Interim Results from the SPECTRA Phase 2a Clinical Trial Evaluating Intravitreal 4D-150 in Adults with Diabetic Macular Edema

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On behalf of the SPECTRA investigators

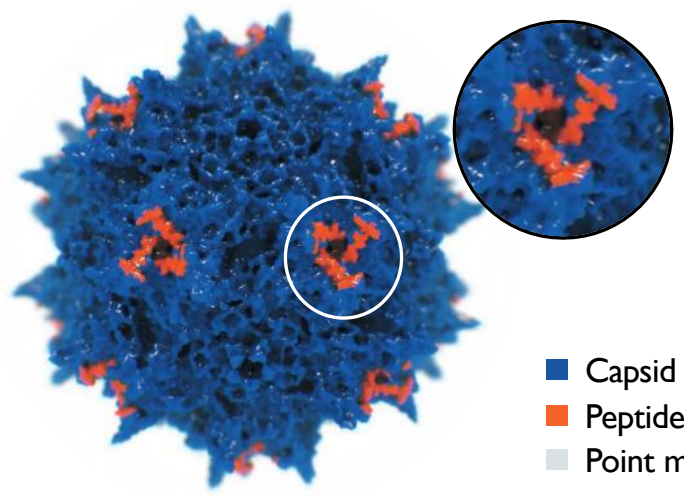
Disclosures

Research Support & Grants Alcon, Allergan/Abbvie, ANI Pharmaceuticals, Boehringer Ingelheim, Eyepoint, Genentech, Novartis, Oculis, Regeneron, Roche
Consulting & Advisory Roles Allergan/Abbvie, ANI Pharmaceuticals, Boehringer Ingelheim, Genentech, Oculis, Regeneron, Unity Biotechnology
Speaking & Honoraria Acelyrin, Alcon, Bayer, Eyepoint, Novartis, Roche
Equity & Leadership: Citrus Therapeutics, Erie Retina Research, The Centers for Advanced Surgical Exploration (CASEx)
Patents CITRUS (CTZ1); NEAR-REAL SURGICAL SPECIMEN (NRSS); STUDY COORDINATOR WORKFLOW
Additional Advisory/Speaking Relationships Acylerin, Alcon, Bayer, Dutch Ophthalmics, Eyepoint, Gyroscope, Novartis, Oculis, Opthea, Regenxbio, Roche, Samsara Vision, Unity Biotechnology

Open Payments: View record at openpaymentsdata.cms.gov/physician/631878

4D-150: Proprietary Capsid Carrying a Dual-Transgene Payload

R100 AAV Capsid



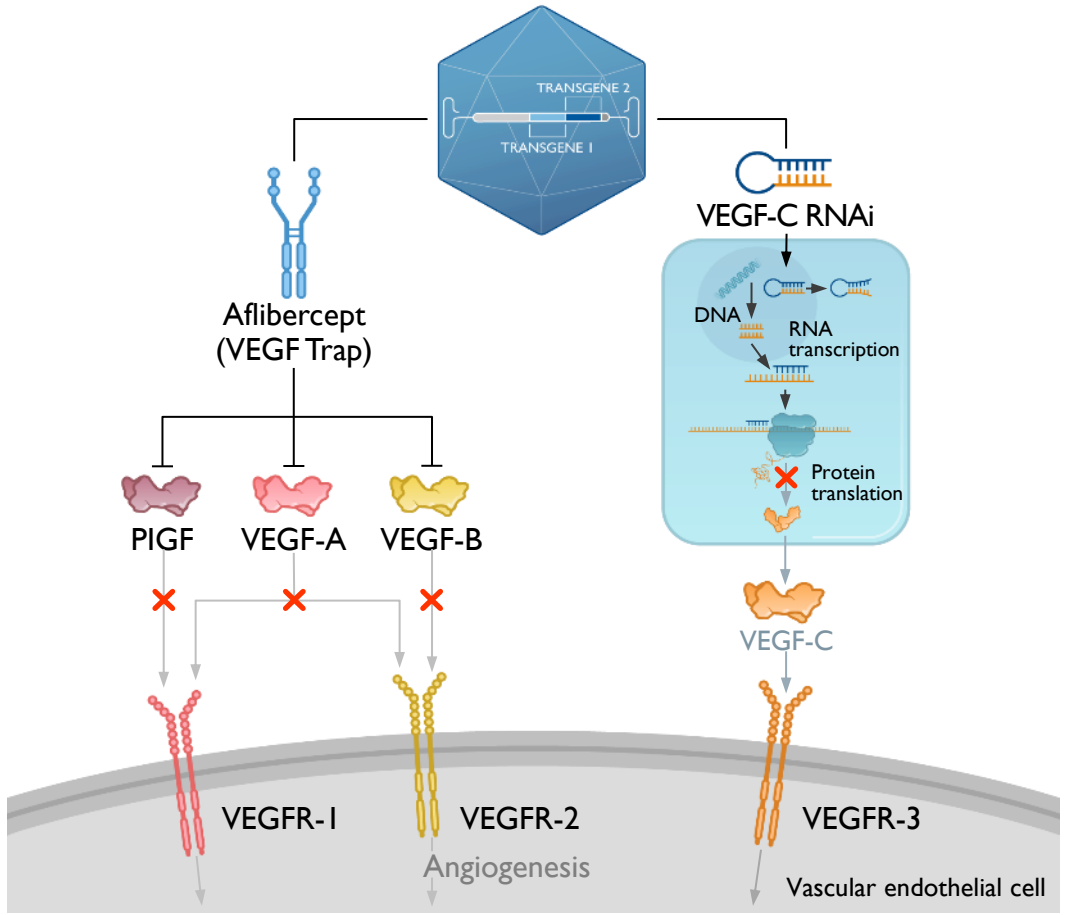
R100 capsid designed for:

Selective tropism for retinal cells

Efficient, low dose gene delivery with no significant inflammation

Administration via routine intravitreal injection

4D-150



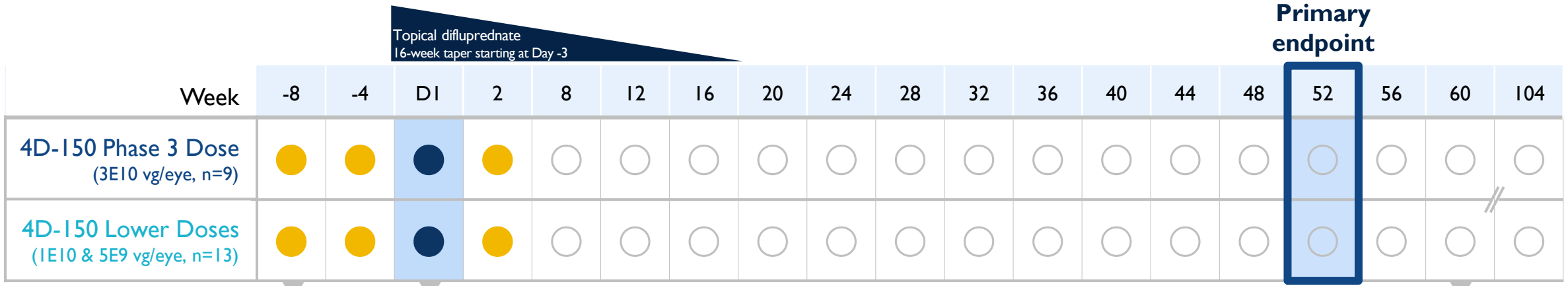
SPECTRA Enrolled DME Patients with Focus on Safety & Dose Selection

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)

- Assessed by SD-OCT and confirmed by independent reading center.

