

EYEPOINT PHARMACEUTICALS

R&D DAY

2024 

UNIVERSITY CLUB | NEW YORK CITY | JUNE 26, 2024

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INTRODUCTIONS AND AGENDA

**JAY DUKER, MD | PRESIDENT AND
CHIEF EXECUTIVE OFFICER**



R&D Day Speakers: Management



Jay Duker, MD
President and CEO

>30 years managing retinal diseases and is a 12-time clinical trial investigator/co investigator; he has started three companies and has published >345 ophthalmic journal articles. Previous Director of the New England Eye Center (NEEC) and Professor and Chair of the Department of Ophthalmology at Tufts Medical Center and the Tufts University School of Medicine in Boston.



George O. Elston
EVP and CFO

>25 years of diverse financial and executive leadership in the biopharmaceutical sector with strong record of execution across strategic, operational, financial goals to drive shareholder value. He has established strong relationships across wall street and pharma/biotech resulting in transformative company-building and M&A transactions.



Ramiro Ribeiro, MD, PhD
CMO

Extensive experience encompassing clinical practice as a retina specialist, academia and the pharmaceutical industry with a strong track record of successfully bringing novel therapies to patients globally. Previous Head of Clinical Development at Apellis where he successfully led the end-to-end clinical process for FDA approval of SYFOVRE.

R&D Day Speakers: KOL Guest Speakers



Carl D. Regillo, MD, FACS

Professor of Ophthalmology at Thomas Jefferson University; Chief of Retina Service at Wills Eye Hospital; Founder of Wills Eye Clinical Retina Research Unit in Philadelphia and Partner, Mid Atlantic Retina



Yasha S. Modi, MD

Associate Professor of Vitreoretinal Surgery, Retinal Disease and Uveitis at New York University; Director of Teleretina

R&D Day: Agenda (1/2)

PRESENTATION SPEAKER

Introductions

Jay Duker, M.D.

Company Overview

Jay Duker, M.D.

DURAVYU™ (vorolanib intravitreal insert) Overview

Jay Duker, M.D.

DURAVYU™: Phase 2 DAVIO 2 Clinical Results and Sub-Group Analyses

Yasha S. Modi, M.D.

DURAVYU™: Phase 2 DAVIO 2 12-Month Topline Results

Carl D. Regillo, M.D.

DURAVYU™ has been conditionally accepted by the FDA as the proprietary name for EYP-1901. DURAVYU is an investigational product; it has not been approved by the FDA. FDA approval and the timeline for potential approval is uncertain.

R&D Day: Agenda (2/2)

PRESENTATION SPEAKER

DURAVYU™: Pivotal Phase 3 Plans for Wet AMD

Jay Duker, M.D.
Ramiro Ribeiro, M.D., Ph.D.

Early Pipeline

Jay Duker, M.D.

Key Opinion Leader Insights and Discussion

Jay Duker, M.D.
Carl D. Regillo, M.D.
Yasha S. Modi, M.D.

Q&A

All

Closing Remarks

Jay Duker, M.D.
Ramiro Ribeiro, M.D., Ph.D.

R&D Day: Agenda

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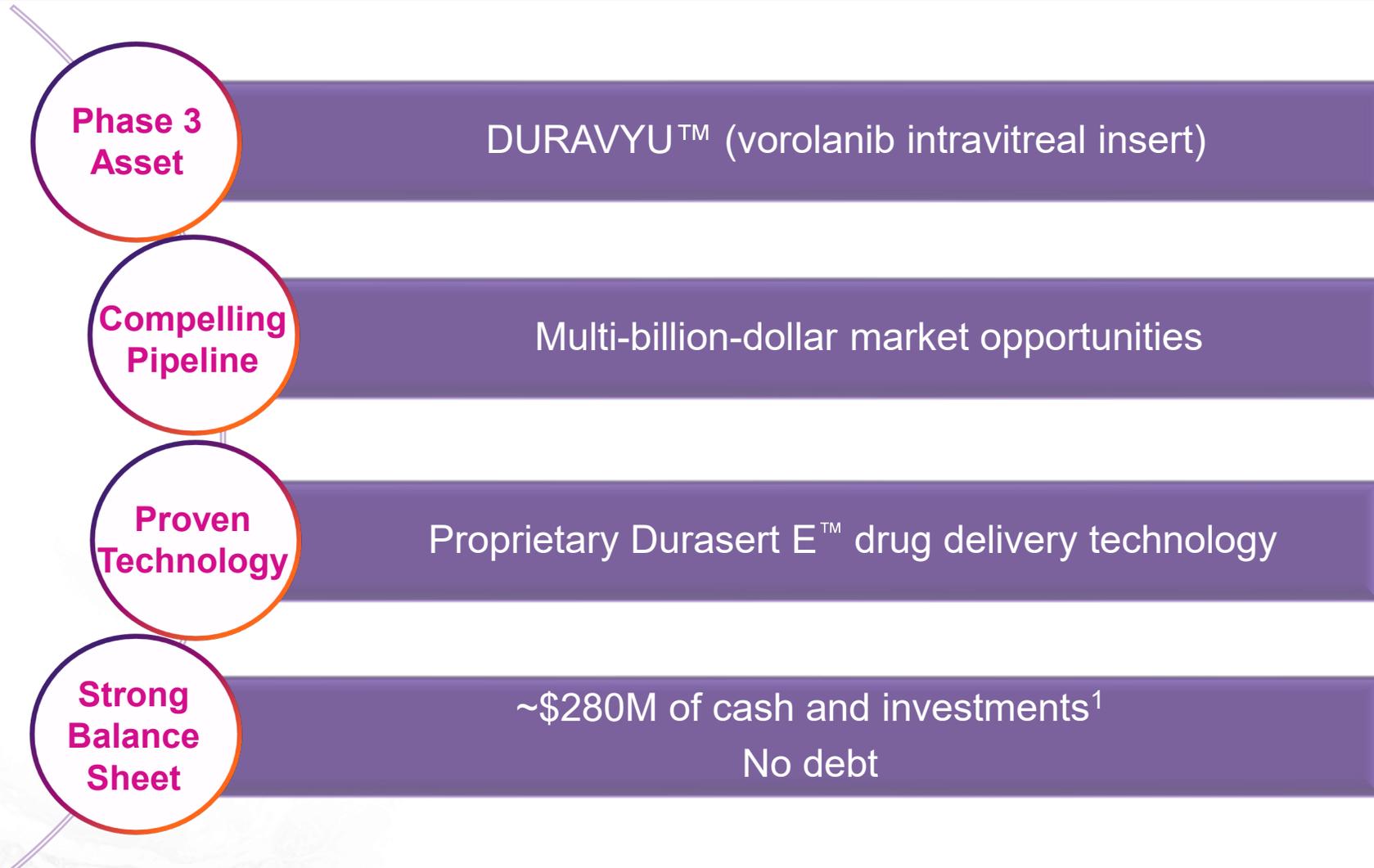
DURAVYU™: Phase 2 DAVIO 2 12-Month Topline Results

Carl D. Regillo, M.D.

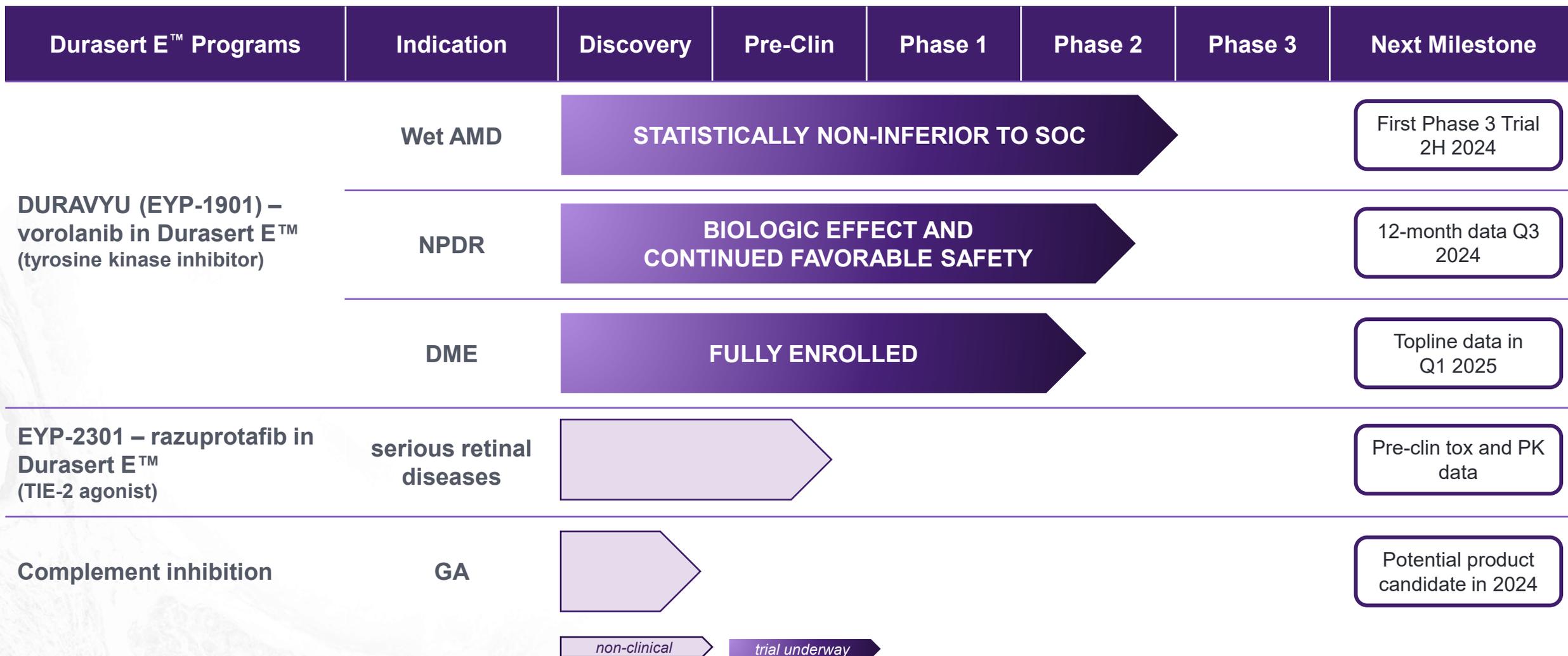
**COMMITTED TO DEVELOPING THERAPEUTICS
TO IMPROVE THE LIVES OF PATIENTS WITH
SERIOUS RETINAL DISEASES**



Phase 3 Clinical Stage Company Leveraging Proven Delivery Technology



Pipeline Represents Potential Multi Billion-Dollar Product Opportunities



wet AMD, wet age-related macular degeneration; EOP2, End of Phase 2; FPI, first patient in; NPDR, non-proliferative diabetic retinopathy; DME, diabetic macular edema; GA, geographic atrophy

TECHNOLOGY

BIOERODIBLE DURASERT E™



Safe, Sustained-Release IVT Drug Delivery

- Delivered via a standard in-office IVT injection
- Continuous, daily therapeutic dose
- Zero-order kinetics drug release

Durasert E™: bioerodible

- Drug embedded within a bioerodible matrix as a solid insert
- Designed to deplete drug load before matrix fully erodes
 - ▶ DURAVYU™

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DURAVYU entering Phase 3 with robust dataset and FDA alignment on approval pathway

