

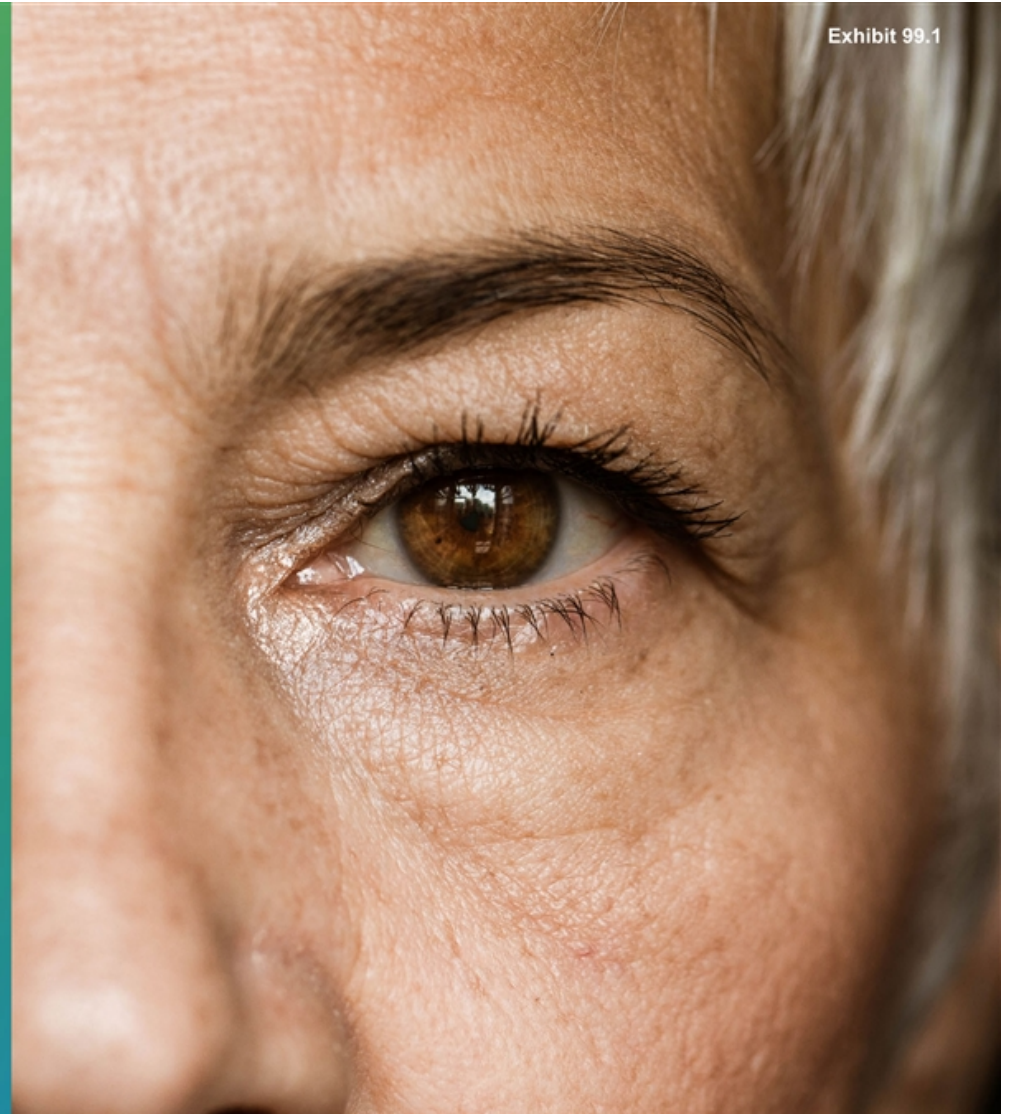
# Preserving Sight for Life<sup>®</sup>

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Webcast to Present 52-Week LUNA and 4-  
Year OPTIC Results and Pivotal Program

November 18<sup>th</sup>, 2024

ADVERUM



# Forward-Looking Statements

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# Today's Agenda

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## Welcome & Key Takeaways

*Laurent Fischer, MD  
President & Chief Executive Officer*

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## Ixo-vec & Wet AMD

*Laurent Fischer, MD  
President & Chief Executive Officer*

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## 4-Year OPTIC & 52-week LUNA Results

*Star Seyedkazemi, PharmD  
Chief Development Officer*

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## Key Pivotal Program Elements

*Rabia Gurses Ozden, MD  
Chief Medical Officer*

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## Patient Preference Survey

*Laurent Fischer, MD  
President & Chief Executive Officer*

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## Commercial Opportunity

*Jason Mitchell  
Chief Commercial Officer*

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07

## KOL Panel

*Moderator:  
Star Seyedkazemi, PharmD  
Chief Development Officer*

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## Conclusions & Q&A

*Adverum Management*

# Adverum Participants



**Laurent Fischer, MD**  
*President and  
Chief Executive Officer*



**Rabia Gurses Ozden, MD**  
*Chief Medical Officer*



**Star Seyedkazemi, PharmD**  
*Chief Development Officer*



**Jason Mitchell**  
*Chief Commercial Officer*



**Peter Soparkar**  
*Chief Operating Officer*



**Linda Rubinstein**  
*Chief Financial Officer*



**Mike Zanoni**  
*Head of Investor Relations*

# Key Opinion Leader Participants



**Charles C. Wykoff, MD, PhD**  
*Director of Research,  
Retina Consultants of Texas*



**Mark Barakat, MD**  
*Director of Clinical Research  
Retina Macula Institute of Arizona*



**Szilárd Kiss, MD**  
*Distinguished Professor of Ophthalmology,  
Director of Retina Service  
Cornell University  
Adverum Board Member*

# Key Takeaways

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# Ixo-vec's Derisked Phase 3 and Commercial Profile

Clinical updates underscore Ixo-vec's potential best-in-class product profile



- **Potential best-in-class product profile**  
>50% injection free and >80% treatment burden reduction in hard-to-treat patients
- **10X safety margin with >4 years follow-up**
- **No OPTIC 2E11 patients had inflammation at Year 1 and through Year 4**
- **No LUNA 6E10 patients had inflammation at 52 weeks or any subsequent visit**  
Favorable safety profile with local prophylaxis
- **LUNA patient survey demonstrates strong patient preference for Ixo-vec**

