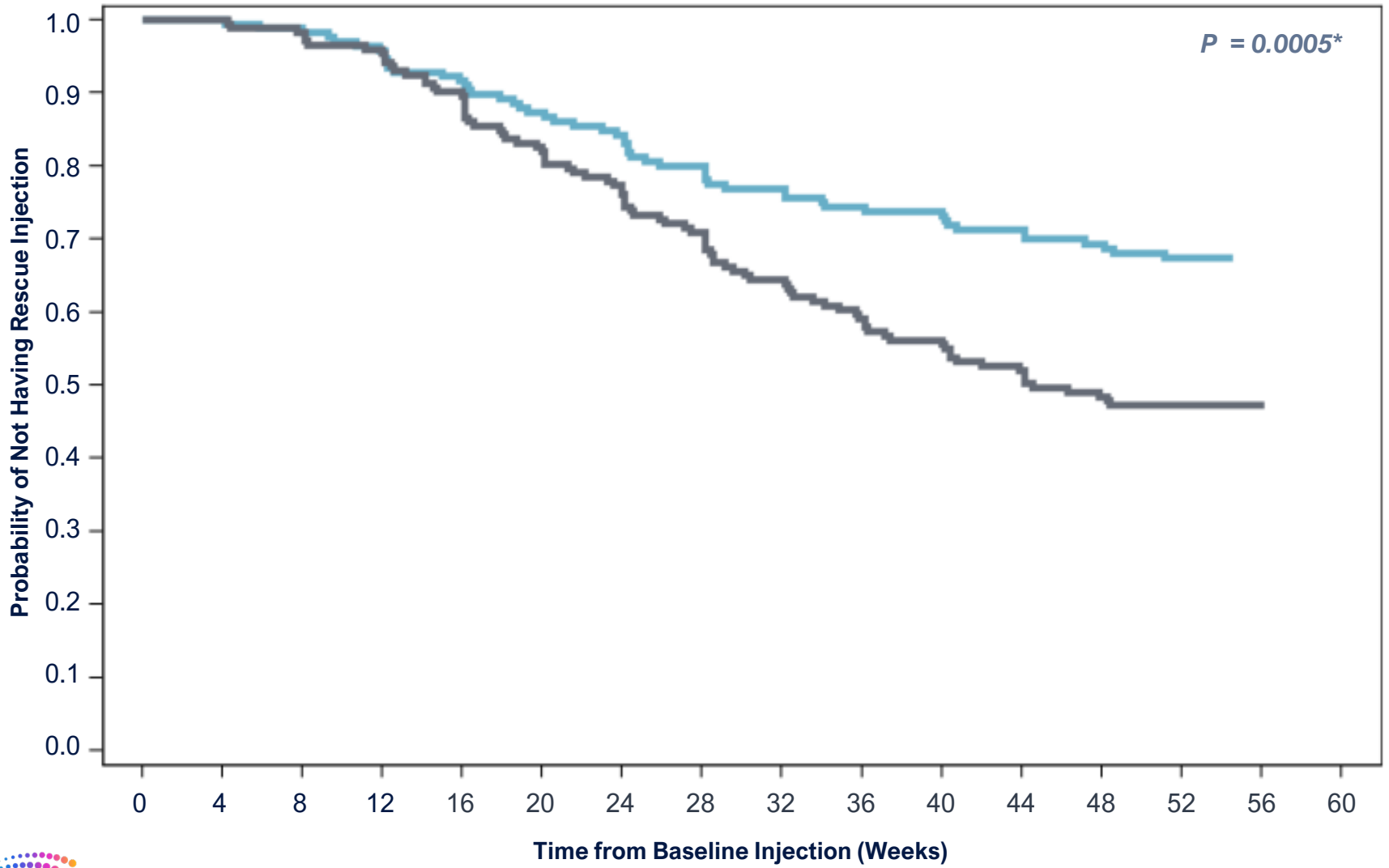
Post Hoc Analysis
*Maintained vision defined as <15 ETDRS letters of loss.
ETDRS, early treatment diabetic retinopathy

Significantly Lower Risk of Rescue During Year 1 with AXPAXLI

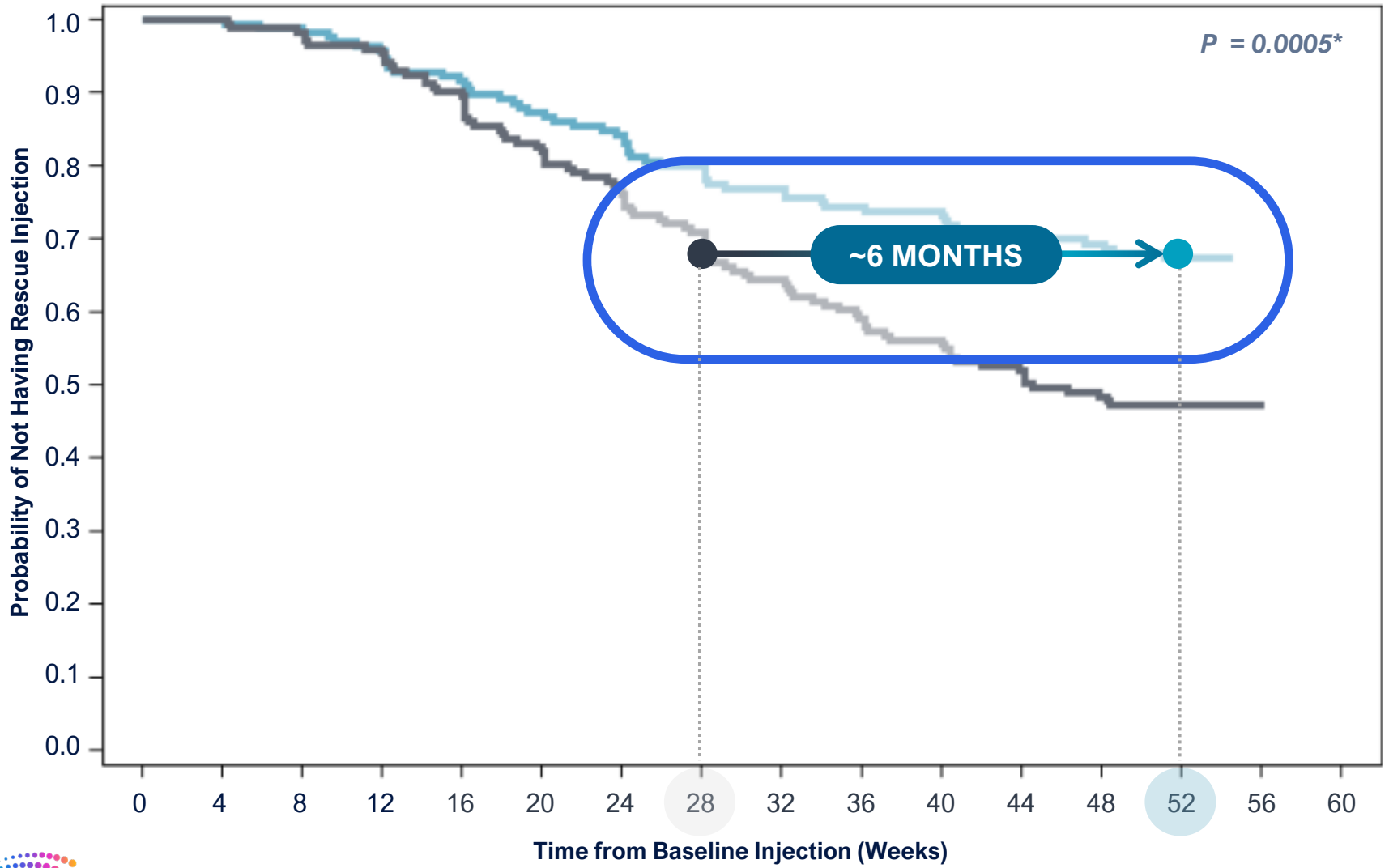


Time to First Rescue Treatment

AXPAXLI 0.45 mg (n=170)
Aflibercept 2 mg (n=172)

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

Significantly Lower Risk of Rescue During Year 1 with AXPAXLI



Time to First Rescue Treatment

~6 Month Difference

AXPAXLI Week 52 rescue rate reflects ***~6-month*** **advantage** over aflibercept

No approved wet AMD intravitreal therapy has ≥6-month dosing label

AXPAXLI 0.45 mg (n=170)
Aflibercept 2 mg (n=172)

Rescue-free subjects include those who did not require rescue injections as specified by the protocol
*Nominal P value
AMD, age-related macular degeneration

SOL-1 Results Highlight AXPAXLI's Groundbreaking Product Profile

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First Successful Superiority Trial of Novel Agent vs Approved anti-VEGF

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Sustained Disease Control

Well-Tolerated

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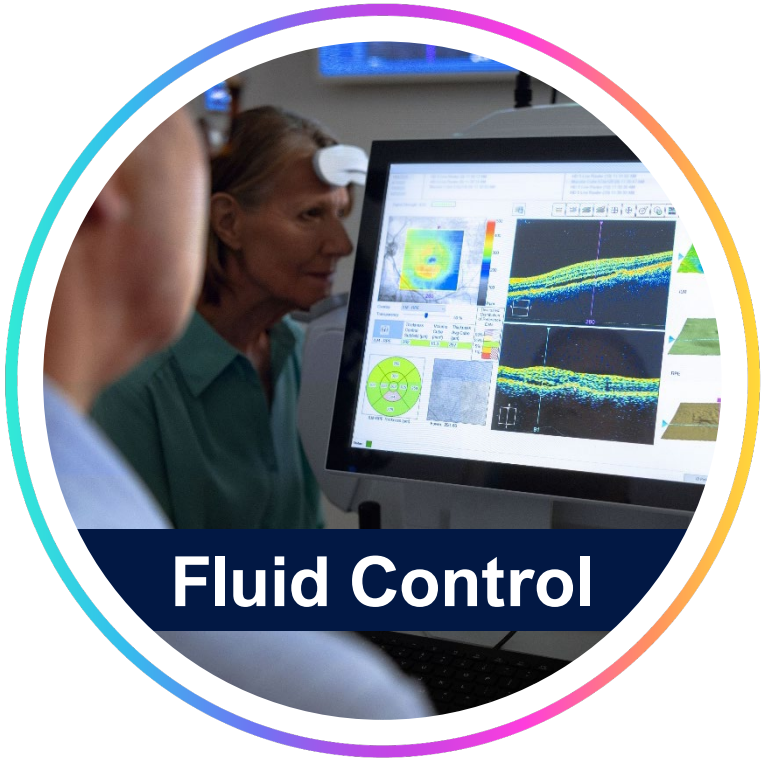
VEGF, vascular endothelial growth factor

Sustained Fluid Control Generally Leads to Strong Vision Control

Anatomic deterioration often precedes visual loss & drives retreatment in clinical practice

Sustained Fluid Control Generally Leads to Strong Vision Control

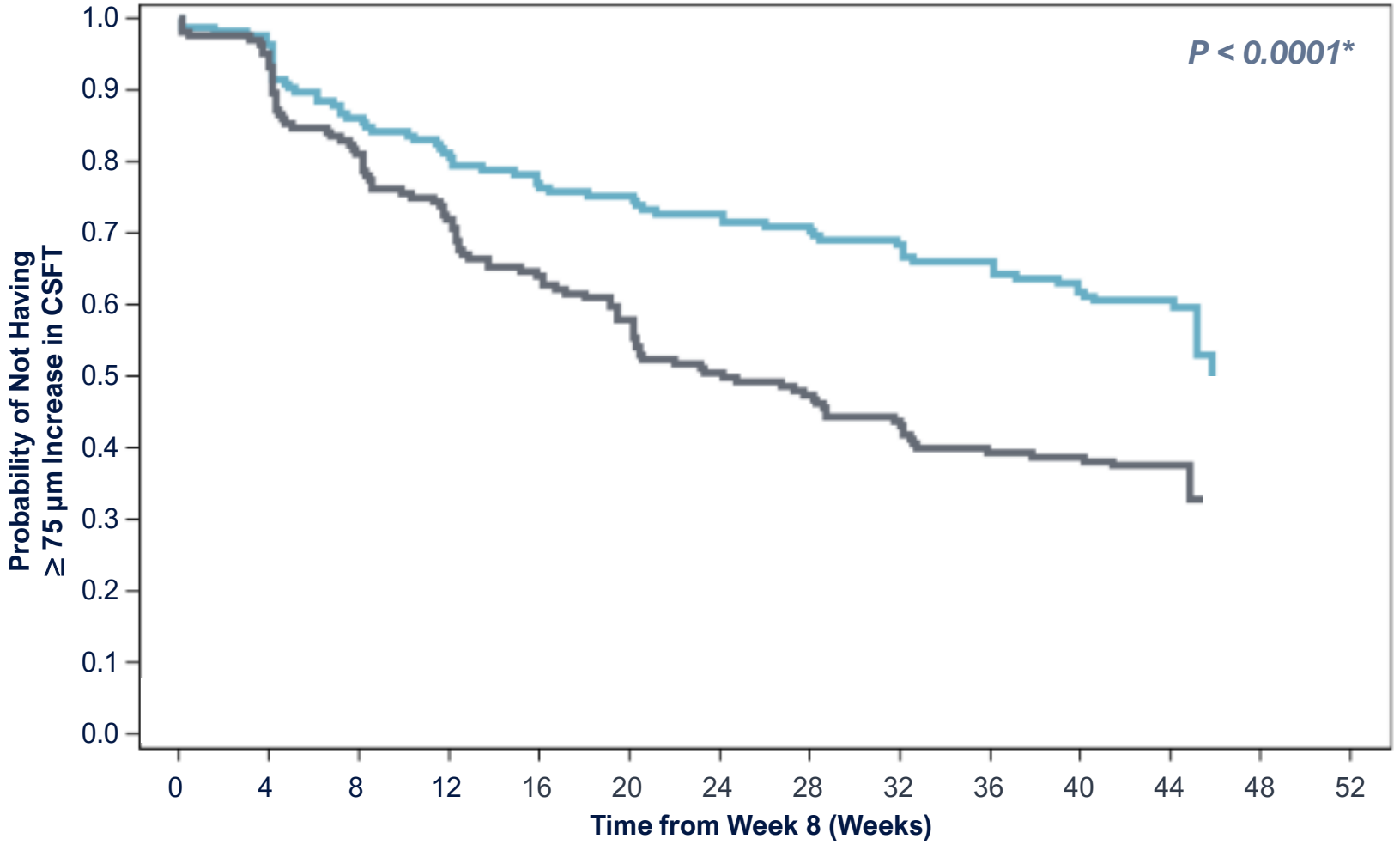


Anatomic deterioration often precedes visual loss & drives retreatment in clinical practice

AXPAXLI Provided Sustained Disease Control Measured Via OCT

SOL-1

Time to ≥ 75 µm Increase in CSFT



What does it all mean?

75 µm CSFT gains often used as re-treatment criteria in wet AMD trials

AXPAXLI 0.45 mg (n=165)

Aflibercept 2 mg (n=164)

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Post Hoc Analysis

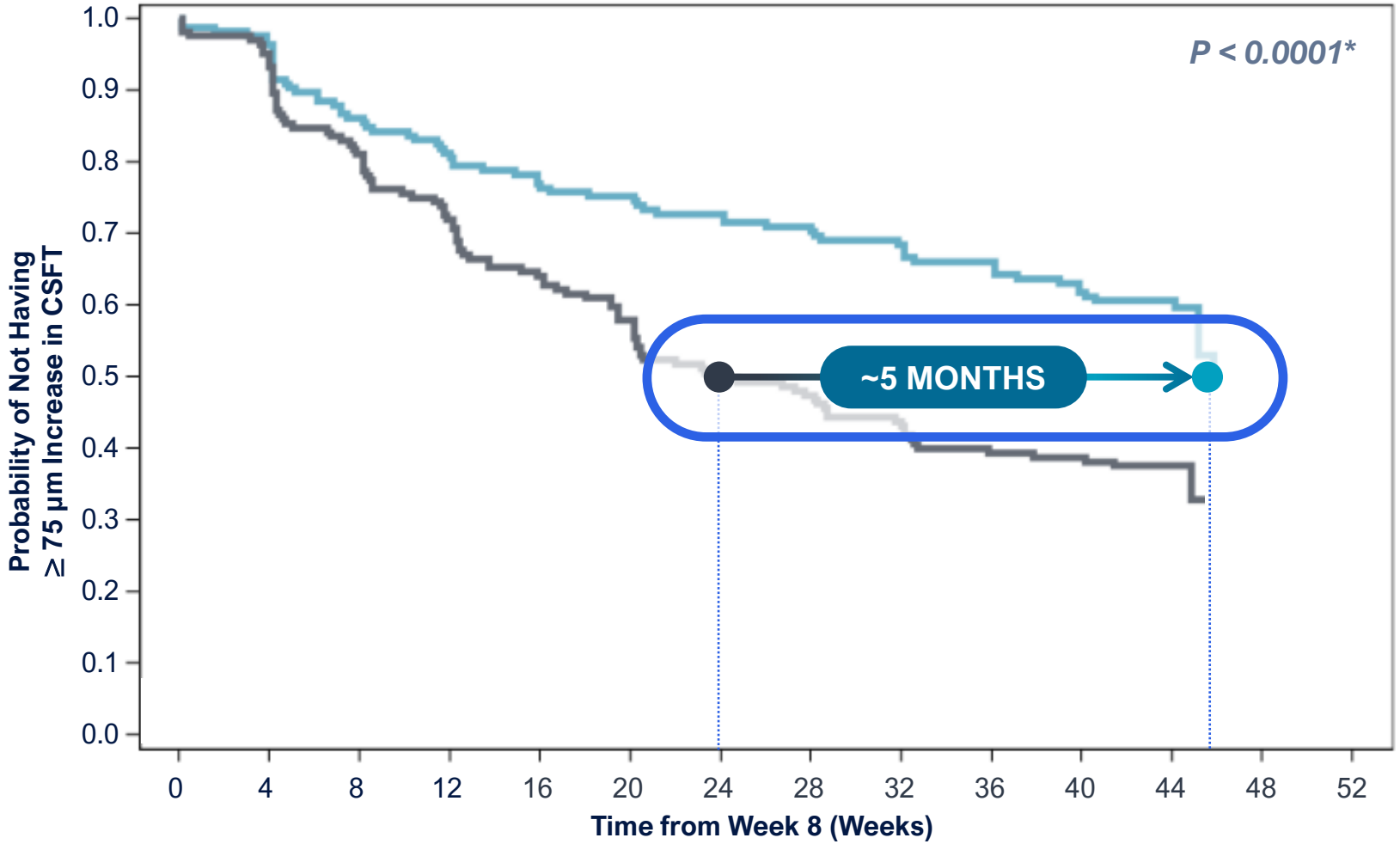
Subjects with CSFT at Week 8 in Full Analysis Set; *Descriptive p-value

CSFT, central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium; OCT, optical coherence tomography; AMD, age-related macular degeneration

AXPAXLI Provided Sustained Disease Control Measured Via OCT

SOL-1

Time to ≥ 75 µm Increase in CSFT



What does it all mean?

75 µm CSFT gains often used as re-treatment criteria in wet AMD trials

~5-month delay in 75 µm CSFT gain with AXPAXLI: evidence of exceptional disease control

AXPAXLI 0.45 mg (n=165)

Aflibercept 2 mg (n=164)

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Post Hoc Analysis

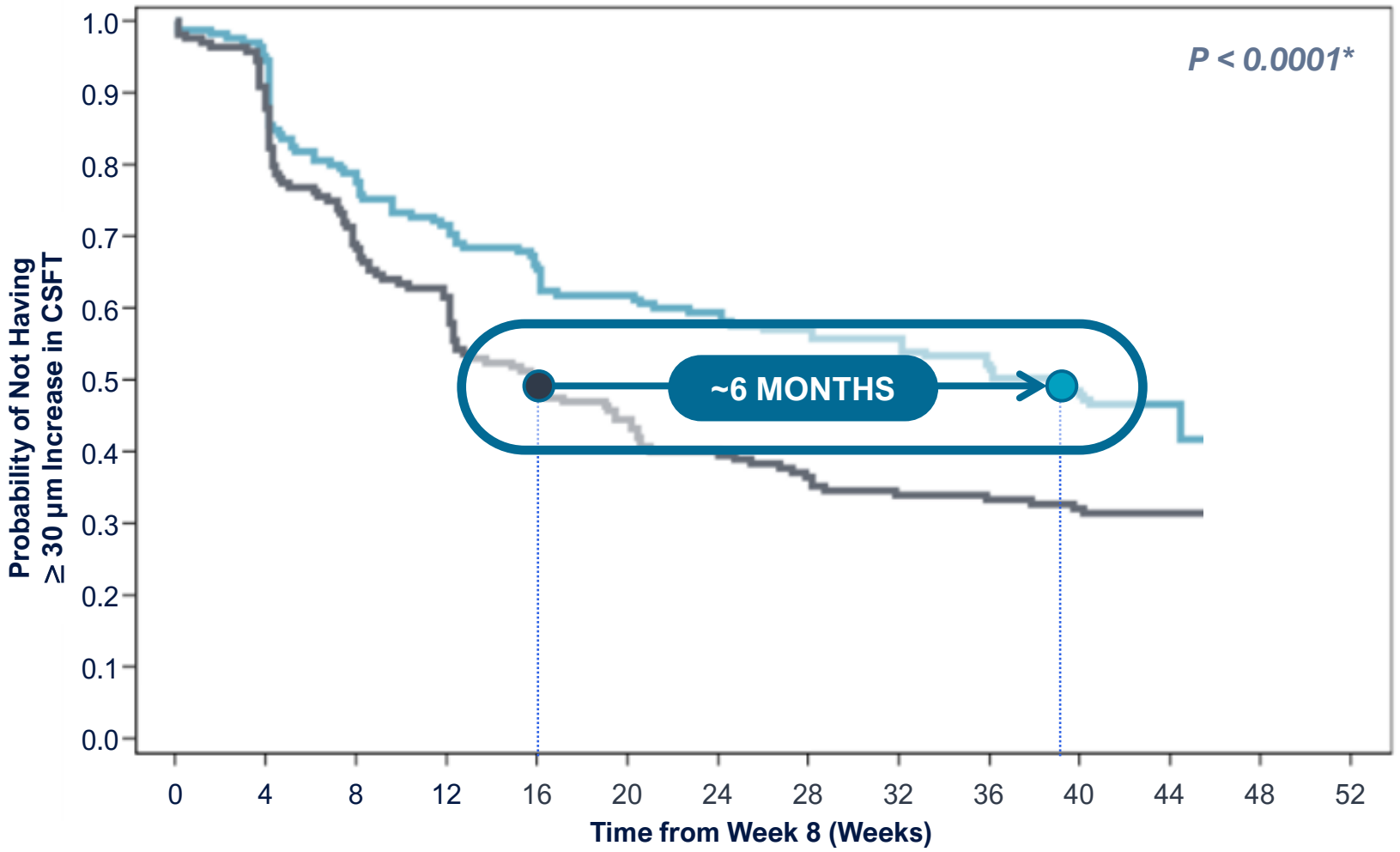
Subjects with CSFT at Week 8 in Full Analysis Set; *Descriptive p-value

CSFT, central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium; OCT, optical coherence tomography ; AMD, age-related macular degeneration

At Even Tighter Anatomic Thresholds – AXPAXLI Demonstrates Stellar Sustained Disease Control

SOL-1

Time to ≥ 30 µm Increase in CSFT



What does it all mean?