SAFETY

No ocular or systemic DURAVYU-related SAEs across clinical trials

FDA

Non-inferiority pathway to approval aligned with FDA

DATA

Most robust dataset of all long-acting treatments in development

TRIAL DESIGN

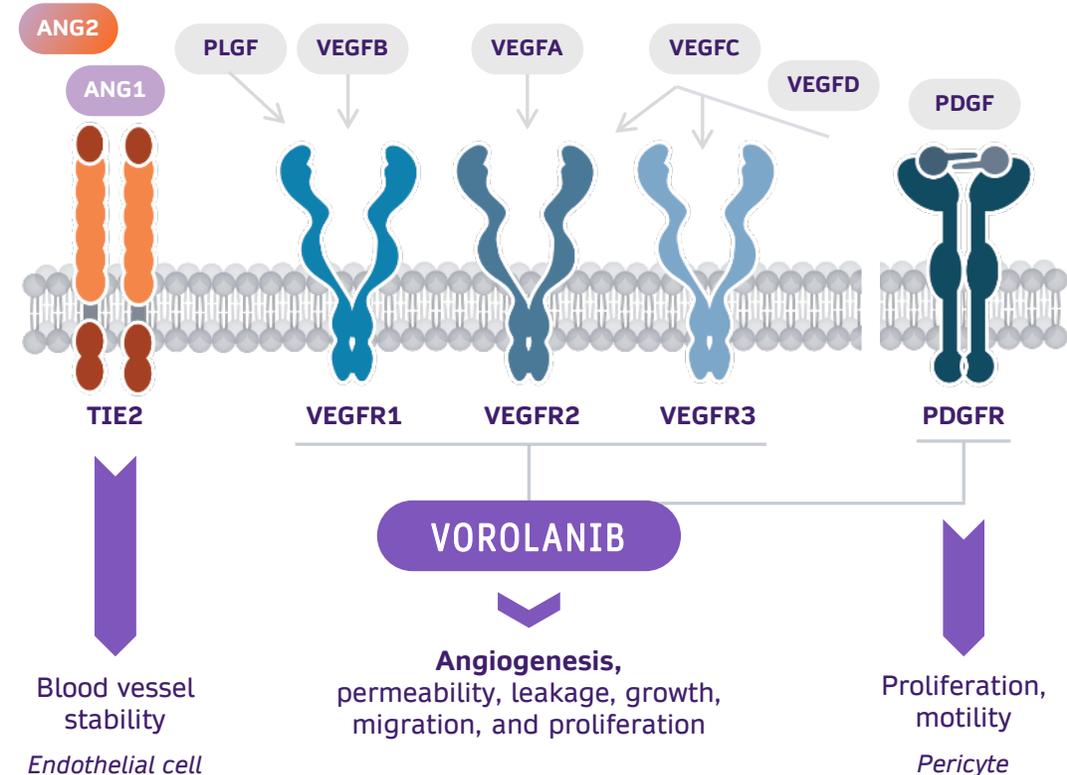
Phase 3 trial design includes re-dosing - aligns with FDA and clinical use

NOVEL

Patented molecule with new MOA and best-in-class delivery technology

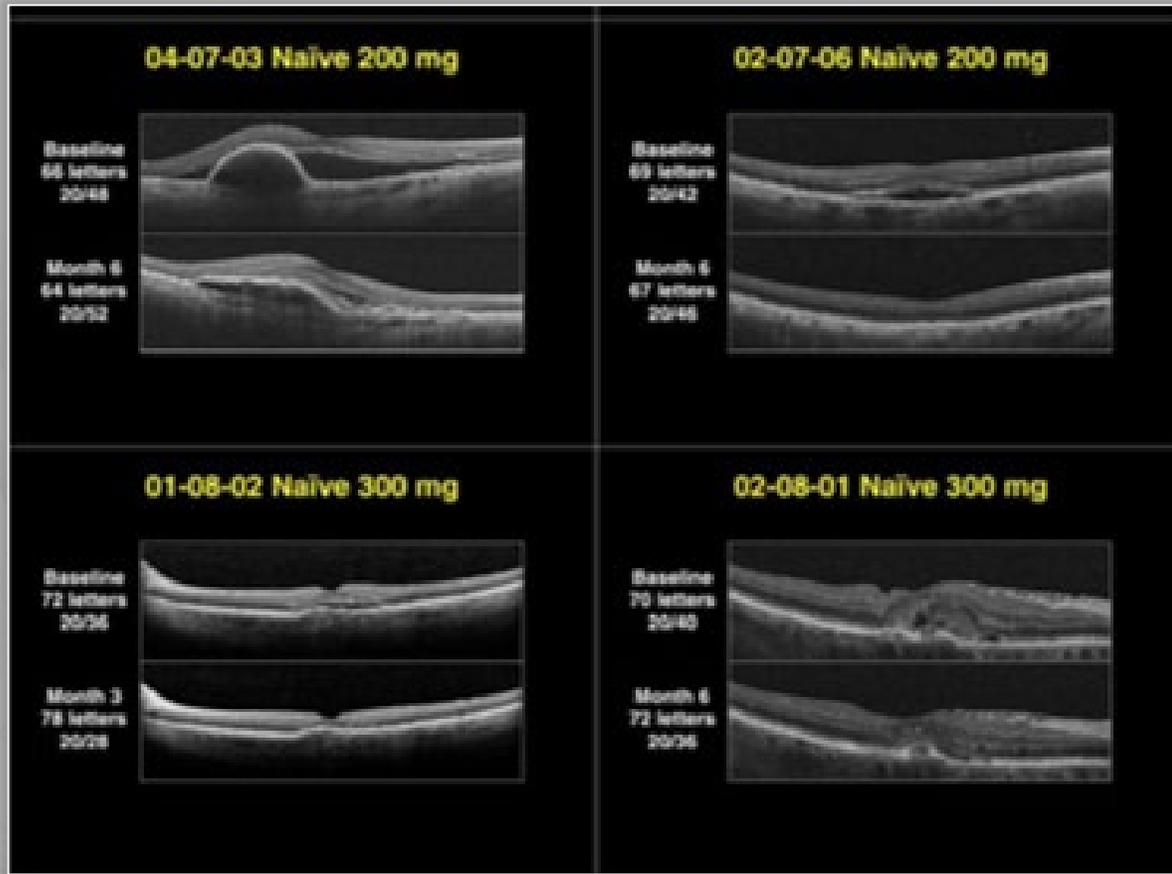
Vorolanib is a Potent and Highly Selective Pan-VEGF Receptor Inhibitor

- **Best-in-class** TKI
- Composition of matter **patent into 2037**
- Demonstrated **neuroprotection**
- Potential **antifibrotic**
- Does **not inhibit TIE-2**¹



Sophie Bakri, M.D., et al. PLOS ONE, <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0304782>, 2024.
VEGF(R), vascular endothelial growth factor (receptor); TKI, tyrosine kinase inhibitor;
PDGF(R), platelet-derived growth factor (receptor); TIE-2, tyrosine-protein kinase receptor

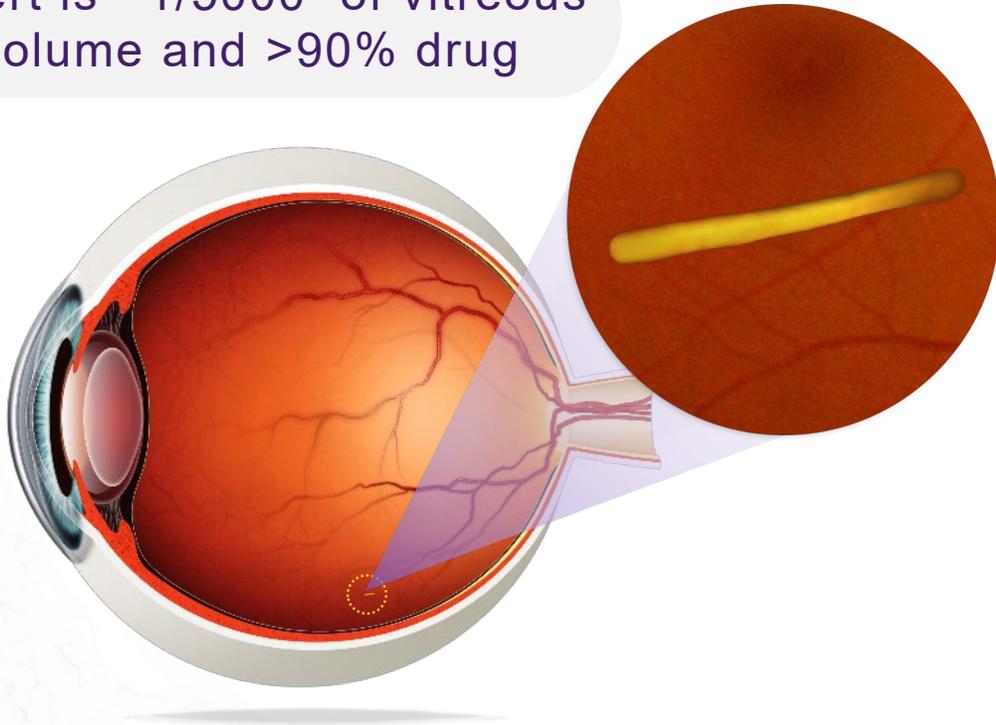
Vorolanib Demonstrated Compelling Clinical Activity in wet AMD Delivered Orally



- **Reduced supplemental therapy** versus anti-VEGF PRN for all doses
- No **ocular toxicity**
- Systemic use **significantly reduced** fellow eye conversion
- Meaningful reduction in mean OCT thickness in **treatment-naive patients**

DURAVYU: Vorolanib in Bioerodible Durasert E™

Insert is ~1/5000 of vitreous volume and >90% drug



- **Immediately** bioavailable
- **Controlled release** for at least six months enables redosing regimen
- **No free-floating drug** - fully eluted prior to bioerosion of matrix
- **Routine** intravitreal injection
- Shipped and stored at **ambient temperature**

DURAVYU Demonstrated Clinically Meaningful Safety and Efficacy Outcomes Across Multiple Indications

DURAVYU HAS BEEN TESTED IN 191 PATIENTS TO DATE ACROSS DIFFERENT INDICATIONS

Trial	n size	Indication	Safety	Key Efficacy Outcomes
DAVIO	17	wet AMD	Favorable safety profile No DURAVYU related ocular or systemic SAEs	<ul style="list-style-type: none"> Stable BCVA and OCT 74% reduction in treatment burden
DAVIO 2	161	wet AMD		<ul style="list-style-type: none"> Statistically non-inferior BCVA >80% reduction in treatment burden Stable OCT
PAVIA	77	NPDR		<ul style="list-style-type: none"> Stable to improved disease severity up to 9-months; trial continuing 12 months
VERONA	27	DME		<ul style="list-style-type: none"> Trial underway

Interim, masked safety as of June 2024

Wet AMD, wet age-related macular degeneration; NPDR, non-proliferative diabetic retinopathy; DME, diabetic macular edema

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There is a Significant Need for More Durable Therapies in Wet AMD



1

• Many patients with wet AMD are chronically undertreated

- >80% of Retina Specialists say undertreatment is due to patient noncompliance, scheduling limitations or provider preference for less frequent dosing¹



2

• Current “treat and extend” protocol still places significant burden on physicians and patients