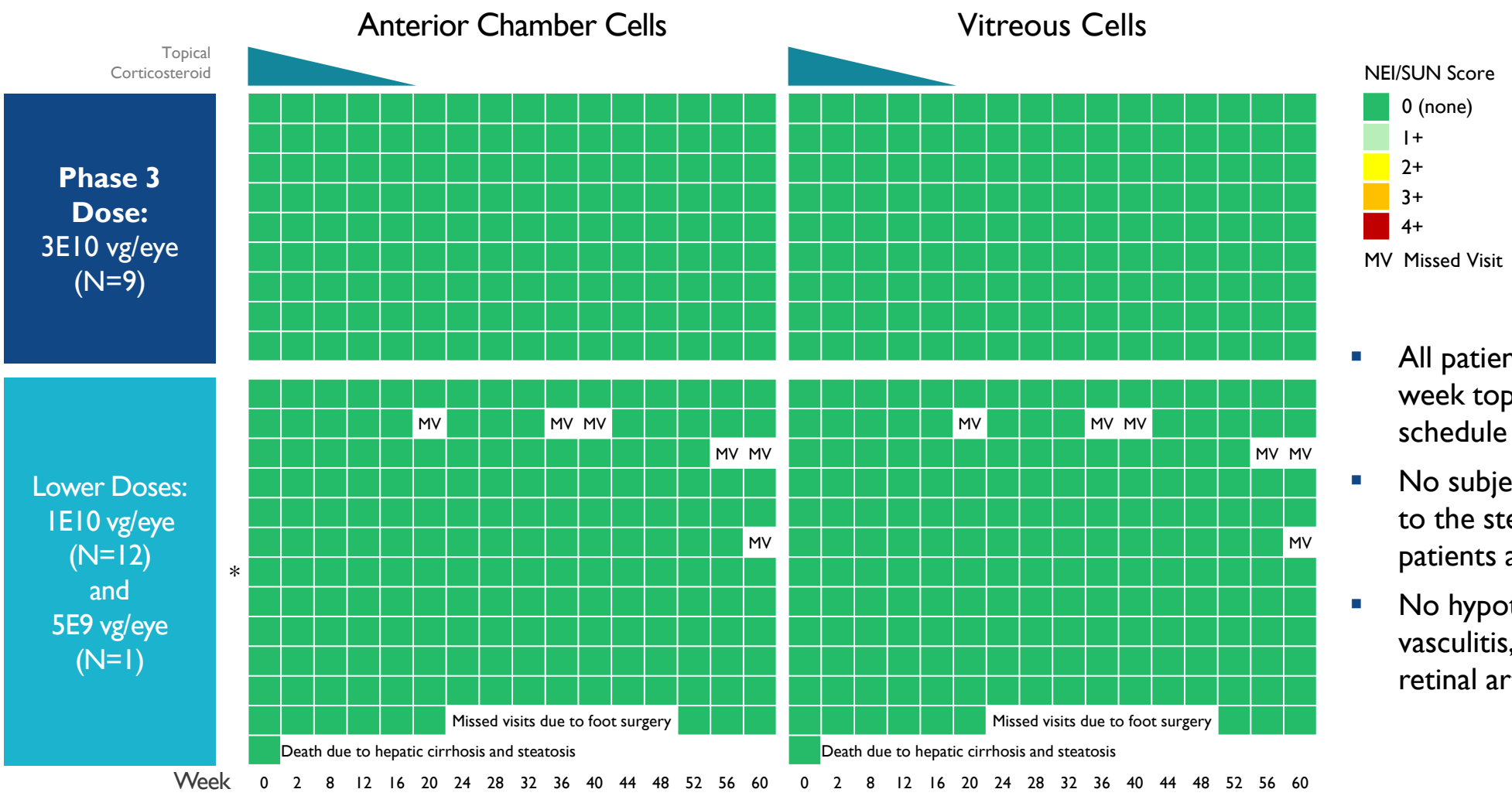


Supplemental Aflibercept Criteria (starting at Week 8)

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

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.

4D-150 Continues to be Well Tolerated Through 60 Weeks with No Intraocular Inflammation at any Timepoint at any Dose Level