~6-month difference in time to a 30 µm CSFT gain in favor of AXPAXLI suggests exceptional disease control

AXPAXLI 0.45 mg (n=165)

Aflibercept 2 mg (n=164)

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;

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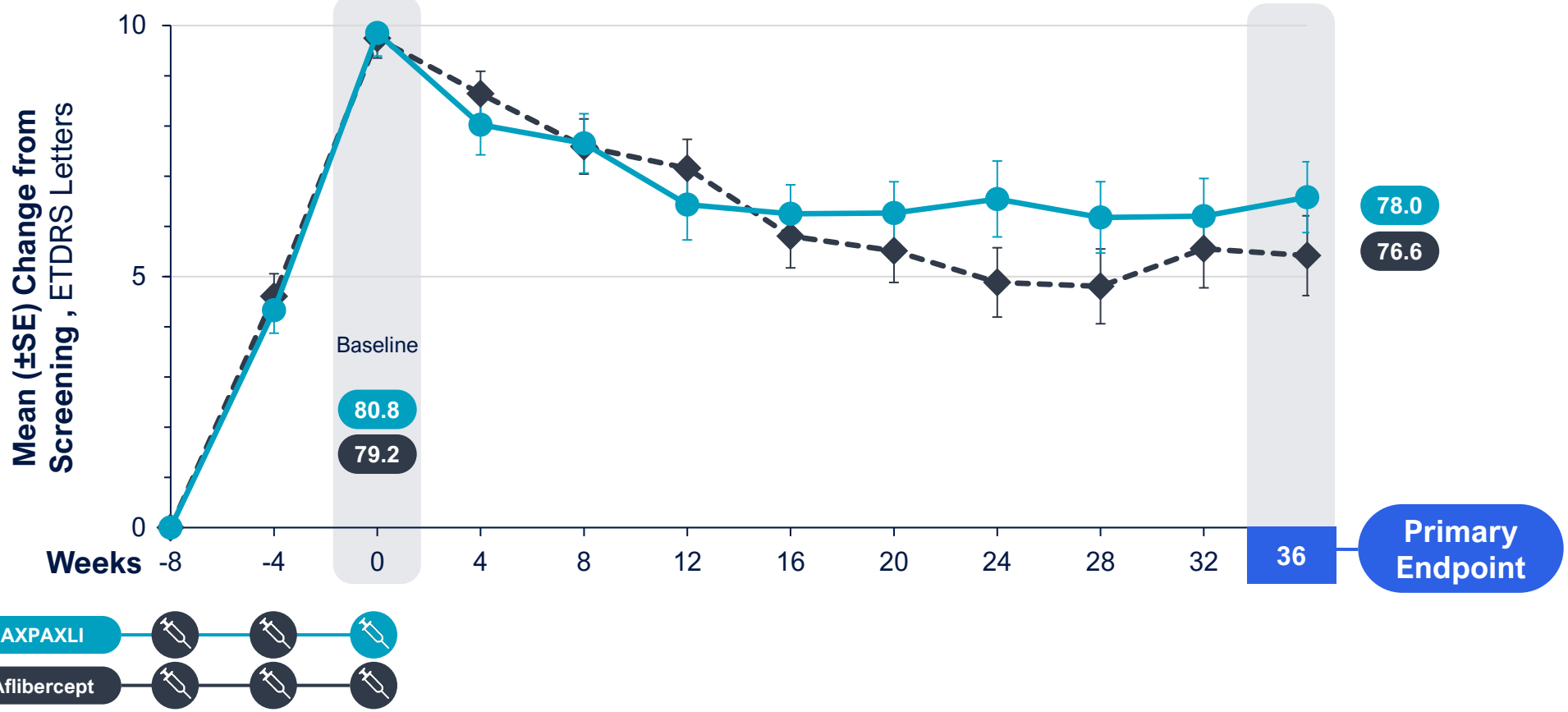
Sustained Fluid Control Generally Leads to Strong Vision Control

Anatomic deterioration often precedes visual loss & drives retreatment in clinical practice

AXPAXLI Demonstrated Strong Vision Control Up to 9 Months With Significantly Fewer Rescues Than Aflibercept (2 mg)

SOL-1

Mean Change in BCVA from Screening in All Subjects



Post Hoc Analysis

Full analysis set. For subjects who received any rescue injections, their observed 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

ETDRS, Early Treatment Diabetic Retinopathy Study; SE, standard error; BCVA, best-corrected visual acuity

AXPAXLI 0.45 mg (n=170)

Aflibercept 2 mg (n=172)

OCULAR THERAPEUTIX Retina experience redefined™

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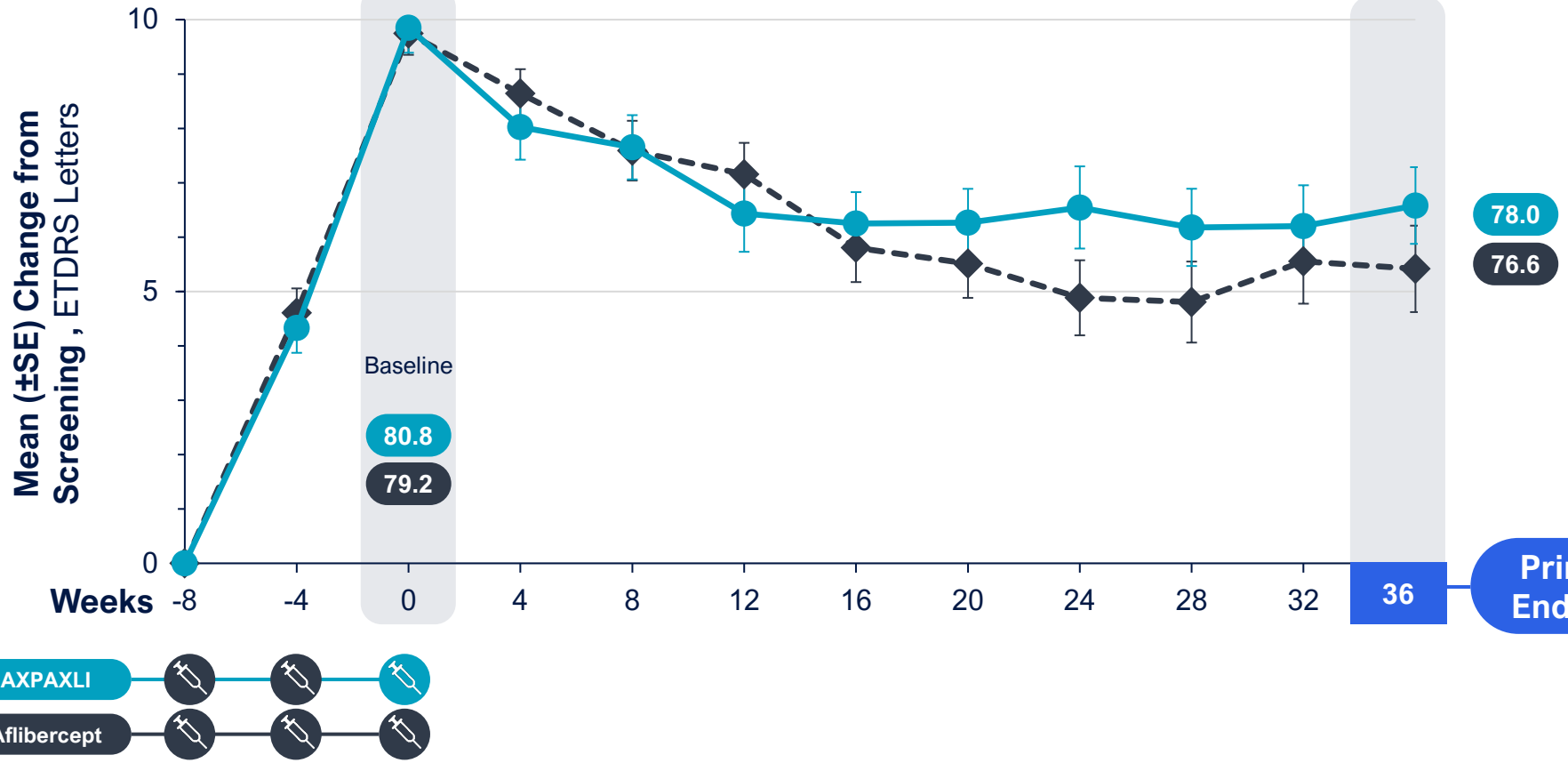
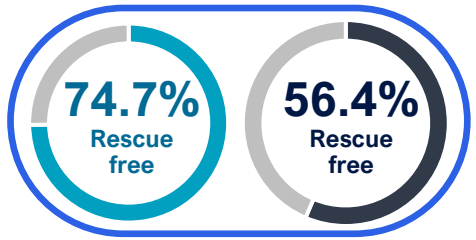


Rescue Free Rate at Week 36



OCULAR THERAPEUTIX Retina experience redefined™

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Aflibercept 2 mg (n=172)

SOL-1 Results Highlight AXPAXLI's Groundbreaking Product Profile

SOL-1

First Successful Superiority Trial of Novel Agent vs Approved anti-VEGF

Unmatched Durability

Sustained Disease Control

Well-Tolerated

OCULAR THERAPEUTIX Retina experience redefined™

VEGF, vascular endothelial growth factor

No Treatment or Procedure Related Ocular SAEs

Ocular Events in the Study Eye

Subjects with Ocular AEs Through Week 52, n (%)	AXPAXLI 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

AXPAXLI was Generally Well Tolerated

Ocular Adverse Events in the Study Eye

Subjects with Ocular AEs (> 2%) Through Week 52, n (%)	AXPAXLI 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)

Safety is Essential in Wet AMD

No cases of endophthalmitis, occlusive or non-occlusive retinal vasculitis

OCULAR THERAPEUTIX Retina experience redefined™

AE, adverse event; AMD, age-related macular degeneration

Year 2 Safety: DSMC Recommends Trial Continuation

SOL-1

SOL-1 THROUGH Week 52

AXPAXLI was generally well-tolerated

No cases of endophthalmitis, occlusive or non-occlusive retinal vasculitis

Detailed results presented globally at multiple medical congresses

SOL-1 FOLLOWING Week 52

SOL-1 remains masked in Year 2, evaluating Q6M dosing

Masked safety data being monitored and DSMC recommends trial continuation

OCULAR THERAPEUTIX Retina experience redefined™

DSMC, data safety monitoring committee; Q6M, every 6 months

Single Injection of AXPAXLI Demonstrated Superiority to a Single Injection of Aflibercept (2 mg) in SOL-1

SOL-1 Results Highlight AXPAXLI's Groundbreaking Profile

First Phase 3 trial to demonstrate durability out to >9 months

~75% of AXPAXLI subjects were rescue free at Week 36

Unmatched Durability

Up to 52 Week visual & anatomic stability

On average, subjects maintained visual & anatomical outcomes with a single AXPAXLI injection

Sustained Disease Control

Well-tolerated safety profile

No cases of endophthalmitis, vasculitis through Week 52

Well-Tolerated

OCULAR THERAPEUTIX Retina experience redefined™

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

What Value Does Each SOL Trial Bring?

SOL Program Potential: Each Trial Designed to Support Unique Value Proposition

SOL-1

Phase 3 Superiority Trial

- **Demonstrates effectiveness** in wet AMD for NDA submission
- **Provides safety data** in wet AMD for NDA submission (Y2, evaluating Q6M dosing)
- **Supports Ex-US regulatory filings**
- **Commercially relevant** potential superiority label

AMD, age-related macular degeneration; NDA, New Drug Application; Q6M, every 6 months

SOL Program Potential: Each Trial Designed to Support Unique Value Proposition

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SOL-R

Phase 3 Non-Inferiority Trial

- **Provides safety data** in wet AMD for NDA submission
- **Supports Ex-US regulatory filings**
- **Commercially relevant** with evaluation of Q6M dosing
- **Commercially relevant** with Eylea HD comparison at W96

OCULAR THERAPEUTIX Retina experience redefined™

AMD, age-related macular degeneration; NDA, New Drug Application; Q6M, every 6 months

SOL Program Potential: Each Trial Designed to Support Unique Value Proposition

SOL-1

Phase 3 Superiority Trial

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SOL-R

Phase 3 Non-Inferiority Trial

- **Provides safety data** in wet AMD for NDA submission
- **Supports Ex-US regulatory filings**
- **Commercially relevant** with evaluation of Q6M dosing
- **Commercially relevant** with Eylea HD comparison at W96

SOL-X

Open-Label Extension

- **Long-term safety** and evaluation of protective impact on fibrosis & atrophy
- **Commercially relevant** with continuous dosing Q6M

OCULAR THERAPEUTIX Retina experience redefined™

AMD, age-related macular degeneration; NDA, New Drug Application; Q6M, every 6 months

How Does SOL-1 Success Impact the HELIOS DR Program?

OCULAR THERAPEUTIX Retina experience redefined™

Streamlining Diabetic Retinopathy Program

2025 Investor Day
Sep. 30, 2025

Announced HELIOS-2* & HELIOS-3 DR Registrational Trials

Evaluations of Q12M and Q6M AXPAXLI Regimens

Superiority Trials Target Broad DR Label, Including DME

Novel Primary Endpoint: Ordinal DRSS 2-Step Change Status

Alignment on Ordinal Endpoint Reached w/ FDA

OCULAR THERAPEUTIX Retina experience redefined™

*HELIOS-2 is a superiority trial comparing AXPAXLI to Ranibizumab (0.3 mg). The trial was granted a Special Protocol Assessment Agreement from FDA. The trial has yet to initiate.
DR, diabetic retinopathy; DME, diabetic macular edema; SPA, special protocol assessment; DRSS, Diabetic Retinopathy Severity Score; Q12M, every 12 months

Streamlining Diabetic Retinopathy Program

2025 Investor Day
Sep. 30, 2025

Announced HELIOS-2* & HELIOS-3 DR Registrational Trials

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Superiority Trials Target Broad DR Label, Including DME

Novel Primary Endpoint: Ordinal DRSS 2-Step Change Status

Alignment on Ordinal Endpoint Reached w/ FDA

Today

Prioritizing One DR Registrational Trial (HELIOS-3)

Evaluation of only Q12M AXPAXLI Regimen vs Sham

Superiority Trial Targeting Broad DR Label, Including DME

Novel Primary Endpoint: Ordinal DRSS 2-Step Change Status

Maintaining FDA-aligned Ordinal DRSS Endpoint

OCULAR THERAPEUTIX Retina experience redefined™

*HELIOS-2 is a superiority trial comparing AXPAXLI to Ranibizumab (0.3 mg). The trial was granted a Special Protocol Assessment Agreement from FDA. The trial has yet to initiate.
DR, diabetic retinopathy; DME, diabetic macular edema; SPA, special protocol assessment; DRSS, Diabetic Retinopathy Severity Score; Q12M, every 12 months

Updated HELIOS-3 Study Design*

Superiority Study

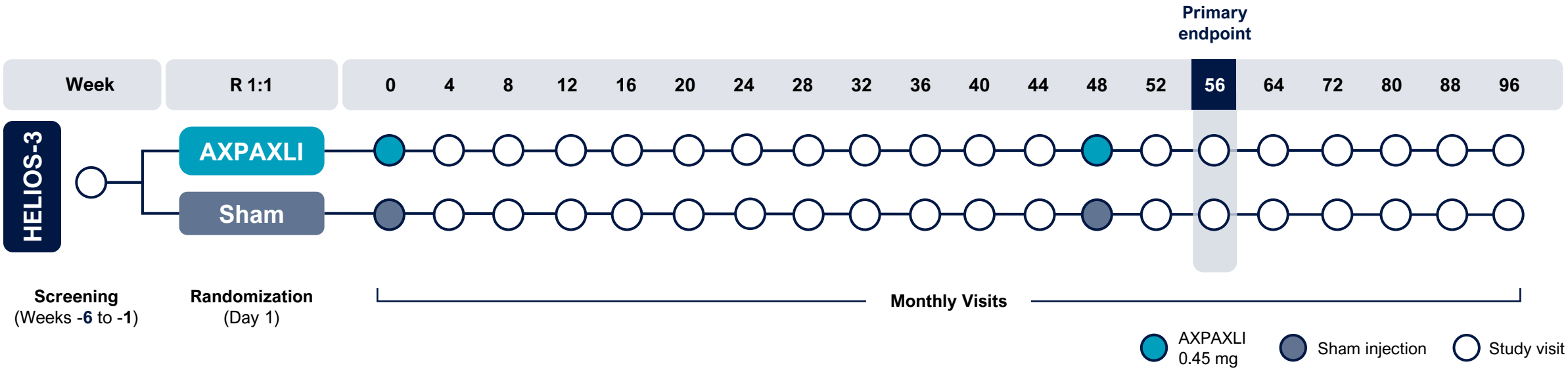
HELIOS-3

Design

Study of AXPAXLI in **~620** subjects with moderately-severe to severe NPDR without CI-DME

Primary Endpoint (Week 56)

Ordinal DRSS 2-step change status at **Week 56** from baseline
(≥ 2 step improvement, ≥ 2-step worsening, < 2-step change in either direction)



Data on File. Ocular Therapeutix.
DRSS, diabetic retinopathy severity scale; NPDR, non-proliferative diabetic retinopathy; CI-DME, center involved diabetic macular edema; Q48W, every 48 weeks
*HELIOS-3 design streamlined from three planned study arms to two (AXPAXLI Q12M vs sham), reducing planned enrollment from approximately 930 to 620 subjects.

HELIOS Program Update

Rationale for Changes to HELIOS Program

1. **Strong SOL-1** results **plus HELIOS-1** data
2. **Demonstrated AXPAXLI durability up to 12 months in SOL-1**
3. **Q12M preferred regimen in DR**
4. **HELIOS-3 supports global regulatory objectives**

OCULAR THERAPEUTIX Retina experience redefined™

Q12M, every 12 months; DR, diabetic retinopathy

Ocular Therapeutix 2026 Investor Day Agenda

Intro & Overview
Pravin U. Dugel, MD

SOL-1 Data & AXPAXLI Clinical Program Review
Nadia K. Waheed, MD, MPH

U.S. Regulatory Strategy in Wet AMD
Peter K. Kaiser, MD

Discussion: AXPAXLI NDA Submission Strategy
Moderator: Peter K. Kaiser, MD

Ocular Panelist: Arthur Ciociola, PhD

Preparing for a Successful Launch
David Robinson

SOL-R: Defining Non-Inferiority Success
Jeffrey S. Heier, MD

KOL Perspectives: Potential to Redefine Retina
Moderator: Jeffrey S. Heier, MD

KOLs: Arshad Khanani, MD; Lejla Vajzovic, MD; Darius Moshfeghi, MD

Summary & Takeaways
Pravin U. Dugel, MD

Audience Q&A
All

OCULAR THERAPEUTIX Retina experience redefined™

U.S. Regulatory Strategy in Wet AMD

Peter K. Kaiser, MD
Chief Development Officer

OCULAR THERAPEUTIX Retina experience redefined™

FDA “Substantial Evidence of Effectiveness” Requirement Likely Met by SOL-1

FDA Pathway Exists

FDA Modernization Act of 1997

FDA Guidance of 1998 and 2023 further defined pathway

>60% of recent FDA approvals based on a single pivotal trial[1]

SOL-1 Trial

Adequate and well-controlled

SPA alignment

High statistical significance

Well-tolerated safety profile and sufficient safety dataset with SOL-R patients

Confirmatory Evidence

Mechanistic Evidence

Pharmacodynamic/ Pharmacokinetic Evidence

Animal Models

Class Consistency

Real World Evidence

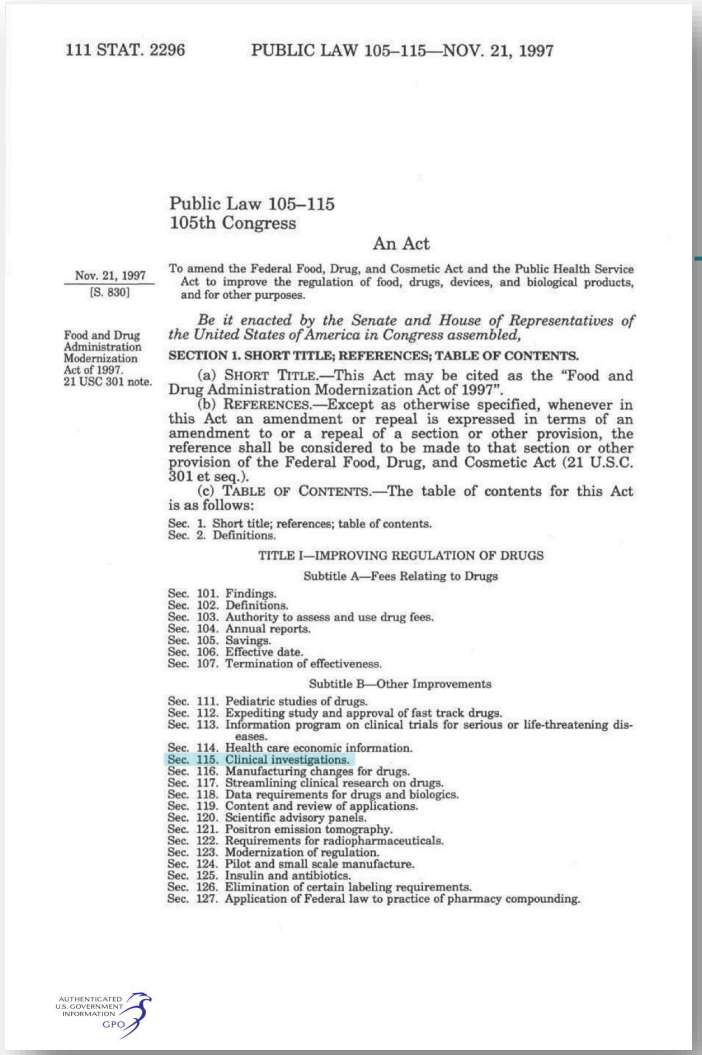
Natural History Evidence

OCULAR THERAPEUTIX Retina experience redefined™

1. OCUL internal analysis of CDER’s novel drugs approvals for 2024 and 2025

SPA, Special Protocol Assessment

Substantial Evidence of Effectiveness with a Single Trial is Well-Established



111 STAT. 2296 PUBLIC LAW 105–115—NOV. 21, 1997

Public Law 105–115
105th Congress

An Act

Nov. 21, 1997
[S. 830]

To amend the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act to improve the regulation of food, drugs, devices, and biological products, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

Food and Drug Administration Modernization Act of 1997.
21 USC 301 note.

SECTION 1. SHORT TITLE; REFERENCES; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the "Food and Drug Administration Modernization Act of 1997".

(b) REFERENCES.—Except as otherwise specified, whenever in this Act an amendment or repeal is expressed in terms of an amendment to or a repeal of a section or other provision, the reference shall be considered to be made to that section or other provision of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.).

(c) TABLE OF CONTENTS.—The table of contents for this Act is as follows:

Sec. 1. Short title; references; table of contents.
Sec. 2. Definitions.

TITLE I—IMPROVING REGULATION OF DRUGS

Subtitle A—Fees Relating to Drugs

Sec. 101. Findings.
Sec. 102. Definitions.
Sec. 103. Authority to assess and use drug fees.
Sec. 104. Annual reports.
Sec. 105. Savings.
Sec. 106. Effective date.
Sec. 107. Termination of effectiveness.

