Jefferies 2025 Healthcare Conference

Corporate Presentation

June 2025

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4D-150 Key Updates

4FRONT-1 Wet AMD Phase 3 enrollment is well underway

- *Over 50 clinical trial sites activated to date*

4D-150 is the <u>first</u> known genetic medicine to receive RMAT designation for both wet AMD and DME

RMAT: Regenerative Medicine Advanced Therapy designation

4D-150: Phase 3 Therapeutic Designed to Disrupt the Global Market for Retinal Vascular Diseases & Improve Patient Outcomes

Multi-Billion Dollar Annual Opportunity	**$17B+ and growing global market** Leveraging expression of validated blockbuster aflibercept
Addresses Primary Clinical Unmet Need	**Backbone therapy with multi-year durability**: Foundational therapy with paradigm-shifting treatment burden reduction & vision preservation
Favorable Safety Profile	**Predictable long-term safety**: Clinically significant IOI rate in-line with aflibercept bolus (remains standard-of-care, >64M eyes treated)
Ease of Clinical & Commercial Adoption	**Single IVT injection**: Seamless integration into retina clinic practice flow and **buy & bill reimbursement model**
Topline Data from wet AMD Pivotal Trials in 2027	Readouts from both Phase 3 studies in 4FRONT global registration program **expected in H2 2027**

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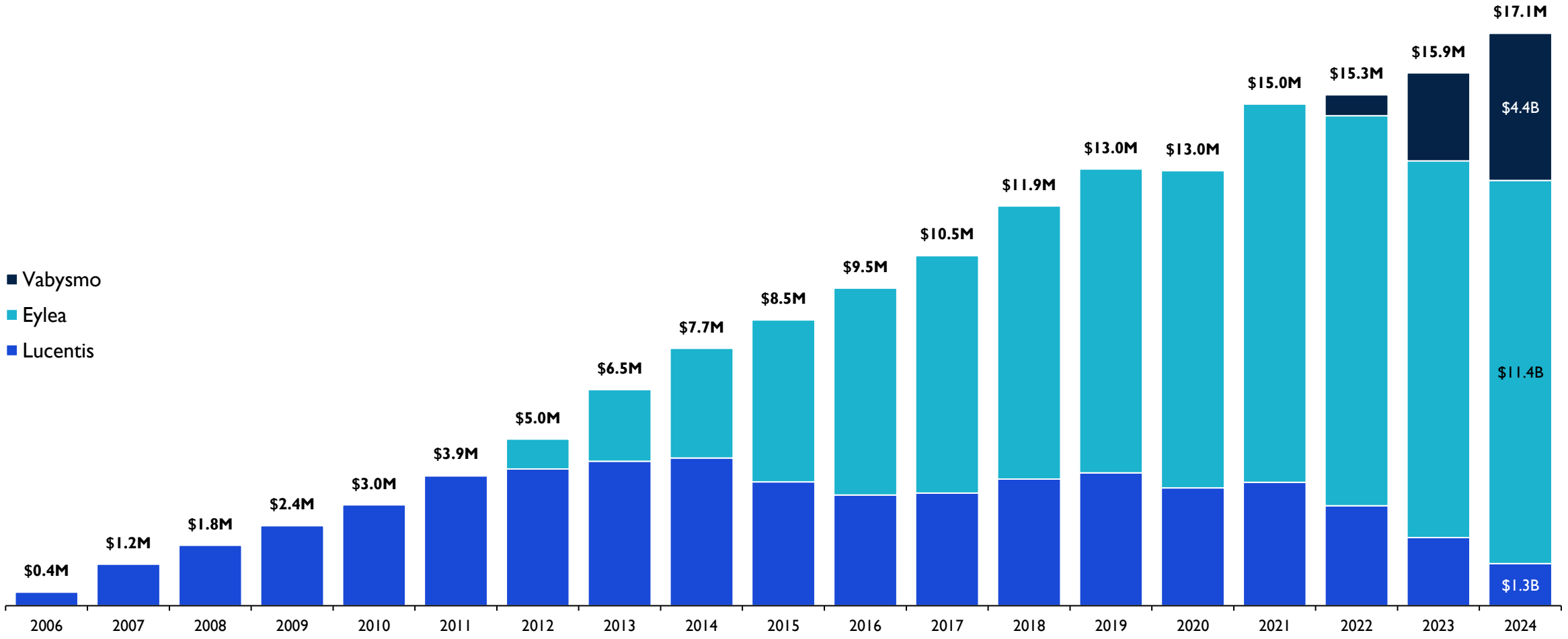
Total Branded Anti-VEGF Market Continues to Grow with Share Driven by Incremental Durability Improvements: Aflibercept Remains Market Leader