**ARTEMIS**  
Phase 3 Trial

**6E10**

With topical  
steroid eyedrops

**EOP2**

US study, incorporates  
FDA feedback

**284**

Patients

**Broad**

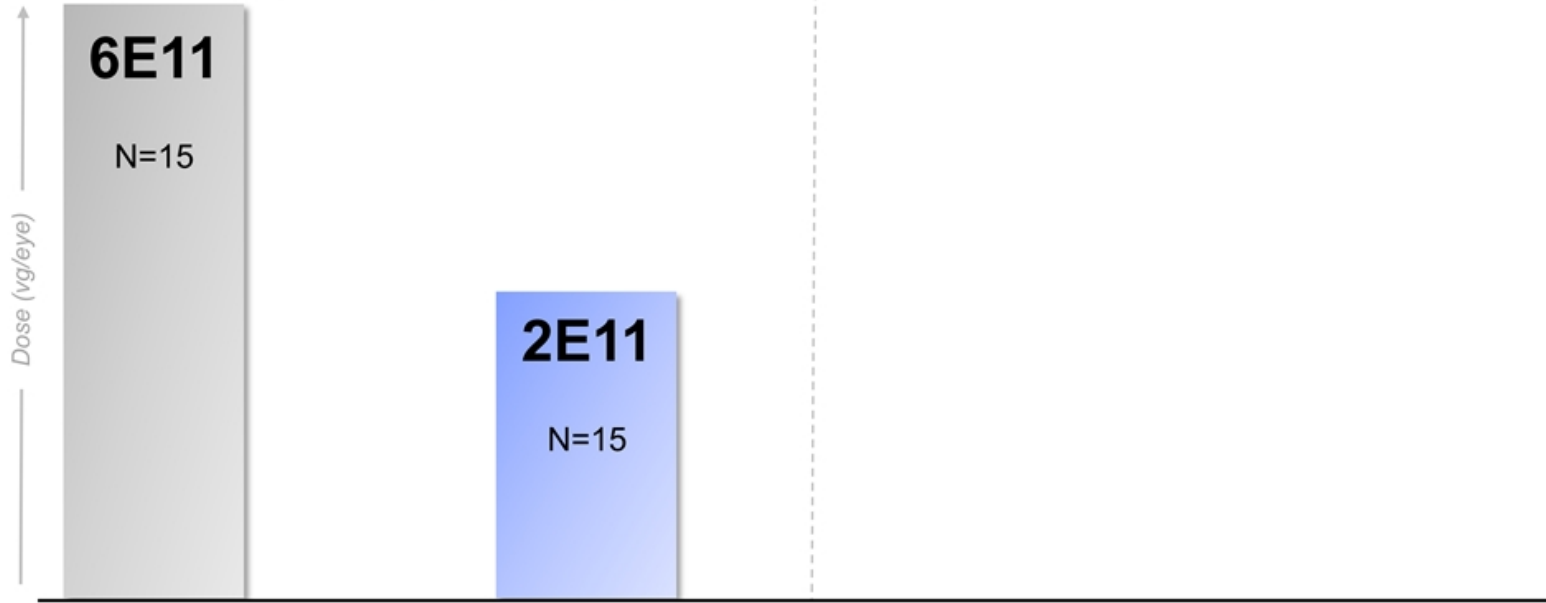
Patient population

**1H25**

Expected Phase 3  
initiation

# 5+ Years of Clinical Experience Establish 10x Safety Margin

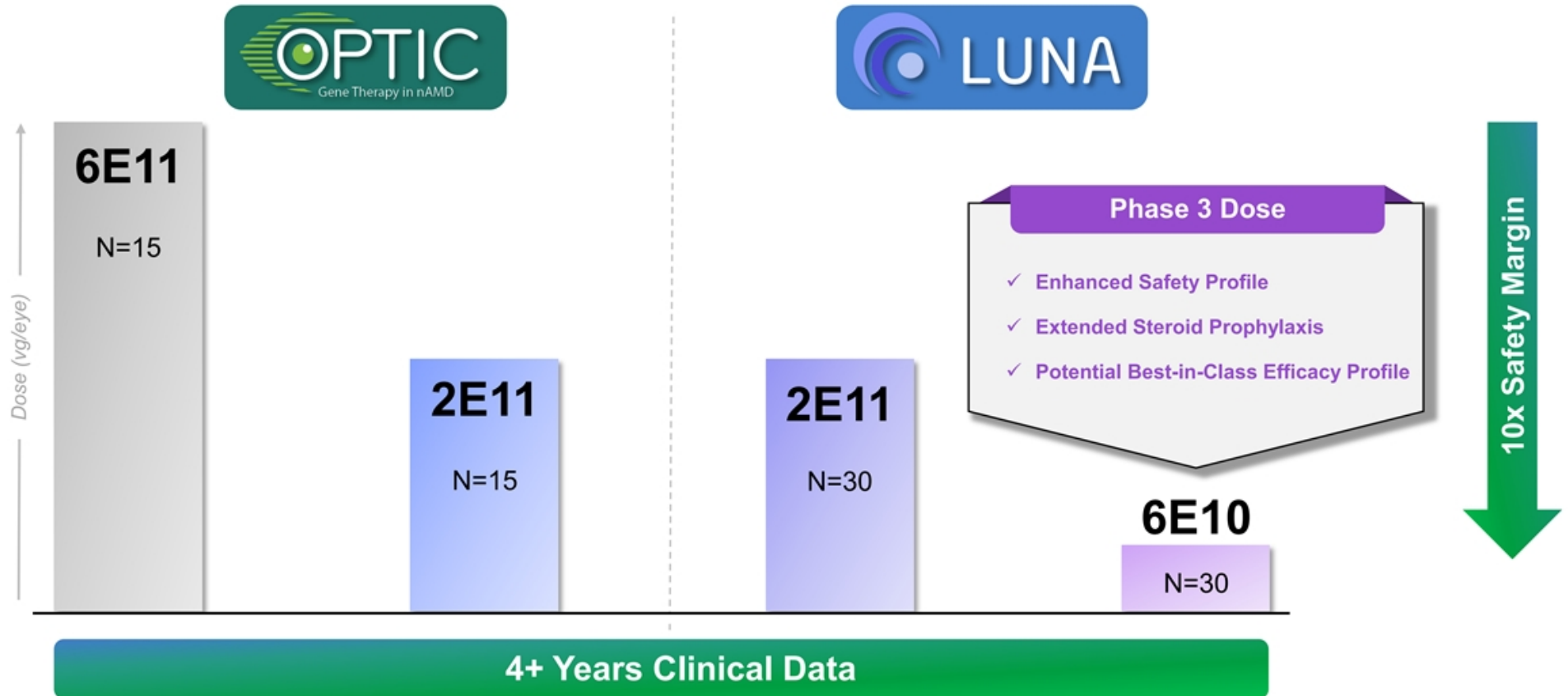
*Ixo-vec 6E10 with extended prophylaxis de-risks Phase 3 & commercialization*











