THE **DAVIO 2** TRIAL:
A Phase 2, Multicenter Study of a Single Injection of EYP-1901 vs Aflibercept for Wet Age-Related Macular Degeneration

Rishi P. Singh, MD

On behalf of the DAVIO 2 trial investigators

Staff Physician, Vice President and Chief Medical Officer, Cleveland Clinic Martin Hospitals, Cleveland Clinic Florida, Stuart, FL

Professor of Ophthalmology, Cleveland Clinic Lerner College Of Medicine, Cleveland, Ohio

Macula Society Annual Meeting 2024

Interim data - database lock pending, final 12m data expected H2 2024

Disclosures

Financial Disclosures

- Consultant for 4DMT, Apellis, AbbVie, Alimera, Bausch + Lomb, EyePoint, Genentech, Gyroscope/Novartis, Ocular Therapeutix, Regeneron

EYP-1901: Pan-VEGF Receptor Inhibitor Vorolanib in Durasert E™, a Bioerodible, Sustained-Delivery, IVT Insert

Vorolanib:

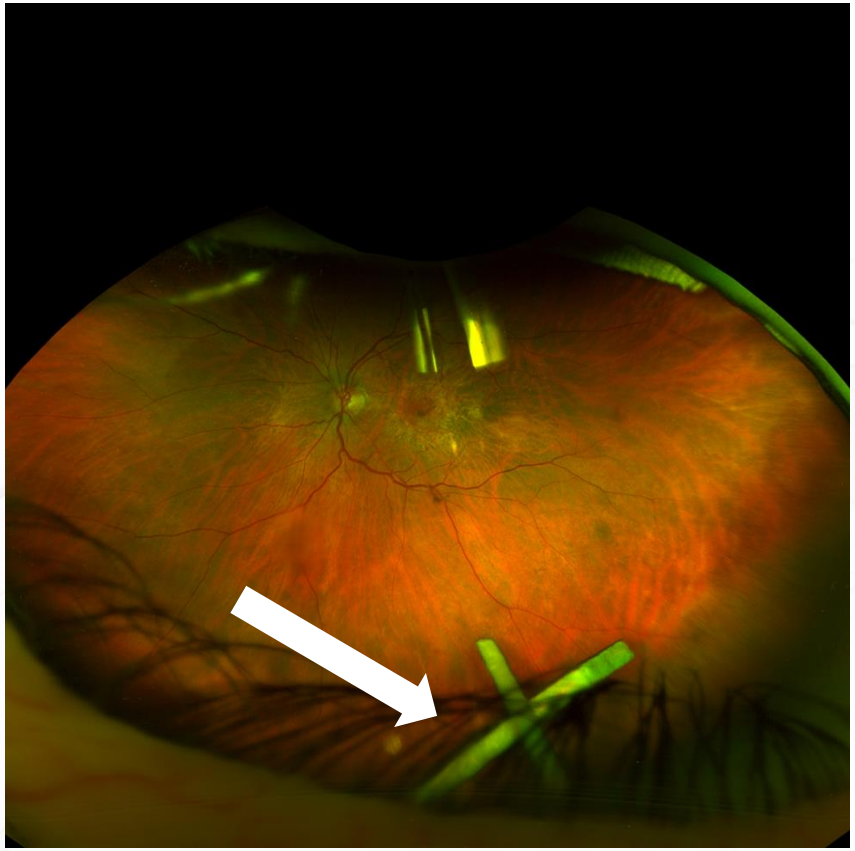
- **Potent and patent-protected pan-VEGFR inhibitor**
  - Inhibits all VEGFRs (1, 2, and 3)—receptors involved in wAMD
  - Does not inhibit **TIE2** receptors at clinically relevant doses*

Bioerodible Durasert E™:

- **Vorolanib reaches targeted tissues within hours** of administration, reaching levels considerably higher than IC_{50} within the day of injection
- **Zero-order kinetics** continuously delivers therapeutic levels of vorolanib for ~9 months at a steady state
- Designed to completely elute vorolanib and then fully **bioerode**
- Stored and shipped at **ambient temperature**

Durasert®: Proven, safe IVT drug delivery technology

- Routine in-office IVT injection
- Safely administered across 4 FDA-approved products with non-erodible formulations

