

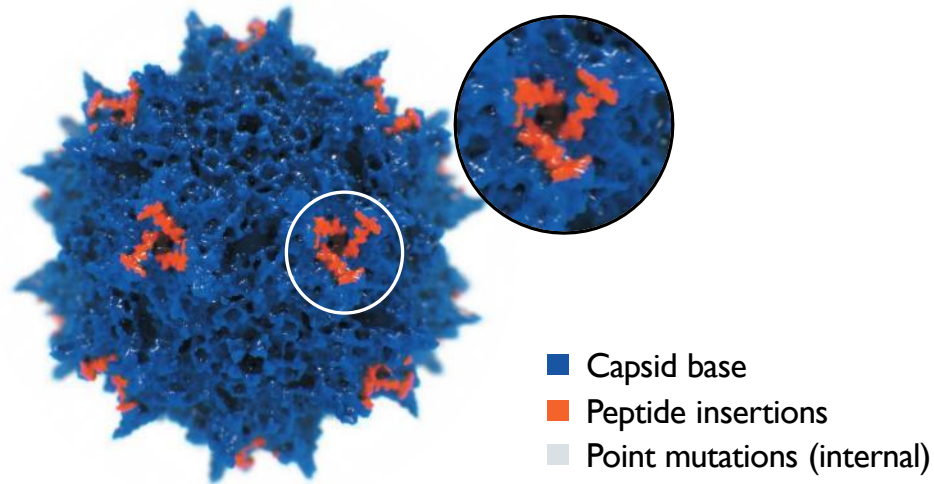


Interim 60-week Results from the
SPECTRA Clinical Trial Evaluating
Intravitreal 4D-150 in Diabetic Macular Edema

July 31, 2025

4D-I50: Proprietary Capsid Carrying a Dual-Transgene Payload

R100 AAV Capsid



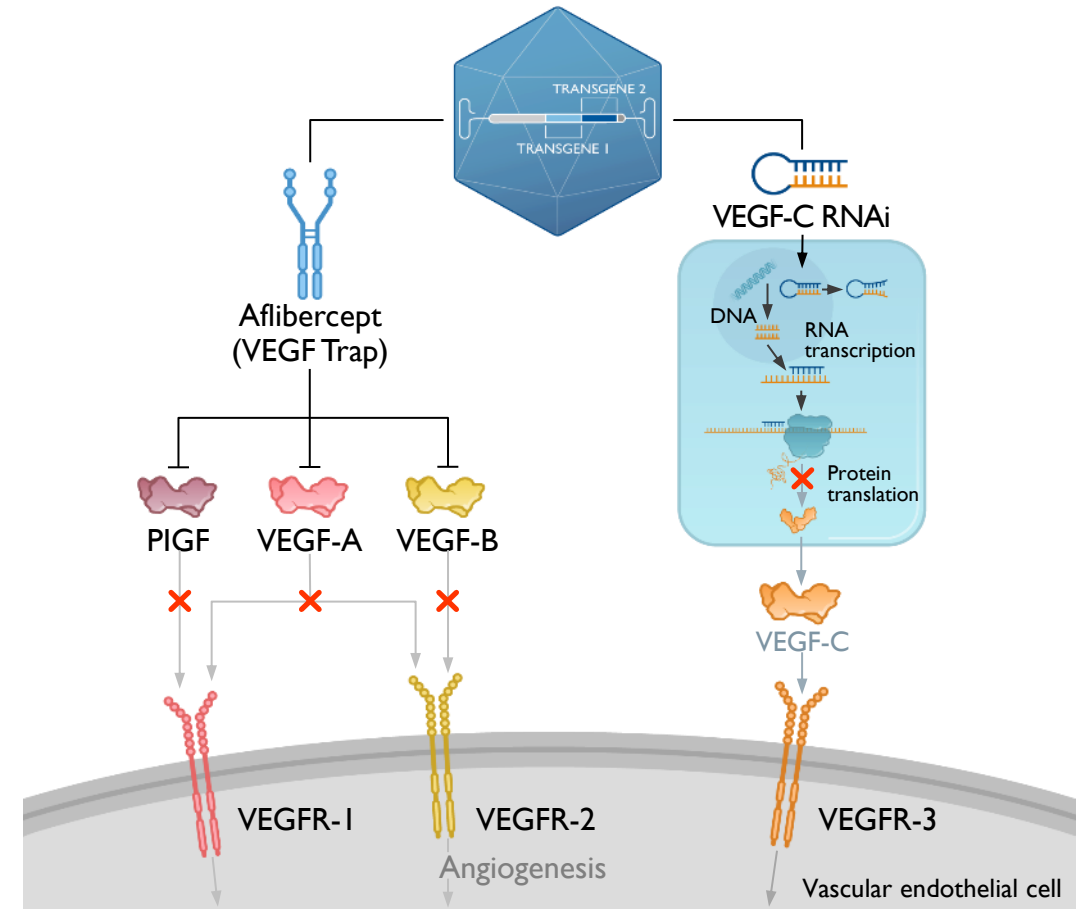
R100 capsid designed to/for:

Selective tropism for retinal cells

Efficient, low dose gene delivery with no significant inflammation

Administration via routine intravitreal injection

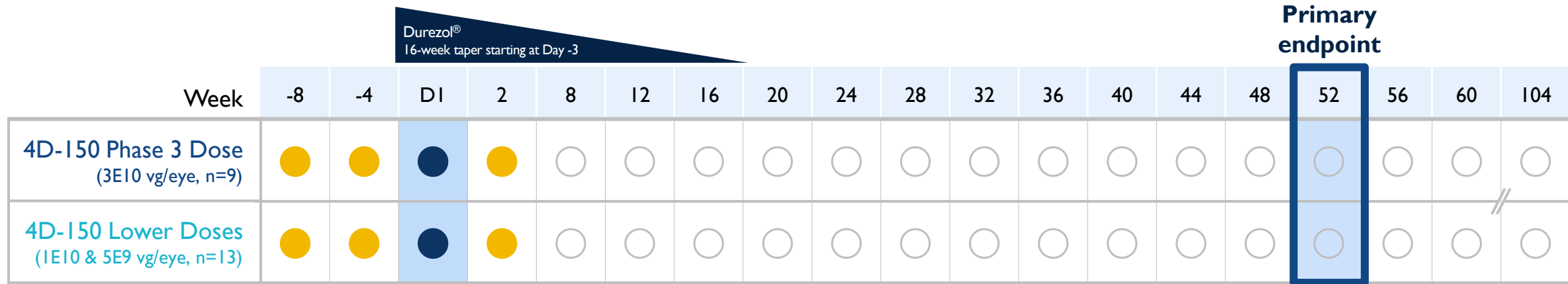
4D-I50



SPECTRA Enrolled DME Patients with Focus on Safety & Dose Selection

Key Eligibility Criteria

- Diagnosis within 2 years, CST $\geq 350 \mu\text{m}$ (includes treatment naïve)
- Confirmed anti-VEGF response (CST decrease $\geq 40 \mu\text{m}$ at Week -1 versus Week -8)
 - Assessed by SD-OCT and confirmed by independent reading center.



● 4D-I50
● Afibercept 2mg

Baseline
Reference for Supplemental Afibercept

Supplemental Afibercept Criteria (starting at Week 8)

- CST increase $\geq 50 \mu\text{m}$
- Injections continue** until change in CST is $\leq 30 \mu\text{m}$ on 2 consecutive visits **or** CST is $\leq 325 \mu\text{m}$

All patients reached 60 weeks as of the cutoff date (May 2, 2025)

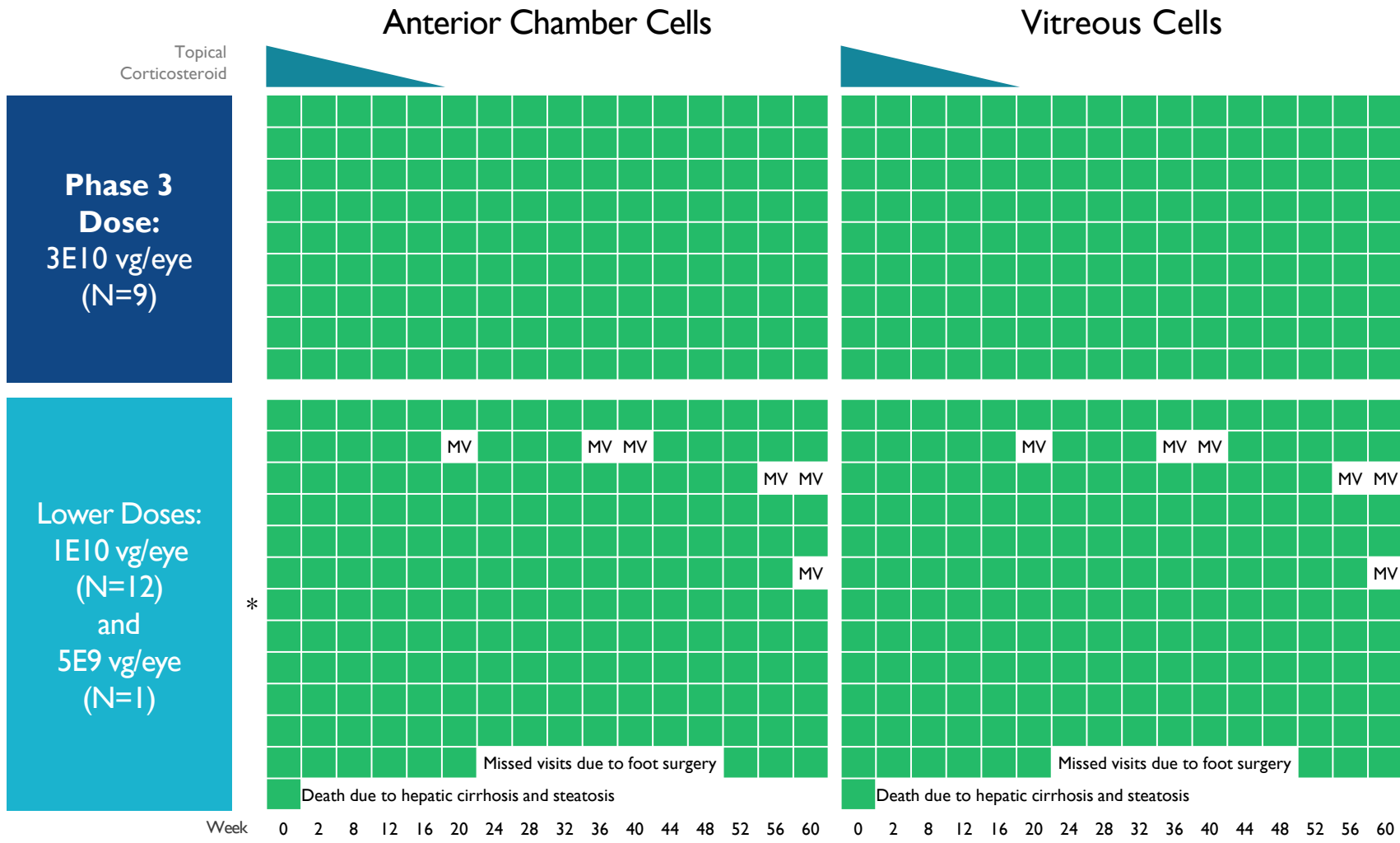
CST, central subfield thickness: defined as thickness of 1mm area from ILM to BM; DME: Diabetic Macular Edema; VEGF: Vascular Endothelial Growth Factor Receptor; vg/eye: viral genomes/eye.

