



# Goldman Sachs 2025 Healthcare Conference

Corporate Presentation

June 2025

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# 4D-150 Key Updates

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

- *Over 50 clinical trial sites activated to date*

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

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



**Multi-Billion Dollar Annual Opportunity**

**Addresses Primary Clinical Unmet Need**

**Favorable Safety Profile**

**Ease of Clinical & Commercial Adoption**

**Topline Data from wet AMD Pivotal Trials in 2027**

**\$17B+ and growing global market**  
Leveraging expression of validated blockbuster aflibercept

**Backbone therapy with multi-year durability:**  
Foundational therapy with paradigm-shifting treatment burden reduction & vision preservation

**Predictable long-term safety:**  
Clinically significant IOI rate in-line with aflibercept bolus (remains standard-of-care, >64M eyes treated)

**Single IVT injection:** Seamless integration into retina clinic practice flow and **buy & bill reimbursement model**

Readouts from both Phase 3 studies in 4FRONT global registration program **expected in H2 2027**

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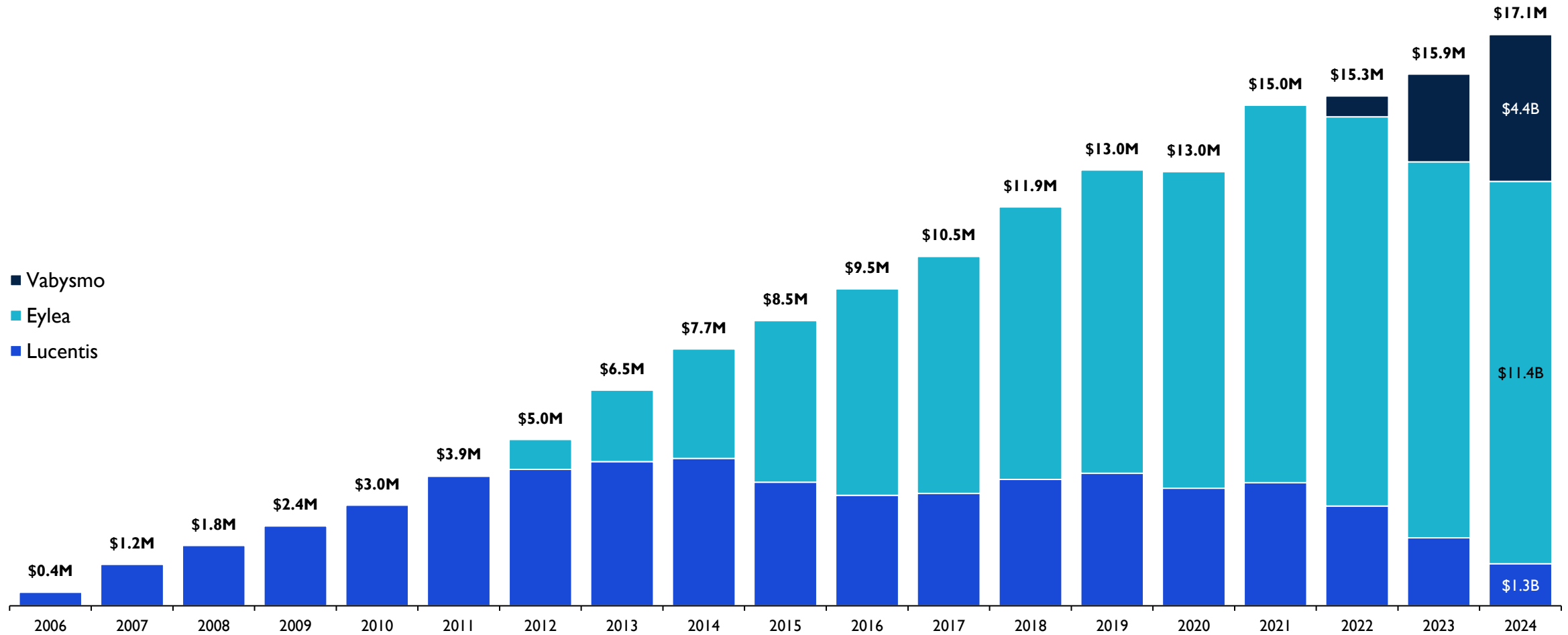
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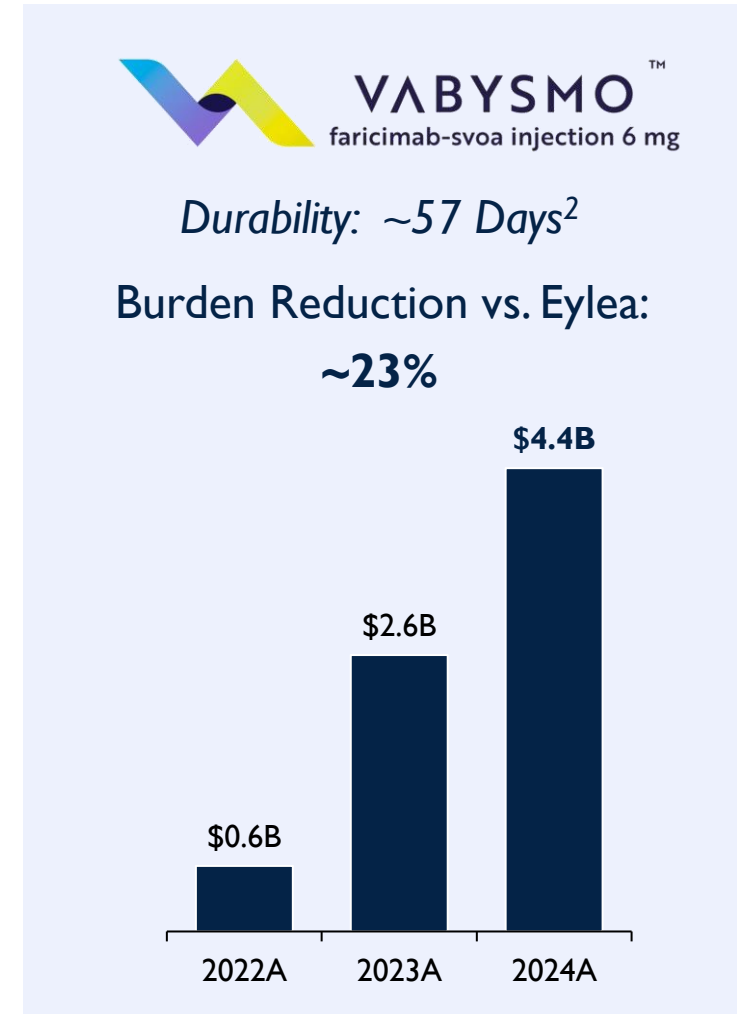
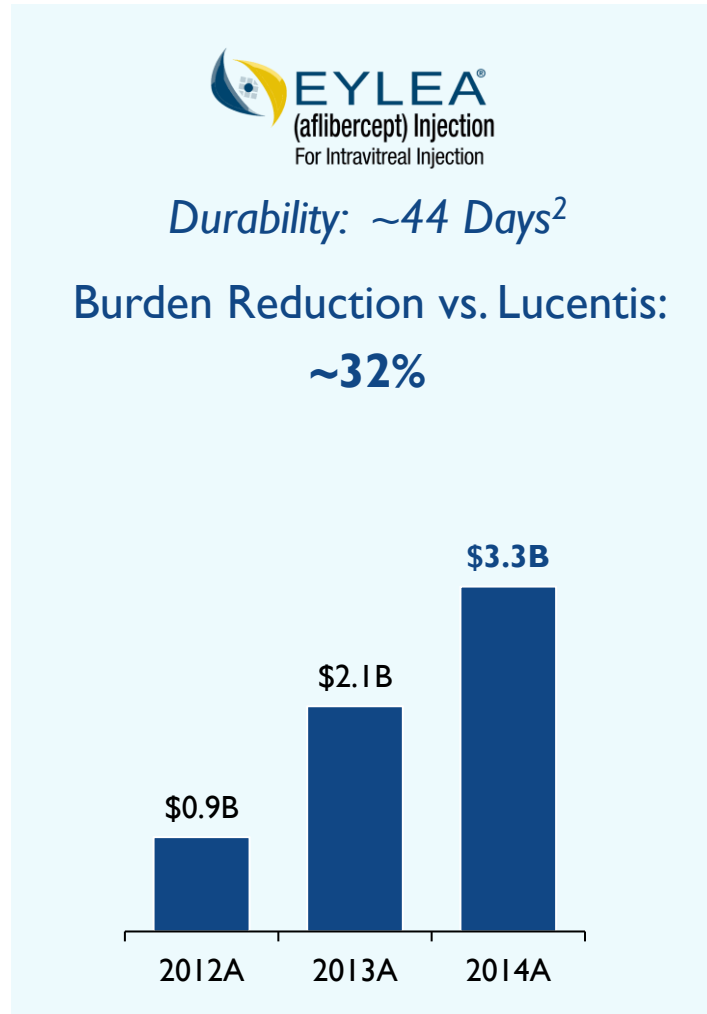
# Total Branded Anti-VEGF Market Continues to Grow with Share Driven by Incremental Durability Improvements: Aflibercept Remains Market Leader