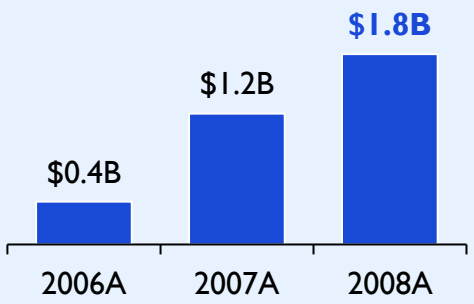


Source: EvaluatePharma Historical and Consensus Estimates as of 3/7/2025.
Note: Product sales reflect sales across manufacturers; Eylea sales include both Eylea and Eylea HD formulations

Incremental Durability Improvements for Bolus Anti-VEGFs Have Resulted in Accelerating Launch Performance

LUCENTIS® RANIBIZUMAB INJECTION

Durability: ~30 Days[1]

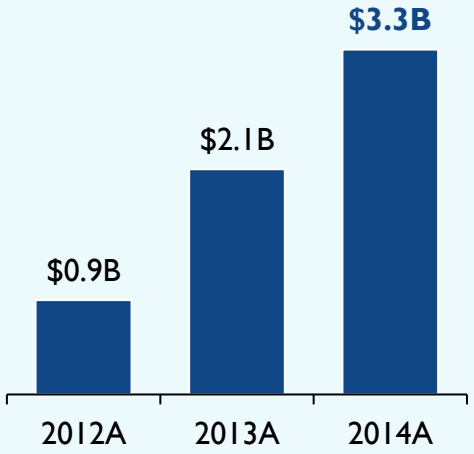


EYLEA® (aflibercept) Injection For Intravitreal Injection

Durability: ~44 Days[2]

Burden Reduction vs. Lucentis:

~32%

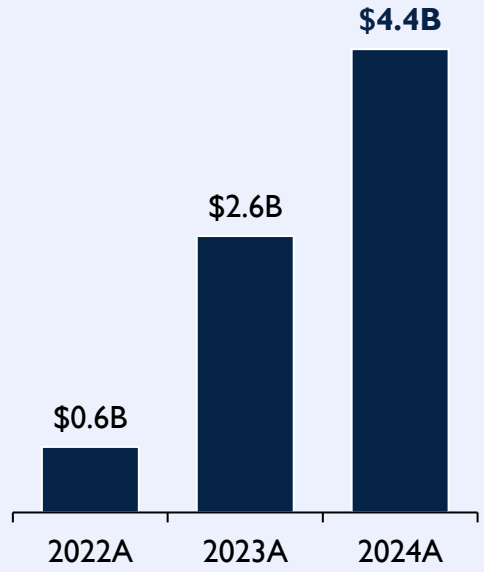


VABYSMO™ faricimab-svoa injection 6 mg

Durability: ~57 Days[2]

Burden Reduction vs. Eylea:

~23%



1. Lucentis package insert; 2. Real-World Evidence (TRUCKEE Study). Injection Burden Reduction vs. prior therapy implied based on difference calculated annual injections based on TRUCKEE durability.

