



# The New Backbone of Retina Care: Moving Beyond Lifelong Injections

Corporate Overview

J.P. Morgan Healthcare Conference | January 2026

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

# Overview

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- 1 4DMT Vision & Pipeline
- 2 4D-I50 Overview & 2025 Accomplishments
- 3 Retinal Vascular Disease Market & Unmet Medical Needs
- 4 Derisking Phase 3 & Commercialization
- 5 2026-27 Catalysts
- 6 Summary













# ***REDEFINING GENETIC MEDICINES:***

**Durable & disease-targeted therapeutics  
for large market diseases**

**Lead Product: 4D-150**

# Next Generation, Locally Delivered AAV Gene Therapy Pipeline: Focused on Rapidly Advancing 4D-150 to Global Commercialization

THERAPEUTIC AREA VECTOR	PRODUCT CANDIDATE	INDICATION	PRE-CLINICAL	PHASE 1	PHASE 2	PIVOTAL	BLA FILING	PARTNERS
<b>RETINA</b> <b>R100</b>  Intravitreal	<b>4D-150</b>	Wet AMD						 <b>Otsuka</b> APAC Rights  <b>4DMT:</b> U.S./EU/ROW
		DME						
	<b>4D-175</b>	Geographic Atrophy						Seeking strategic partnerships
<b>PULMONOLOGY</b> <b>A101</b>  Aerosol	<b>4D-710</b>	CF lung disease						 <b>CYSTIC FIBROSIS FOUNDATION</b> Fully Funded
	<b>4D-725</b>	AIAT lung disease						 <b>CIRM</b> CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE Fully Funded



**4D-150**

## **GOAL**

**Transform** standard of care for  
**large market retinal vascular diseases**  
with **safe, in-office &**  
**durable lifelong backbone therapy**

# 2025: Breakout Year for 4D-I50

- ✓ **Continued Strong Phase 1/2 & 2b Results:**
  - ✓ **Safety:** Well-tolerated & no significant inflammation at Phase 3 dose
  - ✓ **Durability:** Strong consistent clinical activity through 1.5 to 2 years
- ✓ **Execution of Phase 3:** Speed of 4FRONT-1 wet AMD enrollment exceeded expectations
- ✓ **Regulatory for DME:** FDA & EMA alignment on *single* Phase 3 trial for approval; FDA *RMAT*
- ✓ **Team:** Hired industry-leading retina team
- ✓ **Partnership:** Otsuka APAC rights; *4DMT retains U.S., EU & ROW*
- ✓ **Financial:** \$100M raise & cash runway into *H2 2028* (>12-months post-4FRONT-1 data)

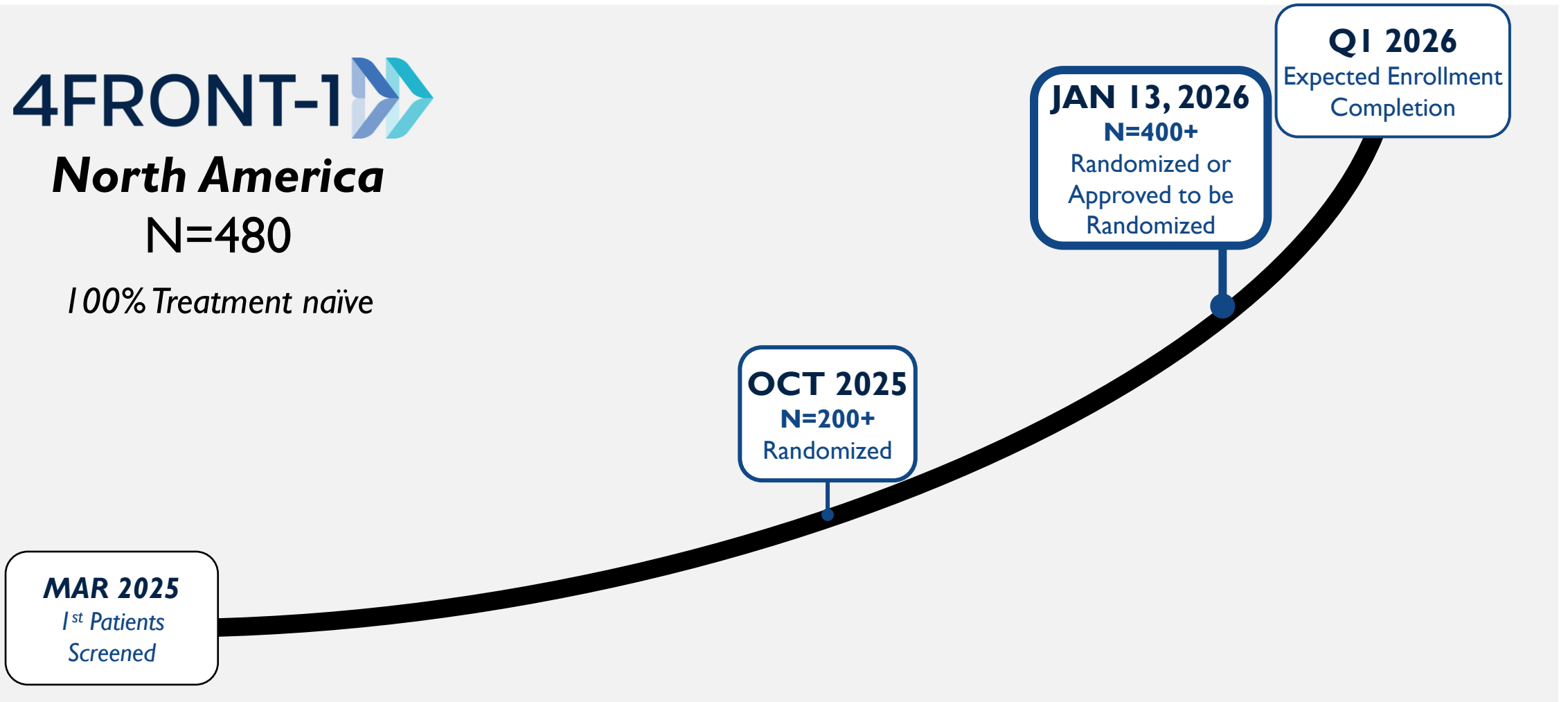
# 4FRONT-1 Enrollment Significantly Exceeding Initial Expectations in Treatment-Naïve Population

**4FRONT-1** 

**North America**

**N=480**

*100% Treatment naïve*



# 4FRONT-2 Rapidly Executing & Enrolling Globally: U.S., EU & Japan Open

**4FRONT-2** 

**Global**

**N=480**

*60% Treatment naïve*

*40% Previously treated\**

**Jun 2025**  
*Trial initiation in  
U.S. sites*

**JAN 2026**  
U.S., EU + APAC  
Sites open &  
screening rapidly

**H2 2026**  
Expected  
Enrollment Completion

\*1-4 prior injections, diagnosed within 6 months.

# Industry-Leading Retina Leadership Team



**Julie Clark, MD**

Chief Medical Officer

**20+ years**

Clinical Development, Regulatory Affairs,  
Biomarkers, Early- & Late-stage Clinical  
Development



**Dhaval Desai, PharmD**

Chief Development Officer

**20+ years**

Late-stage Product Development,  
Medical Affairs & Scientific  
Communications



**Christopher Simms**

Chief Commercial & Business Officer

**25+ years**

Pre-commercial & Commercial,  
Pre-launch Preparations & Development,  
Business Development



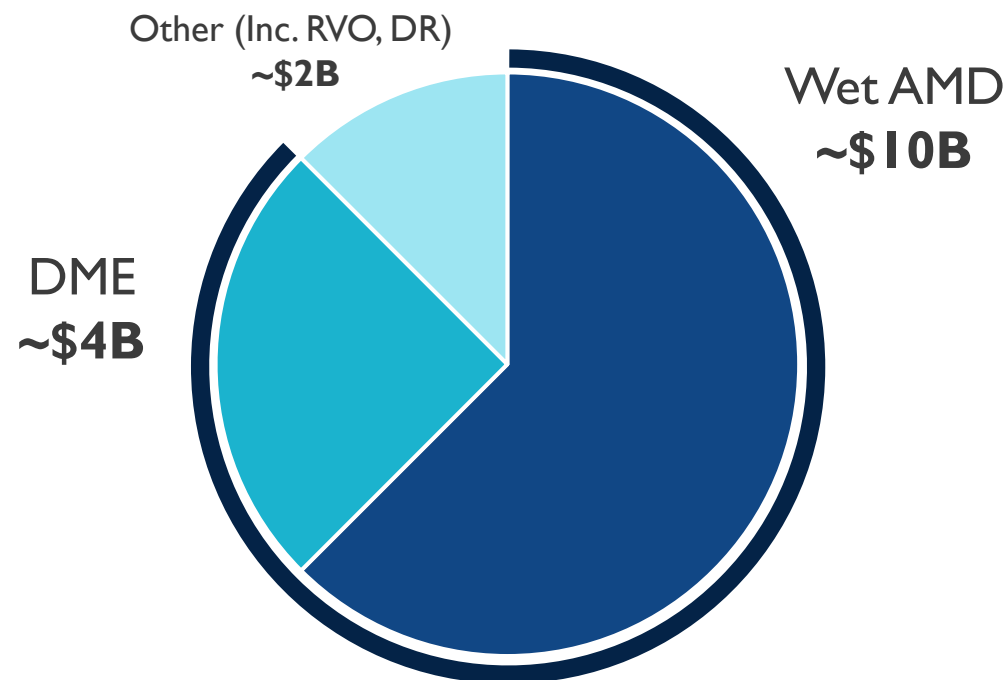
# Retinal Vascular Disease Market & Unmet Medical Needs

