PRISM

24-week Results from the Randomized Phase 2 Dose Expansion Stage of the PRISM Trial Evaluating 4D-150 in High Need nAMD Patients: Injection-free Patient Analyses

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Disclosures

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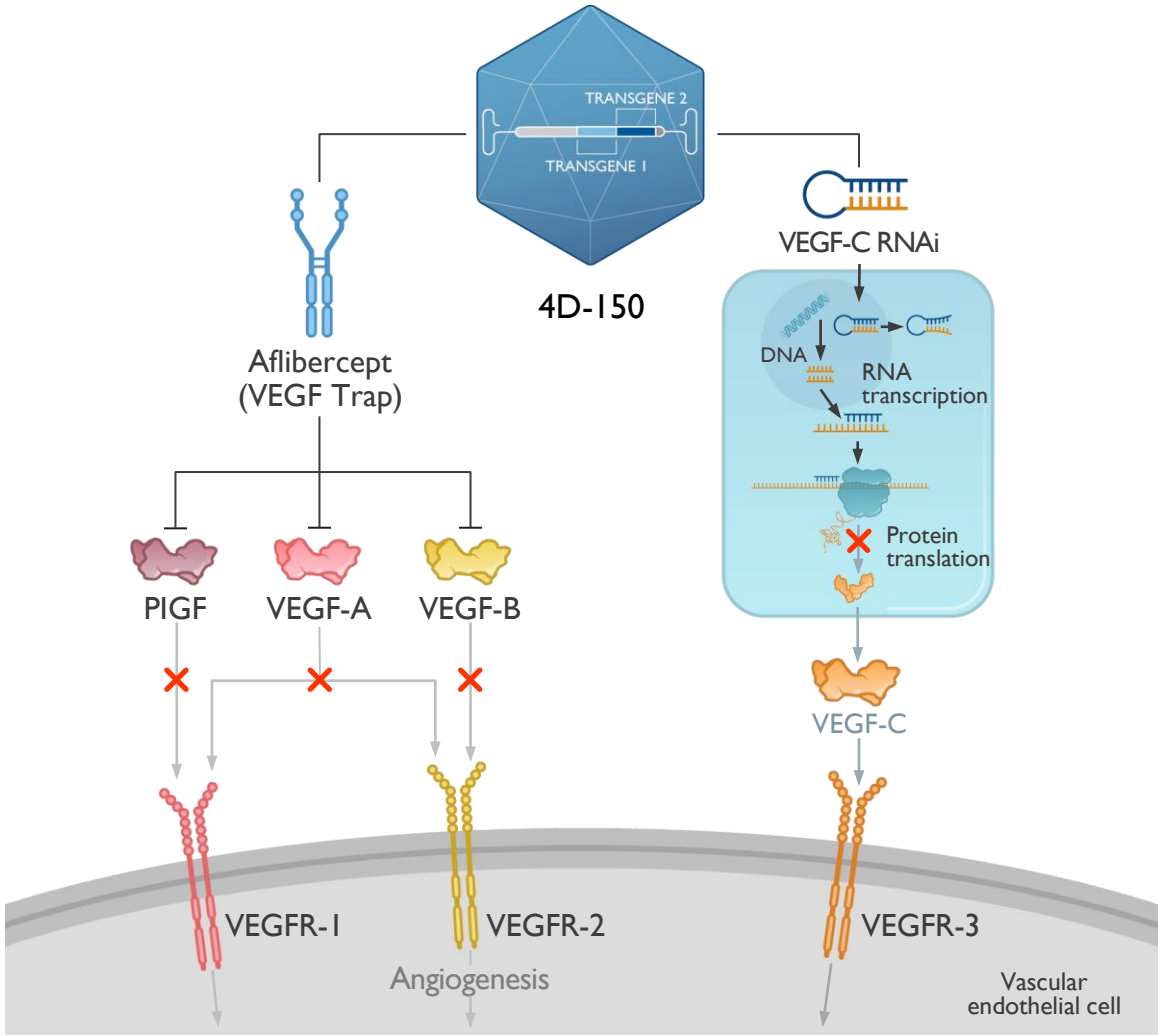
4D-150