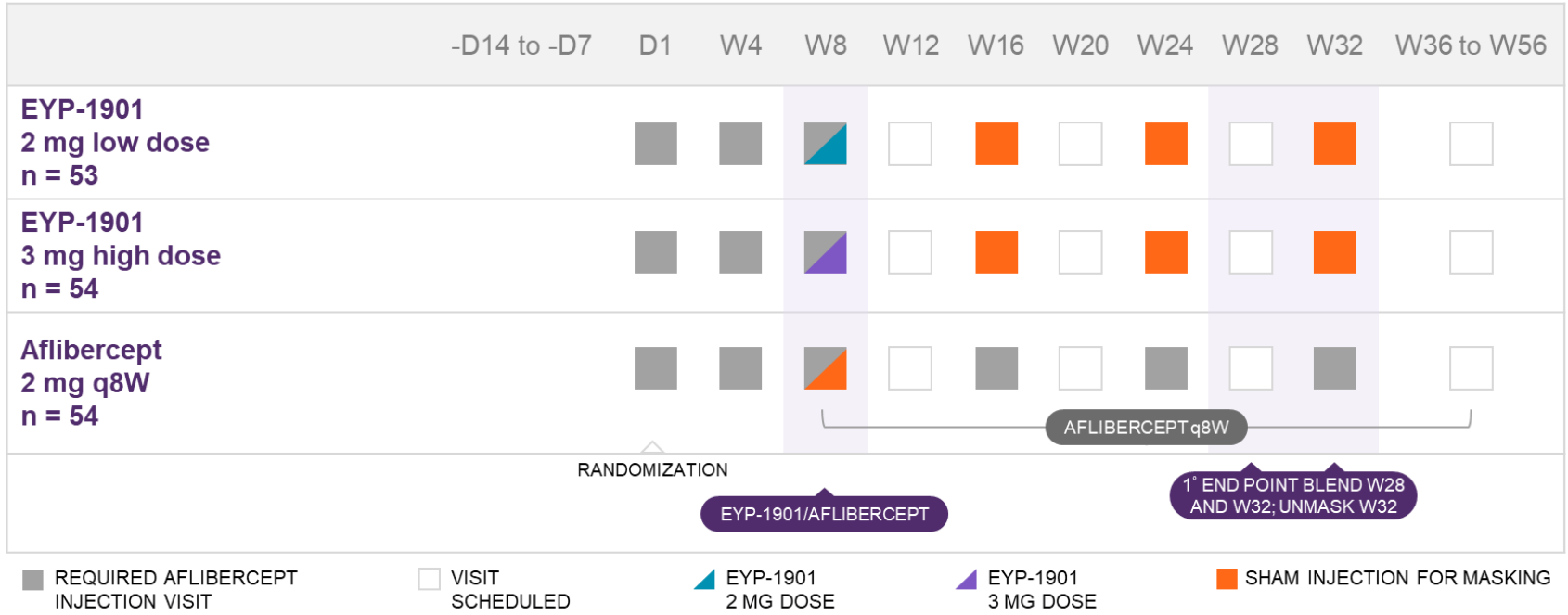


*Avery RL, et al. Presented at AAO 2023.

FDA, Food and Drug Administration; IC_{50}, half-maximal inhibitory concentration; IVT, intravitreal; PDGFR, platelet-derived growth factor receptor; TIE2, tyrosine-protein kinase receptor TIE-2; VEGF(R), vascular endothelial growth factor (receptor); wAMD, wet age-related macular degeneration.

DAVIO 2: Phase 2 Randomized, Double-Masked, Parallel Trial of a Single EYP-1901 Treatment Compared to SoC in Previously Treated Patients with wAMD

Primary endpoint: Combined mean change in BCVA at Weeks 28 and 32 (6 months after EYP-1901 injection)



Key inclusion/exclusion criteria

- Diagnosed with wAMD at any time
- History of documented response to anti-VEGF
- History of at least 2 injections in last 6 months
- BCVA range 85 to 35 letters (20/20 to 20/200)
- Excluded CST >350 µm, IRF >25 µm, RPED >400 µm

Criteria for supplemental injection

BCVA reduction of ≥5 letters from best on-study measurement due to wAMD AND increase in CST of ≥75 µm from lowest on-study measurement

OR

BCVA reduction of ≥10 letters from best on-study measurement due to wAMD

OR

Increase in CST of ≥100 µm from lowest on-study measurement from 2 consecutive visits