# 4D-150 Potential to be Highly Disruptive in a Rapidly Growing, \$14B+ Market

## Prevalence (2025)

- **Wet AMD:**
  - ~5M prevalence in U.S., Europe, Japan
  - ~300K new cases diagnosed annually
- **Diabetic Macular Edema (DME):**
  - ~4M prevalence in U.S., Europe & Japan
  - ~300K new cases diagnosed annually
- Top causes of **permanent vision loss**
- **Rapidly growing population driven by aging demographics**

## \$16B Global Branded Retinal Vascular Disease Anti-VEGF Market (2025E)



**Wet AMD + DME: ~\$14B**

Prevalence sourced from Marketscope Retina Market Report 2023. Anti-VEGF market sourced from GlobalData, GrandView Research.



Typical Age of Wet AMD Patient:  
**~75 years**



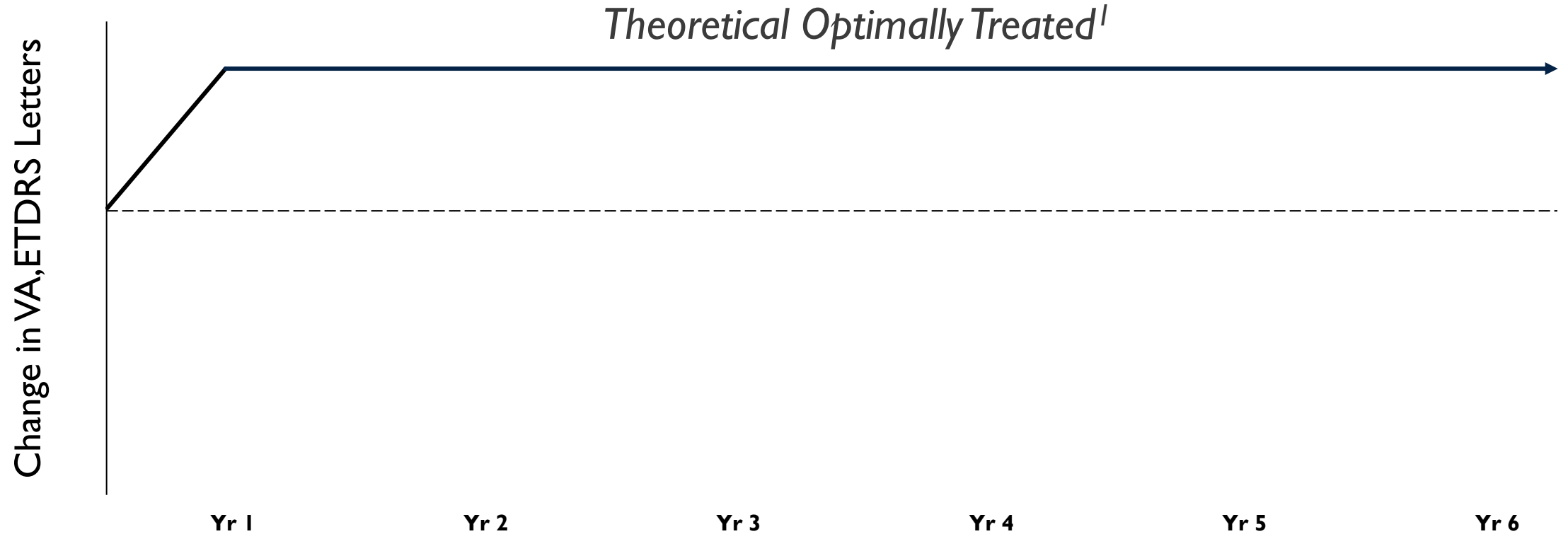
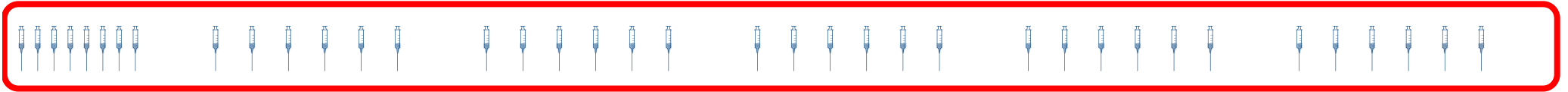
Vision Loss Impact:  
**Isolation, Loss of Autonomy,  
Uncertainty, Fear**



Current  
Standard Of  
Care:  
**Lifelong**  
**Repetitive**  
**Burdensome**  
Anti-VEGF  
Eye Injections

# Lifelong Repetitive & Burdensome Bolus Anti-VEGF Injections Needed to Slow Vision Loss: ~30 Injections over 5 Years

**LIFELONG**  
Bolus Anti-VEGF



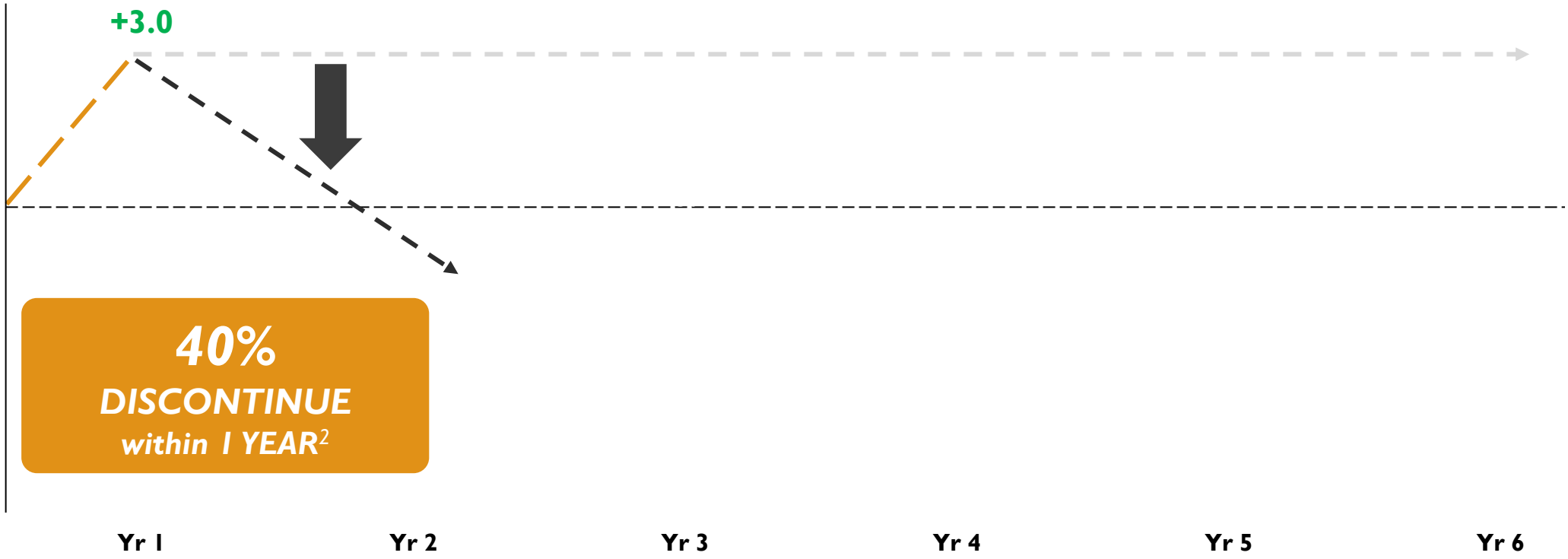
1. Holz FG, et al. *British Journal of Ophthalmol* 2015;99:220-226. More visits and injections appeared to be correlated with more successful maintenance of visual acuity gains, including in SEVEN-UP (Seven Year Observational Update of Macular Degeneration Patients Post-MARINA/ANCHOR and HORIZON Trials),