# 5+ Years of Clinical Experience Establish 10x Safety Margin

*Ixo-vec 6E10 with extended prophylaxis de-risks Phase 3 & commercialization*



# 6E10 Dose Selected to Maximize Phase 3 and Commercial Success

Demonstrates potential best-in-class product profile

	Ph3 Go-Forward Dose	Benefit			Safety	
		Treatment Burden Reduction	≤ 1 Injection	Injection Free	% With AC ≥1+	% Receiving Steroids for IOI
	 <b>6E10</b> (n = 28)	<b>88%</b>	<b>75%</b>	<b>54%</b>	<b>0%</b>	<b>4%</b> <i>N=1</i>
	 <b>2E11</b> (n = 29)	92%	79%	69%	3%	7%
	 <b>2E11</b> (n = 15)	84%	73%	60%	0%	27%
	 <b>6E11</b> (n = 15)	97%	87%	87%	0%	60%

Potential *best-in-class clinical activity* with *enhanced safety profile* of 6E10 for pivotal studies

# Reliable Benefit & Predictable Safety Profile Enable True Paradigm Shift

4-year OPTIC & 52-week LUNA data underscore Ixo-vec's profile

## Demonstrated Reliable Long-Term Benefit

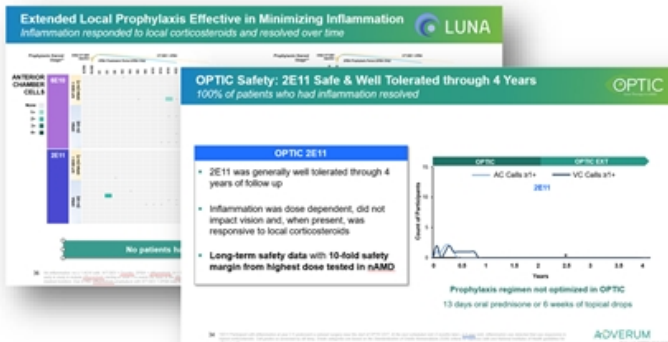
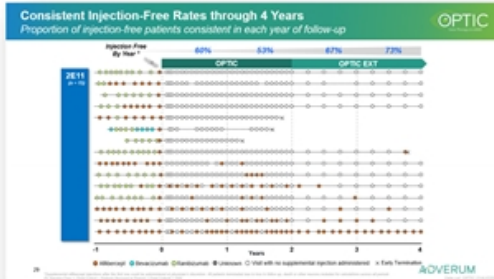
**78%** of patients who were injection free through year 1 remained injection free through year 4

**88%** of patients who were injection free through year 2 remained injection free through year 4

## Demonstrated Predictable Safety Profile with Extended Local Prophylaxis

**NO** new onset of inflammation after week 30

**100%** of inflammation resolved by year 1



# Ixo-vec & wet AMD

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# Large and Growing Global Market Opportunity

*Wet AMD physicians and patients embrace innovation*

## Wet Age-Related Macular Degeneration

*A leading cause of vision loss among older adults*

**1.5M**  
US Patients

**20M**  
Worldwide

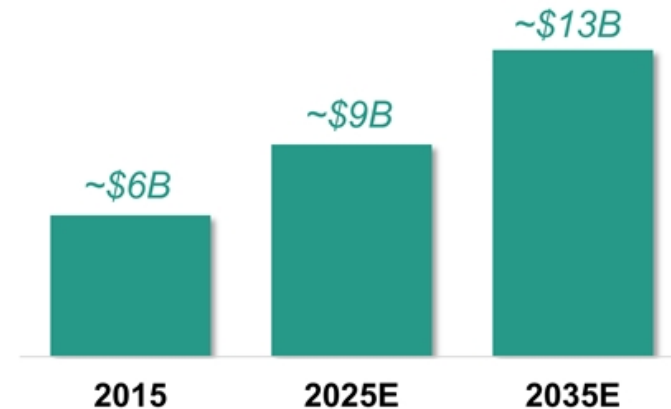
*~200k US patients diagnosed annually*

**Up to 42% of patients develop bilateral disease within 2-3 years of initial diagnosis**

## Multi-Billion Dollar Market Opportunity

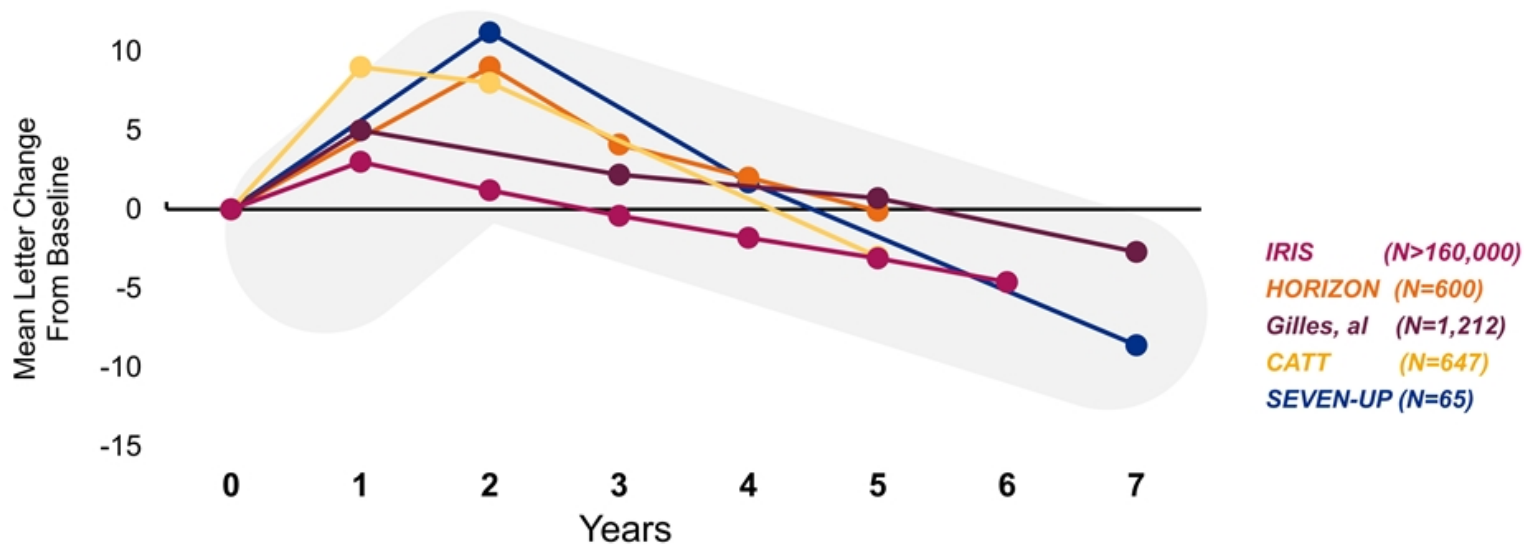
*Growth driven by aging population and product innovation*