Subtitle B—Other Improvements

Sec. 111. Pediatric studies of drugs.
Sec. 112. Expediting study and approval of fast track drugs.
Sec. 113. Information program on clinical trials for serious or life-threatening diseases.
Sec. 114. Health care economic information.
Sec. 115. Clinical investigations.
Sec. 116. Manufacturing changes for drugs.
Sec. 117. Streamlining clinical research on drugs.
Sec. 118. Data requirements for drugs and biologics.
Sec. 119. Content and review of applications.
Sec. 120. Scientific advisory panels.
Sec. 121. Positron emission tomography.
Sec. 122. Requirements for radiopharmaceuticals.
Sec. 123. Modernization of regulation.
Sec. 124. Pilot and small scale manufacture.
Sec. 125. Insulin and antibiotics.
Sec. 126. Elimination of certain labeling requirements.
Sec. 127. Application of Federal law to practice of pharmacy compounding.

AUTHENTICATED U.S. GOVERNMENT INFORMATION GPO

Precedent is Well-Established

Section 115 of the **FDA Modernization Act of 1997** amended and clarified FD&C Act § 505(d) to define **"substantial evidence"** and **explicitly allow one adequate and well-controlled trial plus confirmatory evidence**[1]

The **1998 FDA Guidance** reiterated that the **"substantial evidence" requirement** for effectiveness…**could be met by a single trial plus confirmatory evidence**[2]

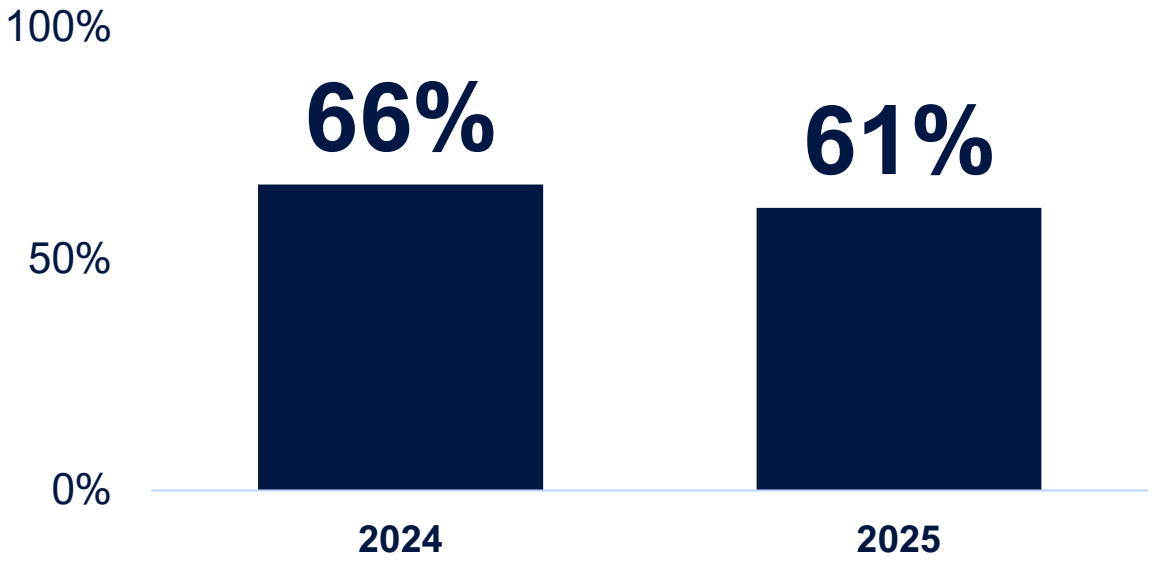
The **2023 FDA Guidance** explained even more clearly how **one trial plus confirmatory evidence** can meet the statutory **"substantial evidence"** standard[3]

OCULAR THERAPEUTIX Retina experience redefined™

1. FDAMA § 115, Pub. L. No. 105-115, amending Federal Food, Drug, and Cosmetic Act § 505(d), 21 U.S.C. § 355(d). 2. FDA, Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products: Guidance for Industry (May 1998). 3. FDA, Demonstrating Substantial Evidence of Effectiveness With One Adequate and Well-Controlled Clinical Investigation and Confirmatory Evidence: Draft Guidance for Industry (Sept. 2023).

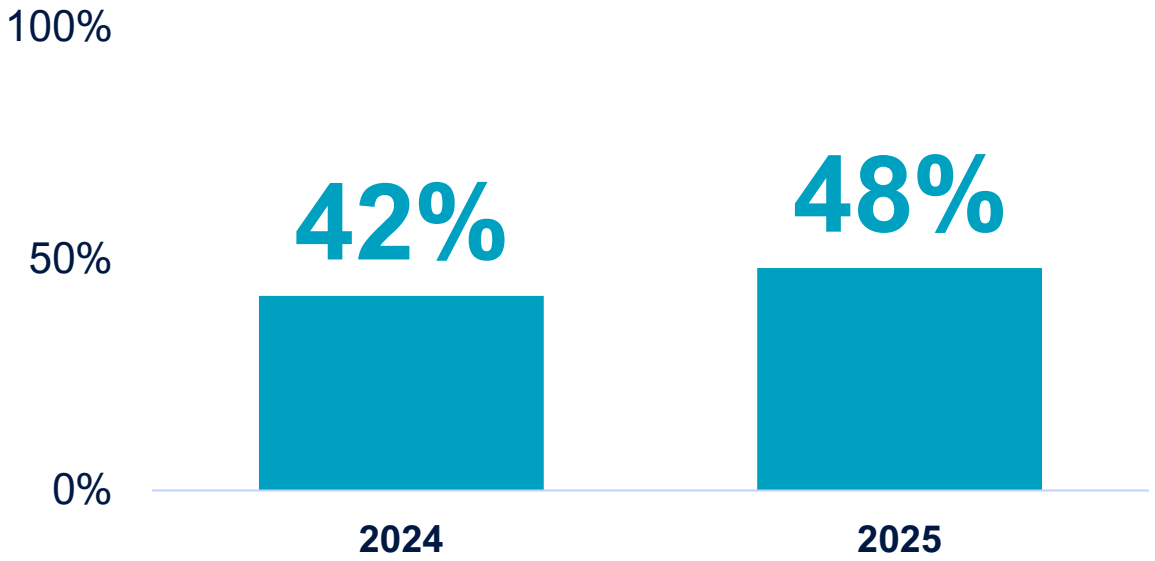
Approvals based on a Single Trial are Common and Increasingly Frequent

Percent of All CDER NDAs Approved with a Single Trial[1]



Majority of **recent CDER approvals** based on **single pivotal trial**[1]

Percent of Non-Orphan CDER NDAs Approved with a Single Trial[1]



Over 40% of recent non-orphan CDER approvals based on a single-trial[1]

OCULAR THERAPEUTIX Retina experience redefined™

1. Ocular internal analysis of CDER's novel drugs approvals for 2024 and 2025 CDER, Center for Drug Evaluation and Research.

Meeting The Evidentiary Standard for Effectiveness with a Single Pivotal Trial

Pre-Data

- ☐ **Adequate & Well-Controlled Trial**
- ☐ Protocol Aligned with FDA

Post-Data

- ☐ Superiority Primary Endpoint Met
- ☐ Clinically Meaningful Results
- ☐ Safety Dataset Meeting FDA Submission Requirements
- ☐ Supporting Confirmatory Evidence

Code of Federal Regulation
21 CFR § Part 314 defined what qualifies as an **"adequate and well-controlled" study**

Evidence from clinical trials that are **not adequate and well-controlled** (eg. sham introduces bias) can be corroborative, but **cannot stand alone**

OCULAR THERAPEUTIX Retina experience redefined™

1. 21 C.F.R. § 314.126 — Adequate and well-controlled studies.

Meeting The Evidentiary Standard for Effectiveness with a Single Pivotal Trial

Pre-Data

- [x] **Adequate & Well-Controlled Trial**
- [ ] Protocol Aligned with FDA

Post-Data

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Code of Federal Regulation
21 CFR § Part 314 defined what qualifies as an **"adequate and well-controlled" study**

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SOL-1 was prospectively designed to meet the standards of an **adequate and well-controlled clinical trial** under 21 CFR § 314

OCULAR THERAPEUTIX Retina experience redefined™

1. 21 C.F.R. § 314.126 — Adequate and well-controlled studies.

Meeting The Evidentiary Standard for Effectiveness with a Single Pivotal Trial

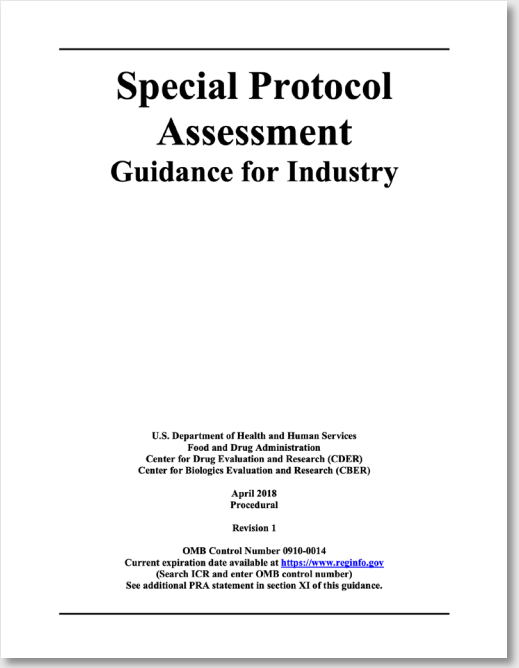
Pre-Data

- [x] Adequate & Well-Controlled Trial
- [ ] **Protocol Aligned with FDA**

Post-Data

- [ ] Superiority Primary Endpoint Met
- [ ] Clinically Meaningful Results
- [ ] Safety Dataset Meeting FDA Submission Requirements
- [ ] Supporting Confirmatory Evidence

A SPA means the FDA has agreed that the **study design, endpoints, study size, and analysis plan** are adequate to address the scientific and regulatory requirements for a study that could support approval[1]



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™

1. Special Protocol Assessment; Guidance for Industry; Availability, 83 Fed. Reg. 16356, Apr. 16, 2018.; "An SPA agreement indicates concurrence by FDA with the adequacy and acceptability of specific critical elements of overall protocol design (e.g., entry criteria, dose selection, endpoints, and planned analyses) for a study intended to support a future marketing application... However, an SPA agreement does not indicate FDA concurrence on every protocol detail."

Meeting The Evidentiary Standard for Effectiveness with a Single Pivotal Trial

Pre-Data

- ☑ Adequate & Well-Controlled Trial
- ☑ **Protocol Aligned with FDA**

Post-Data

- ☐ Superiority Primary Endpoint Met
- ☐ Clinically Meaningful Results
- ☐ Safety Dataset Meeting FDA Submission Requirements
- ☐ Supporting Confirmatory Evidence

SOL-1 conducted under SPA

Only active wet AMD trial conducted under SPA

"The special protocol assessment is an official agreement between a sponsor & the agency that we will accept a certain trial design… **If you successfully complete that protocol, that will be highly supportive of approval of the product."**

W. Boyd – FDA Deputy Division Director of Ophthalmology | Retina World Congress, May 2026

OCULAR THERAPEUTIX Retina experience redefined™

SPA, Special Protocol Assessment; AMD, age-related macular degeneration

Meeting The Evidentiary Standard for Effectiveness with a Single Pivotal Trial

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- ☐ Supporting Confirmatory Evidence

FDA Division of Ophthalmology considers p values ≤ 0.001 to be **potentially supportive** for **single trial approval**

"Single adequate and well-controlled trials can support approval…often with very strong p-values (e.g., <0.001)"

W. Boyd – FDA Deputy Division Director of Ophthalmology | Retina World Congress, May 2026

OCULAR THERAPEUTIX Retina experience redefined™

Meeting The Evidentiary Standard for Effectiveness with a Single Pivotal Trial

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FDA Division of Ophthalmology considers p values ≤ 0.001 to be **potentially supportive** for **single trial approval**

Xipere approved for UME on single trial (PEACHTREE) with **p value <0.001** (trial included 96 subjects, safety package with 296 subjects incl. patients from open-label AZALEA)(Oct 2021)

OCULAR THERAPEUTIX Retina experience redefined™

1. Godoy CB et al Ramachandran R, Sapre P, Ross JS. Confirmatory evidence supporting single pivotal trial new drug approvals by the Food and Drug Administration, 2015 through 2023. *Clin Trials*. 2026;23(1):109-112.

Meeting The Evidentiary Standard for Effectiveness with a Single Pivotal Trial

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FDA Division of Ophthalmology considers p values ≤ 0.001 to be **potentially supportive** for **single trial approval**

SOL-1 reported highly statistically significant (p value = 0.0006) risk difference of **17.5%** for patients treated with AXPAXLI vs control in maintenance of vision at week 36

All six pre-specified sensitivity analyses also statistically significant

OCULAR THERAPEUTIX Retina experience redefined™

1. Puthumana J, Wallach JD, Ross JS. Single pivotal trial evidence supporting FDA approval of original drug and biologic indications, 2015–2023. Clinical Trials. 2025. doi:10.1177/17407745251376620.

Meeting The Evidentiary Standard for Effectiveness with a Single Pivotal Trial

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- ☑ Protocol Aligned with FDA

Post-Data

- ☑ Superiority Primary Endpoint Met
- ☑ **Clinically Meaningful Results**
- ☐ Safety Dataset Meeting FDA Submission Requirements
- ☐ Supporting Confirmatory Evidence

- First trial to show **superiority** in preventing vision loss against an active anti-VEGF control, aflibercept 2mg
- **69% of AXPAXLI Subjects Rescue-Free** at 12 months
- **Time to first rescue injection** ~6 months difference with aflibercept
- **3 hierarchically controlled key secondary** endpoints **met with statistical significance**

SOL-1 demonstrated superiority on the prespecified primary endpoint, strengthening effect size over time, consistent visual outcomes, and supportive anatomic benefit creating a highly persuasive efficacy statement

OCULAR THERAPEUTIX Retina experience redefined™

Hierarchical testing: endpoints are tested in a prespecified order and significance is claimed only if prior endpoints are met.
VEGF, vascular endothelial growth factor

Meeting The Evidentiary Standard for Effectiveness with a Single Pivotal Trial

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Post-Data

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- ☐ Supporting Confirmatory Evidence

- FDA notes one trial may establish effectiveness, but FDA still requires adequate safety exposure
- The **2023 nAMD Guidance** defines a **minimum of 300 patients with at least 9 months follow up**

OCULAR THERAPEUTIX Retina experience redefined™

nAMD, neovascular age-related macular degeneration; NDA, New Drug Application

Meeting The Evidentiary Standard for Effectiveness with a Single Pivotal Trial

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- FDA notes one trial may establish effectiveness, but FDA still requires adequate safety exposure
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AXPAXLI safety dataset will include **>300 patients on AXPAXLI for 12 months** at time of planned NDA submission

- SOL-1 52-week safety (n=170 at 52 weeks) plus
- SOL-R Interim 52-week safety (n >130 patients)
  - 0.0001 alpha penalty, no additional SOL-R analysis
- SOL-1 masking maintained through Year 2 for labeling
- At 120-day safety update, Year 2 SOL-1 safety data submission intended to support repeat dosing

OCULAR THERAPEUTIX Retina experience redefined™

nAMD, neovascular age-related macular degeneration; NDA, New Drug Application

Meeting The Evidentiary Standard for Effectiveness with a Single Pivotal Trial

Pre-Data

- ☑ Adequate & Well-Controlled Trial
- ☑ Protocol Aligned with FDA

Post-Data

- ☑ Superiority Primary Endpoint Met
- ☑ Clinically Meaningful Results
- ☑ Safety Dataset Meeting FDA Submission Requirements
- ☐ **Supporting Confirmatory Evidence**

2023 FDA Guidance[1] defined "confirmatory evidence"

1. Clinical Evidence from a Related Indication
2. Mechanistic or Pharmacodynamic Evidence
3. Evidence from a Relevant Animal Model
4. Evidence from Other Members of the Same Pharmacological Class
5. Natural History Evidence
6. Real-World Data/Evidence
7. Evidence from Expanded Access Use

OCULAR THERAPEUTIX Retina experience redefined™

1. FDA, Demonstrating Substantial Evidence of Effectiveness With One Adequate and Well-Controlled Clinical Investigation and Confirmatory Evidence: Draft Guidance for Industry (Sept. 2023).

Meeting The Evidentiary Standard for Effectiveness with a Single Pivotal Trial

Pre-Data

- ✓ Adequate & Well-Controlled Trial
- ✓ Protocol Aligned with FDA

Post-Data

- ✓ Superiority Primary Endpoint Met
- ✓ Clinically Meaningful Results
- ✓ Safety Dataset Meeting FDA Submission Requirements
- ✓ **Supporting Confirmatory Evidence**

2023 FDA Guidance[1] defined "confirmatory evidence"

1. Clinical Evidence from a Related Indication
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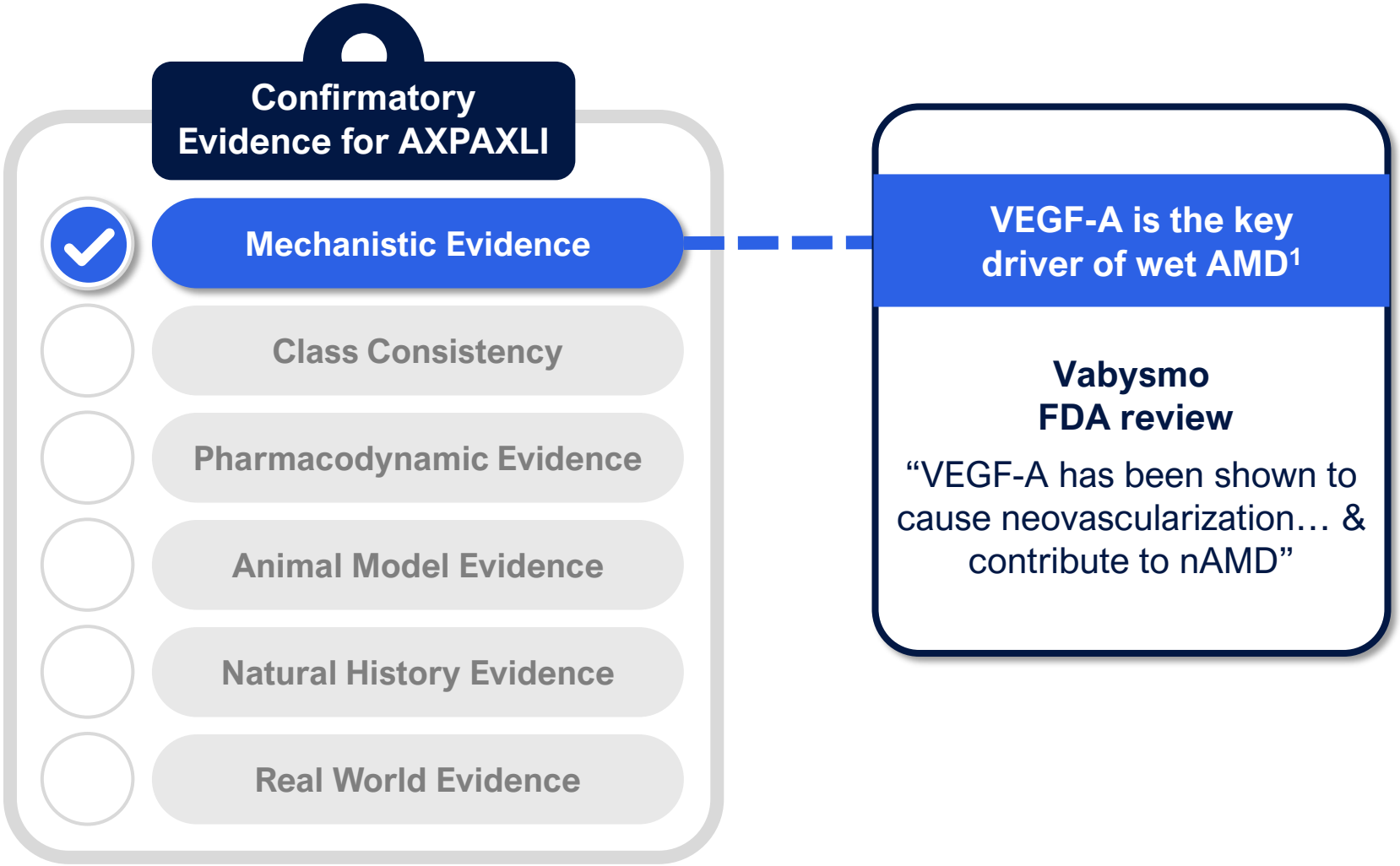
6. Real-World Data/Evidence
7. Evidence from Expanded Access Use

AXPAXLI's Substantial Evidence of Effectiveness supported by broad confirmatory evidence

OCULAR THERAPEUTIX Retina experience redefined™

1. FDA, Demonstrating Substantial Evidence of Effectiveness With One Adequate and Well-Controlled Clinical Investigation and Confirmatory Evidence: Draft Guidance for Industry (Sept. 2023).