# Real World Data - Treatment Discontinuation is Extremely Common: Current Bolus Treatment Regimens are NOT Sustainable

**LIFELONG**  
Bolus Anti-VEGF



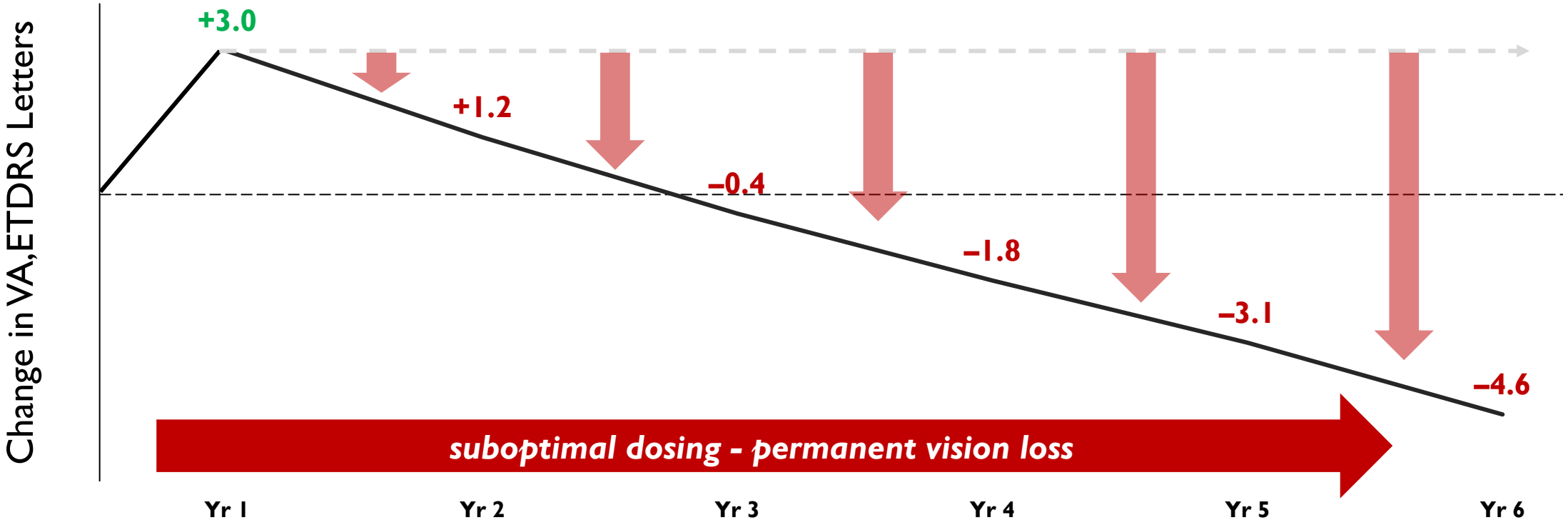
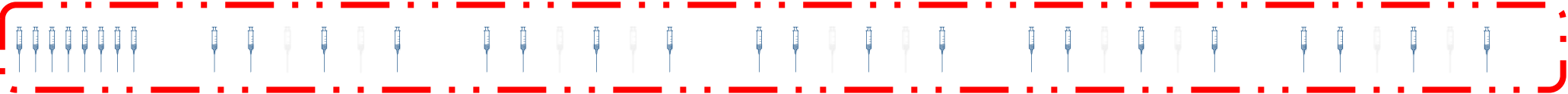
Change in VA, ETDRS Letters



1. Wykoff et al.: *Ophthalmol Sci.* 2023 Oct 31;4(2):100421.; n=135,384 at Yr 1; 6,878 at Yr 6. 2. Khanani AM, et al. *Ophthalmol Retina.* 2020;4(2):122-133

# Real World Data - Patients Remaining on Treatment: Inability to Maintain Burdensome Injection Regimen Leads to Unrelenting Vision Loss<sup>1</sup>

**LIFELONG**  
Bolus Anti-VEGF



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

# Solving the Unmet Need: Provide Continuous Backbone Treatment to Control Disease & Protect Vision Without Repetitive Lifelong Injections