Dual-Transgene Intravitreal Gene Therapy

- Primate-evolved intravitreal R100 capsid carrying a dual-transgene payload
  - Aflibercept & VEGF-C RNAi
- Single-dose intravitreal administration
- Widespread delivery to all major regions and layers of the macula
- Robust pan-retinal transgene expression
- Inhibition of 4 distinct VEGF family members: VEGF-A, B, C and PlGF



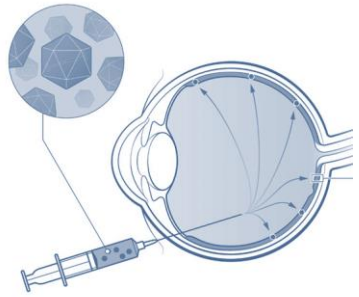
PlGF, placental growth factor; VEGF, vascular endothelial growth factor.

PRISM Met All Objectives in wAMD Patients with Severe Disease Activity & High Anti-VEGF Treatment Burden*

PRISM

Administration

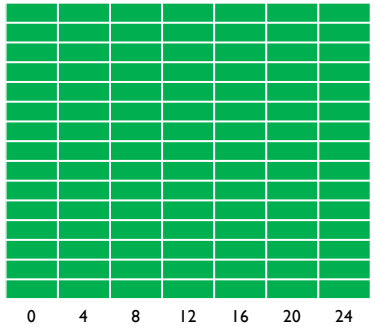
✓ Single clinically routine intravitreal injection



Safety

✓ Favorable safety profile

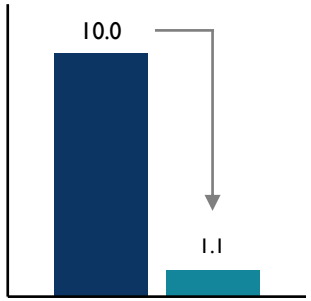
No significant or recurrent inflammation



Reduced Injection Burden

4D-150
(3E10 vg/eye)†

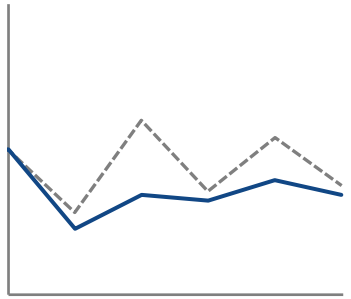
✓ 89% reduction
✓ 84% 0–1 injection
✓ 63% injection-free