Global Wet AMD Sales



13 Sources: Bright Focus Foundation. Age-Related Macular Degeneration: Facts & Figures.; Wong WL, et al. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. *Lancet Glob Health*. 2014;2:106-16.; Gangnon RE et al. (2015) *JAMA Ophthalmol*; 133 (2): 125-132.; 2023 Cowen Equity Research – Therapeutic Categories Outlook.; Company estimates.

# Real-World Vision Declines Due to Chronic Undertreatment

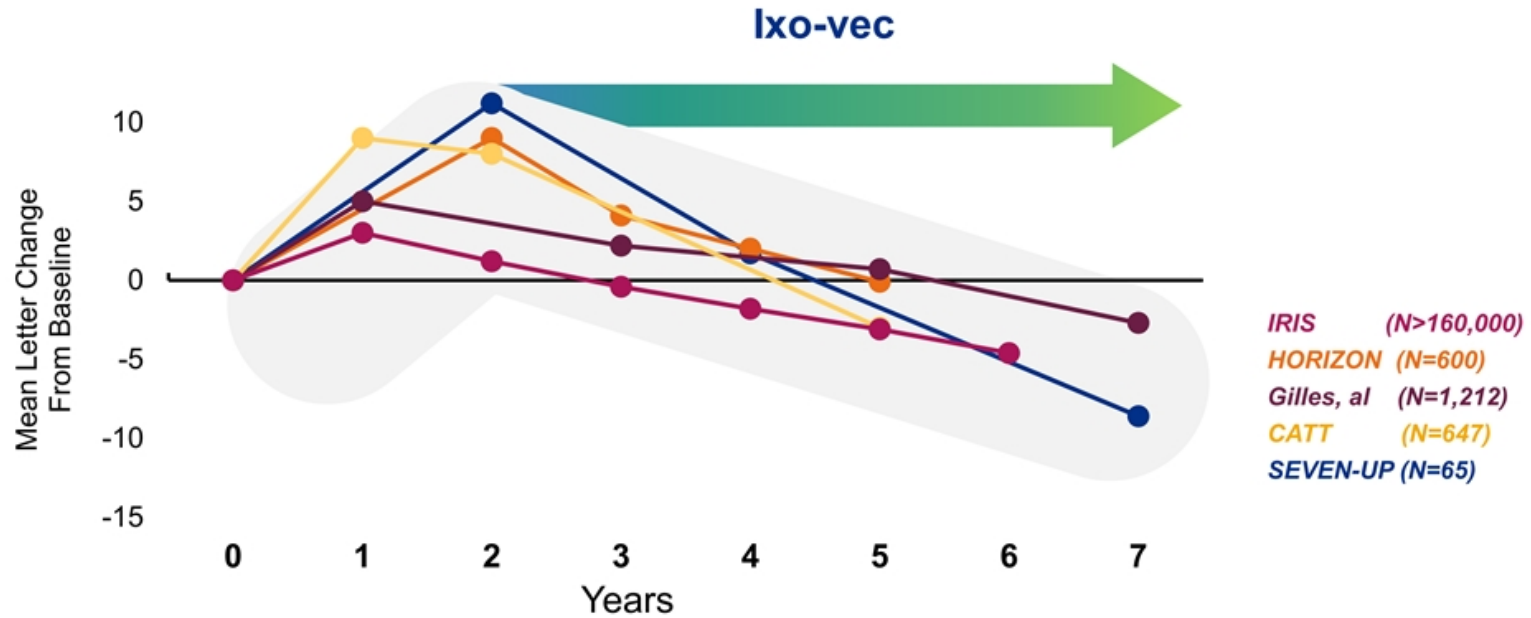


Up to ~40% STOP anti-VEGF over 2 years and up to 57% stop over 5 years

14 Sources: <https://futureofvision.global/home/the-reality-of-retinal-disease.html>. Adapted from Singer MA, et al. *Ophthalmology*. 2012;119(6):1175-1183. Adapted from Gillies MC, et al. *Ophthalmology*. 2015;122(9):1837-1845. Adapted from Comparison of Age-related Macular Degeneration Treatments Trials (CATT) Research Group, Maguire MG, et al. *Ophthalmology*. 2016;123(8):1751-1761. Adapted from Rofagha S, et al.; *Ophthalmology*. 2013;120(11):2292-2299. Wykoff CC, Garmo V, Tabano D, et al. *Ophthalmol Sci*. 2023;4(2):100421.

# Real-World Vision Declines Due to Chronic Undertreatment

*Ixo-vec designed to deliver stable aflibercept to maintain long-term vision*



Up to ~40% STOP anti-VEGF over 2 years and up to 57% stop over 5 years

15 \*Potential long-term vision outcome with Ixo-vec. Sources: <https://futureofvision.global/home/the-reality-of-retinal-disease.html>. Adapted from Singer MA, et al. Ophthalmology. 2012;119(6):1175-1183. Adapted from Gillies MC, et al. Ophthalmology. 2015;122(9):1837-1845. Adapted from Comparison of Age-related Macular Degeneration Treatments Trials (CATT) Research Group, Maguire MG, et al. Ophthalmology. 2016;123(8):1751-1761. Adapted from Rofagha S, et al. Ophthalmology. 2013;120(11):2292-2299. Wykoff CC, Garmo V, Tabano D, et al. Ophthalmol Sci. 2023;4(2):100421.

