4DMT

Intravitreal 4D-150

Phase 2 Population Extension in Broad Disease Activity Wet AMD Patients

PRISM

July 17, 2024

Forward-Looking Statements

This Presentation contains forward looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Presentation, including statements regarding our clinical development plans, strategy, future operations, future financial position, prospects, plans, and objectives of management, are forward looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "target," "should," "would," and similar expressions are intended to identify forward looking statements, although not all forward looking statements contain these identifying words. We may not actually achieve the plans, intentions, or expectations disclosed in these forward looking statements, and you should not place undue reliance on these forward looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward looking statements. In addition, the forward looking statements included in this Presentation represent our views as of the date of this Presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward looking statements in the future, we specifically disclaim any obligation to do so. These forward looking statements should not be relied upon as representing our views as of any date subsequent to the date of this Presentation.

This Presentation discusses our product candidates that are under preclinical study and in clinical trials, and which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of our product candidates for the therapeutic use for which they are being studied.

This Presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

This Presentation shall not constitute an offer to sell or the solicitation of an offer to buy securities.

Today's Presenters

David Kirn, MD
Co-Founder & CEO

Robert Kim, MD
Chief Medical Officer

Arshad Khanani, MD, MA, FASRS
Director of Clinical Research at Sierra Eye Associates, Clinical Associate Professor, Reno School of Medicine

Key Highlights for Today for 4D-150

1. **CONTINUES TO BE SAFE & WELL-TOLERATED:**
   In Both Wet AMD & DME

2. **STRONG CLINICAL ACTIVITY DEMONSTRATED IN BROAD WET AMD DISEASE ACTIVITY POPULATION:**
   Planned Phase 3 Population

3. **DEMONSTRATED DURABLE CLINICAL ACTIVITY**

4. **PROVIDES FURTHER SUPPORT FOR PLANNED WET AMD PHASE 3 PROGRAM**

Data cutoff date, June 24, 2024.

Key Takeaways

PRISM

Phase 2 Population Extension:

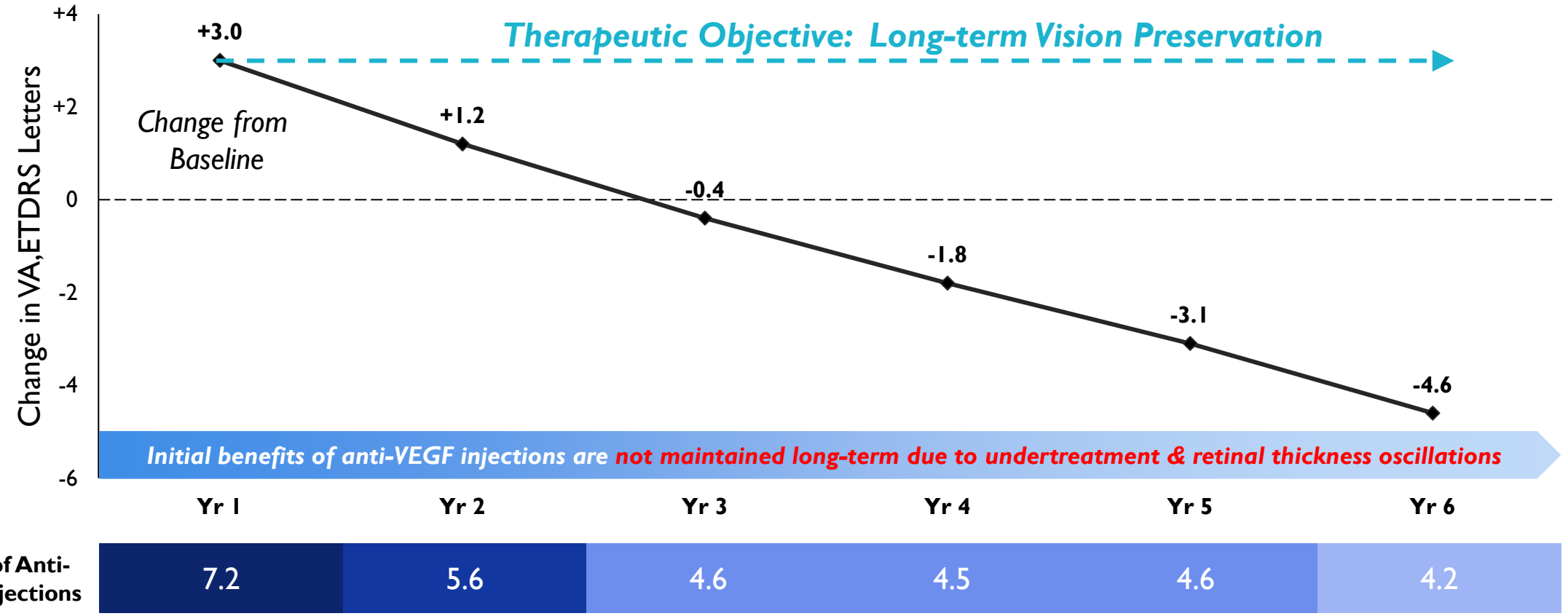
24-week Landmark

- **45 PATIENTS WITH BROAD WET AMD DISEASE ACTIVITY TREATED**
- **SAFE & WELL TOLERATED, INCLUDING PHASE 3 DOSE (N=30; 3E10 VG/EYE)**
  - ✓ **100% (30 of 30) No** anterior chamber inflammation
  - ✓ **100% (30 of 30) No** significant vitreous inflammation (n=1 trace, no intervention)
  - ✓ **100% (30 of 30)** completed local steroid prophylactic regimen on schedule and did not resume
- **STRONG CLINICAL ACTIVITY THROUGH 24-WEEKS (3E10 VG/EYE)**
  - ✓ **Robust reduction in anti-VEGF injection treatment burden:**
    - **89%** reduction in annualized injection rate
    - **93%** 0–1 injection
    - **77%** injection-free
  - ✓ **BCVA improved: +4.2 letters** from baseline; **+5.7 letters** vs low dose
  - ✓ **CST: sustained and greater anatomic control without fluctuations**
- **FURTHER SUPPORTS PLANNED PHASE 3 PROGRAM:** Study design, patient population, safety, primary endpoint (BCVA), treatment burden reduction

Data cutoff date, June 24, 2024.

Current Bolus Anti-VEGF Therapies for Wet AMD Do Not Preserve Vision Long-Term

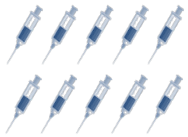
Vision Loss Over Time in the Real World with Current Standard of Care[1]



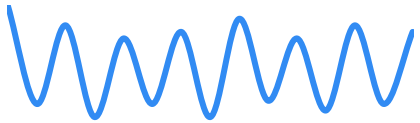
1. Wykoff et al.: Ophthalmol Sci. 2023 Oct 31;4(2):100421.; n=135,384 at Yr 1; 6,878 at Yr 6

4D-150 Solution: Designed to Preserve Vision by Addressing the Limitations of Current Wet AMD Therapeutic Regimens

Vision Loss Over Time
Due to Limitations of Current Standard of Care

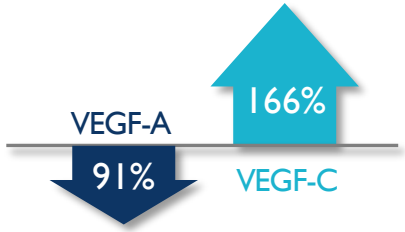


Limited durability & high treatment burden → **suboptimal compliance & undertreatment**



Oscillating peak-trough anti-VEGF concentrations → **CST fluctuations**

Aqueous Concentrations Following Bevacizumab Injections[1]*



VEGF-A inhibitors result in **increased VEGF-C levels**

4D-150 Designed to Preserve Vision
Transform Treatment Paradigm

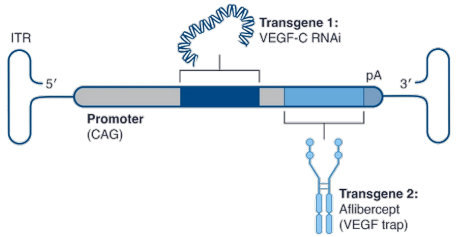
1

Single routine intravitreal injection optimizes treatment with durable expression of anti-VEGF

