



# 4D-I50 Business & PRISM Wet AMD Long-term Data Update

November 6, 2025

# Legal Disclaimer

---

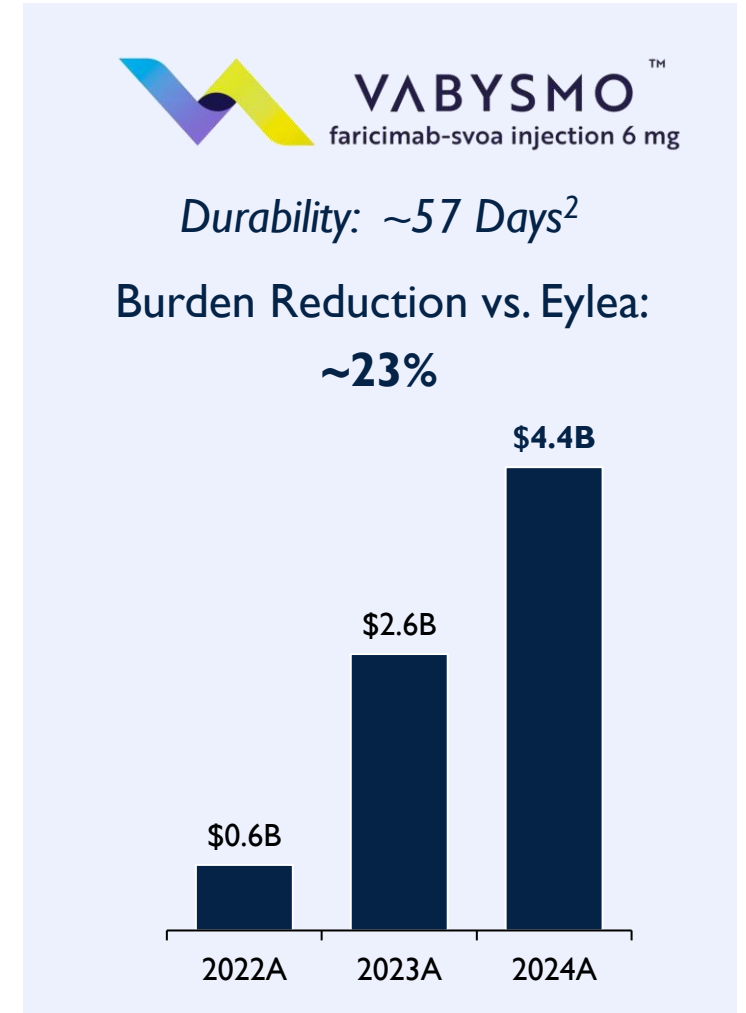
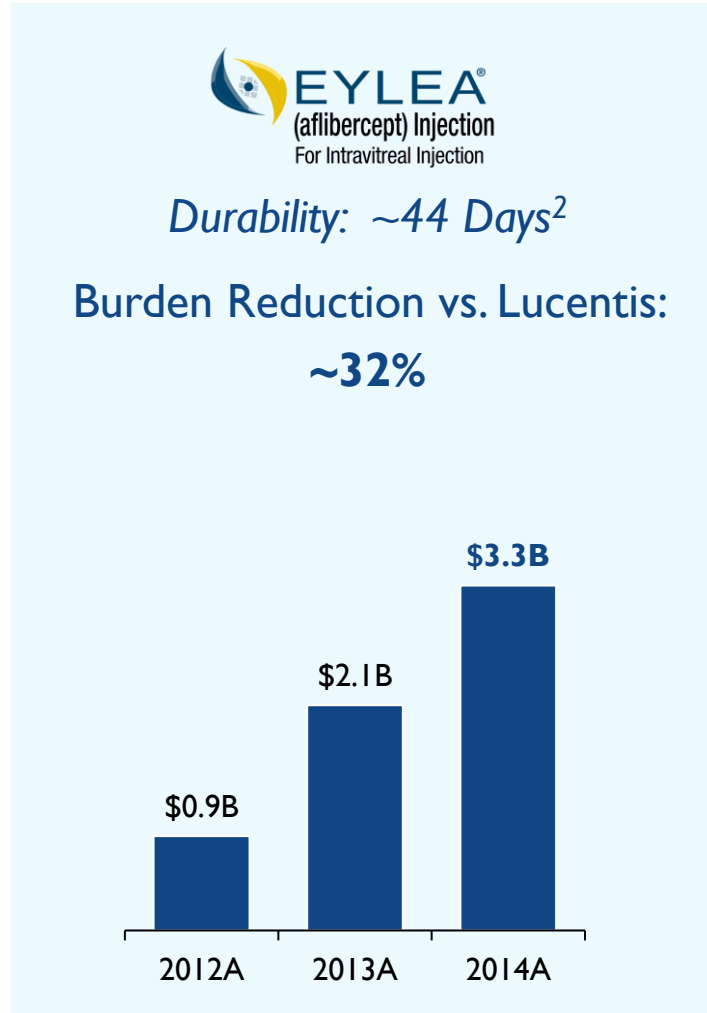
This Presentation contains forward looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Presentation, including statements regarding our clinical development plans, strategy, future operations, future financial position, prospects, plans, objectives of management, and implied and express statements regarding the therapeutic potential, clinical benefits of and market potential of our product candidates 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.

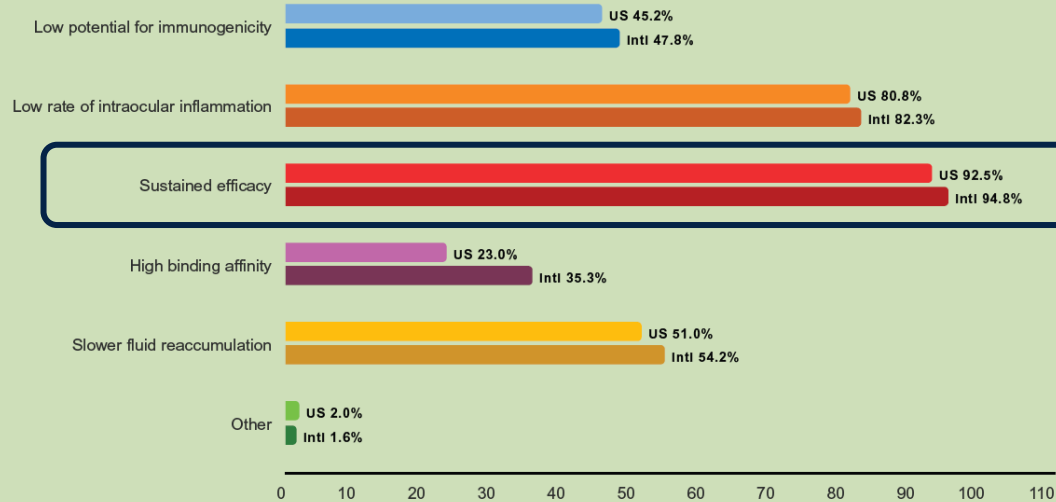
# Incremental Durability Improvements for Bolus Anti-VEGFs Have Resulted in Accelerating Launch Performance



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.

# ASRS Preferences and Trends (PAT) Survey 2025: Retina Specialists Are Excited to Utilize Gene Therapy for Wet AMD

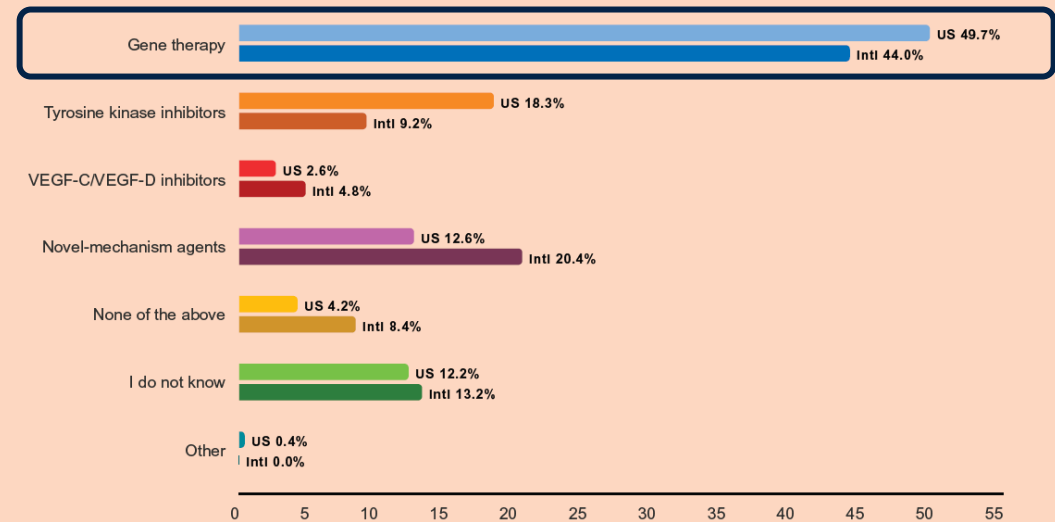
## Which factors are important when selecting an anti-VEGF agent?



34. Which of these factors are important considerations when selecting an anti-VEGF agent?  
(Select all that apply.)

*n* = 984

## Which pipeline treatment for wet AMD excites you most?

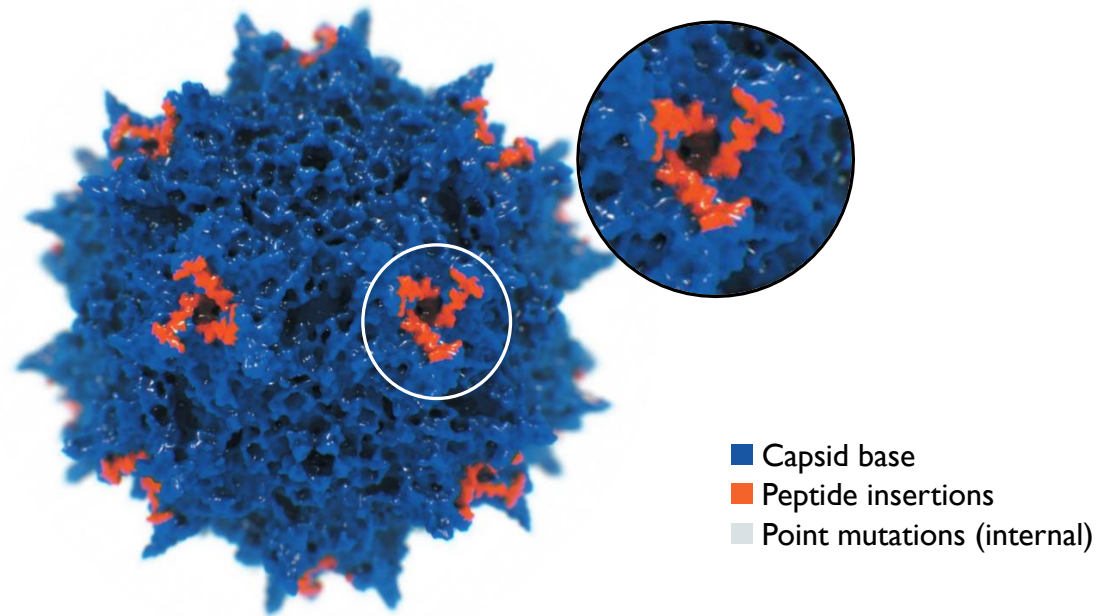


10. Which of the following pipeline treatments for wet AMD excites you most?

*n* = 987

# 4D-150 Designed for Sustained Intraretinal Expression of Anti-VEGF & Blockade of VEGF-C Production to Address Key Unmet Needs