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

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

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

4D-I50 Continues to be Well Tolerated Through 60 Weeks with No Intraocular Inflammation at any Timepoint at any Dose Level



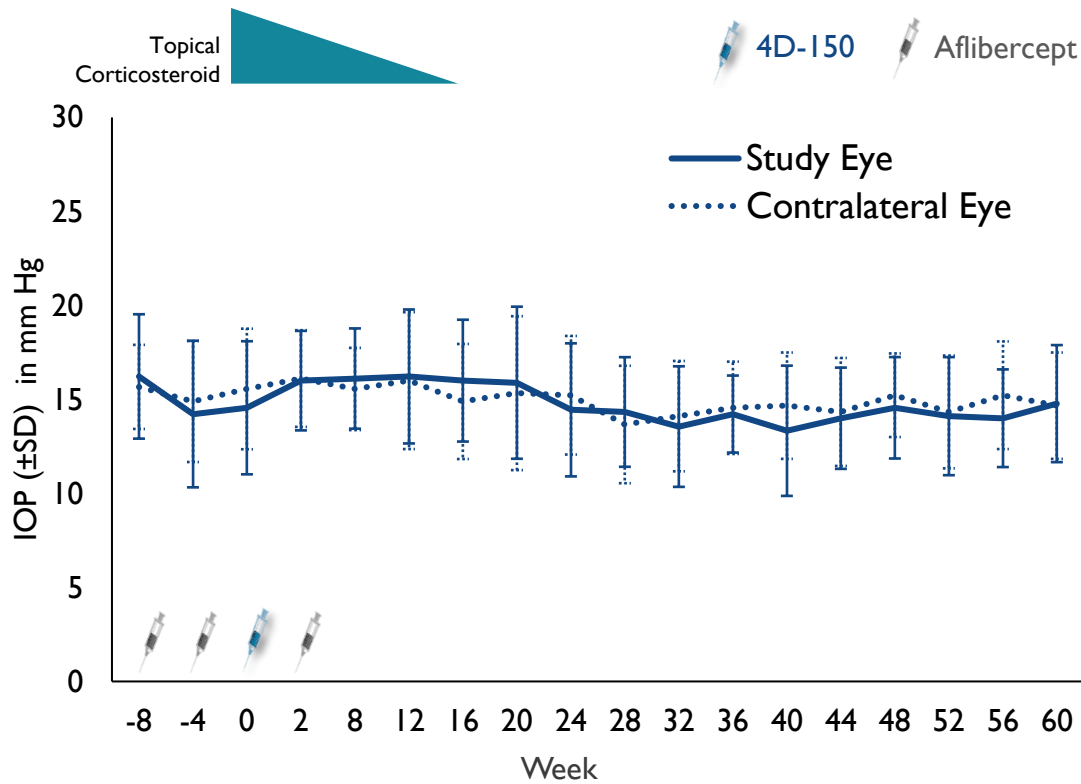
- All patients completed the 16-week topical steroid taper on schedule
- No subjects required modification to the steroid regimen and all patients are currently off steroids
- No hypotony, endophthalmitis, vasculitis, choroidal effusions or retinal artery occlusions

*Subject dosed with 5E9 vg/eye. NEI: National Eye Institute; SUN: Standardization of Uveitis Nomenclature; IOI: intraocular inflammation
Data cutoff as of May 2, 2025

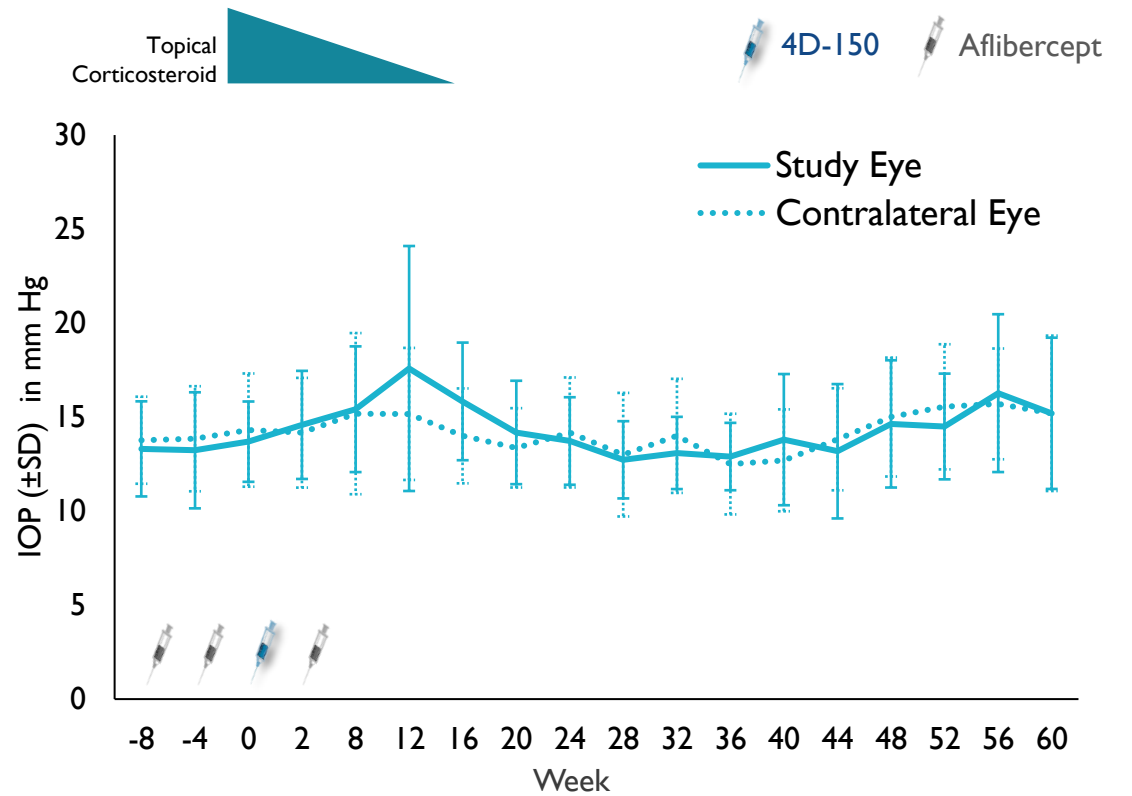
Mean IOP Within Normal Limits

No IOP <6 mmHg at any visit

Phase 3 Dose: 3E10 vg/eye (N=9)