2

Sustained local expression of anti-VEGF reduces CST fluctuations

3

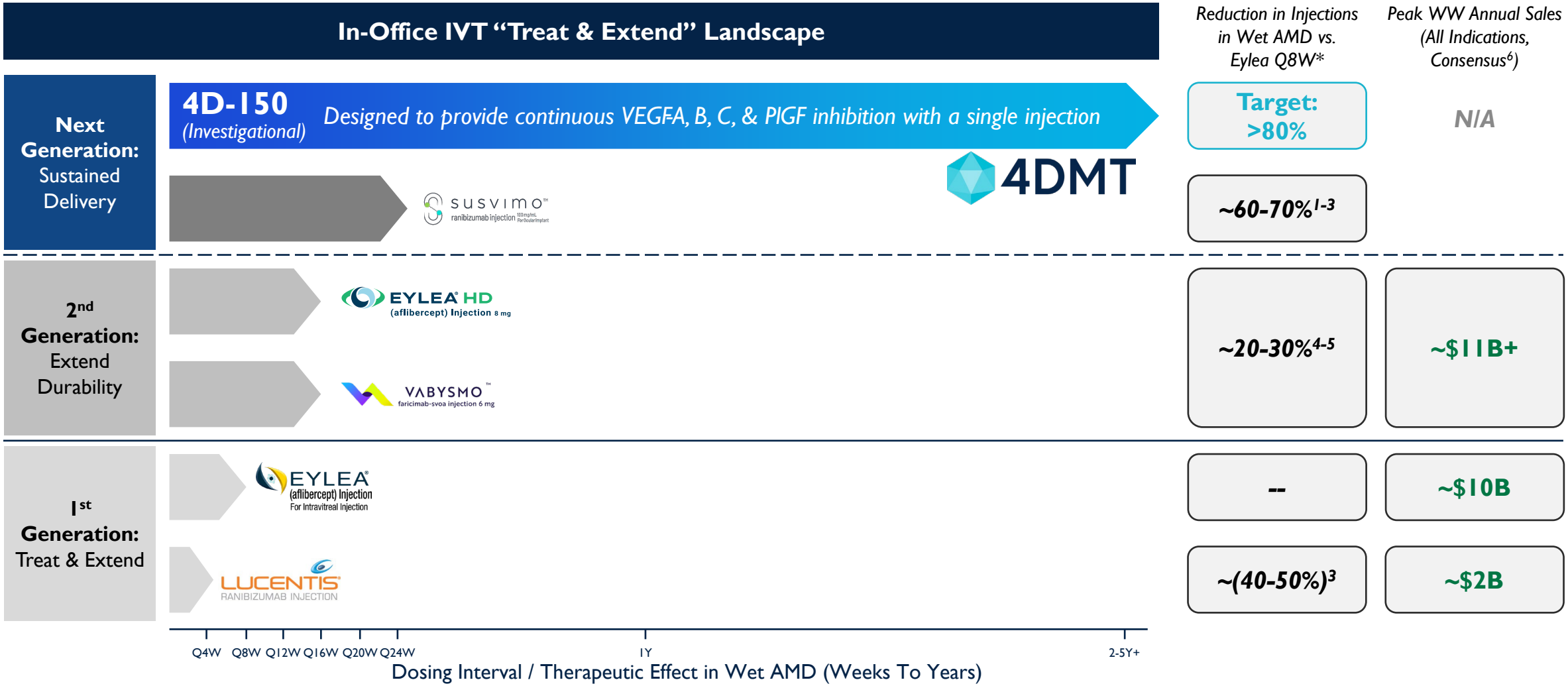


Dual-transgene payload targets **4 VEGF family members**

Goal: ***Vision Preservation*** *for Millions with a* ***Safe, Routine, One-time IVT Treatment***

1. Cabral et al. *Ophthalmol Retina* 2018;2:31–7. CST, central retinal thickness. *2 months post administration of bevacizumab

Products with Incremental Improvements in Durability & Reduction in Treatment Burden Have Become Commercial Blockbusters



Mean no. of injections over Year 0-2: Susvimo (ARCHWAY) vs. Eylea Q8W (VIEW 1 & 2) 2. Regillo et al. *Ophthalmology* 2023; 130:735-7 (ARCHWAY). 3. Schmidt-Erfurth et al. *Ophthalmology* 2014; 121:193-201 (VIEW 1 & 2) 4. Eylea HD: Regeneron publicly available information/company website as of 8/10/23 (PULSAR data) 5. Vabysmo: CDER statistical review; Khanani et al., *Ophthalmology* 2024; 1-13 (TENAYA and LUCERNE) 6. FactSet 2028E WW sales for Eylea HD and Vabysmo; FactSet for Eylea and Lucentis peak WW sales *The data presented above are based on cross-study comparisons and are not based on any head-to-head clinical trials. Cross-study comparisons are inherently limited and may suggest misleading similarities and differences. The values shown in the cross-study comparisons are directional and may not be directly comparable.

Potential Multi-billion Annual Revenue Opportunity for 4D-150 in Broad Wet AMD Patient Population in the U.S. if Approved

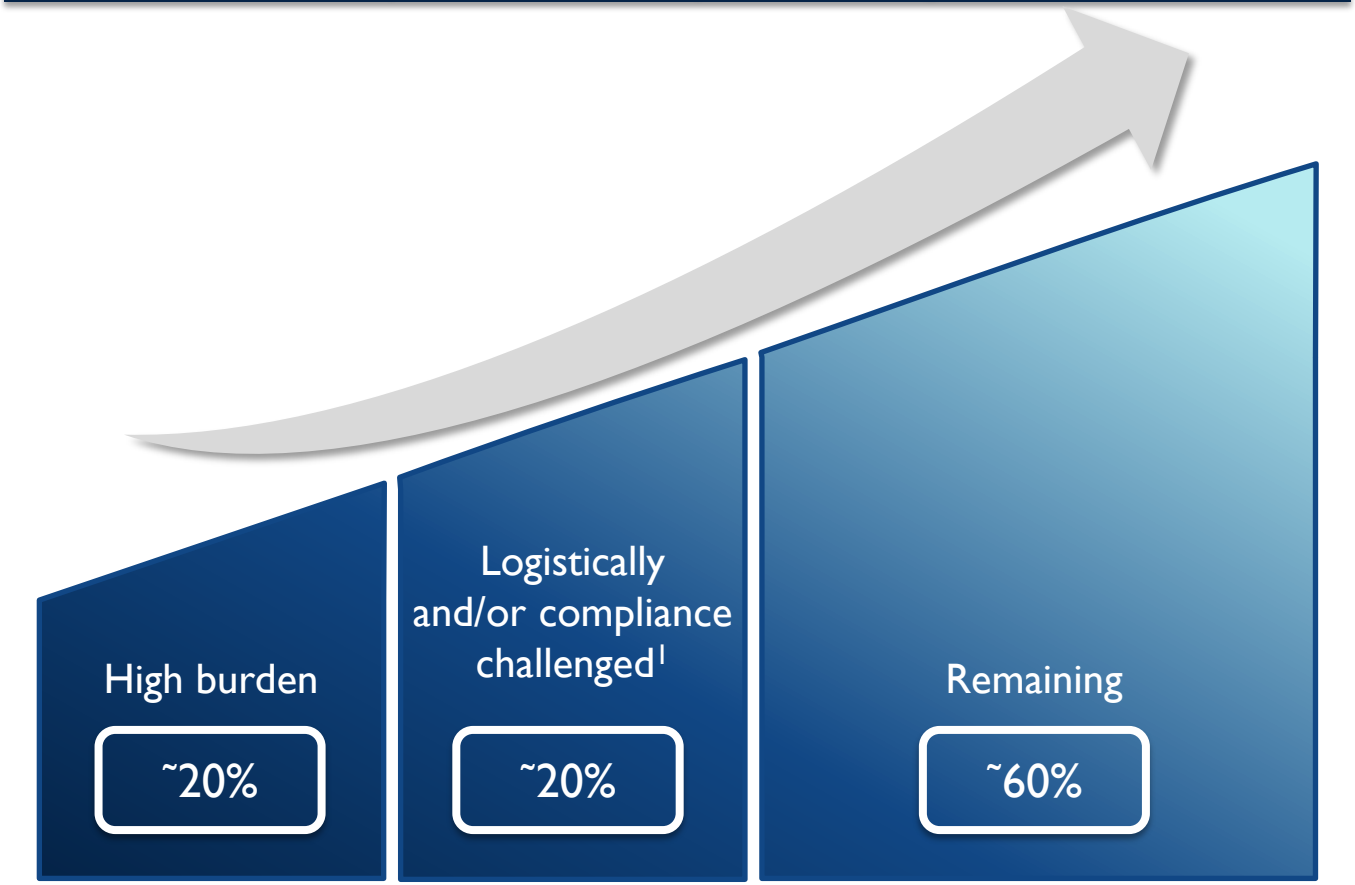
Wet AMD U.S. Opportunity

Estimated in 2035

~$10B
annual*

1% share
translates to **$300M to $500M**
(assumes 3-5 years of benefit)