Anatomical Control

4D-150
(3E10 vg/eye)†

✓ Sustained reduction in retinal thickness
✓ Stabilization of CST



Durable Clinical Activity

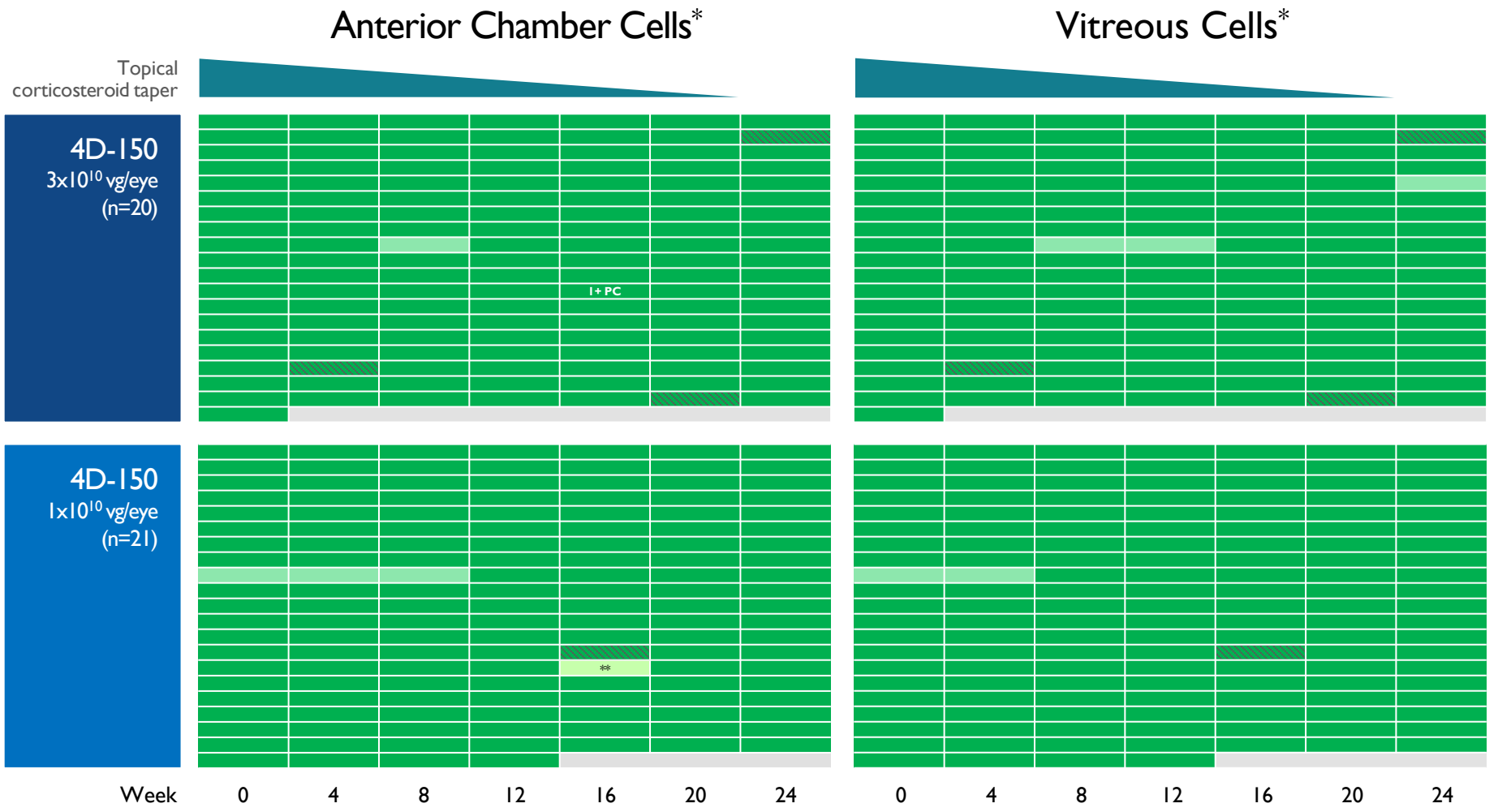
✓ Multi-year durability (up to 2 years)‡

Potential for long-term vision preservation

*Duration of follow up, ≥24 weeks. †Assessed at Week 24. ‡Dose exploration cohort (3E10 vg/eye). CST, central subfield thickness.