OR

Presence of new or worsening vision-threatening hemorrhage due to wAMD

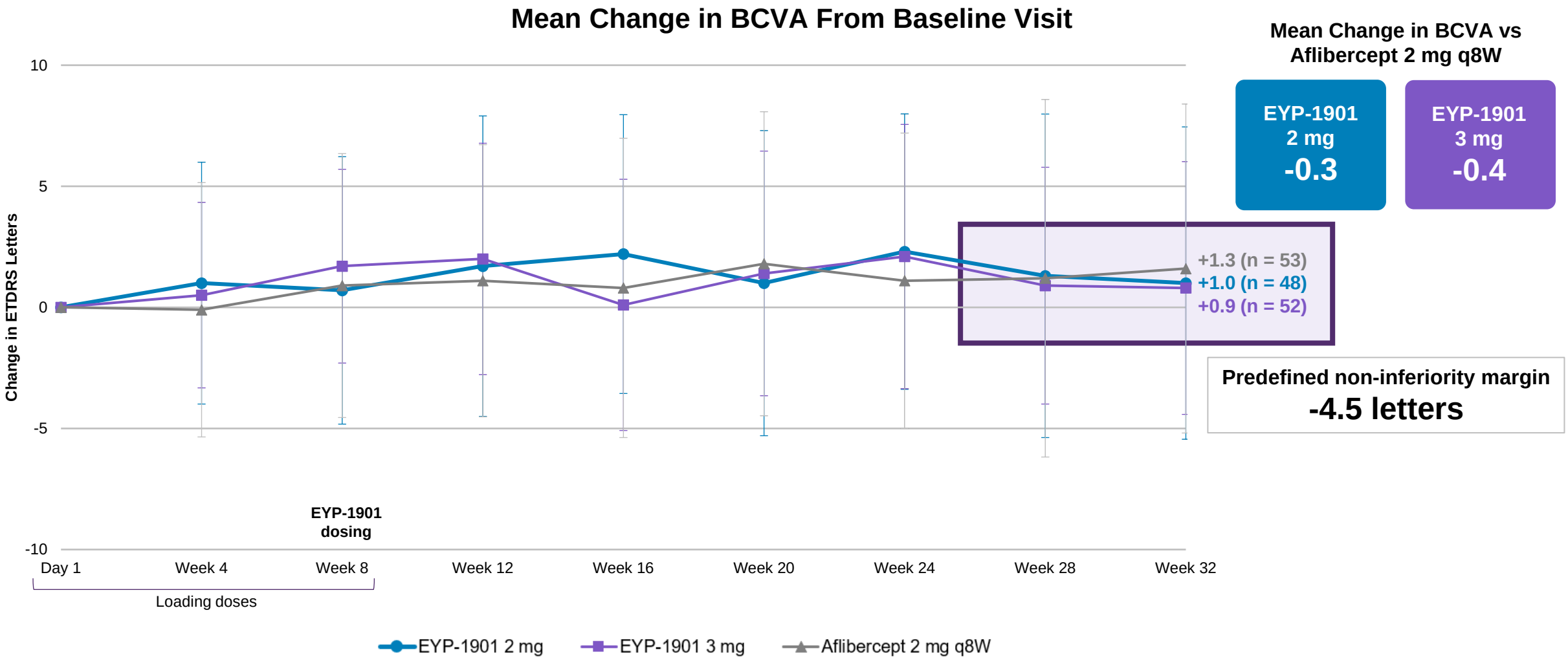
BCVA, best corrected visual acuity; CST, central subfield thickness; IRF, intraretinal fluid; q8W, every 8 weeks; RPED, retinal pigment epithelium detachment; VEGF, vascular endothelial growth factor; wAMD, wet age-related macular degeneration.

DAVIO 2 Baseline Characteristics Well Balanced Across Arms

Baseline Characteristics (N = 156)	Aflibercept 2 mg q8W (n = 54)	EYP-1901 2 mg (n = 50)	EYP-1901 3 mg (n = 52)
Mean age, years (range)	75.9 (52–93)	76.4 (61–93)	75.4 (56–89)
Female, %	53.7%	64.0%	67.3%
Mean BCVA, ETDRS letters (range) (Snellen equivalent)	73.4 (41–85) (~20/32)	73.9 (52–84) (~20/32)	74.9 (46–85) (~20/32)
Mean CST, µm (range)	265.7 (178–348)	267.0 (192–400)	262.9 (186–345)
Median length of time for wAMD diagnosis prior to screening, months (range)	28.1 (2.4–273.8)	24.3 (2.4–168.1)	28.1 (2.4–145.3)
Mean number of injections in the 12 months prior to screening (range)*	**9.5 (2–12)**	**10.2 (2–13)**	**10.0 (2–13)**

*Normalized values using topline Table 9-1. Other data are from topline Tables 2 and 3.
BCVA, best-corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; q8W, every 8 weeks; VEGF, vascular endothelial growth factor; wAMD, wet age-related macular degeneration.