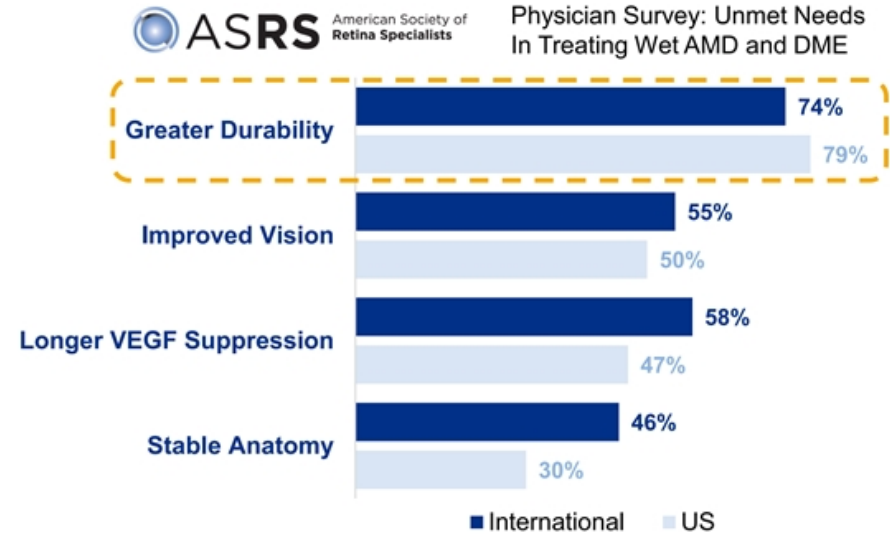
# Undertreatment Often Results from Barriers to Treatment

Physician ASRS survey underscores need for more durable treatments

## Barriers to Treatment



## More Durable Treatment Options Are Needed



Ixo-vec may address unmet need in wet AMD by delivering stable aflibercept



# Ixo-vec Positioned to Transform Treatment Paradigm

In contrast, 2nd generation wet AMD treatments are only incremental advancements

Ixo-vec designed to deliver stable and continuous aflibercept 5+ years

% Injection Free Potential 2024 US Revenue

Paradigm Shift

Ixo-vec

>50%

2<sup>nd</sup> Generation



[Discontinued and Relunched]

\$1.6B

\$4.3B

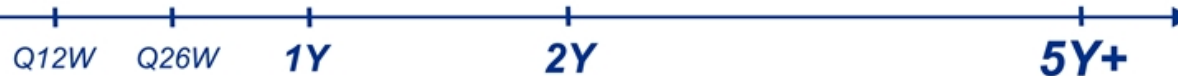
0%

1<sup>st</sup> Generation



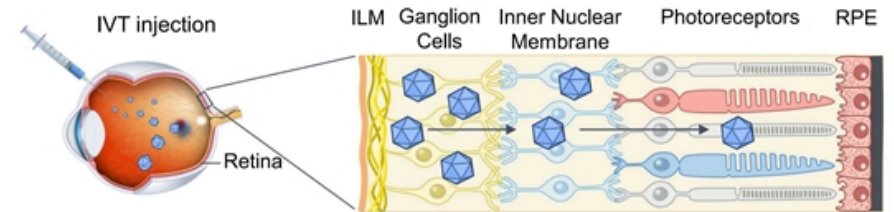
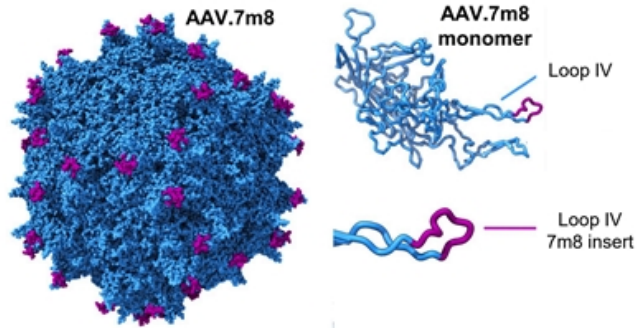
\$4.6B

\$23M



# Ixo-vec Delivers Anti-VEGF Aflibercept via Single Intravitreal Injection

*7m8 capsid enables delivery of stable aflibercept levels into the retina*

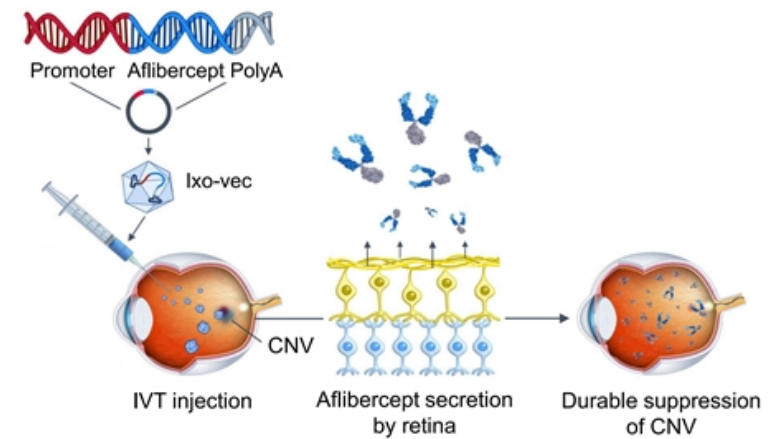


## AAV.7m8: Created by Directed Evolution

- Engineered for IVT administration; peptide loop enables 7m8 to cross the inner limiting membrane (ILM)
- AAV.7m8 delivers aflibercept to the retina

## AAV.7m8 for IVT Gene Therapy

- Validated in 3 clinical programs
- Published in peer reviewed journals



# 4-Year OPTIC & 52-week LUNA Results

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# OPTIC First-in-Human Trial Design