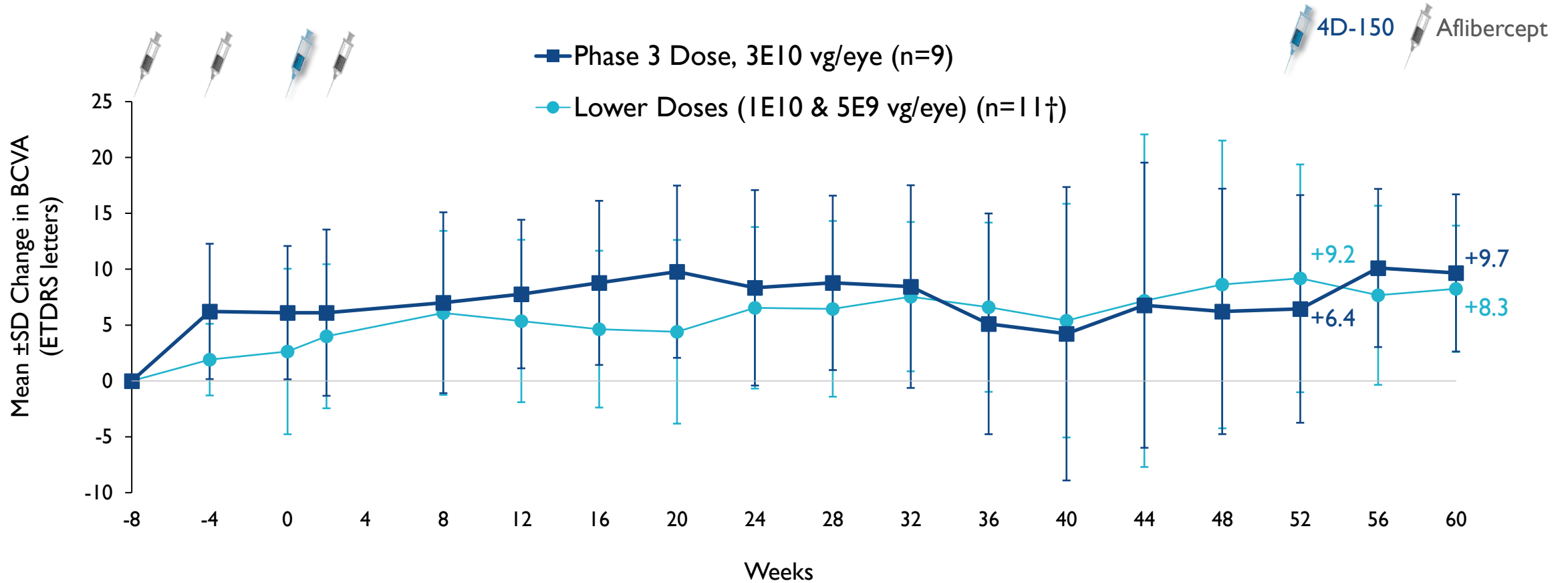


Lower Doses: 1E10 vg/eye (N=12) and 5E9 vg/eye (N=1)



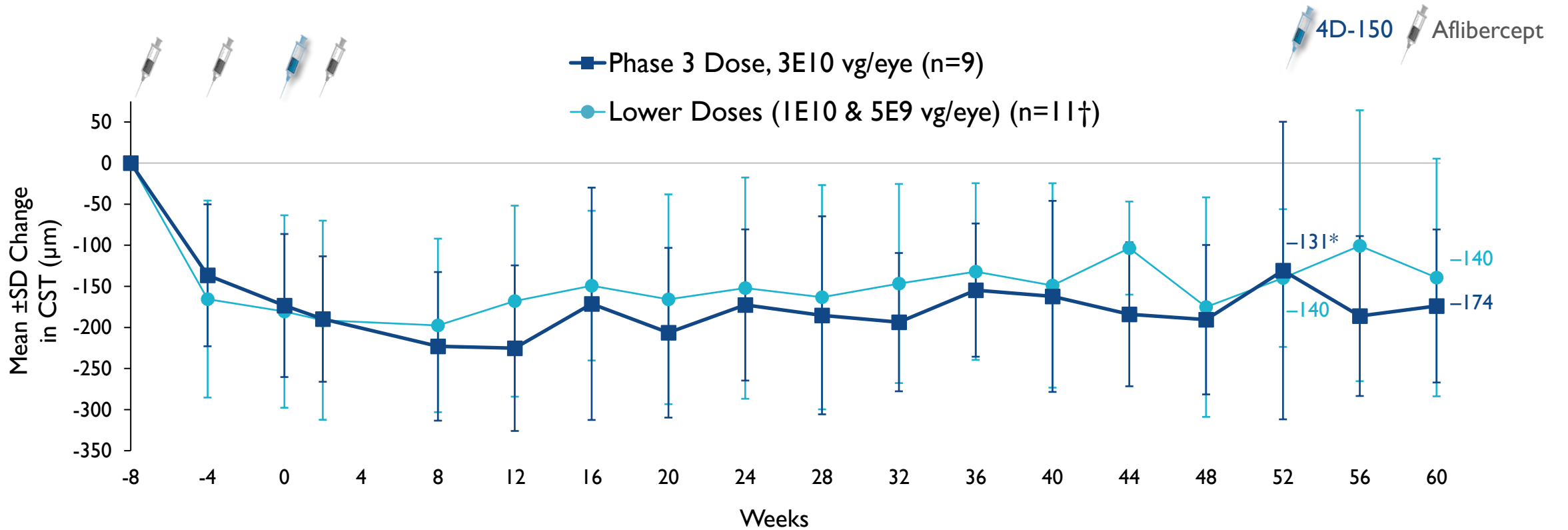
IOP: Intraocular Pressure
Data cutoff as of May 2, 2025.