Primary Endpoint: EYP-1901 Statistically Non-Inferior to SoC in Maintaining BCVA Over 32 Weeks



Mean Change in BCVA vs Aflibercept 2 mg q8W

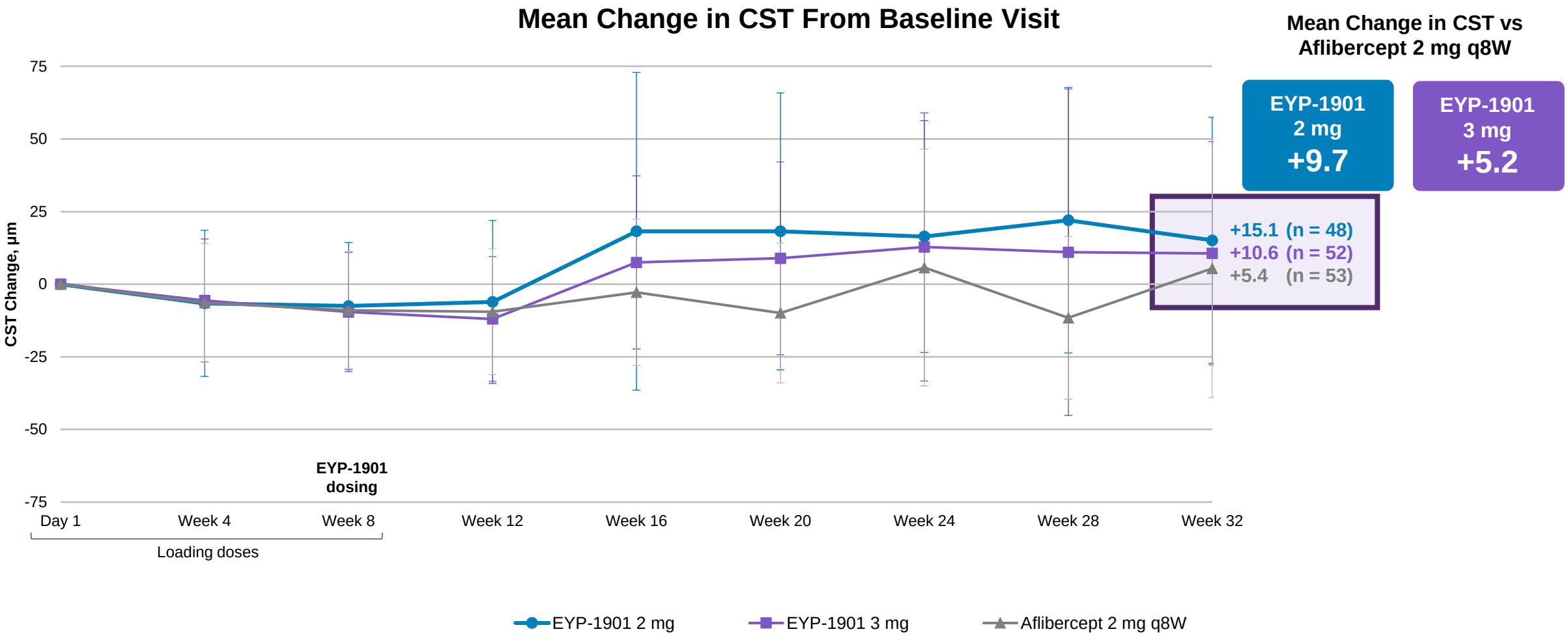
EYP-1901 2 mg	EYP-1901 3 mg
-0.3	-0.4

Predefined non-inferiority margin
-4.5 letters

Data from topline Table 4-1. Error bars represent the standard deviation. BCVA units were ETDRS letters.
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; q8W, every 8 weeks; SoC, standard of care.

DAVIO 2 INTERIM DATA NOV23: DATABASE LOCK PENDING

Secondary Endpoint: Central Subfield Thickness Was Similar to SoC Over 32 Weeks with EYP-1901