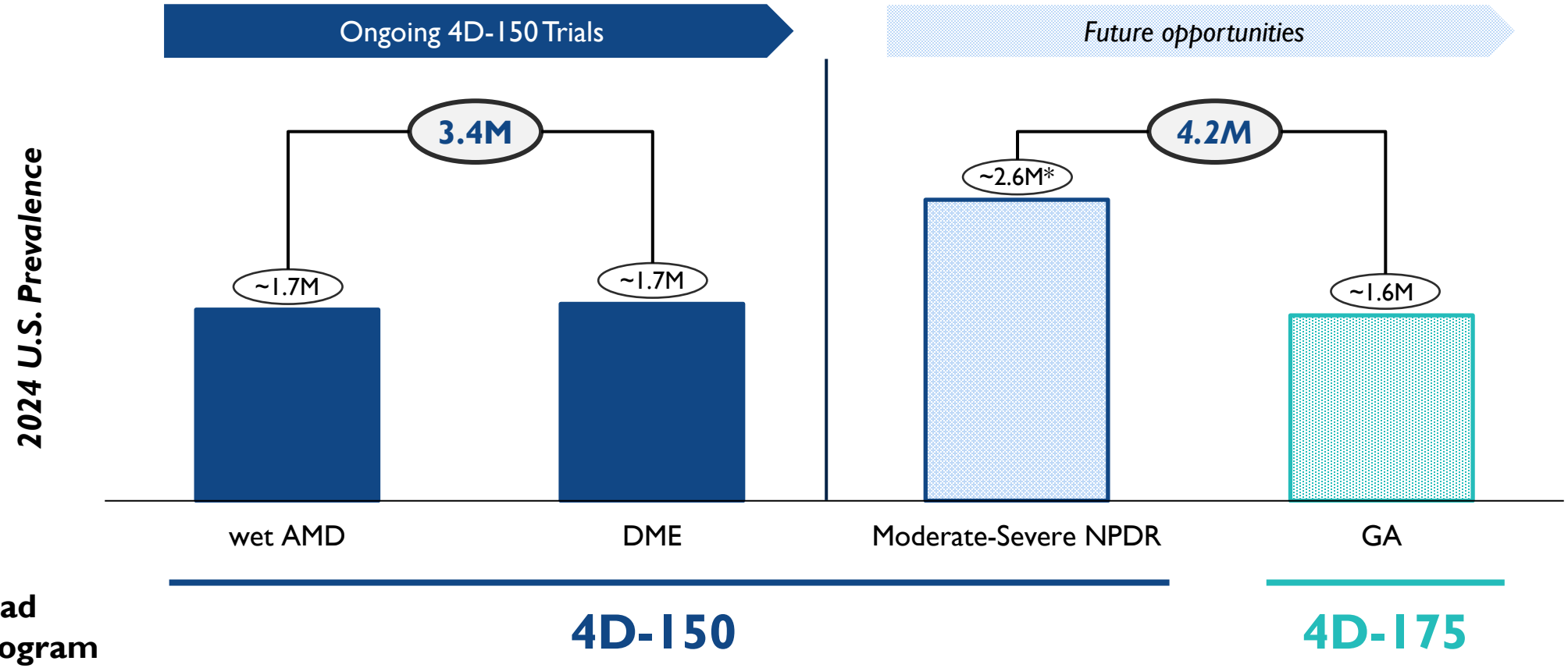
Market Unlocked Through Potential Adoption Across Key Patient Segments



*Company estimates. 1. Patients receiving less than or equal to 4 injections from Ciulla et al: Ophthalmol Retina. 2020 Jan;4(1):19-30.

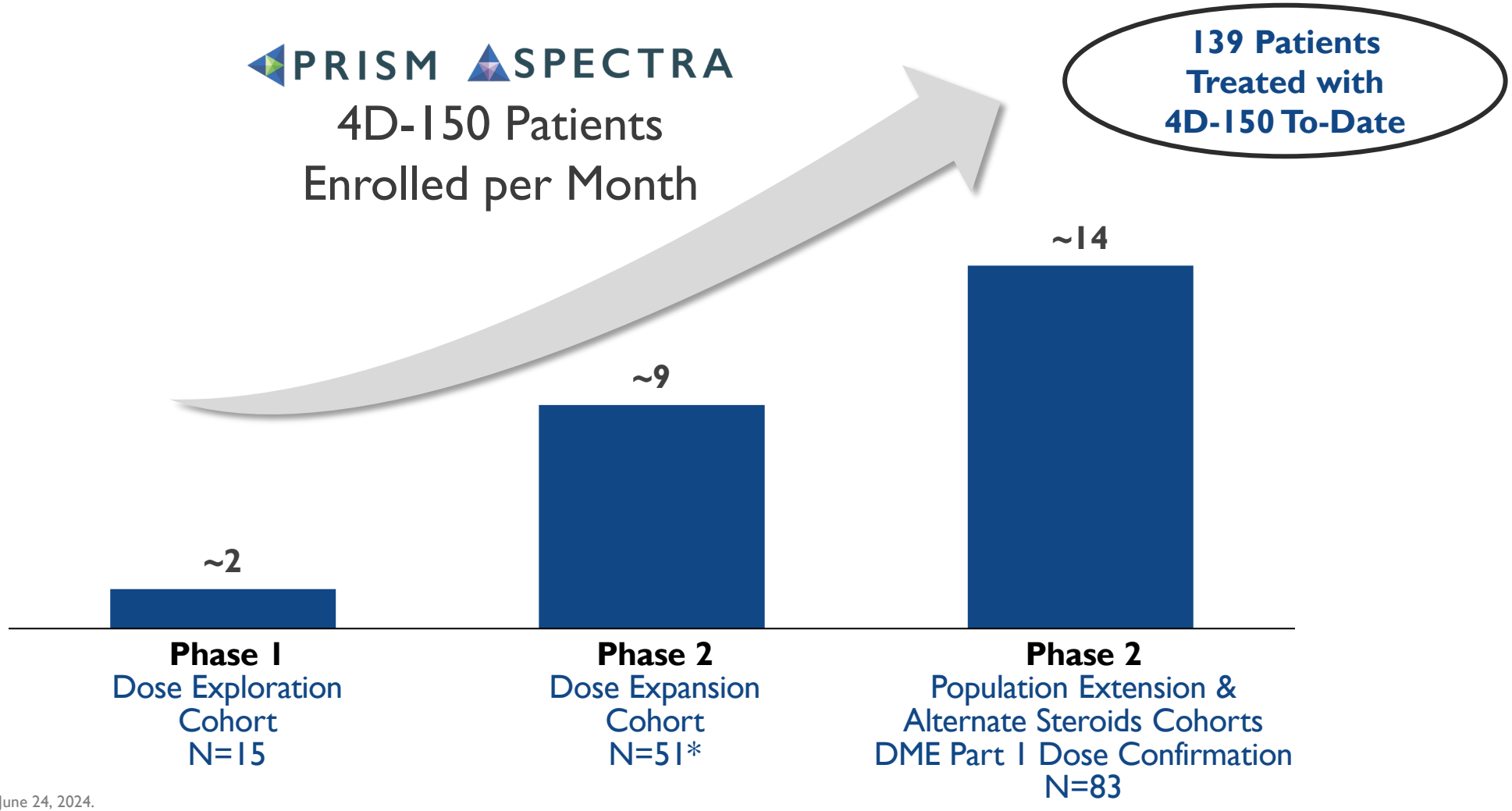
Wet AMD is the First of Four Large Market Retina Indications for 4DMT

~7.6 Million Patients in U.S.



Market Scope 2023 Retinal Pharmaceuticals Market Report, published Aug 2023. * Excludes patients with DME.

Significant Investigator & Patient Interest Following Clinical Data Drove Strong & Accelerating Enrollment Rates



4DMT internal data. Data cutoff date, June 24, 2024.
*Including n=10 in aflibercept control arm.

139 Patients Treated with 4D-150 To Date Across Multiple Populations in Wet AMD and DME

CLINICAL TRIAL	STAGE COHORT	DISEASE SEVERITY (Inj, Prior Year)	TOTAL N= *Dose Range*	FOLLOW-UP (UP TO)*	*Planned Phase 3 Dose (3E10 vg/eye)* N=
PRISM Wet AMD	**Phase 1** Dose Exploration	**Severe** (≥6)	**15** *6E9 – 3E10 vg/eye*	**2.5 years**	5
	Phase 2 Dose Expansion	**Severe** (≥6)	**41** *1E10 – 3E10 vg/eye*	**72 weeks**	20
	Phase 2 Population Extension	**Broad** (1-6)	**45** *1E10 – 3E10 vg/eye*	**40 weeks**	30
	Phase 2 Alternate Steroids	**Severe/Broad** (≥1)	**16** *3E10 vg/eye*	**44 weeks**	16
SPECTRA DME	**Phase 2 Part 1** Dose Confirmation	**Broad**	**22** *5E9 – 3E10 vg/eye*	**36 weeks**	9
Total			**139**	**2.5 years**	80

*Data cutoff date, June 24, 2024.

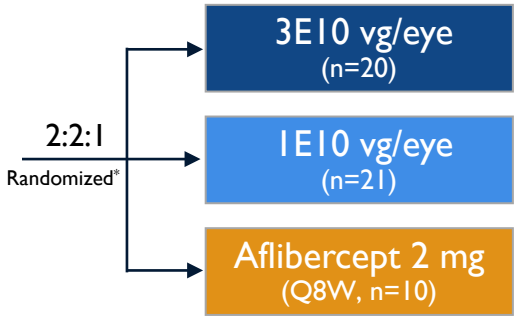
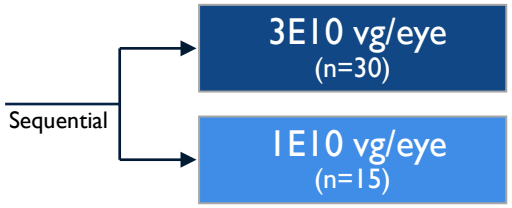
4DMT