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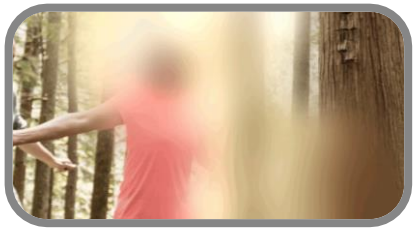
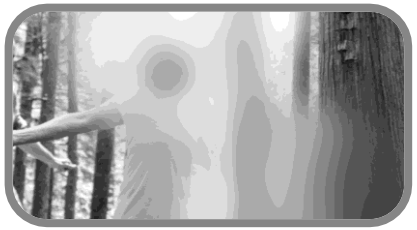
Short Durability of Wet AMD Standard of Care Leads to Poor Vison Outcomes

	Durability	Impact on Retinal Anatomy	Vision
Current Standard of Care	Bolus loading doses, followed by… 4 weeks 4-8 weeks 8 weeks 8-12 weeks 8-12-16 weeks 8-16 weeks	Central Retinal Thickness *Associated with **greater vision loss**[1] & **fibrosis**[2]*	

[1]Guo et al. *Ophthal Res* 2023; 66:406-12. [2]Evans et al. *JAMA Ophtalmol* 2020;138:1043-51.

Markedly Improving Outcomes with a Multi-year Backbone Therapy

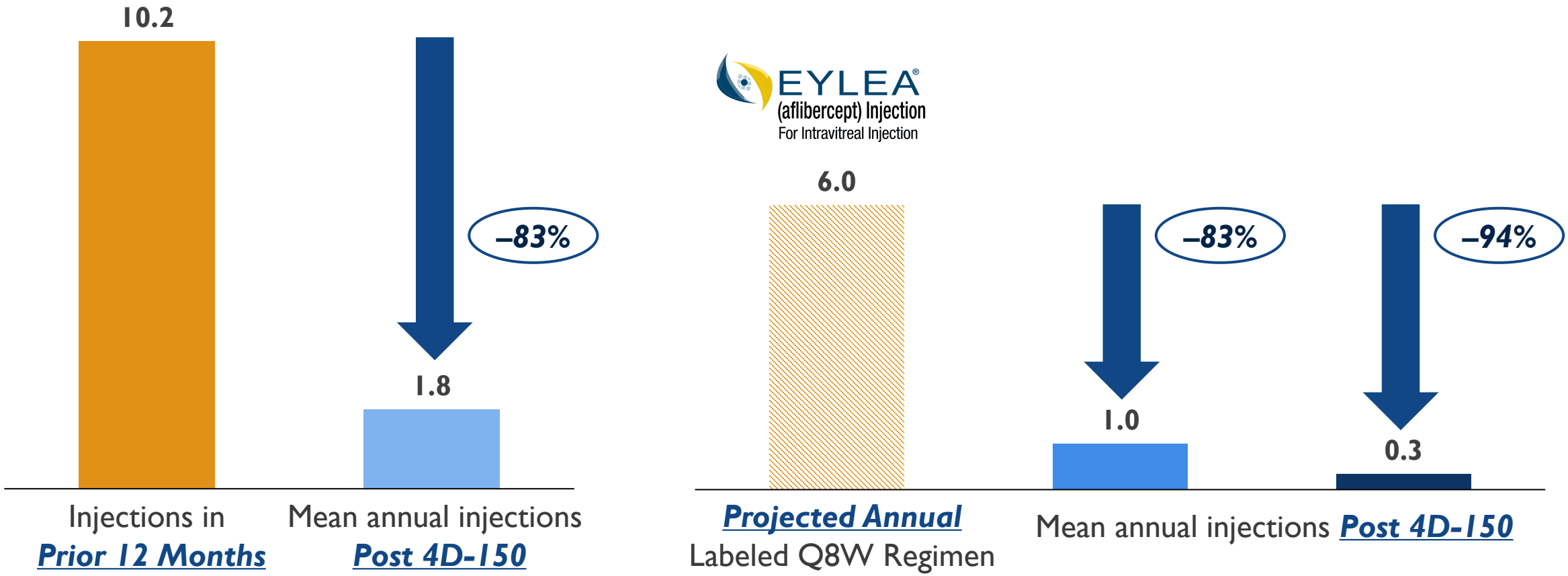
	Durability	Impact on Retinal Anatomy	Vision
Current Standard of Care	Bolus loading doses, followed by… 4 weeks 4-8 weeks 8 weeks 8-12 weeks 8-12-16 weeks 8-16 weeks	Central Retinal Thickness *Associated with **greater vision loss**[1] & **fibrosis**[2]*	
Solution: 4D-150 Backbone Therapy	Bolus loading doses, followed by… **4D-150** ***Multiple years***	**Goal Post–4D-150** *Bolus supplement as needed* Central Retinal Thickness *Low retinal variability to **preserve vision***	