Ophthalmic Examination in 4D-150 Treated Patients

No Clinically Significant or Recurrent Intraocular Inflammation*



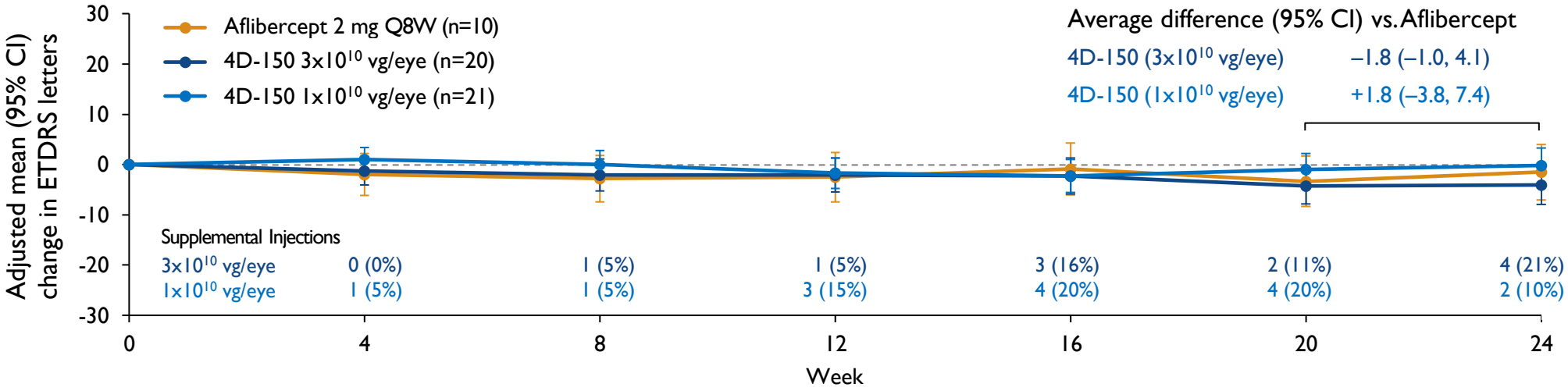
- 97% (38 of 39) completed 20-week corticosteroid taper on schedule
  - Single participant** with increase in topical steroid dose, completed taper by week 26
- No participants restarted steroids during follow-up for up to 48 weeks

*SUN and NEI Scores for white blood cells. **Mixed WBC and pigmented cells; managed with temporary increase in topical corticosteroid dose (taper completed by Week 26).
†Unrelated to study treatment. NEI, National Eye Institute; PC, pigmented cells; SUN, Standardization of Uveitis Nomenclature.

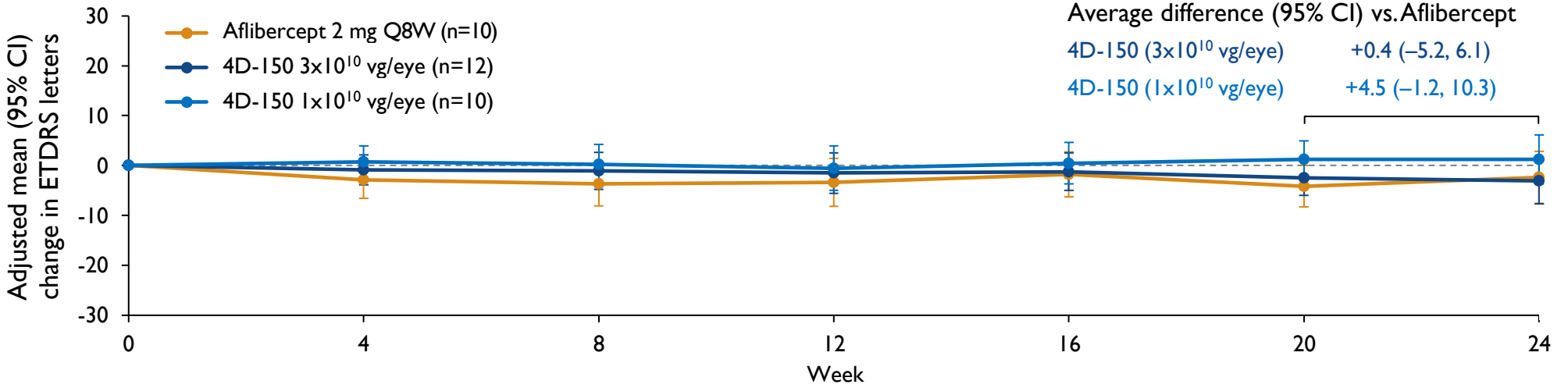
Best Corrected Visual Acuity: Supplemental Injection-free