PRISM

Phase 2 Population Extension Cohort (N=45): 24-week Landmark Analysis

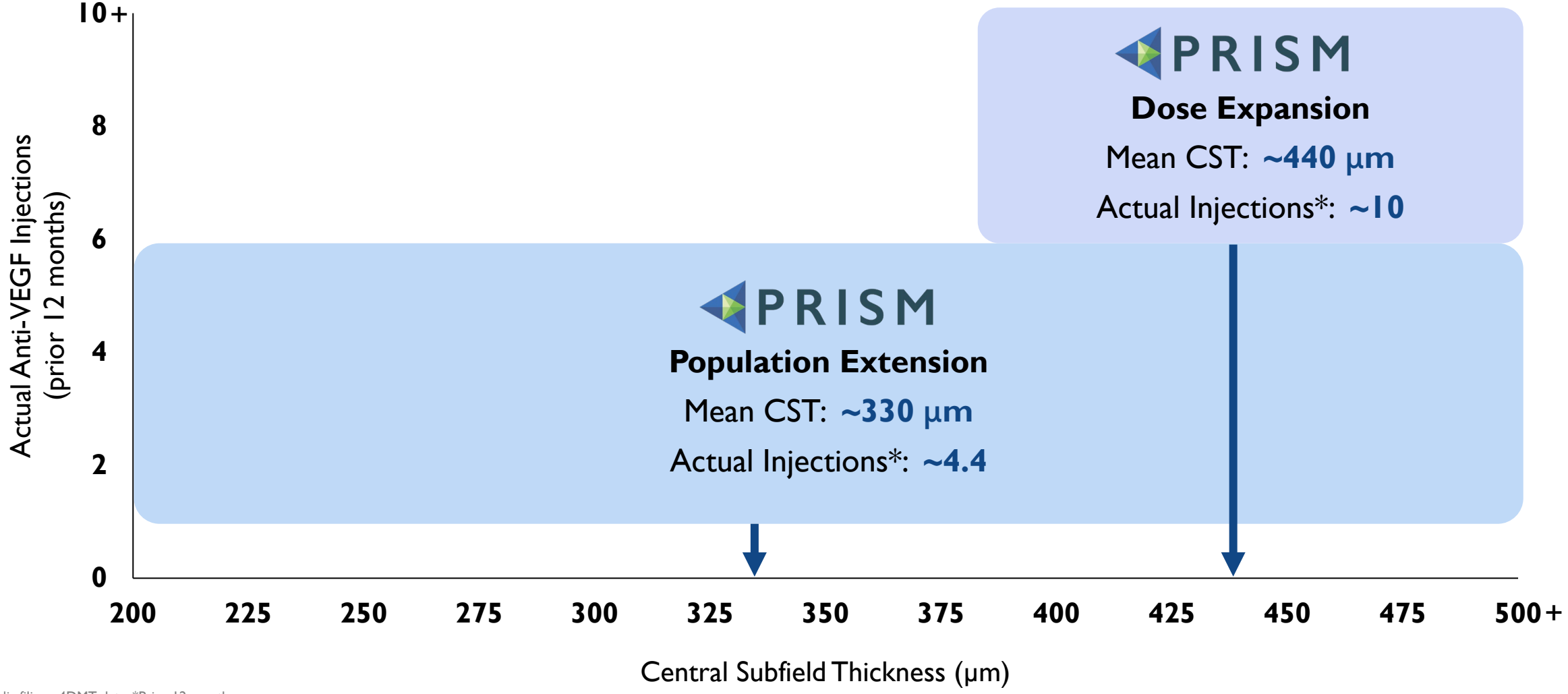
Data cutoff date: June 24, 2024

Phase 2 Population Extension Cohort Designed to Evaluate 4D-150 in Wet AMD Patients With a Broad Range of Disease Activity

Population:	Severe & High Treatment Burden	Broad Disease Activity
Cohort:	Dose Expansion	Population Extension
		
Key Inclusion Criteria:		
Anti-VEGF Injections in prior 12 months	≥6	**1-6** (≥1 in last 12 weeks)
CST at Screening	≥325 µm AND retinal fluid	**No minimum or maximum**
BCVA at Screening	34–83 ETDRS letters	34–83 ETDRS letters

*Stratified by prior injections <9 vs. ≥9. BCVA, best corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; VEGF, vascular endothelial growth factor.

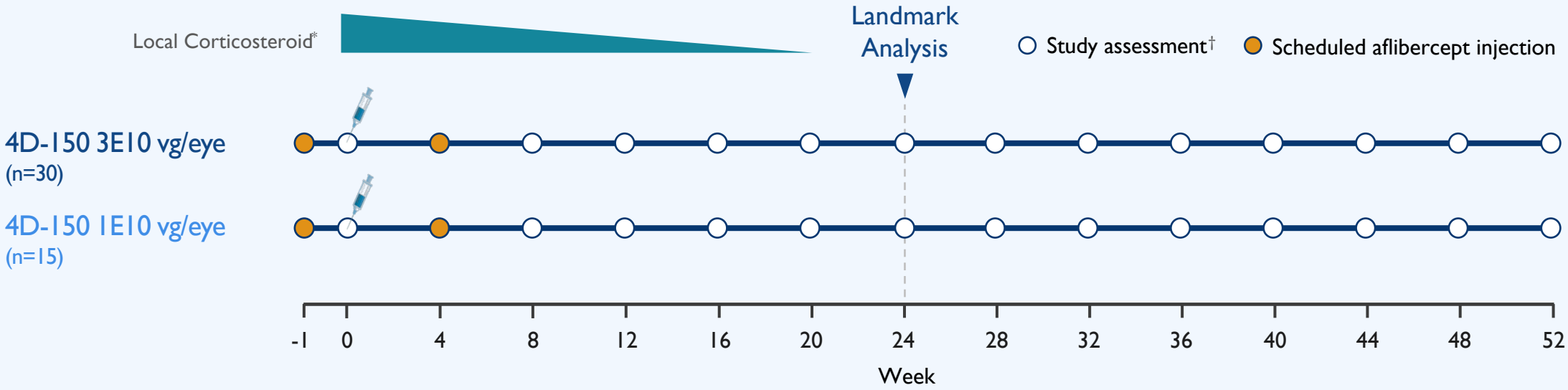
Phase 2 Population Extension Cohort Focuses on a Previously Treated Wet AMD Population with Broad Disease Activity



Public filings, 4DMT data. *Prior 12 months.

Phase 2 Population Extension Cohort Treatment Schema & Endpoints

Population Extension Cohort Study Schema



Key Endpoints

- Safety and tolerability
- Annualized anti-VEGF injection rate
- % requiring supplemental aflibercept injection
- Change from baseline in BCVA and CST

Supplemental Injection Criteria

- BCVA: Loss of ≥10 letters from average of Day -7 and Day 1 attributable to retinal fluid
- CST: Increase ≥75 µm from average of Day -7 and Day 1 values
- New vision-threatening hemorrhage due to wet AMD per investigator

*Participants received one of: (a) difluprednate (Durezol) ophthalmic emulsion (3E10 & 1E10 vg/eye), (b) triamcinolone acetonide with prednisolone taper (3E10 vg/eye), or (c) dexamethasone (3E10 vg/eye). †Visual acuity, optical coherence tomography, ophthalmic exam.

Baseline Characteristics Showed Dose Arms are Well Balanced

	3E10 vg/eye (N=30)	1E10 vg/eye (N=15)	Total (N=45)
Mean ±SD age, years	77 ±7.7	78 ±8.6	77 ±7.9
Mean ±SD BCVA, ETDRS letters	71 ±9.9	73 ±8.8	72 ±9.5
Mean ±SD CST (central subfield thickness), μm	**336 ±135.0**	**314 ±70.8**	**329 ±117.1**
Mean ±SD time since diagnosis, years	1.8 ±3.5	0.7 ±0.9	1.4 ±2.9
Mean ±SD *actual* anti-VEGF injections in prior 12 months*	**4.4 ±2.0**	**4.3 ±2.1**	**4.4 ±2.0**
Mean *annualized* injection rate, prior 12 months*	8.3	10.7	9.0

*Includes Day -7 aflibercept injection. BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; SD, standard deviation; VEGF, vascular endothelial growth factor.