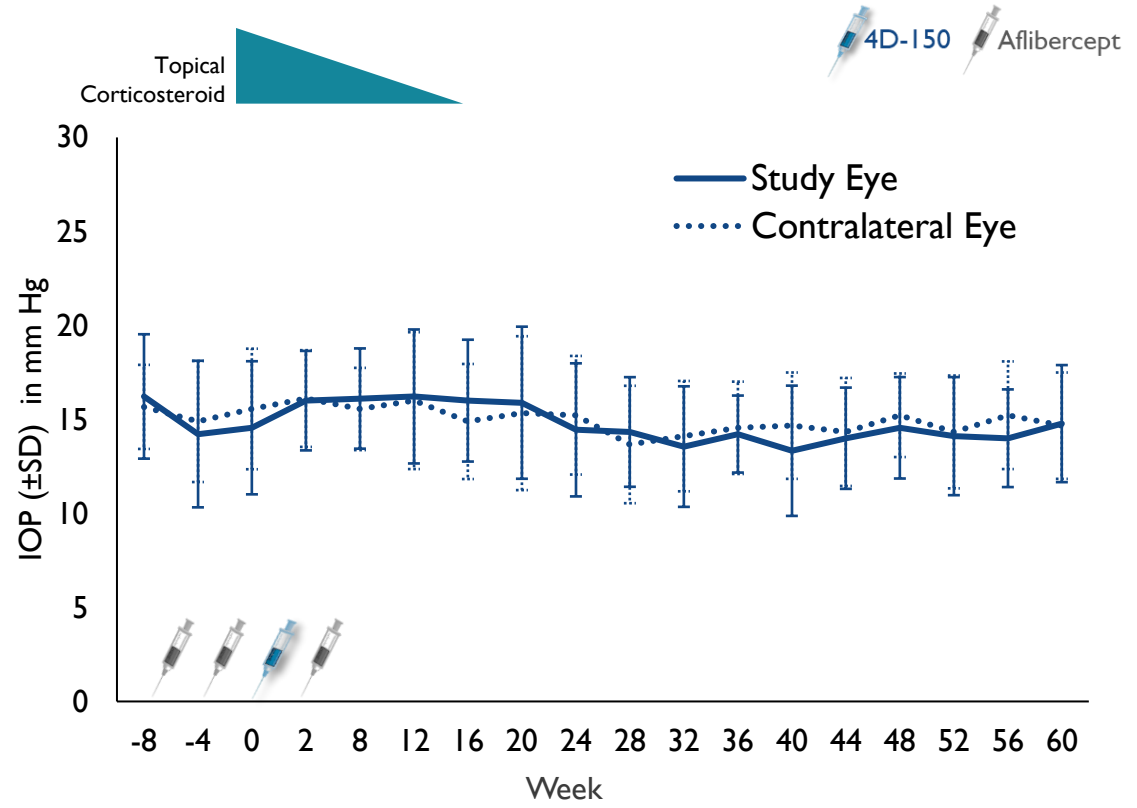
- All patients completed the 16-week topical steroid taper on schedule
- No subjects required modification to the steroid regimen and all patients are currently off steroids
- No hypotony, endophthalmitis, vasculitis, choroidal effusions or retinal artery occlusions