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



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 Vision Outcomes

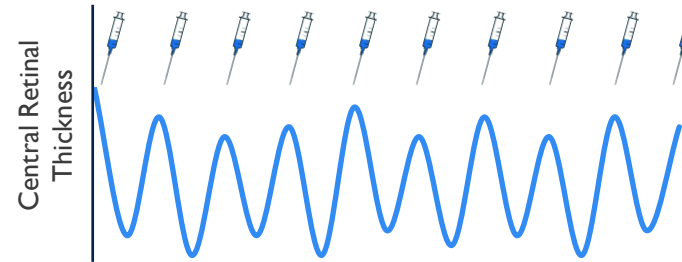
Durability

Impact on Retinal Anatomy

Vision

Current  
Standard of  
Care

Bolus loading doses, followed by...



Associated with **greater vision loss<sup>1</sup>** & **fibrosis<sup>2</sup>**



<sup>1</sup>Guo et al. *Ophthalm Res* 2023; 66:406-12. <sup>2</sup>Evans et al. *JAMA Ophthalmol* 2020;138:1043-51.

# Markedly Improving Outcomes with a Multi-year Backbone Therapy

## Current Standard of Care

**Durability**

Bolus loading doses, followed by...

- 4 weeks
- 4-8 weeks
- 8 weeks
- 8-12 weeks
- 8-12-16 weeks
- 8-16 weeks

**Impact on Retinal Anatomy**

Associated with **greater vision loss<sup>1</sup> & fibrosis<sup>2</sup>**

**Vision**

## Solution: 4D-I50 Backbone Therapy

Bolus loading doses, followed by...

**4D-I50**

**Multiple years**

**Goal Post-4D-I50**

Bolus supplement as needed

Low retinal variability to **preserve vision**

<sup>1</sup>Guo et al. *Ophthalm Res* 2023; 66:406-12. <sup>2</sup>Evans et al. *JAMA Ophthalmol* 2020;138:1043-51.