- Chronic disease treated with short acting anti-VEGF biologics



3

• A delay in care/missed visit can result in vision loss

- A delay in treatment of only 5.34 weeks resulted in vision loss²

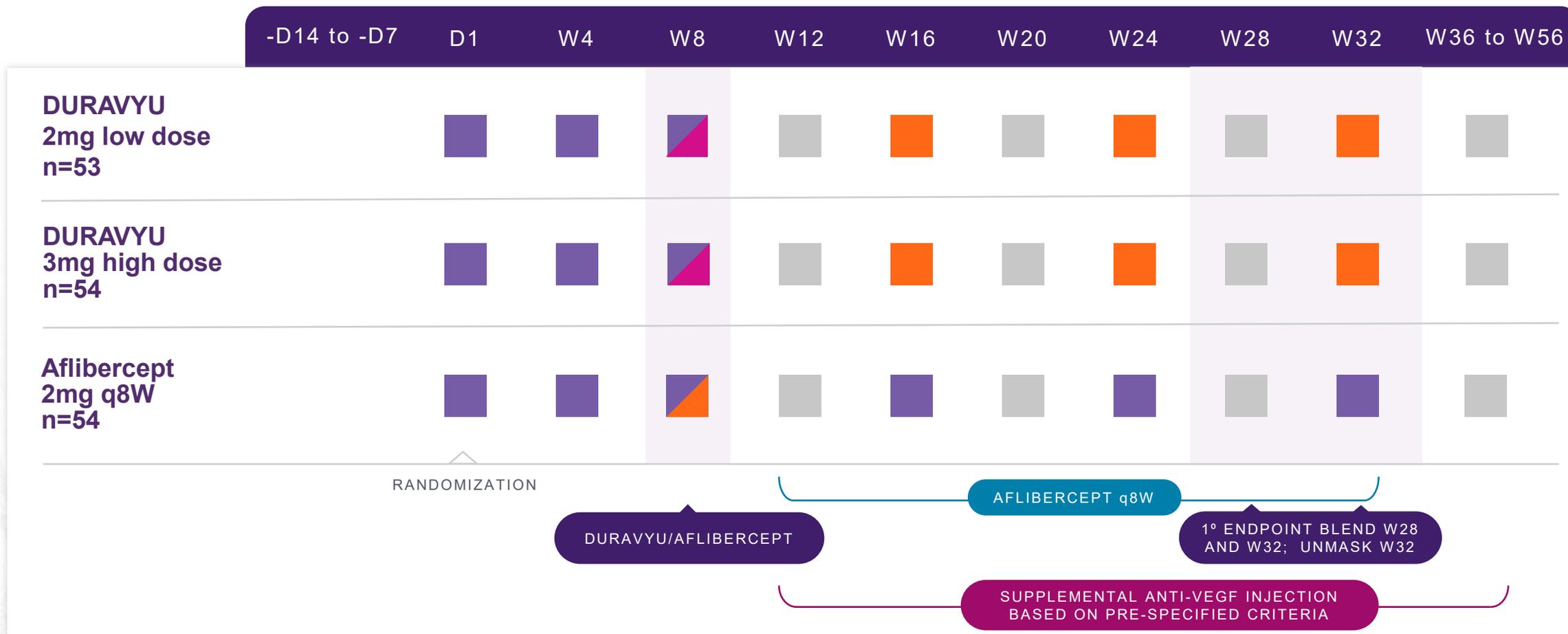


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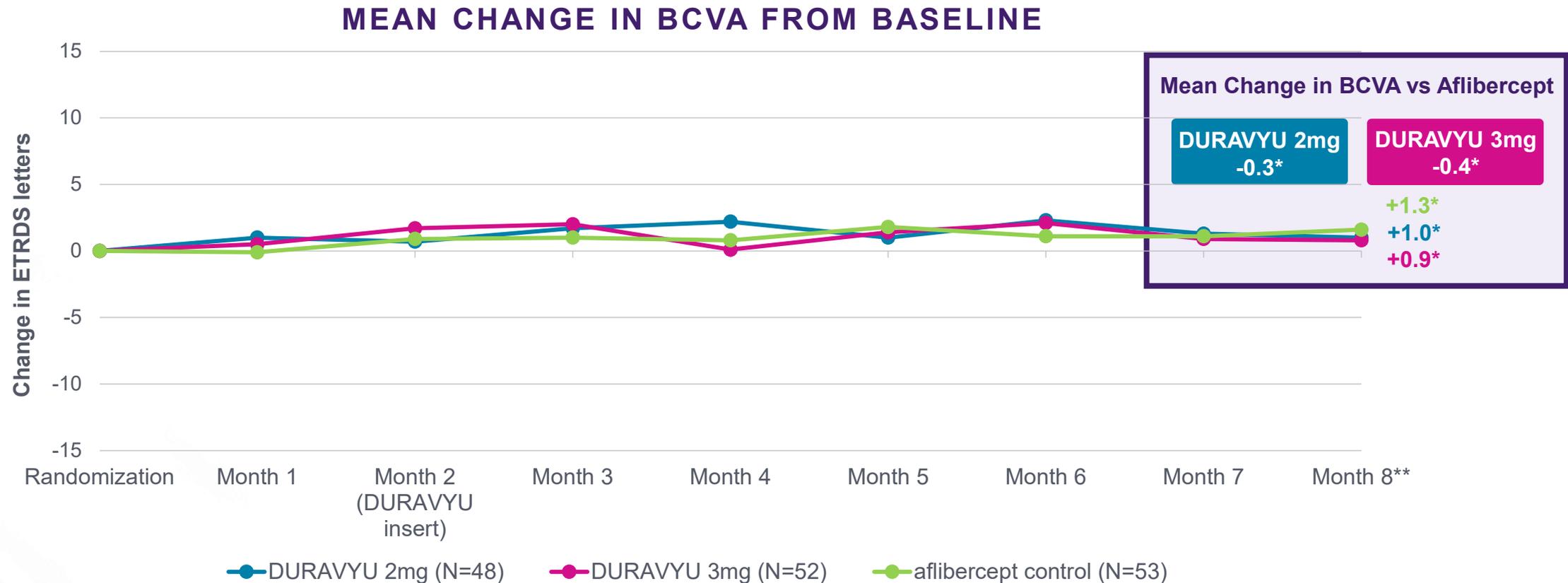
• An aging population means significantly more injections in a patient’s lifetime

- Current anti-VEGF treatments are dosed on average every two months in the United States³

DAVIO 2 Clinical Trial is Randomized, Double-Masked, Aflibercept Controlled* with a Single DURAVYU Treatment at Two Doses



DURAVYU was Statistically Non-Inferior in Change in BCVA Compared to the Aflibercept Control (95% CI)



In the Pulsar trial, HD Eylea (16-week 8mg arm) change in BCVA vs. 2mg Eylea was -1.4 letters¹

*Blended week 28 and week 32 change vs. baseline
 **Month 8 represents 6 months after DURAVYU injection
 CI, Confidence Interval
 PRELIMINARY DATA – PENDING FINAL ANALYSIS

Clinically Meaningful Reduction in Treatment Burden Retrospectively Supports DURAVYU as a Maintenance Treatment For Wet AMD

	DURAVYU 2mg	DURAVYU 3mg
Mean number of injections week 8 through week 32	0.55	0.73
Mean number of injections 6 months prior to screening*	4.98	5.02
Reduction in treatment burden vs. 6 months prior (%)	89%	85%

*Normalized
PRELIMINARY DATA – PENDING FINAL ANALYSIS

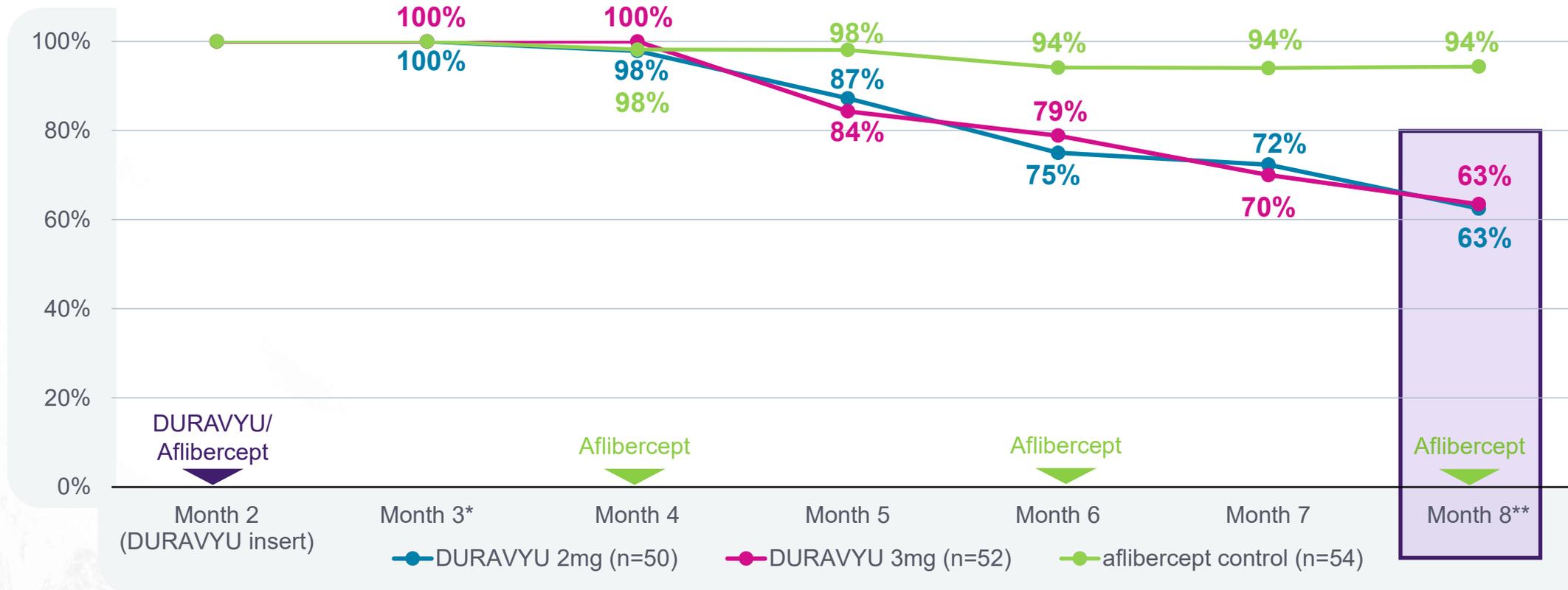
DURAVYU Demonstrated a Meaningful Reduction in Treatment Burden Prospectively vs. the Aflibercept Control Arm

	DURAVYU 2mg	DURAVYU 3mg	Aflibercept 2mg q8W
Mean number of injections week 8 through week 32	0.55	0.73	3.28
Reduction in treatment burden vs. aflibercept control (%)	83%	78%	NA

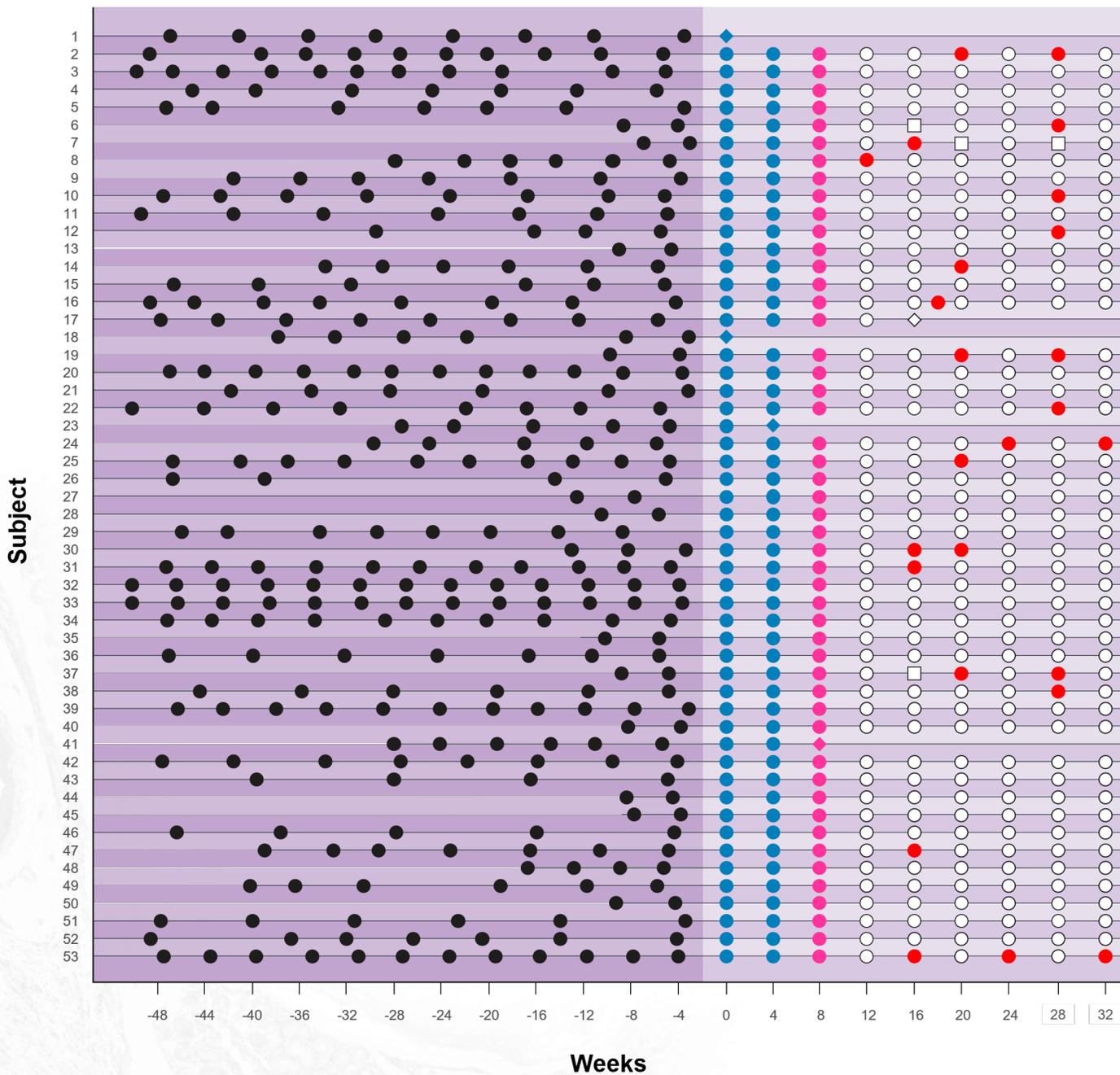
Nearly Two-Thirds of Eyes Treated with DURAVYU were Supplement-Free up to Six Months