Stable Visual Acuity Equivalent to Standard Aflibercept Through Week 24 in Injection-free Participants

Total Population
(4D-150, n=41)



Supplemental Injection-free
(4D-150, n=22)

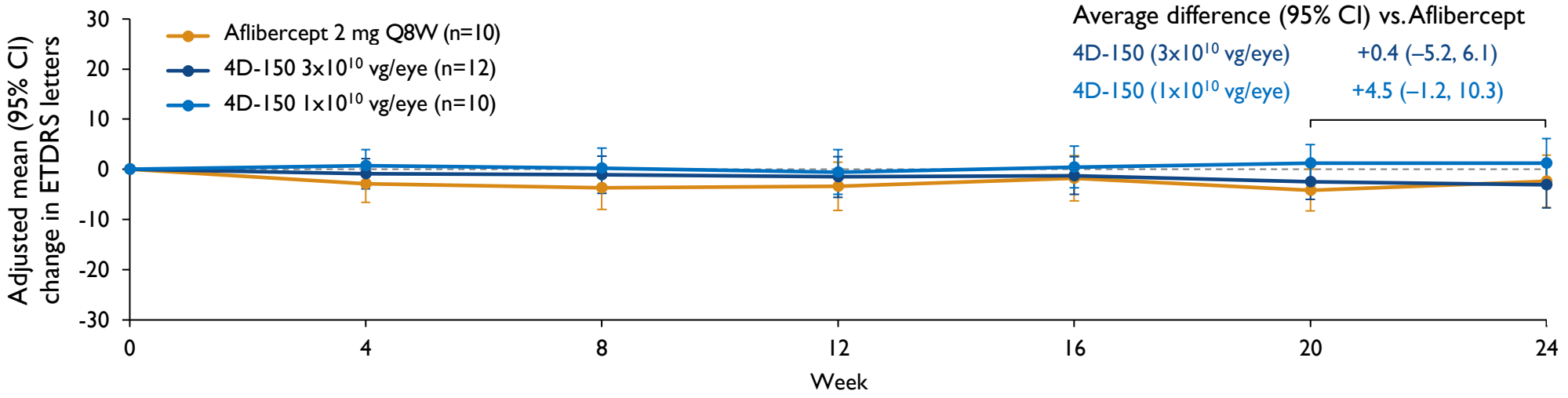


Baseline=Day -7. Adjusted mean (95% CI) estimated from a mixed–effect model for repeated measures (weeks 4-24) without imputation of missing values. Excludes participants (n=1 per dose group) with missing data due to early termination. ETDRS, Early Treatment Diabetic Retinopathy Study.

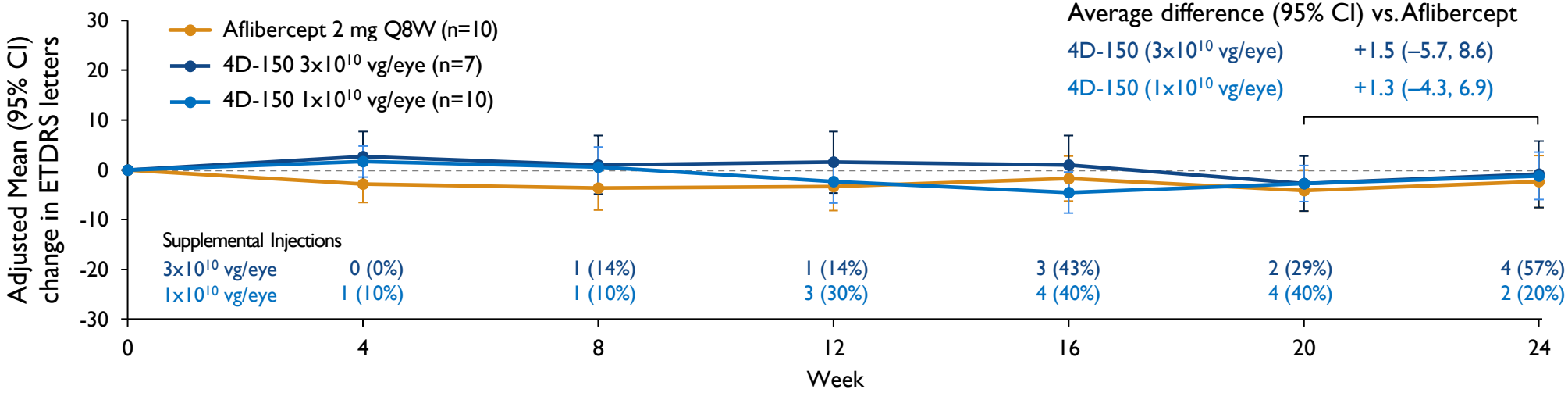
Best Corrected Visual Acuity By Supplemental Injection Status