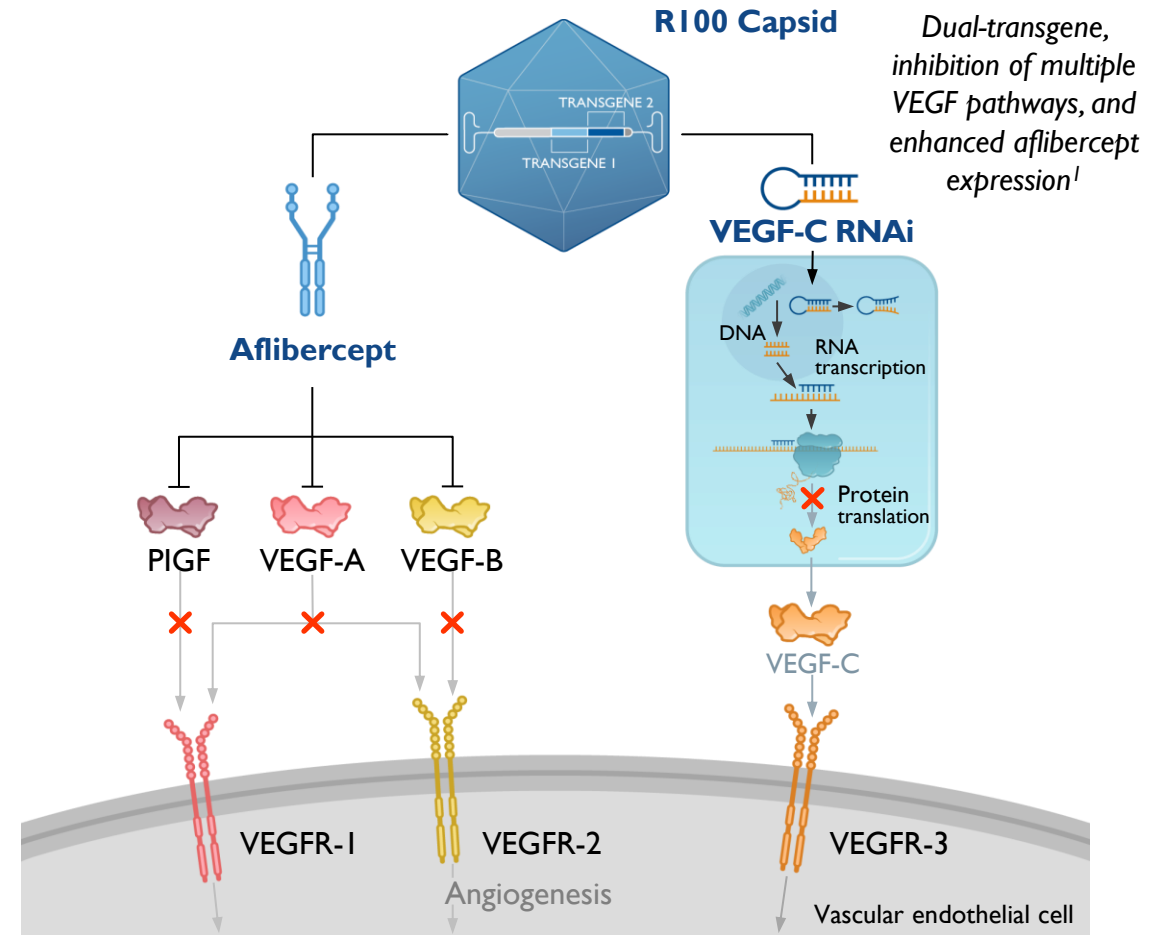
## R100 Capsid



- ✓ Minimal inflammation potential based on clinical data to date
- ✓ Robust delivery to multiple retinal layers
- ✓ Durable expression of transgenes

I. Calton et al. *Invest Ophthalmol Vis Sci* 2024;65:1.

## 4D-150



# 4D-150 Updates Today

**STRATEGIC  
PARTNERSHIP**



*Exclusive license  
for development and  
commercialization of **4D-150** in  
**Asia-Pacific region***

*Retained **substantial economic  
value** and leadership of global  
development*

**Enables DME Phase 3 initiation**

**POSITIVE WET AMD  
CLINICAL DATA**



*Consistency of  
**durability and safety data**  
across diverse populations  
through 1.5 & 2-years demonstrates  
**4D-150's potential to  
become a backbone therapy for  
retinal vascular diseases***

**STRONG  
PHASE 3 EXECUTION**



**4FRONT-1**  
*Treatment Naïve*  
**Over 200 patients randomized\***

**4FRONT-2**  
*Treatment Naïve & Experienced*  
**Enrollment on track,  
ex-U.S. sites expected to open in  
Nov'25**

Data cutoff of August 22, 2025.  
\*As of October 30, 2025

# Exclusive License Agreement with Otsuka Pharmaceutical for Development & Commercialization of 4D-I50 in Asia-Pacific Region



## **4D-I50 APAC License**

- **\$85M** *upfront*
- **At least \$50M** *cost sharing expected over next three years*
- **Up to \$336M** *in potential regulatory and commercial milestones*
- **Tiered, double-digit** *royalties on net sales in Otsuka territory*

### ✓ **Complementary Strengths:**

- **4DMT:** expertise in AAV genetic medicine, retina product development and manufacturing
  - **Otsuka:** global pharma with expertise in APAC regulatory and commercialization
- ✓ 4DMT retains full development and commercialization rights for 4D-I50 outside the APAC region
  - ✓ 4DMT continues to **lead global Phase 3 clinical development and manufacturing**
  - ✓ Upfront proceeds and cost reimbursement expected to support **global Phase 3 clinical trial in DME and retina pre-commercial activities**
  - ✓ APAC territory represents **~10% of global retinal anti-VEGF market**



# 4D-150

## PRISM Phase 1/2 Clinical Trial in Wet AMD

Long-term Clinical Data Update

# 4D-150 PRISM Phase 1/2 Update: 1.5- & 2-Year Clinical Activity Follow-up



## Key Takeaways

**Consistent,  
Durable and  
Clinically  
Meaningful  
Clinical Activity  
through 1.5 & 2  
Years**

- Visual acuity & anatomic control **maintained**
- **Consistent treatment burden reduction observed** over time and across diverse wet AMD disease activity populations:
  - **Recently diagnosed\*** subgroup (Phase 2b, 1.5 Years): **92%**
  - **Broad** (Phase 2b, 1.5 Years): **82%**
  - **Severe, recalcitrant** (Phase 1/2a, 2 Years): **79%**
- **Strong dose response** favoring Phase 3 dose (3E10 vg/eye)

Data cutoff of August 22, 2025.  
\*Disease duration  $\leq 0.5$  years.

# 4D-150 PRISM Phase 1/2 Update: Up to 3+ Years of Safety Follow-up



## Key Takeaways

Consistent,  
Durable and  
Clinically  
Meaningful  
Clinical Activity  
through 1.5 & 2  
Years

No New Safety  
or IOI Events

- Visual acuity & anatomic control maintained
- Consistent treatment burden reduction observed over time and across diverse wet AMD disease activity populations:
  - Recently diagnosed\* subgroup (Phase 2b, 1.5 Years): 92%
  - Broad (Phase 2b, 1.5 Years): 82%
  - Severe, recalcitrant (Phase 1/2a, 2 Years): 79%
- Strong dose response favoring Phase 3 dose (3E10 vg/eye)

- No related SAE, hypotony, vasculitis, hypotony, endophthalmitis, occlusive/non-occlusive retinal vasculitis, or choroidal effusions
- Phase 3 dose (3E10 vg/eye, N=71):
  - No new intraocular inflammation (IOI) since last update
  - Overall, no IOI in 97.2%
  - Through 28 weeks: 2 cases of mild, transient IOI, as previously reported
  - From after 28 weeks through 3.5 years+: No IOI

Data cutoff of August 22, 2025.  
\*Disease duration ≤0.5 years.

# 4D-I50 Wet AMD Development Program: Robust & Comprehensive Global Strategy, Studying Increasingly Early-Stage Populations

## PRISM Phase I/2

**Phase I/2a**  
Safety,  
Proof of Concept

24

*Severe,  
Recalcitrant*

10.2

425  $\mu\text{m}$

3.7 years

**Phase 2b**  
Clinical Activity in  
Broader Population

30

*Broad*

4.4

336  $\mu\text{m}$

1.8 years

**Phase 2b  
Subgroup**  
Phase 3-Comparable

15

*Recently  
Diagnosed\*\**

2.7

304  $\mu\text{m}$

0.2 years

**4FRONT-1**  
**4FRONT-2**  
**Phase 3**

~400

*Tx Naïve / Recently  
Diagnosed\*\**

0-4

$\leq 500 \mu\text{m}$

$\leq 0.5$  years

**Phase 3 Dose**  
3E10 vg/eye (N=)\*

**Population:**

**Mean Injections in  
Last 12 Mo.**

**Mean CST**

**Mean Time Since Dx**

\*Phase 3 dose. \*\* $\leq 0.5$  years with previous treatment.

# 4D-I50 Wet AMD Development Program: Robust & Comprehensive Global Strategy, Studying Increasingly Early-Stage Populations

## PRISM Phase I/2

**Phase 3 Dose**  
3E10 vg/eye (N=)\*

**Population:**

**Mean Injections in Last 12 Mo.**

**Mean CST**

**Mean Time Since Dx**

Phase I/2a  
Safety,  
Proof of Concept

24

Severe,  
Recalcitrant

10.2

425 µm

3.7 years

Phase 2b  
Clinical Activity in  
Broader Population

30

Broad

4.4

336 µm

1.8 years

**Phase 2b  
Subgroup**  
Phase 3-Comparable

15

**Recently  
Diagnosed\*\***

2.7

304 µm

0.2 years

4FRONT-1  
4FRONT-2  
Phase 3

~400

Tx Naïve / Recently  
Diagnosed\*\*

0-4

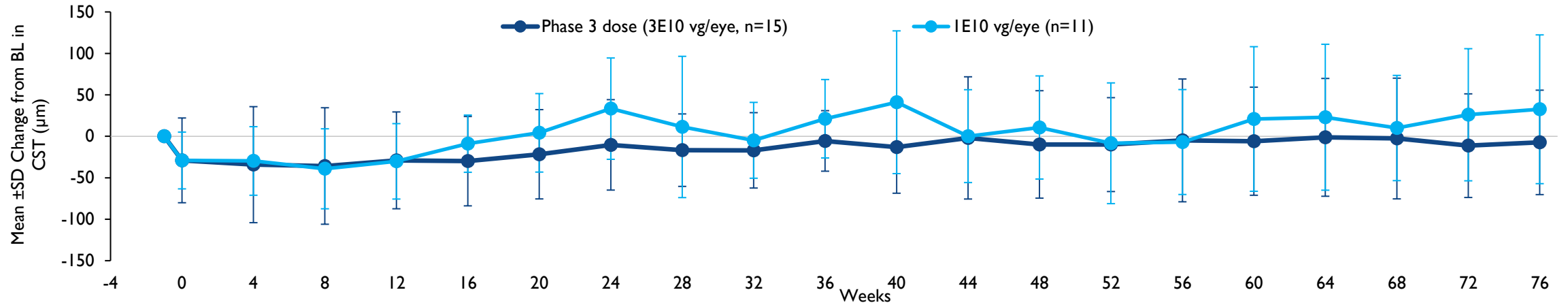
≤500 µm

≤0.5 years

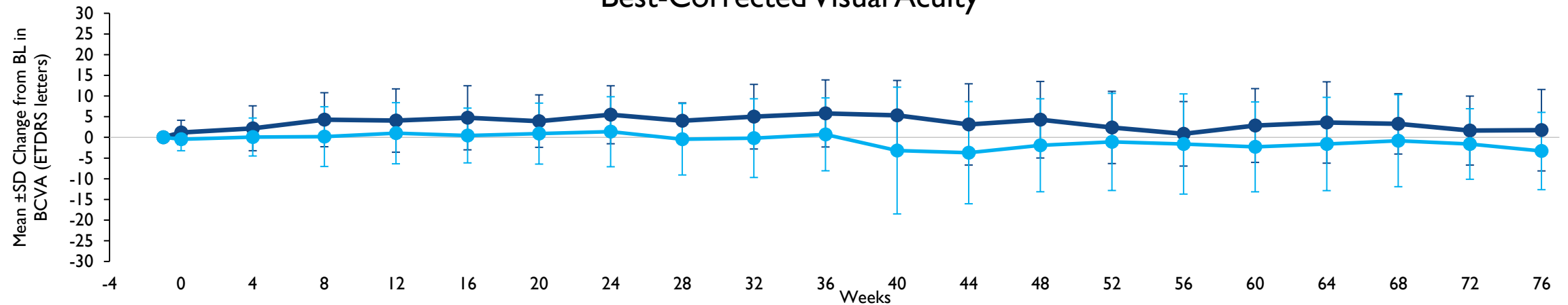
\*Phase 3 dose. \*\*≤0.5 years with previous treatment.