Confirmatory Evidence Supports Substantial Evidence of Effectiveness for the Use of AXPAXLI in the Treatment of nAMD



OCULAR THERAPEUTIX Retina experience redefined™

1. U.S. Food and Drug Administration. Vabysmo (Faricimab) Non-Clinical Review – application number 761235. 2. U.S. Food and Drug Administration. Inlyta (Axitinib) Medical Review – application number 202324
AMD, age-related macular degeneration; nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor

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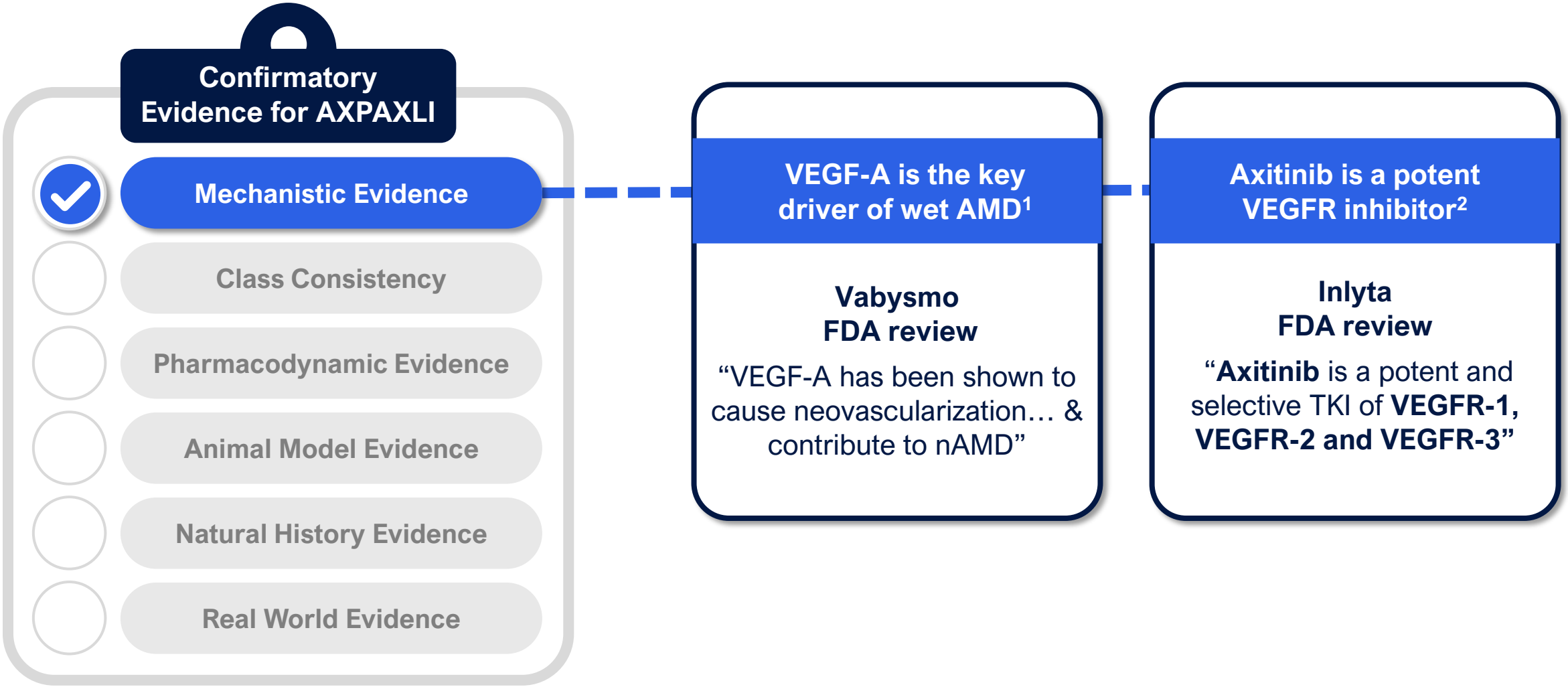

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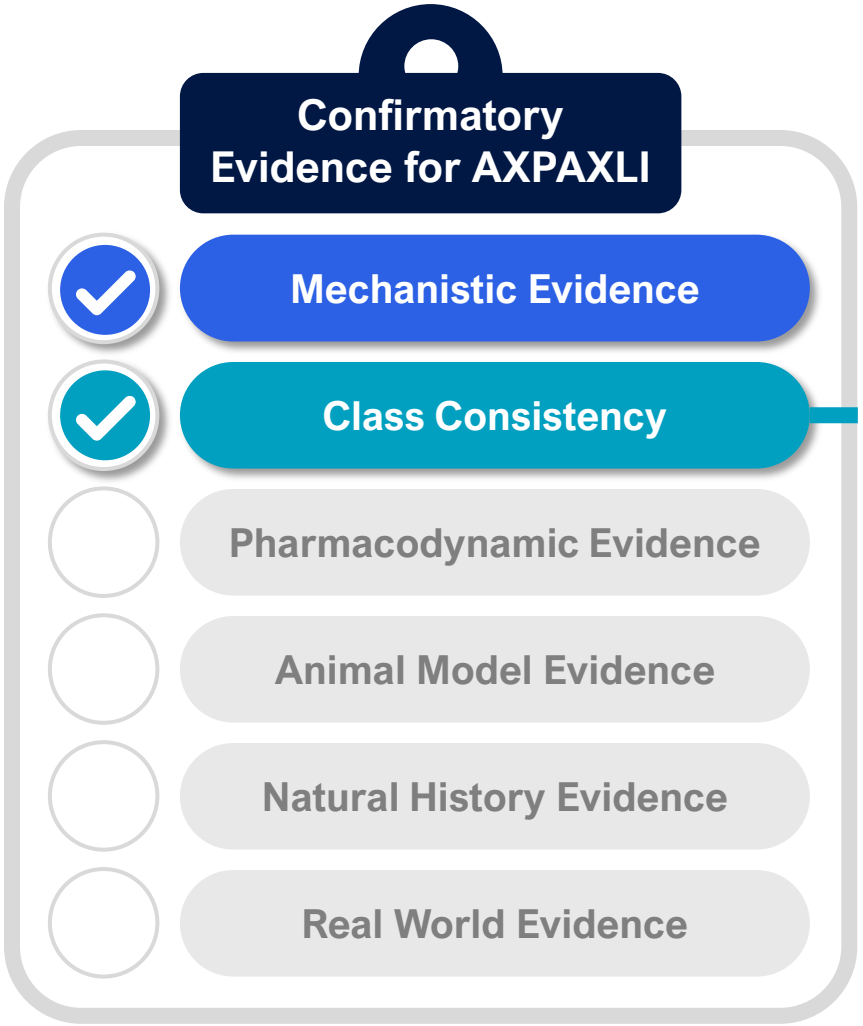


FDA recognizes evidence from other members of the same pharmacologic class

Observed effect is **consistent with what is already known for the same therapeutic class, mechanism, disease setting, endpoint, and direction of effect**

Anti-VEGF pathway has a long record of vision and anatomic benefit in wet AMD trials and real-world studies

AXPAXLI effect is in the expected direction, magnitude, time course, anatomic relationships, and safety for this therapeutic class in same disease

OCULAR THERAPEUTIX Retina experience redefined™

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

Confirmatory Evidence Supports Substantial Evidence of Effectiveness for the Use of AXPAXLI in the Treatment of nAMD

Confirmatory Evidence for AXPAXLI

- ✓ Mechanistic Evidence
- ✓ Class Consistency
- ✓ Pharmacodynamic Evidence
- Animal Model Evidence
- Natural History Evidence
- Real World Evidence

Highly selective for *all* VEGF and PDGF receptors, minimal off target inhibition

Physiologic Levels for Testing

1µM*

Axitinib intraocular conc = 1.03 to 1.13 µM
Vorolanib intraocular conc = 0.23 to 0.95 µM[3,4,6]

Kinase[1,2]	Axitinib	Vorolanib[3-5]	Sunitinib
VEGF RECEPTORS			
VEGFR1	100%	39%	83%
VEGFR2	97%	28%	71%
VEGFR3	95%	59%	72%
OTHER RECEPTORS			
PDGFRα	79%	65%	70%
PDGFRβ	88%	64%	87%

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.

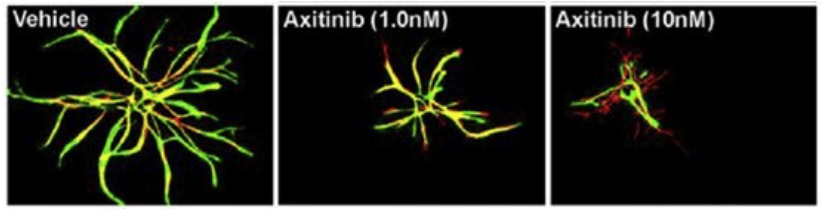
1. Data on file, Ocular Therapeutix. 2. Patel C, et al. Target and Selectivity Profiling of Axitinib in Cell-Based and Biochemical Assays. Presented at the Association for Research in Vision and Ophthalmology. May 8, 2025, Salt Lake City, UT. 3. Singh RP, et al. A 12-Month, Ocular Pharmacokinetic Study 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; 6. Saim, S., Howard-Sparks, M., Paggiarino, D., Karzoun, B. and Chen, J., Eyepoint Pharmaceuticals Inc, 2026. Bioerodible ocular drug delivery insert and therapeutic method. U.S. Patent 12,551,368.;
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

Confirmatory Evidence Supports Substantial Evidence of Effectiveness for the Use of AXPAXLI in the Treatment of nAMD

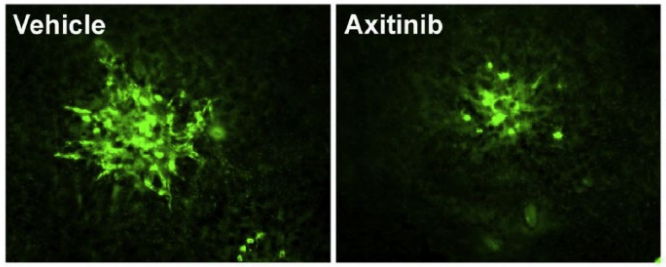
Confirmatory Evidence for AXPAXLI

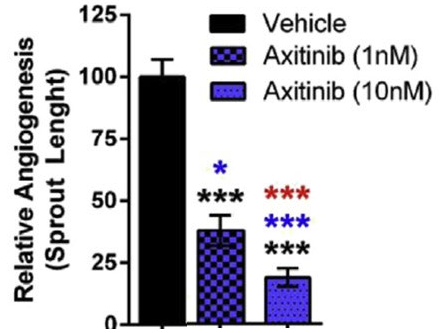
- ✓ Mechanistic Evidence
- ✓ Class Consistency
- ✓ Pharmacodynamic Evidence
- ✓ Animal Model Evidence
- Natural History Evidence
- Real World Evidence

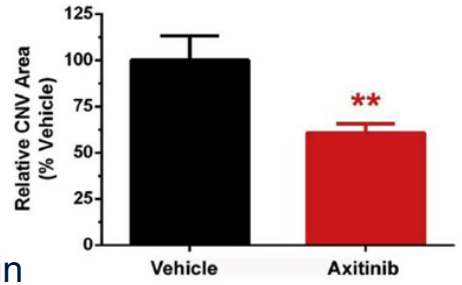
Axitinib inhibits VEGF & PDGF mediated angiogenic sprouts in human retinal microvascular endothelial cells and pericytes



The sprouts in green are endothelial cells and sprouts in red are pericytes







Axitinib inhibits angiogenesis and vascular leakage in the *in vivo* rat choroidal neovascularization (CNV) model

OCULAR THERAPEUTIX Retina experience redefined™

Data on File. Ocular Therapeutix. 2026.
VEGFR, vascular endothelial growth factor receptor; nAMD, neovascular age-related macular degeneration; PDGFR, platelet-derived growth factor receptor

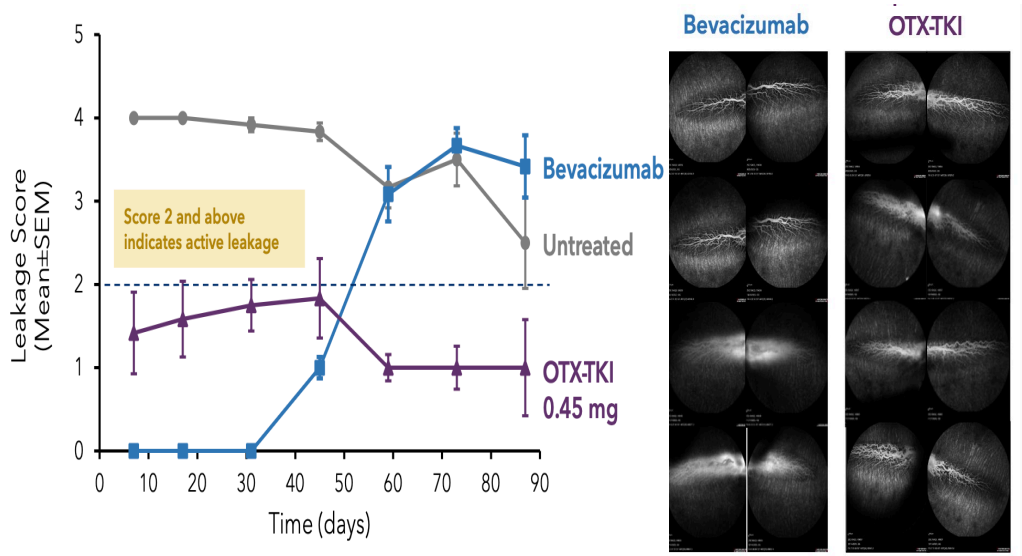
Confirmatory Evidence Supports Substantial Evidence of Effectiveness for the Use of AXPAXLI in the Treatment of nAMD

Confirmatory Evidence for AXPAXLI

- ✓ Mechanistic Evidence
- ✓ Class Consistency
- ✓ Pharmacodynamic Evidence
- ✓ Animal Model Evidence
- Natural History Evidence
- Real World Evidence

AXPAXLI Demonstrated Leakage Suppression in Rabbit VEGF Challenge model

Figure 7 Suppression of Vascular Leakage in the Rabbit VEGF Challenge Model Following Administration of OTX-TKI Formulated with 0.45 mg Form IV



- **Rabbit VEGF-challenge model** a well-established animal model to evaluate efficacy
- **Positive & negative controls** validate test methods
- **AXPAXLI** demonstrates durable suppression of vascular leakage in validated test

OCULAR THERAPEUTIX Retina experience redefined™

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.

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

Confirmatory Evidence Supports Substantial Evidence of Effectiveness for the Use of AXPAXLI in the Treatment of nAMD

Confirmatory Evidence for AXPAXLI

- ✓ Mechanistic Evidence
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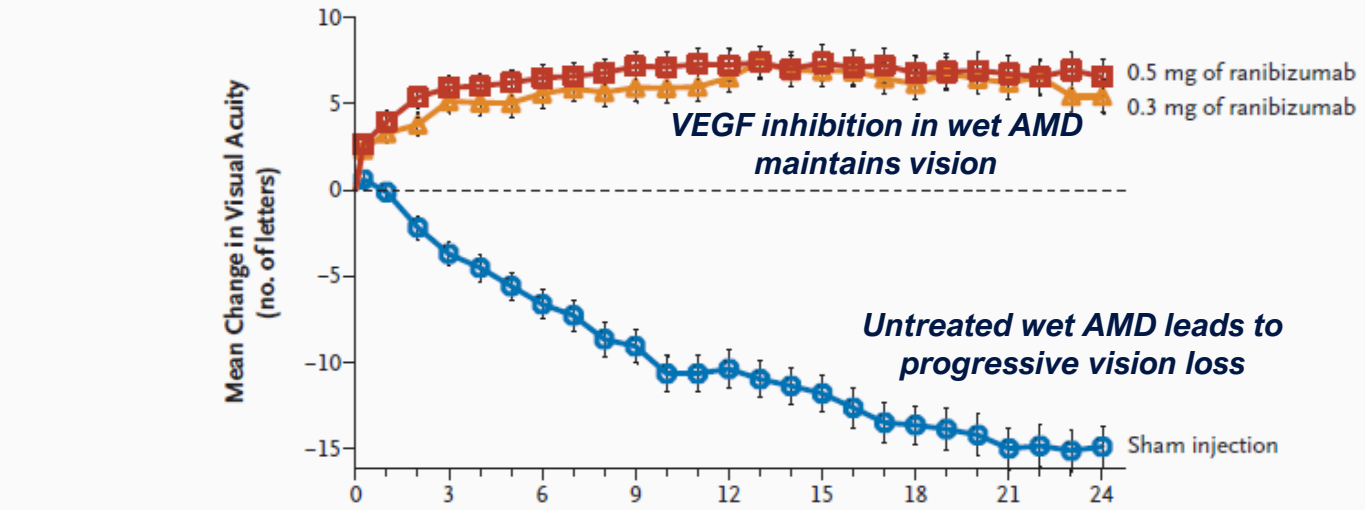
- Real World Evidence

Natural History Evidence[1]



Mean Change from Baseline	(day 7)								
0.5 mg of ranibizumab	+2.6	+5.9	+6.5	+7.2	+7.2	+7.4	+6.8	+6.7	+6.6
0.3 mg of ranibizumab	+2.3	+5.1	+5.6	+5.9	+6.5	+6.9	+6.1	+6.2	+5.4
Sham injection	+0.6	−3.7	−6.6	−9.1	−10.4	−11.8	−13.6	−15.0	−14.9

OCULAR THERAPEUTIX Retina experience redefined™

1. Rosenfeld PJ, et al. *N Engl J Med*. 2006;355(14):1419-1431

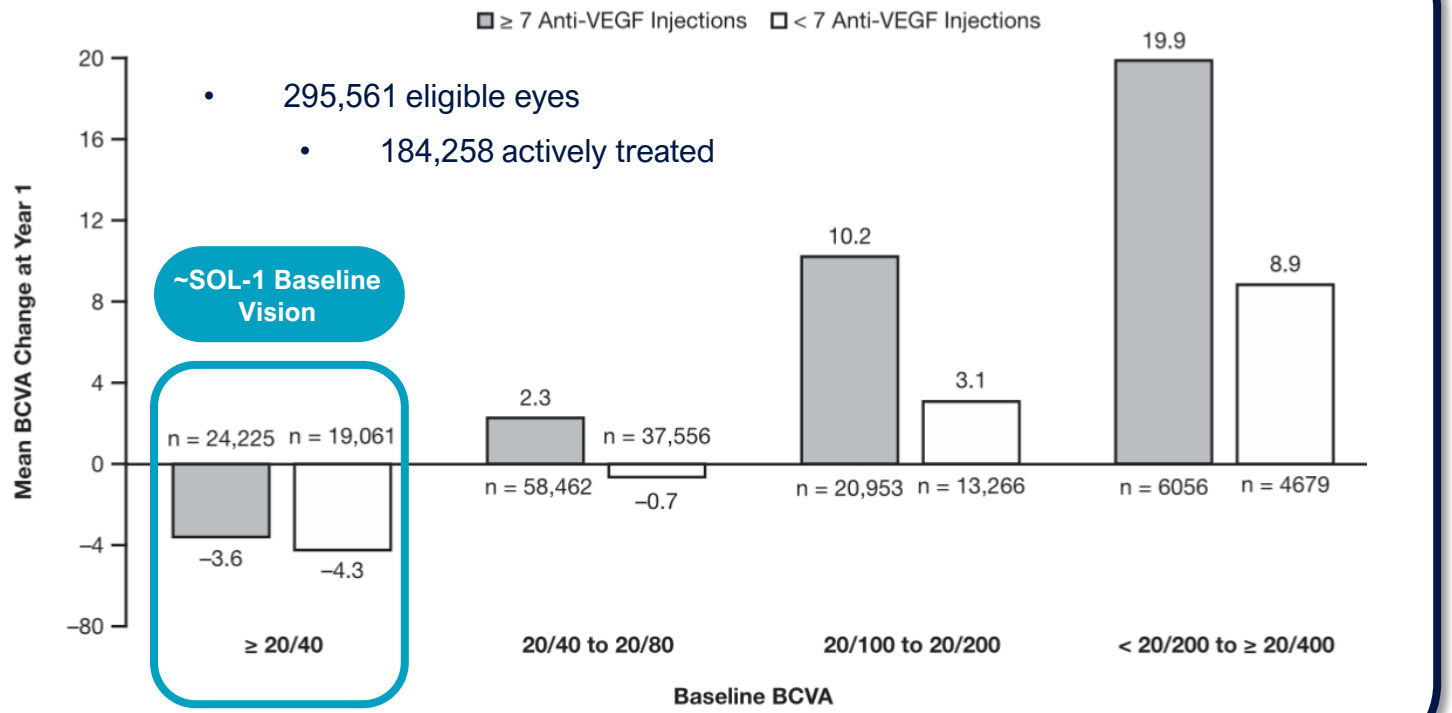
VEGF, vascular endothelial growth factor; AMD, age-related macular degeneration

Confirmatory Evidence Supports Substantial Evidence of Effectiveness for the Use of AXPAXLI in the Treatment of nAMD

Confirmatory Evidence for AXPAXLI

- Mechanistic Evidence
- Class Consistency
- Pharmacodynamic Evidence
- Animal Model Evidence
- Natural History Evidence
- Real World Evidence

Real World Evidence of anti-VEGF Treatment



OCULAR THERAPEUTIX Retina experience redefined™

Barikian et al. *Ophthalmology Retina* 2026;10:71-80
BCVA, best-corrected visual acuity; VEGF, vascular endothelial growth factor

Confirmatory Evidence Supports Substantial Evidence of Effectiveness for the Use of AXPAXLI in the Treatment of nAMD

Confirmatory Evidence for AXPAXLI

- Mechanistic Evidence
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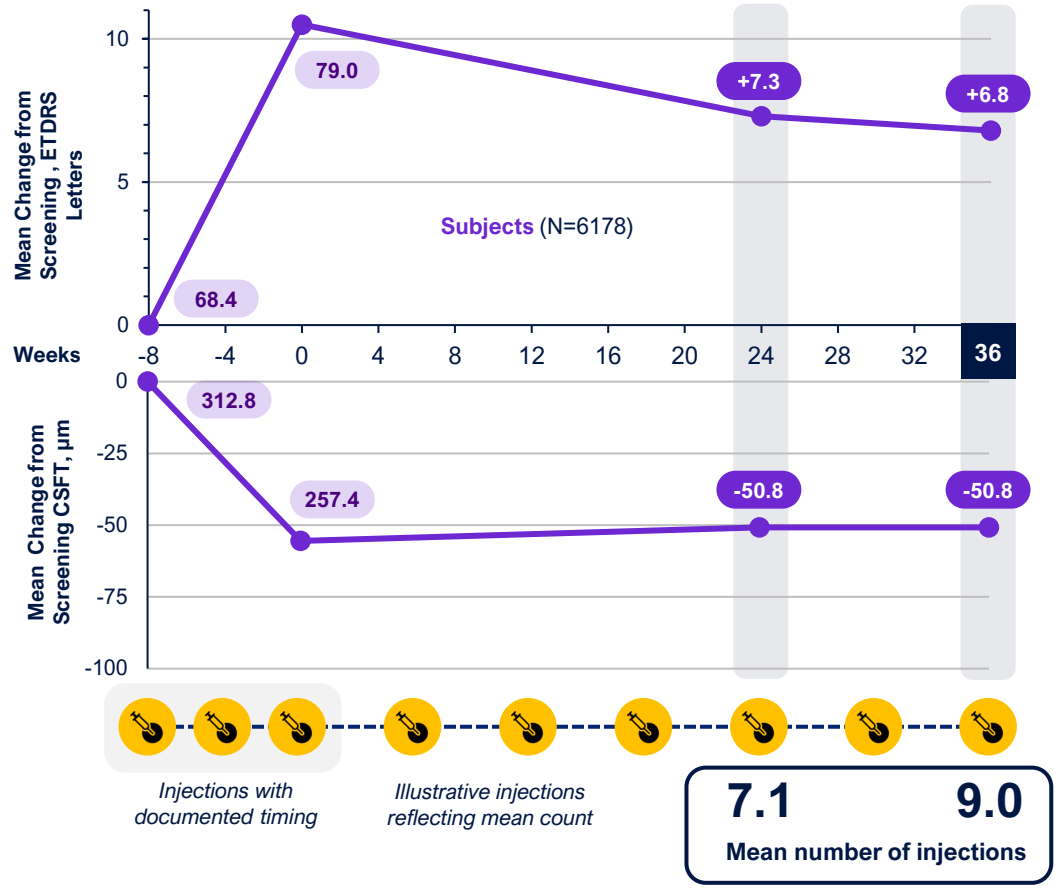
- Natural History Evidence
- Real World Evidence

SOL-1 Emulated Population
IRIS Registry



OCULAR THERAPEUTIX Retina experience redefined™

ETDRS, early treatment diabetic retinopathy study; CSFT, central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium

What's Going into the AXPAXLI NDA Package, per Type C Meeting Minutes

AXPAXLI NDA Package

	SOL-1	SOL-R
Efficacy	**Week 52 Data**	**None**
Safety	Week 52 Data	Interim Analysis
120 Day Safety Update	Week 104 Data	None

AXPAXLI Efficacy for NDA

Efficacy Data from
SOL-1 Week 52 data

No SOL-R Efficacy Data
included in the NDA

What's Going into the AXPAXLI NDA Package, per Type C Meeting Minutes

AXPAXLI NDA Package

	SOL-1	SOL-R
Efficacy	Week 52 Data	None
Safety	**Week 52 Data**	**Interim Analysis**
120 Day Safety Update	Week 104 Data	None