DESPITE EOM AFLIBERCEPT INJECTIONS, 6% OF THE CONTROL GROUP REQUIRED ADDITIONAL SUPPLEMENTATION

SUMMARY OF SUPPLEMENT-FREE RATES BY MONTH



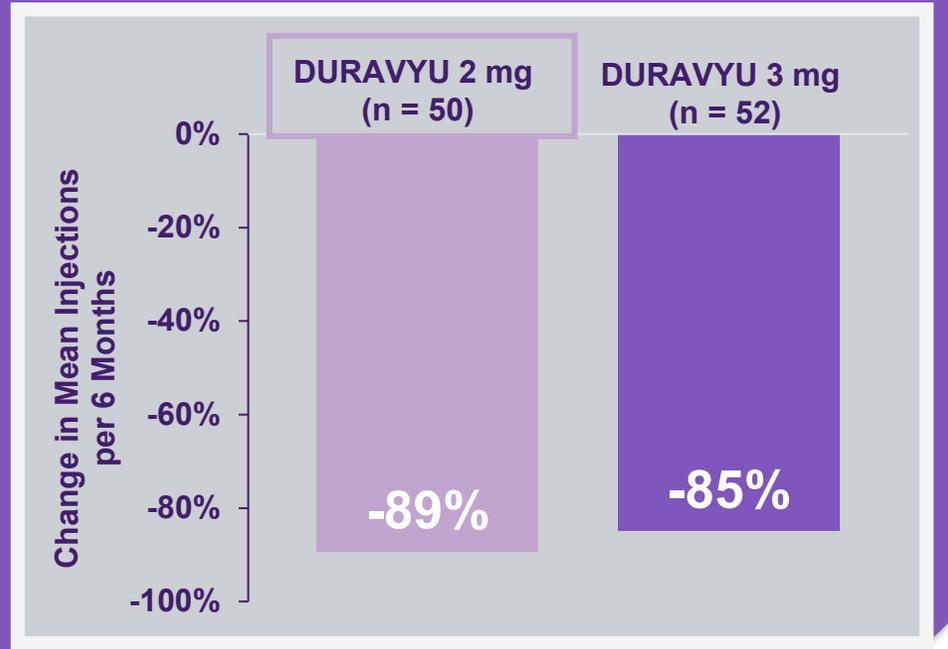
*First visit patients are eligible to be supplemented EOM, every-other-month
PRELIMINARY DATA – PENDING FINAL ANALYSIS



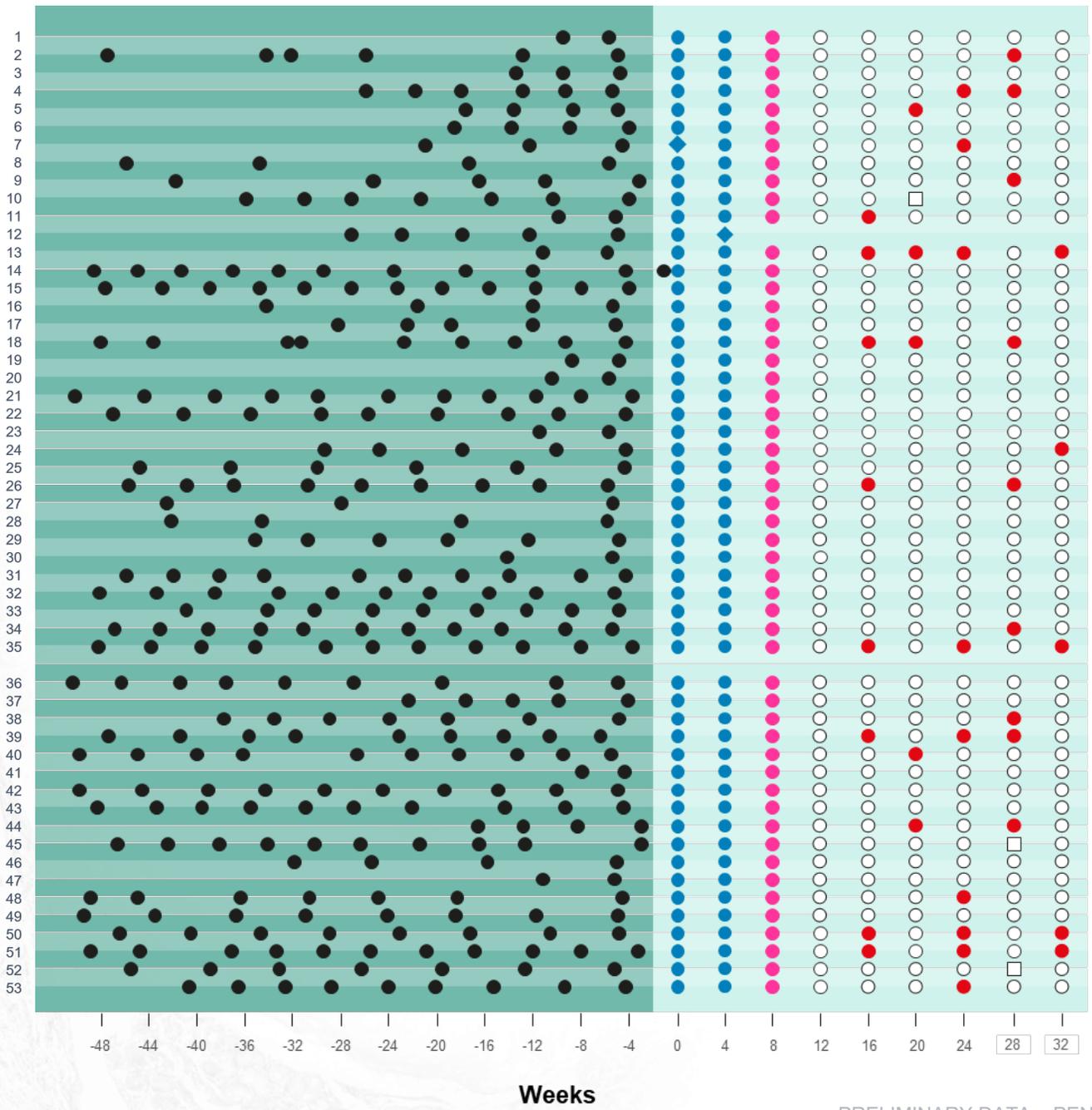
DURAVYU 2mg Dose Reduced Treatment Burden by 89% Compared to Prior 6 Months

Injections in year prior and during the DAVIO 2 trial

- Anti-VEGF injection
- Afibercept loading dose
- Afibercept + DURAVYU
- No injection
- Missed Visit
- Supplemental injection



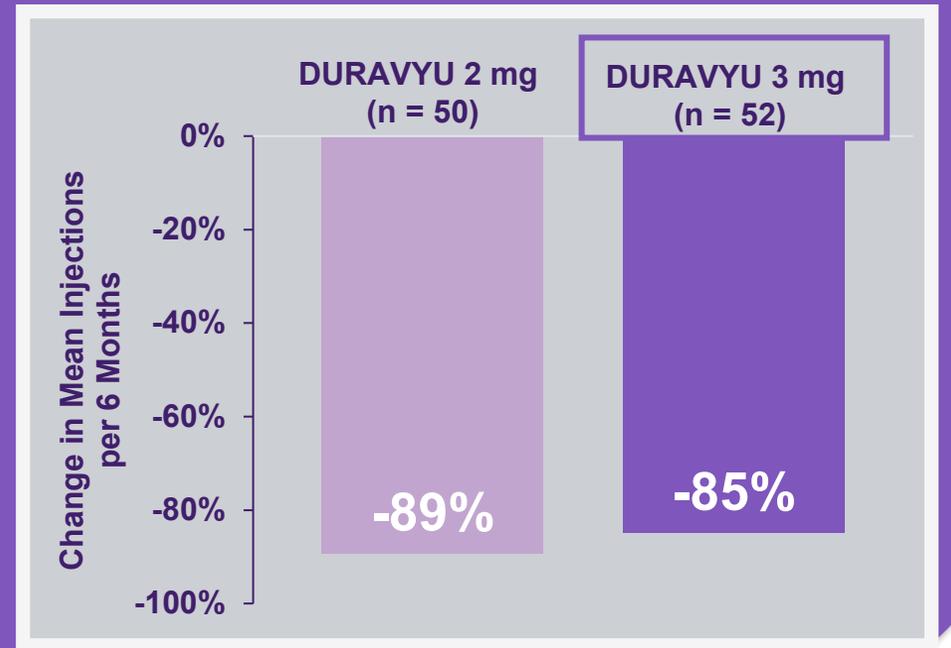
Subject



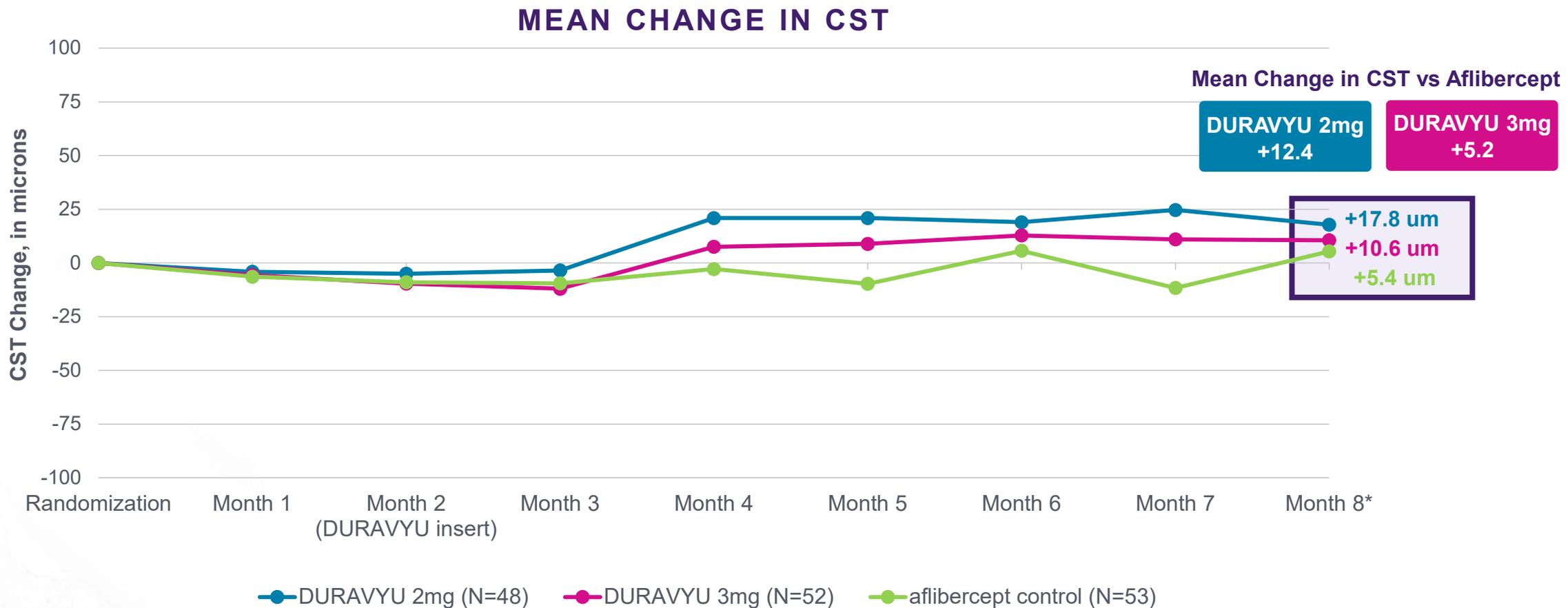
DURAVYU 3mg Dose Reduced Treatment Burden by 85% Compared to Prior 6 Months