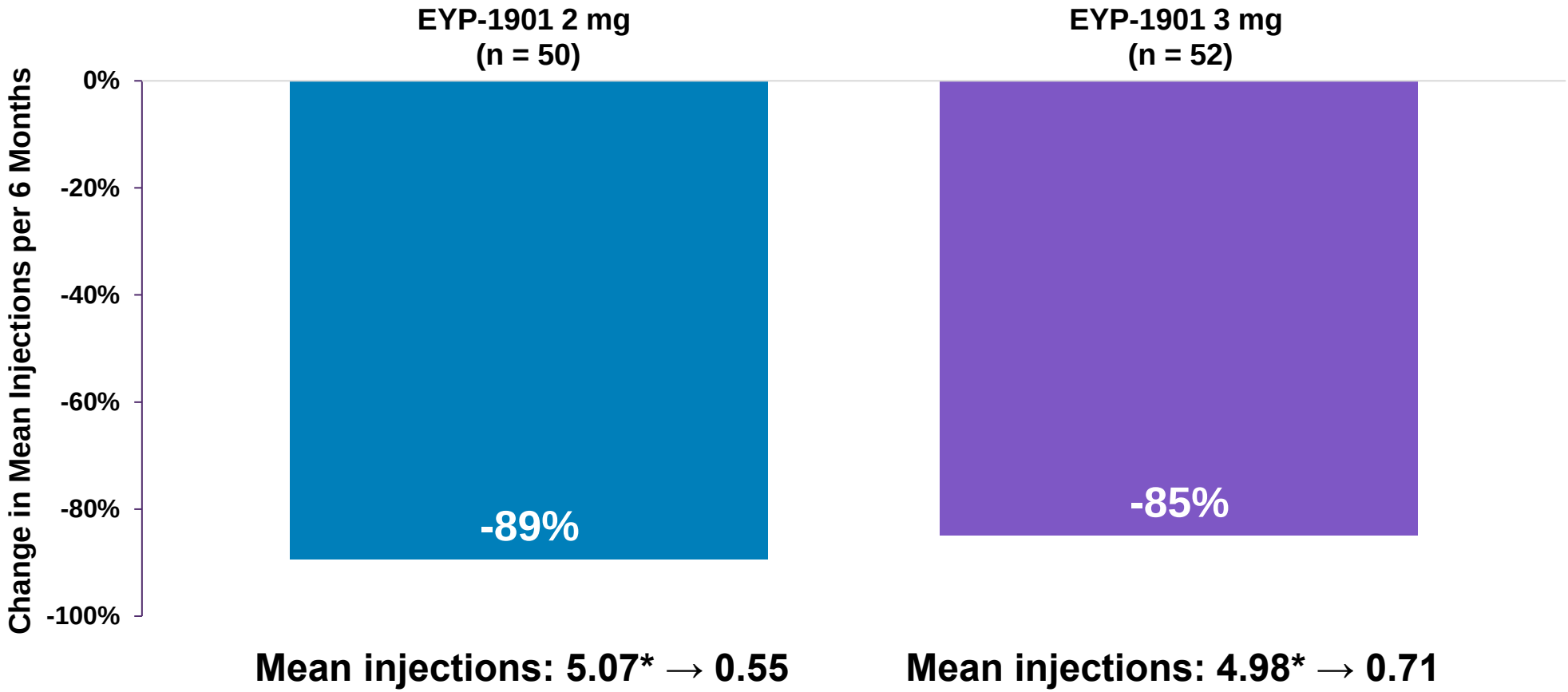


Data from topline Table 6. Error bars represent the standard deviation. CST units were µm.
CST, central subfield thickness; q8W, every 8 weeks; SoC, standard of care.