# In Phase 3-Comparable Wet AMD Population, Visual Acuity & Anatomy Stable Through 1.5 Years

### Central Subfield Thickness



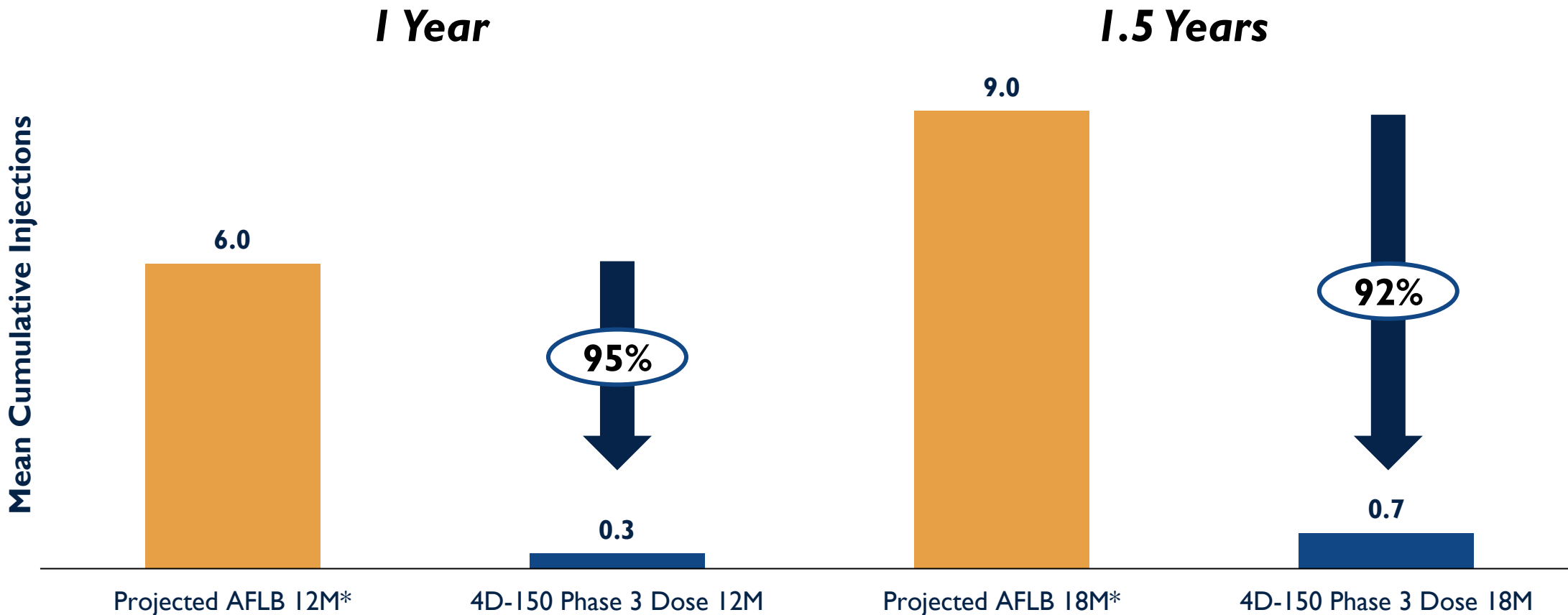
### Best-Corrected Visual Acuity



Data cutoff of August 22, 2025.

CST, central subfield thickness; BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study.

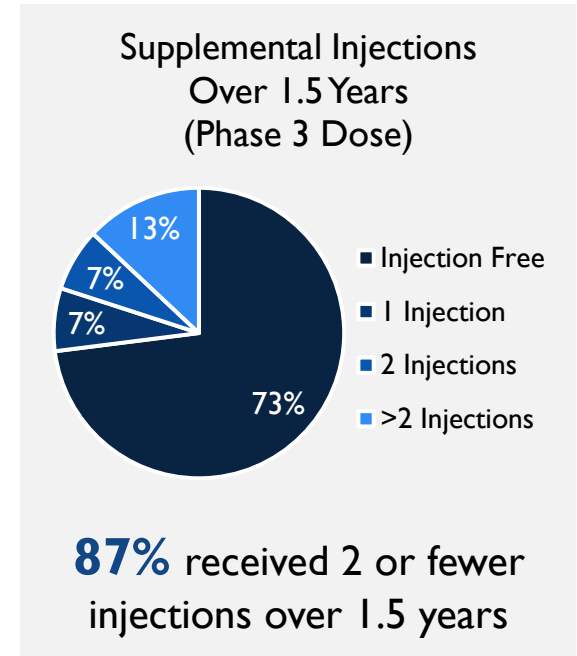
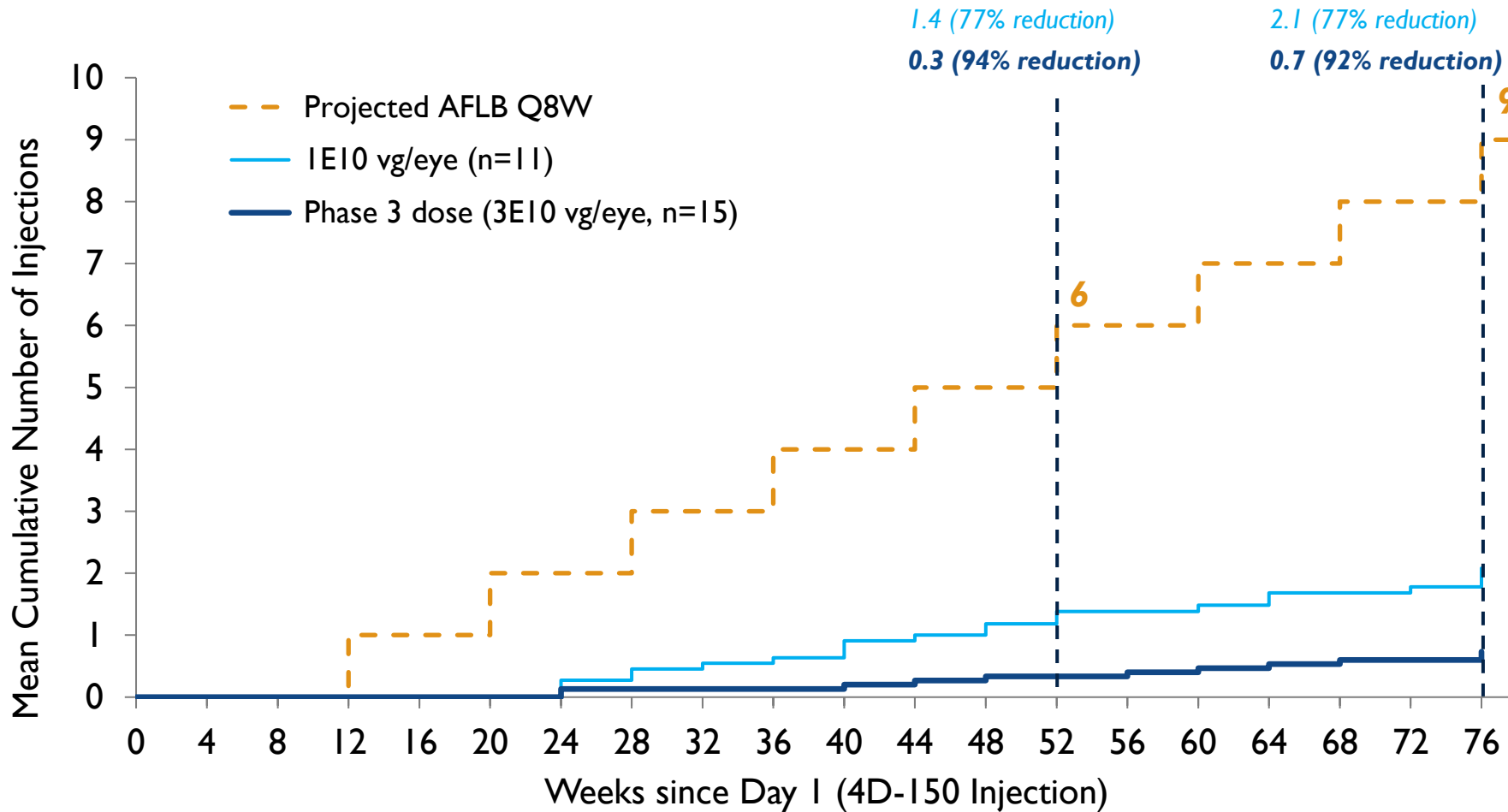
# Consistent and Durable Treatment Burden Reductions in Phase 3-Comparable Wet AMD Population Over 1.5 Years



Data cutoff of August 22, 2025.

\*Projection based on approved dosing schedule for aflibercept 2mg in wet AMD after loading doses.

# 3E10 vs. 1E10 vg/eye: Consistent Dose Response in Mean Cumulative Supplemental Injections Through 1.5 Years



Data cutoff of August 22, 2025.

MCF, mean cumulative function derived from a single-arm Cox proportional hazard regression model. Projection based on approved dosing schedule for aflibercept in wet AMD after loading doses.

# 4D-I50 Wet AMD Development Program: Robust & Comprehensive Global Strategy, Studying Increasingly Early-Stage Populations

## PRISM Phase I/2

**Phase 3 Dose**  
3E10 vg/eye (N=)\*

**Population:**

**Mean Injections in Last 12 Mo.**

**Mean CST**

**Mean Time Since Dx**

Phase I/2a  
Safety,  
Proof of Concept

24

Severe,  
Recalcitrant

10.2

425  $\mu$ m

3.7 years

**Phase 2b**  
Clinical Activity in  
Broader Population

**30**

**Broad**

4.4

336  $\mu$ m

1.8 years

Phase 2b  
Subgroup  
Phase 3-Comparable

15

Recently  
Diagnosed\*\*

2.7

304  $\mu$ m

0.2 years

4FRONT-1  
4FRONT-2  
**Phase 3**

~400

Tx Naïve / Recently  
Diagnosed\*\*

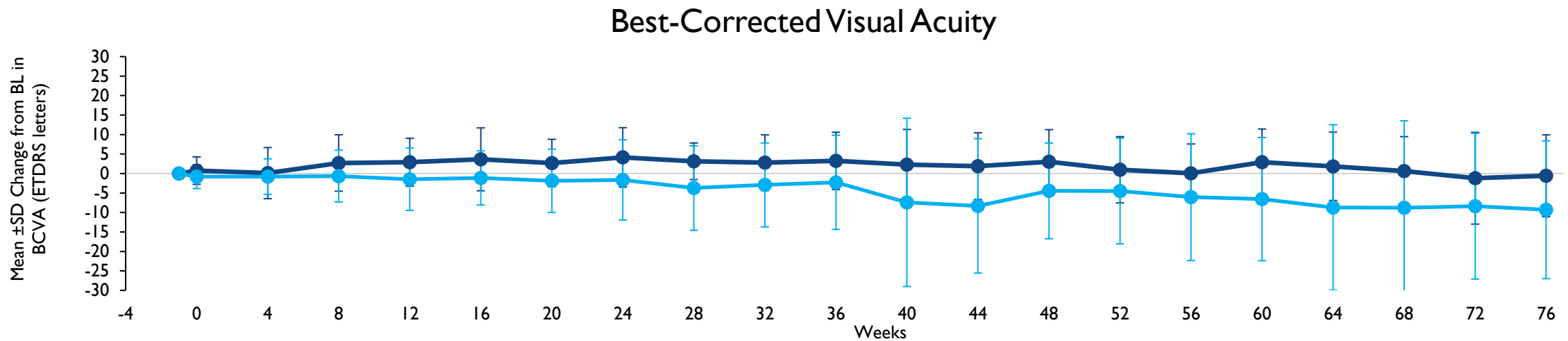
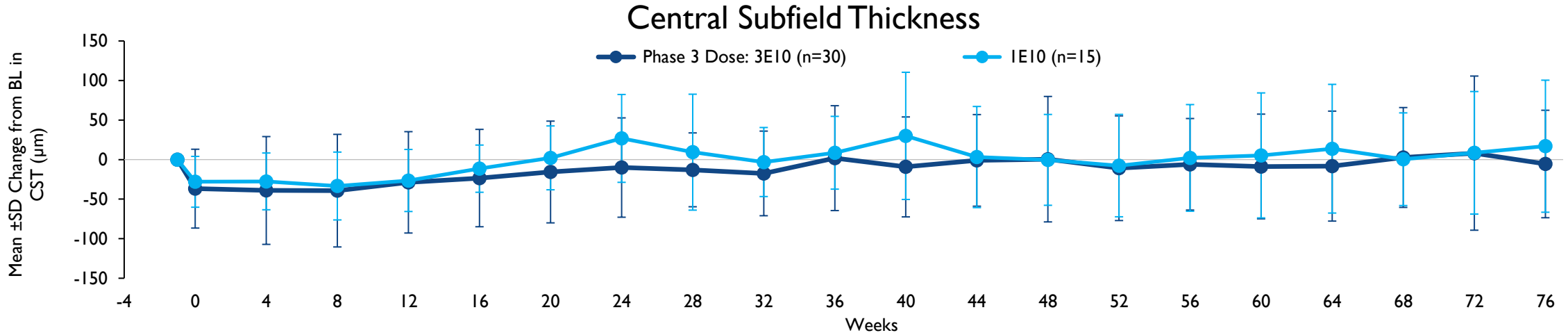
0-4

$\leq$ 500  $\mu$ m

$\leq$ 0.5 years

\*Phase 3 dose. \*\* $\leq$ 0.5 years with previous treatment.