Injections in year prior and during DAVIO 2 trial

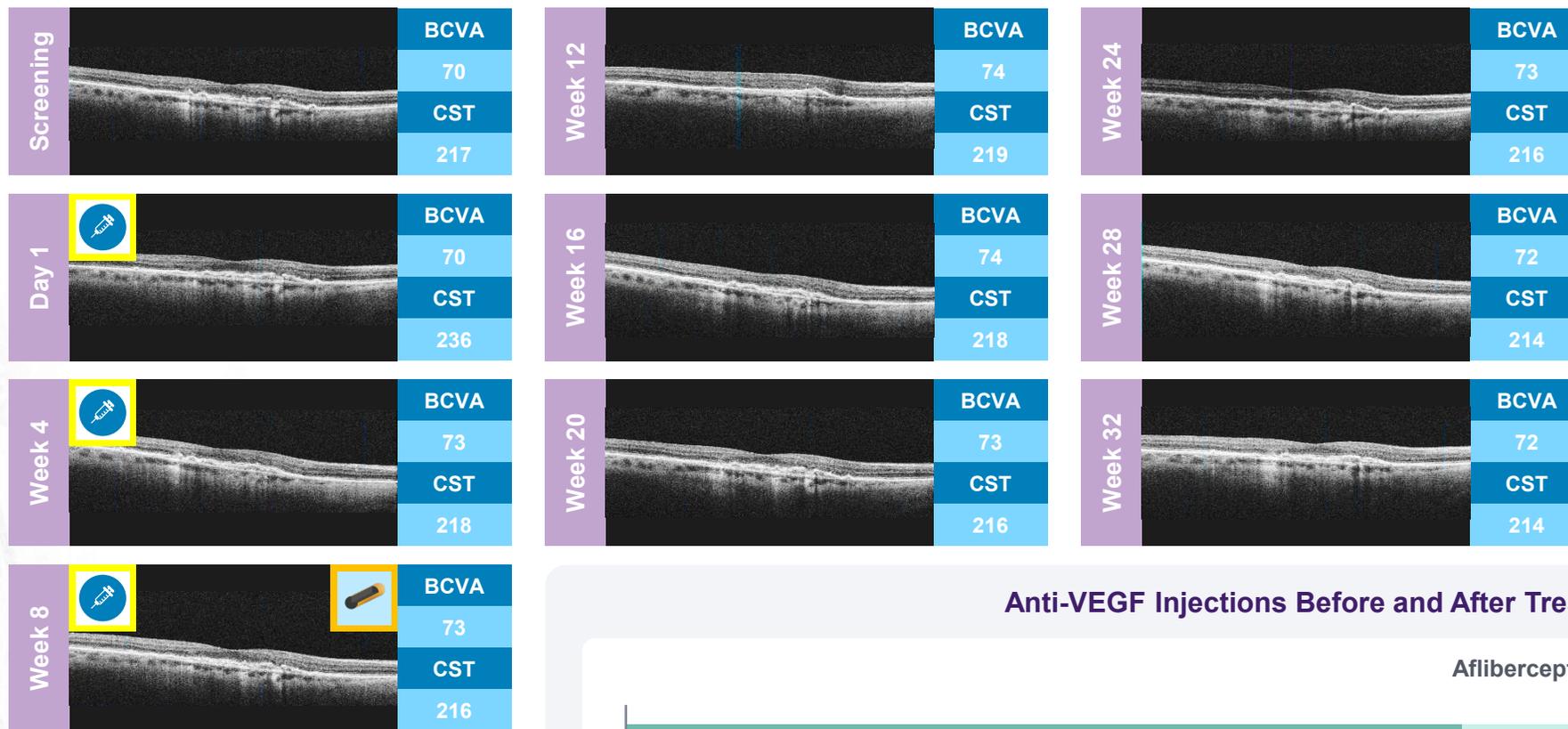
- Anti-VEGF injection
- Afibercept loading dose
- Afibercept + DURAVYU
- No injection
- Missed Visit
- Supplemental injection



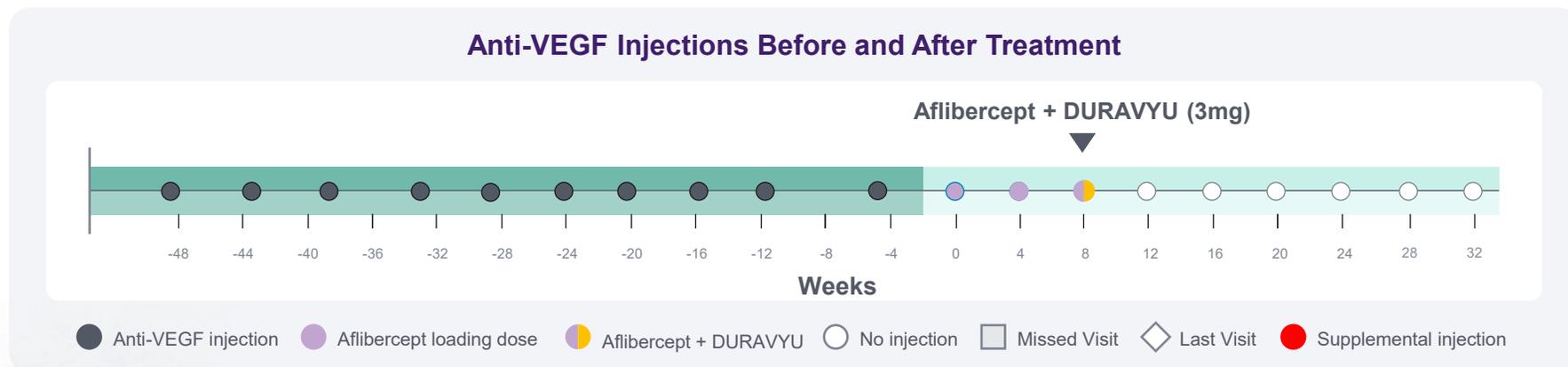
Data from DAVIO 2 Suggests Strong Anatomic Control at 6-Months Compared to the Aflibercept Control



DAVIO 2 Case Study: Patient with Frequent Anti-VEGF Injections Was Maintained for at Least Six Months After Receiving DURAVYU

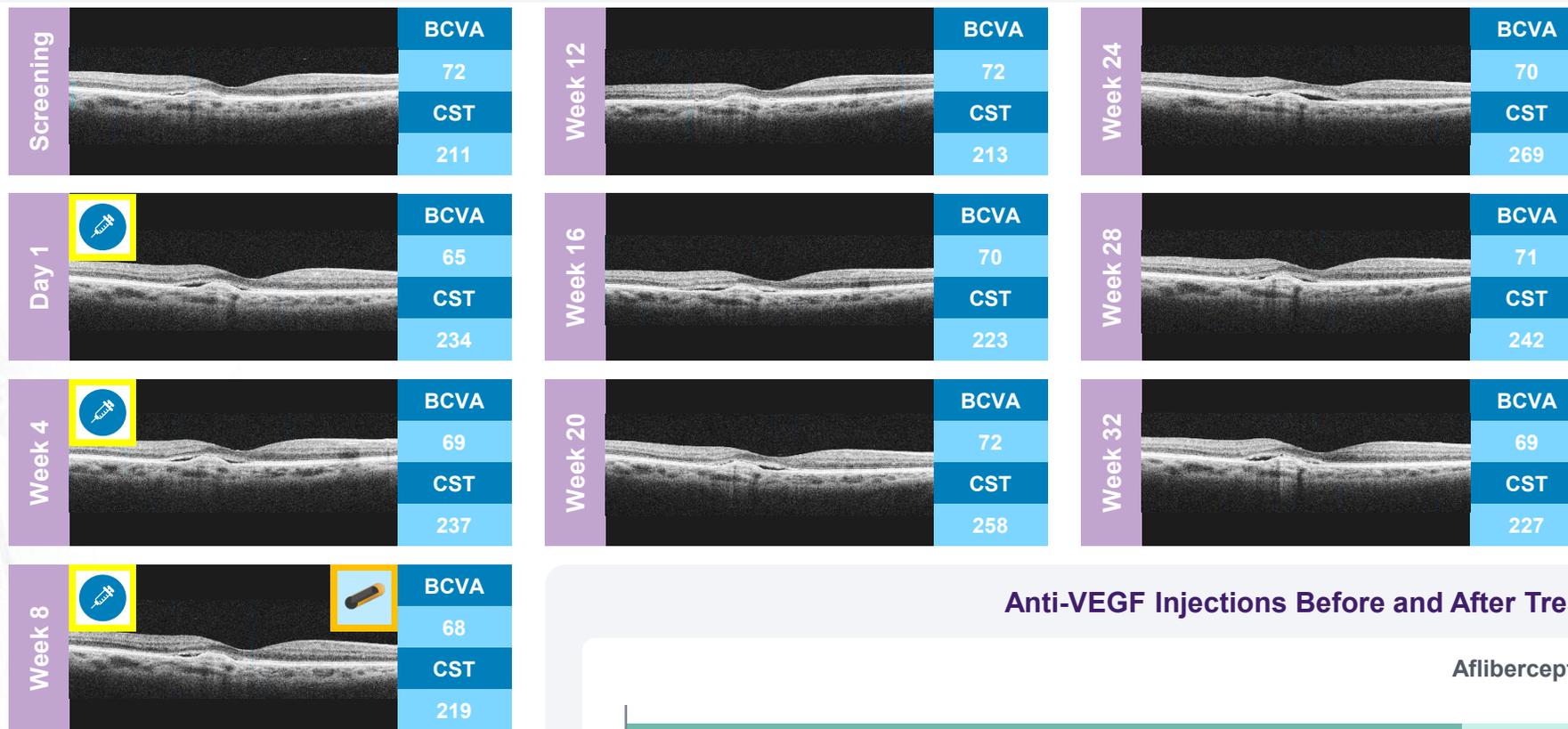


- = administration of aflibercept
- = administration of DURAVYU (3mg)

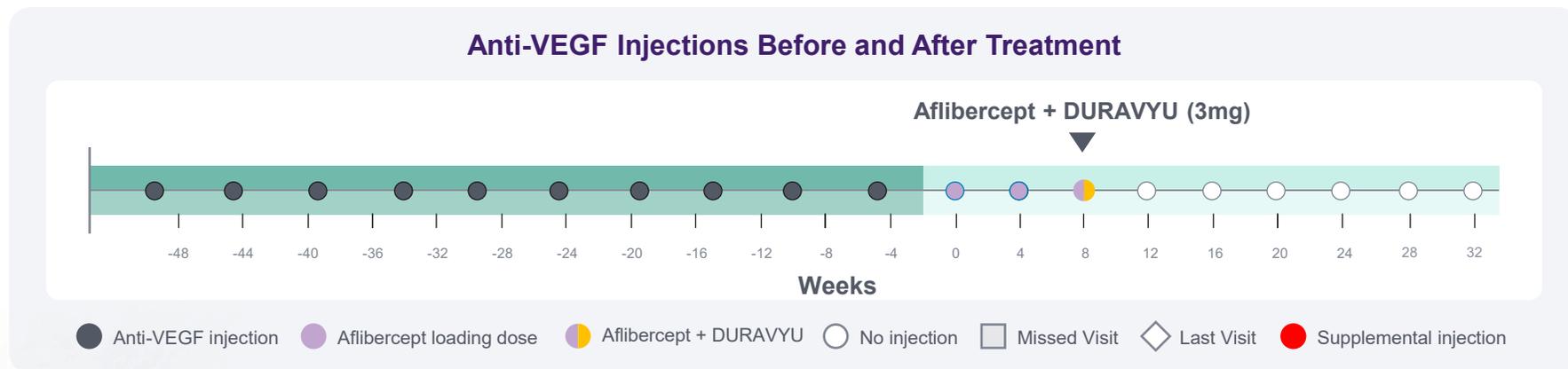


BCVA, best-corrected visual acuity; CST, central subfield thickness.