DAVIO 2 INTERIM DATA NOV23: DATABASE LOCK PENDING

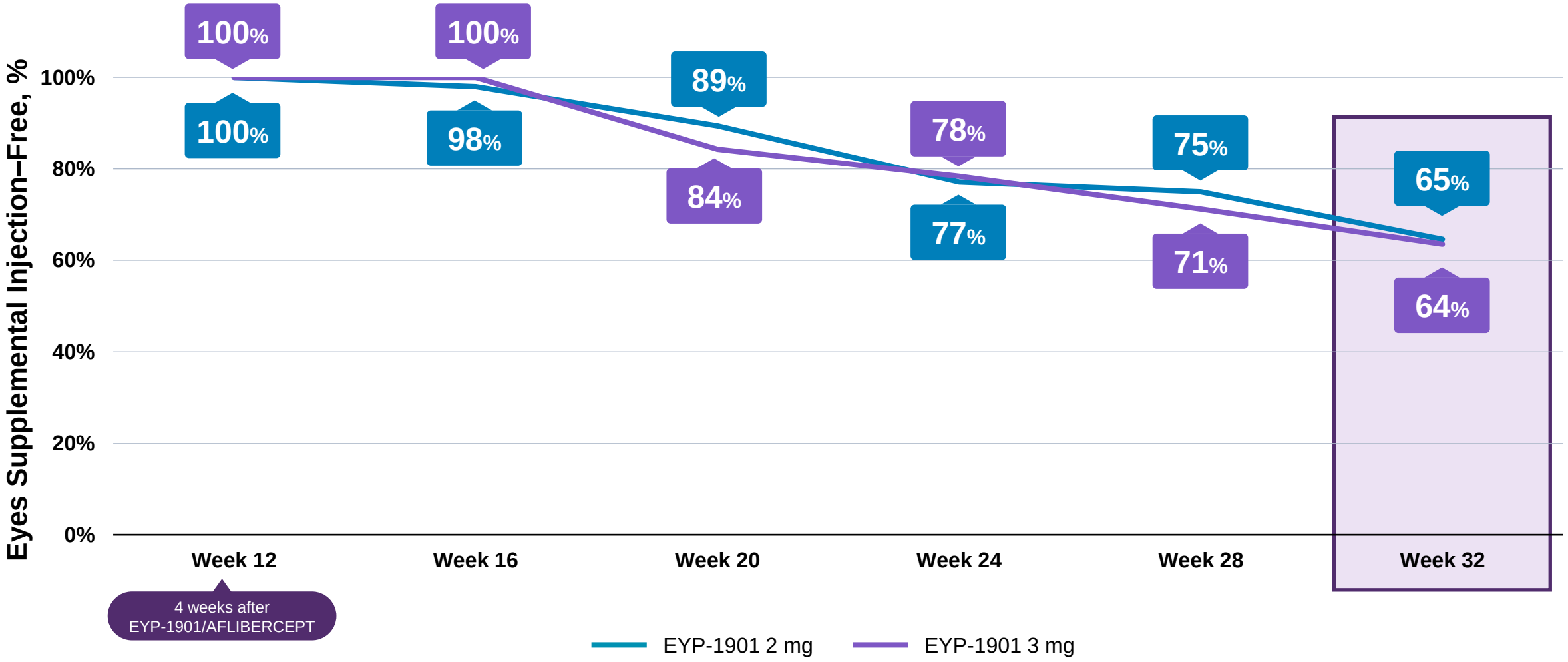
EYP-1901 Reduced Treatment Burden by ≥85% Compared to Prior 6 Months

Treatment Burden on Study (Up to Week 32) vs Prior 6 Months



*Normalized values using data from topline Table 9-2.

≥64% of Eyes Receiving EYP-1901 Were Supplemental Injection–Free Up to Week 32

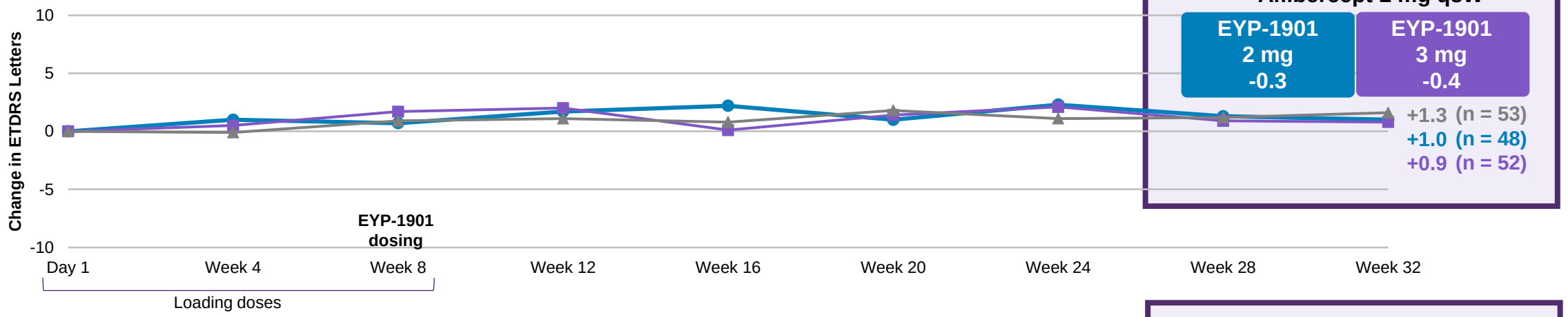


Data from topline Table 7.