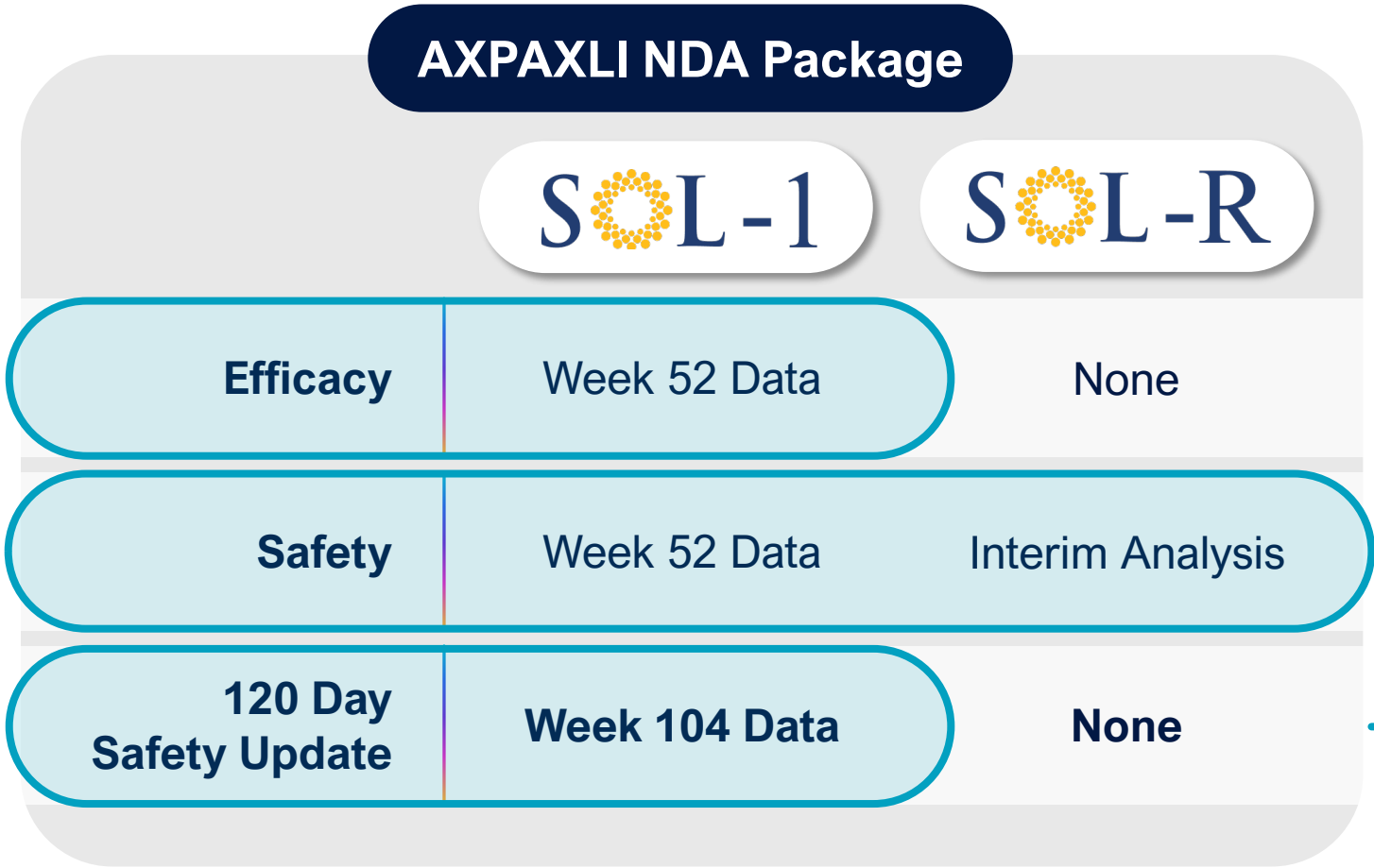
AXPAXLI Safety for NDA

Aligned with FDA to conduct unscheduled interim safety review of SOL-R

Will incur **0.0001 alpha penalty** for unscheduled analysis

Enables NDA submission with >300 patients for safety review

What's Going into the AXPAXLI NDA Package, per Type C Meeting Minutes



120 Day Safety Update

Year 2 Safety from SOL-1 for repeat dosing

No additional data that would trigger a major amendment will be submitted during NDA review

OCULAR THERAPEUTIX Retina experience redefined™

NDA, New Drug Application

Timeline to AXPAXLI NDA Submission Package

Feb 2026 — **Positive SOL-1 Week 52 results** announced on February 17, 2026

May 2026 — **Early Alignment at Type C Meeting:**
FDA agreed in writing on NDA submission with SOL-1 trial plus confirmatory evidence

3Q 2026 — **Pre-NDA meeting:**
To align on format and content of information to be submitted in NDA

4Q 2026 — **SOL-R interim safety database lock** to reach >300 patients planned

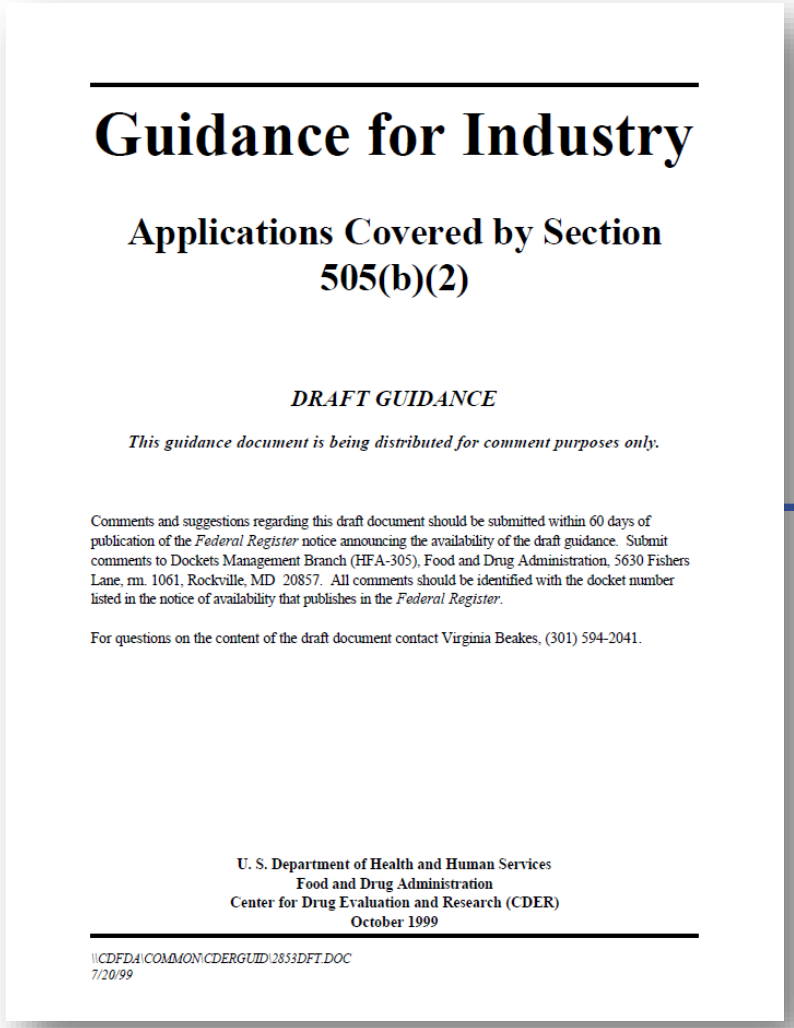
4Q 2026 — **Complete AXPAXLI NDA package to be submitted to FDA**

Post-NDA — **Year 2 Safety from SOL-1**
Intended to support repeat dosing to be submitted at 120-day safety update

OCULAR THERAPEUTIX Retina experience redefined™

NDA, New Drug Application

Next Steps: AXPAXLI NDA Submission Leveraging the 505(b)(2) Pathway



Guidance for Industry

Applications Covered by Section 505(b)(2)

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication of the *Federal Register* notice announcing the availability of the draft guidance. Submit comments to Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20857. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions on the content of the draft document contact Virginia Beakes, (301) 594-2041.

U. S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
October 1999

\\CDFDA\COMMON\CDERGUID\2853DFT.DOC
7/20/99

505(b)(2) Pathway

- **Hybrid new drug application** for approval of drugs that are **similar to, but not identical, to previously approved drugs**
- Allows reliance on established safety and efficacy
- **Accelerates approval for new formulations**, dosages, **routes of administration** or indications

Axitinib approved for renal cell carcinoma in 2012

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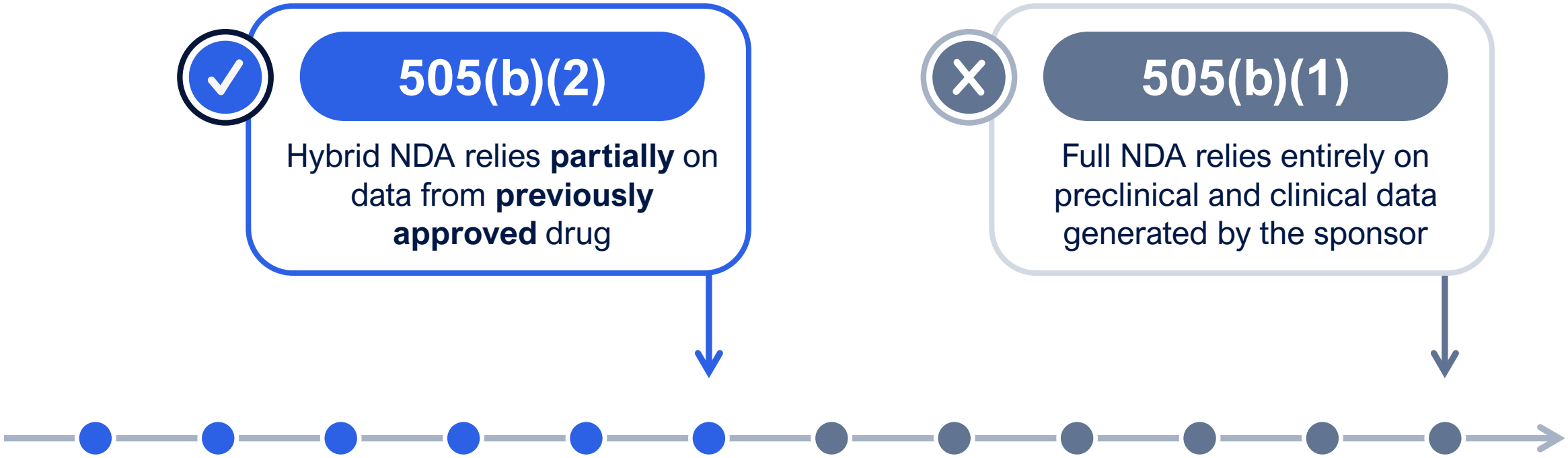
The 505(b)(2) Pathway vs 505(b)(1) Pathway



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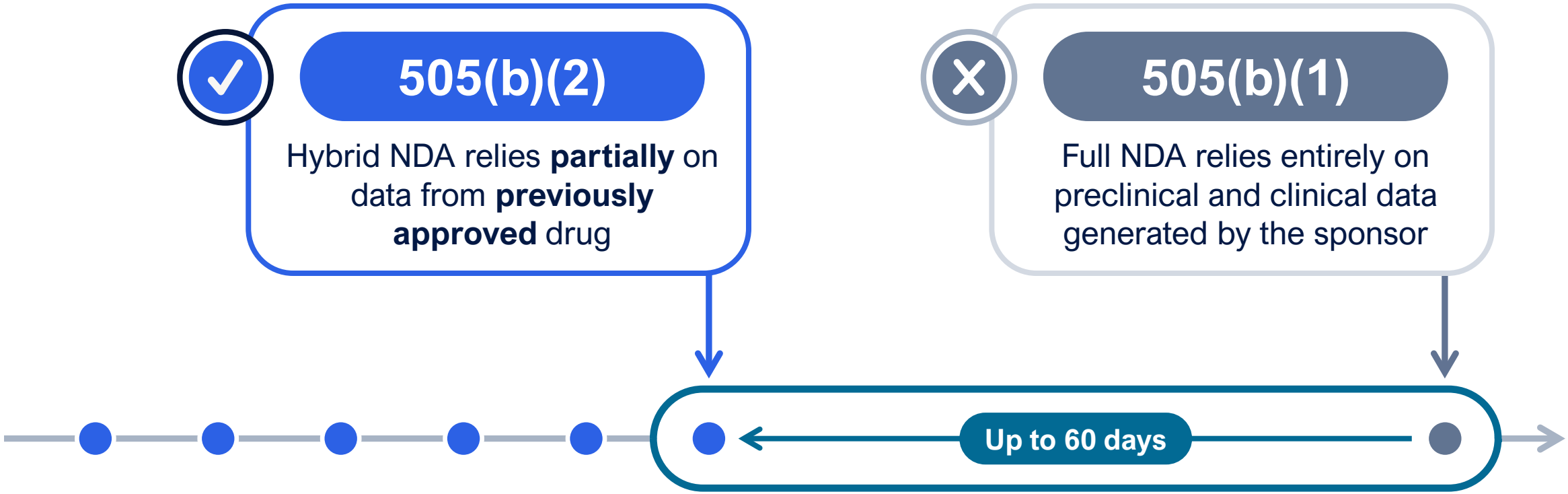
Goldstein, Beth, and Science Analyst. OVERVIEW of the 505(B)(2) REGULATORY PATHWAY for NEW DRUG APPLICATIONS. www.fda.gov/media/156350/download.
NDA, New Drug Application

The 505(b)(2) Pathway Provides Up to 60 Days Advantage over 505(b)(1)



Using the 505(b)(2) pathway compared to 505(b)(1)

Goldstein, Beth, and Science Analyst. OVERVIEW of the 505(B)(2) REGULATORY PATHWAY for NEW DRUG APPLICATIONS. www.fda.gov/media/156350/download.
NDA, New Drug Application

AXPAXLI NDA Package Designed to Meet FDA "Substantial Evidence of Effectiveness" and Safety Requirements

Highly Positive SOL-1 Trial Aligned with FDA through SPA + **Safety** + **Confirmatory Evidence** =

Positive, Adequate, Well-Controlled Trial	Highly Stat Sig Results	Clinical Coherence & Consistency	Sufficient Safety Package	Broad Confirmatory Evidence
SOL-1 has SPA Agreement w/ FDA	**SOL-1 superiority trial is highly stat sig**	**3 of 5 key secondaries met in hierarchical fashion w/ stat sig**	**>300 patients for one year at NDA submission**	**Strong confirmatory evidence as part of NDA**
Design, endpoints, study size, and SAP aligned in advance	17.5% risk dif. for AXPAXLI vs control at Week 36 (p=0.0006)	Superiority in maintaining vision, anatomic results, rescue-free all supportive	Will include 170 from SOL-1 and >130 from SOL-R	Mechanistic, PD, PK, class consistency, animal model, natural history, and real-world evidence

AXPAXLI NDA Submission in 4Q 2026 Following Interim SOL-R Safety Analysis

OCULAR THERAPEUTIX Retina experience redefined™

wAMD, wet age-related macular degeneration; SPA, Special Protocol Assessment; SAP, statistical analysis plan; NDA, New Drug Application

Ocular Therapeutix 2026 Investor Day Agenda

Intro & Overview
Pravin U. Dugel, MD

SOL-1 Data & AXPAXLI Clinical Program Review
Nadia K. Waheed, MD, MPH

U.S. Regulatory Strategy in Wet AMD
Peter K. Kaiser, MD

Discussion: AXPAXLI NDA Submission Strategy
Moderator: Peter K. Kaiser, MD

Ocular Panelist: Arthur Ciociola, PhD

Preparing for a Successful Launch
David Robinson

SOL-R: Defining Non-Inferiority Success
Jeffrey S. Heier, MD

KOL Perspectives: Potential to Redefine Retina
Moderator: Jeffrey S. Heier, MD

KOLs: Arshad Khanani, MD; Lejla Vajzovic, MD; Darius Moshfeghi, MD

Summary & Takeaways
Pravin U. Dugel, MD

Audience Q&A
All

OCULAR THERAPEUTIX Retina experience redefined™

Discussion: AXPAXLI NDA Submission Strategy

Peter K. Kaiser, MD

Chief Development Officer

Arthur Ciociola, PhD

Chief Regulatory and
Quality Officer

OCULAR THERAPEUTIX Retina experience redefined™

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Preparing for a Successful Launch

David Robinson
Global Chief Commercial Officer

OCULAR THERAPEUTIX Retina experience redefined™

Preparing For An Accelerated Launch of AXPAXLI

Following successful Type C meeting with FDA, NDA submission planned for 4Q 2026

Preparing for launch in 2027, if approved

OCULAR THERAPEUTIX Retina experience redefined™

NDA, New Drug Application

AXPAXLI Potential

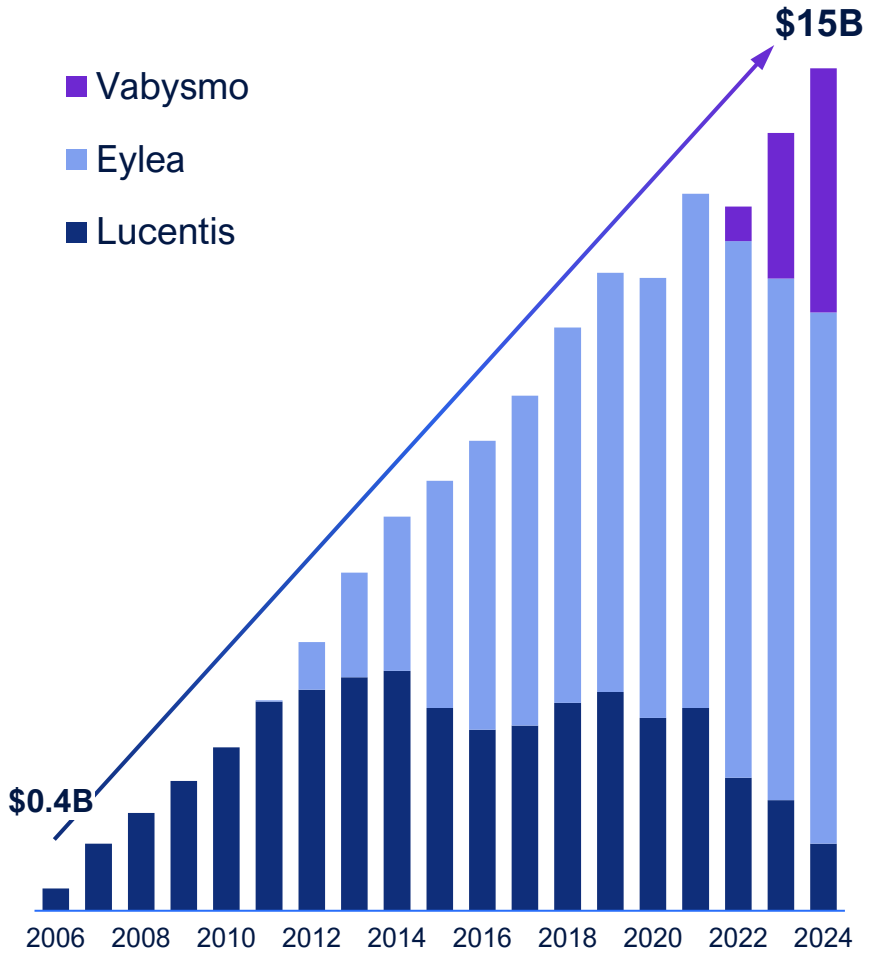
Positive Feedback

Launch Preparation

OCULAR THERAPEUTIX Retina experience redefined™

Current Anti-VEGF Landscape

Global Branded Anti-VEGF Revenue[1]



Strong growth despite shortfalls

Globally, the branded anti-VEGF market has grown to ~$15B

Treatment is currently defined by short acting aVEGF therapies

- Lucentis – 30 days[2]
- EYLEA - 44 days[3] (+ 2 weeks)
- VABYSMO - 57 days[3] (+ 2 weeks after 6 injections)

Marginal improvements in durability typically lead to quick and significant market share

- VABYSMO offers ~2-week improvement in durability over EYLEA
- Within 3 years of launch generated $4.4B in WW revenue

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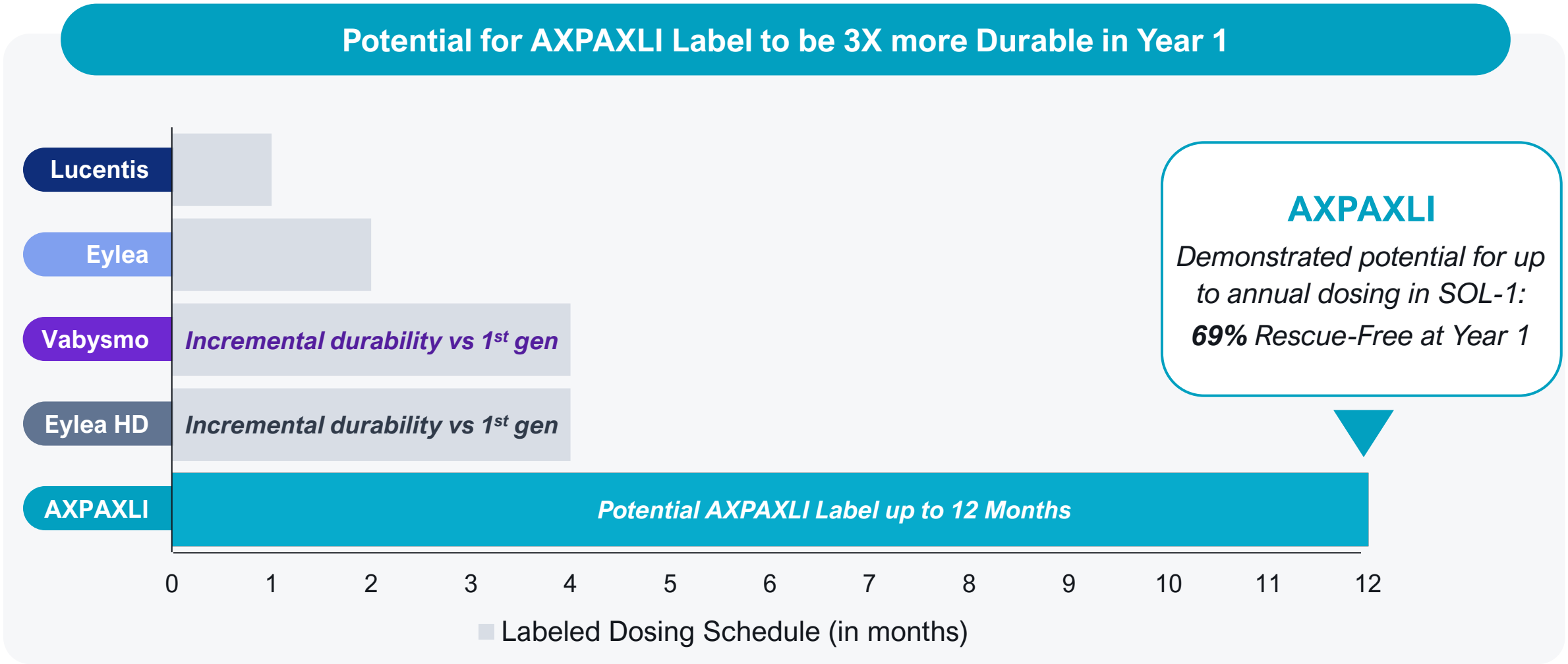
1. Data aggregated from company reports. Captures revenue across all labeled indications. Figure excludes BEOVU®. EYLEA® HD FDA approved in August 2023 captured in EYLEA® sales figures. 2. LUCENTIS® package insert. San Francisco, CA: Genentech, Inc. 2018. 3. Real-World Evidence (TRUCKEE Study): VABYSMO® offers 1-2 week extension over EYLEA® in switch patients. Study Results presented at Roche Ophthalmology Day, July 2024.
VEGF, vascular endothelial growth factor