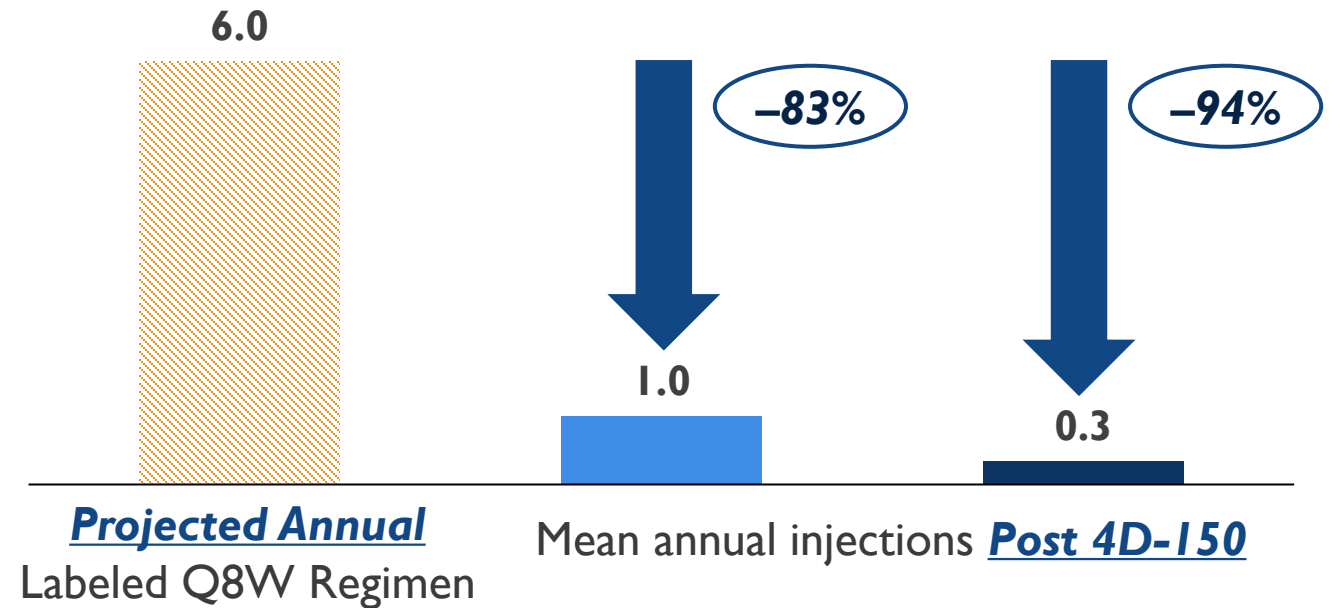
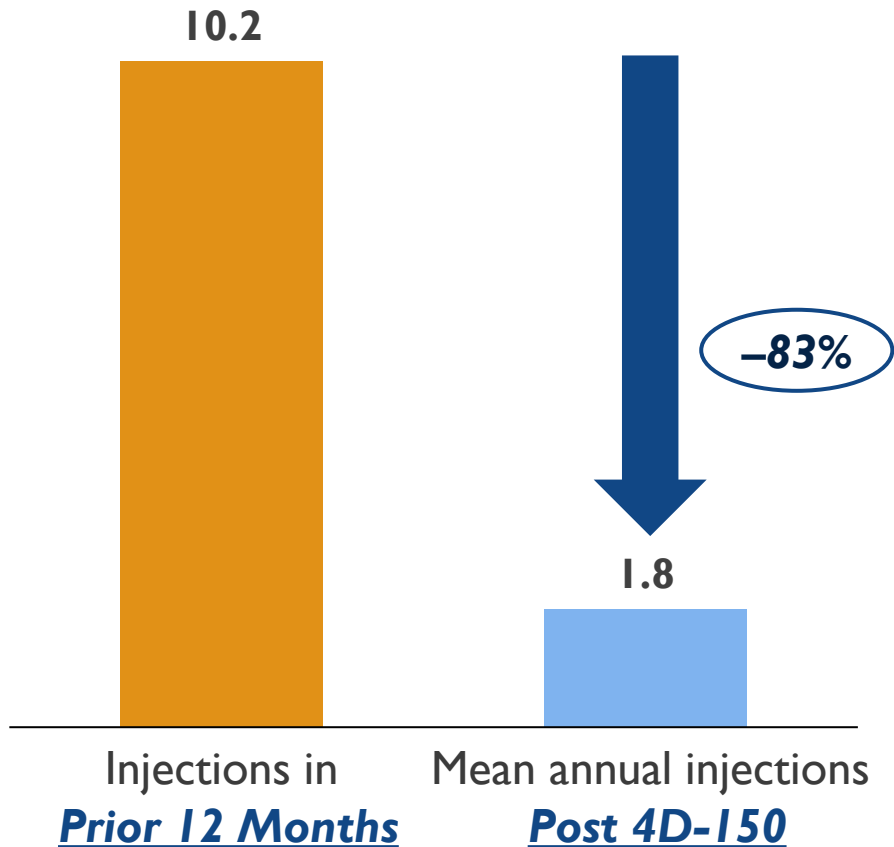
# 4D-I50 Demonstrated Transformative Treatment Burden Reduction & Durability in Multiple Wet AMD Patient Populations

Phase 1/2a Population: Severe, Recalcitrant

Phase 2b Populations:

Broad

Recently Diagnosed



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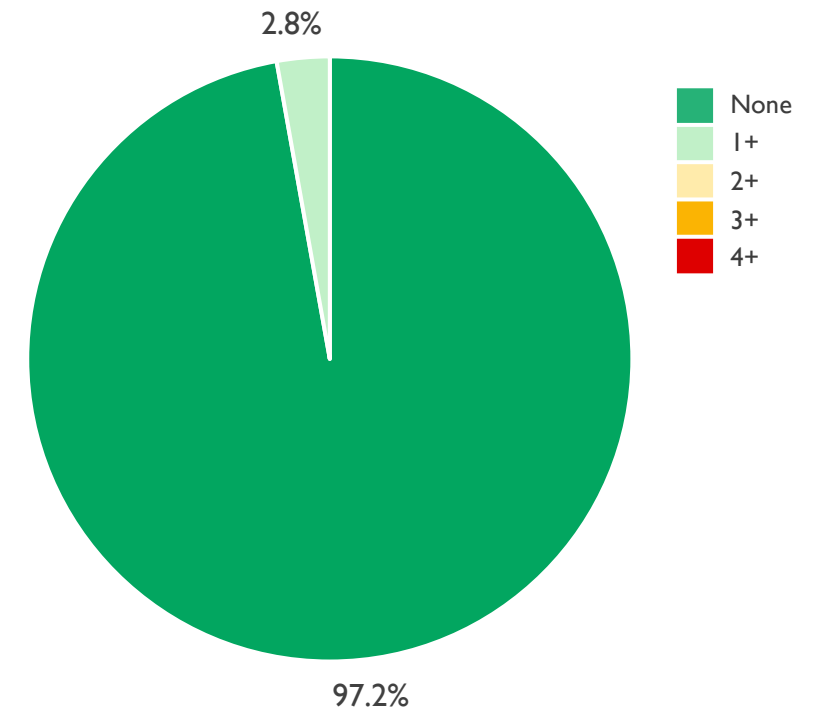
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# 4D-150 Has Been Well Tolerated in Broad Wet AMD Population: Safety In-Line With Aflibercept Protein to Date