Stable Visual Acuity Equivalent to Standard Aflibercept Through Week 24 in Both 4D-150 Dose Groups

Supplemental Injection-free
(4D-150, n=22)



Supplemental Injection (+)
(4D-150, n=17)



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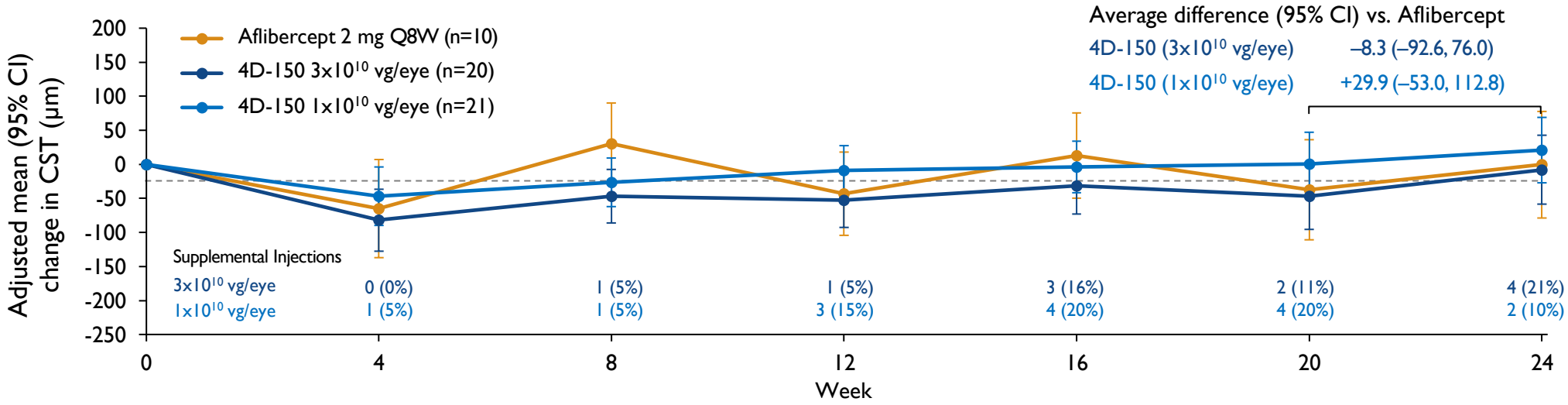
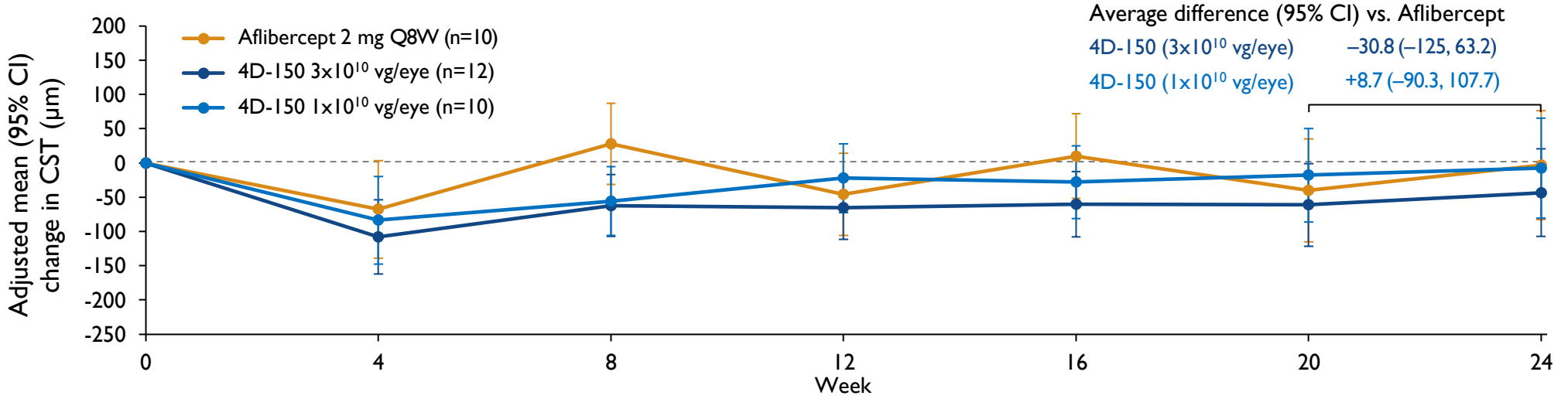
Central Subfield Thickness (CST): Supplemental Injection-free

