Intravitreal 4D-150

ASRS Data Discussion

PRISM

July 2024

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4D-150 Population Extension Data Discussion Points

1. **Addition of Week 4 loading dose to protocol**
2. **Wet AMD is a heterogenous patient population**
3. **CST curve**
4. **Long term durability update expected in September at a medical conference (52-landmark guidance on Dose Expansion & Population Extension Cohorts in February 2025 remains unchanged)**
5. **Consistency of Safety Data**

Data cutoff date, June 24, 2024.

Loading Doses for Phase 3-Ready Long-Acting wet AMD Agents: 2nd Anti-VEGF Loading Dose as Phase 3 Approaches is **Industry Standard**

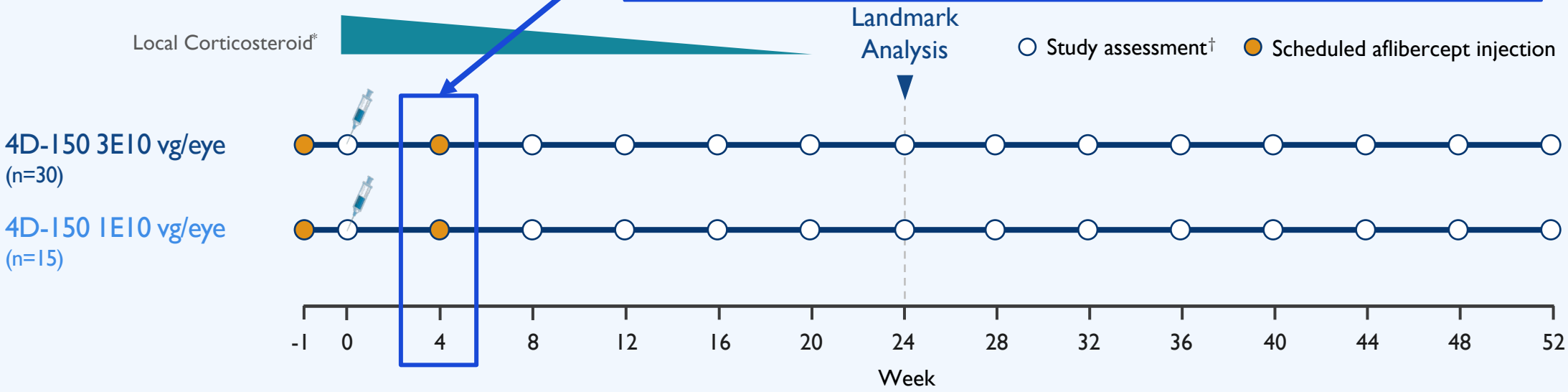
*Dose after Study Treatment

Asset (Mechanism)	Study Name	Phase	Total Loading Doses
ABBV-RGX-314 SR Gene Therapy	ATMOSPHERE/ASCENT	3	**3***
ABBV-RGX-314 SCS Gene Therapy	AAVIATE	2	**3***
AXPAXLI TKI implant	SOL-1	3	**3**
	SOL-R	3	**5**
DURAVYU TKI implant	DAVIO2	2	**3**
	LUGANO/ LUCIA	3	**3**
4D-150 IVT Gene Therapy	PRISM	2	**2***

Phase 2 Population Extension Cohort Treatment Schema & Endpoints

Population Extension Cohort Study Schema

Design Finalized ~Mid-2023:
1) Patient safety during gene expression ramp-up (~1-8 weeks to maximize)
2) Similar to expected Phase 3 design (and precedents)