Sustained Gains in Visual Acuity Through Week 60



†2 subjects missed >50% of study visits and are not considered evaluable for injection burden or other efficacy parameters.
 BCVA: Best Corrected Visual Acuity; SD: Standard Deviation.
 Data cutoff as of May 2, 2025

Sustained Improvement in Anatomic Control Through Week 60



*One subject received supplemental aflibercept at W52 due to post-cataract surgery edema.
 †2 subjects missed >50% of study visits and are not considered evaluable for evaluation of injection burden or other efficacy parameters.
 CST: Central Subfield Thickness; SD: Standard Deviation.
 Data cutoff as of May 2, 2025

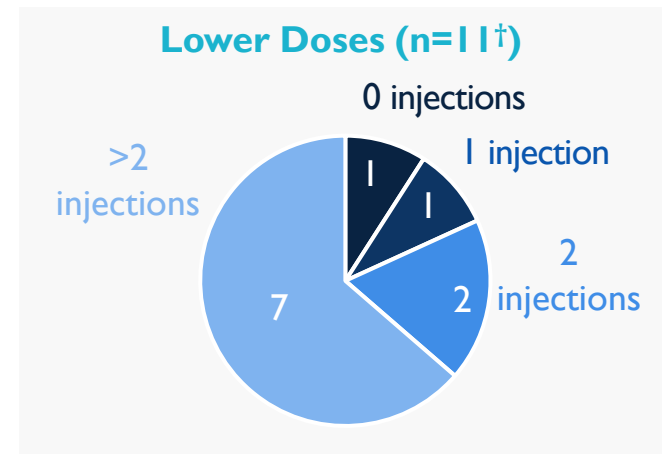
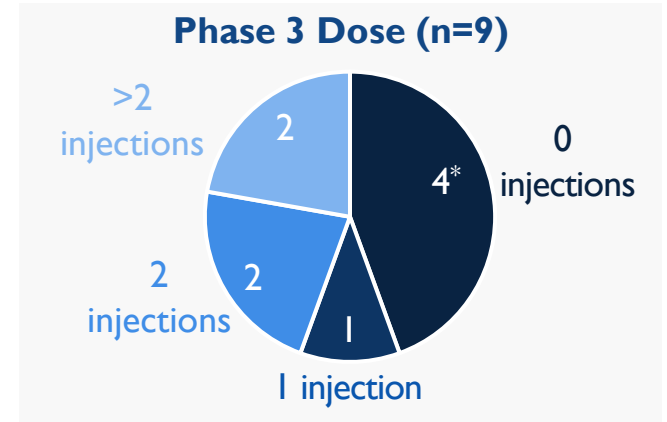
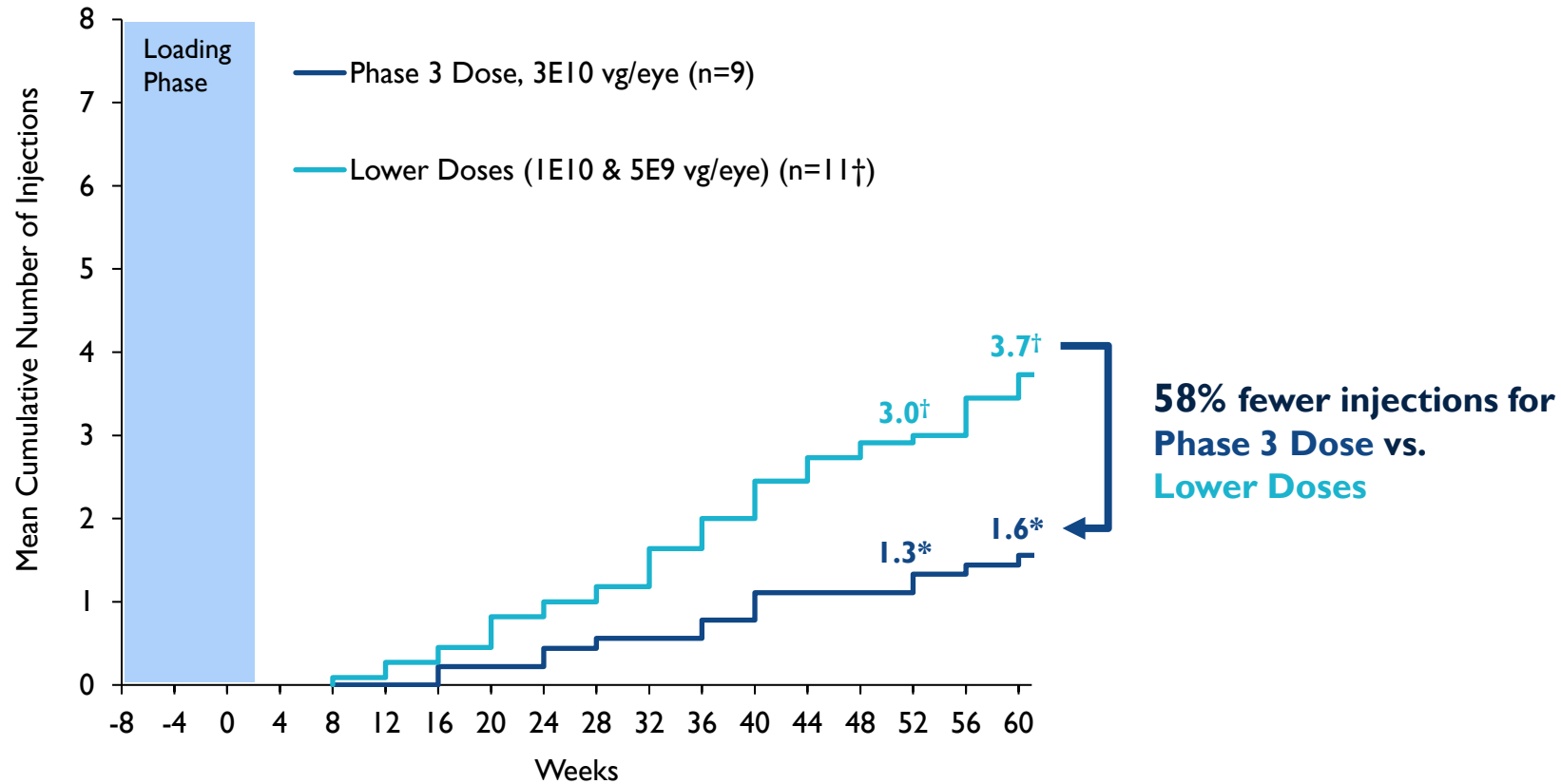
SPECTRA Disease Activity Criteria for Supplemental Treatment Are Stringent Compared to Other Trials and Did Not Require Vision Decrease

Product	Trial	Disease Activity Criteria for Supplemental Treatment or Shortened Dose Interval
 EYLEA [®] (afibercept) 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 (afibercept) 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 I	≥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.