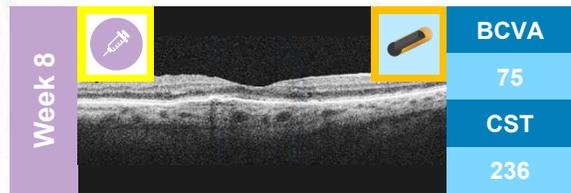
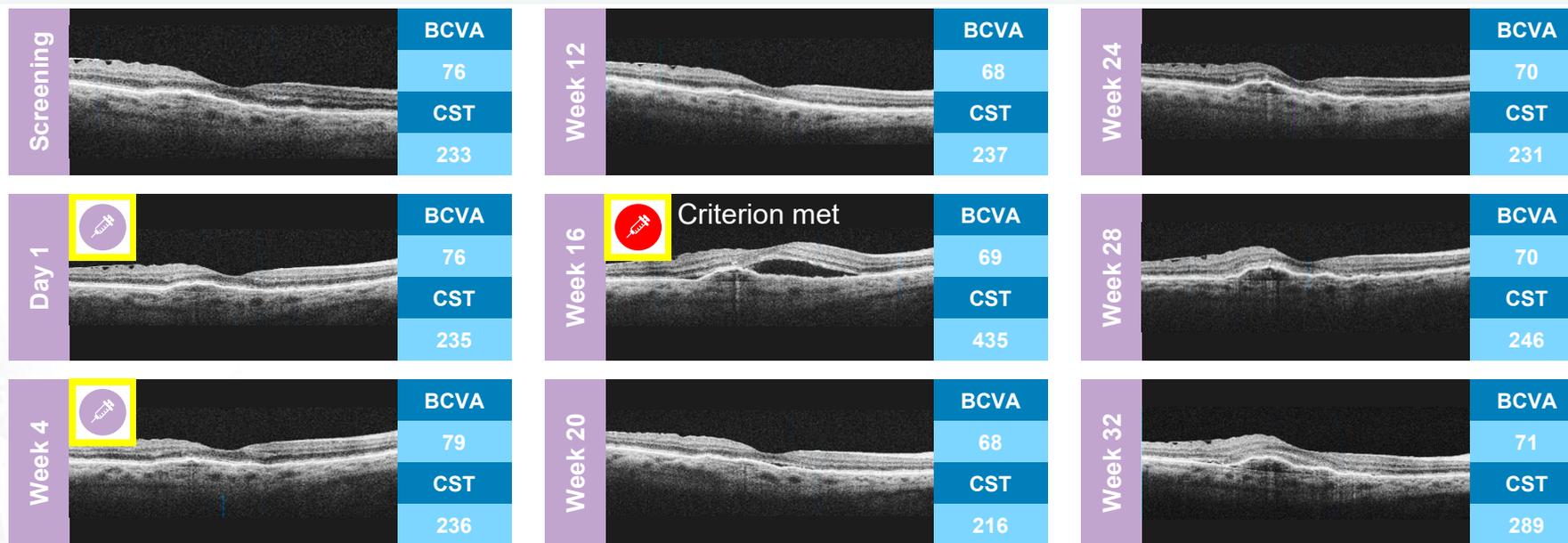
DAVIO 2 Case Study: Patient Treated with DURAVYU had Fluctuations in Fluid without Impact on Vision



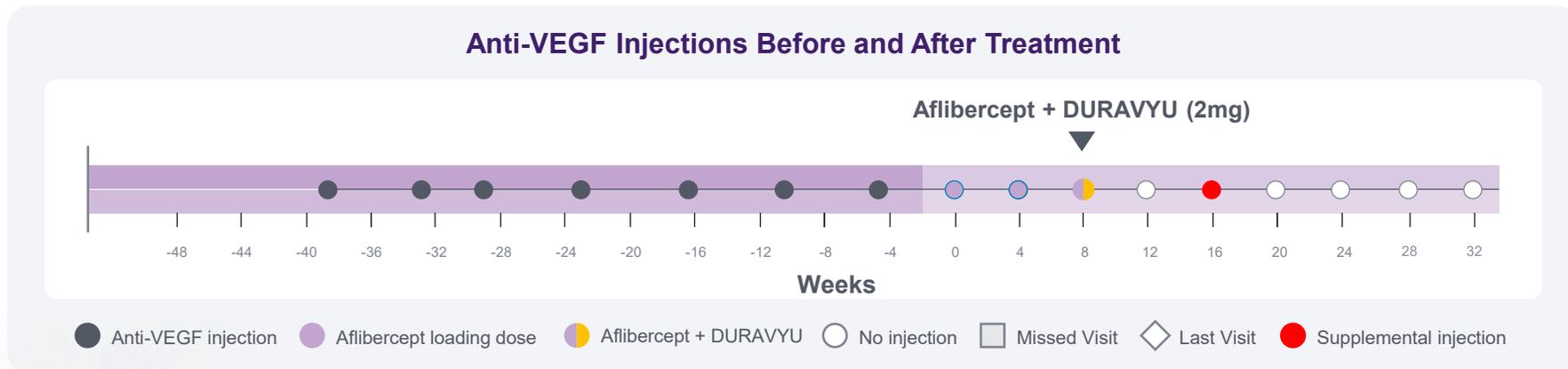
- = administration of aflibercept
- = administration of DURAVYU (3mg)



DAVIO 2 Case Study: Patient Treated with DURAVYU Remained Dry with Only One Supplemental Injection



-  = administration of aflibercept loading dose
-  = administration of DURAVYU (2mg)
-  = administration of aflibercept supplemental injection



BCVA, best-corrected visual acuity; CST, central subfield thickness.

DURAVYU Phase 2 DAVIO 2 Clinical Trial in Wet AMD Met All Primary and Secondary Endpoints

Endpoint	2mg	3mg
✓ Primary: Non-inferior change in BCVA vs. aflibercept	- 0.3 letters	- 0.4 letters
✓ Secondary: Favorable safety profile ¹	No DURAVYU-related SAEs	
✓ Secondary: Reduction in treatment burden vs. 6 mos prior	89%	85%
✓ Secondary: Reduction in treatment burden vs. aflibercept	83%	78%
✓ Secondary: Supplement-free up to 6 months	63% 88% of eyes had 0 or only 1 supplemental injections	63% 83% of eyes had 0 or only 1 supplemental injections
✓ Secondary: Anatomical control vs. aflibercept	+12.4um	+5.2um



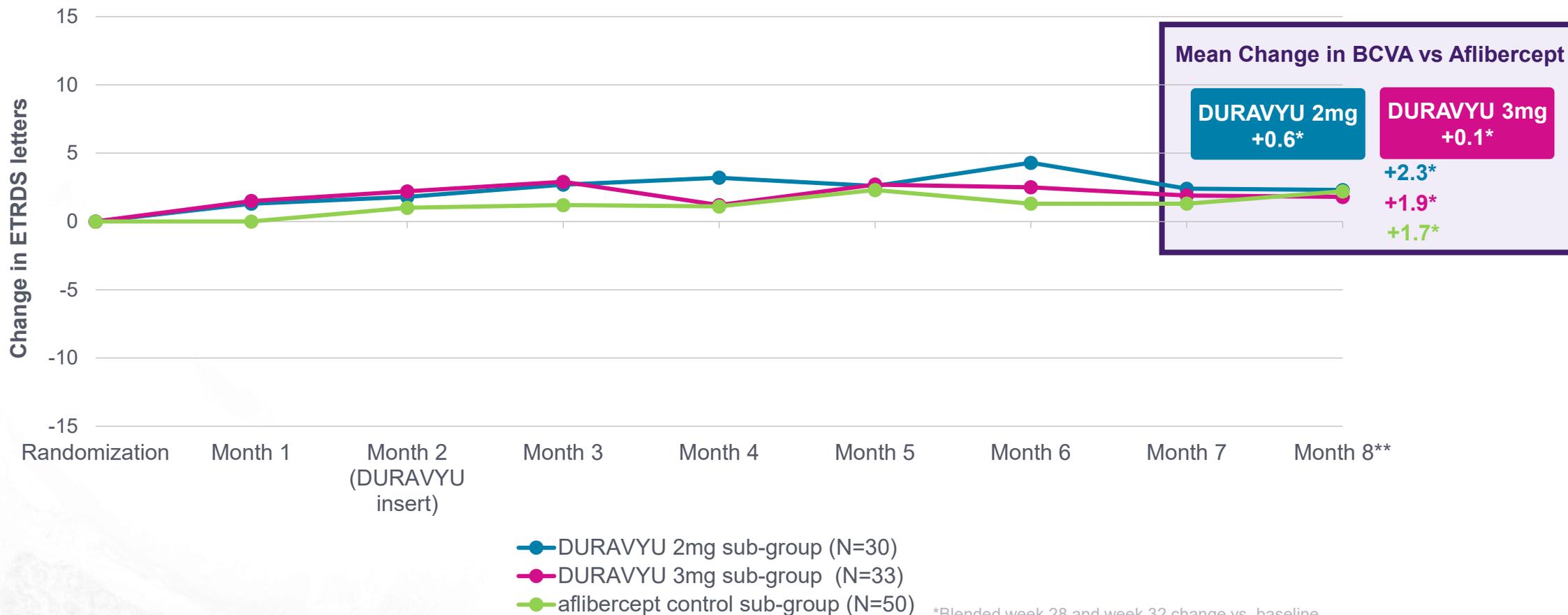
PHASE 2 DAVIO 2 TRIAL IN WET AMD

SUB-GROUP ANALYSIS



Sub-Group Analysis of Supplement-Free Patients Demonstrated Eyes Treated with DURAVYU had Numerically Better Visual Acuity vs. Control

SUB-GROUP ANALYSIS OF PATIENTS SUPPLEMENT-FREE UP TO SIX MONTHS MEAN CHANGE IN BCVA FROM BASELINE

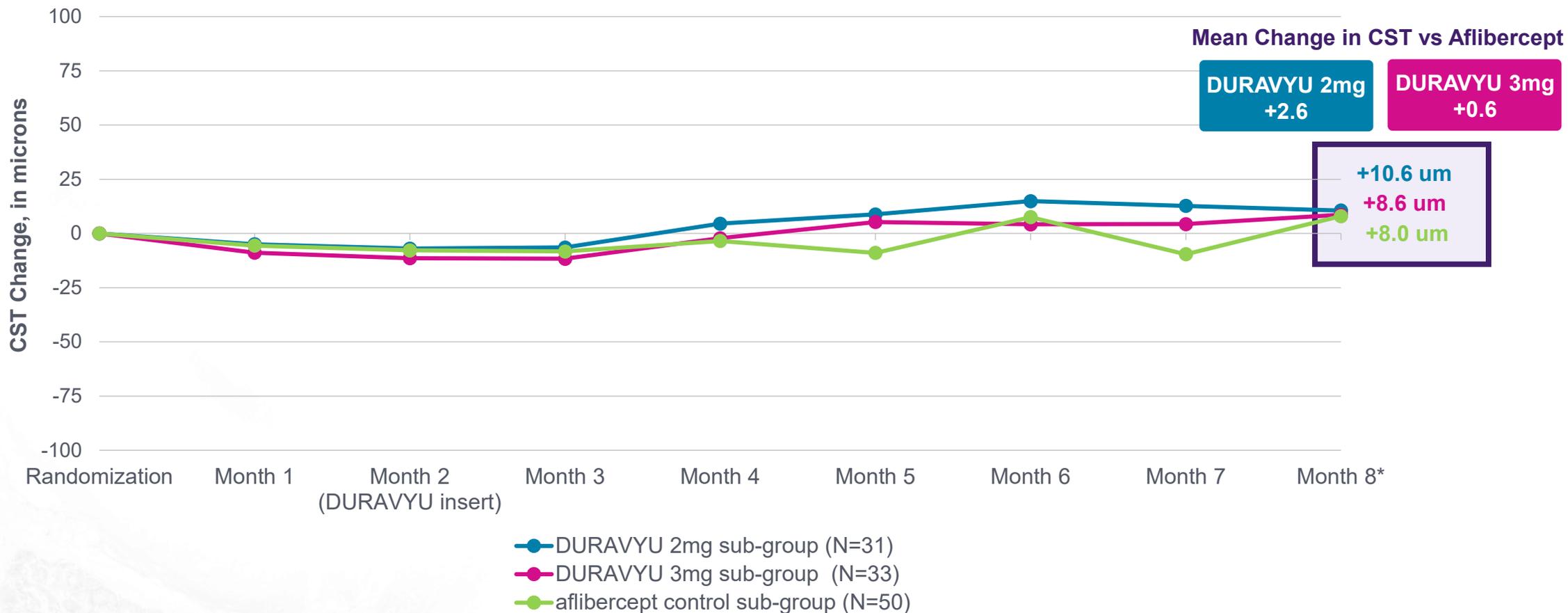


*Blended week 28 and week 32 change vs. baseline
 **Month 8 represents 6 months after DURAVYU injection
 PRELIMINARY DATA – PENDING FINAL ANALYSIS