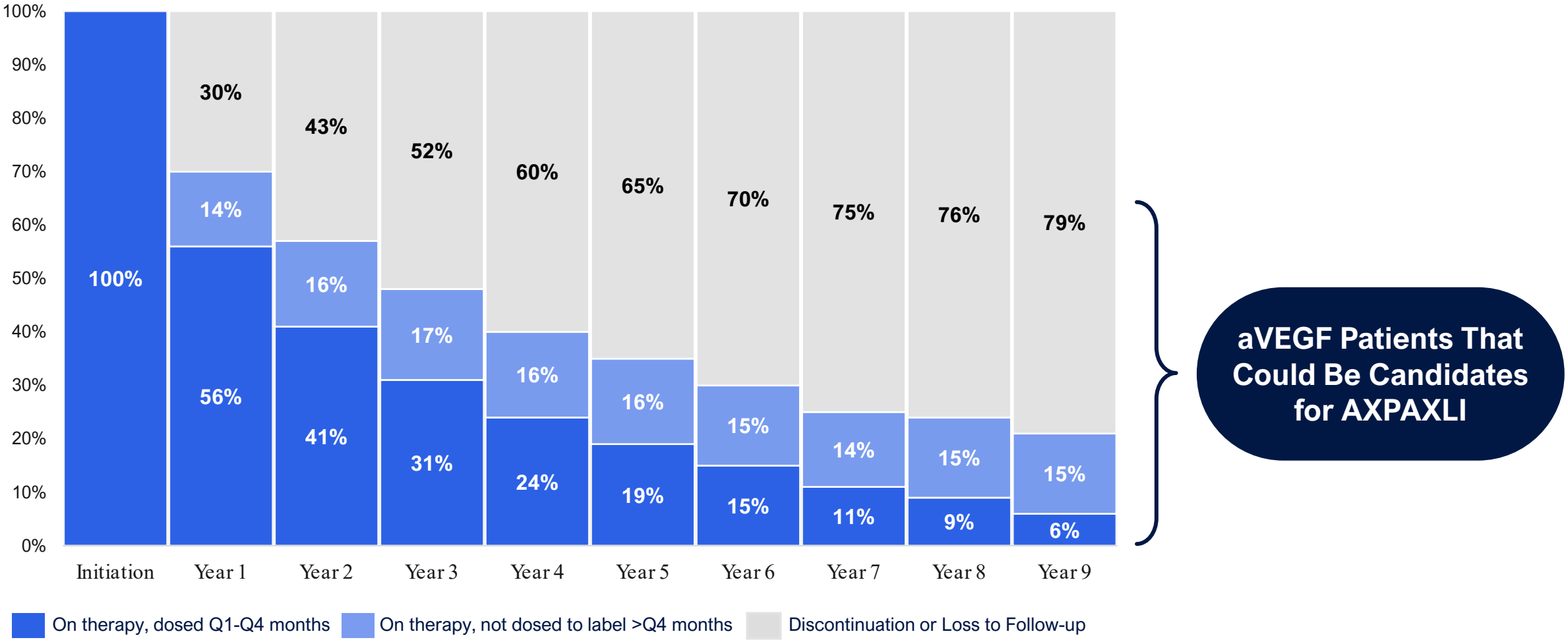
Durability of AXPAXLI is Unmatched Relative to Current Agents



OCULAR THERAPEUTIX Retina experience redefined™

Dosing Schedules Illustrated for Year 1; Eylea HD approved for up to 5-month dosing after 1 year of treatment in patients who have a successful visual and anatomic response

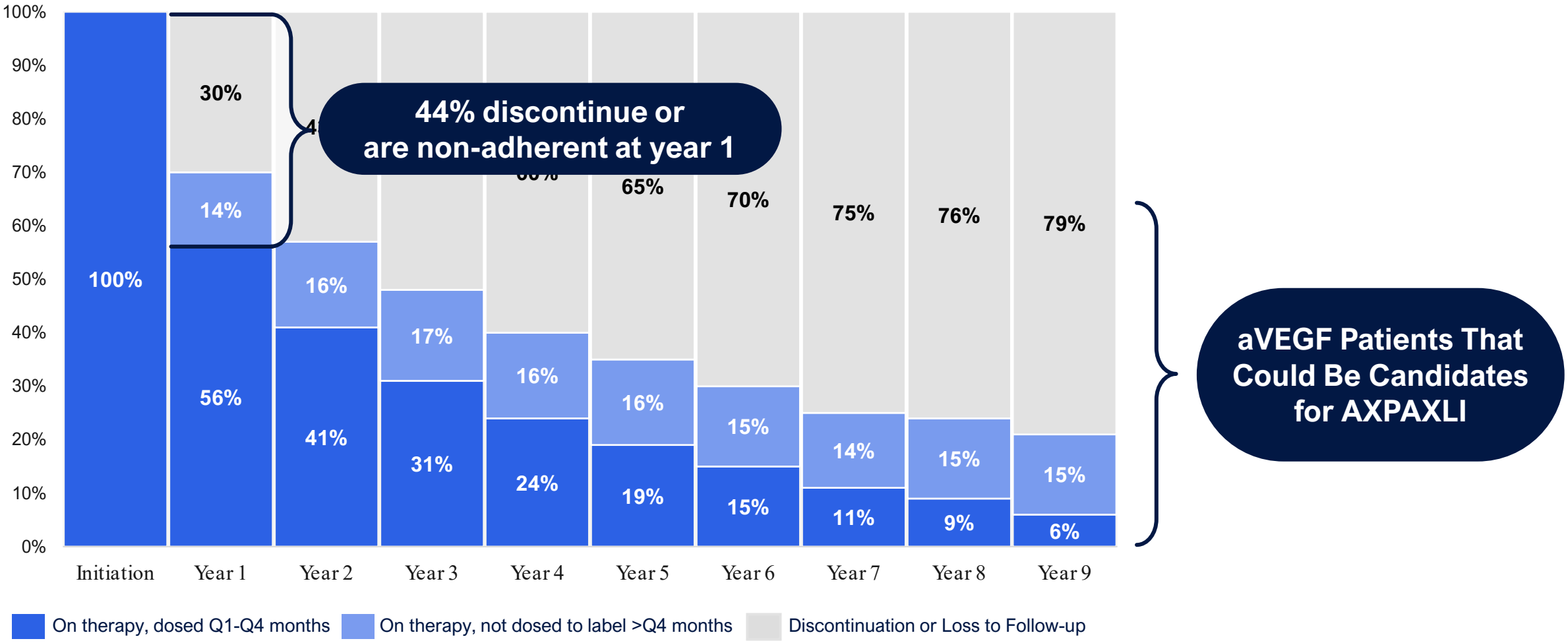
AXPAXLI Potential to Significantly Improve Long-Term Treatment Dynamics



OCULAR THERAPEUTIX Retina experience redefined™

OCUL Internal Analysis of aVEGF adherence in IRIS and Vestrum Databases
Q1, every month; Q4, every 4 months

AXPAXLI Potential to Significantly Improve Long-Term Treatment Dynamics



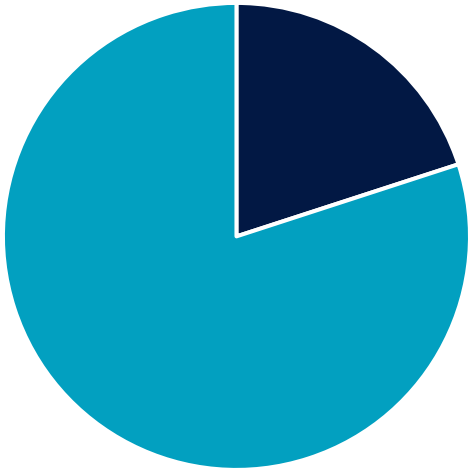
OCULAR THERAPEUTIX Retina experience redefined™

OCUL Internal Analysis of aVEGF adherence in IRIS and Vestrum Databases
Q1, every month; Q4, every 4 months

AXPAXLI Anticipated Use By Patient Segment

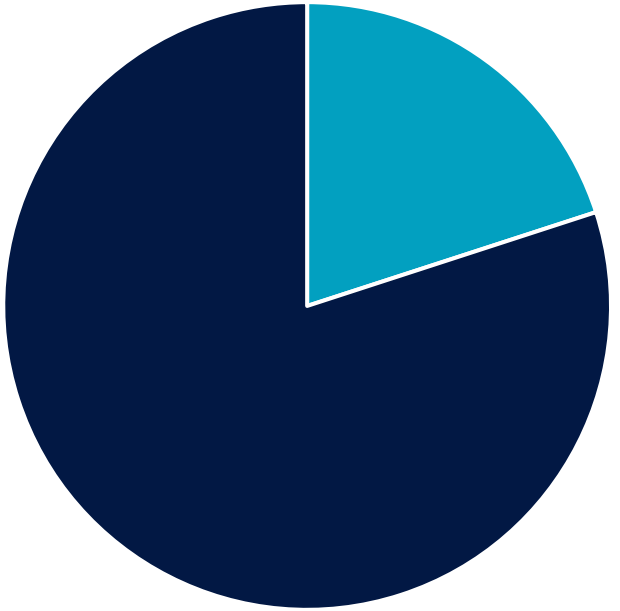
Projected Dynamics: Early-Launch Phase

Greatest near-term opportunity **post-launch is in aVEGF** conversions



Illustrative

Projected Mature Market Dynamics



Illustrative

Market expansion & increase in Tx naïve starts expected over time with improved adherence & long-term outcomes

AXPAXLI is well suited for immediate adoption across treatment naïve patients and those already receiving aVEGF therapy

aVEGF Conversions to AXPAXLI

Treatment Naïve Starts on AXPAXLI

OCULAR THERAPEUTIX Retina experience redefined™

aVEGF, anti-vascular endothelial growth factor; Tx, treatment

AXPAXLI Potential

Positive Feedback

Launch Preparation

Key Insights: Retina Specialists

Rapid Adoption

>90% of retina specialists would adopt AXPAXLI **within 1st year of launch**[1,2]

~25% would rapidly adopt within the first 3 months of availability[1,2]

Broad Utilization

Improved disease control and **predictable 6+ month** durability drives broad use[3,4]

99% would utilize AXPAXLI in future wet AMD patients[1,2]

Seamless Practice Integration

Pre-filled intravitreal injection facilitates smooth practice integration[3,4]

Increased patient capacity and **fewer anticipated scheduling challenges** with AXPAXLI[3,4]

OCULAR THERAPEUTIX Retina experience redefined™

1. Ocular Therapeutix Sponsored Quantitative Market Research (n=100 Retina Specialists) Conducted September-October 2025; 2. Ocular Therapeutix Sponsored Quantitative Market Research (n=100 Retina Specialists) Conducted June 2025; 3. Ocular Therapeutix Sponsored Qualitative Market Research (n=25 Retina Specialists) Conducted December 2024 – January 2025; 4. Ocular Therapeutix Sponsored Qualitative Market Research (n=16 Retina Specialists) Conducted December 2024 – January 2025
AMD, age-related macular degeneration

Retina Specialist Feedback Post-SOL-1

Following SOL-1 data, we have been very busy gathering feedback from the Retina Specialist community

~80%

Of Retina Specialists surveyed[1] were likely or extremely likely to utilize AXPAXLI based on SOL-1 Data Alone

OCULAR THERAPEUTIX Retina experience redefined™

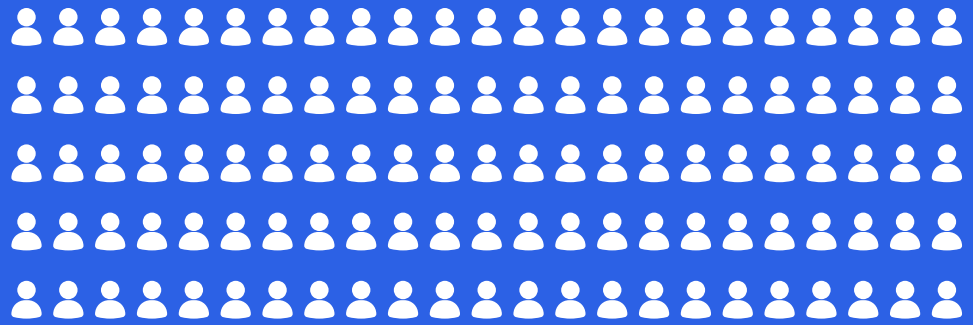
1.Ocular Therapeutix Market Research (n=53 Retina Specialists) Conducted February-May 2026, Retina Specialists surveyed at Medical Presentations of SOL-1 Data

Early Payer Engagement is Validating the Unmet Need for Durability, Adherence and Long-Term Visual Outcomes

Experienced payer team early engagements have covered:

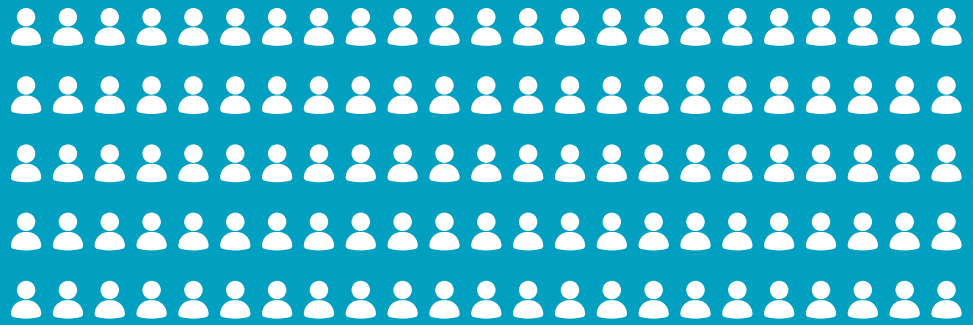
100%

of Tier 1 **MEDICARE ADVANTAGE** Lives



100%

of Tier 1 **COMMERCIAL** Lives



OCULAR THERAPEUTIX Retina experience redefined™

Payer Insights Indicate Strong Potential for Premium Pricing

Superiority Label

Payers acknowledge that a **label with superior durability** potentially **transforms the market** and may command **premium pricing**

> **Superiority in durability would get our attention relative to Total Cost of Care**

Adherence and LT Outcomes

Payers agree that **improving adherence** could **improve long-term patient outcomes**

Real World Evidence

- Cost Avoidance (Blindness/Vision Loss)
- Cost Effectiveness
- Easing Capacity Constraints
- Lowering Healthcare Resource Utilization

OCULAR THERAPEUTIX Retina experience redefined™

AXPAXLI Potential

Positive Feedback

Launch Preparation

OCULAR THERAPEUTIX Retina experience redefined™

Current Treatment Challenges Represent a Clear Market Opportunity

No Superiority Label

- Approvals based on non-inferiority trial design
- Minimal efficacy or durability differentiation
- Payers cite lack of differentiation among approved treatments[1]

Market Dynamics

- Biosimilar entrants
- Increased competitive pressure to rebate/discount
- Focus on financial not safety, efficacy and durability parameters

Clear market opportunity to differentiate for Superiority label with Predictive, Durable dosing and Positive long-term vision maintenance outcomes

OCULAR THERAPEUTIX Retina experience redefined™

1. Data on File. Ocular Therapeutix. 2026.

Current Market Dynamics Put Ocular In A Position to Win

1.8M wet AMD Patients in the U.S. Alone

Concentrated Call Point

2.5 – 3K Retina Specialists in U.S.

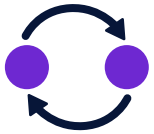
~600 HCPs account for 80% of claims volume[1]

High Treatment Initiation Rate

71% initiate within 1st month of diagnosis[2]

Dropouts due to insufficient durability

High Switch Rate



Patients often request most durable product[3]

Low RS tolerance for underperforming products

OCULAR THERAPEUTIX Retina experience redefined™

1.Analysis of Symphony Clams Data; 2. Acharya B, et al.; IRIS® Analytic Center Consortium. Disparities in Presentation and Anti-VEGF Therapy Initiation for Neovascular Age-Related Macular Degeneration: An Analysis of the Academy IRIS® Registry (Intelligent Research in Sight). Ophthalmology. 2025; 3. Roche Q2 2022 Earnings Call

AMD, age-related macular degeneration; HCPs, healthcare providers; RS, retina specialist

Our Team is Ready

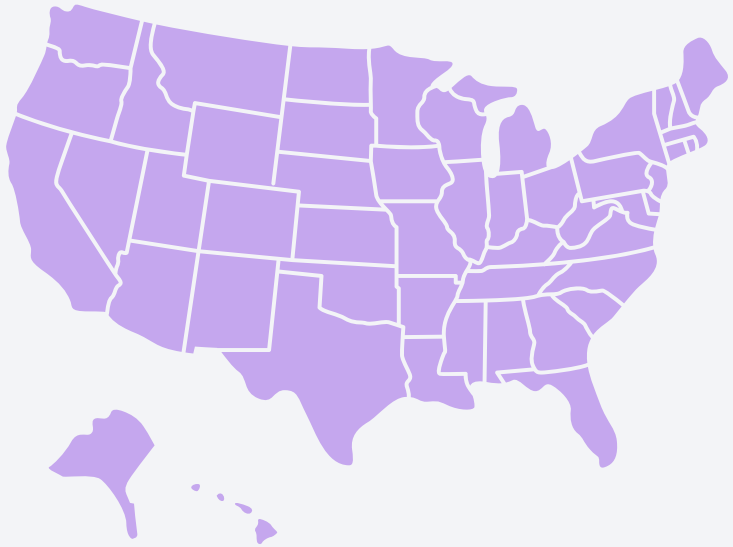
Powered by Existing Field Expertise

Existing National Coverage

Total Team of 65

~50-person Field Team

~15-person Reimbursement Team



World Class Retina Leadership

David Robinson
Global CCO

Steve Meyers
CCO

Namrata Saroj
CBO

Nicole Harris
SVP, Marketing

Kelley Allison
SVP, Market Access

Andrea Gibson
SVP, Medical Collab

John France
VP, Comm Ops

Decades of combined experience in industry and retina

Proven history of launching retina treatments:

LUCENTIS® RANIBIZUMAB INJECTION

EYLEA® (aflibercept) Injection For Intravitreal Injection

izervay™ (avacincaptad pegol intravitreal solution)

Beovu® (brolucizumab-dbll) Injection

OCULAR THERAPEUTIX Retina experience redefined™

Key Launch Preparation Activities - Ongoing

Commercial Strategy

Key Account Segmentation and Prioritization

Launch Scenario Planning

Distribution Network Strategy

Launch Infrastructure

Patient Support Hub Buildout

Data and Analytics Enablement

Organizational Enablement

Talent Planning and Organization

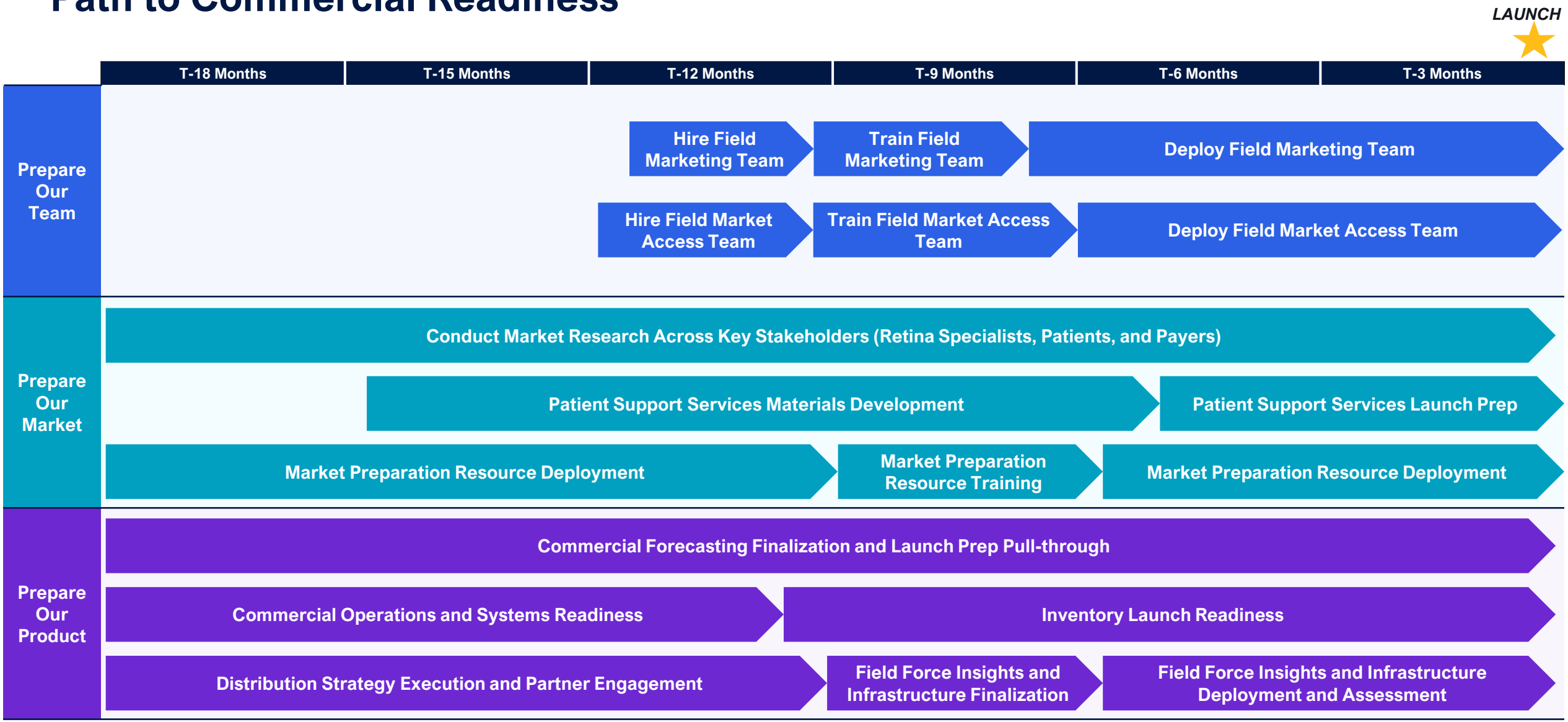
Cross-functional Operating Model

Training Readiness

Preparing for AXPAXLI Launch in 2027, if Approved

OCULAR THERAPEUTIX Retina experience redefined™

Path to Commercial Readiness



OCULAR THERAPEUTIX Retina experience redefined™

AXPAXLI Potential to Redefine the Retina Market

1. Large Market Size and a Global Opportunity
2. Redefines Retina Treatment Dosing
3. Superiority Label Positions AXPAXLI in a Class of One
4. Economic Predictability for Payers, Physicians & Patients