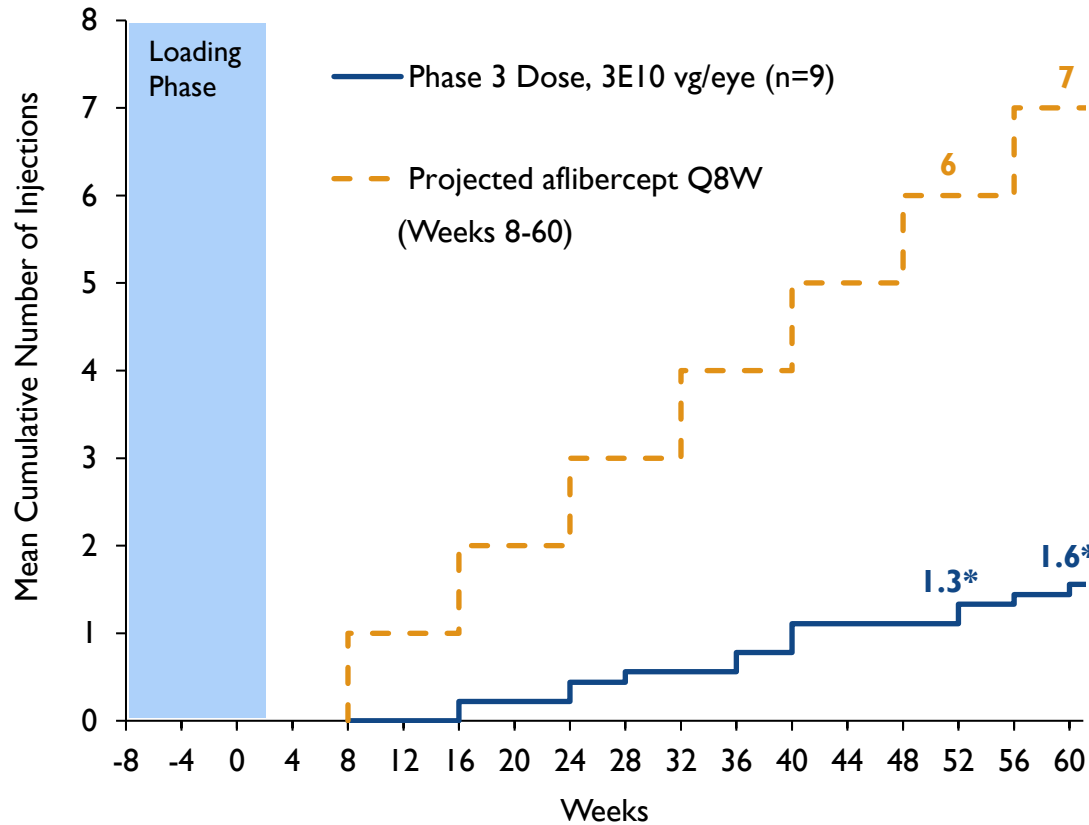
1. Korobelnik et al. *Ophthalmology* 2014;121:2247–54. 2. Brown et al. *Lancet* 2024;403:1153–63. 3. Wykoff et al. *Lancet* 2022;399:741–55. 4. EyePoint Corporate Presentation, October 2024.

4D-I50 Phase 3 Dose Demonstrated Strong Treatment Burden Reduction and Clear Dose Response vs. Lower Doses Through Week 60

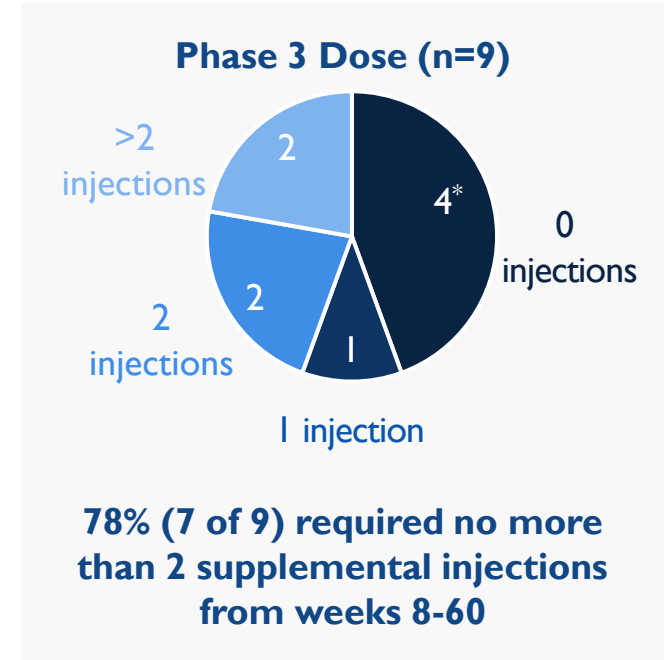


*One subject received supplemental aflibercept at W52 due to post-cataract surgery edema. The injection was not accounted in the subsequent supplemental aflibercept analyses.
 †2 subjects missed >50% of study visits and are not considered evaluable for evaluation of injection burden or other efficacy parameters.
 Mean cumulative function from Cox proportional hazard regression model for recurrent events was used to estimate the mean cumulative number of supplemental aflibercept injections.
 Data cutoff as of May 2, 2025

4D-I50 Phase 3 Dose Demonstrated Strong Treatment Burden Reduction vs. Expected Phase 3 Comparator Through Week 60