*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

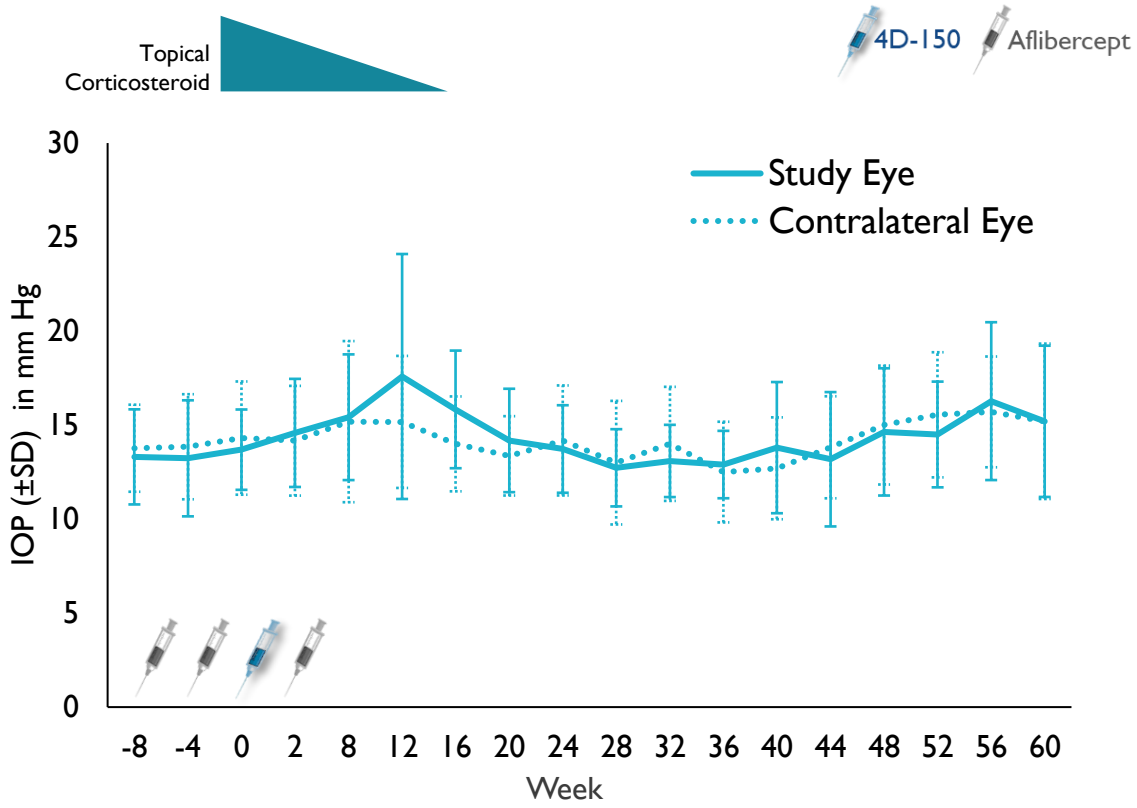
Mean IOP Within Normal Limits

No IOP <6 mmHg at any visit

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

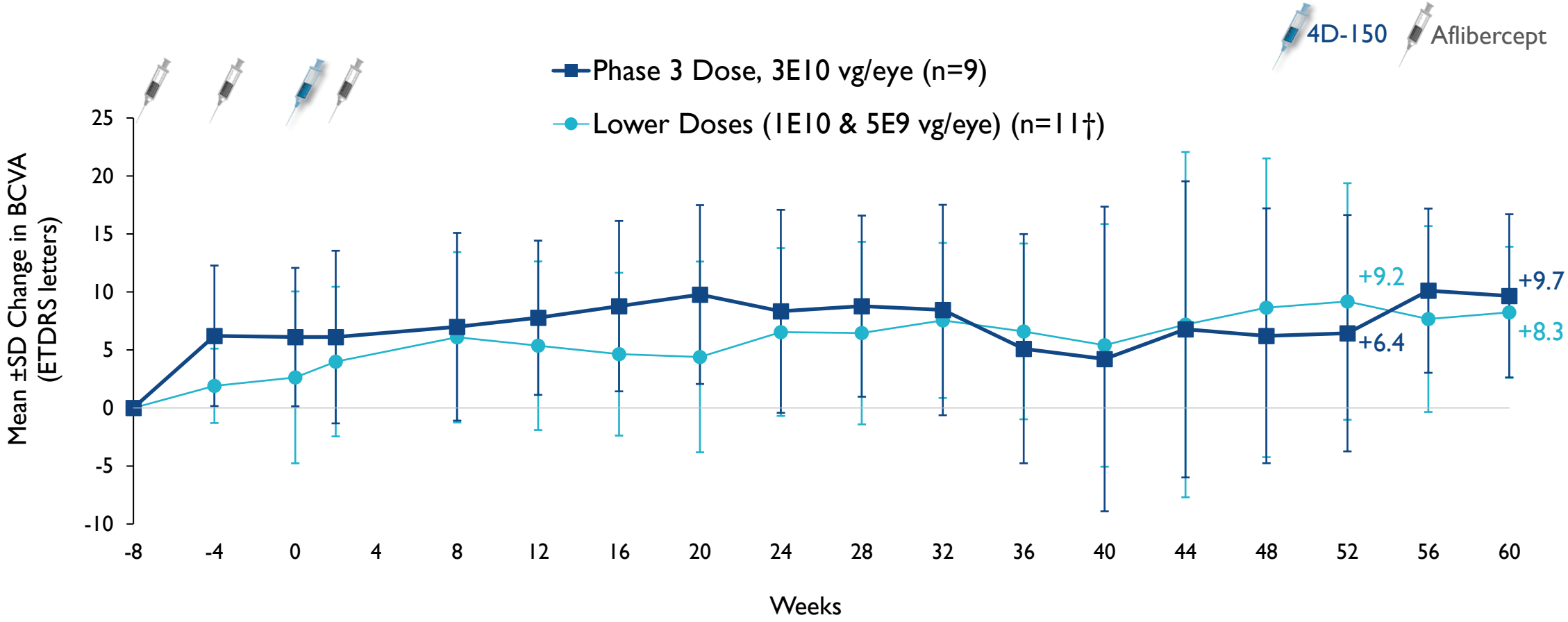


Lower Doses: 1E10 vg/eye (N=12) and 5E9 vg/eye (N=1)