Sub-Group Analysis of Supplement-Free Patients Demonstrated Strong Anatomic Control Up to 6-Months Compared to the Aflibercept Control

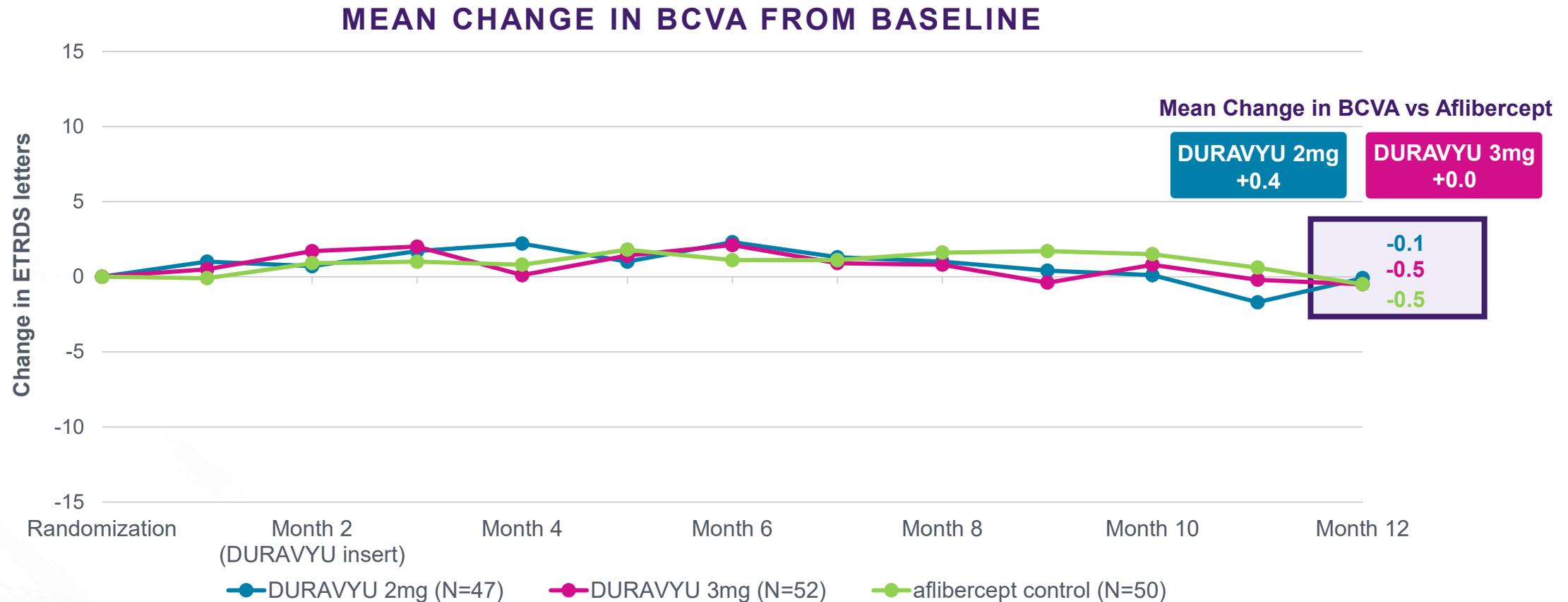
SUB-GROUP ANALYSIS OF PATIENTS SUPPLEMENT-FREE UP TO SIX MONTHS MEAN CHANGE IN CST



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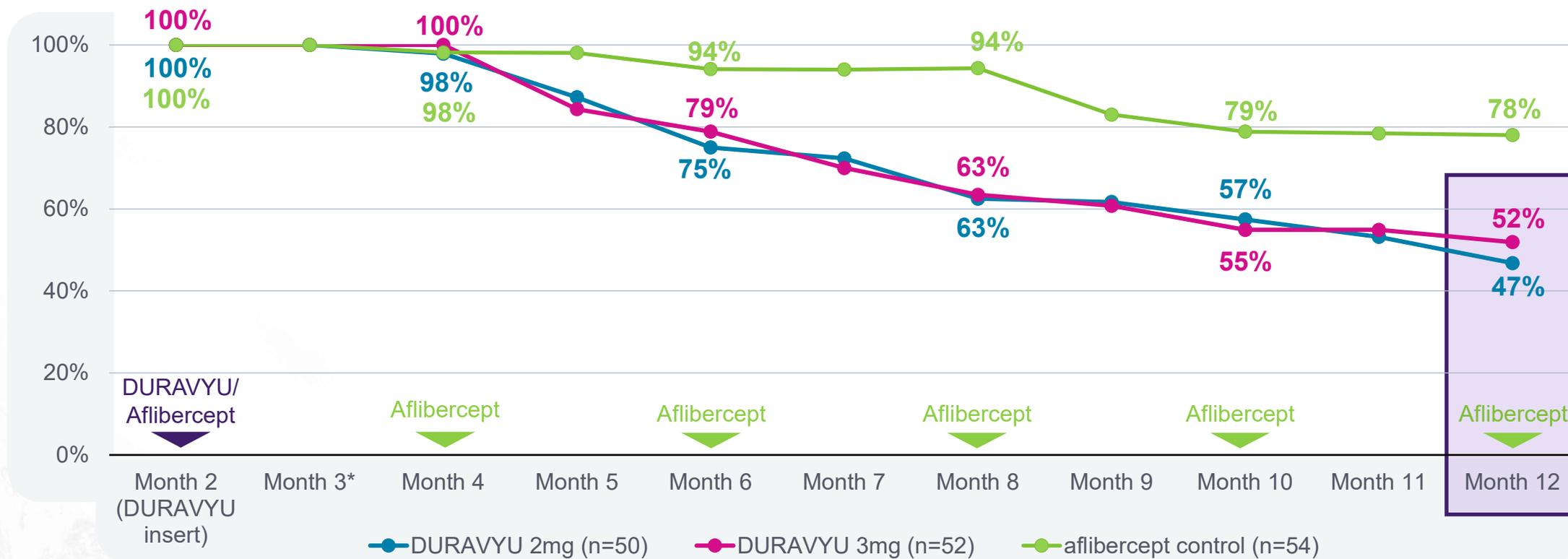
Nearly Identical BCVA Compared to Aflibercept Through 12-Months After a Single Injection; Statistically Significant (95% CI)



Clinically Meaningful Supplement-Free Rates in DURAVYU Treated Eyes After Single Injection

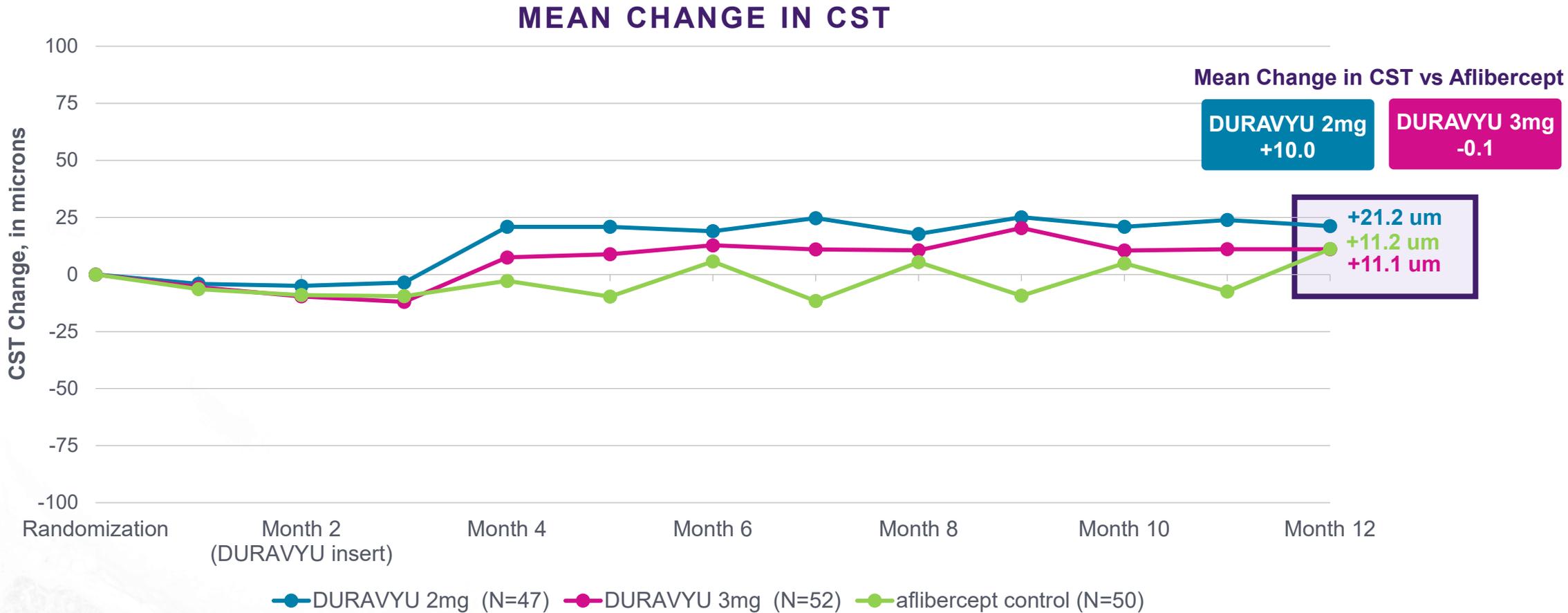
DESPITE EOM AFLIBERCEPT INJECTIONS, 22% OF THE CONTROL GROUP REQUIRED ADDITIONAL SUPPLEMENTATION

SUMMARY OF SUPPLEMENT-FREE RATES BY MONTH



*First visit patients are eligible to be supplemented EOM, every-other-month
PRELIMINARY DATA – PENDING FINAL ANALYSIS

Data from DAVIO 2 Demonstrates Strong Anatomic Control in Eyes Treated with DURAVYU without Saw-Toothing Seen in Aflibercept Arm



DURAVYU Demonstrated a Favorable Safety Profile in the Phase 2 DAVIO 2 Clinical Trial

- No DURAVYU-related ocular or systemic SAEs
- No insert migration into the anterior chamber
- No retinal occlusive vasculitis
- Low patient discontinuation rate
 - No discontinuations were related to DURAVYU treatment

1. As deemed by the investigator

Data as of June 14, 2024

SAE, serious adverse event; AE, adverse event; IVT, intravitreal injection
PRELIMINARY DATA CUT– PENDING FINAL ANALYSIS



Topline 12- Month DAVIO 2 Data Underscores Highly Positive Results

Efficacy:

- After a single injection, eyes treated with DURAVYU **maintained stable visual acuity** with **strong anatomical control**
- Approximately **half of DURAVYU-treated eyes were supplement-free** up to 12 months

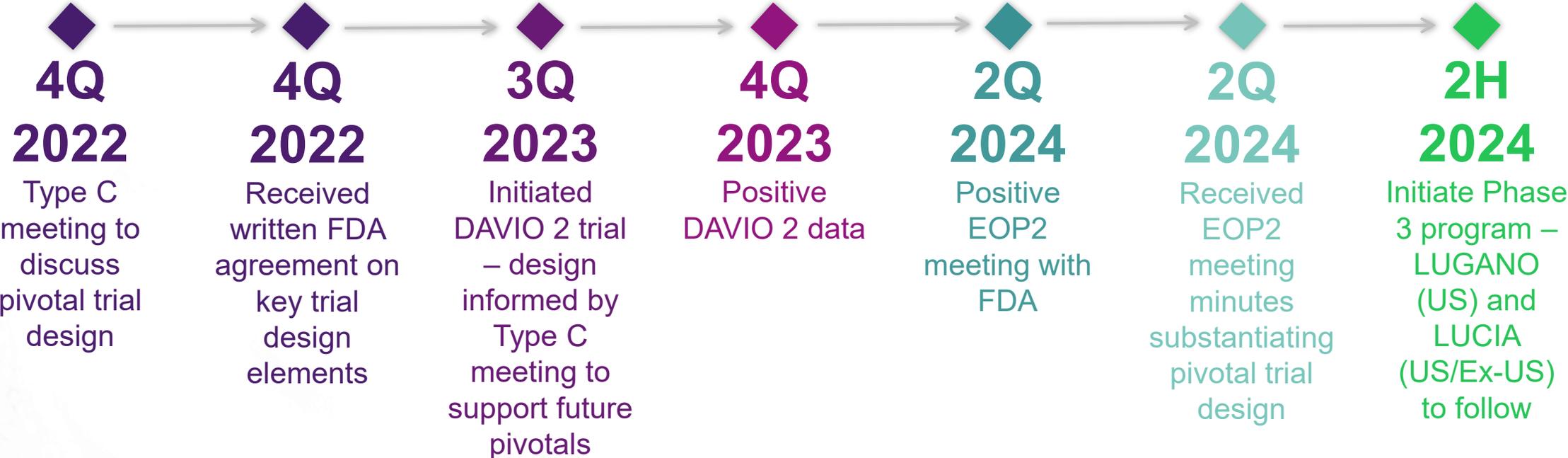
Safety:

- **No ocular or systemic DURAVYU-related SAEs**

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Early Pipeline	Jay Duker, M.D.
Key Opinion Leader Insights and Discussion	Jay Duker, M.D. Carl D. Regillo, M.D. Yasha S. Modi, M.D.
Q&A	All
Closing Remarks	Jay Duker, M.D.