4D-150 3×10[10] vg/eye: Sustained Reduction in CST and Reduced CST Fluctuation Compared to Aflibercept

Total Population
(4D-150, n=41)



Supplemental Injection-free
(4D-150 n=22)

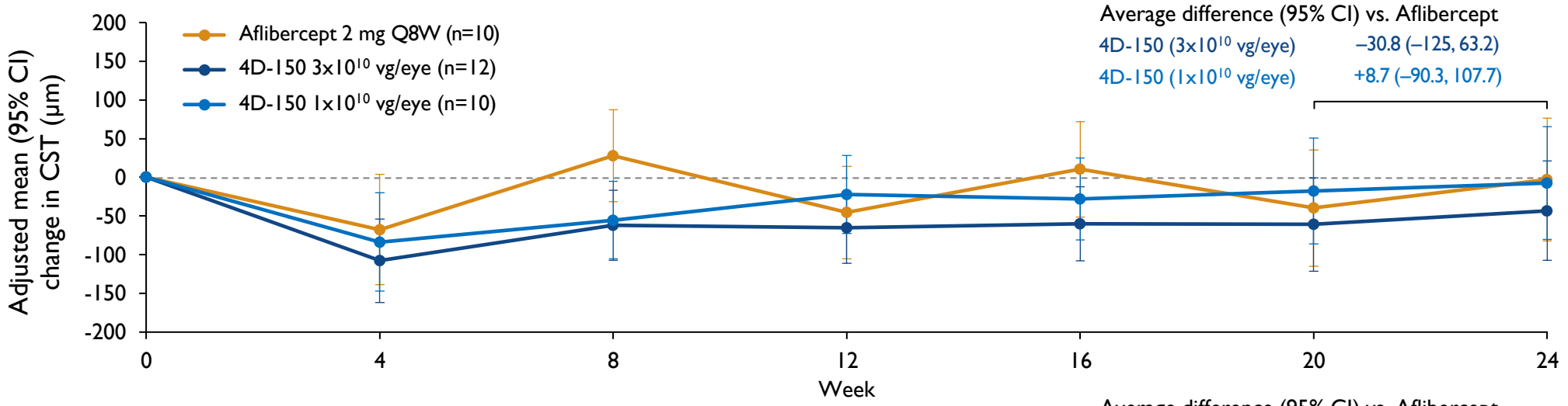


Baseline=Day -7. Adjusted mean (95% CI) estimated from a mixed–effect model for repeated measures (weeks 4-24) without imputation of missing values. Excludes participants (n=1 per dose group) with missing data due to early termination.