Ocular Therapeutix 2026 Investor Day Agenda

Intro & Overview
Pravin U. Dugel, MD

SOL-1 Data & AXPAXLI Clinical Program Review
Nadia K. Waheed, MD, MPH

U.S. Regulatory Strategy in Wet AMD
Peter K. Kaiser, MD

Discussion: AXPAXLI NDA Submission Strategy
Moderator: Peter K. Kaiser, MD

Ocular Panelist: Arthur Ciociola, PhD

Preparing for a Successful Launch
David Robinson

SOL-R: Defining Non-Inferiority Success
Jeffrey S. Heier, MD

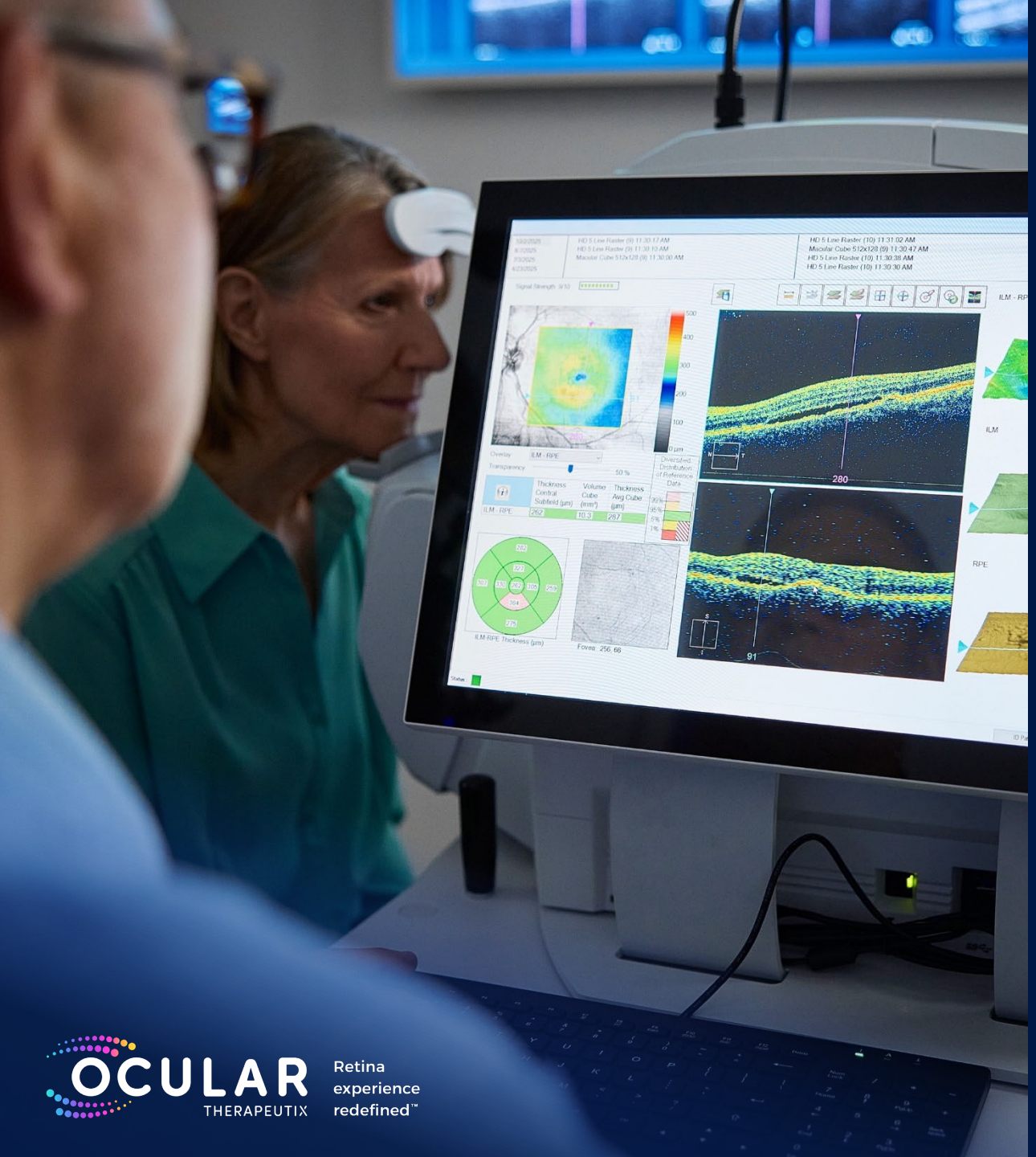
KOL Perspectives: Potential to Redefine Retina
Moderator: Jeffrey S. Heier, MD

KOLs: Arshad Khanani, MD; Lejla Vajzovic, MD; Darius Moshfeghi, MD

Summary & Takeaways
Pravin U. Dugel, MD

Audience Q&A
All

OCULAR THERAPEUTIX Retina experience redefined™



SOL-R: Defining Non-Inferiority Success

Jeffrey S. Heier, MD
Chief Scientific Officer

OCULAR THERAPEUTIX
Retina experience redefined™

FDA Alignment

Careful Patient Selection

Interpreting Outcomes

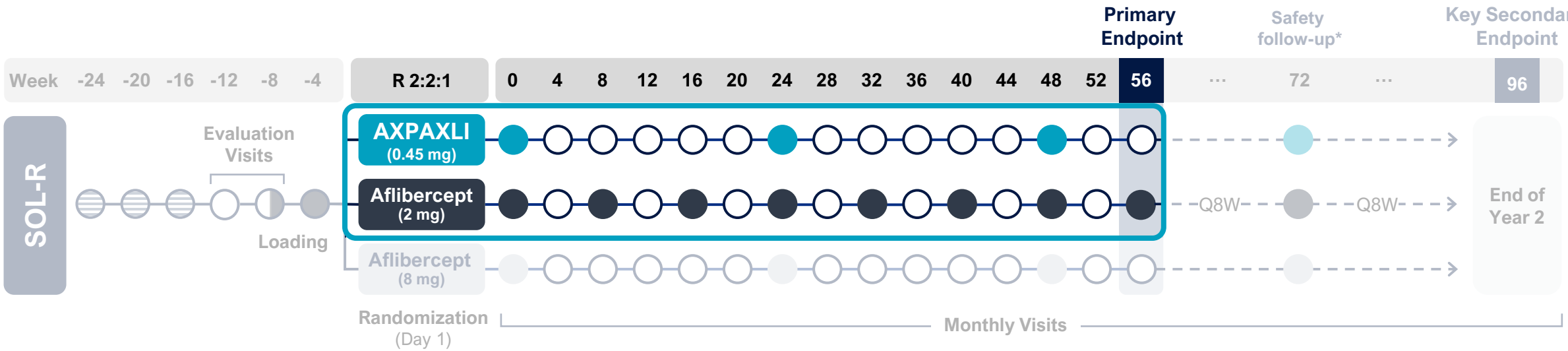
FDA Alignment

Careful Patient Selection

Interpreting Outcomes

OCULAR THERAPEUTIX Retina experience redefined™

SOL-R Design: Updates & Considerations



FDA Guidance for Non-Inferiority Trials

Compare to labeled dosing of Aflibercept 2 mg or Ranibizumab 0.5 mg **(-4.5 letter margin)**[1]

SOL-R Trial Design

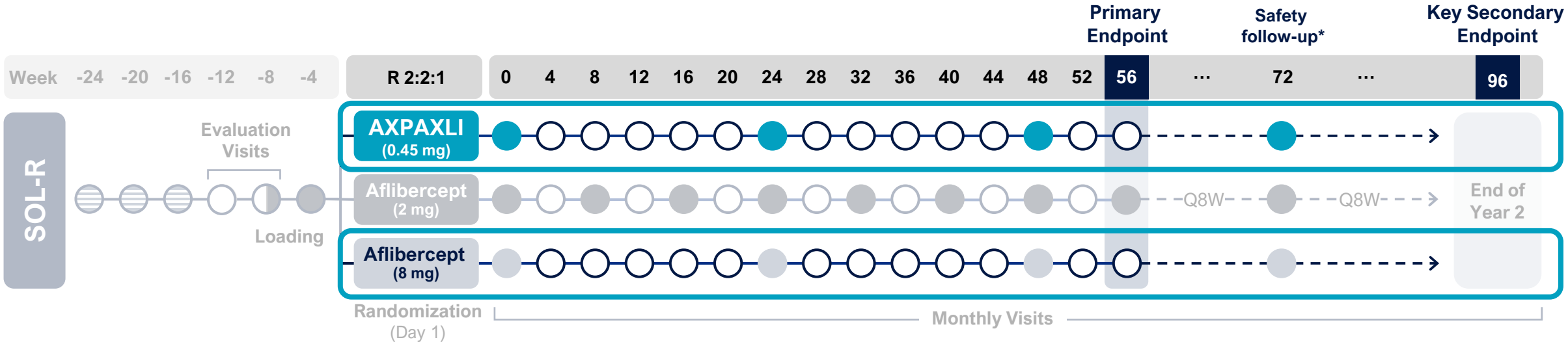
Primary analysis: AXPAXLI dosed Q24W versus Aflibercept 2mg Q8W

Screening Dose, Any Anti VEGF† | 2nd evaluation & Aflibercept 2mg | AXPAXLI 0.45mg | Aflibercept 2 mg | Aflibercept 8 mg | Study visit

OCULAR THERAPEUTIX Retina experience redefined™

1. U.S. Food and Drug Administration. Neovascular AMD: Developing Drugs for Treatment Guidance for Industry. 2023
Q24W, every 24 weeks; Q8W, every 8 weeks; VEGF, vascular endothelial growth factor; † Any anti-VEGF except Beovu

SOL-R Design: Updates & Considerations



FDA Guidance for Wet AMD Trials

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

SOL-R Trial Design

Aflibercept 8mg dosing identical with key secondary endpoint at week 96

Screening Dose, Any Anti VEGF† | 2nd evaluation & Aflibercept 2mg | AXPAXLI 0.45mg | Aflibercept 2 mg | Aflibercept 8 mg | Study visit

OCULAR THERAPEUTIX Retina experience redefined™

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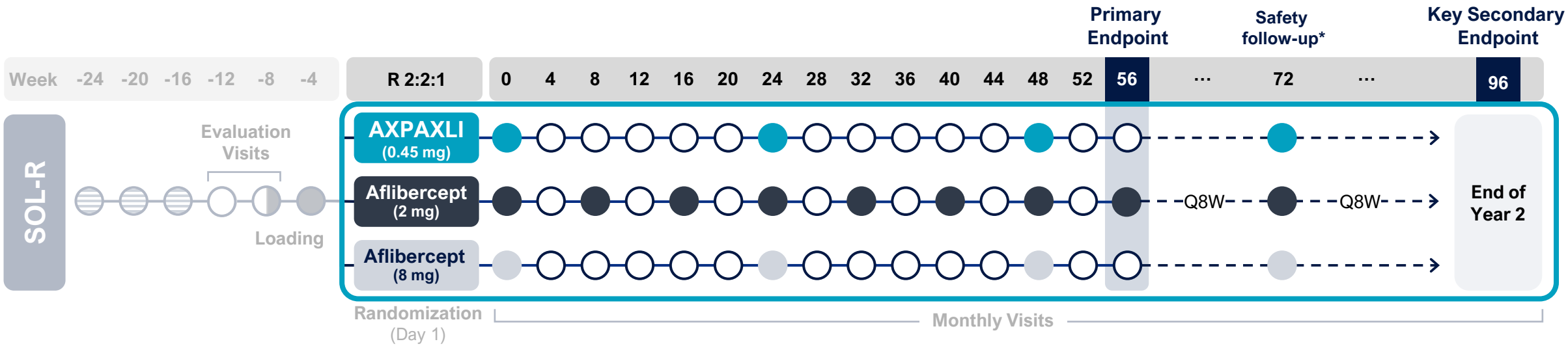
AMD, age-related macular degeneration; Q8W, every 8 weeks; VEGF, vascular endothelial growth factor; † Any anti-VEGF except Beovu

SOL-R Design: Updates & Considerations



FDA Guidance for Wet AMD Trials

Sham injections are not recommended
due to inadequate masking[1,2]

SOL-R Trial Design

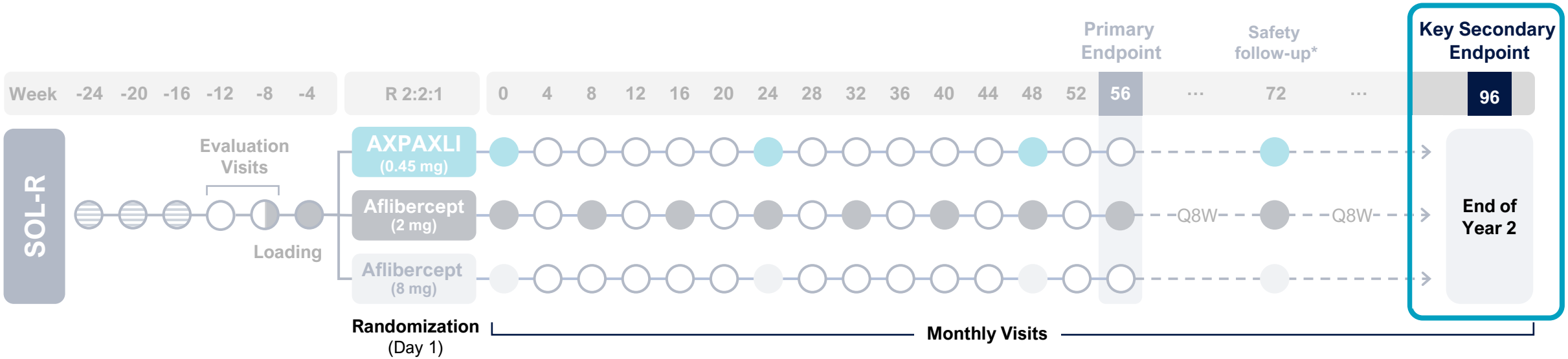
No sham injections

Screening Dose, Any Anti VEGF† | 2nd evaluation & Aflibercept 2mg | AXPAXLI 0.45mg | Aflibercept 2 mg | Aflibercept 8 mg | Study visit

OCULAR THERAPEUTIX Retina experience redefined™

1. Type C WRO [written response only] Aug 2024. 2. Weiss J, Boyd B, Event: Q&A with FDA, at the American Academy of Ophthalmology Annual Meeting, October 20, 2024
AMD, age-related macular degeneration; Q8W, every 8 weeks; VEGF, vascular endothelial growth factor; † Any anti-VEGF except Beovu

SOL-R Design: Updates & Considerations



SOL-R Year 1 Efficacy No Longer Part of AXPAXLI NDA Review

New Plan to Maintain Masking until Week 96 AXPAXLI Secondary Endpoints

vs. aflibercept (8 mg)

Key Secondary Endpoint:
Evaluating superiority in BCVA

vs. aflibercept (2 mg)

Secondary Endpoint: Evaluating prevention of fibrosis and atrophy

Screening Dose, Any Anti VEGF† | 2nd evaluation & Aflibercept 2mg | AXPAXLI 0.45mg | Aflibercept 2 mg | Aflibercept 8 mg | Study visit

OCULAR THERAPEUTIX Retina experience redefined™

1. Type C WRO [written response only] Aug 2024. 2. Weiss J, Boyd B, Event: Q&A with FDA, at the American Academy of Ophthalmology Annual Meeting, October 20, 2024
AMD, age-related macular degeneration; Q8W, every 8 weeks; VEGF, vascular endothelial growth factor; BCVA, best corrected visual acuity; † Any anti-VEGF except Beovu

SOL-R

FDA Alignment

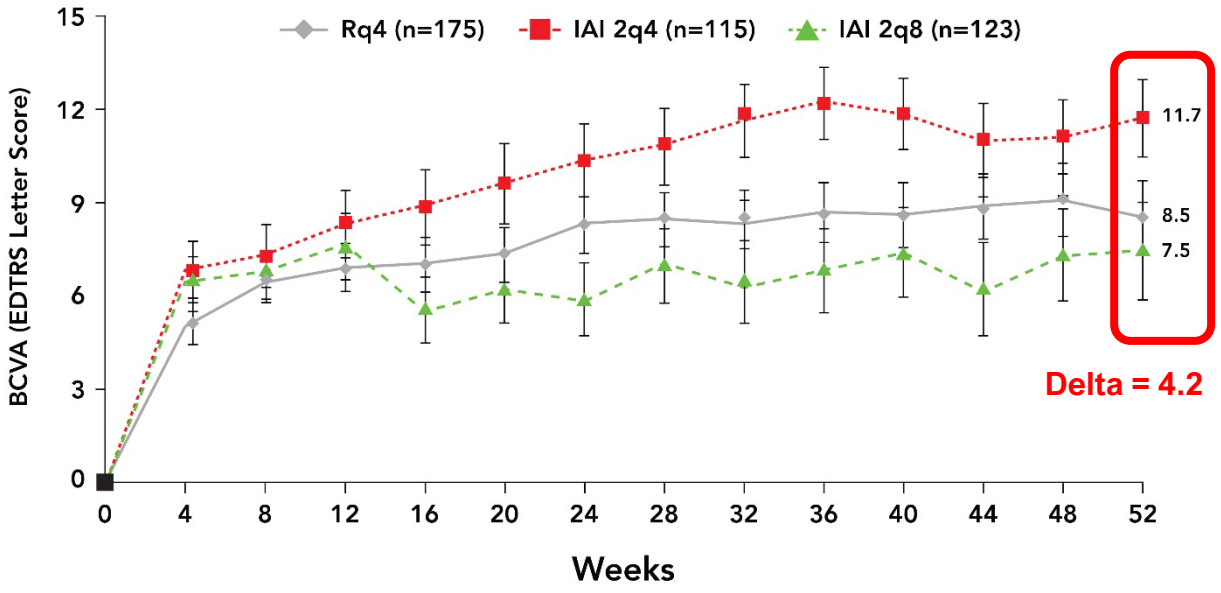
Careful Patient Selection

Interpreting Outcomes

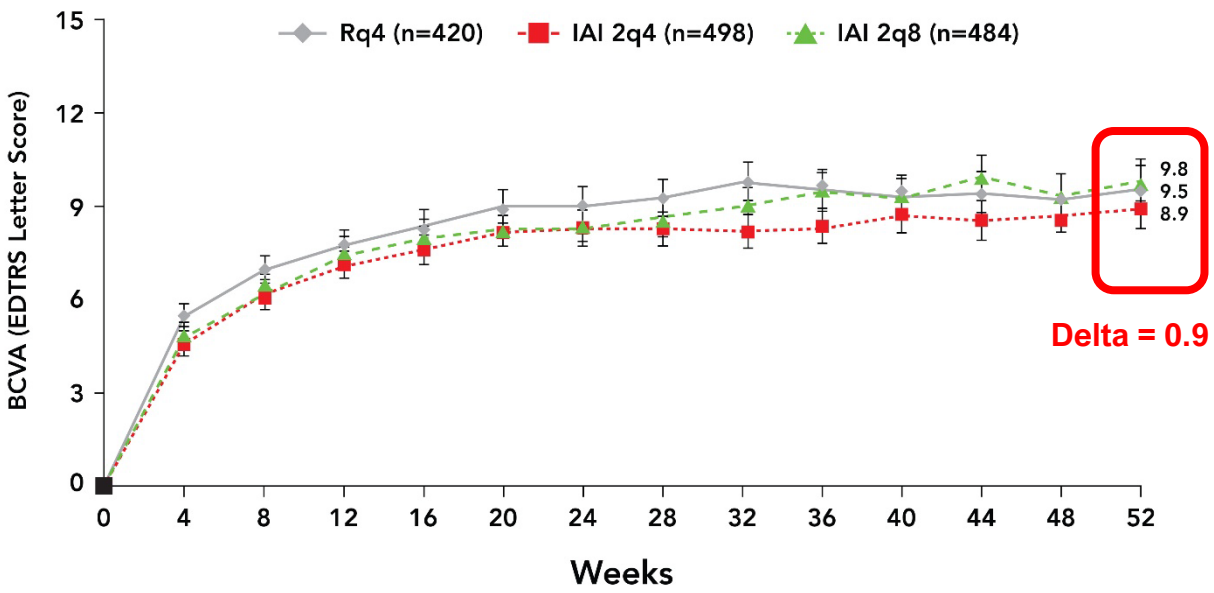
OCULAR THERAPEUTIX Retina experience redefined™

Patients with Early Persistent Fluid Can Disrupt Non-Inferiority Trials

Vision in Patients *with* Early Persistent Fluid



Vision in Patients *without* Early Persistent Fluid



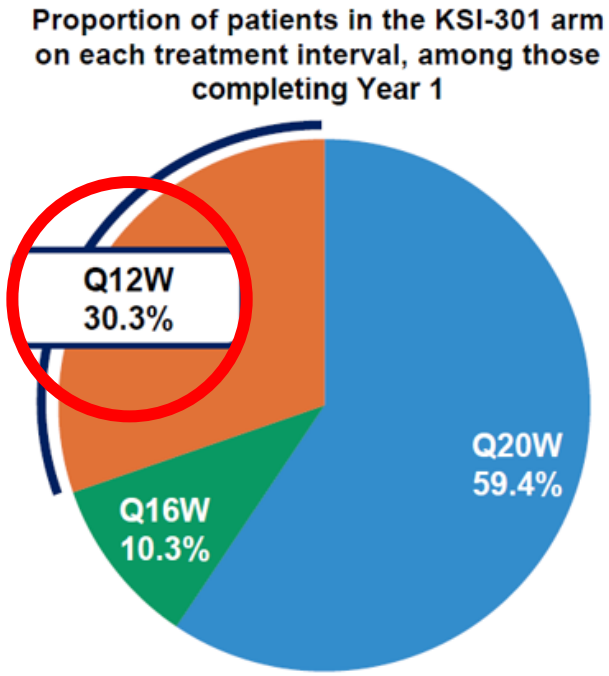
Screening to exclude subjects with early persistent fluid may be critical for trial success

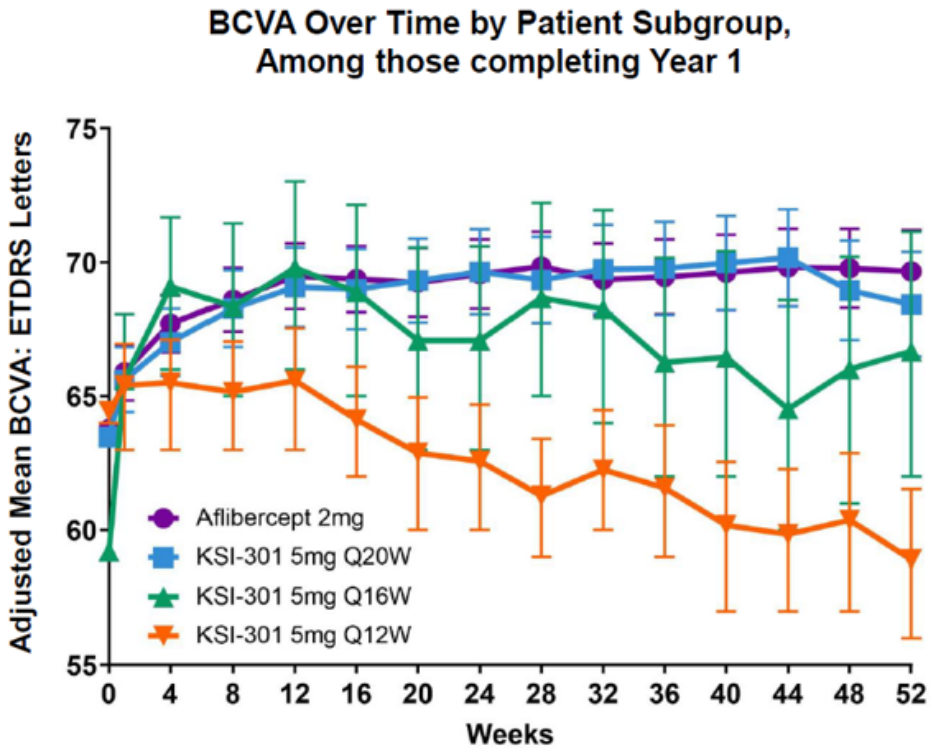
OCULAR THERAPEUTIX Retina experience redefined™

"Early Persistent Fluid" group captures patients that had retinal fluid as defined earlier on all initial 4 visits (baseline and weeks 4, 8, and 12). This period included all 3 visits during the initial loading dose period when all eyes were treated every 4 weeks, as well as 4 weeks after the third treatment.
Jaffe GJ, et al. Ophthalmology. 2016;123(9):1856-1864.
BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study

Learnings from Kodiak's DAZZLE Trial in Wet AMD

DAZZLE Trial Failed To Meet Primary Endpoint[1]
Original Zenkuda/KSI-301 Formulation*