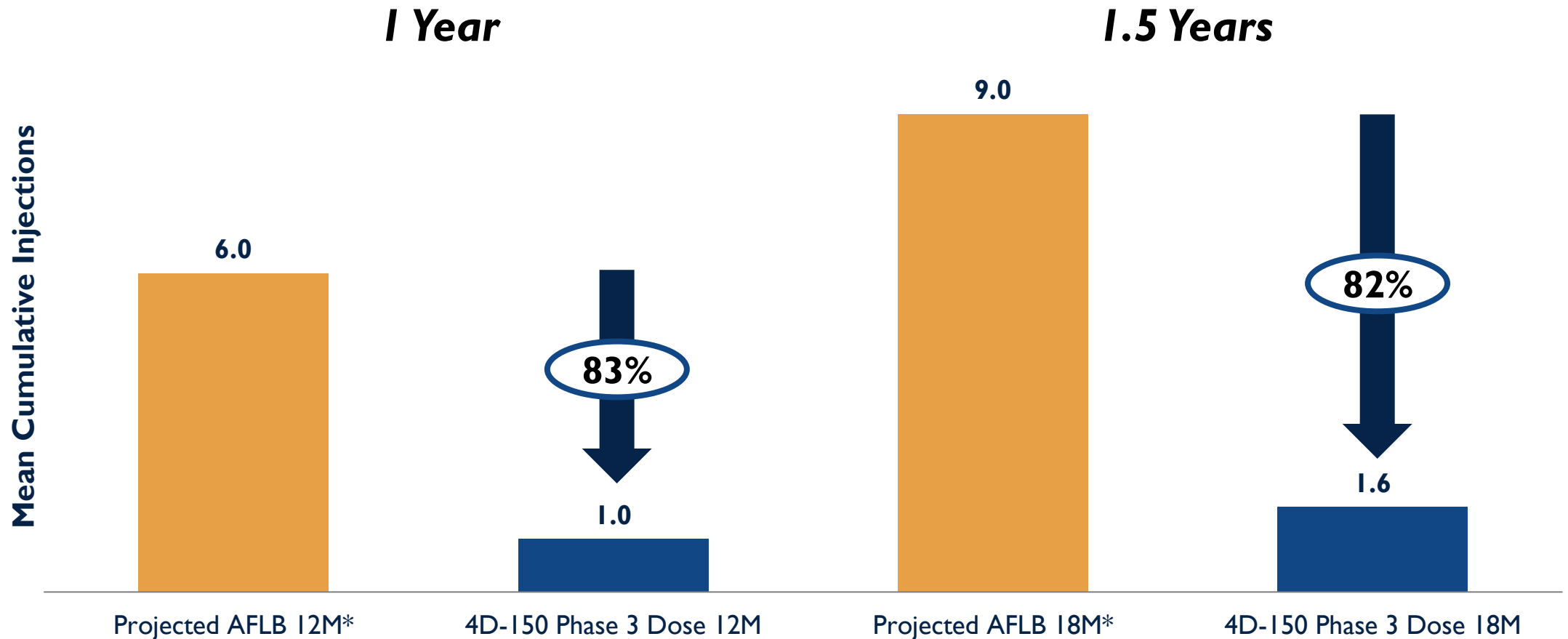
# In a Broad Wet AMD Population, Visual Acuity & Anatomy Stable Through 1.5 Years



Data cutoff of August 22, 2025.

CST, central subfield thickness; BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study.

# Consistent and Durable Treatment Burden Reductions in a Broad Wet AMD Population Over 1.5 Years

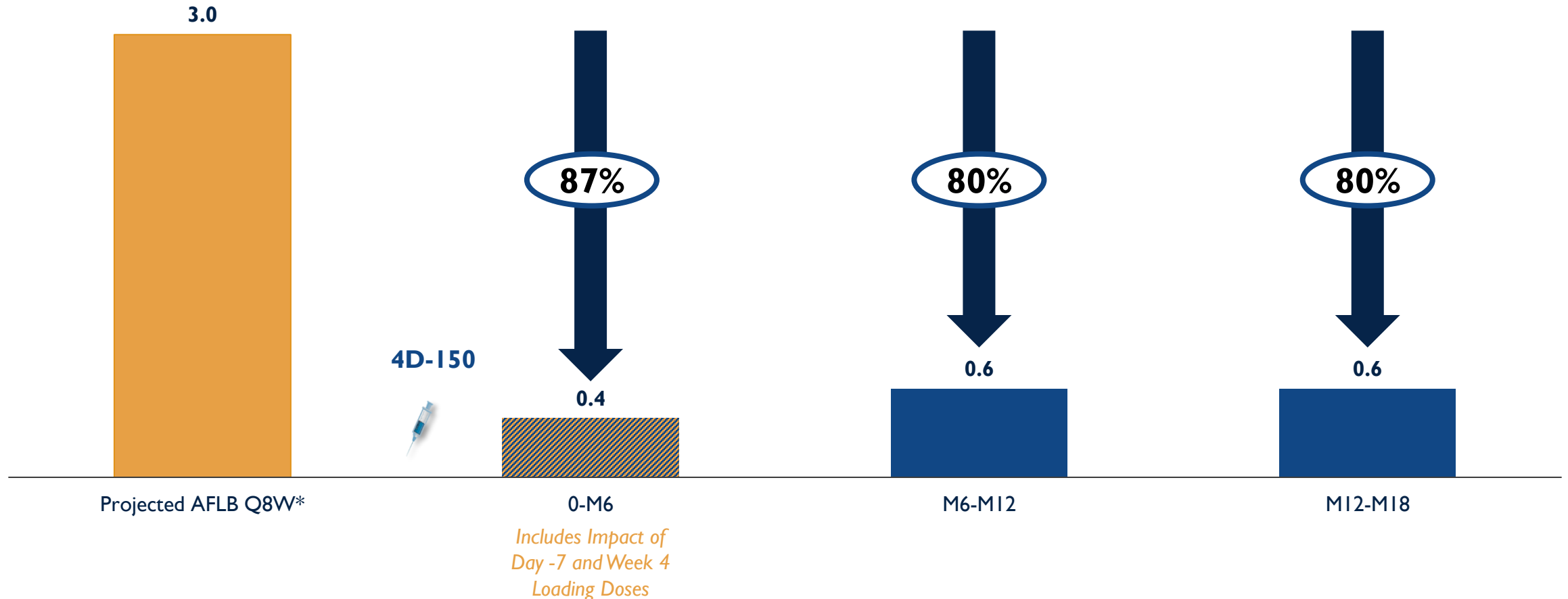


Data cutoff of August 22, 2025.

\*Projection based on approved dosing schedule for aflibercept 2mg in wet AMD after loading doses.

# Consistent and Durable Treatment Burden Reductions in a Broad Wet AMD Population Over 1.5 Years: 6-Month Segments

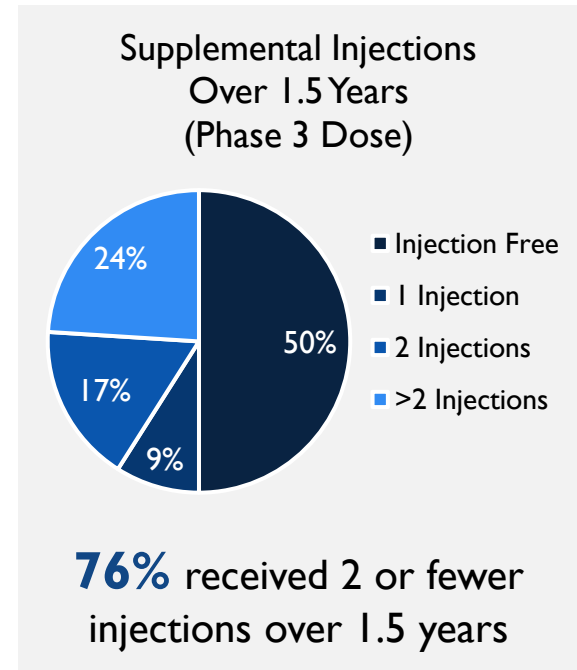
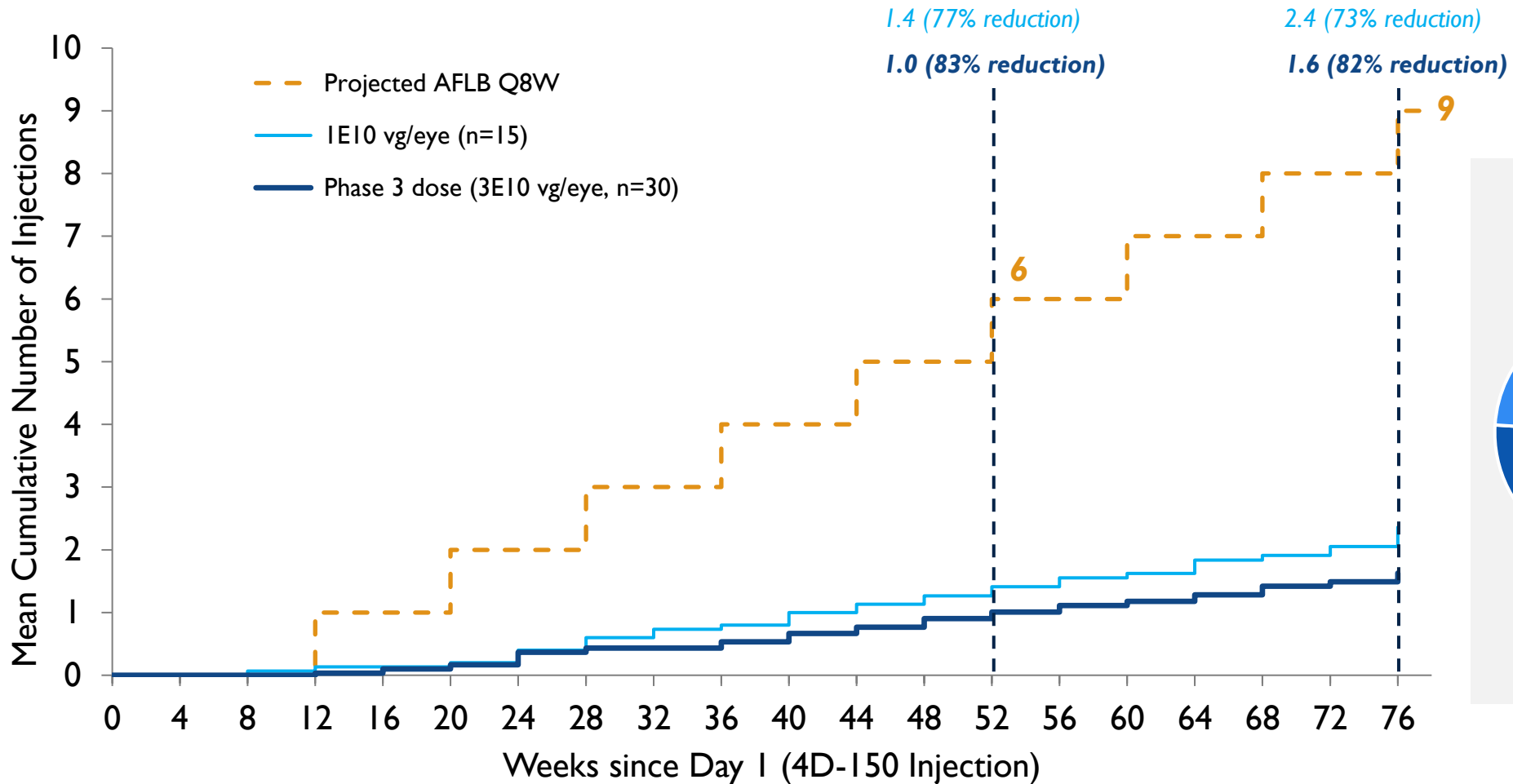
Treatment Burden Reduction in 4D-I50 Phase 3 Dose vs. Projected AFLB 2mg Q8W (6-month Segment)



Data cutoff of August 22, 2025.

\*Projection based on approved dosing schedule for aflibercept 2mg in wet AMD after loading doses.

# 3E10 vs. 1E10 vg/eye: Consistent Dose Response in Mean Cumulative Supplemental Injections Through 1.5 Years



Data cutoff of August 22, 2025.