[1]Guo et al. *Ophthal Res* 2023; 66:406-12. [2]Evans et al. *JAMA Ophtalmol* 2020;138:1043-51.

4D-150 Demonstrated Transformative Treatment Burden Reduction & Durability in Multiple Wet AMD Patient Populations

Phase 1/2a Population: Severe, Recalcitrant

Phase 2b Populations: *Broad* *Recently Diagnosed*



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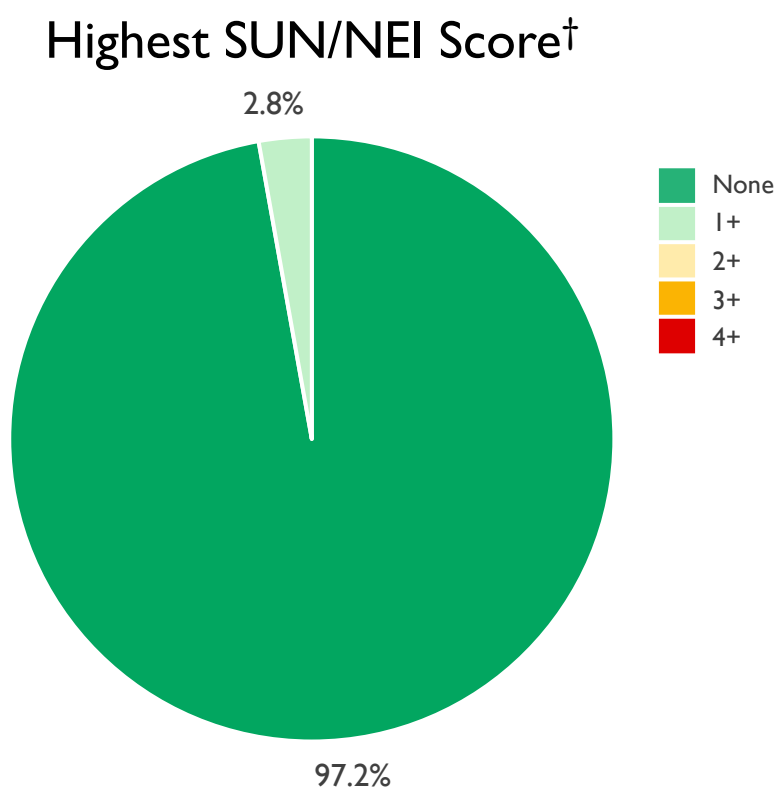
4D-150 Has Been Well Tolerated in Broad Wet AMD Population: Safety In-Line With Aflibercept Protein to Date