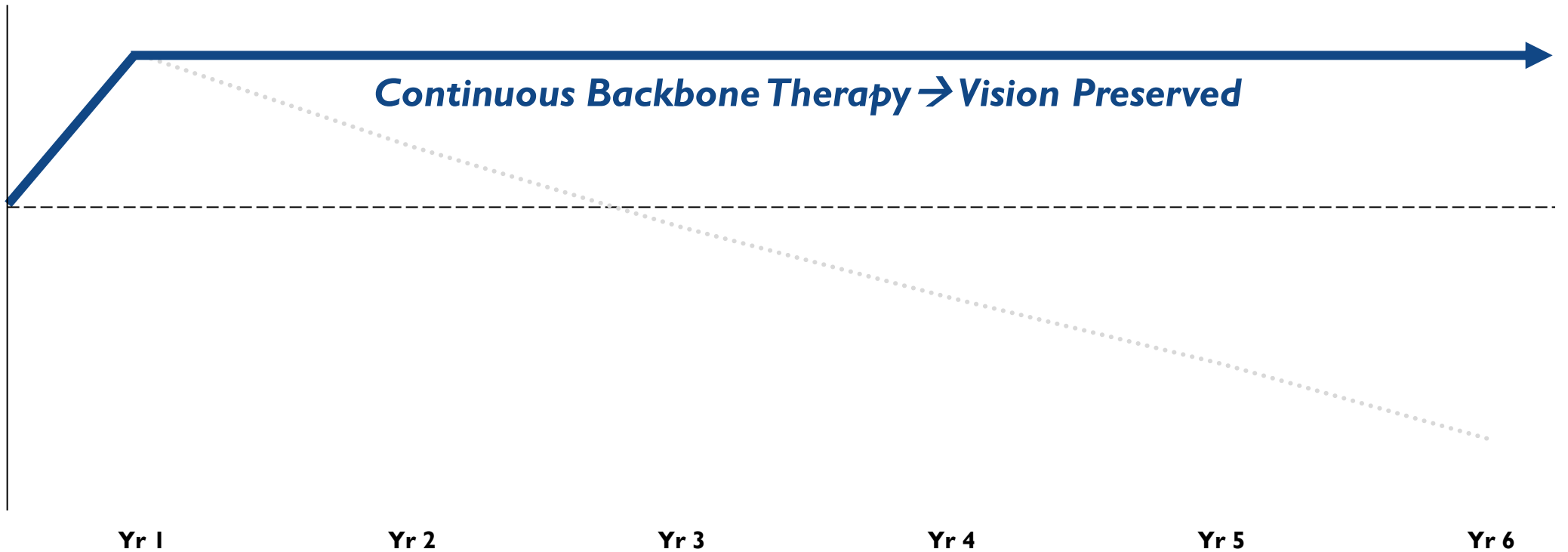
~~LIFELONG  
Dosis Anti-VEGF~~



**BACKBONE**  
Anti-VEGF



Change in VA, ETDRS Letters

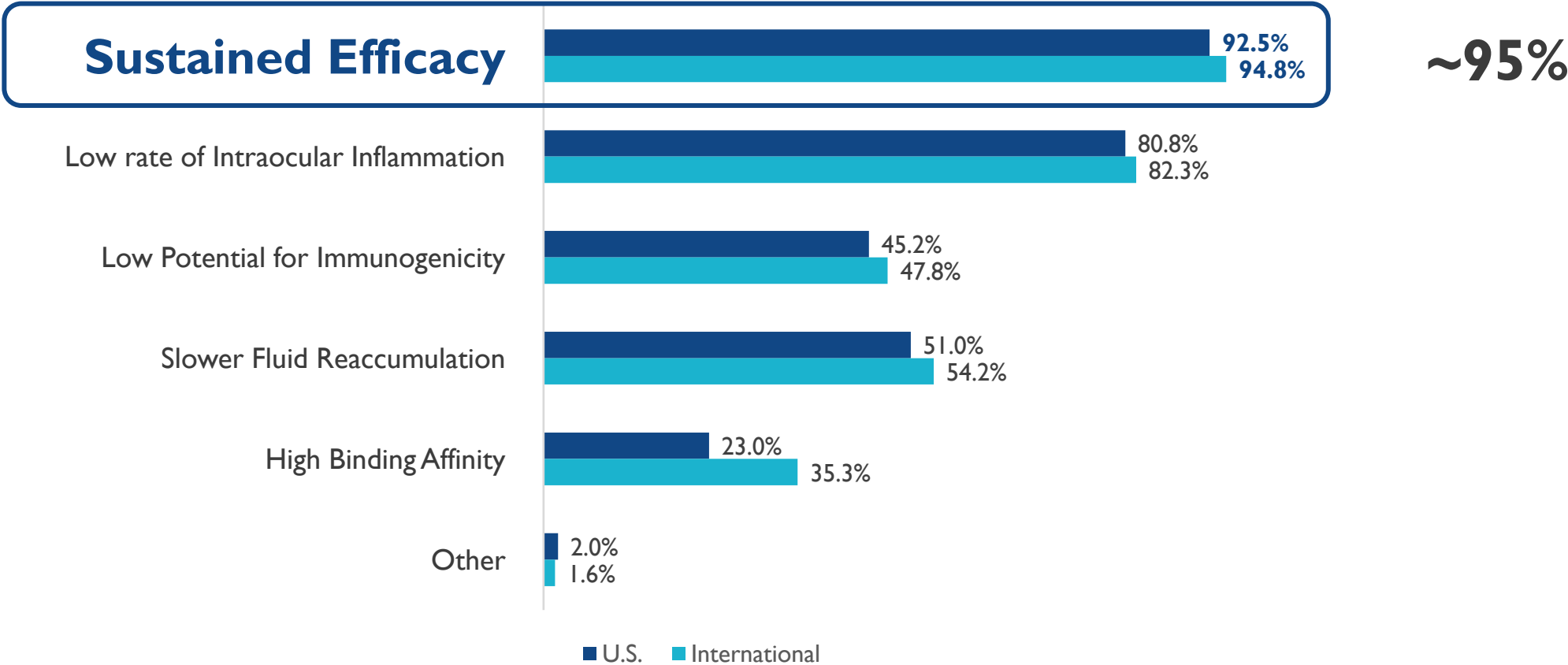


Wykoff et al.: Ophthalmol Sci. 2023 Oct 31;4(2):100421.; n=135,384 at Yr 1; 6,878 at Yr 6

# Durability Remains the Priority for Retina Doctors & Patients: Long-term Disease Control is Still the #1 Unmet Need

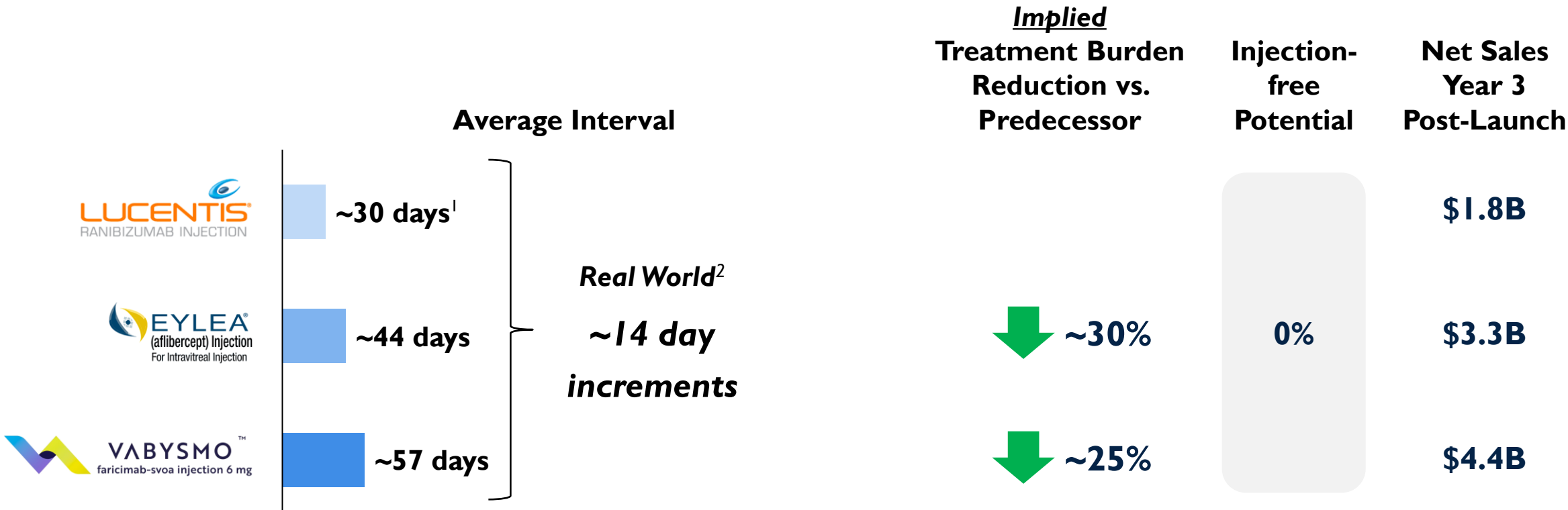
## ASRS Preferences and Trends (PAT) Survey 2025

Which factors are most important to you when selecting anti-VEGF agent?



Hahn P, ed. ASRS 2025 Preferences and Trends Membership Survey. Chicago, IL. American Society of Retina Specialists; 2025

# Despite Incremental Durability Improvements, Eylea & Vabysmo Had Rapid, Blockbuster Commercial Success

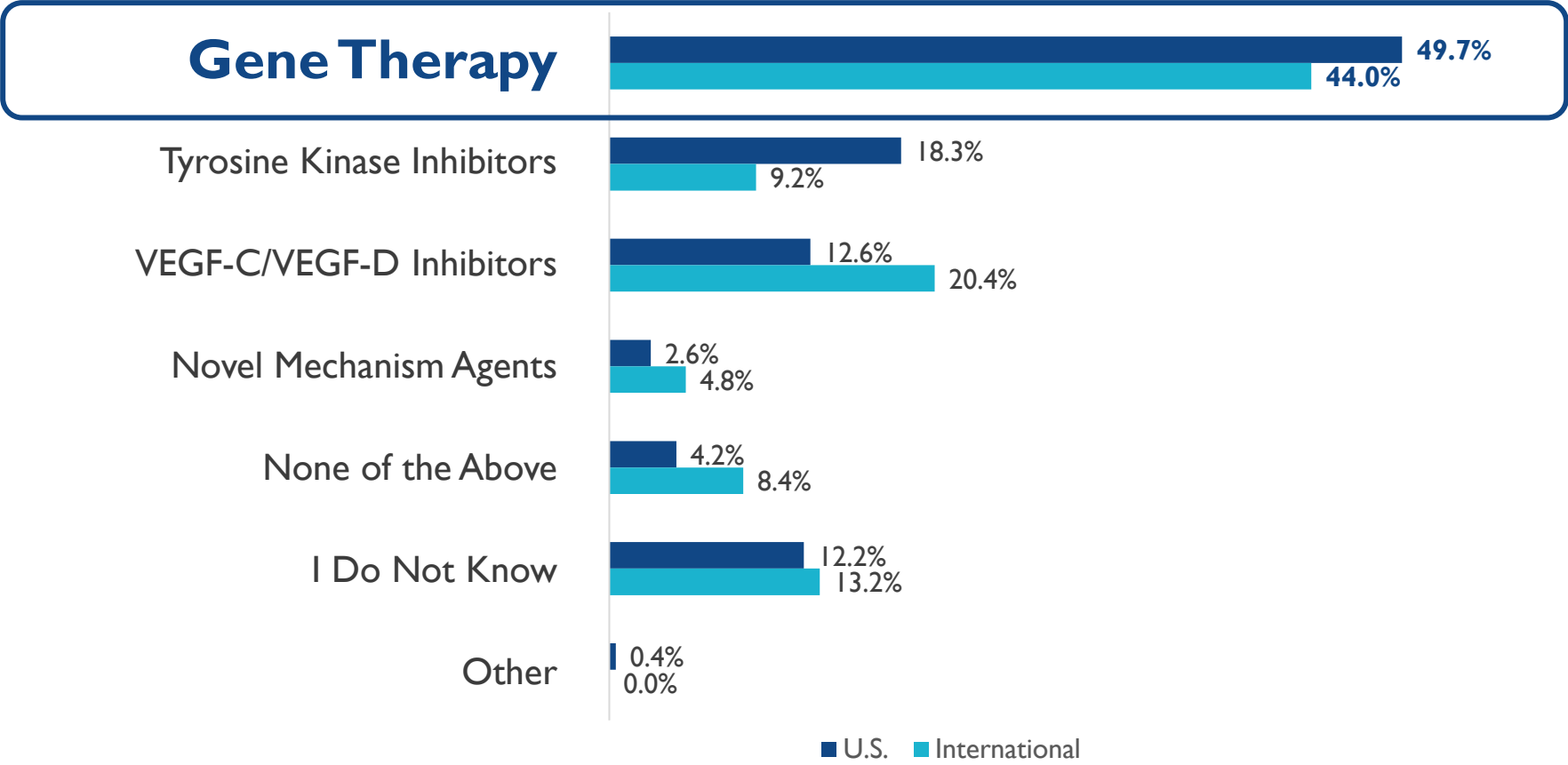


1. Lucentis package insert; 2. Real-World Evidence (TRUCKEE Study). Injection Burden Reduction vs. prior therapy implied based on difference calculated annual injections based on TRUCKEE durability.