DAVIO 2 INTERIM DATA NOV23: DATABASE LOCK PENDING

Eyes with Supplemental Injections Did Not Drive BCVA Outcomes

Mean Change in BCVA, All Eyes

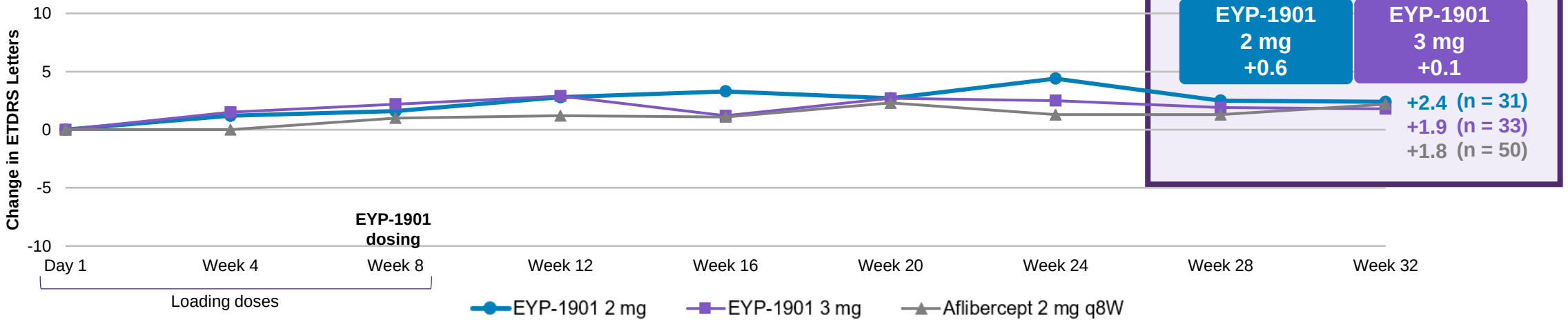


Mean Change in BCVA vs Aflibercept 2 mg q8W

EYP-1901 2 mg	EYP-1901 3 mg
-0.3	-0.4

+1.3 (n = 53)
+1.0 (n = 48)
+0.9 (n = 52)

Mean Change in BCVA, Eyes Without Supplemental Injections



Mean Change in BCVA vs Aflibercept 2 mg q8W

EYP-1901 2 mg	EYP-1901 3 mg
+0.6	+0.1

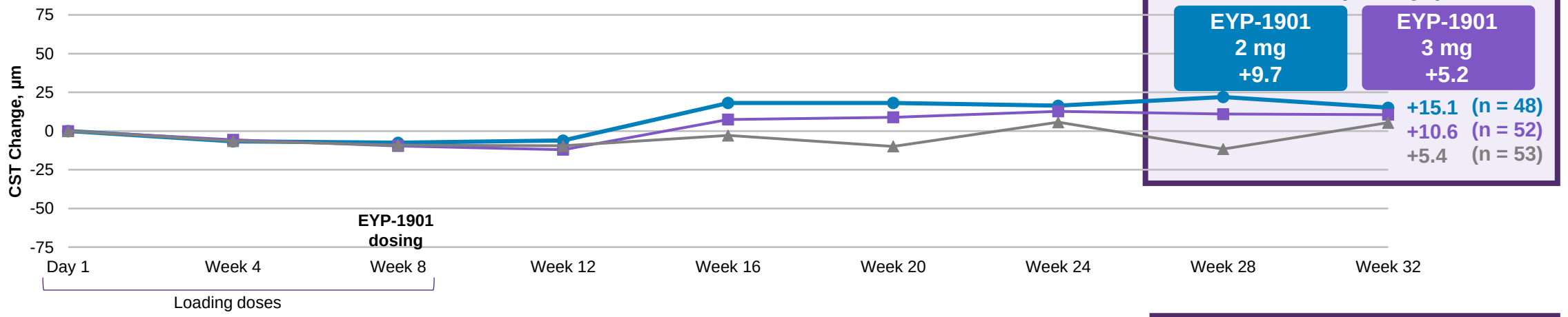
+2.4 (n = 31)
+1.9 (n = 33)
+1.8 (n = 50)

Data from IA-SG01 Table 1. BCVA units were ETDRS letters.
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; q8W; every 8 weeks.