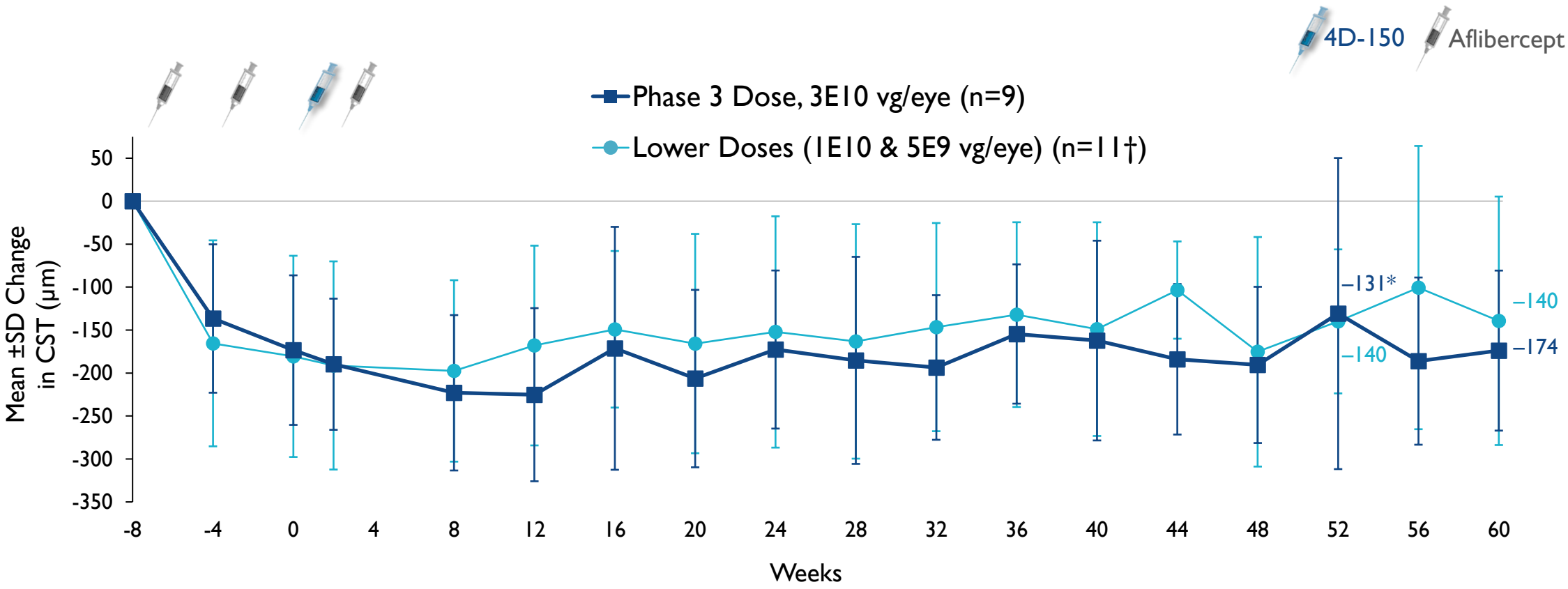
IOP: Intraocular Pressure
Data cutoff as of May 2, 2025.

Sustained Gains in Visual Acuity Through Week 60



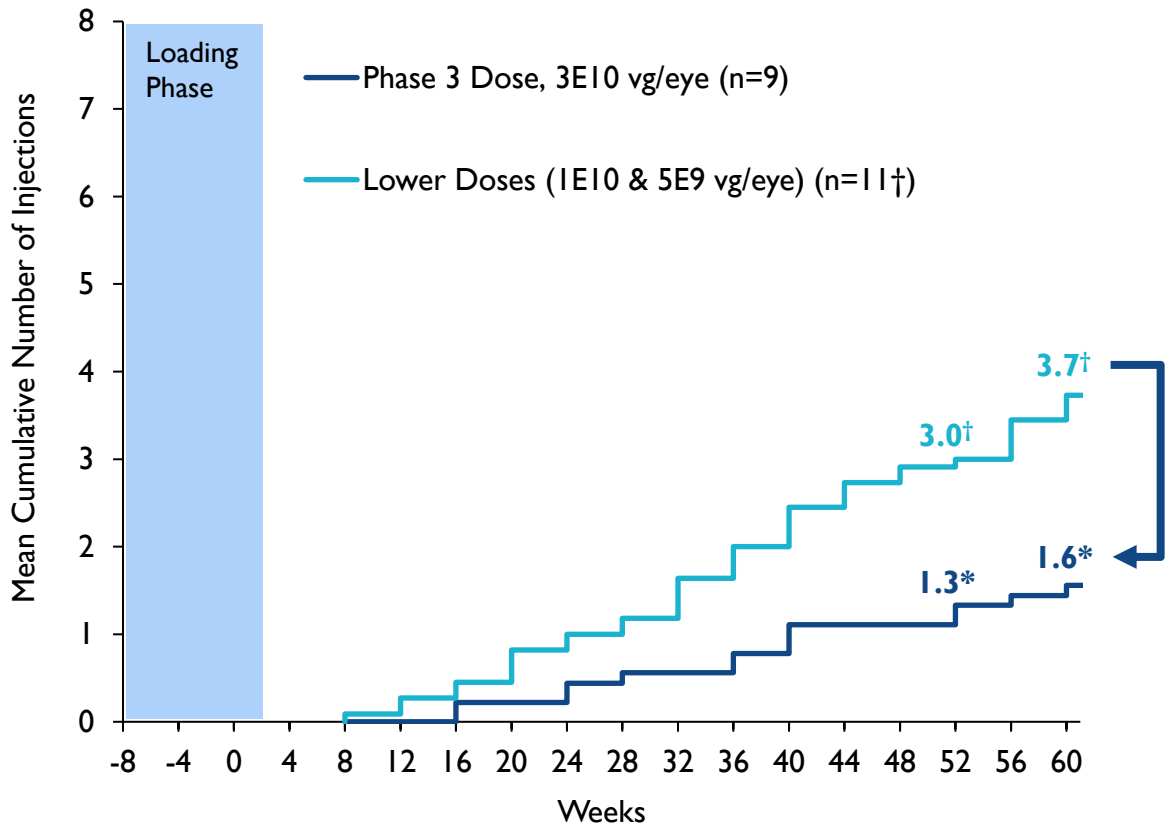
†2 subjects missed >50% of study visits and are not considered evaluable for injection burden or other efficacy parameters. BCVA: Best Corrected Visual Acuity.
Data cutoff as of May 2, 2025