# Gene Therapy (e.g. 4D-I50) is the Most Exciting Pipeline Treatment: Highest Potential to Achieve True Continuous Disease Control

## ASRS Preferences and Trends (PAT) Survey 2025

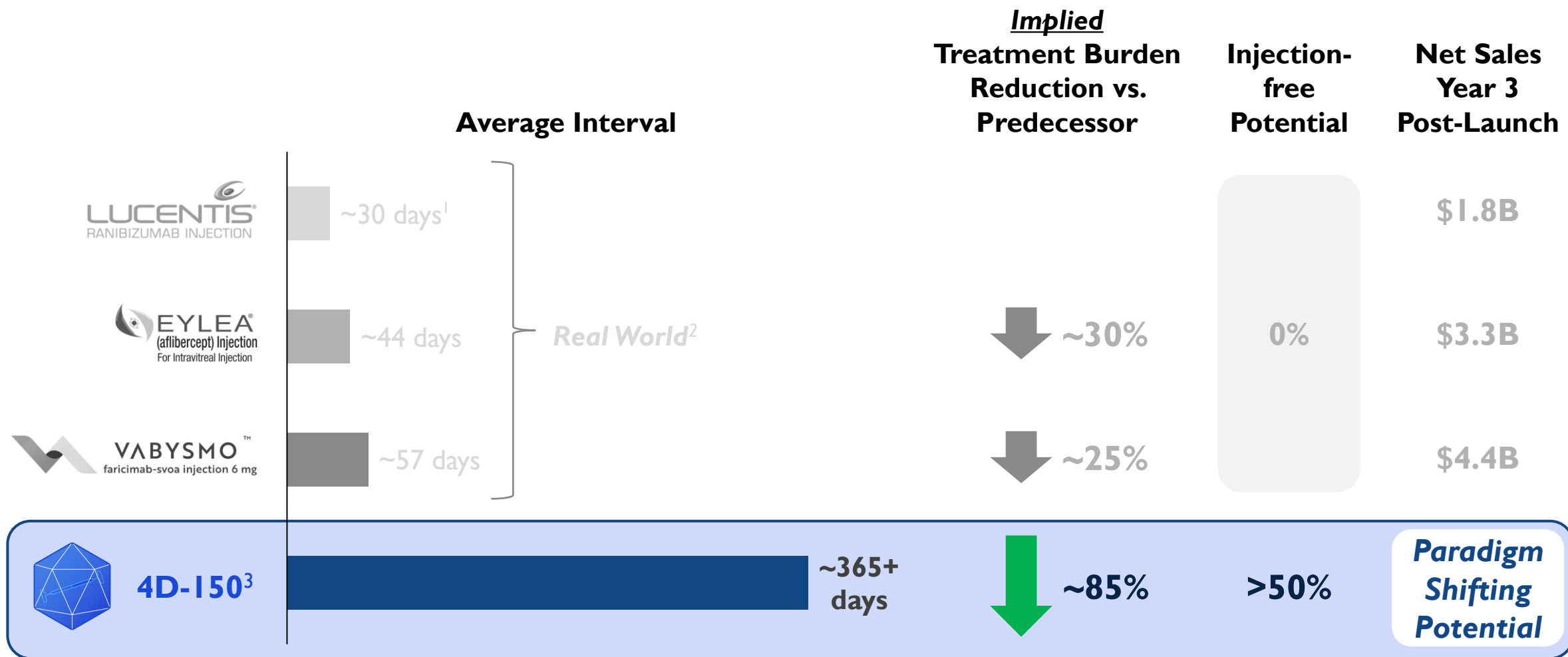
Which pipeline treatment for wet AMD excites you most?



~50%

Hahn P, ed. ASRS 2025 Preferences and Trends Membership Survey. Chicago, IL. American Society of Retina Specialists; 2025

# 4D-I50 Durability Profile would be Paradigm-Shifting



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. 3. 4DMT PRISM Phase 2b data, average interval based on 1.0 mean supplemental injections through 1 year in 3E10 vg/eye arm.



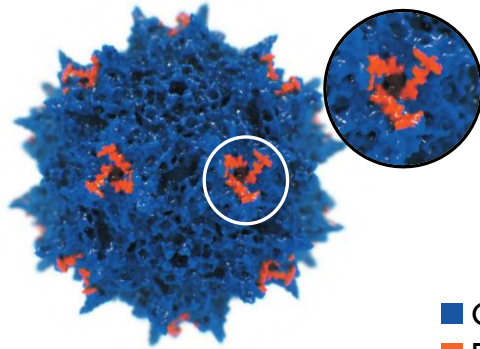
**4D-150**

**GOAL: To transform the standard of care for large market retinal vascular diseases with a safe, in-office & durable lifelong backbone therapy**

- I. Continuous disease control** enabled by **durable** retinal expression of **aflibercept**

# 4D-I50 is Designed as Backbone Therapy to Provide Safe & Continuous Disease Control with Lifelong Anti-VEGF Expression Potential

## R100 Capsid



■ Capsid base  
■ Peptide insertions

- ✓ Robust delivery to multiple retinal layers
- ✓ Low doses and minimal inflammation potential



## Anti-VEGF Transgenes



Aflibercept  
(VEGF Trap)

- ✓ >64 million doses administered WW since launch\*



VEGF-C RNAi

- ✓ Enhanced aflibercept expression in preclinical studies<sup>1</sup>

## 4D-I50 Backbone Therapy Target Profile

Single, in-office IVT Injection

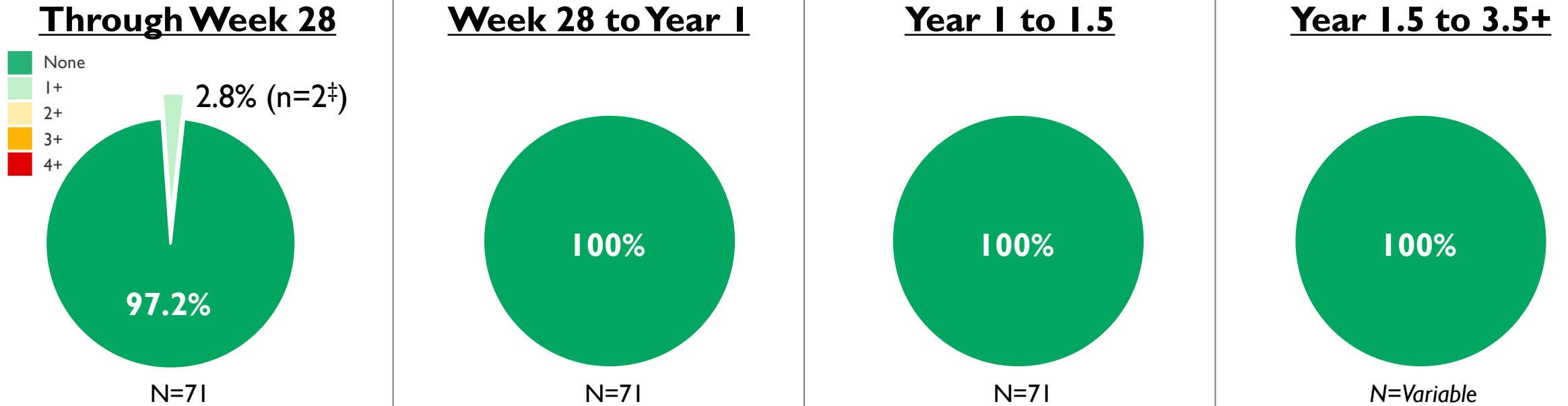
Predictable, prophylactic steroid eyedrop taper


Potential for lifelong durability<sup>2</sup>

\*Regeneron data on file. 1. Calton et al. *Invest Ophthalmol Vis Sci* 2024;65:1. 2. Based on 4DMT and other AAV-based retinal gene therapies.