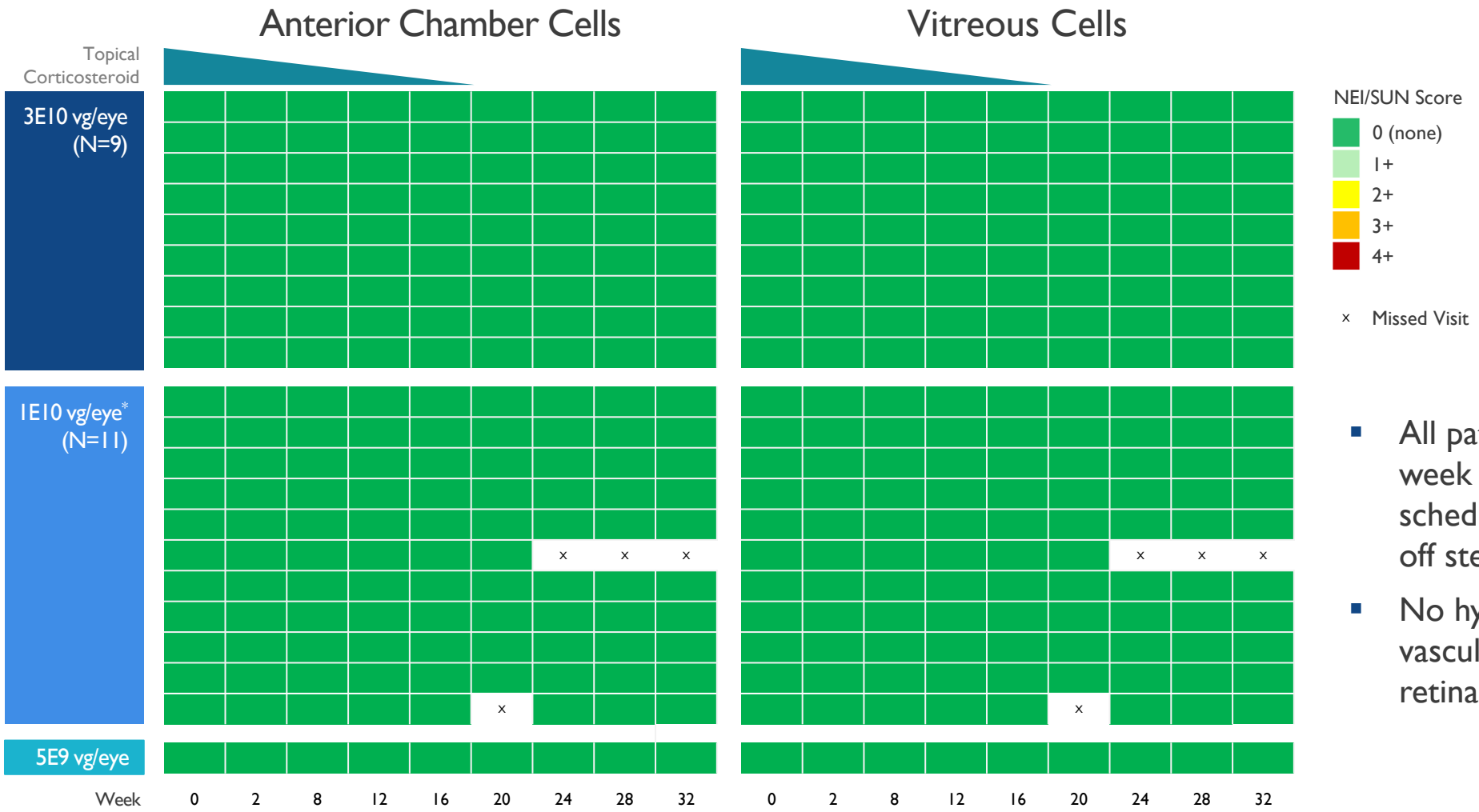
- No 4D-150–related serious adverse events
- No 4D-150–related hypotony, endophthalmitis, occlusive/non-occlusive retinal vasculitis, or choroidal effusions
- Treatment-related **1+** vitreous cells at a single timepoint observed in 2 of 71 (**2.8%**)
- **99%** (70 of 71) completed prophylactic topical steroid taper on schedule
- **99%** (70 of 71) remain completely off steroids

4D-150 3E10 vg/eye (N=71)*



*Duration of follow up, ≤3 years. †4D-150–related.
VC, Vitreous cell; NEI, National Eye Institute; SUN, Standardization of Uveitis Nomenclature.