Clear Regulatory Pathway for Phase 3 Pivotal Trials in wet AMD Informed by Multiple FDA Interactions



Phase 3 Trials are Designed to Enable Global Regulatory Approval of DURAVYU

LUGANO/LUCIA: GLOBAL, RANDOMIZED, DOUBLE-MASKED, AFLIBERCEPT CONTROLLED

OBJECTIVE

Demonstrate DURAVYU, when administered **every six months**, achieves similar visual outcomes to **on-label aflibercept** while **reducing treatment burden**

DESIGN

- Two pivotal, **non-inferiority** trials
- **~400** patients per trial
- **Two arms:** 2.7mg DURAVYU vs. aflibercept control

ENDPOINTS

Primary Endpoint: difference in mean change in BCVA from Day 1 to Week 52 and 56 (blended) versus aflibercept control

Secondary endpoints: safety, reduction in treatment burden, percent of eyes supplement-free, anatomical stability

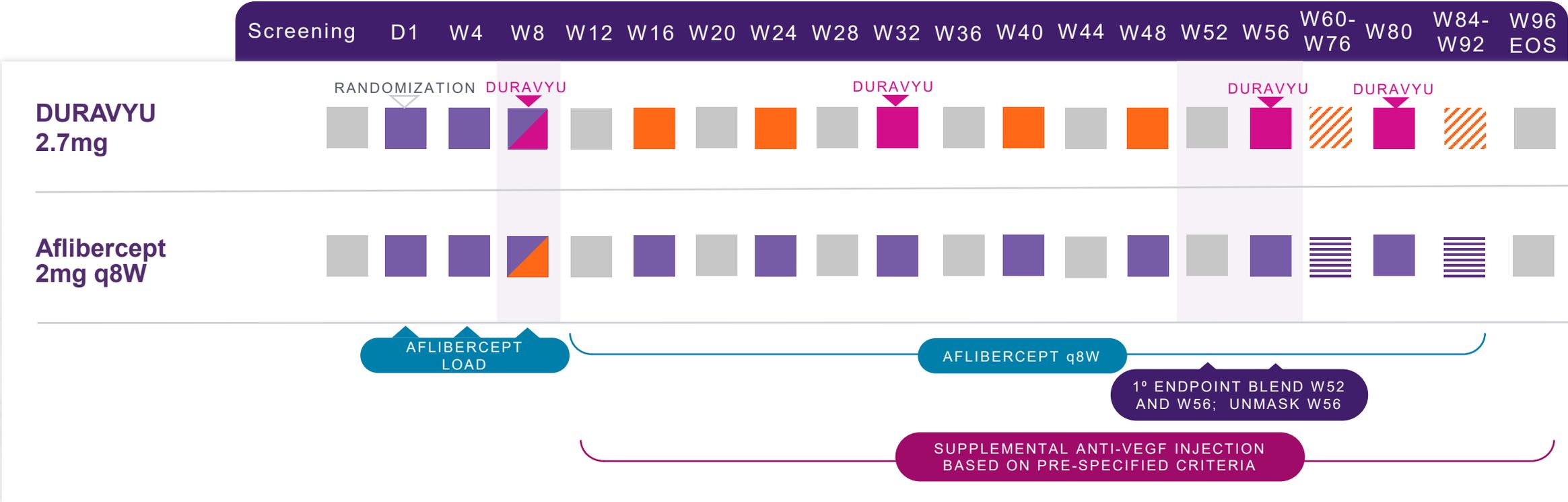
Phase 3 Program is Designed to Drive Global Regulatory and Commercial Success

KEY TRIAL DESIGN ELEMENTS

- Only sustained release wet AMD program to evaluate reinjection for label
- Trials will enroll patients with active wet AMD (previously treated and treatment naïve)
- All patients will receive three loading doses of aflibercept
- Sham injections will be used for masking
- Primary efficacy endpoint at 12 months (basis for NDA submission)
 - Safety will be monitored for 24 months

On track to be first sustained release wet AMD program with two pivotal trials to enable NDA submission to the FDA

DURAVYU in Wet AMD Phase 3 Pivotal Trial Design



- REQUIRED AFLIBERCEPT INJECTION VISIT
- VISIT SCHEDULED
- DURAVYU DOSE
- SHAM INJECTION FOR MASKING
- ≡ AFLIBERCEPT Q8W
- ▨ SHAM INJECTION TO MASK FOR AFLIBERCEPT INJECTION

A Broad Patient Population in the Phase 3 Pivotal Trials has the Potential to Enhance Trial Outcomes and Increase Commercial Opportunity

- ✓ Enriches trial to have **more supplement-free eyes**, which had better outcomes in DAVIO 2
- ✓ Ensures **broad label** and global **reimbursement**
- ✓ **Speeds enrollment**; >80 sites already selected
- ✓ Supports **real-world clinical use** for physicians and patients
- ✓ **Three loading doses of aflibercept**; all patients will be previously treated when receiving DURAVYU

A Broad Patient Population in the Phase 3 Pivotal Trials has the Potential to Enhance Trial Outcomes and Increase Commercial Opportunity

Highly positive, statistically non-inferior DAVIO 2 results despite tough to treat population

- Average of 10 injections per year prior to enrollment
- Aflibercept arm (q8w) had nearly 25% supplementation rate despite receiving on-label injections
- Supplement-free eyes did the best visually and, in those eyes, DURAVYU performed numerically better than aflibercept visually

In DAVIO 2, eyes that were pseudo naïve¹ had fewer supplements than the overall cohort

We believe the inclusion of treatment naïve patients not only expands the potential patient population but also increases the probability of success

Commercial Manufacturing Facility



New manufacturing site for clinical and commercial products



Conveniently located in Northbridge, MA, near EyePoint headquarters



Built to EYPT specifications with no capital investment required preserving cash



Built to US FDA and EU EMA standards



40,000 sqft cGMP manufacturing facility



FDA, Federal Drug Administration; EMA, European Medicines Agency

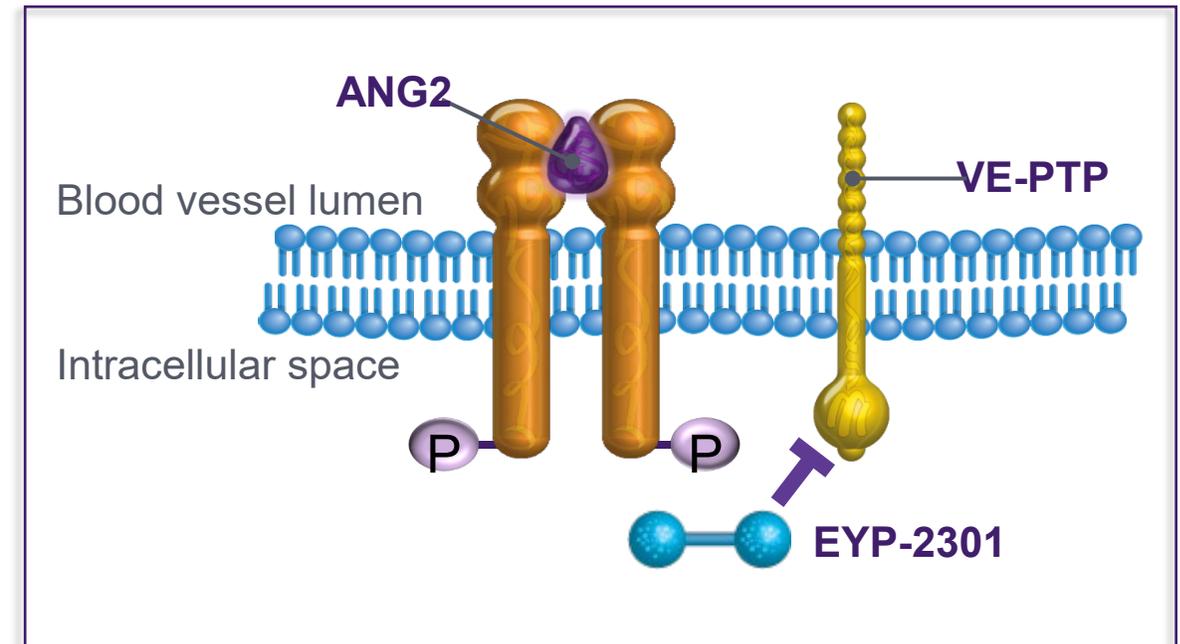
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Key Opinion Leader Insights and Discussion	Jay Duker, M.D. Carl D. Regillo, M.D. Yasha S. Modi, M.D.
Q&A	All
Closing Remarks	Jay Duker, M.D.

EYP-2301: Razuprotafib in Durasert E™ is a Patented TIE-2 Agonist as a Potential New MOA for Treating Serious Retinal Diseases

EYP-2301 targets vascular endothelial protein tyrosine phosphatase (VE-PTP) to promote TIE-2 activation and maintain vascular stability in the retina

- Tie-2 activation combined with VEGF inhibition has the potential to **enhance efficacy and extend durability**¹ of treatment
- Razuprotafib (f/k/a AKB-9778) delivered subcutaneously demonstrated preclinical and **clinical proof of concept** in posterior segment disease^{2,3}



1. Heier et al. Retina, 2021;41:1-19. and Joussen et al. Eye 2021; 35:1305-1316.; 2. Hammes, et. Al – Diabetes.2011 Jan 1; 3. Shen et al. JCI, 2014; 124:4564; 4. Campochiaro et al. Ophthalmology, 2016; 123:1722-1730

R&D Day: Agenda

	PRESENTATION SPEAKER
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R&D Day: Agenda

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Data from Clinical and Preclinical Studies will be Presented at Multiple Upcoming Meetings

Medical Conference	Data	Timing
ASRS	New DAVIO 2 sub-group analyses	July 2024
American Retina Forum	DAVIO 2 encore presentation	August 2024
Retina Society	Topline DAVIO 2 12-month data	September 2024
EURetina	DAVIO 2 sub-group analyses Topline DAVIO 2 12-month data	September 2024
AAO	DAVIO 2 12-month sub-group analyses	October 2024
FloRetina	DAVIO 2 encore presentation*	December 2024

Publications	Link
Phase I DAVIO Trial: EYP-1901 Bioerodible, Sustained-Delivery Vorolanib Insert in Patients With Wet Age-Related Macular Degeneration Patel S, Storey P, Barakat M, et al. <i>Ophthalmology Science</i> . 2024 Apr 8:4(5)	https://www.ophtalmologyscience.org/article/S2666-9145(24)00063-0/fulltext
Vorolanib, sunitinib, and axitinib: A comparative study of vascular endothelial growth factor receptor inhibitors and their anti-angiogenic effects Bakri S, Lynch J, Howard-Sparks M, et al. <i>PLOS One</i> . 2024 June 4	https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0304782

DURAVYU entering Phase 3 with robust dataset and FDA alignment on approval pathway

SAFETY

No ocular or systemic DURAVYU-related SAEs across clinical trials

FDA

Non-inferiority pathway to approval aligned with FDA

DATA

Most robust dataset of all long-acting treatments in development

**TRIAL
DESIGN**

Phase 3 trial design including re-dosing - aligns with FDA and clinical use

NOVEL

Patented molecule with new MOA and best-in-class delivery technology

EYEPOINT PHARMACEUTICALS

R&D DAY

2024 

UNIVERSITY CLUB | NEW YORK CITY | JUNE 26, 2024