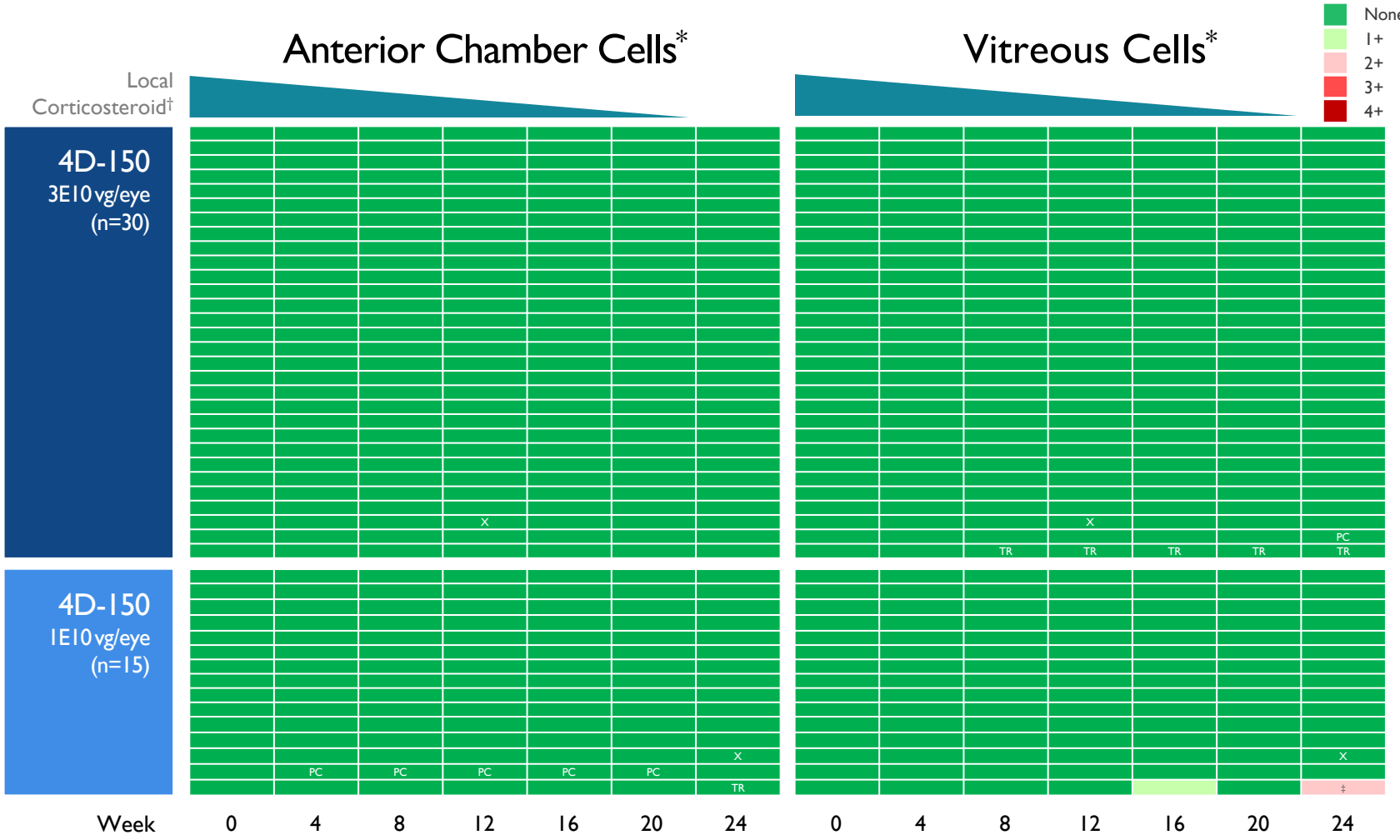
4D-150 Was Safe & Well Tolerated

- No 4D-150–related serious adverse events
- No hypotony, endophthalmitis, vasculitis, choroidal effusions, or retinal artery occlusions
- No significant inflammation reported in patients treated with 3E10 vg/eye dose and topical corticosteroid regimen (N=30)
  - All 30 patients completed local corticosteroid prophylactic regimen on schedule and did not resume

Data cutoff date, June 24, 2024.

No Significant Inflammation Observed in the Planned Phase 3 Dose Arm

Population Extension Cohort Scoring per Principal Investigator Through Week 24



3E10 vg/eye:

- **No** anterior chamber inflammation (30 of 30)
- **No** significant vitreous inflammation (30 of 30; trace vitreal cells noted in one patient)
- **All 30 patients completed steroid prophylaxis on schedule and did not resume**

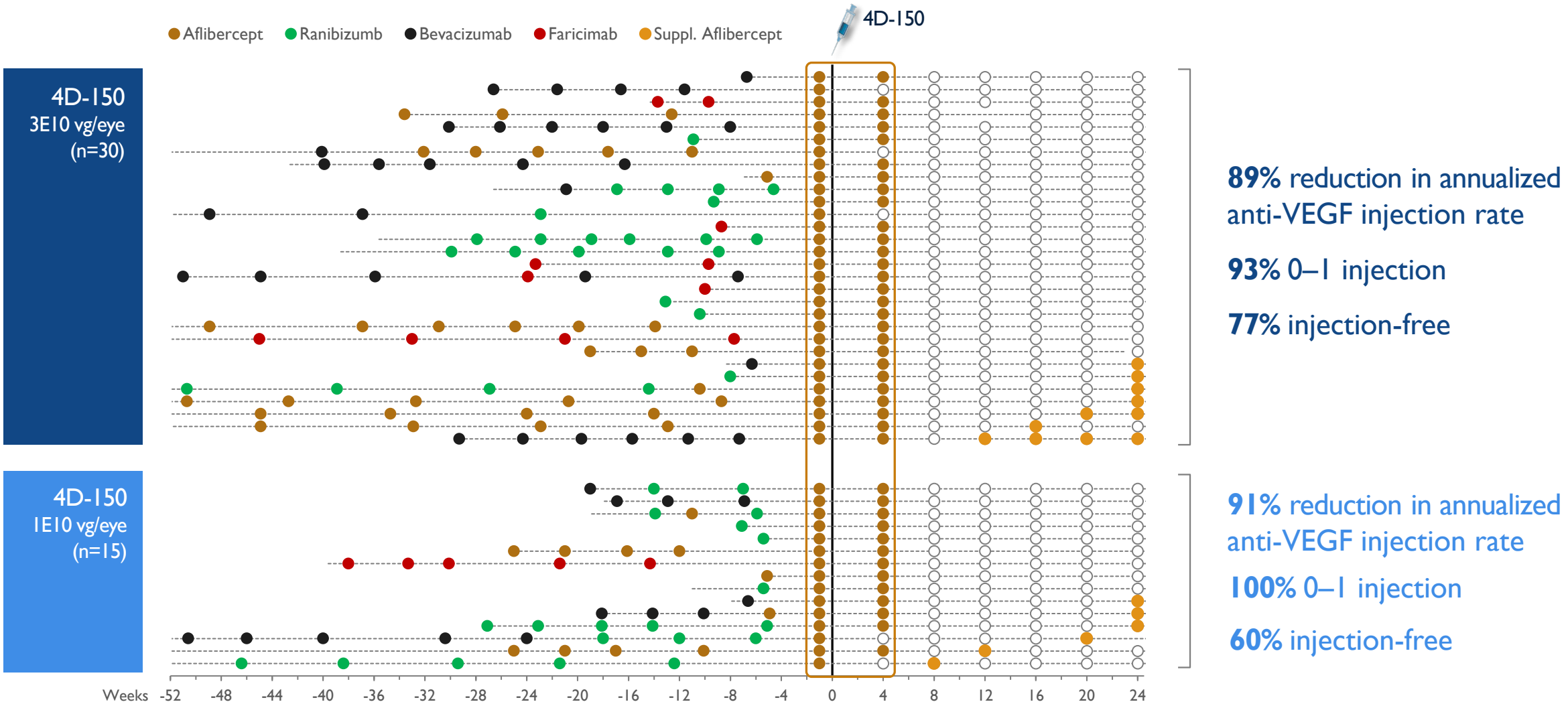
1E10 vg/eye:

- **No** significant anterior chamber inflammation
- **No** vitreous inflammation in 14 of 15 patients
  - One patient with mild to moderate inflammation (1 of 45 total, ~2%); vitreous cells also observed in untreated fellow eye

Data cutoff date, June 24, 2024. *SUN and NEI Scores for white blood cells. †Either difluprednate ophthalmic emulsion, triamcinolone acetonide with prednisolone taper, or dexamethasone. ‡Vitreous cells observed in non-injected contralateral eye at same visit; history of syphilis; assessed as 2+ by primary investigator next day after initial assessment by sub-investigator as 3+. NEI, National Eye Institute; PC, pigmented cells; SUN, Standardization of Uveitis Nomenclature; TR=trace; X=missed visit.

Robust Anti-VEGF Treatment Burden Reduction Observed through 24 Weeks

Patients Receiving Planned Phase 3 Dose of 3E10: 77% Injection-Free & 93% Had 0-1 Injection



89% reduction in annualized anti-VEGF injection rate

93% 0–1 injection

77% injection-free

91% reduction in annualized anti-VEGF injection rate

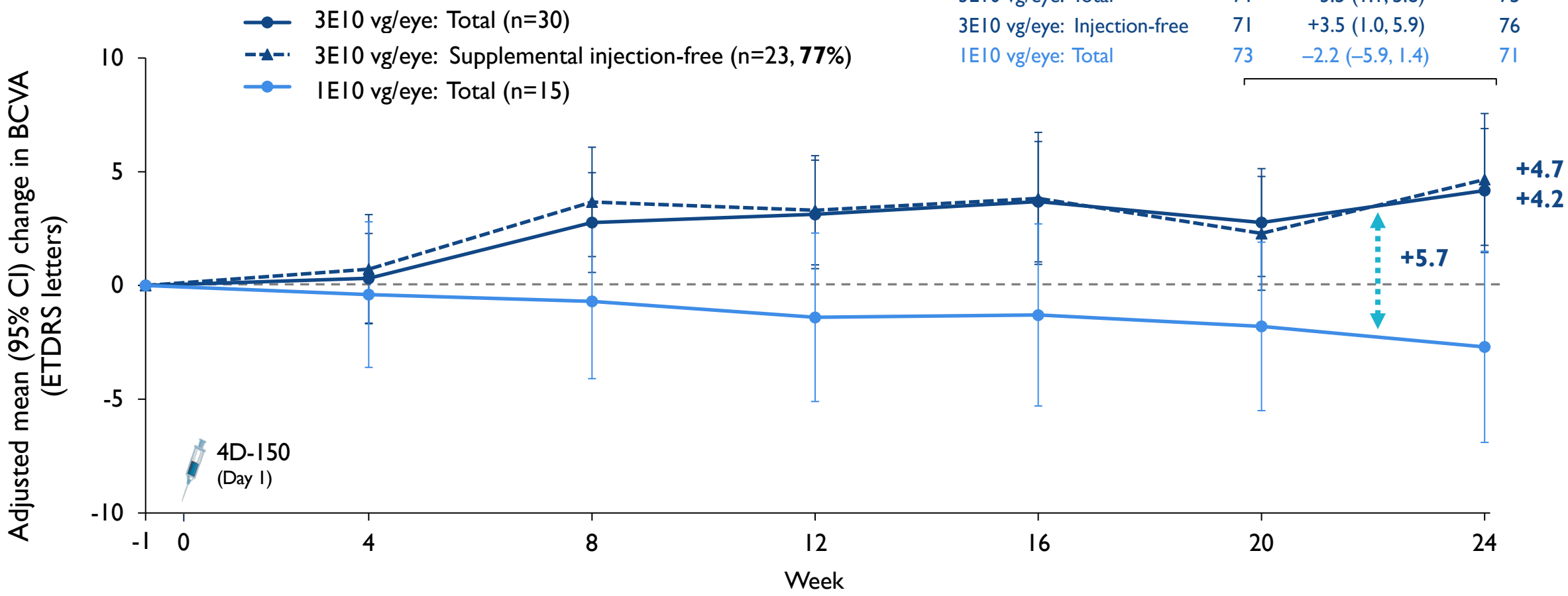
100% 0–1 injection

60% injection-free

Data cutoff date, June 24, 2024. *Scheduled on-study aflibercept injection administered at Weeks -1 and 4; post-4D-150 annualized anti-VEGF injection rate calculated from Week 4 onward (time of last loading aflibercept dose)