78% reduction



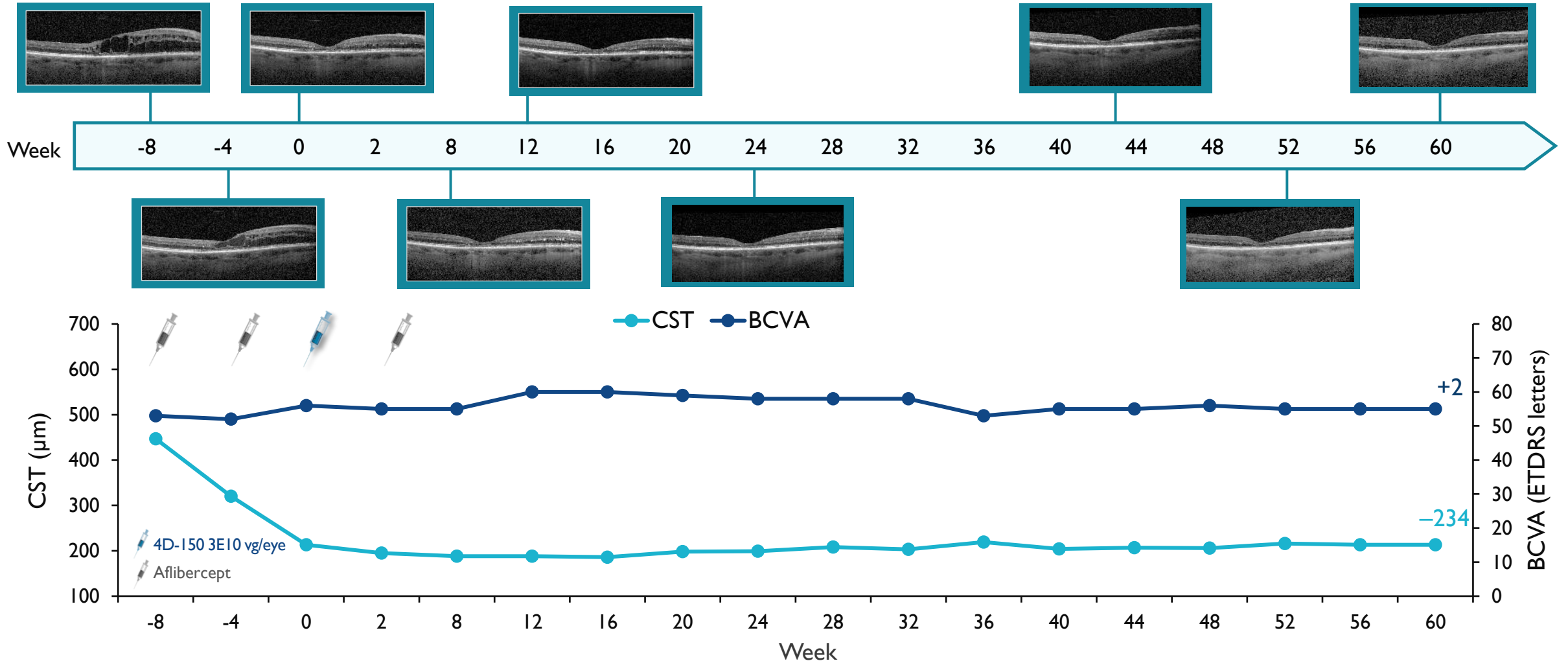
Clinically meaningful treatment burden reduction compared to expected Phase 3 comparator arm with:

- 2 fewer loading doses (VIVID/VISTA Eylea DME Phase 3's had 5)
- Stringent supplemental criteria

*One subject received supplemental aflibercept at W52 due to post-cataract surgery edema. The injection was not accounted for the subsequent supplemental aflibercept analyses. Mean cumulative function from Cox proportional hazard regression model for recurrent events was used to estimate the mean cumulative number of supplemental aflibercept injections. Data cutoff as of May 2, 2025

3E10 vg/eye Case Study: 50-year-old Male Injection-Free Participant

Time Since Diagnosis: 11 Months, One Anti-VEGF in Prior 12 Months



CST: Central Subfield Thickness; BCVA: Best Corrected Visual Acuity; ETDRS: Early Treatment Diabetic Retinopathy Study

SPECTRA Conclusions Through Week 60

Safety Data

- **No intraocular inflammation** (No SUN/NIH score >0) observed at any timepoint or dose level
- No hypotony, endophthalmitis, vasculitis, choroidal effusions or retinal artery occlusions
- All patients completed the 16-week topical steroid taper on schedule and are currently off steroids
- No serious ocular TEAEs have been reported to date
 - No TEAEs related to 4D-I50

Efficacy Data (Phase 3 Dose)

- Sustained vision gains
- Sustained anatomic control
- Supplemental injections (weeks 8-60):
 - **Clear dose response** observed for Phase 3 dose vs. lower doses
 - **78% reduction** for Phase 3 dose vs. projected on-label aflibercept 2mg Q8W