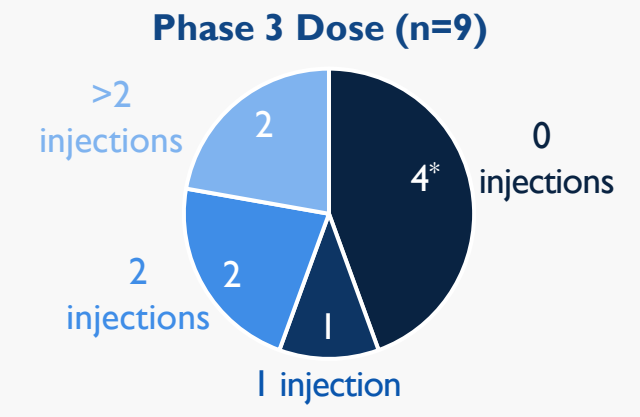
Sustained Improvement in Anatomic Control Through Week 60

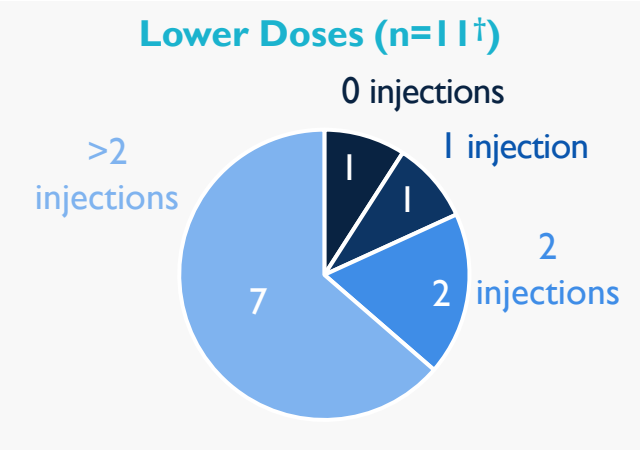


*One subject received supplemental AFLB at W52 due to post-cataract surgery edema. †2 subjects missed >50% of study visits and are not considered evaluable for evaluation of injection burden or other efficacy parameters. CST: Central Subfield Thickness.
Data cutoff as of May 2, 2025

4D-150 3E10 vg/eye: Strong Treatment Burden Reduction and Dose Response vs. Lower Doses Through Week 60