MCF, mean cumulative function derived from a single-arm Cox proportional hazard regression model. Projection based on approved dosing schedule for aflibercept in wet AMD after loading doses.

# 4D-I50 Wet AMD Development Program: Robust & Comprehensive Global Strategy, Studying Increasingly Early-Stage Populations

## PRISM Phase I/2

**Phase 3 Dose**  
3E10 vg/eye (N=)\*

**Population:**

**Mean Injections in Last 12 Mo.**

**Mean CST**

**Mean Time Since Dx**

**Phase I/2a**  
Safety,  
Proof of Concept

24

*Severe,  
Recalcitrant*

10.2

425 µm

3.7 years

**Phase 2b**  
Clinical Activity in  
Broader Population

30

*Broad*

4.4

336 µm

1.8 years

**Phase 2b**  
Subgroup  
Phase 3-Comparable

15

*Recently  
Diagnosed\*\**

2.7

304 µm

0.2 years

4FRONT-1  
4FRONT-2  
**Phase 3**

~400

*Tx Naïve / Recently  
Diagnosed\*\**

0-4

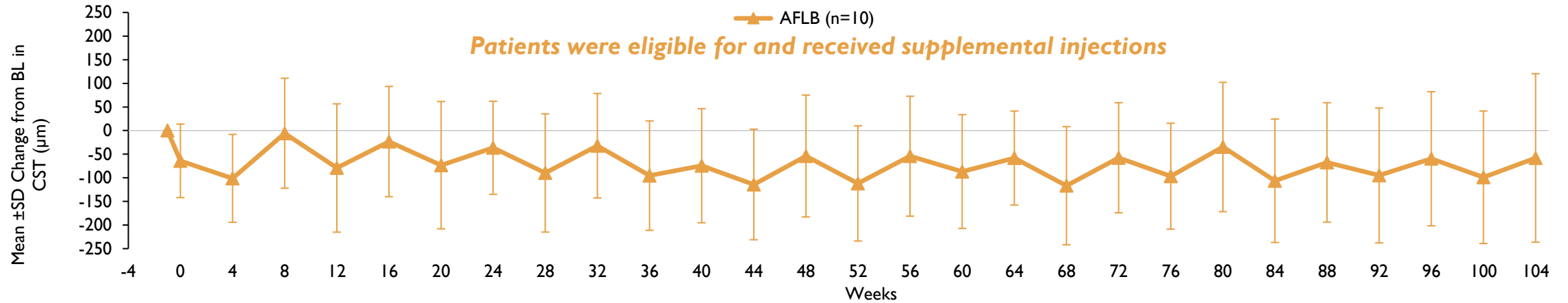
≤500 µm

≤0.5 years

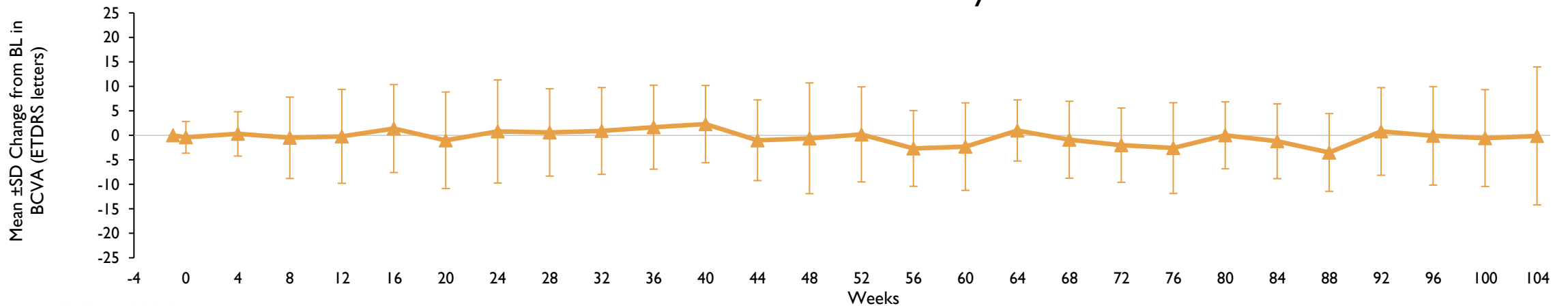
\*Phase 3 dose. \*\*≤0.5 years with previous treatment.

# In Severe, Recalcitrant Population, Stable Visual Acuity with Large Anatomic Fluctuations in Aflibercept 2mg Q8W through 2 Years

### Central Subfield Thickness



### Best-Corrected Visual Acuity

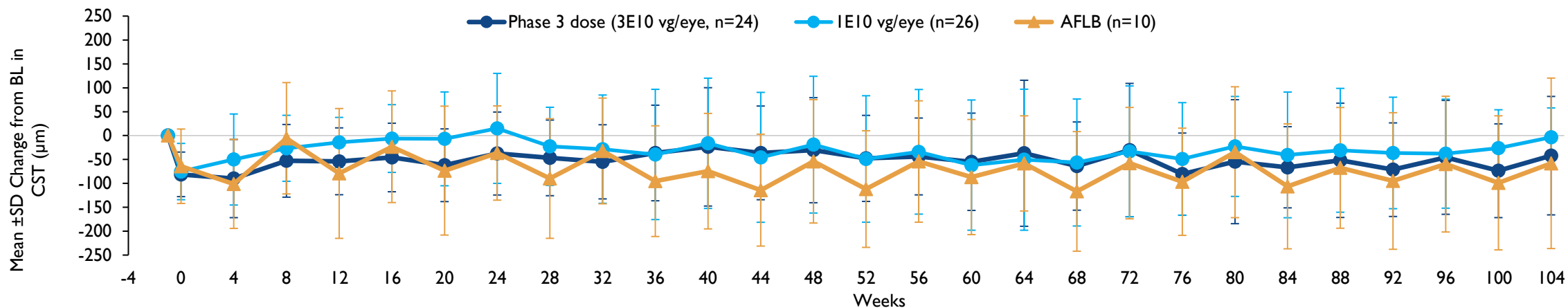


Data cutoff of August 22, 2025.

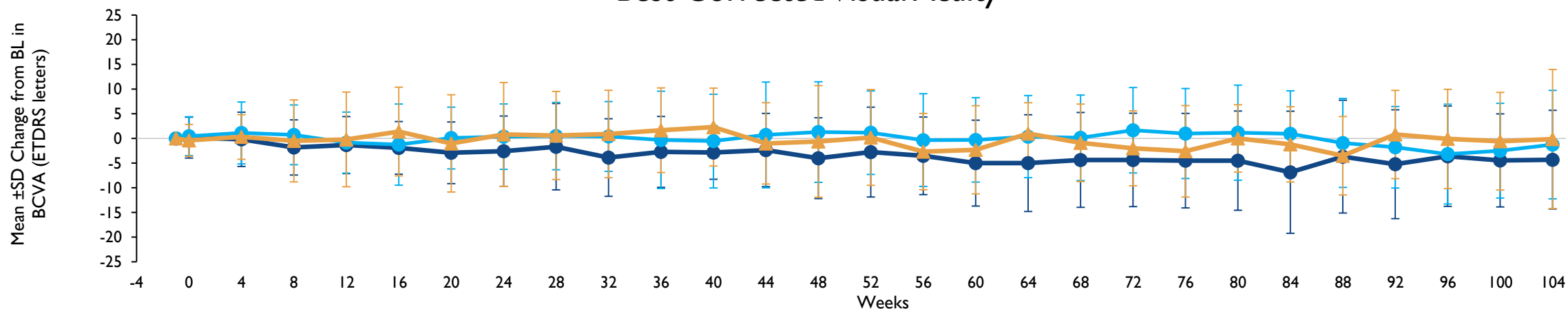
CST, central subfield thickness; BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study.

# 4D-I50 Visual Acuity Comparable to Aflibercept 2mg Q8W Through 2 Years, With Fewer Anatomic Fluctuations

### Central Subfield Thickness



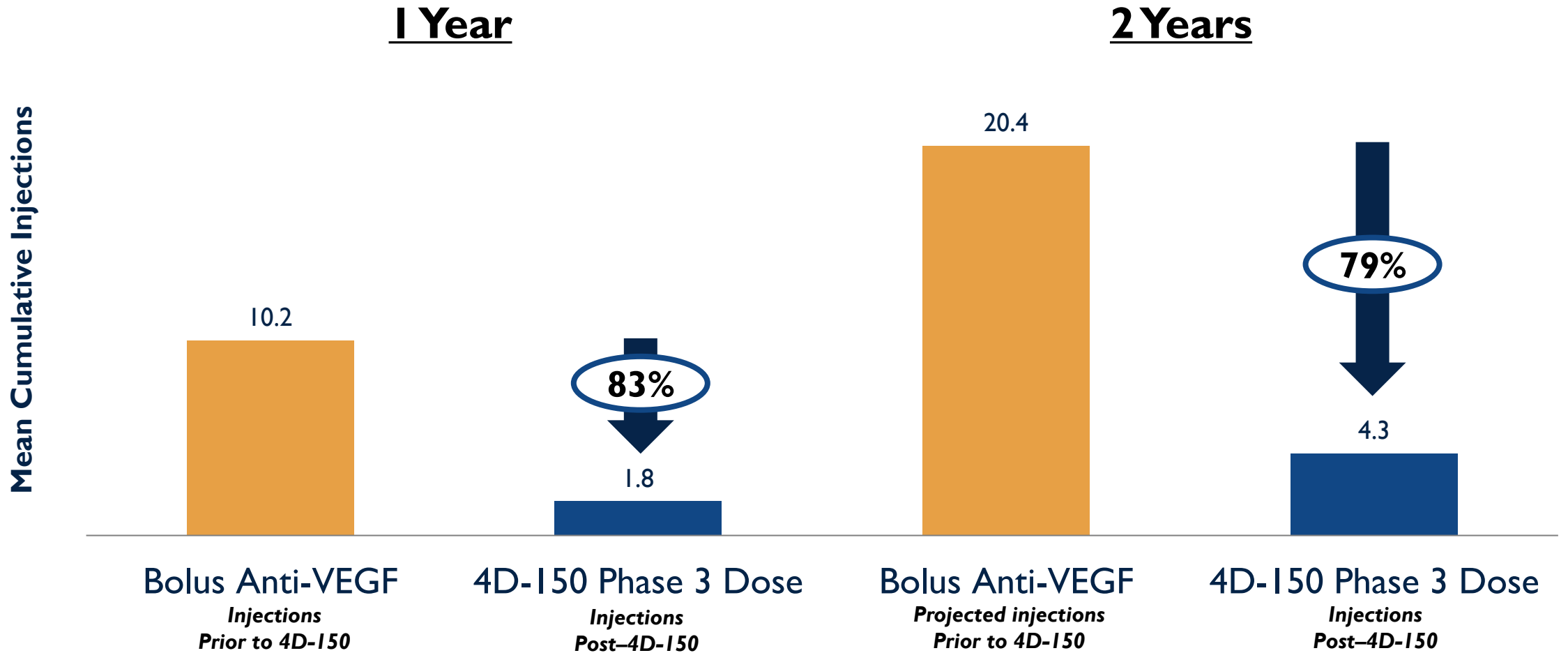
### Best-Corrected Visual Acuity



Data cutoff of August 22, 2025.

CST, central subfield thickness; BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study.

