4DMT

Intravitreal 4D-150

SPECTRA

DME Clinical Trial: Part 1
Interim 32-week Results

January 10, 2025

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SPECTRA

Positive Interim Data & FDA Feedback Supports Advancement of 4D-150 to Phase 3 in DME

Interim data support potential for maintenance of vision and anatomy improvements with substantially fewer injections than standard of care

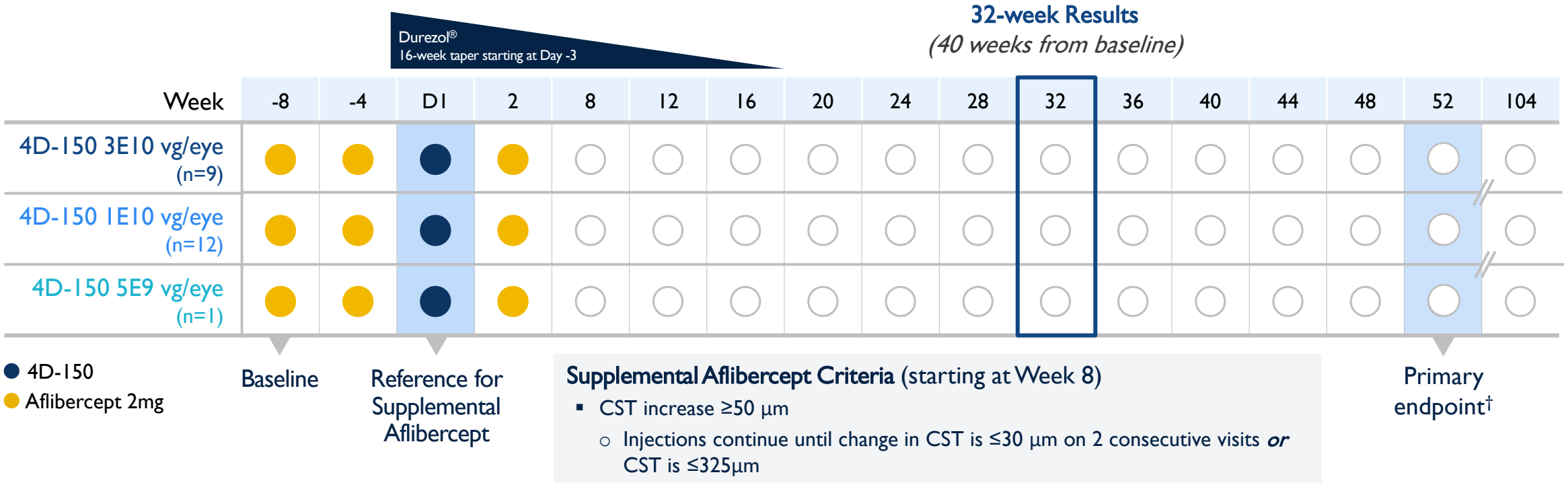
Additional details at Corporate Webcast February 10, 2025

- 4D-150 continues to be **well tolerated**:
  - **No intraocular inflammation** observed at any timepoint or dose level
  - All patients completed the 16-week topical steroid taper on schedule and remained completely off steroids
  - No hypotony, endophthalmitis, vasculitis, choroidal effusions or retinal artery occlusions
- 4D-150 (3E10 vg/eye, n=9) 32-week efficacy results:
  - Sustained gain in BCVA: **+8.4 letters**
  - Sustained reduction of CST: **–194 µm**
  - **86% reduction** in injection burden vs. projected on-label aflibercept 2mg Q8W
  - **61% reduction** in injection burden vs. 1E10 vg/eye, **dose response observed**
- FDA alignment:
  - **Single Phase 3 clinical trial** acceptable for BLA submission in DME, based on review of interim data from SPECTRA and PRISM and planned global Phase 3 program for wet AMD
  - Company may proceed to Phase 3 per FDA feedback, SPECTRA Part 2 no longer needed
- Next steps:
  - 3E10 vg/eye selected as Phase 3 dose
  - Detailed results to be presented in corporate webcast on February 10, 2025
  - **SPECTRA 52-week interim data update**: Mid-2025 at scientific conference

Data cutoff date, December 13, 2024. DME, diabetic macular edema; BCVA, best corrected visual acuity; CST, central subfield thickness.