# Wet AMD: Consistent & Predictable Safety Data To-date

Highest SUN/NEI Score<sup>†</sup> with 4D-150 Phase 3 Dose, 3E10 vg/eye (N=71)

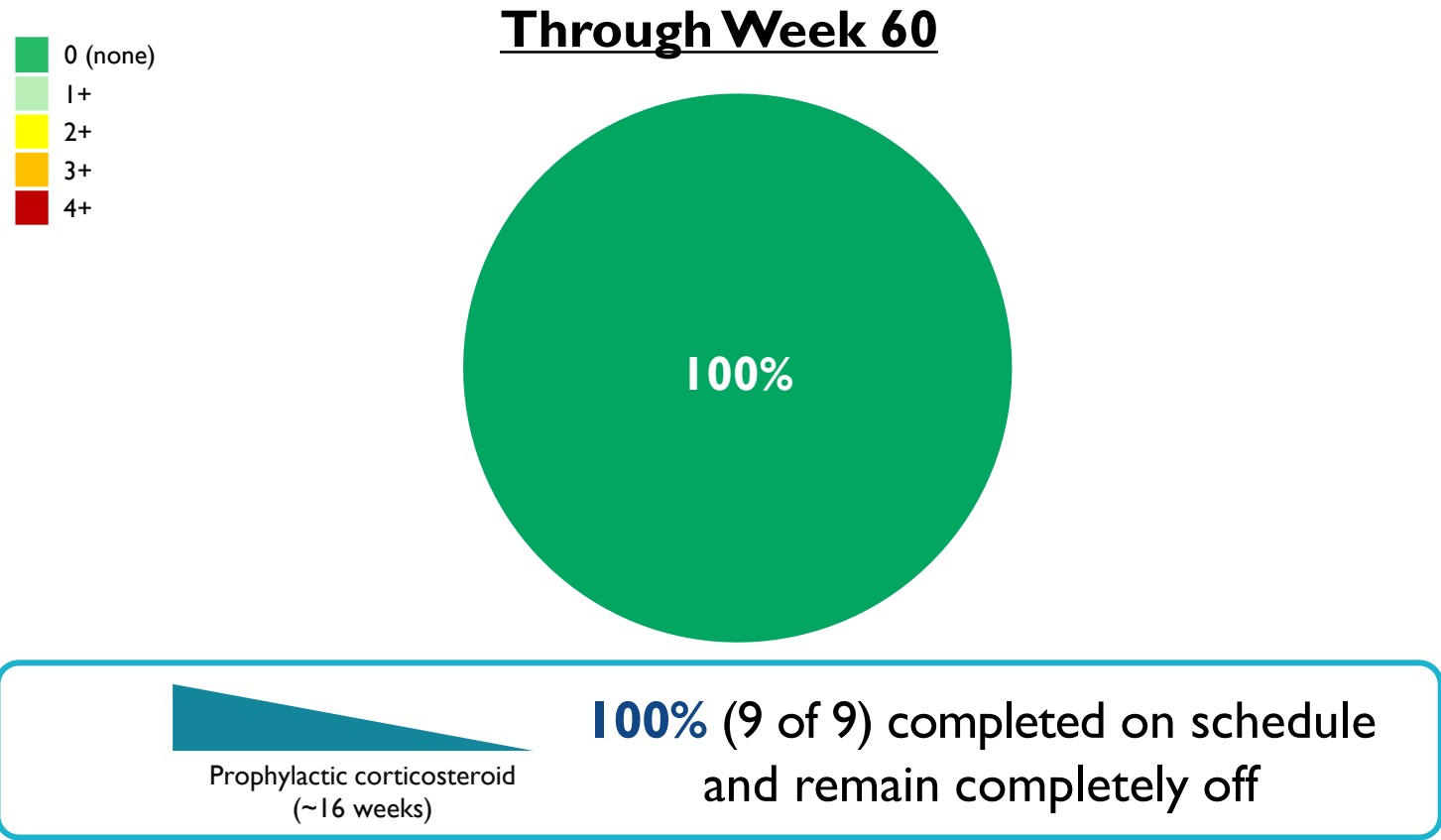



 Prophylactic corticosteroid (~20 weeks)
 
**99%** (70 of 71) completed on schedule and remain completely off

Data cutoff of August 22, 2025.  
<sup>†</sup>4D-150-related. <sup>‡</sup>1+ VC cell in 1 patient at Week 4 & 1 patient Week 28.  
 NEI, National Eye Institute; SUN, Standardization of Uveitis Nomenclature.

# DME: Consistent & Predictable Safety Data To-date

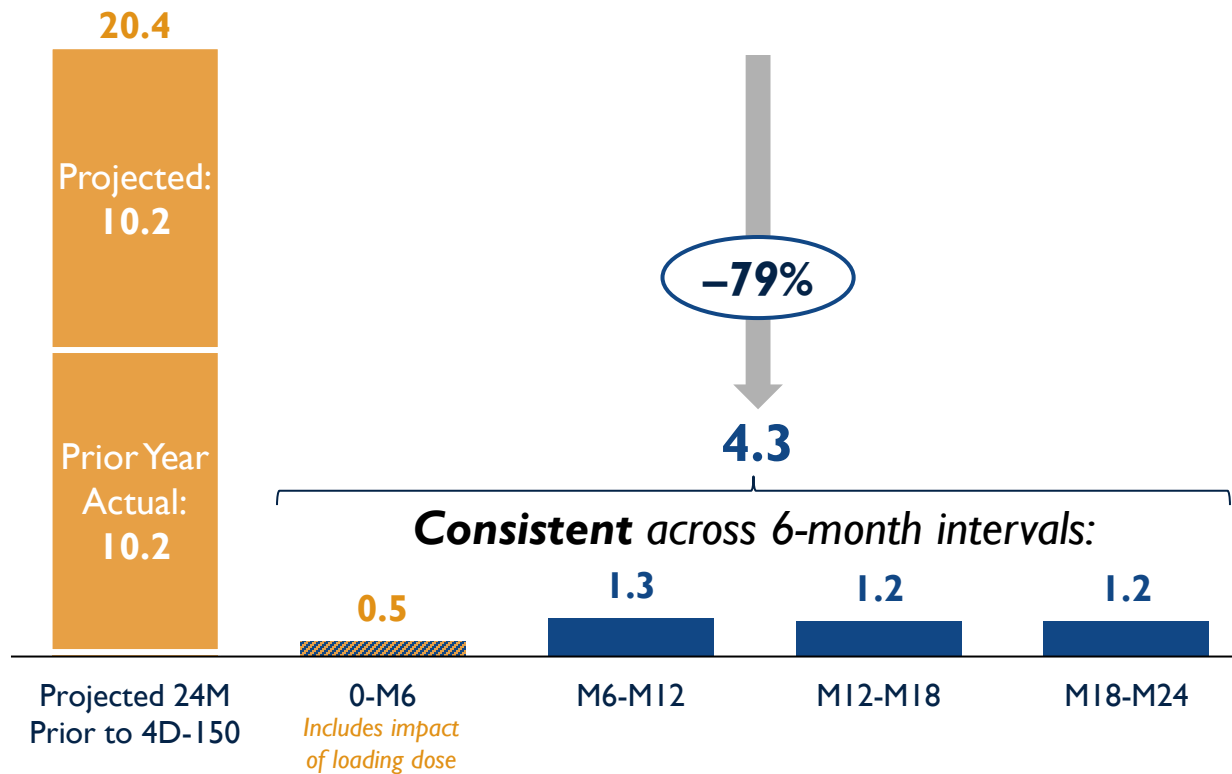
Highest SUN/NEI Score with 4D-I50 Phase 3 Dose, 3E10 vg/eye (N=9)



NEI: National Eye Institute; SUN: Standardization of Uveitis Nomenclature.  
Data cutoff as of May 2, 2025.

# Phase I/2a 2-year Data Demonstrates Durable Disease Control: Severe, Recalcitrant Wet AMD Population

## Treatment Burden\* Reduction Post-4D-150 vs. Prior



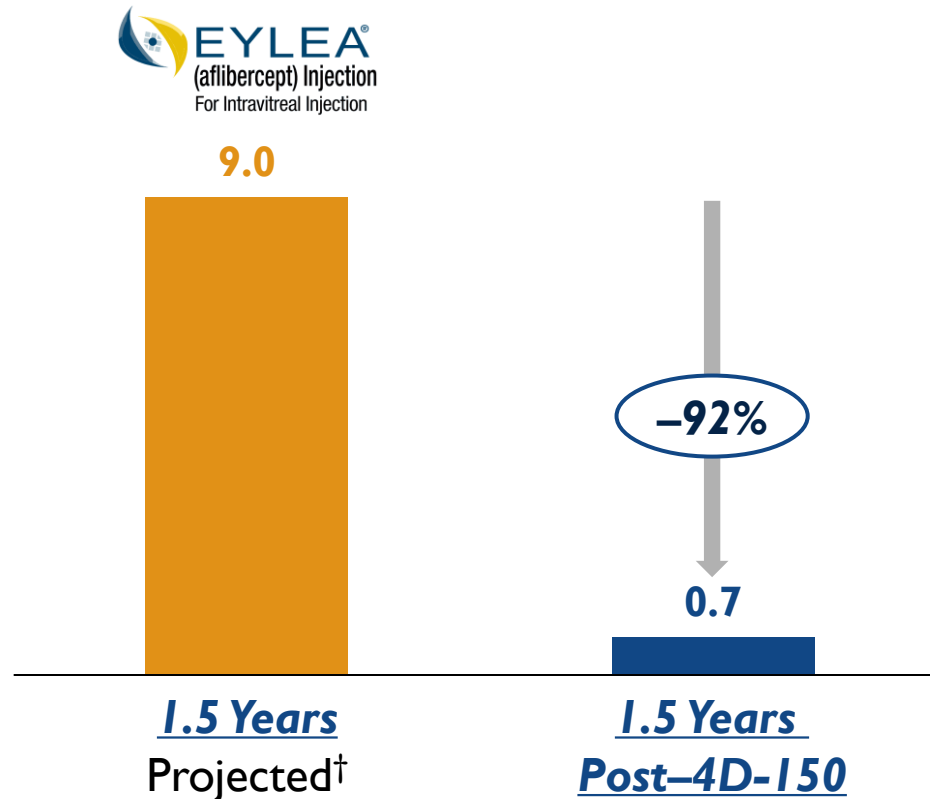
- Visual acuity: **stable & equivalent** to aflibercept control
- Retinal anatomy: stable **with fewer fluctuations** vs. aflibercept control
- Inflammation: **no meaningful signal**

Data cutoff of August 22, 2025.