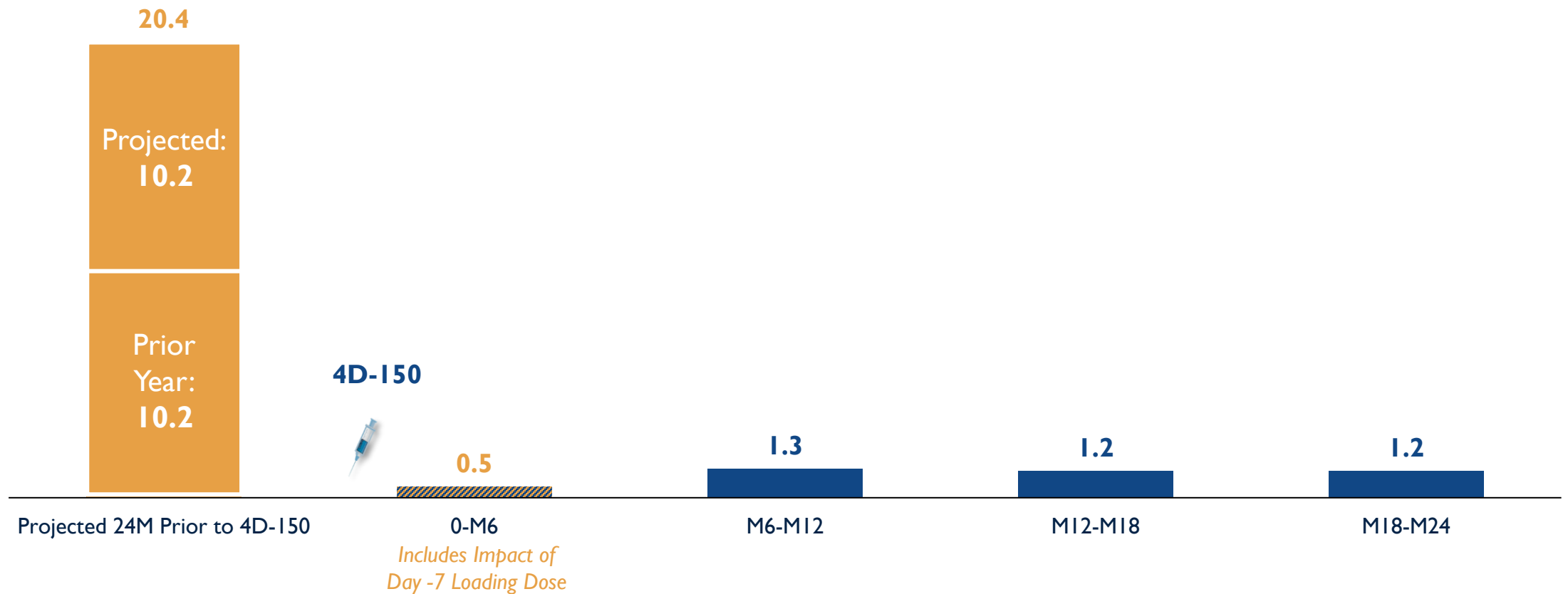
# Robust, Consistent, and Durable Treatment Burden Reductions Over 2 Years in Severe, Recalcitrant Wet AMD Population



Data cutoff of August 22, 2025.  
VEGF, vascular endothelial growth factor.

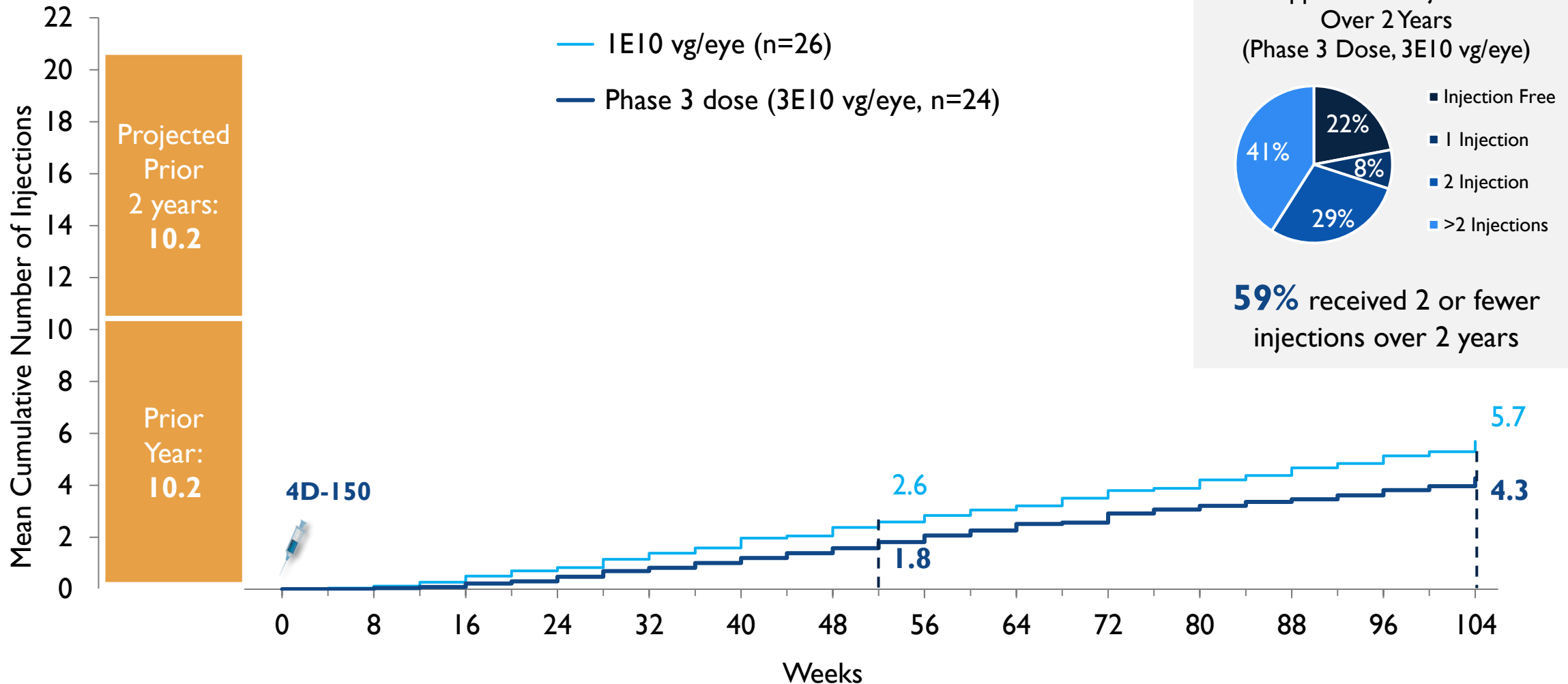
# Robust, Consistent, and Durable Treatment Burden Reductions Over 2 Years in Severe, Recalcitrant Wet AMD Population: Over 6-month Segments

Treatment Burden Reduction in Phase 3 Dose vs. Prior (6-month Segments)



Data cutoff of August 22, 2025.

# 3E10 vs. 1E10 vg/eye: Consistent Dose Response in Mean Cumulative Supplemental Injections Through 2 Years



Data cutoff of August 22, 2025.

# 4D-I50 Continues to be Well Tolerated: No Change Since Last Update

- No 4D-I50–related serious adverse events
- No 4D-I50–related hypotony, endophthalmitis, occlusive/non-occlusive retinal vasculitis, or choroidal effusions
- 4D-I50–related intraocular inflammation (SUN/NEI):
  - Through Week 28 post-4D-I50: **1+** vitreous cells at a single timepoint in 2 of 71 (**2.8%**), as previously reported\*
  - After Week 28 post-4D-I50: **No inflammation reported**
  - **99%** (70 of 71) completed prophylactic topical steroid taper on schedule
  - **99%** (70 of 71) remain completely off steroids

Data cutoff of August 22, 2025.

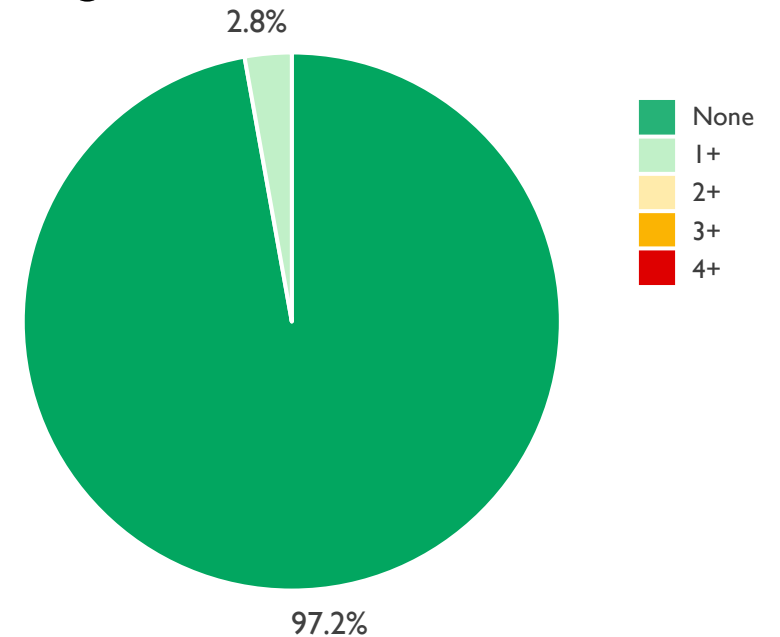
†4D-I50–related. \*One case at Week 4 and one case at Week 28.

Intraocular inflammation defined as presence of  $\geq 1$  anterior chamber or vitreous white blood cells on SUN/NEI scale.

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

4D-I50 3E10 vg/eye (N=71)\*

Highest SUN/NEI Score†

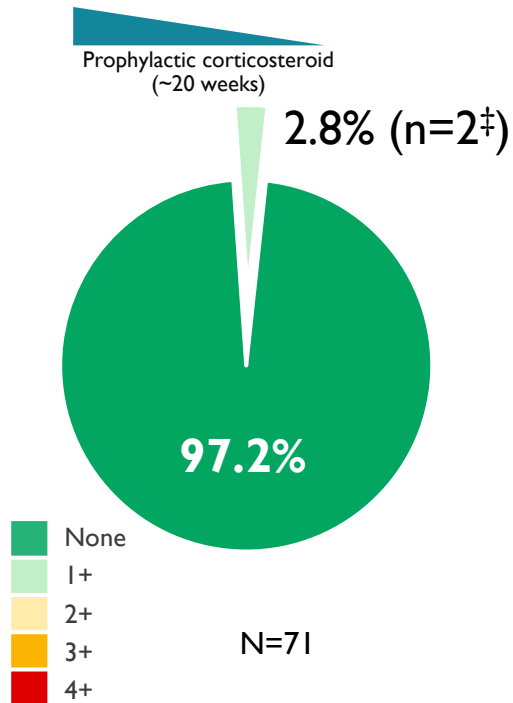


Patients have reached  
**1.5 to 3.5+ years** of follow-up

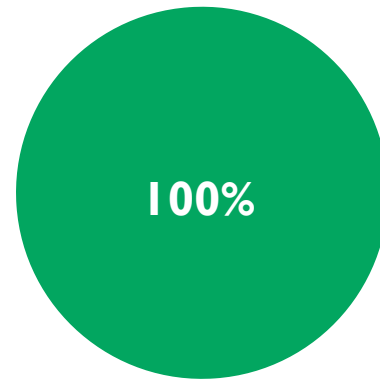
# Follow-up Through 1.5 to 3.5+ Years Suggests a Consistent and Predictable Intraocular Inflammation Profile with Phase 3 Dose

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

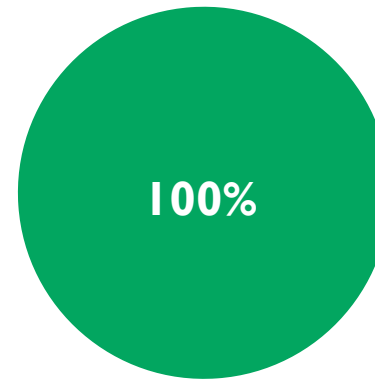
## Through Week 28



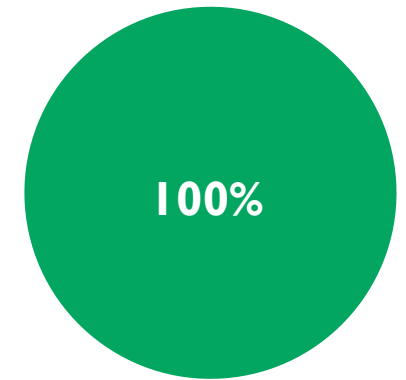
## After Week 28 to Year 1



## Year 1 to 1.5



## Year 1.5 to 3.5+



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.

# 4D-150 PRISM Phase 1/2 Update: 1.5- & 2-Year Follow-up



## Key Takeaways

**Consistent, Durable and Clinically Meaningful Clinical Activity through 1.5 & 2 Years**

**No New Safety or IOI Events**

- Visual acuity & anatomic control **maintained**
- **Consistent treatment burden reduction observed** over time and across diverse wet AMD disease activity populations:
  - **Severe, recalcitrant** (Phase 1/2a, 2 Years): **79%**
  - **Broad** (Phase 2b, 1.5 Years): **82%**
  - **Recently diagnosed\* subgroup** (Phase 2b, 1.5 Years): **92%**
- **Strong dose response** favoring Phase 3 dose (3E10 vg/eye)

- No related SAE, hypotony, vasculitis, hypotony, endophthalmitis, occlusive/non-occlusive retinal vasculitis, or choroidal effusions
- Phase 3 dose (3E10 vg/eye, N=71):
  - **No new intraocular inflammation (IOI) since last update**
  - **Overall, no IOI in 97.2%**
  - **Through 28 weeks**: 2 cases of mild, transient IOI, *as previously reported*
  - **From after 28 weeks through 3.5 years+**: **No IOI**

Data cutoff as of August 22, 2025.  
\*Disease duration ≤0.5 years.