Part 1: Designed to Enroll Patients with High CST and Employed Stringent Supplemental Criteria, with Focus on Safety & Dose Selection

Key Objectives	Evaluate **safety & tolerability** Identify dose level for further evaluation
Key Eligibility Criteria	Diagnosis within 2 years, CST ≥350 µm (includes treatment naïve) Confirmed anti-VEGF response (CST decrease ≥40 µm at Week –1 versus Week –8)*



Supplemental Aflibercept Criteria (starting at Week 8)

- CST increase ≥50 µm
  - Injections continue until change in CST is ≤30 µm on 2 consecutive visits ***or*** CST is ≤325µm

*Assessed by SD-OCT and confirmed by independent reading center.
†Safety and tolerability (frequency and severity of treatment emergent adverse events). CST, central subfield thickness: defined as thickness of 1mm area from ILM to BM.

SPECTRA Disease Activity Criteria for Supplemental Treatment Are Stringent Compared to Other Trials and Did Not Require Vision Decrease

Product	Trial	Disease Activity Criteria for Supplemental Treatment or Shortened Dose Interval
EYLEA® (aflibercept) Injection For Intravitreal Injection	VIVID/VISTA[1]	≥10 letter loss on 2 consecutive visits or ≥15 letter loss at any visit from the best previous measurement *AND* BCVA worse than baseline*
EYLEA® HD (aflibercept) Injection 8 mg	PHOTON[2]	>10 letter loss in BCVA from Week 12 due to persistent or worsening DME *AND* >50 µm increase in CRT from Week 12
VABYSMO™ faricimab-svoa injection 6 mg	YOSEMITE/RHINE[3]	≥5 letter loss in BCVA *AND* ≥10% increase in CST from reference CST ≥20% increase in CST from reference CST independent of any BCVA change
DURAVYU	VERONA[4]	≥10 letter loss in BCVA due to DME 5-9 letters loss in BCVA *AND* >75 µm of new fluid at two consecutive visits ≥100 µm increase in CST (new fluid) vs. baseline Lack of 10% reduction in CST compared to baseline†
4D-150	SPECTRA Part 1	≥50 µm increase in CST‡ (supplemental injections continue until change in CST is ≤30 µm on 2 consecutive visits or CST ≤325 µm)

*After Week 24. †After Week 12. ‡After Week 8. BCVA, best corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study.

1. Korobelnik et al. *Ophthalmology* 2014;121:2247–54. 2. Brown et al. *Lancet* 2024;403:1153–63. 3. Wykoff et al. *Lancet* 2022;399:741–55. 4. EyePoint Corporate Presentation, October 2024.

Study Population: Baseline CST, BCVA, and Prior Treatment Status Balanced Across Dose Arms

	3E10 vg/eye (n=9)	1E10 vg/eye (n=12)	5E9 vg/eye (n=1)	Total (N=22)
Central subfield thickness, µm				
Mean	**513**	**488**	**515**	**499**
(range)	(382–671)	(356–669)		(356–671)
BCVA, ETDRS letters				
Mean	63	62	68	63
(range)	(41–79)	(32–84)		(32–84)
Treatment Experienced, n (%)	7 (78)	9 (75)	0	16 (73)

- 1 patient in 1E10 vg/eye arm terminated the study due to death unrelated to 4D-150 prior to completion of a post-baseline assessment

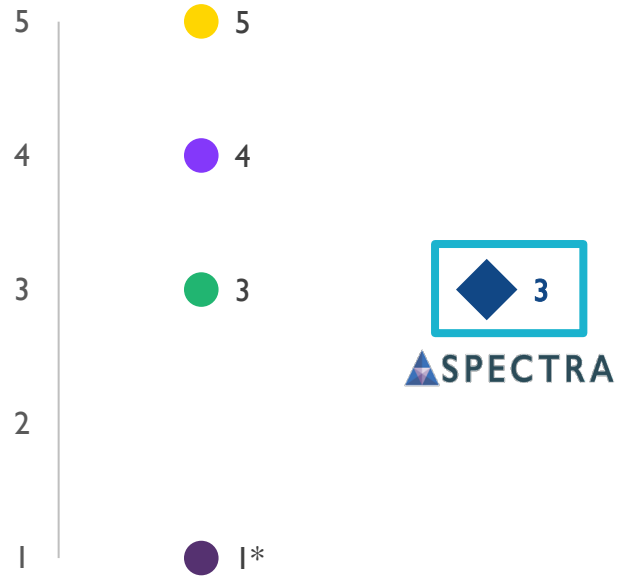
BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study.