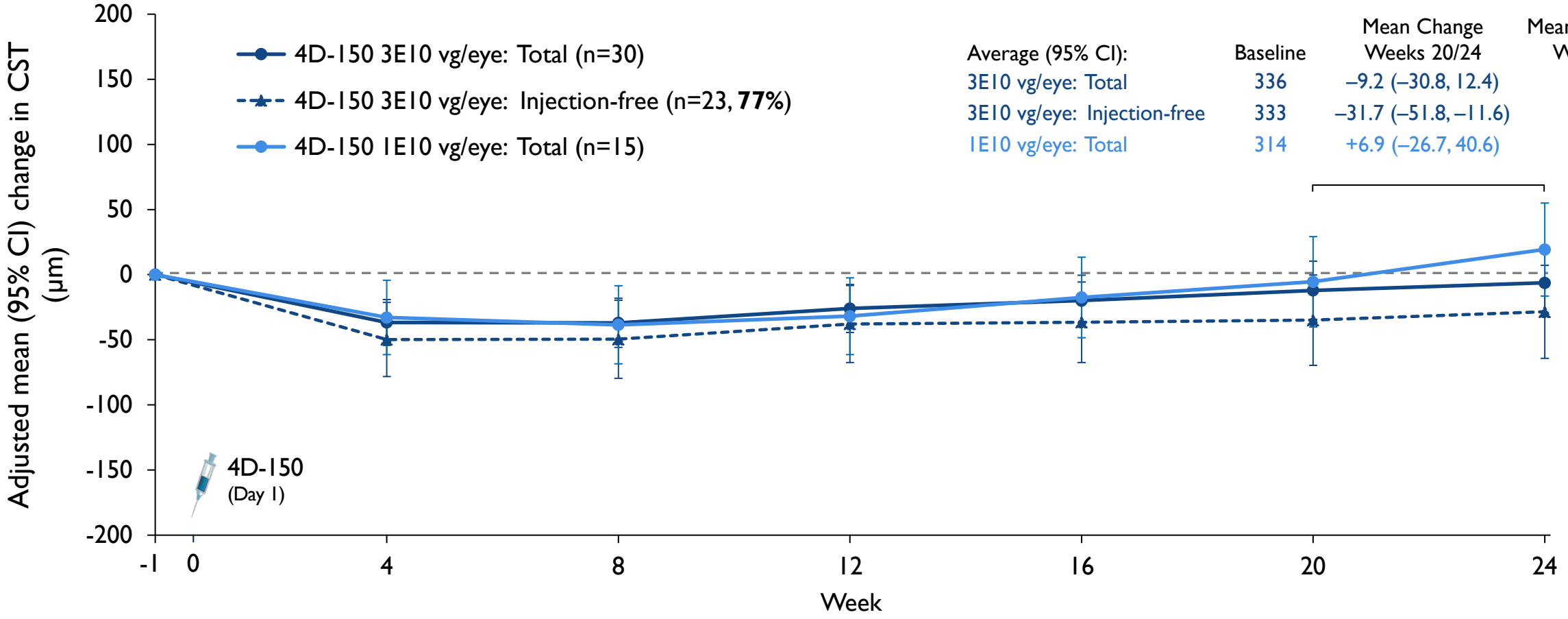
Planned Phase 3 Dose Demonstrated Higher BCVA Gains That Were Maintained Over Time, Including in Injection-Free Patients

Average (95% CI):	Baseline	Mean Change Weeks 20/24	Mean Absolute Week 24
3E10 vg/eye: Total	71	+3.5 (1.1, 5.8)	75
3E10 vg/eye: Injection-free	71	+3.5 (1.0, 5.9)	76
1E10 vg/eye: Total	73	–2.2 (–5.9, 1.4)	71



Data cutoff date, June 24, 2024.
Adjusted mean and 95% CI estimated from a mixed–effect model for repeated measures (MMRM) including observed data (weeks 4-24) without imputing missing values.
CI, confidence interval; ETDRS, Early Treatment Diabetic Retinopathy Study.

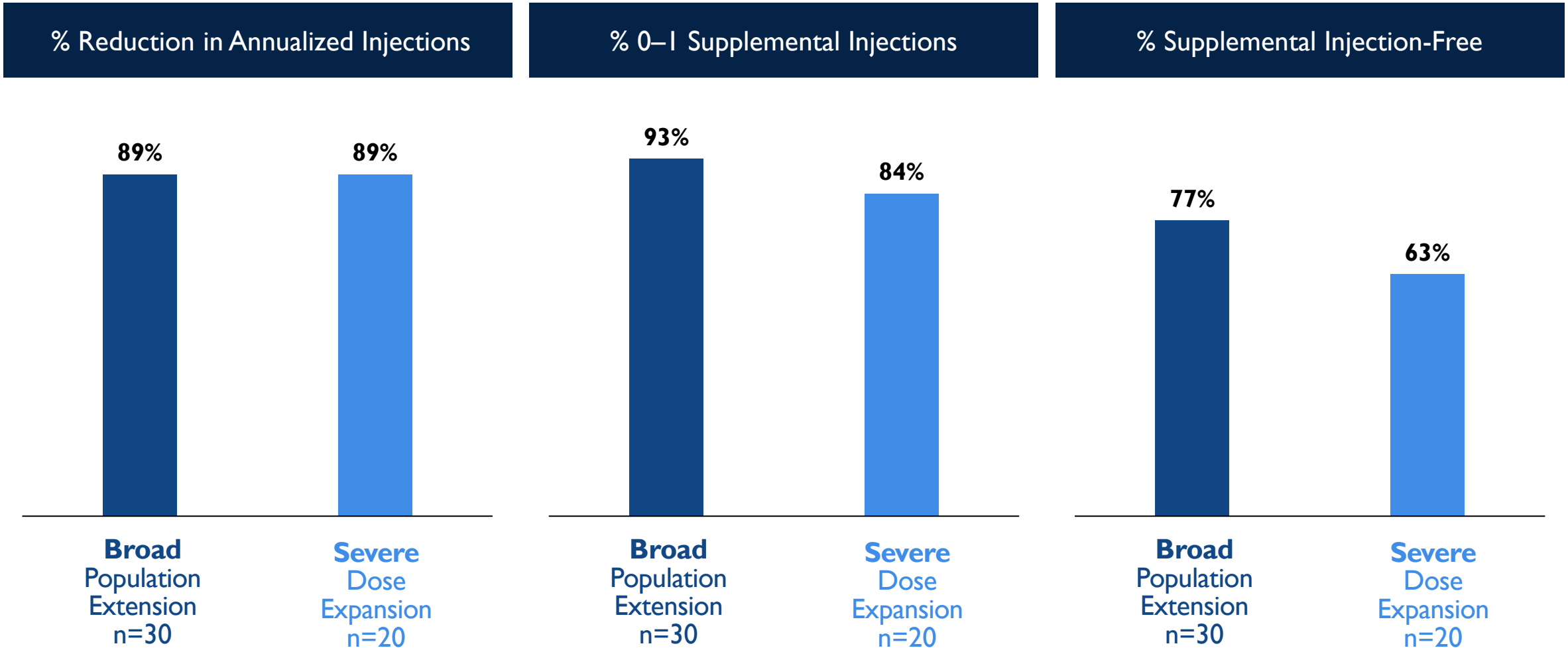
Planned Phase 3 Dose Demonstrated Sustained & Greater Anatomic Control Without Fluctuations, Including in Injection-Free Patients



Average (95% CI):	Baseline	Mean Change Weeks 20/24	Mean Absolute Week 24
3E10 vg/eye: Total	336	–9.2 (–30.8, 12.4)	326
3E10 vg/eye: Injection-free	333	–31.7 (–51.8, –11.6)	308
1E10 vg/eye: Total	314	+6.9 (–26.7, 40.6)	334

Data cutoff date, June 24, 2024.
Adjusted mean and 95% CI estimated from a mixed–effect model for repeated measures (MMRM) including observed data (weeks 4-24) without imputing missing values.
CI, confidence interval; CST, central subfield thickness.