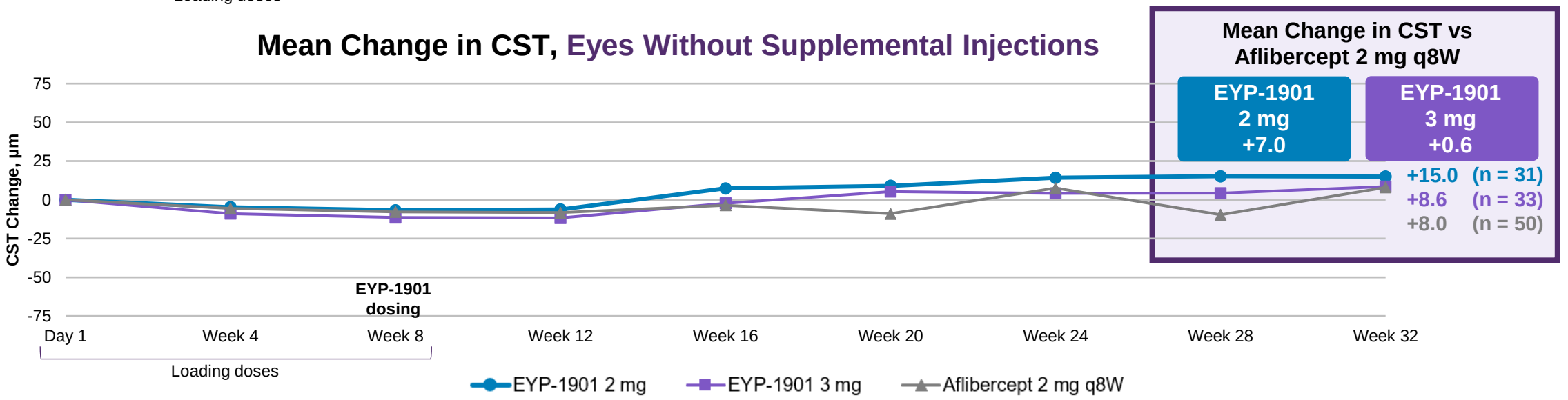
DAVIO 2 INTERIM DATA NOV23: DATABASE LOCK PENDING

Eyes with Supplemental Injections Did Not Drive Anatomical Outcomes

Mean Change in CST, All Eyes



Mean Change in CST, Eyes Without Supplemental Injections



Data from IA-SG01 Table 2. CST units were µm.
CST, central subfield thickness; q8W, every 8 weeks.

DAVIO 2 INTERIM DATA NOV23: DATABASE LOCK PENDING

EYP-1901: Well Tolerated With an Acceptable Safety Profile Through Week 32 and No Ocular SAEs Related to EYP-1901

Key ocular findings

- No reported EYP-1901–related ocular SAEs
- Four ocular SAEs reported in a study eye – none deemed related to EYP-1901
- No reported EYP-1901–related systemic SAEs
- >97% of AEs reported were mild or moderate and generally expected with IVT injection
- No cases of:
  - Insert migration into the anterior chamber
  - Retinal occlusive vasculitis
- No discontinuations were related to EYP-1901 treatment

AE, adverse event; IVT, intravitreal; SAE, serious adverse event.

Ocular AEs Reported in ≥5% of Study Eyes

n (%)	Aflibercept 2 mg q8W (n = 54)	EYP-1901 2 mg (n = 53)	EYP-1901 3 mg (n = 53)
Study eyes with AEs	20 (37.0)	30 (56.6)	29 (54.7)
Worsening wAMD	2 (3.7)	7 (13.2)	6 (11.3)
Conjunctival hemorrhage	2 (3.7)	6 (11.3)	3 (5.7)
Vitreous floaters	0 (0)	3 (5.7)	4 (7.5)
Retinal hemorrhage	1 (1.9)	1 (1.9)	5 (9.4)
Cataract	3 (5.6)	2 (3.8)	3 (5.7)
Eye pain	1 (1.9)	2 (3.8)	3 (5.7)
Vitreous detachment	2 (3.7)	3 (5.7)	2 (3.8)
Subretinal fluid	1 (1.9)	3 (5.7)	0 (0.0)

Data from topline Table 11-2.
AE, adverse event; q8W, every 8 hours; IOI, intraocular inflammation; wAMD, wet age-related macular degeneration.

Summary: EYP-1901 Demonstrated Non-Inferiority to SoC With Stable BCVA, a Favorable Safety Profile, and Durability Up to 6 Months in Eyes With wAMD

DAVIO 2

- Prospective, randomized, aflibercept-controlled phase 2 trial evaluating a single injection of EYP-1901

Primary endpoint

- BCVA: Statistically non-inferior change vs aflibercept; stable over 6 months

Secondary endpoints

- Strong anatomical control: **<10 µm** OCT difference vs SoC at 6 months
- **≥64%** of eyes were supplemental injection–free up to 6 months
- **≥85%** mean reduction in treatment burden vs prior 6 months

Favorable safety profile

- Most ocular AEs were expected with IVT injection; no EYP-1901–related ocular SAEs

Subgroup assessments of EYP-1901

- Multiple subgroups showed treatment durability across a variety of patients with wAMD

Phase 2 DAVIO 2 12m readout H2 2024; DME first patient enrolled Jan 2024;
Phase 2 NPDR topline mid-2024; Global Phase 3 wAMD planned initiation H2 2024

AE, adverse event; BCVA, best corrected visual acuity; DME, diabetic macular edema; IVT, intravitreal; NPDR, nonproliferative diabetic retinopathy; OCT, optical coherence tomography; SAE, serious adverse event; SoC, standard of care; wAMD, wet age-related macular degeneration.