6E11 & 2E11 with short prophylaxis in hard-to-treat population



<b>Primary Objective</b>  Long-term safety and efficacy of Ixo-vec IVT in treatment experienced patients	<b>Secondary Objectives</b> <ul style="list-style-type: none"> <li>• Vision maintenance (BCVA)</li> <li>• Anatomy (SD-OCT)</li> <li>• Need for supplemental therapy</li> </ul>
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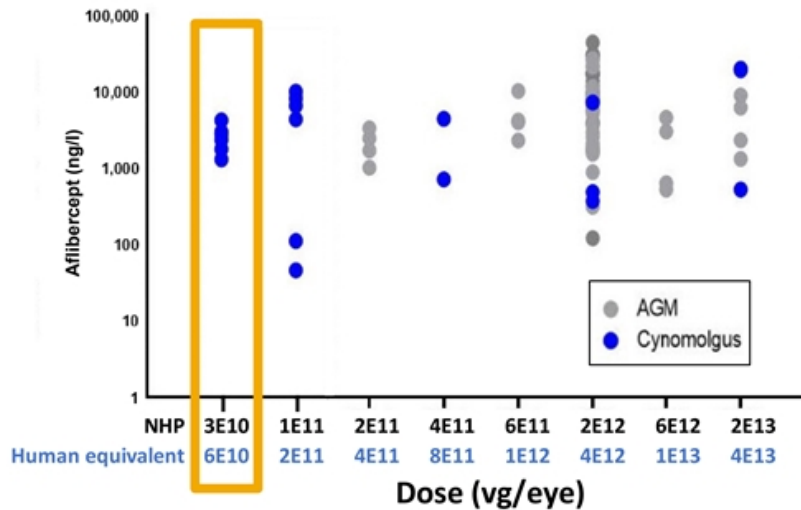
	Ixo-vec Dose	Corticosteroid Prophylaxis	Extension Scheduled Visits	Supplemental Aflibercept (2 mg IVT) Criteria:
<b>Cohort 1</b> (n=6)	6E11	Oral, 13d	Quarterly assessments following completion of 2-year OPTIC parent study	<ul style="list-style-type: none"> <li>• <math>\geq 10</math> letters BCVA (ETDRS) loss from baseline <b>OR</b>,</li> <li>• CST <math>&gt;75 \mu\text{m}</math> increase from baseline <b>OR</b>,</li> <li>• New Vision-threatening hemorrhage due to AMD</li> <li>• After initial supplemental injection subsequent injections administered at investigator discretion</li> </ul>
<b>Cohort 2</b> (n=6)	2E11	Oral, 13d		
<b>Cohort 3</b> (n=9)	2E11	Eye Drops, 6 wks		
<b>Cohort 4</b> (n=9)	6E11	Eye Drops, 6 wks		

# Preclinical Data Suggest Best-in-Class Potential of Ixo-vec at 6E10 Dose

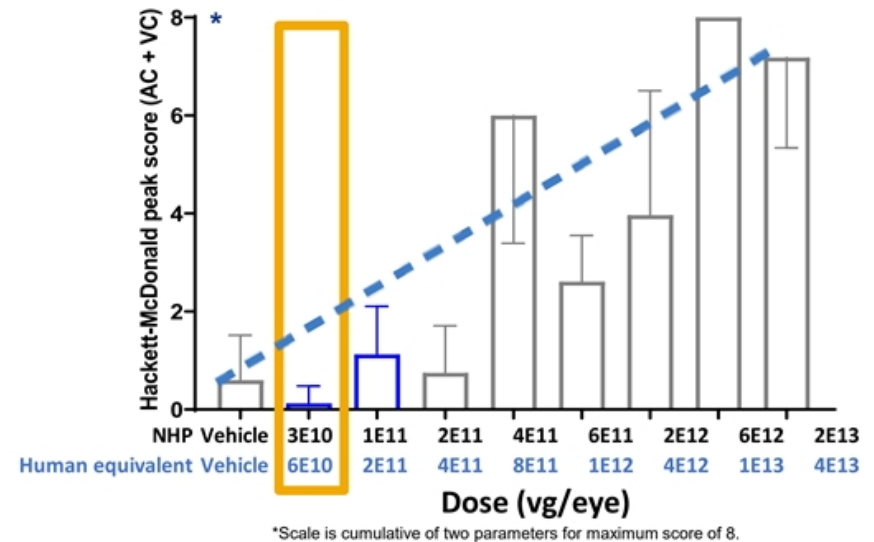
*NHP studies demonstrate consistent aflibercept production with low inflammation*

**Less-than-dose-proportional aflibercept levels across 3 logs**  
**Improved inflammation scores with lower doses (no prophylaxis)**

**Aqueous Humor Aflibercept Levels**



**Inflammation Scores**





## Objective I

**Determine the Optimal  
Dose for Phase 3**



## Objective II

**Determine the  
Phase 3 Prophylactic  
Regimen**

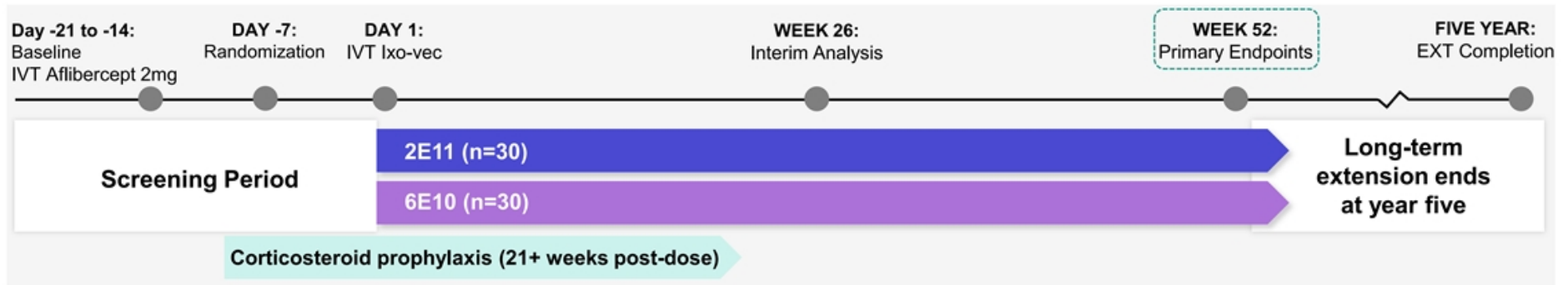
# LUNA Phase 2 Trial Design

6E10 & 2E11 with extended prophylaxis in hard-to-treat patients



## Multicenter, double-masked, randomized, parallel-group Phase 2 study

Key inclusion criteria: demonstrated response to anti-VEGF therapy and under active treatment for CNV secondary to nAMD (received a minimum of 2 injections within 4 months of entry), study eye BCVA in the range of 25 – 83 ETDRS letters