SPECTRA Designed With Fewer Loading Doses and Enrolled Population With High CST and Majority Treatment Experienced

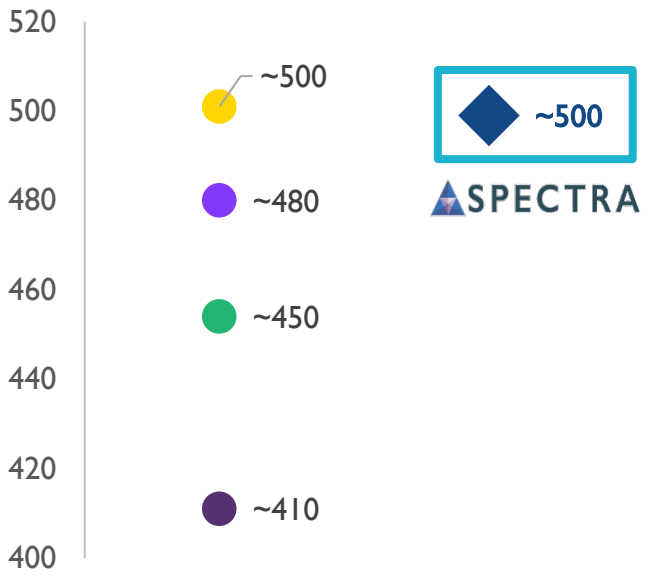
Selected Studies:

Phase 3			Phase 1/2	
EYLEA (aflibercept) Injection For Intravitreal Injection	EYLEA HD (aflibercept) Injection 8 mg	VABYSMO faricimab-svoa injection 6 mg	DURAVYU	4D-150
VIVID/VISTA[1]	PHOTON[2]	YOSEMITE/RHINE[3]	VERONA[4]	SPECTRA

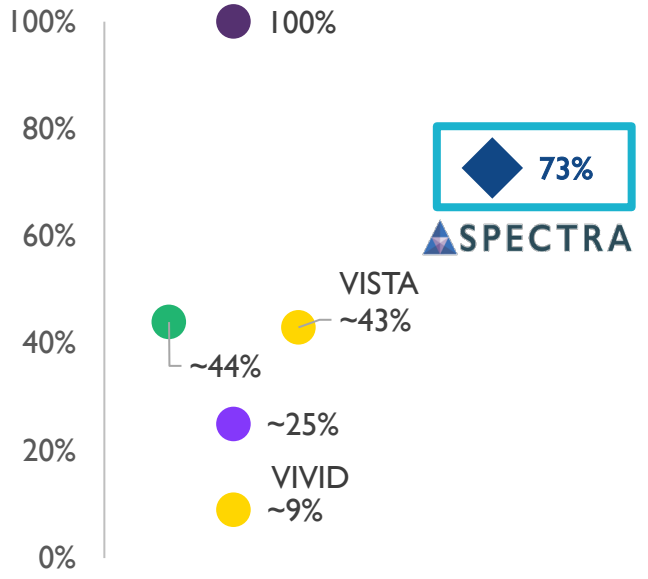
Anti-VEGF Loading Doses



Mean CST at Baseline (µm)



Treatment Experienced at Baseline (%)



CST, central subfield thickness; BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study.

Sources: 1. Korobelnik et al. *Ophthalmology* 2014;121:2247–54. 2. Brown et al. *Lancet* 2024;403:1153–63. 3. Wykoff et al. *Lancet* 2022;399:741–55. 4. EyePoint Corporate Presentation, October 2024.