\*Anti-VEGF injections. CST, central subfield thickness; BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; AFLB, aflibercept. Mean cumulative function from Cox proportional hazard regression model for recurrent events was used to estimate the mean cumulative number of supplemental aflibercept injections.

# Phase 2b 1.5-year Data Demonstrates Durable Disease Control: Recently Diagnosed, Phase 3 Comparable Wet AMD Population

## Treatment Burden\* Reduction Post-4D-150

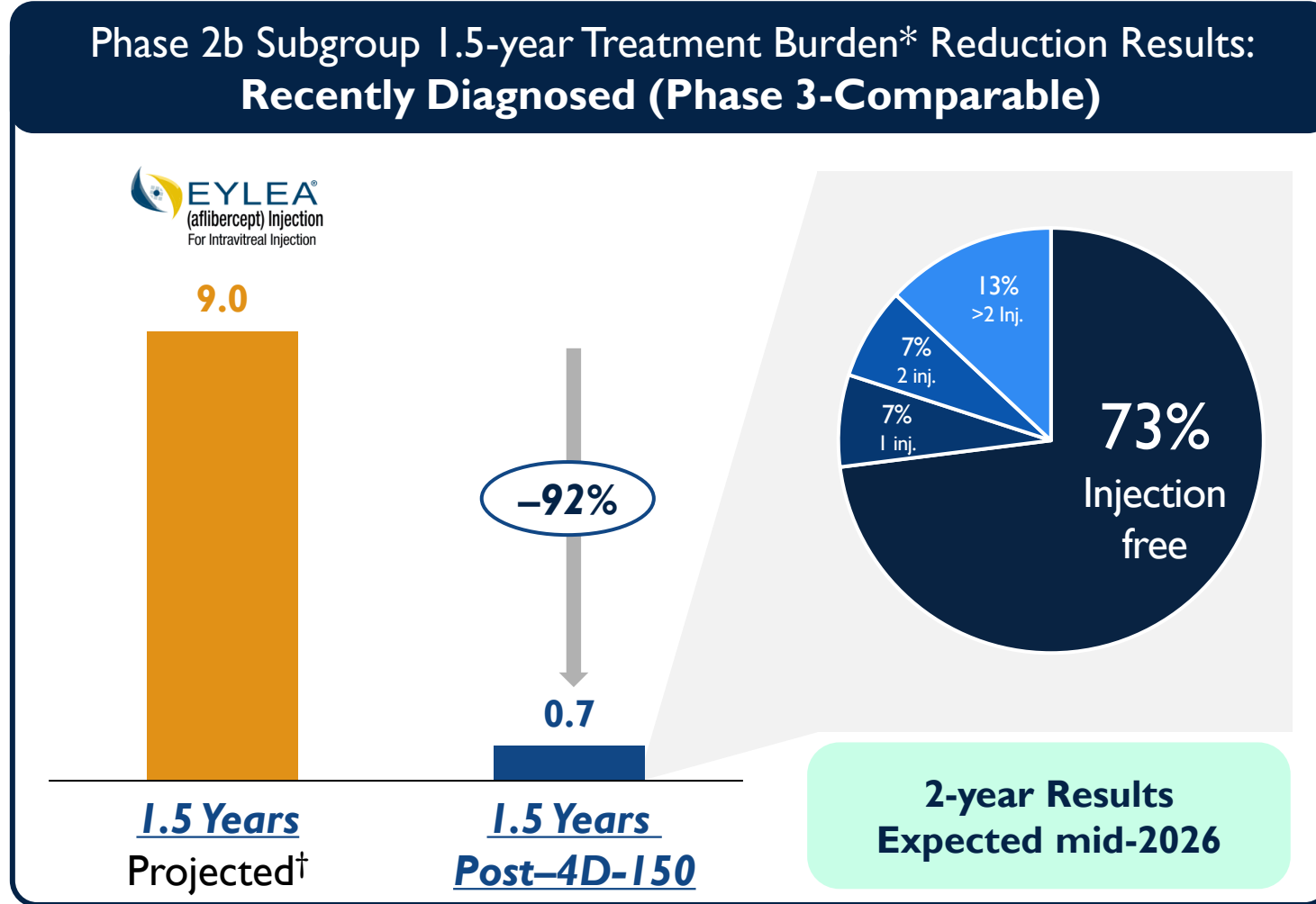


- Visual acuity: **stable**
- Retinal anatomy: **stable without fluctuations**
- Inflammation: **no meaningful signal**

Data cutoff of August 22, 2025.

\*Anti-VEGF Injections. †Projection based on last loading dose in Phase 2b and approved dosing schedule for aflibercept in wet AMD. Mean cumulative function from Cox proportional hazard regression model for recurrent events was used to estimate the mean cumulative number of supplemental aflibercept injections.

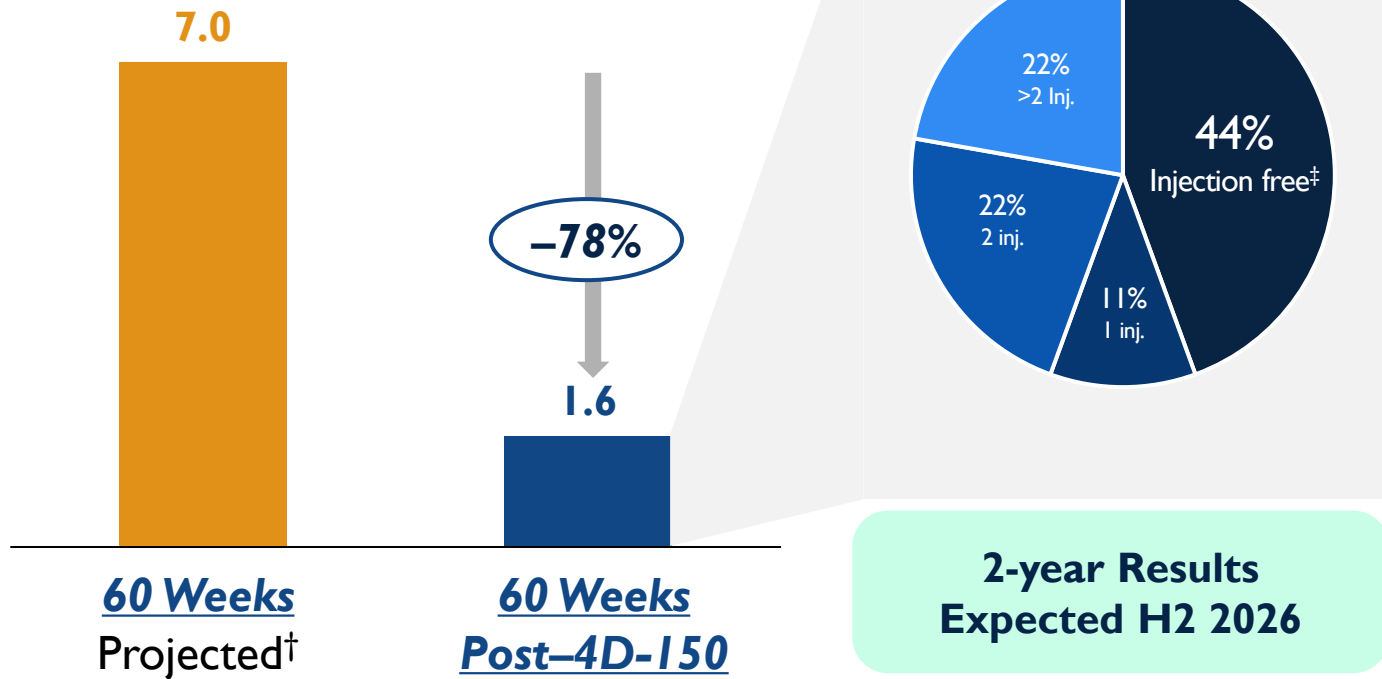
# Phase 2b 1.5-year Data: 73% Injection-free in Phase 3 Comparable Wet AMD Population



Data cutoff of August 22, 2025. \*Anti-VEGF Injections. †Projection based on last loading dose in Phase 2b and approved dosing schedule for aflibercept in wet AMD. Mean cumulative function from Cox proportional hazard regression model for recurrent events was used to estimate the mean cumulative number of supplemental aflibercept injections.