### Corticosteroid Prophylaxis Regimen

- Difluprednate 22 wks ± prednisone oral 10 wks
- Ozurdex IVT + difluprednate after week 4 ± prednisone oral 10 wks\*
- Randomized 2:1 local versus local + oral

### Supplemental Injection Criteria

- Increase in CST > 75  $\mu$ m from BL confirmed by the CRC **OR**
- Loss of  $\geq$  10 letters in BCVA from BL due to new/worsening IRF or SRF **OR**
- New vision-threatening hemorrhage due to nAMD

# Demographics and Baseline Characteristics

OPTIC & LUNA evaluated hard-to-treat patients

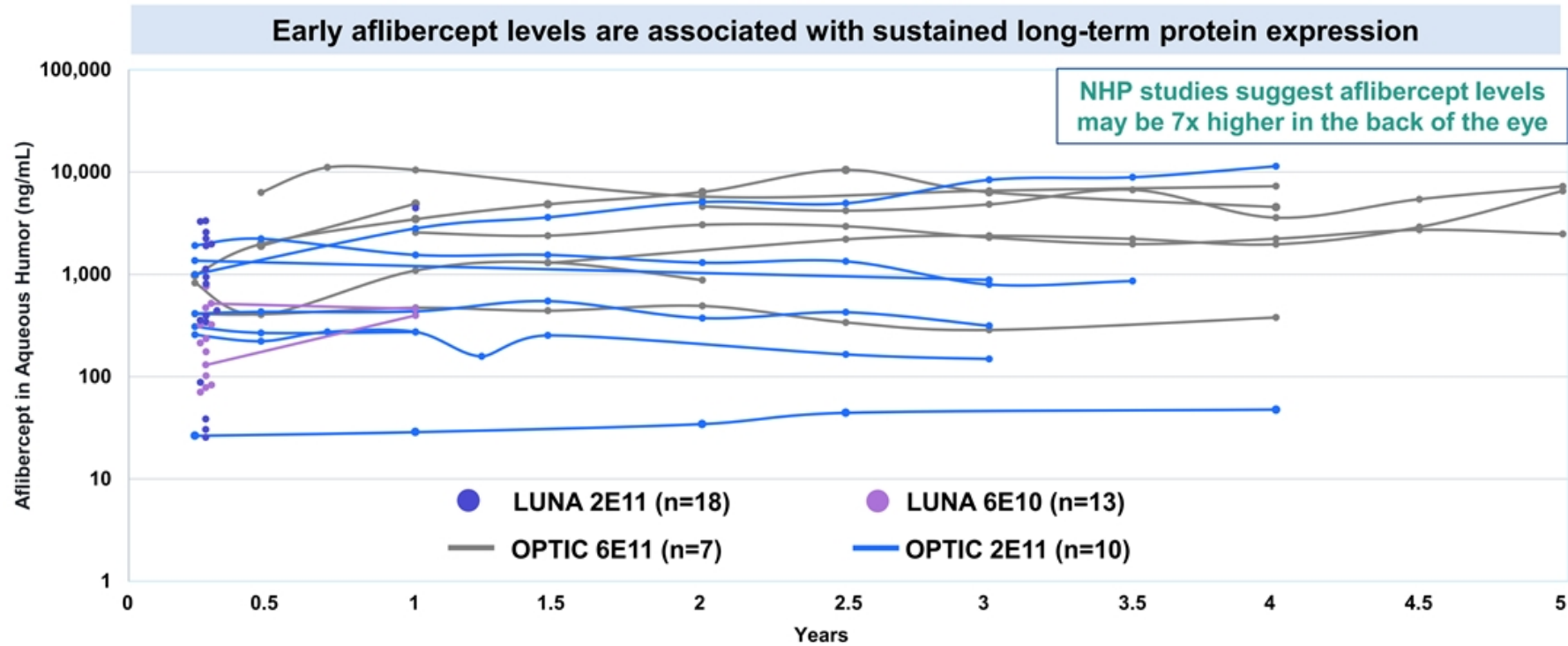


Demographics and Baseline Characteristics	LUNA 6E10 N = 30	LUNA 2E11 N = 30	LUNA Total N = 60	OPTIC Total N = 30
Mean age, years (SD)	75.4 (8.2)	77.7 (7.4)	76.6 (7.8)	79.0 (7.3)
Female, n (%)	16 (53%)	18 (60%)	34 (57%)	15 (50%)
Race, n (%)				
White	27 (90%)	28 (93%)	55 (92%)	30 (100%)
Asian	2 (7%)	2 (7%)	4 (7%)	0
Mean years since nAMD diagnosis in the study eye (SD)	3.0 (2.9)	3.0 (3.1)	3.0 (2.9)	3.7 (2.8)
Mean annualized anti-VEGF injections in year prior to Day 1 (SD)	10.2 (1.7)	10.0 (3.3)	10.1 (2.6)	9.9 (1.9)
Mean BCVA, ETDRS letters (SD)	72.9 (8.8)	71.8 (6.4)	72.3 (7.7)	65.4 (7.2)
Mean CST, $\mu\text{m}$ (SD)	360.6 (112.0)	340.5 (119.3)	350.6 (115.2)	397.0 (137.3)
Phakic lens status, n (%)	11 (37%)	11 (37%)	22 (37%)	10 (33.3%)