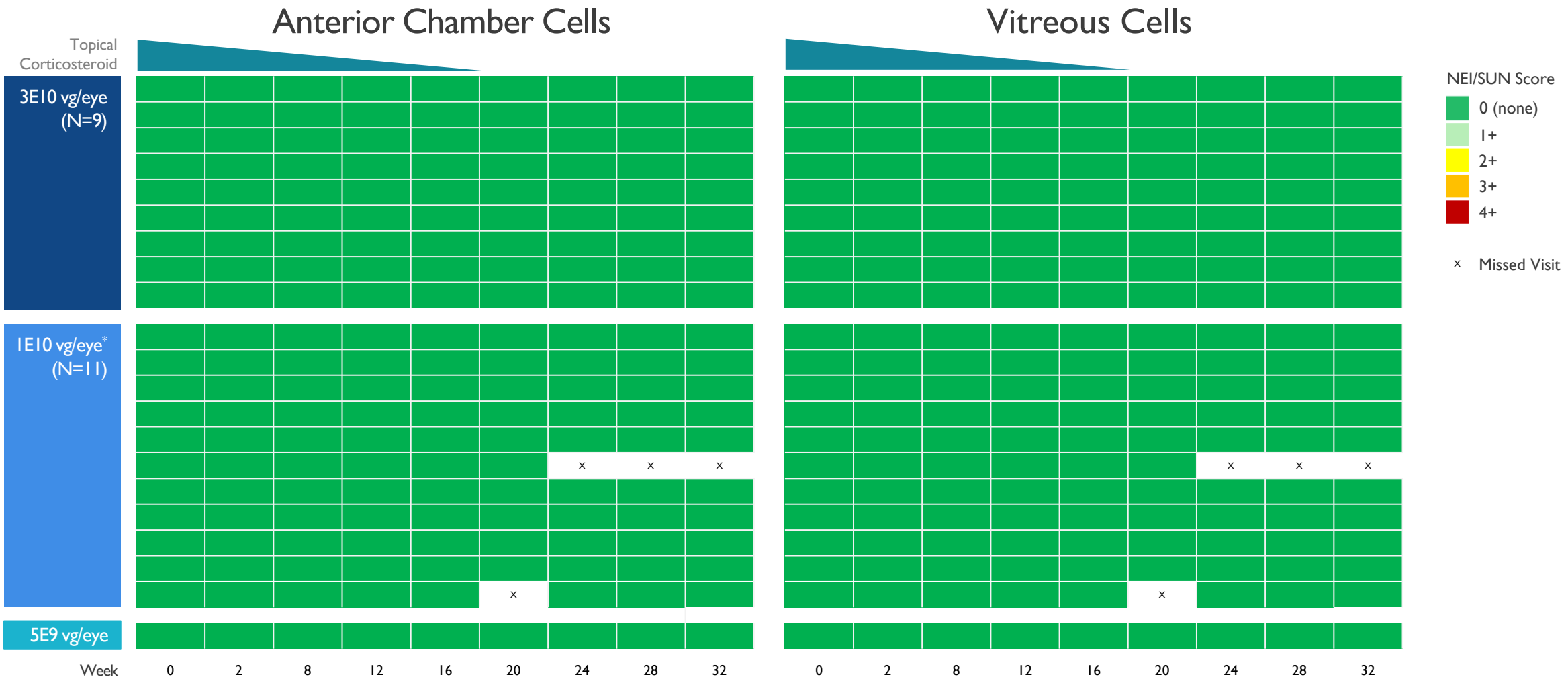
*Given concurrently with DURAVYU.

4D-150 Continues to be Well Tolerated

- 4D-150 continues to be well tolerated with no intraocular inflammation at any timepoint at any dose level
  - All patients completed the 16-week topical steroid taper on schedule and remained completely off steroids
- No hypotony, endophthalmitis, vasculitis, choroidal effusions or retinal artery occlusions

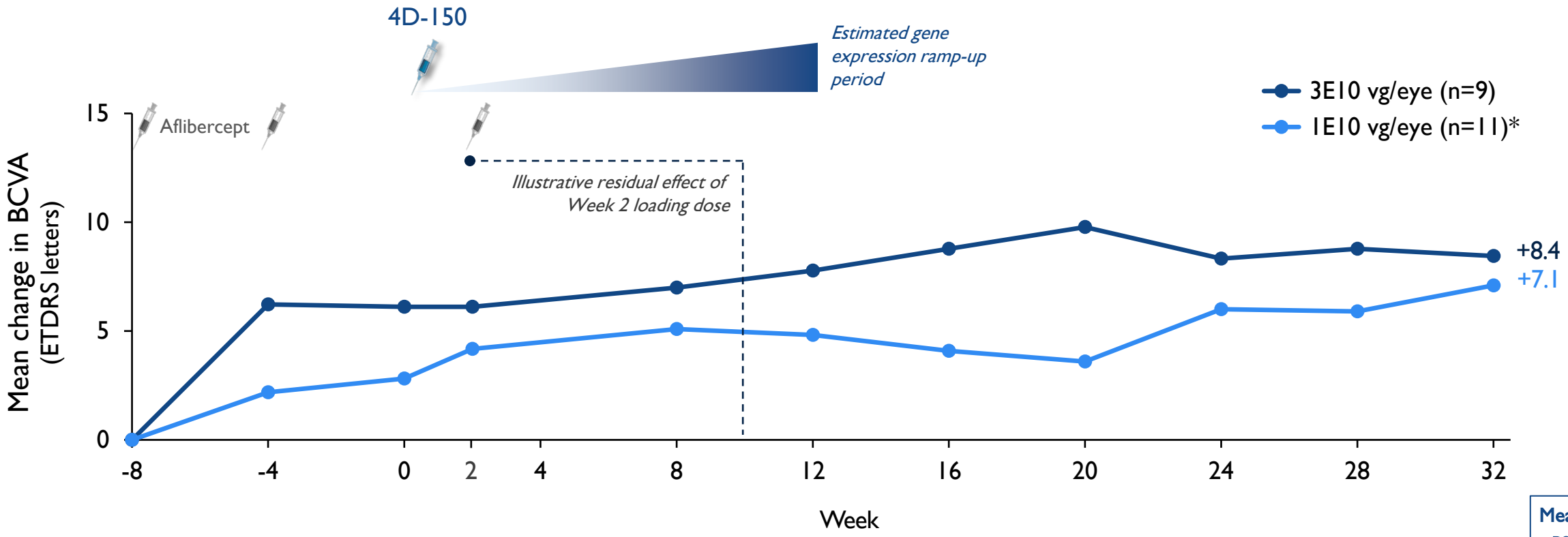
Data cutoff date, December 13, 2024.