*One subject received supplemental AFLB at W52 due to post-cataract surgery edema. The injection was not counted in 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.
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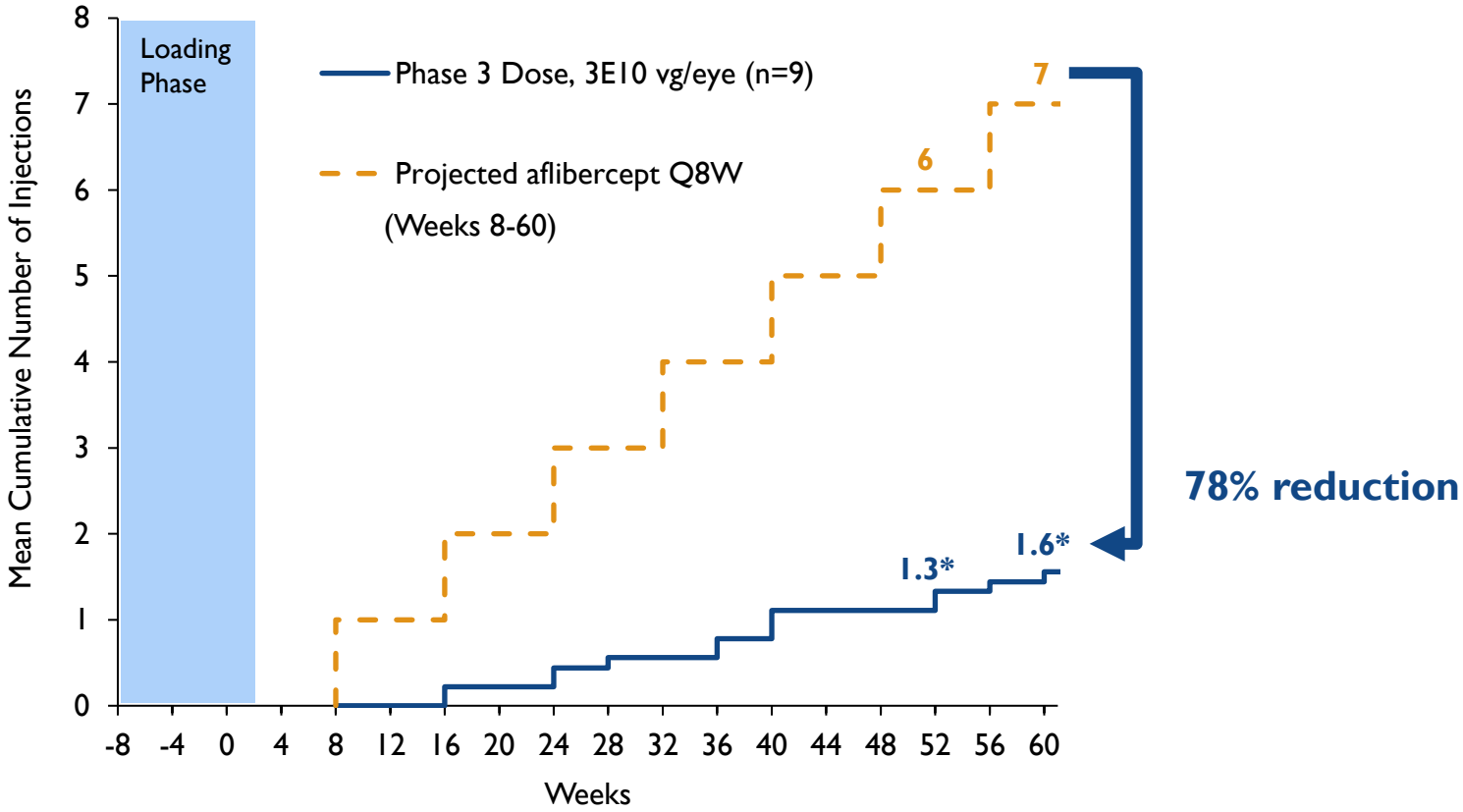
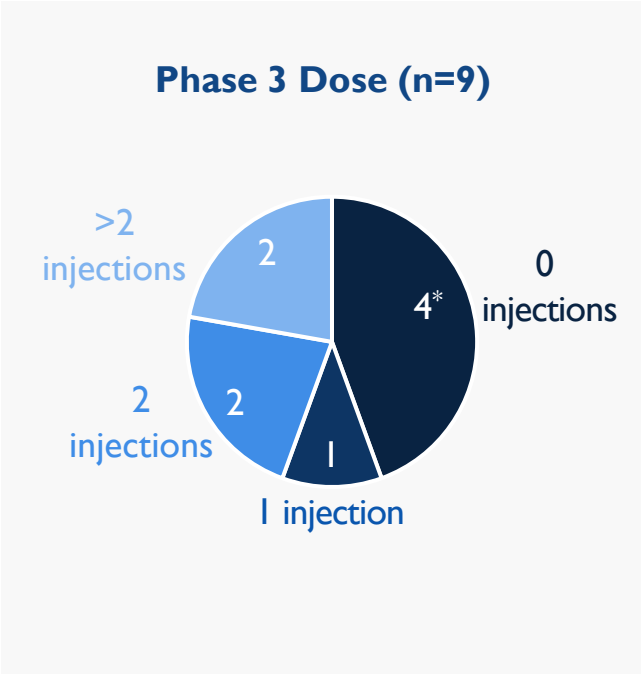
4D-150 3E10 vg/eye: Strong Treatment Burden Reduction and Dose Response vs. Lower Doses Through Week 60





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SPECTRA Conclusions Through Week 60

Safety Data

- **No intraocular inflammation** (No SUN/NEI 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-150

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-150 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.

Thank you to all trial investigators, research staff, patients, and caregivers who contributed to this work

SPECTRA Investigators

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