- 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)\*

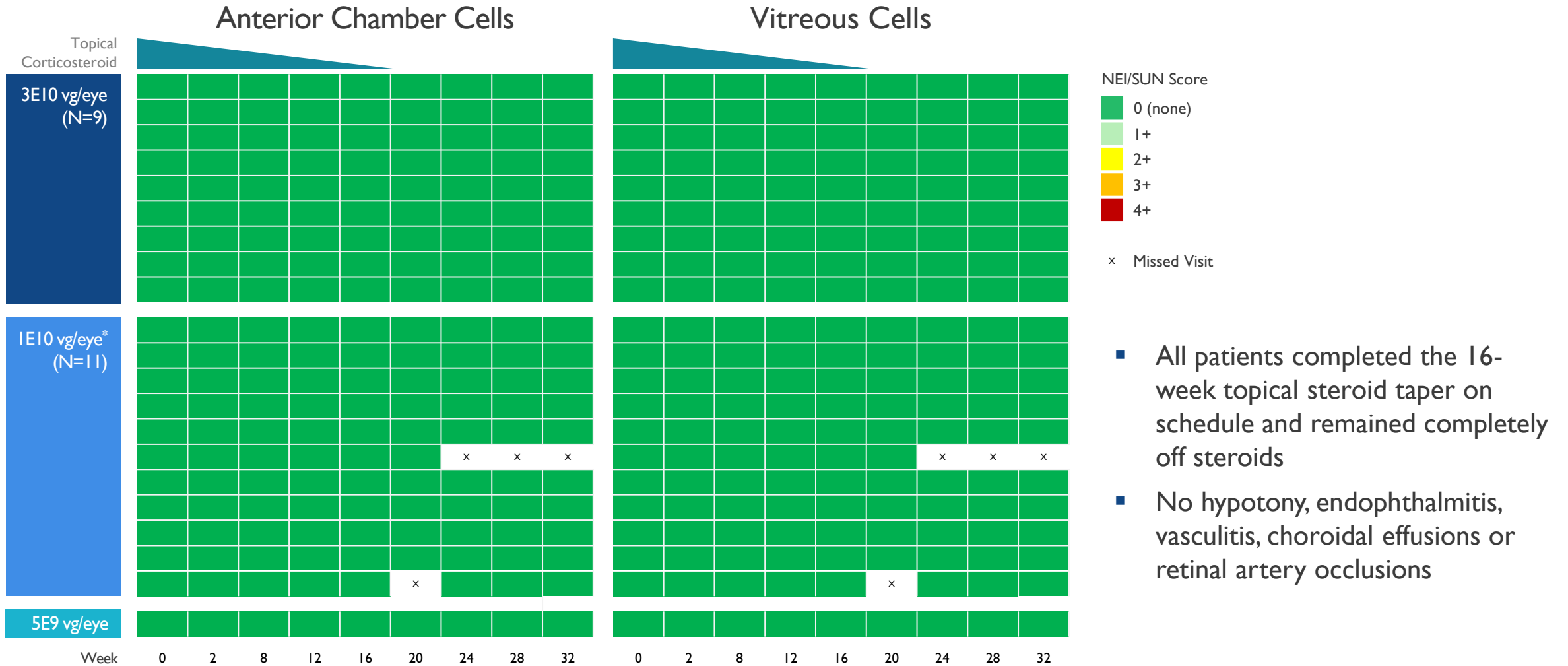
Highest SUN/NEI Score<sup>†</sup>



\*Duration of follow up,  $\leq 3$  years. <sup>†</sup>4D-150–related.

VC, Vitreous cell; NEI, National Eye Institute; SUN, Standardization of Uveitis Nomenclature.

# 4D-I50 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-I50). 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-I50

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## 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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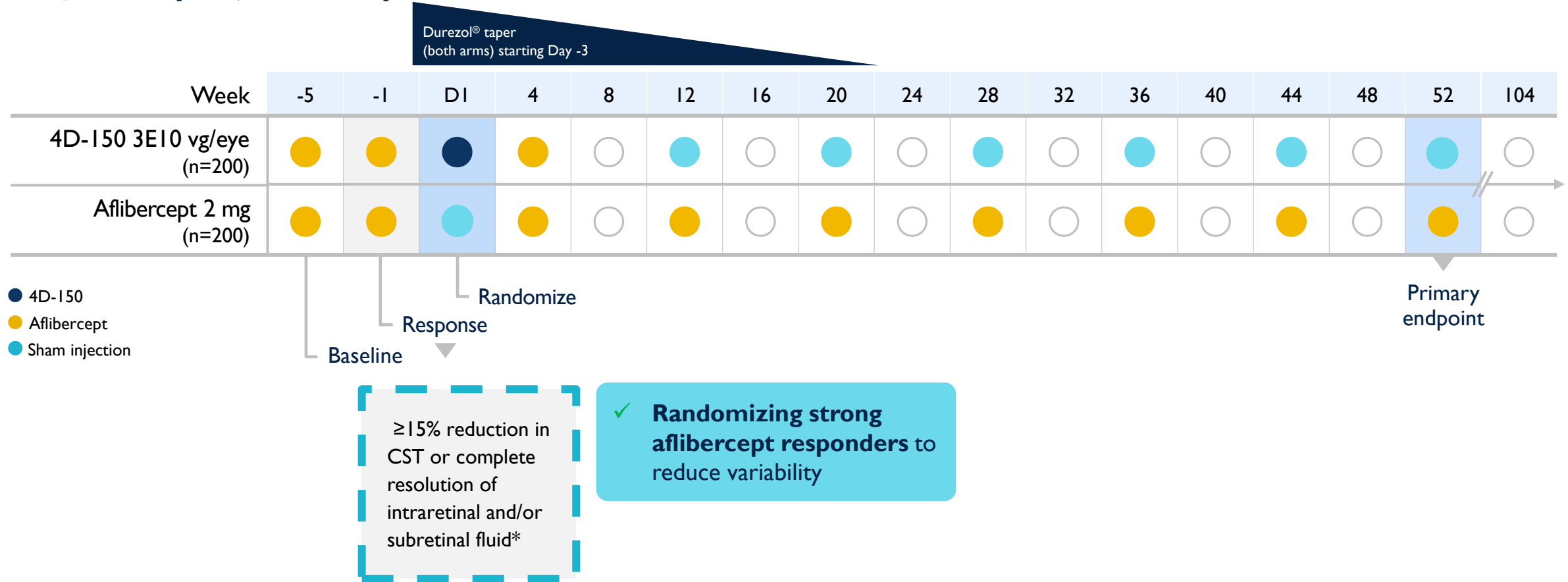
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# Global 4FRONT Phase 3 Trial Design