No Intraocular Inflammation and All Patients Completed Prophylactic Topical Steroids on Schedule and Remained Completely Off Steroids



Data cutoff date, December 13, 2024. *Excludes patient with early termination due to death (unrelated to 4D-150) prior to completion of a post-baseline assessment. NEI, National Eye Institute; SUN, Standardization of Uveitis Nomenclature; TR, trace (not observed); PC, pigmented cells (not observed); X, missed visit.

4D-150 3E10 vg/eye: Sustained Improvement in Visual Acuity Through 32 Weeks (+8.4 Letters vs Baseline)

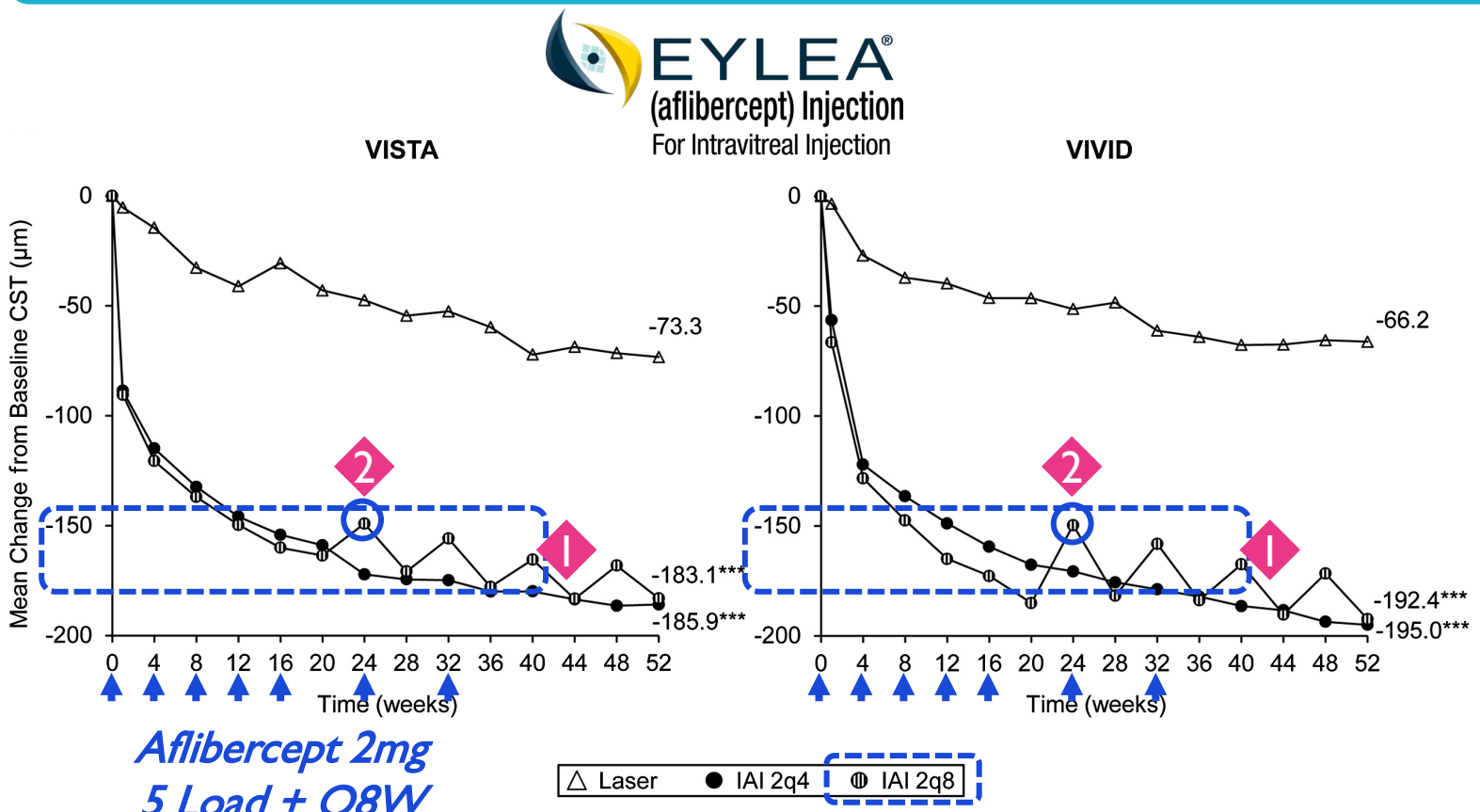


Supplemental Injections**, n									Mean per patient
	3E10 vg/eye (n=9)	0	0	2	0	2	1	0	0.6
	1E10 vg/eye (n=11)	1	2	2	4	2	1	3	1.4