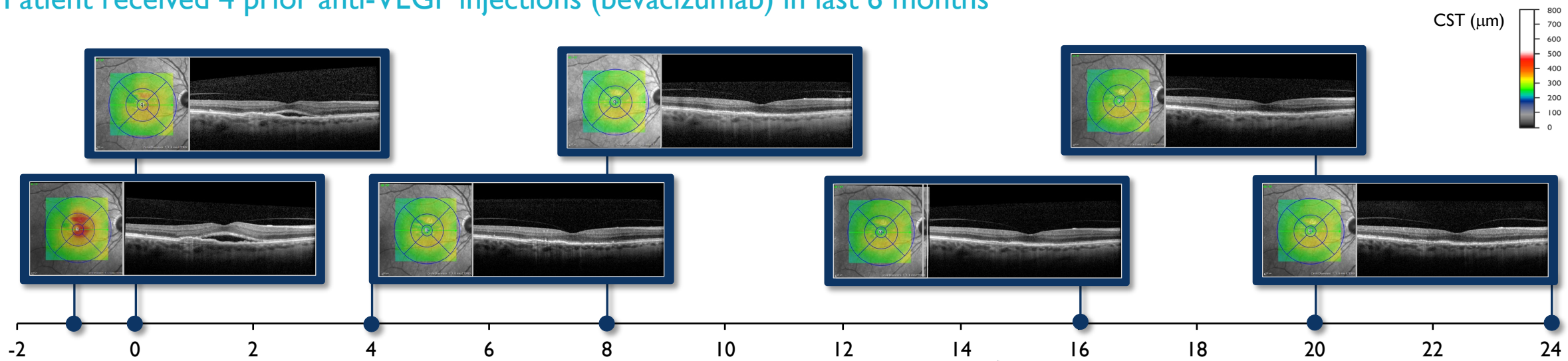
Robust & Consistent Reduction in Treatment Burden Observed Across All Wet AMD Populations Studied at the 3E10 vg/eye Dose Through 24 Weeks

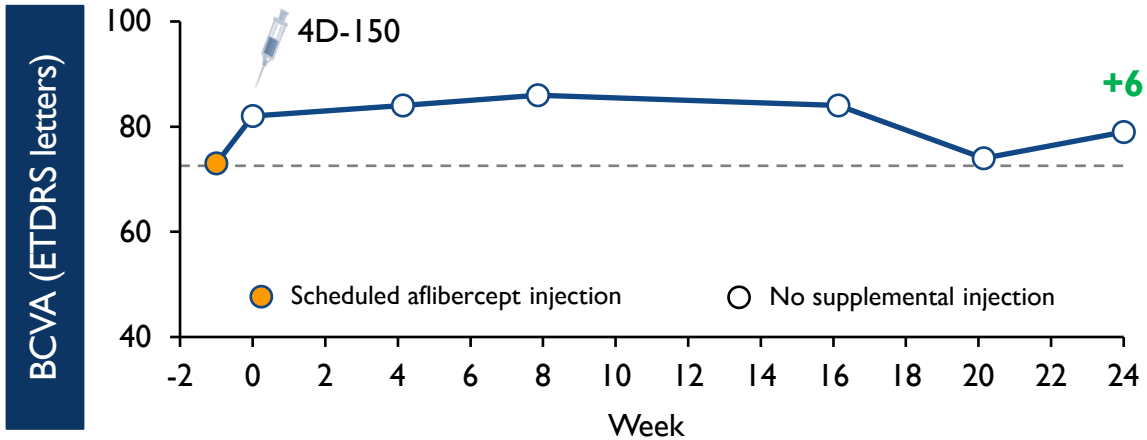


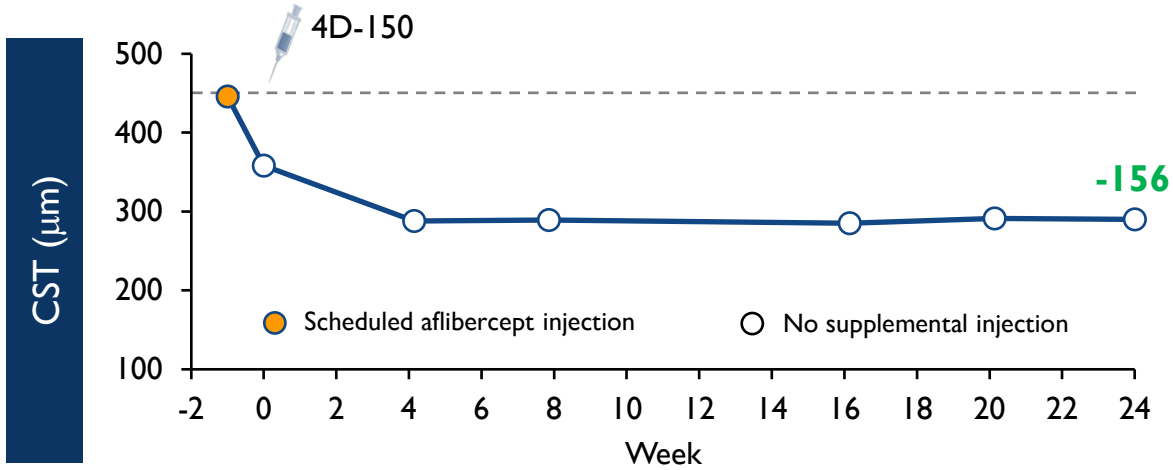
Data cutoff dates: Dose Expansion, January 19, 2024; Population Extension, June 24, 2024.

Patient Case Highlighting the Benefit of a Single Injection of 4D-150 3E10: BCVA & CST Improved and Maintained Over Time and Injection-free

Patient received 4 prior anti-VEGF injections (bevacizumab) in last 6 months

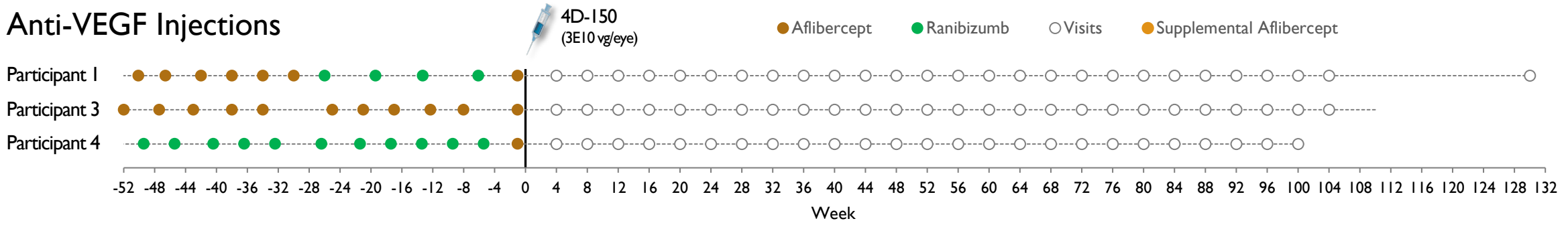


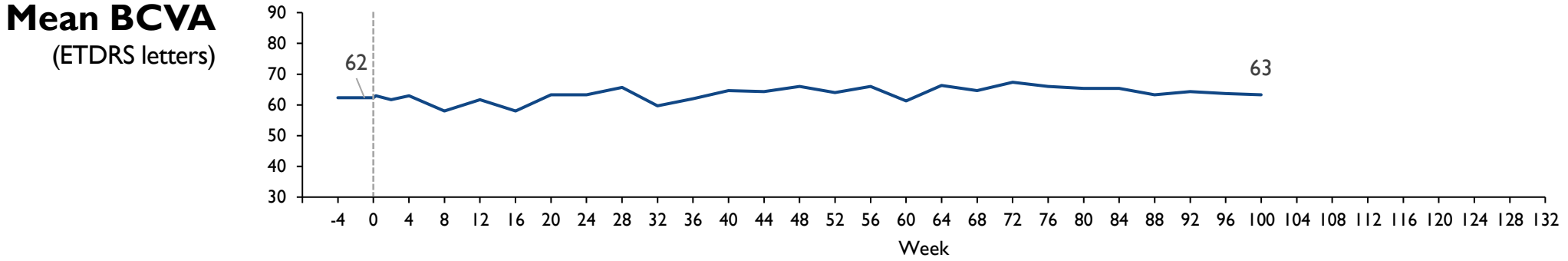


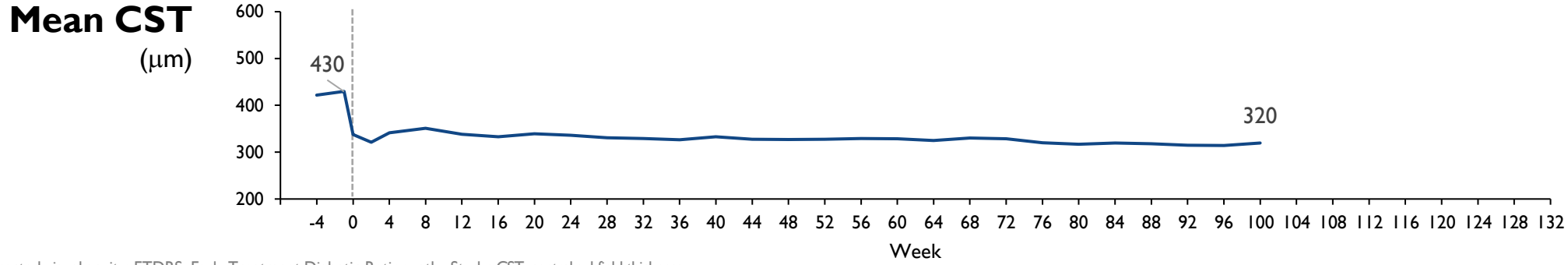


Data cutoff date, June 24, 2024. BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; CST, central subfield thickness.