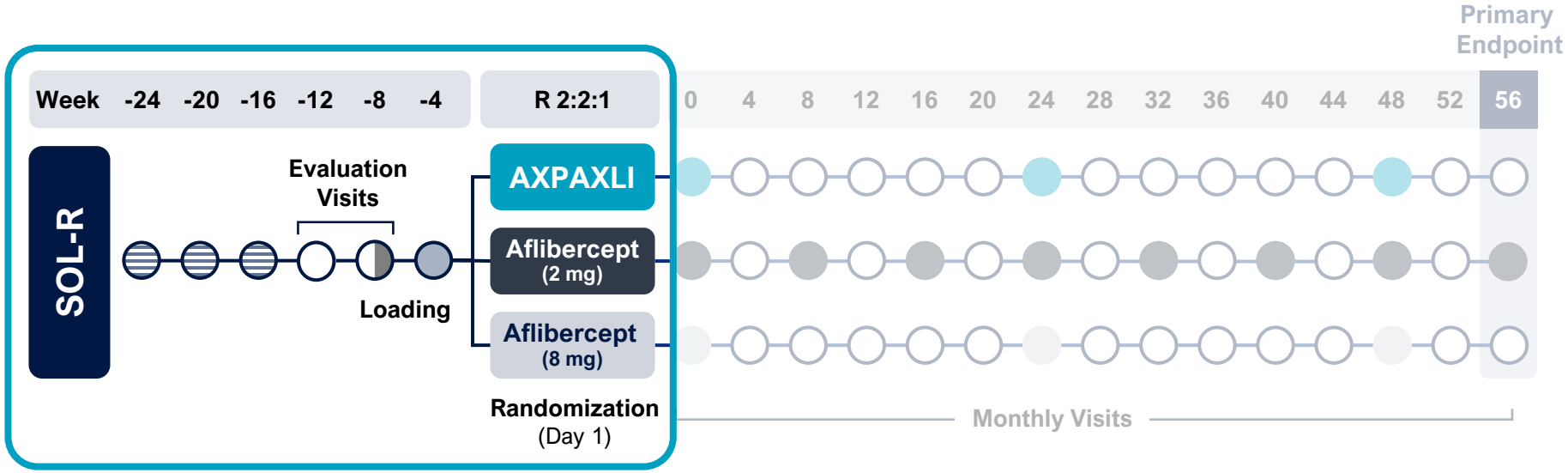
Kodiak's Commentary[1]

"Allowing treatment with **KSI-301 no more often than every 12** weeks after the loading phase **turned out to be insufficient** for some patients"

OCULAR THERAPEUTIX Retina experience redefined™

*Kodiak modified the Zenkuda formulation after initial pivotal trials including DAZZLE. Ongoing pivotal studies of Zenkuda are evaluating the modified formulation
1. C. Regillo ARVO 2022: Efficacy, Durability and Safety of KSI-301 antibody biopolymer conjugate in wet AMD; Primary results of the Phase 2b/3 DAZZLE Study
BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; AMD, age-related macular degeneration; Q20W, every 20 weeks

SOL-R Population Carefully Selected



Two Evaluation Visits

CSFT ≤350 µm at Wk -12 & Wk -8

— AND —

CSFT ≤35 µm increase from the lowest CSFT at any prior visits

SOL-R Trial Design

Careful patient selection

Screening Dose, Any Anti VEGF†

2nd evaluation & Aflibercept 2mg

AXPAXLI

Aflibercept 2 mg

Aflibercept 8 mg

Study visit

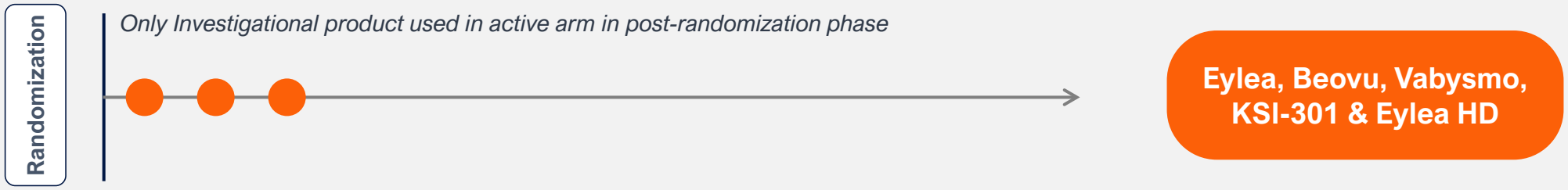
† Any anti-VEGF except Beovu

aVEGF, vascular endothelial growth factor; CSFT, central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium

Why do we insist on monotherapy <u>after</u> randomization?

Non-Inferiority Designs: Active Arm Dosing*

Non-Inferiority Trials for 1st & 2nd Generation anti-VEGFs



OCULAR THERAPEUTIX Retina experience redefined™

*Active arm dosing is abbreviated and reflects scheduled treatments provided during the initial dosing phase (randomization through Month 3). Actual Dosing Schedules vary thereafter.
VEGF, vascular endothelial growth factor

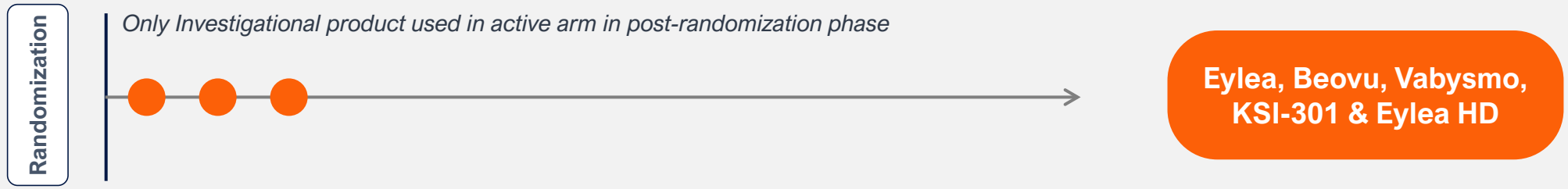
Control product

Investigational product

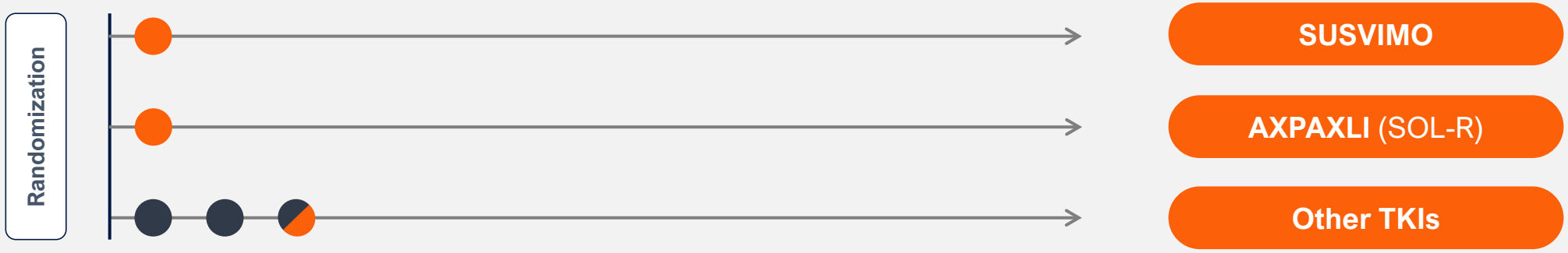
Investigational + control product

Non-Inferiority Designs: Active Arm Dosing*

Non-Inferiority Trials for 1st & 2nd Generation anti-VEGFs



Non-Inferiority Trials for Extended Duration Products



OCULAR THERAPEUTIX Retina experience redefined™

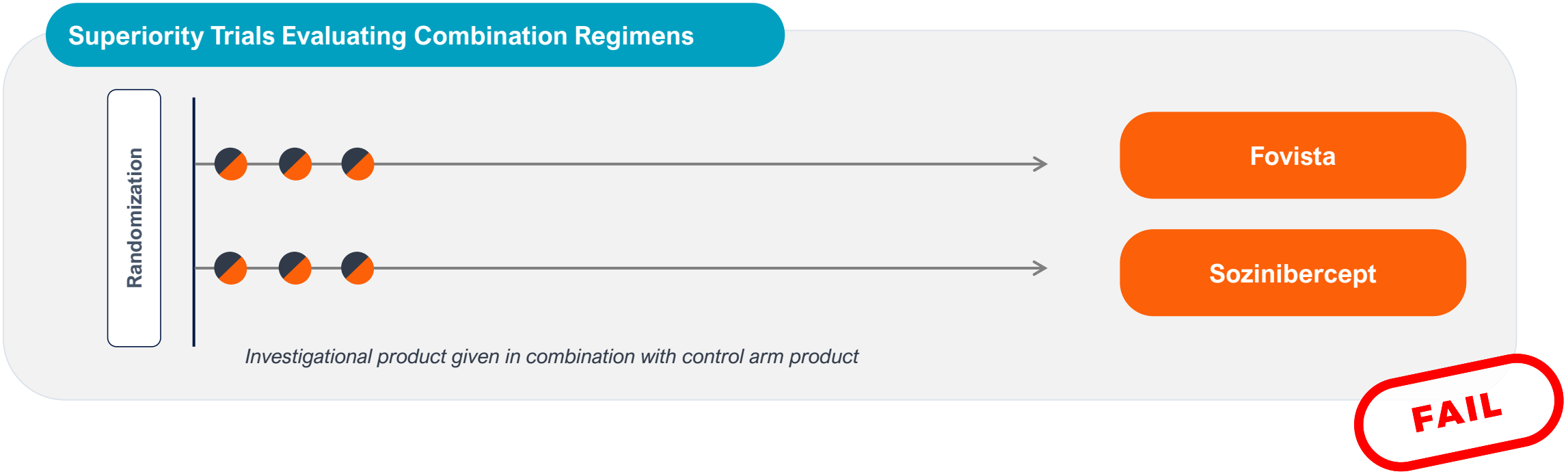
*Active arm dosing is abbreviated and reflects scheduled treatments provided during the initial dosing phase (randomization through Month 3). Actual Dosing Schedules vary thereafter.
VEGF, vascular endothelial growth factor

Control product

Investigational product

Investigational + control product

Combination Regimen Trials Were Designed to Evaluate Superiority



Active arm dosing is abbreviated and reflects scheduled treatments provided during the initial dosing phase (randomization through Month 3). Actual Dosing Schedules vary thereafter

Control product

Investigational product

Investigational + control product

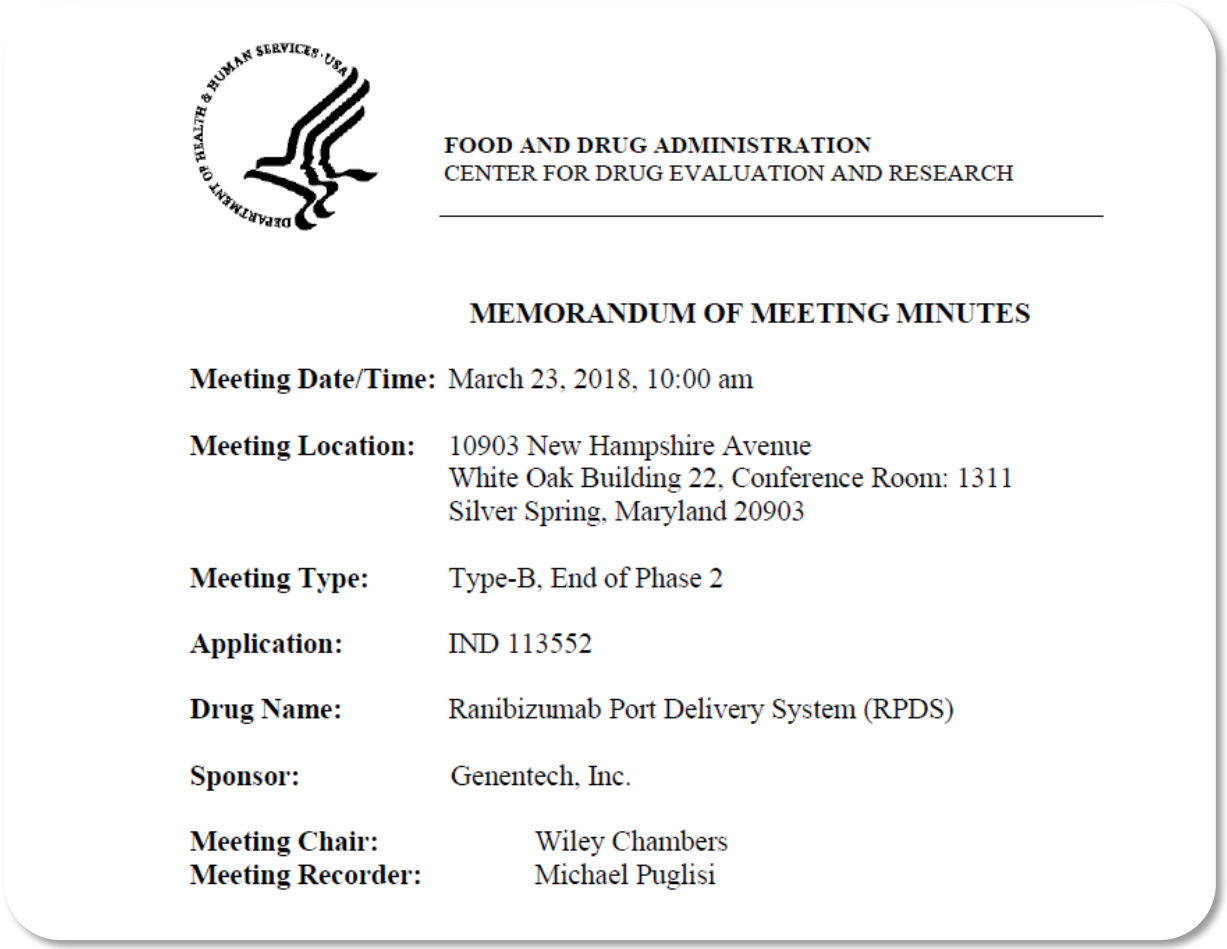
FDA Alignment

Careful Patient Selection

Interpreting Outcomes

OCULAR THERAPEUTIX Retina experience redefined™

Key Learning From Susvimo's FDA Review in Wet AMD



FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF MEETING MINUTES

Meeting Date/Time: March 23, 2018, 10:00 am

Meeting Location: 10903 New Hampshire Avenue
White Oak Building 22, Conference Room: 1311
Silver Spring, Maryland 20903

Meeting Type: Type-B, End of Phase 2

Application: IND 113552

Drug Name: Ranibizumab Port Delivery System (RPDS)

Sponsor: Genentech, Inc.

Meeting Chair: Wiley Chambers
Meeting Recorder: Michael Puglisi

Susvimo FDA Review

"The Agency stated that the primary analysis should include consideration of patients who receive rescue therapy that may impact the efficacy outcomes"

Susvimo Archway Trial permitted rescue with Intravitreal Ranibizumab

OCULAR THERAPEUTIX Retina experience redefined™

1. U.S. Food and Drug Administration. Susvimo wet AMD FDA Review, 2021.

Key Considerations about Rescues in Non-Inferiority Wet AMD Trials

SOL-R

Number of Rescues

Timing of Rescues

AMD, age-related macular degeneration

Key Considerations about Rescues in Non-Inferiority Wet AMD Trials

SOL-R

Number of Rescues

Timing of Rescues

Subjects requiring frequent rescue therapy may be considered **treatment failures[1] (or combination therapy)**

FDA generally does not consider **a single rescue as a treatment failure[1]**

OCULAR THERAPEUTIX Retina experience redefined™

1. Weiss J, Boyd B, Event: Q&A with FDA, at the American Academy of Ophthalmology Annual Meeting, October 20, 2024

AMD, age-related macular degeneration

Key Considerations about Rescues in Non-Inferiority Wet AMD Trials

SOL-R

Number of Rescues

Timing of Rescues

Rescues in close proximity (<3 months) to the primary endpoint will fall under greater regulatory scrutiny[1]

EX: A W48 rescue for a trial with a W52/56 endpoint may be considered to have impacted the primary outcome

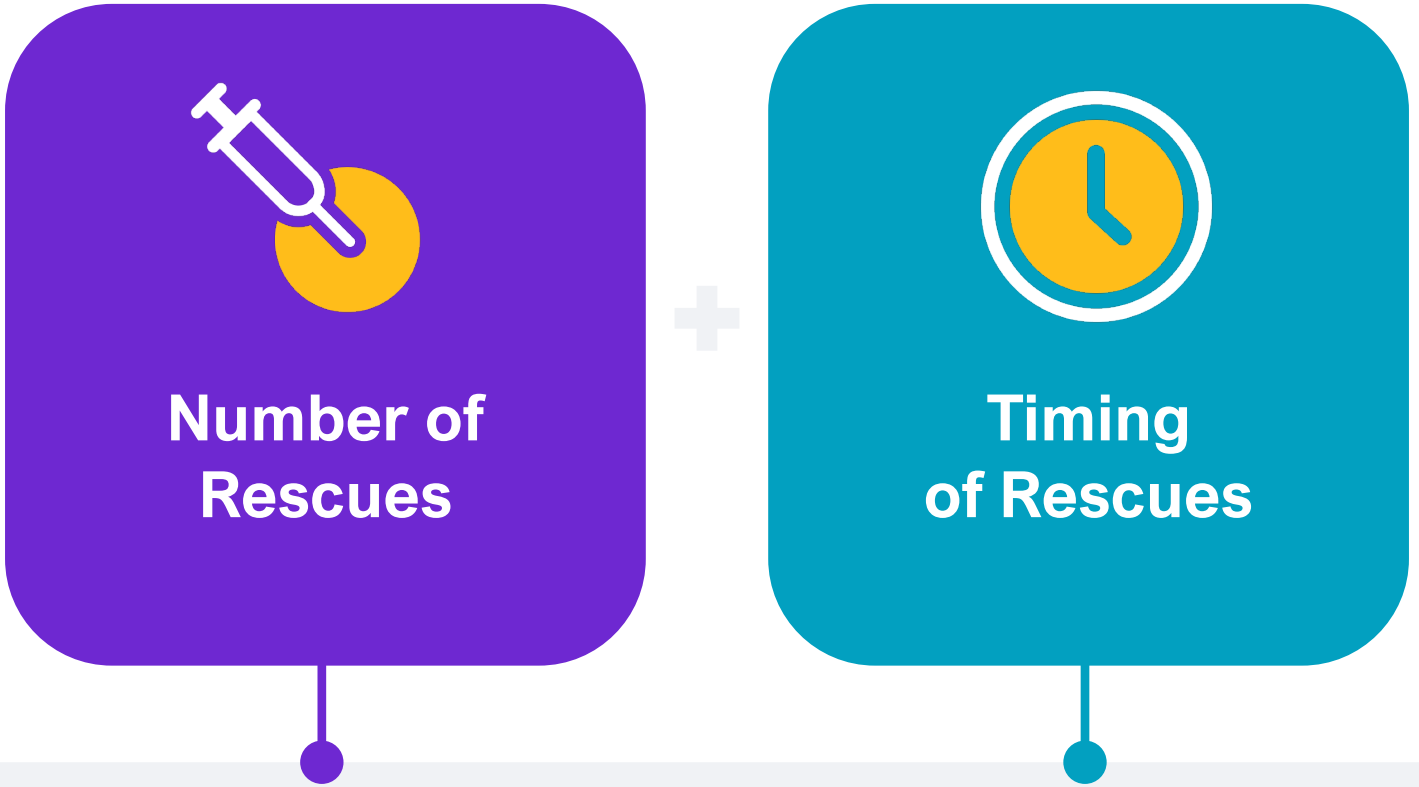
OCULAR THERAPEUTIX Retina experience redefined™

1. FDA communication to OCUL

AMD, age-related macular degeneration

Key Considerations about Rescues in Non-Inferiority Wet AMD Trials

SOL-R



Clear interpretation of a non-inferiority trial requires understanding of each

AMD, age-related macular degeneration

Key Questions of a Non-Inferiority Trial Evaluating Extended Durability Agents

1

Did the trial meet the NI margin?

NI, non-inferiority

Key Questions of a Non-Inferiority Trial Evaluating Extended Durability Agents

1

Did the trial meet the NI margin?

2

How many subjects were rescued?

NI, non-inferiority

Key Questions of a Non-Inferiority Trial Evaluating Extended Durability Agents

1. Did the trial meet the NI margin?

2. How many subjects were rescued?

3. How many subjects were rescued more than once?

NI, non-inferiority

Key Questions of a Non-Inferiority Trial Evaluating Extended Durability Agents

1. 

Did the trial meet the NI margin?

2. 

How many subjects were rescued?

3. 

How many subjects were rescued more than once?

4. 

How many rescues near the primary endpoint?

OCULAR THERAPEUTIX Retina experience redefined™

NI, non-inferiority

Key Questions of a Non-Inferiority Trial Evaluating Extended Durability Agents

1. Did the trial meet the NI margin?
2. How many subjects were rescued?
3. How many subjects were rescued more than once?
4. How many rescues near the primary endpoint?
5. Was the trial protocol in alignment with FDA?

OCULAR THERAPEUTIX Retina experience redefined™

NI, non-inferiority

Key Questions of a Non-Inferiority Trial Evaluating Extended Durability Agents

1. Did the trial meet the NI margin?
2. How many subjects were rescued?
3. How many subjects were rescued more than once?
4. How many rescues near the primary endpoint?
5. Was the trial protocol in alignment with FDA?
6. Does the use of other agents constitute a combination design *requiring superiority*?

OCULAR THERAPEUTIX Retina experience redefined™

NI, non-inferiority

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Pravin U. Dugel, MD

Audience Q&A
All

OCULAR THERAPEUTIX Retina experience redefined™

KOL Perspectives: AXPAXLI's Potential to Redefine Retina

MODERATOR

Jeffrey S. Heier, MD

Chief Scientific Officer

PANELISTS

Arshad M. Khanani, MD, MA, FASRS

Sierra Eye Associates
Reno, Nevada

Lejla Vajzovic, MD, FASRS

Duke University
Durham, North Carolina

Darius M. Moshfeghi, MD

Stanford University
Stanford, California

OCULAR THERAPEUTIX Retina experience redefined™

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Preparing for a Successful Launch
David Robinson

SOL-R: Defining Non-Inferiority Success
Jeffrey S. Heier, MD

KOL Perspectives: Potential to Redefine Retina
Moderator: Jeffrey S. Heier, MD

KOLs: Arshad Khanani, MD; Lejla Vajzovic, MD; Darius Moshfeghi, MD

Summary & Takeaways
Pravin U. Dugel, MD

Audience Q&A
All

OCULAR THERAPEUTIX Retina experience redefined™

Summary & Takeaways

Pravin U. Dugel, MD
Executive Chairman, President & CEO

OCULAR THERAPEUTIX Retina experience redefined™

AXPAXLI:
Positioned to Redefine Retina

Groundbreaking Profile

Unmatched Durability with Sustained Disease Control in SOL-1

Clear Path to Market

FDA Aligned on NDA Submission in 4Q 2026

Focused on Commercial Success

Preparing to Meet Immediate Demand (if Approved)

OCULAR THERAPEUTIX Retina experience redefined™

NDA, New Drug Application

Ocular Therapeutix 2026 Investor Day Agenda

Intro & Overview
Pravin U. Dugel, MD

SOL-1 Data & AXPAXLI Clinical Program Review
Nadia K. Waheed, MD, MPH

U.S. Regulatory Strategy in Wet AMD
Peter K. Kaiser, MD

Discussion: AXPAXLI NDA Submission Strategy
Moderator: Peter K. Kaiser, MD

Ocular Panelist: Arthur Ciociola, PhD

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