Data cutoff date, December 13, 2024.
*Excludes patient with early termination due to death (unrelated to 4D-150) prior to completion of a post-baseline assessment. **No patient in 3E10 or 1E10 vg/eye arm would have received a supplemental injection based on disease activity measurement at time of first supplemental injection based on disease activity worsening criteria in VIVID/VISTA or PHOTON.
BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study.

On-label Eylea Improves CST ~165 µm But Requires High Treatment Burden

Eylea Phase 3 Studies in DME[1] Compared 5 Loading Doses + Q4W or Q8W vs. Laser

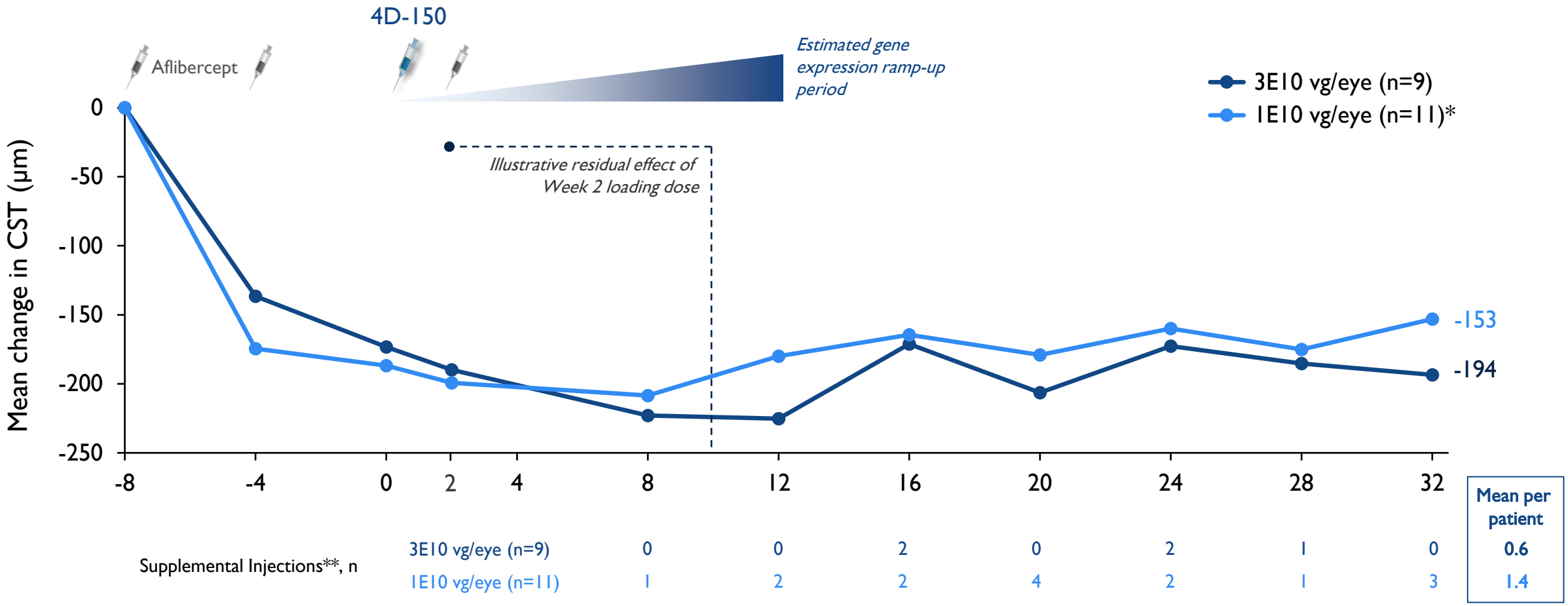


1 Eylea consistently achieved CST improvements of ~165 µm in DME patients

2 Eylea saw CST rebounds ~8 weeks after last dose of the loading dose regimen, rebounds continue in Q8W arms

1. Korobelnik et al. *Ophthalmology* 2014;121:2247–54.

4D-150 3E10 vg/eye: Sustained Improvement in Anatomic Control Through 32 Weeks (–194 µm vs Baseline)