## Noninferiority Trials to Enable Global Registration in Wet AMD

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

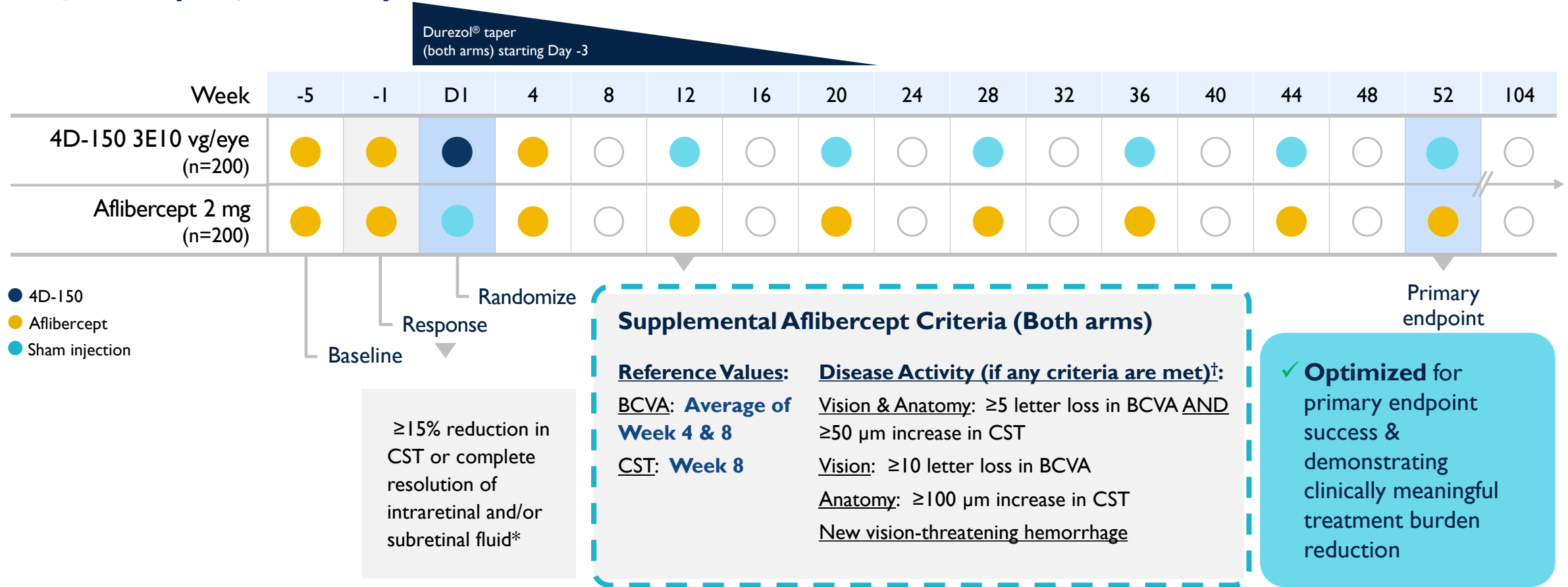


\*Determined by SD-OCT and confirmed by an independent Reading Center. †PI discretion not allowed.

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# 4D-I50 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
<b>LARGE MARKET OPHTHALMOLOGY</b>  <b>RI00</b> Intravitreal	<b>4D-150</b>	Wet AMD	~3M U.S./EUMM				<ul style="list-style-type: none"> <li>✓ PRISM Ph2b 52-week interim data: <b>Feb 10, 2025</b></li> <li>✓ 4FRONT-1 Initiation: <b>Mar 2025</b></li> <li>▪ 4FRONT-2 Initiation: <b>Q3 2025</b></li> <li>▪ PRISM Ph 1/2a 2-year &amp; Ph2b 1.5-year data: <b>Q4 2025</b></li> <li>▪ 4FRONT-1 &amp; -2 topline data: <b>H2 2027</b></li> </ul>
		DME	~5M U.S./EUMM				Part I: <ul style="list-style-type: none"> <li>✓ 32-week interim data</li> <li>▪ 52-week interim data: <b>Q3 2025</b></li> </ul>
<b>PULMONOLOGY</b>  <b>A101</b> Aerosol	<b>4D-710</b>	CF lung disease (mod. ineligible/intolerant)	~15K WW				<ul style="list-style-type: none"> <li>▪ Interim data: <b>H2 2025</b></li> </ul>

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



# THANK YOU

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