4D-150 Has Been Well Tolerated in DME Patients: No Intraocular Inflammation at Any Timepoint at Any Dose Level



- All patients completed the 16-week topical steroid taper on schedule and remained completely off steroids
- No hypotony, endophthalmitis, vasculitis, choroidal effusions or retinal artery occlusions

Data cutoff date, December 13, 2024. *Excludes patient with early termination due to death. The subject had a prior history of hepatic cirrhosis and died prior to any study visits due to liver failure (assessed by PI as unrelated to 4D-150).
NEI, National Eye Institute; SUN, Standardization of Uveitis Nomenclature; X, missed visit. One of the subjects missed three consecutive study visits due to recovery from foot surgery.

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Potential to Improve Economic Value for Payors and Clinics with 4D-150

Payors

- **Adherence by design**, leading to long term preservation of vision
- **Reduction in treatment burden**, leading to patient freedom and quality-of-life
- **Preservation of vision**, leading to socio-economic benefit
- **Low expected COGS**, leading to pricing flexibility

Clinics

- **IVT dosing with seamlessly adoption** into current practice flow
- **Seamless integration into current distribution networks & clinic storage**
- **Improved cash flow & clinic capacity**, esp with Buy & Bill reimbursement model

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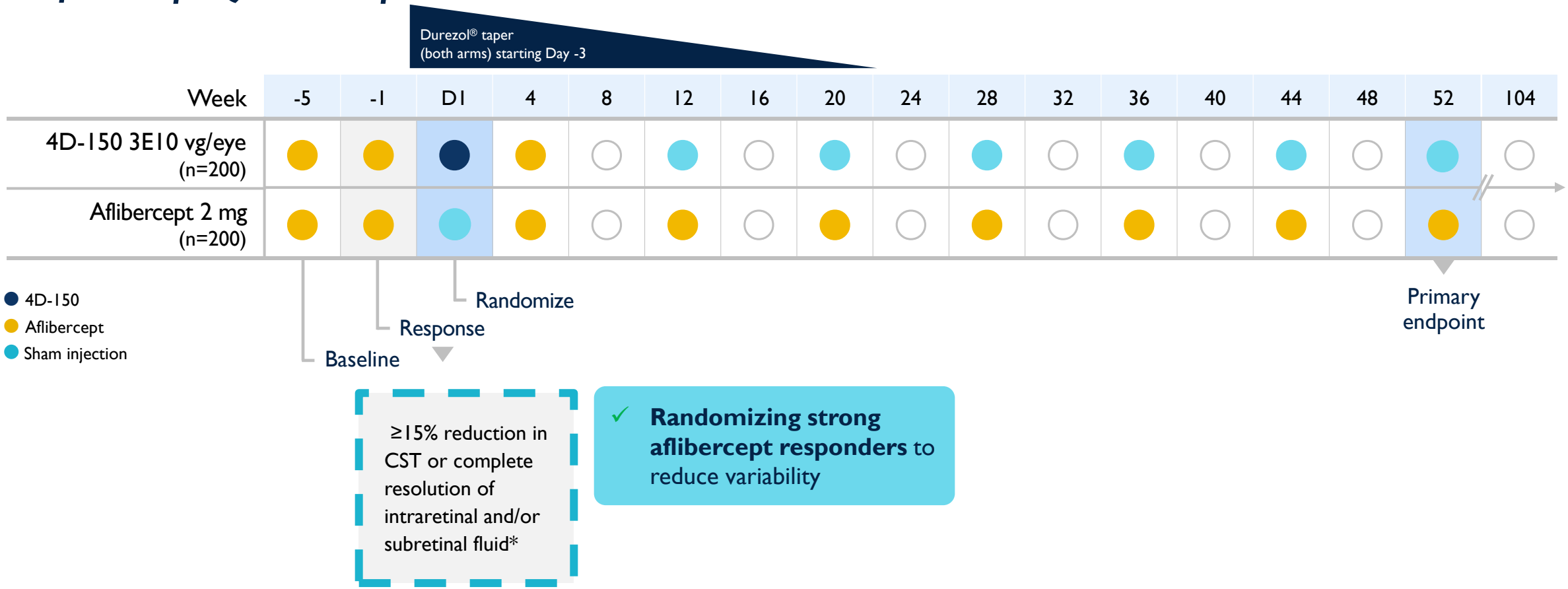
Global 4FRONT Phase 3 Trial Design