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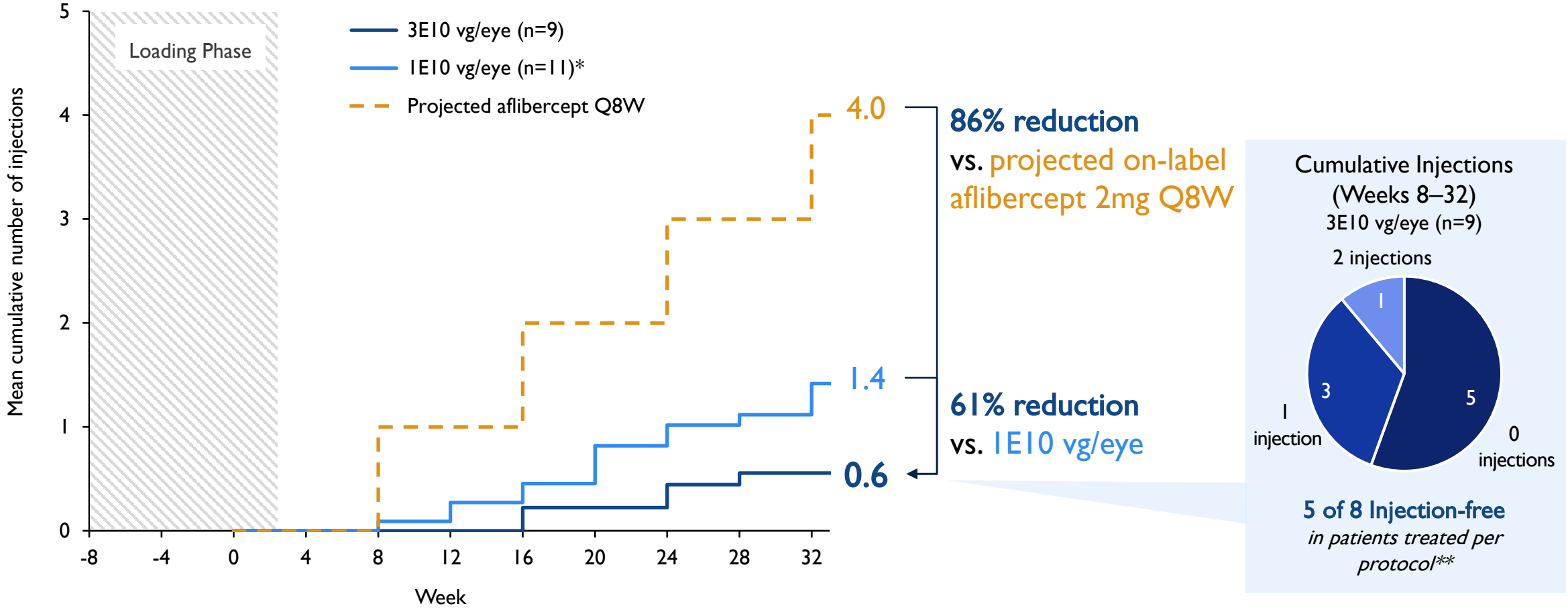
CST, central subfield thickness.

3E10 vg/eye Post-loading Phase: 86% Reduction in Treatment Burden vs. Projected On-label Aflibercept 2mg Q8W; Dose Response in Favor of 3E10



Data cutoff date, December 13, 2024.

*Excludes patient with early termination due to death (unrelated to 4D-150) prior to completion of a post-baseline assessment. **Excludes n=1 patient who did not receive the Week 2 aflibercept. This patient received 1 supplemental injection through 32 weeks. Mean cumulative function from Cox proportional hazard regression model for recurrent events was used to estimate the mean cumulative number of supplemental aflibercept injections.