# Phase I/2 Data Demonstrates Durable Disease Control: 78% Treatment Burden Reduction in DME

## Phase I/2 60-week Treatment Burden\* Reduction Results: Diabetic Macular Edema



- Visual acuity: **stable**
- Retinal anatomy: **stable without fluctuations**
- Inflammation: **no signal**

Data cutoff of May 2, 2025. \*Anti-VEGF Injections. †Projection based on last loading dose and approved dosing schedule for aflibercept in DME. Mean cumulative function from Cox proportional hazard regression model for recurrent events was used to estimate the mean cumulative number of supplemental aflibercept injections. ‡One subject received supplemental aflibercept at W52 due to post-cataract surgery edema.



**4D-150**

**GOAL: To transform the standard of care for large market retinal vascular diseases with a safe, in-office & durable lifelong backbone therapy**

1. **Continuous disease control** enabled by **durable** retinal expression of aflibercept
2. **Global Phase 3 program** for Wet AMD & DME

# Wet AMD Global 4FRONT Phase 3 Program Overview: Derisking Strategy for Global Regulatory & Commercial Success

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- ✓ Continued strong Phase 1/2 & 2b results in broad patient populations
- ✓ Industry standard Phase 3 trial designs (Noninferiority to aflibercept)
- ✓ Optimized Phase 3 patient population
- ✓ Global regulatory alignment with FDA (RMAT), EMA (PRIME), PMDA

# DME Global Phase 3 Program Overview: Derisking Strategy for Global Regulatory & Commercial Success

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- ✓ Continued strong Phase 1/2 results
- ✓ Industry standard trial design (Noninferiority to aflibercept)
- ✓ Global regulatory alignment with FDA (RMAT) & EMA: Single Phase 3 trial sufficient to file for approval

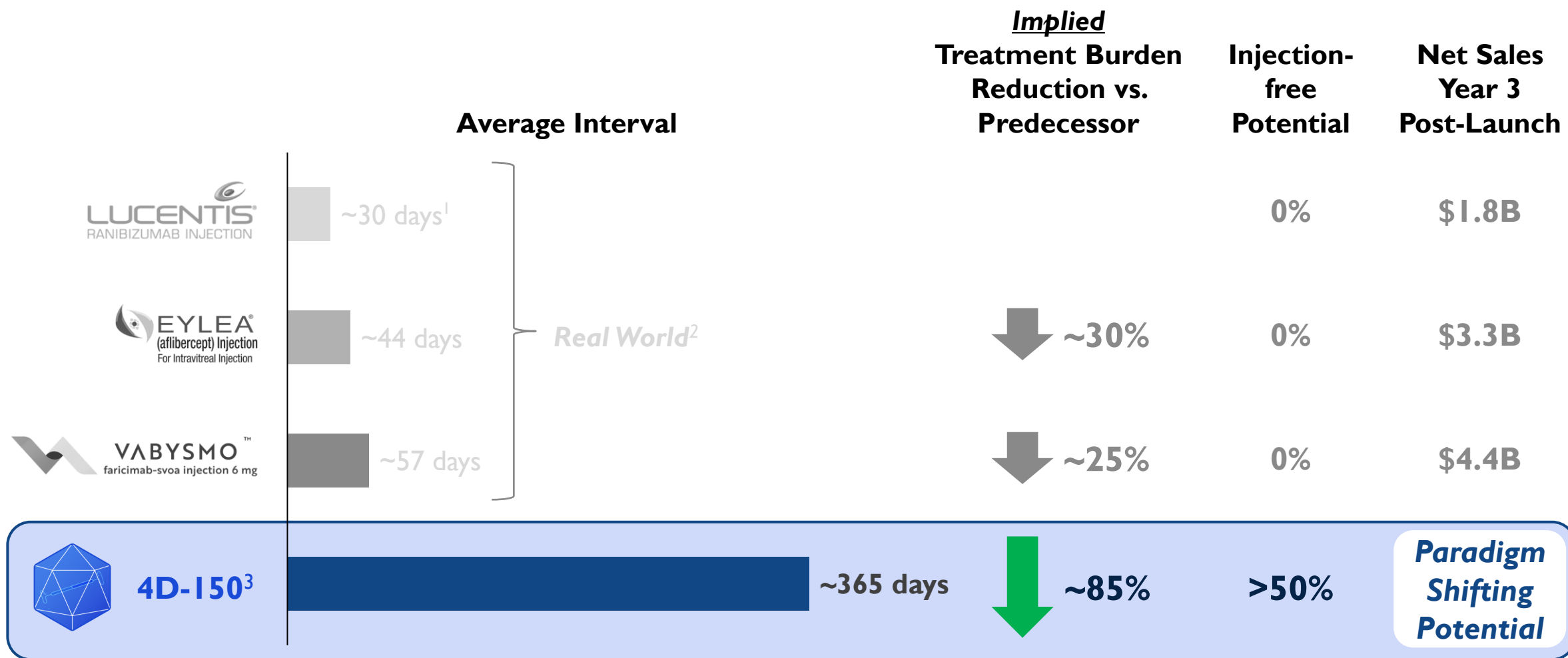


**4D-150**

**GOAL: To transform the standard of care for large market retinal vascular diseases with a safe, in-office & durable lifelong backbone therapy**

1. **Continuous disease control** enabled by **durable** retinal expression of aflibercept
2. **Global Phase 3 program** for Wet AMD & DME
3. **Paradigm-shifting durability** from incremental interval extension to potential **lifelong disease control & vision preservation**

# 4D-I50 Durability Profile is Paradigm-Shifting



1. Lucentis package insert; 2. Real-World Evidence (TRUCKEE Study). 3. 4DMT PRISM Phase 2b data, average interval based on 1.0 mean supplemental injections through 1 year in 3E10 vg/eye arm. Injection Burden Reduction vs. prior therapy implied based on difference calculated annual injections based on TRUCKEE durability.

# Commercial Model: Designed for Seamless Adoption & Global Scalability



## GLOBAL SCALABILITY

- **Manufacturing** scalability
- **Favorable COGS** margin
- **Efficient commercial infrastructure in U.S.** to reach ~2,500 retina specialists (<100 field reps)
- **Otsuka** infrastructure in APAC

## PAYORS

- **Unique value proposition** aligns incentives to long-term disease control and **vision protection**
- **Buy & bill model** fit (U.S.)
- **Flexible pricing** enabled by low COGS

## PRACTICE WORKFLOW & ECONOMICS

- **In-office routine IVT dosing**
- **Standard refrigeration**
- **Practice economics enhanced**
- **Clinic capacity increased**

# Key Catalysts: Poised for Strong Clinical Data & Phase 3 Execution

## Milestones followed by Topline Phase 3 Data

### Wet AMD

- **Q1 2026:** 4FRONT-1 randomization complete
- **Mid-2026:** PRISM Phase 2b 2-year data
- **H2 2026:** 4FRONT-2 randomization complete
- **H1 2027:** 4FRONT-1 topline data
- **H2 2027:** 4FRONT-2 topline data

### Diabetic Macular Edema

- **Mid-2026:** Finalize global Phase 3 design
- **Q3 2026:** Initiate global Phase 3 trial
- **H2 2026:** SPECTRA Trial 2-year data

**\$514M Cash\*** at YE2025, Runway Expected into **H2 2028**

\*Cash, cash equivalents and marketable securities (unaudited) as of December 31, 2025.

# Key Takeaways for 2026 & Beyond

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- **Continue reporting strong Phase 1/2 & 2b clinical data in wet AMD & DME**
- **Continue Phase 3 execution momentum**
  - Complete Phase 3 enrollment in Wet AMD (4FRONT-1/4FRONT-2)
  - Initiate Phase 3 in DME
- **Deliver topline Wet AMD Phase 3 data in H1 2027 & H2 2027**

**GOAL:** To transform the standard of care for large market retinal vascular diseases with a safe, in-office & durable lifelong backbone therapy



# THANK YOU

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