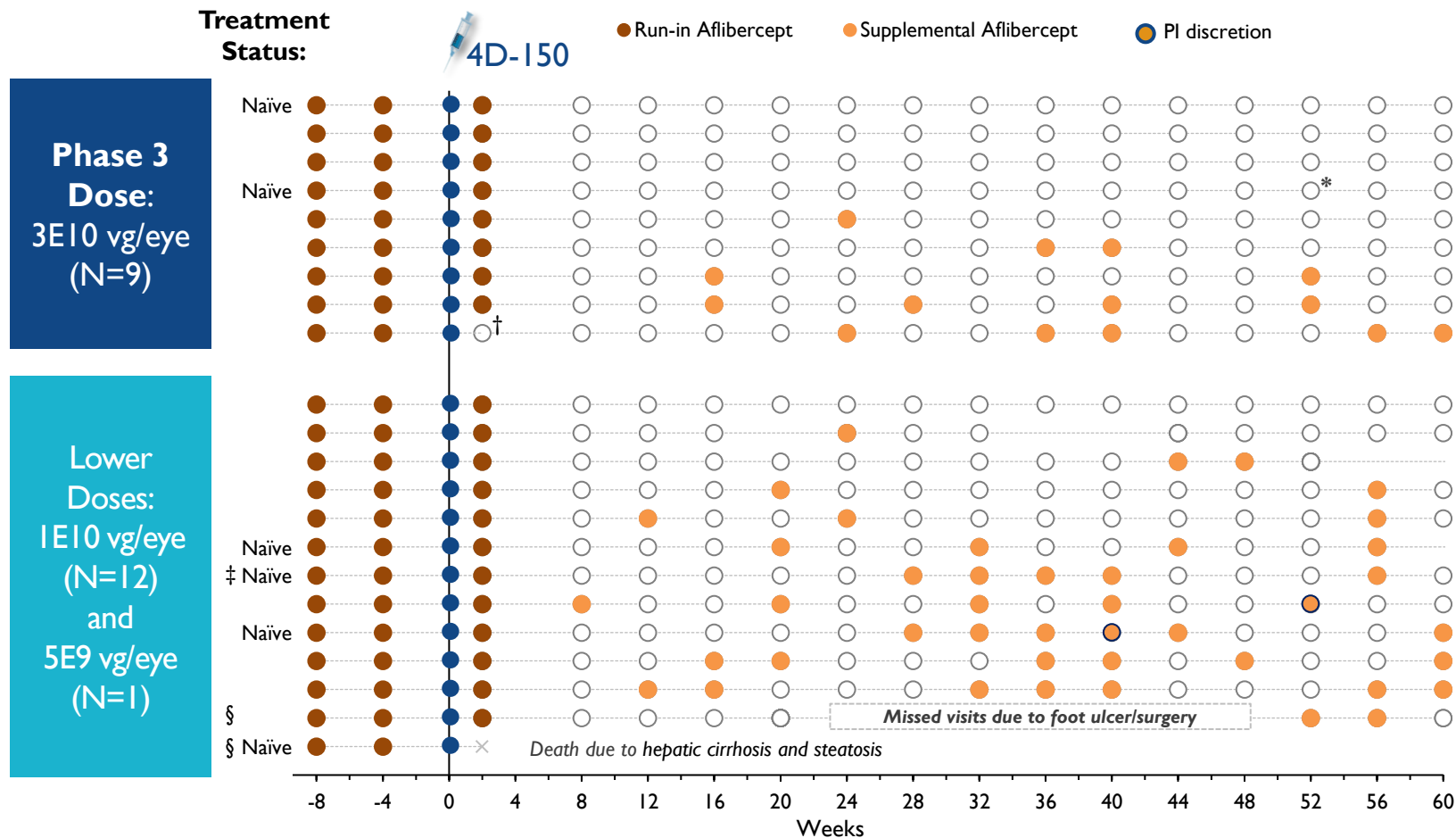
Next Steps: FDA & EMA aligned that in conjunction with 4FRONT wet AMD program, a **single Phase 3 trial** would be acceptable for BLA/MAA submission for 4D-I50 in DME

NEI, National Eye Institute; SUN, Standardization of Uveitis Nomenclature; TEAE, Treatment Emergent Adverse Event; BCVA: Best Corrected Visual Acuity; CST: Central Subfield Thickness; FDA: Food & Drug Administration; BLA: Biologics License Agreement; MAA: Marketing Authorization Application; DME: Diabetic Macular Edema.

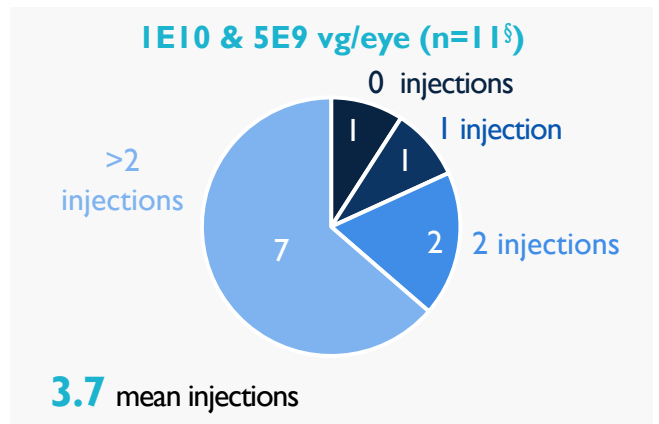
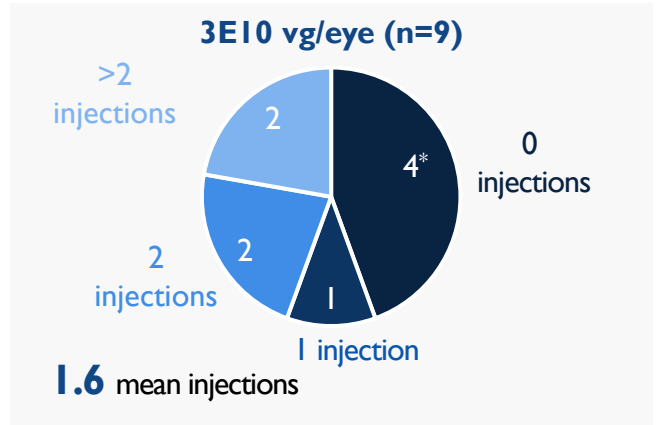


Supplementary Materials

4D-I50 Phase 3 Dose Demonstrated Robust Treatment Burden Reduction through 60 Weeks with Strong Dose Response vs. Lower Doses



Through Week 60



*One patient received supplemental aflibercept at W52 due to post-cataract edema. †Patient refused the per protocol aflibercept injection. ‡Patient dosed with 5E9 vg/eye.

§2 patient missed >50% of study visits and were not considered evaluable for injection burden or other efficacy parameters.

Protocol specified criteria for supplemental aflibercept (from Week 8): CST increase $\geq 50 \mu\text{m}$ compared to Day 1. Supplemental injections continue until change in CST decreases is $\leq 30 \mu\text{m}$ on 2 consecutive visits or CST is $\leq 325 \mu\text{m}$

Data cutoff as of May 2, 2025