Key Endpoints

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

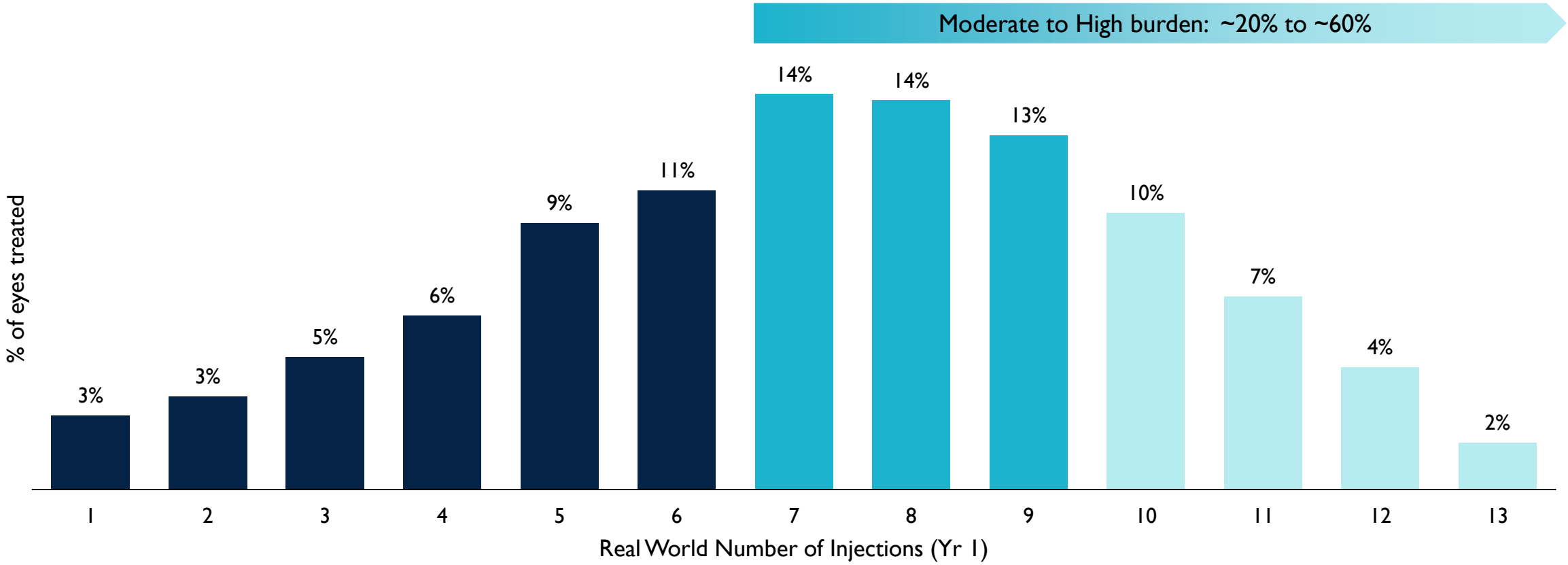
Supplemental Injection Criteria

- 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.

Wet AMD Patients is a **Heterogenous** Patient Population with Varying Anti-VEGF Needs

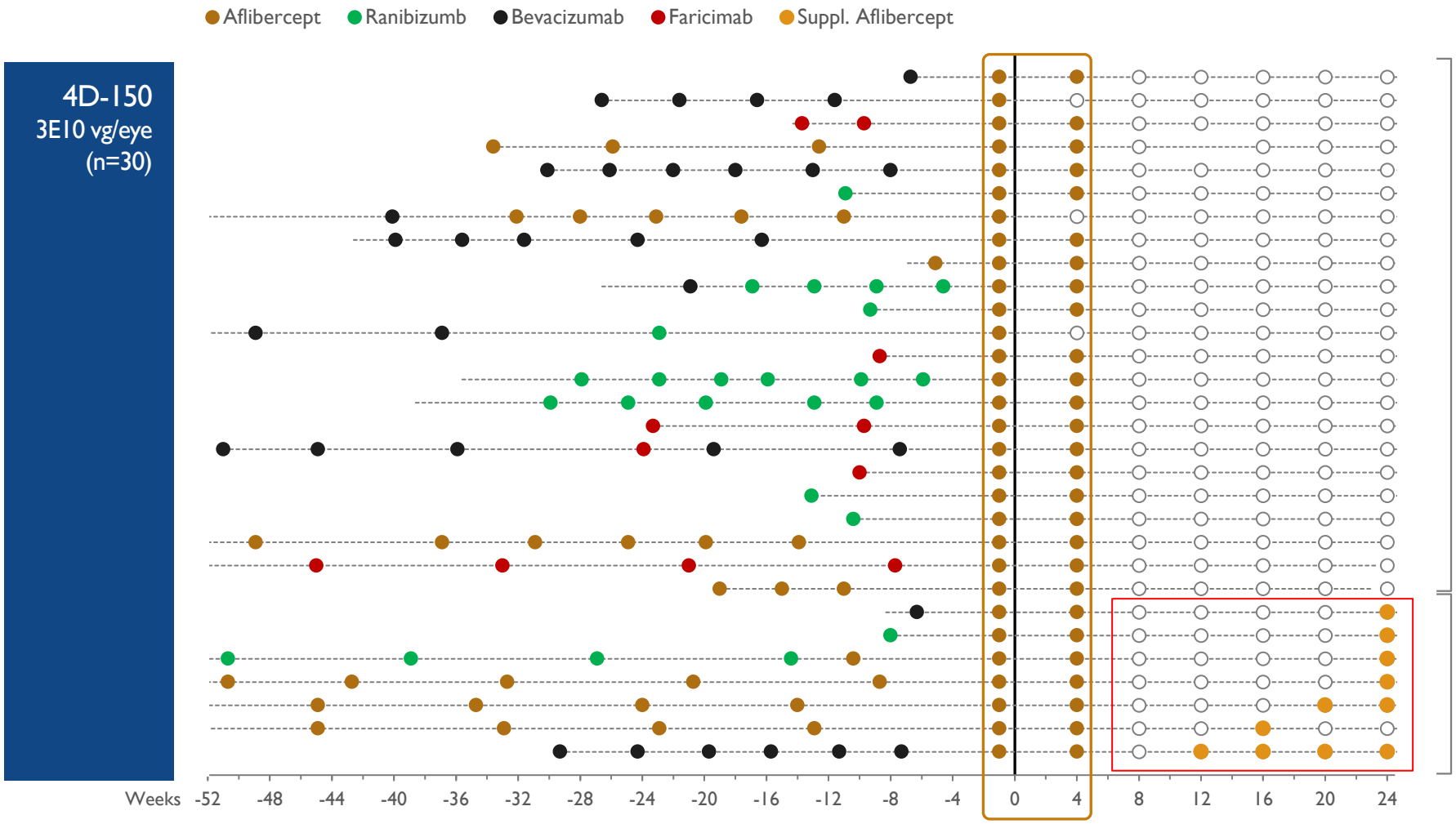
Real World Injection Frequency[1]