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THANK YOU

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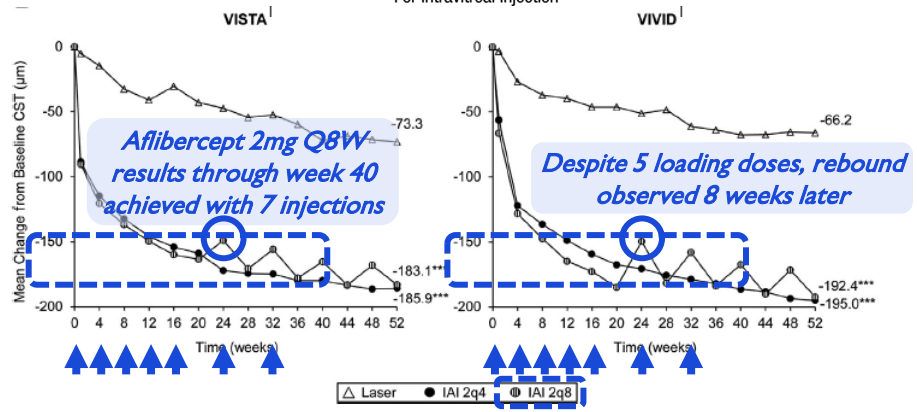
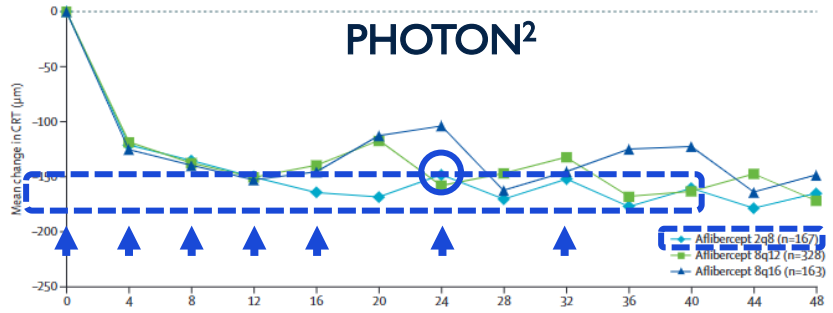
On-label Aflibercept Improves CST by ~150-180 µm with 7 Total Injections Through 40 Weeks; Rebound Observed at Week 24 Despite 5 Loading Doses

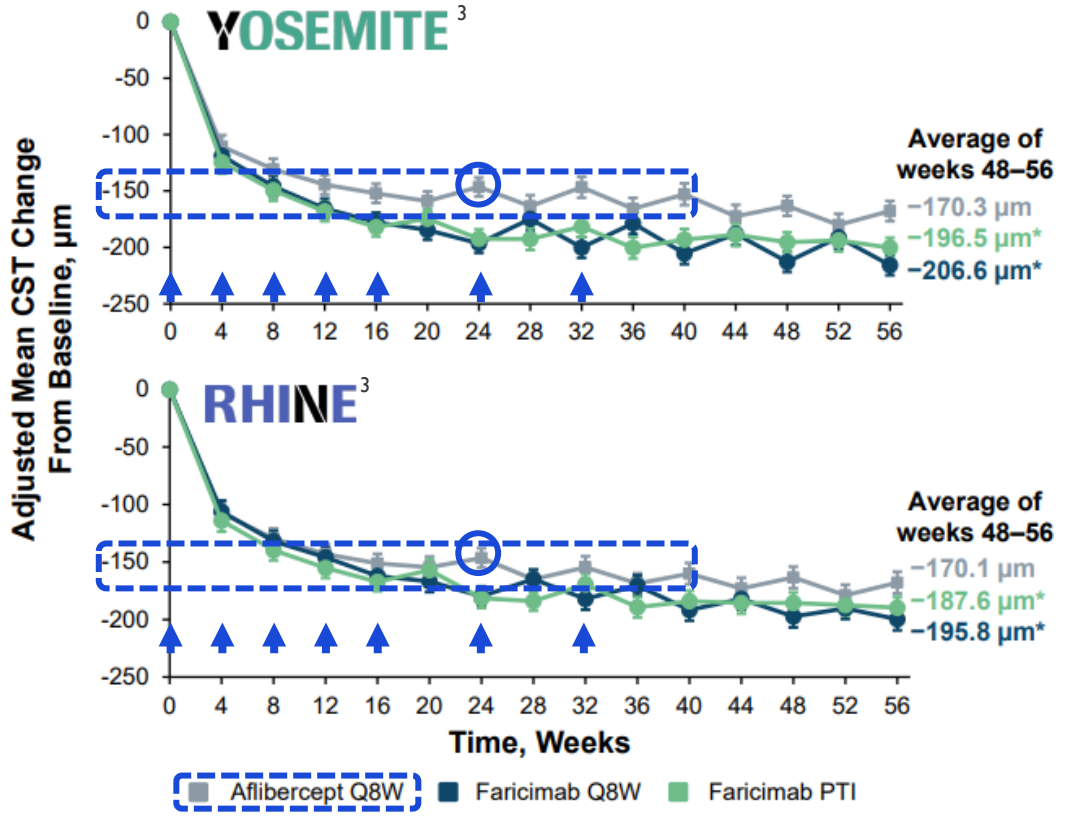
EYLEA® (aflibercept) Injection
For Intravitreal Injection



EYLEA HD™ (aflibercept) Injection
8 mg/0.07 mL | For Intravitreal Use



VABYSMO™ faricimab-svoa injection 6 mg



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