3 Patients from Phase 1 Treated with 4D-150 3E10 vg/eye Remain Injection-free Through ~2 to 2.5 Years







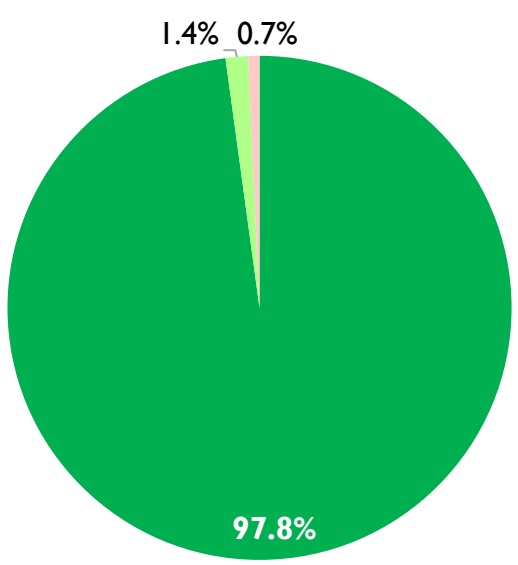
Data cutoff date, June 24, 2024.
Baseline = Week -1. BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; CST, central subfield thickness.

4D-150 Continues to be Safe and Well Tolerated in Wet AMD & DME (N=139)

No Significant Inflammation in Patients Treated with Planned Phase 3 Dose & Durezol Regimen

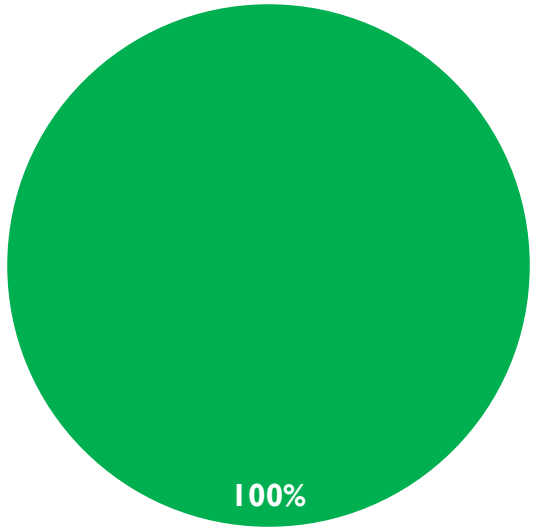
Highest SUN/NEI Score Observed*

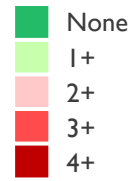
All Doses & Steroid Regimens Tested†
(5E9 to 3E10 vg/eye, N=139)



Includes 22 DME patients (follow-up ≤36 weeks): No inflammation, completed topical steroid prophylactic regimen on schedule and did not resume

Planned Phase 3 Dose & Durezol Regimen (3E10 vg/eye, N=51)





No recurrent inflammation post local steroid taper

No 4D-150–related hypotony, endophthalmitis, vasculitis, choroidal effusions or retinal artery occlusions observed to date

Data cutoff date, June 24, 2024.
*Duration of follow up, ≤2.5 years. NEI, National Eye Institute; SUN, Standardization of Uveitis Nomenclature. †N=29 3E10 vg/eye patients received one of the following: (a) triamcinolone acetonide with prednisolone taper or (b) dexamethasone.

Planned 4D-150 Phase 3 Registrational Trials in Wet AMD

Preliminary Phase 3 Design

- **Primary Endpoint:** Noninferiority (BCVA) 4D-150 **3E10 vg/eye** **vs.** aflibercept 2mg Q8 weeks
- **Study Size:** ~450 patients per study, two studies
- **Target Population:** **broad** wet AMD disease activity

FDA RMAT & EMA PRIME Designations

- **Increased collaboration** between the FDA & EMA with opportunity for **expedited product development**
- **Plan to have an aligned global development pathway**

Final Phase 3 design update expected September 2024
1st Phase 3 initiation expected Q1 2025

Such designations do not guarantee faster approval or approval of the product

Key Takeaways

4D-150 Program in Wet AMD and DME

- **CONTINUES TO BE SAFE & WELL-TOLERATED:**
  In Both Wet AMD & DME
- **STRONG CLINICAL ACTIVITY DEMONSTRATED IN BROAD WET AMD DISEASE ACTIVITY POPULATION:**
  Planned Phase 3 Population
- **DEMONSTRATED DURABLE CLINICAL ACTIVITY**
- **PROVIDES FURTHER SUPPORT FOR PLANNED WET AMD PHASE 3 PROGRAM**
- **NEXT STEPS:**
  - **PHASE 3 WET AMD PROGRAM UPDATE:** Expect to share final study design in **September 2024** and initiate first trial in **Q1 2025**
  - **PHASE 2 PRISM WET AMD 52-WEEK DATA:** Expect update from both Dose Expansion & Population Extension cohorts in **February 2025**
  - **PHASE 2 SPECTRA DME 24-WEEK DATA:** Expect update from Part 1 (N=22) in **Q4 2024**
- **$589M CASH* AS OF MARCH 31, 2024; RUNWAY INTO H1 2027**

Data cutoff date, June 24, 2024.
*Includes cash equivalents and marketable securities

THANK YOU

5858 Horton Street, Suite 455 | Emeryville, California 94608

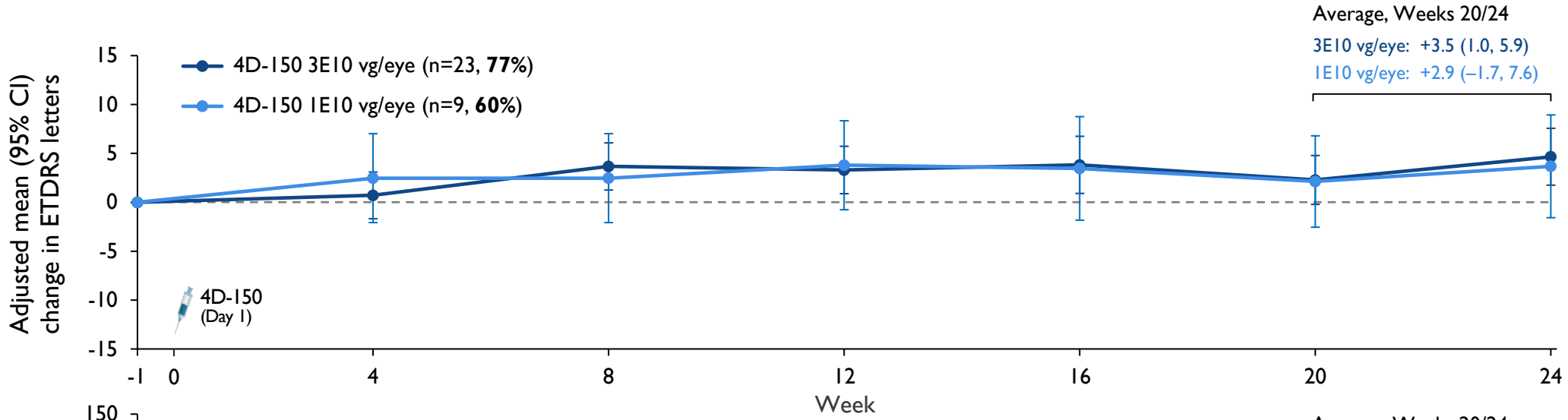
(510) 505-2680 | Investor.Relations@4DMT.com

IR.4DMT.com | LinkedIn

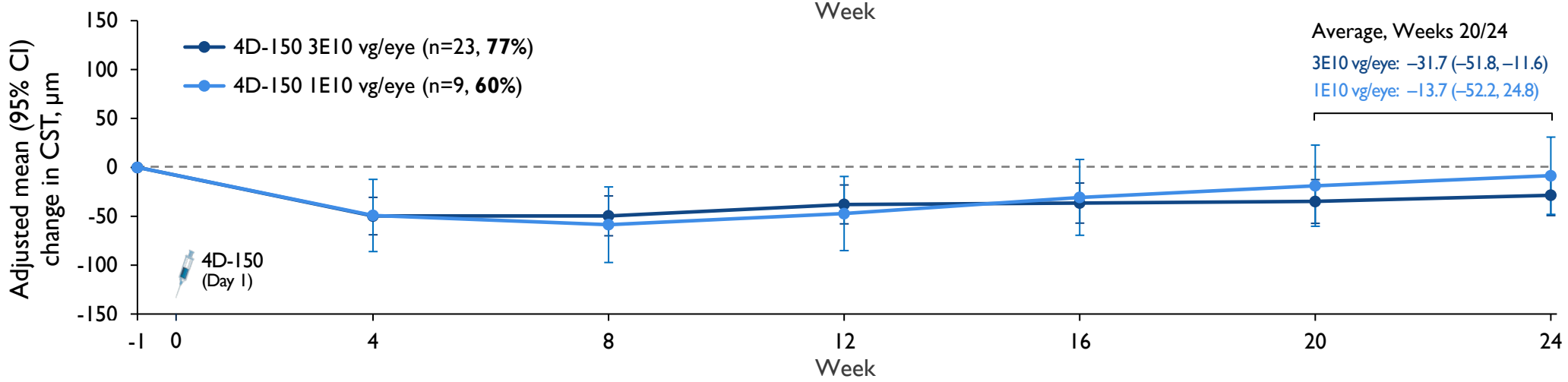
Supplemental Injection-free Participants

3E10 vg/eye: Durable Improvement in Visual Acuity and Sustained Reduction in CST

BCVA



CST



Data cutoff, June 24, 2024. Adjusted mean, difference in adjusted mean, and 95% CI estimated from a mixed–effect model for repeated measures (MMRM) including observed data (weeks 4-24) without imputing missing values. BCVA, best corrected visual acuity; CI, confidence interval; CST, central retina thickness; ETDRS, Early Treatment Diabetic Retinopathy Study.