1. Adapted from Ciulla et al: Ophthalmol Retina. 2020 Jan;4(1):19-30.; n = 49,485 eye.

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



Overall:

89% reduction in annualized anti-VEGF injection rate

93% 0–1 injection

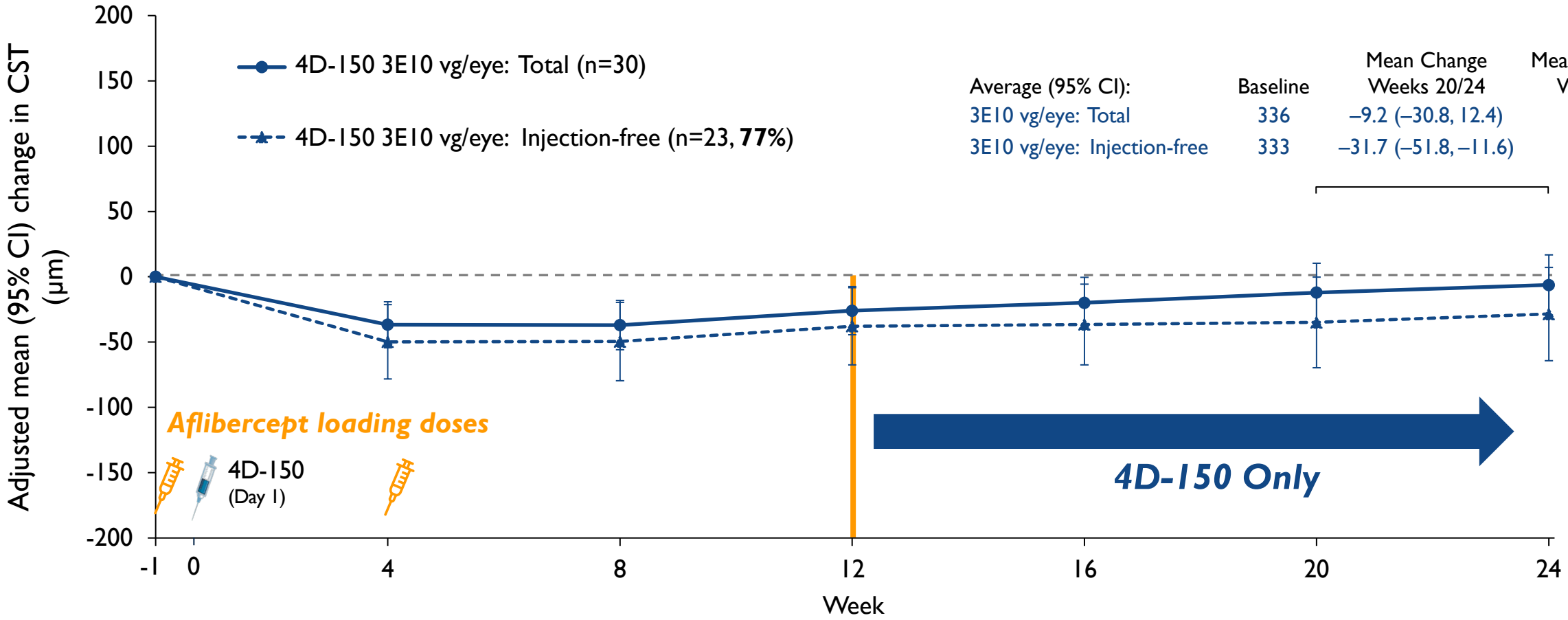
77% injection-free

23% injection (+)