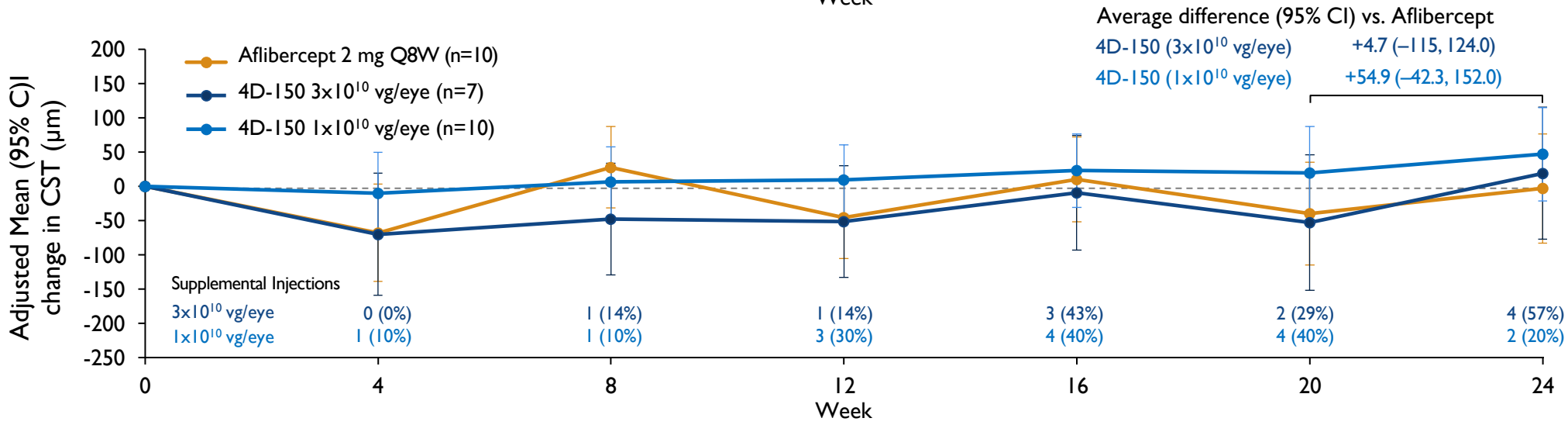
Central Subfield Thickness (CST): +/- Supplemental Injection

4D-150 3×10[10] vg/eye: Reduced CST Fluctuation Compared to Aflibercept

Supplemental Injection-free
(4D-150, n=22)



Supplemental Injection (+)
(4D-150, n=17)



Baseline=Day -7. Adjusted mean (95% CI) estimated from a mixed–effect model for repeated measures (weeks 4-24) without imputation of missing values. Excludes participants (n=1 per dose group) with missing data due to early termination.

Conclusion: Promising Clinical Outcomes in Participants with Severe Disease Activity and High Treatment Burden

- 4D-150 was safe and well tolerated (through Week 24)
  - No clinically significant or recurrent intraocular inflammation
  - No patients restarted steroids through up to 48 weeks of follow-up
  - No hypotony, endophthalmitis, retinal vasculitis, choroidal effusions, or retinal artery occlusions
- Injection-free subgroup analysis: BCVA
  - Stable visual acuity observed through Week 24 in both 4D-150 dose groups +/- supplemental injections
  - BCVA equal to or numerically higher than aflibercept at all time points in both dose groups
- Injection-free subgroup analysis: CST
  - 4D-150 dose response demonstrated with CST stability in injection-free patients
  - 4D-150 high dose ($3x10^{10}$ vg/eye): CST stability and reduced CST fluctuation compared to bimonthly aflibercept
- Phase 3 clinical trial: Initiation targeted in Q1 2025