# Global 4FRONT Phase 3 Wet AMD Program: Evaluating the Efficacy, Safety, and Durability of a Single IVT Injection of 4D-150 vs. Aflibercept 2mg Q8W

## Primary Objective

Demonstrate non-inferiority in the mean change in BCVA from baseline to Week 52 of a single injection of 4D-150 compared to aflibercept 2mg (Q8W) after three aflibercept doses

Costs for both trials to be shared Otsuka

## 4FRONT-1

**North America**  
N=400

100% Treatment naïve

Initiated in March 2025

## 4FRONT-2

**Global**  
N=400

60% Treatment naïve; 40% Previously treated  
(1-4 prior injections, diagnosed within 6 months)

Initiated in June 2025

## Key Inclusion Criteria

**BCVA:**  
25-78 letters

**Active disease**

**CST:**  
≤500 μm

**Anti-VEGF responsive**

Primary 52-week topline data expected:  
4FRONT-1 in H1 2027 & 4FRONT-2 in H2 2027

CST, central subfield thickness; BCVA, best corrected visual acuity; VEGF, vascular endothelial growth factor.

# 4D-I50 Expected Milestones in 2026 to 2027: Significant Execution and Value Inflection Planned



*Backbone therapy with the potential to transform the treatment paradigm and provide unprecedented benefits to patients with retinal vascular diseases*






**Wet AMD**

**Diabetic Macular Edema**

## **Key Expected Milestones:**

- ✓ **Oct 2025:** >200 patients randomized in 4FRONT-1
  - **Mid-2026:** PRISM Phase 2b 2-year data
  - **2026:** Complete enrollment in 4FRONT Phase 3's
  - **H1 2027:** 4FRONT-1 topline data
  - **H2 2027:** 4FRONT-2 topline data
  - **2026-27:** Commercial preparations
  - **H1 2028:** File BLA, assuming positive 4FRONT results
- ✓ Upfront proceeds and cost sharing from Otsuka partnership **enables initiation of the single global Phase 3 study required for approval**
  - **Mid-2026:** Phase 3 design to be shared after ongoing alignment with Otsuka and APAC regulatory agencies

# Rapidly Progressing Late-Stage 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	2025-2027 EXPECTED MILESTONES
<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 1-year data</li> <li>✓ 4FRONT-1 Ph3 Initiation</li> <li>✓ 4FRONT-2 Ph3 Initiation</li> <li>✓ PRISM Ph1/2 1.5- &amp; 2-year data</li> <li>▪ PRISM Ph2b 2-year data: <b>Mid-2026</b></li> <li>▪ 4FRONT Ph3 enroll. complete: <b>2026</b></li> <li>▪ 4FRONT-1 topline: <b>H1 2027</b></li> <li>▪ 4FRONT-2 topline: <b>H2 2027</b></li> </ul>
		DME	~5M U.S./EUMM				SPECTRA Trial: <ul style="list-style-type: none"> <li>✓ 32-week data</li> <li>✓ 60-week data</li> </ul> Phase 3 Trial: <ul style="list-style-type: none"> <li>▪ Finalize trial design: <b>Mid-2026</b></li> </ul>
<b>PULMONOLOGY</b>   <b>AI01</b>  Aerosol	<b>4D-710</b>	CF lung disease (mod. Ineligible or intolerant)	~15K WW				<ul style="list-style-type: none"> <li>▪ Interim data &amp; program update: <b>YE 2025</b></li> </ul>

**Seeking Partnerships or Additional Financing to Advance Other Pipeline Candidates:**

4D-175 for Geographic Atrophy and 4D-725 for AIAT



# THANK YOU

5858 Horton Street, Suite 455 | Emeryville, California 94608

(510) 505-2680 | [Investor.Relations@4DMT.com](mailto:Investor.Relations@4DMT.com)

[IR.4DMT.com](http://IR.4DMT.com) | [LinkedIn](#)

# Baseline Characteristics: Phase I/2a (Dose Exploration/Expansion)

Characteristic	4D-150 3E10 vg/eye N=24	4D-150 1E10 vg/eye N=26	AFLB 2mg Q8W N=10	All N=60
Mean $\pm$ SD age, years	77 $\pm$ 7.9 59–91	77 $\pm$ 8.6 57–92	80 $\pm$ 4.1 74–85	77 $\pm$ 7.7 57–92
Mean $\pm$ SD BCVA, ETDRS letters	67 $\pm$ 11.0 35–80	70 $\pm$ 11.7 39–82	71 $\pm$ 13.2 43–87	69 $\pm$ 12.5 35–87
Mean $\pm$ SD central subfield thickness, $\mu$ m	425 $\pm$ 89.8 302–742	443 $\pm$ 114.5 295–816	419 $\pm$ 64.3 326–521	432 $\pm$ 97.1 295–816
Mean $\pm$ SD time since diagnosis, years	<b>3.7</b> $\pm$ 2.9 0.7–11.1	<b>2.9</b> $\pm$ 2.1 0.7–8.2	<b>2.1</b> $\pm$ 1.5 1.0–5.7	3.1 $\pm$ 2.4 0.7–11.1
Mean prior <i>annualized</i> injection rate*	<b>10.1</b>	<b>9.7</b>	<b>9.0</b>	9.7
Mean $\pm$ SD <i>number</i> injections, prior 12 months*	<b>10.2</b> $\pm$ 2.4 7–13	<b>9.2</b> $\pm$ 2.1 7–14	<b>9.3</b> $\pm$ 0.9 8–11	9.6 $\pm$ 2.1 7–14

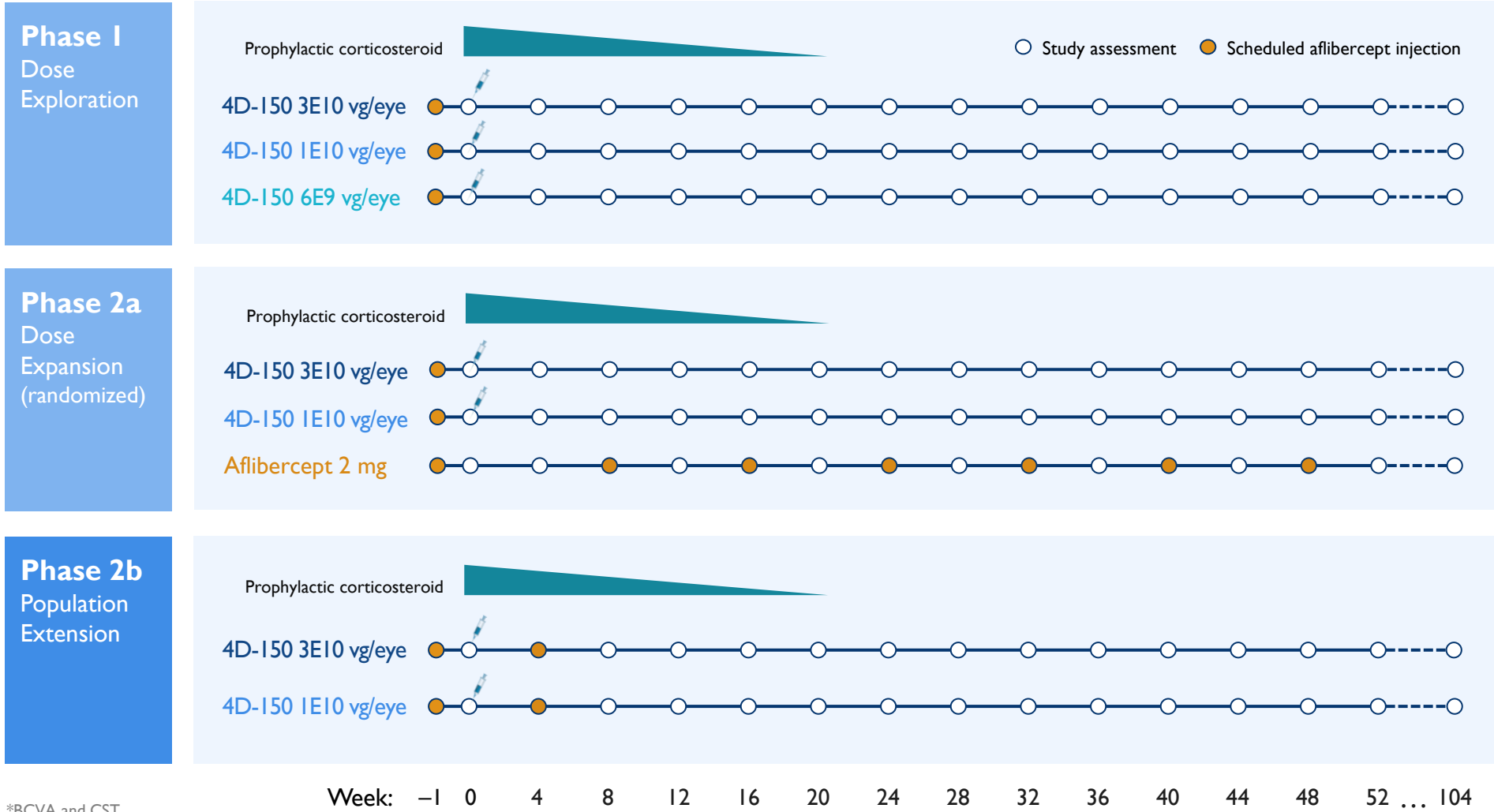
\*Includes Day -7 AFLB injection. BCVA, best corrected visual acuity; VEGF, vascular endothelial growth factor.

## Baseline Characteristics: Phase 2b (Population Extension)

	3E10 vg/eye (N=30)	1E10 vg/eye (N=15)	Total (N=45)
Mean $\pm$ SD age, years	77 $\pm$ 7.7 62–92	78 $\pm$ 8.6 63–90	77 $\pm$ 7.9 62–92
Female, n (%)	20 (67)	6 (40)	26 (58)
Race, n (%)			
White	30 (100)	14 (93)	44 (98)
Asian	0	1 (7)	1 (2)
Mean $\pm$ SD BCVA, ETDRS letters	71 $\pm$ 9.9 45–83	73 $\pm$ 8.8 51–80	72 $\pm$ 9.5 45–83
Mean $\pm$ SD central subfield thickness, $\mu$ m	336 $\pm$ 135.0 188–702	314 $\pm$ 70.8 225–441	329 $\pm$ 117.1 188–702
Mean $\pm$ SD time since diagnosis, years	1.8 $\pm$ 3.4 0.1–13.9	0.7 $\pm$ 0.9 0.1–3.0	1.4 $\pm$ 2.9 0.1–13.9
Mean prior <i>annualized</i> injection rate*	8.3	10.7	9.0
Mean $\pm$ SD <i>number</i> injections, prior 12 months*	4.4 $\pm$ 2.0 2–7	4.3 $\pm$ 2.1 2–9	4.4 $\pm$ 2.0 2–9

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

# Wet AMD Phase 1/2 Schemas



## Supplemental Injection Criteria

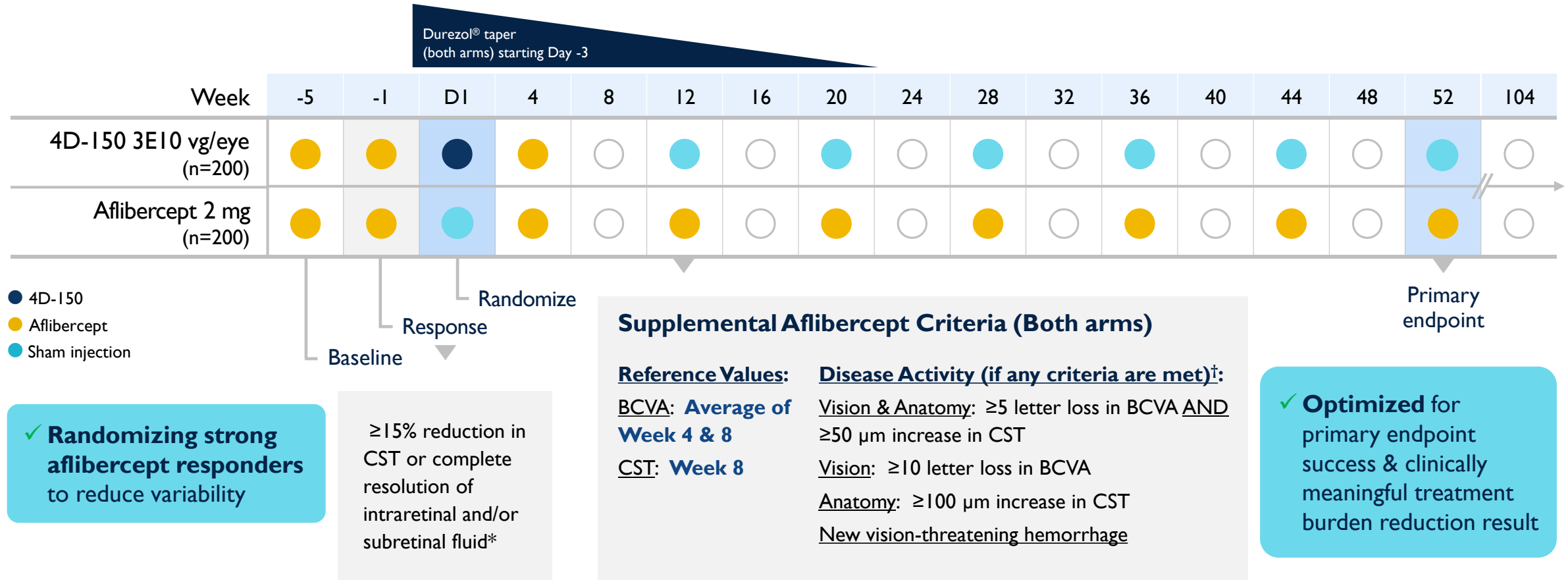
- Reference Values\***
- Average of Week -1 and Day 1
- Disease Activity**
- BCVA: Loss of  $\geq 10$  letters attributable to retinal fluid,
  - OR
  - CST: Increase of  $\geq 75 \mu\text{m}$
  - OR
  - New vision-threatening hemorrhage due to wet AMD per investigator

\*BCVA and CST.  
CST, central subfield thickness; BCVA, best corrected visual acuity.