9 of 11 (82%) "Recently Dx" patients were 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 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

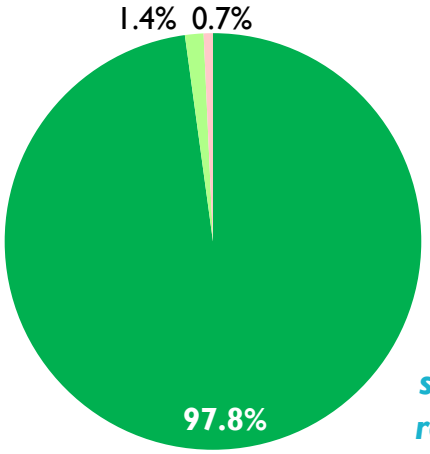
Data cutoff date, June 24, 2024.
Adjusted mean and 95% CI estimated from a mixed–effect model for repeated measures (MMRM) including observed data (weeks 4-24) without imputing missing values.
CI, confidence interval; CST, central subfield thickness.

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

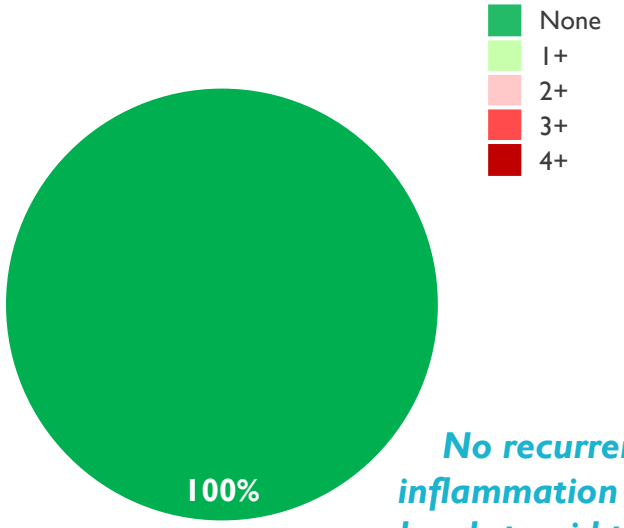
Highest SUN/NEI Score Observed*

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



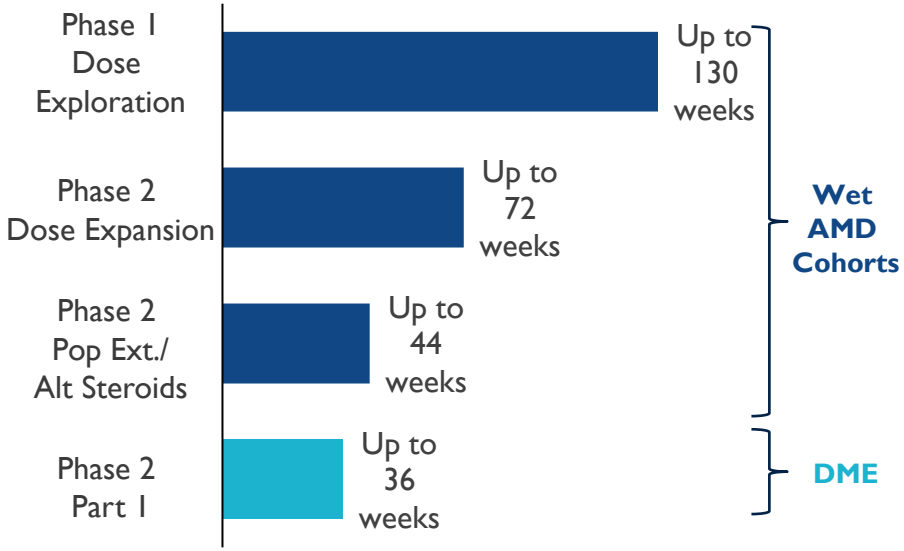
Includes DME (N=22): No inflammation, completed topical steroid prophylactic regimen on schedule and did not resume

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



No recurrent inflammation post local steroid taper

Range of Maximum Follow-up†
(5E9 to 3E10 vg/eye, N=139)



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.

Key Highlights from 4D-150 Interim Data Presented at ASRS

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

2. **DEMONSTRATED DURABLE CLINICAL ACTIVITY**

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

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

Data cutoff date, June 24, 2024.

THANK YOU

5858 Horton Street, Suite 455 | Emeryville, California 94608

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

IR.4DMT.com | LinkedIn