Noninferiority Trials to Enable Global Registration in Wet AMD

Global, Multicenter, Randomized, Double Masked, Aflibercept Q8W Comparator Controlled Studies



*Determined by SD-OCT and confirmed by an independent Reading Center. †PI discretion not allowed.

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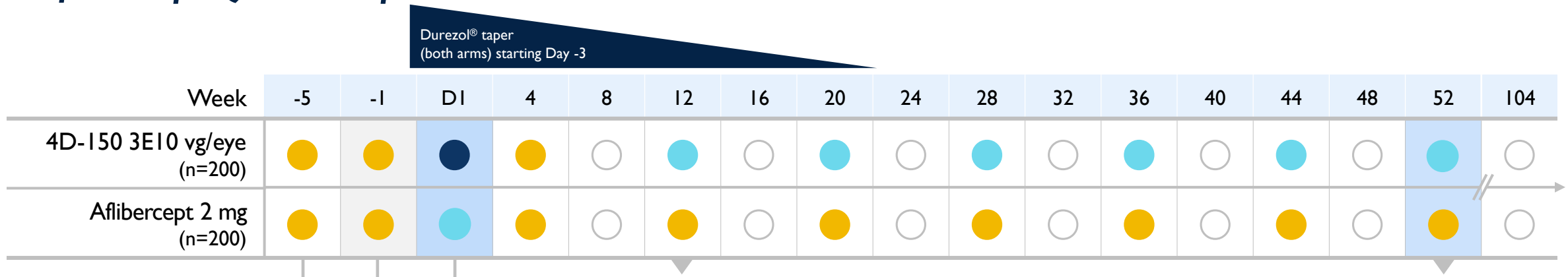


≥15% reduction in CST or complete resolution of intraretinal and/or subretinal fluid*

Supplemental Aflibercept Criteria (Both arms)

Reference Values:

BCVA: **Average of Week 4 & 8**

CST: **Week 8**

Disease Activity (if any criteria are met)†:

Vision & Anatomy: ≥5 letter loss in BCVA AND ≥50 µm increase in CST

Vision: ≥10 letter loss in BCVA

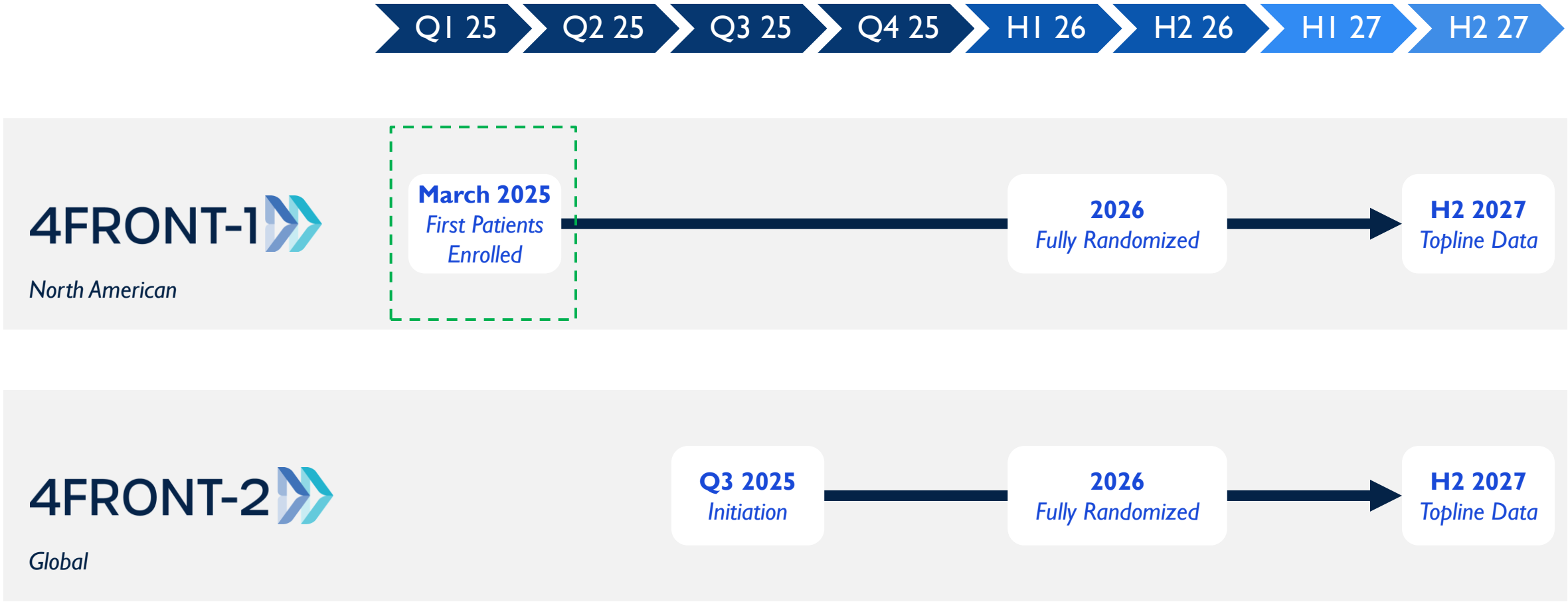
Anatomy: ≥100 µm increase in CST

New vision-threatening hemorrhage

✓ **Optimized** for primary endpoint success & demonstrating clinically meaningful treatment burden reduction

*Determined by SD-OCT and confirmed by an independent Reading Center. †PI discretion not allowed.

4D-150 Wet AMD Phase 3 Expected Milestones



Pipeline Focused on Large Market Indications with High Unmet Need

THERAPEUTIC AREA VECTOR ROUTE OF ADMIN	PRODUCT CANDIDATE	INDICATION	ESTIMATED PREVALENCE	PHASE 1	PHASE 2	PIVOTAL	STATUS
LARGE MARKET OPHTHALMOLOGY **R100** Intravitreal	4D-150	Wet AMD	*~3M U.S./EUMM*				✓ PRISM Ph2b 52-week interim data: **Feb 10, 2025** ✓ 4FRONT-1 Initiation: **Mar 2025** ▪ 4FRONT-2 Initiation: **Q3 2025** ▪ PRISM Ph1/2a 2-year & Ph2b 1.5-year data: **Q4 2025** ▪ 4FRONT-1 & -2 topline data: **H2 2027**
		DME	*~5M U.S./EUMM*				Part 1: ✓ 32-week interim data ▪ 52-week interim data: **Q3 2025**
PULMONOLOGY **A101** Aerosol	4D-710	CF lung disease (mod. ineligible/ intolerant)	*~15K WW*				▪ Interim data: **H2 2025**

$458M cash as of March 31, 2025; Runway into 2028

THANK YOU

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