# 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



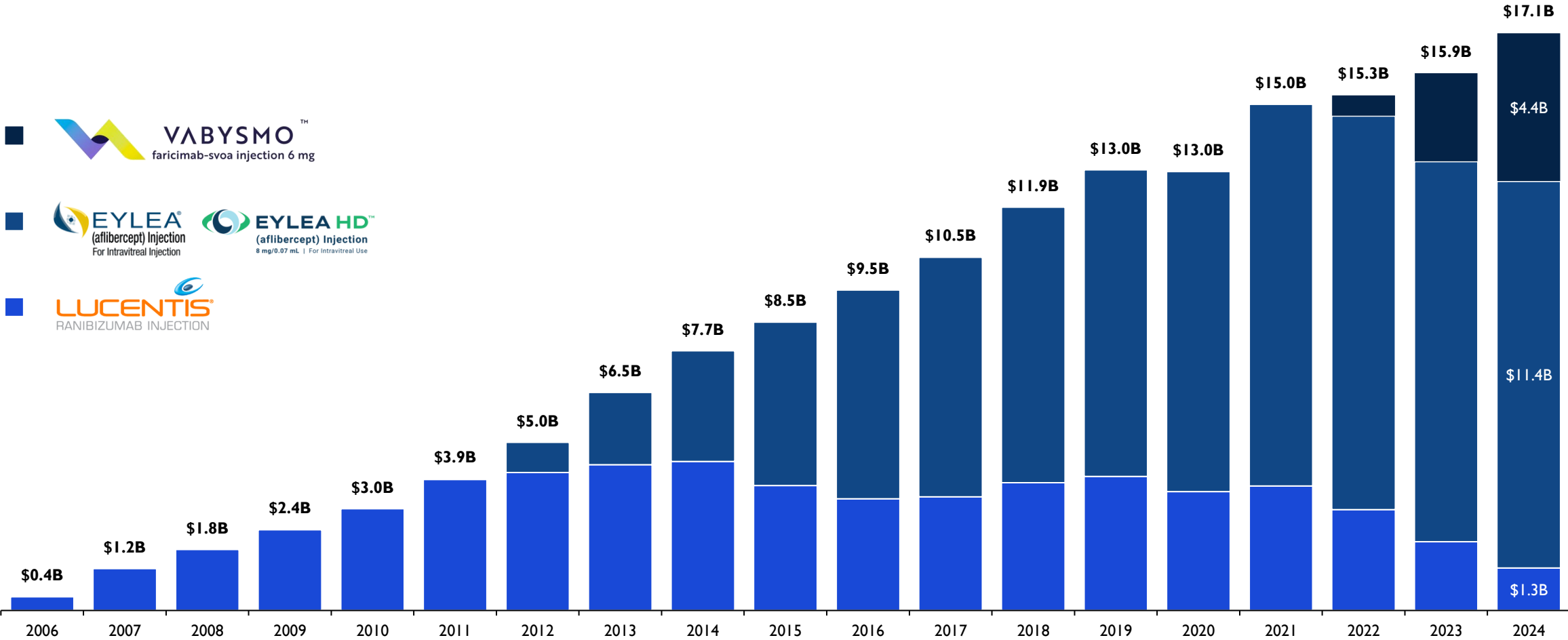
\*Determined by SD-OCT and confirmed by an independent Reading Center. †PI discretion not allowed.

# 4FRONT Supplemental Criteria Optimized for Phase 3 Success & Clinically Meaningful Treatment Burden Reduction



Reference Measurement	Post 1 loading dose: ▪ <u>BCVA &amp; CST</u> : Average of Week -1 and Day 1	Post 2-3 loading doses: ▪ <u>BCVA</u> : <b>Average of Week 4 &amp; 8</b> ▪ <u>CST</u> : <b>Week 8</b>
Vision & Anatomy	None	<b>≥5 letter loss in BCVA AND ≥50 μm increase in CST</b>
Vision Only	≥10 letter loss in BCVA <b>OR</b>	≥10 letter loss in BCVA <b>OR</b>
Anatomy Only	≥75 μm increase in CST <b>OR</b>	≥ <b>100 μm</b> increase in CST <b>OR</b>
Hemorrhage	Presence of vision-threatening new macular hemorrhage <b>OR</b>	Presence of vision-threatening new macular hemorrhage
PI Discretion	Allowed	<b>Not Allowed</b>

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



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

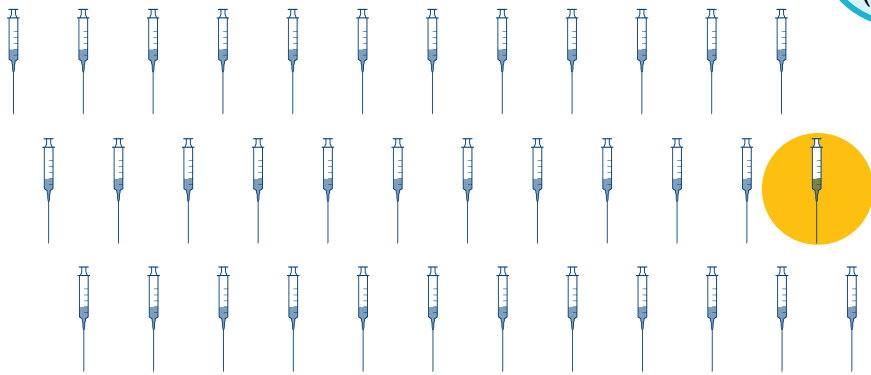
# Current Standard of Care Paradigm for Treating Retinal Vascular Diseases Relies on Frequent and Burdensome Bolus Injections

## Bolus Anti-VEGF Therapies in Today's Standard of Care



TKI Inserts (future potential)

## Bolus Injection Regimen over 5 years<sup>1</sup>



~36 (average)

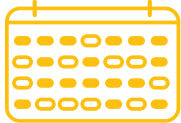


4 hours/visit

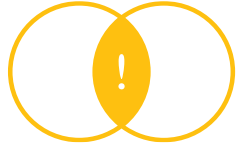
## Injections Carry High Burden



Caregiver commitment



Missed life events



Conflict with care for comorbidities



Needle anxiety

**#1 Unmet Need<sup>2</sup>: Durability and Lower Injection Burden**

1. Ciulla, et al, 2022. *Ophthalmology. Retina*, 6(9), 796–806. 2. Han P, ASRS 2024 PAT Survey.

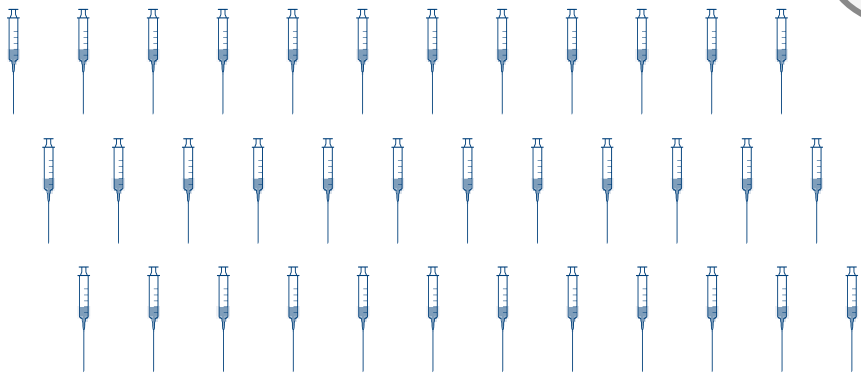
# From Bolus Injections to 4D-I50 Backbone Therapy: Becoming the Foundation for Treatment of Retinal Vascular Diseases

## Bolus Anti-VEGF Therapies in Today's Standard of Care



TKI Inserts (future potential)

Bolus Injection Regimen over 5 years<sup>1</sup> **~36** (average)



1. Ciulla, et al, 2022. Ophthalmology. Retina, 6(9), 796–806.

### Future Target Paradigm: 4D-I50 Backbone Therapy

+ bolus supplementation as needed

**~7**

80+% fewer injections Over 5 yrs (Target)

# Low Durability of SOC Associated with Poor Vision Outcomes in Wet AMD; 4D-I50 Multi-year Backbone Therapy Aims to Markedly Improve Outcomes

## Durability

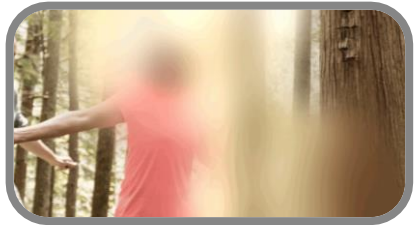
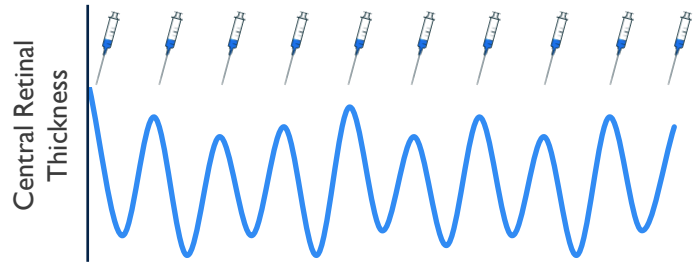
## Retinal Anatomy

## Vision

**Current Standard of Care**

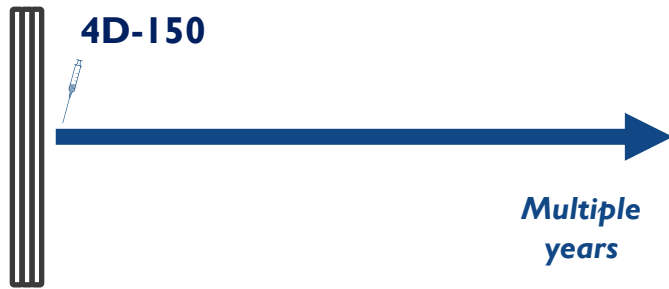
Bolus loading doses, followed by...

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

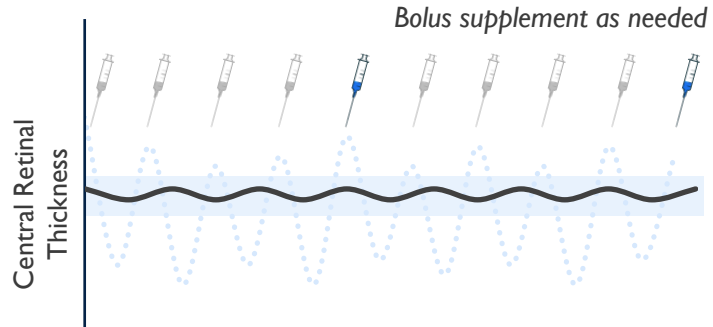


**Solution: 4D-I50 Backbone Therapy**

Bolus loading doses, followed by...



## Goal Post-4D-I50



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