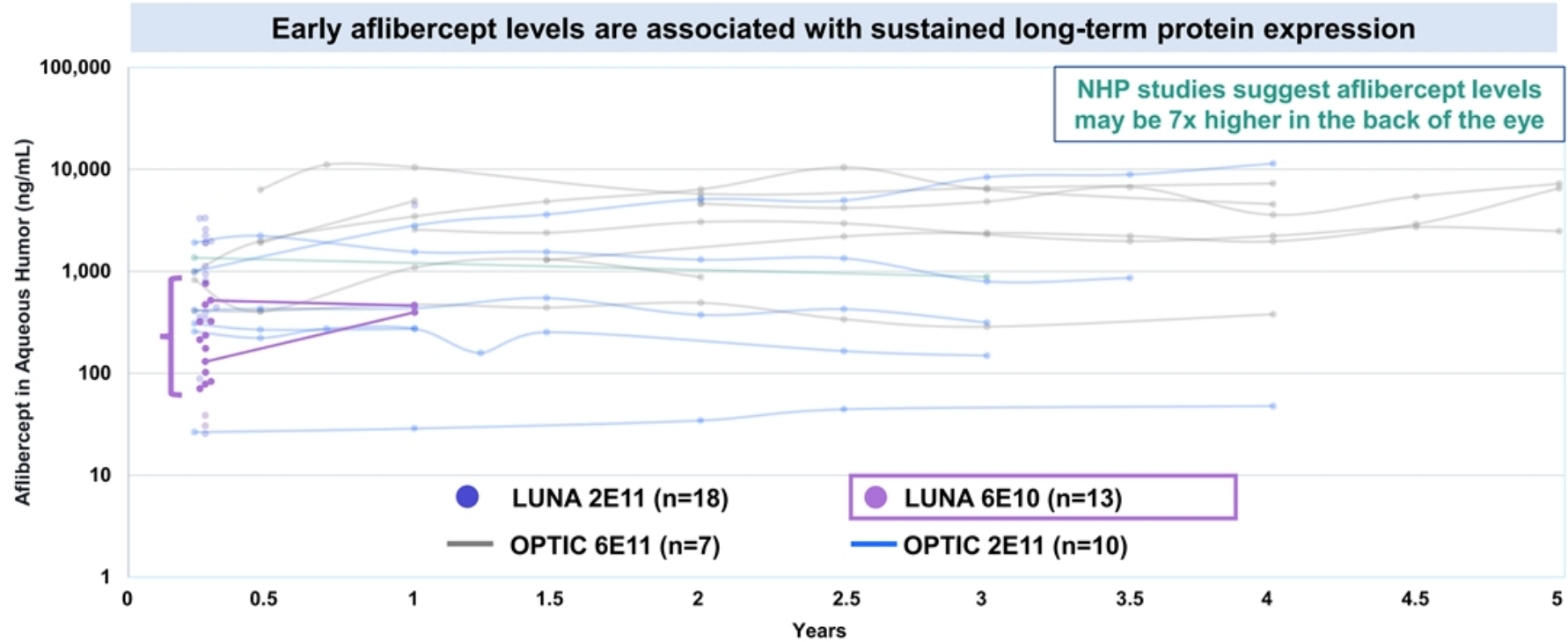
# Ixo-vec Demonstrates Durable Therapeutic Levels After One Injection

*Sustained aqueous aflibercept levels up to 5 years*



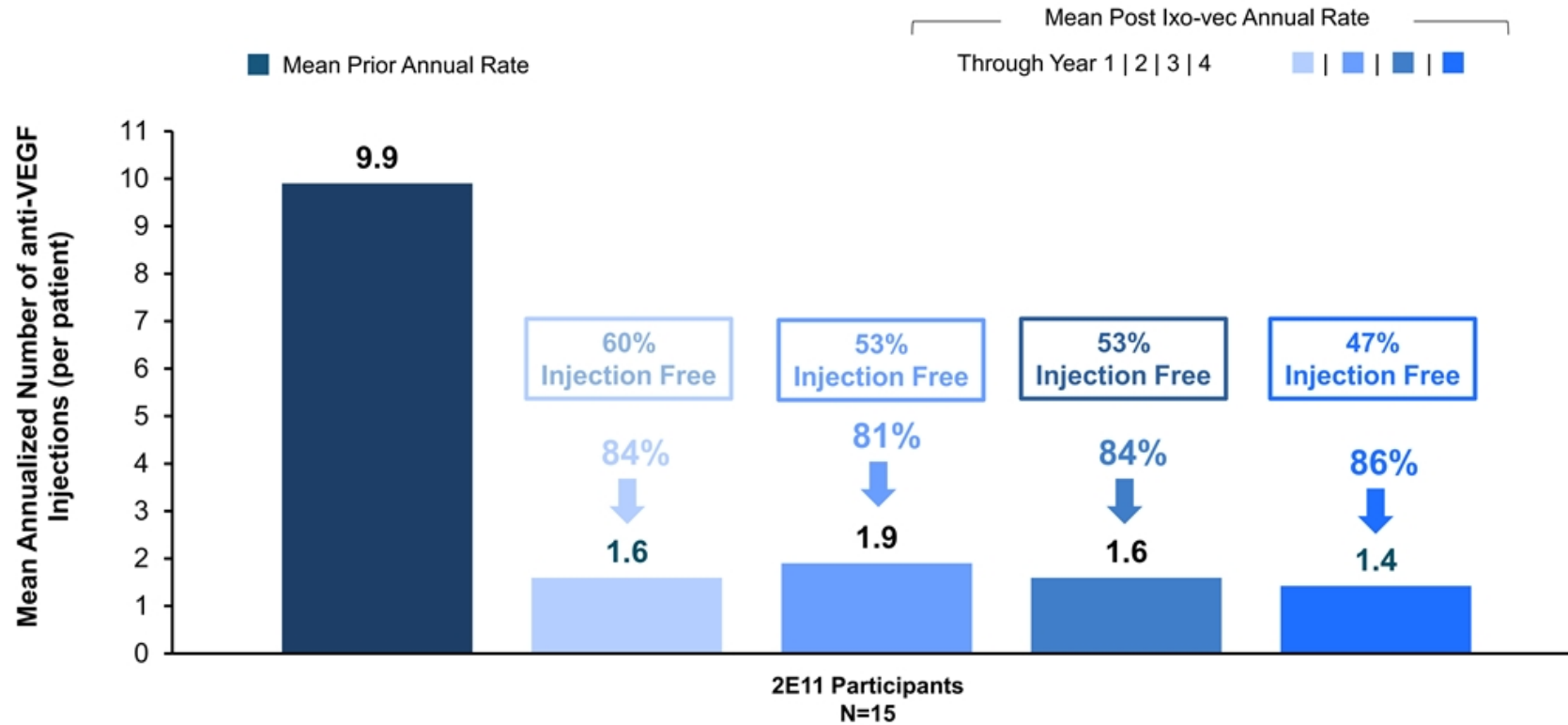
# Ixo-vec Demonstrates Durable Therapeutic Levels After One Injection

*Sustained aflibercept levels measured with 6E10 at year 1*



# Ixo-vec Reduced Treatment Burden Through 4 Years

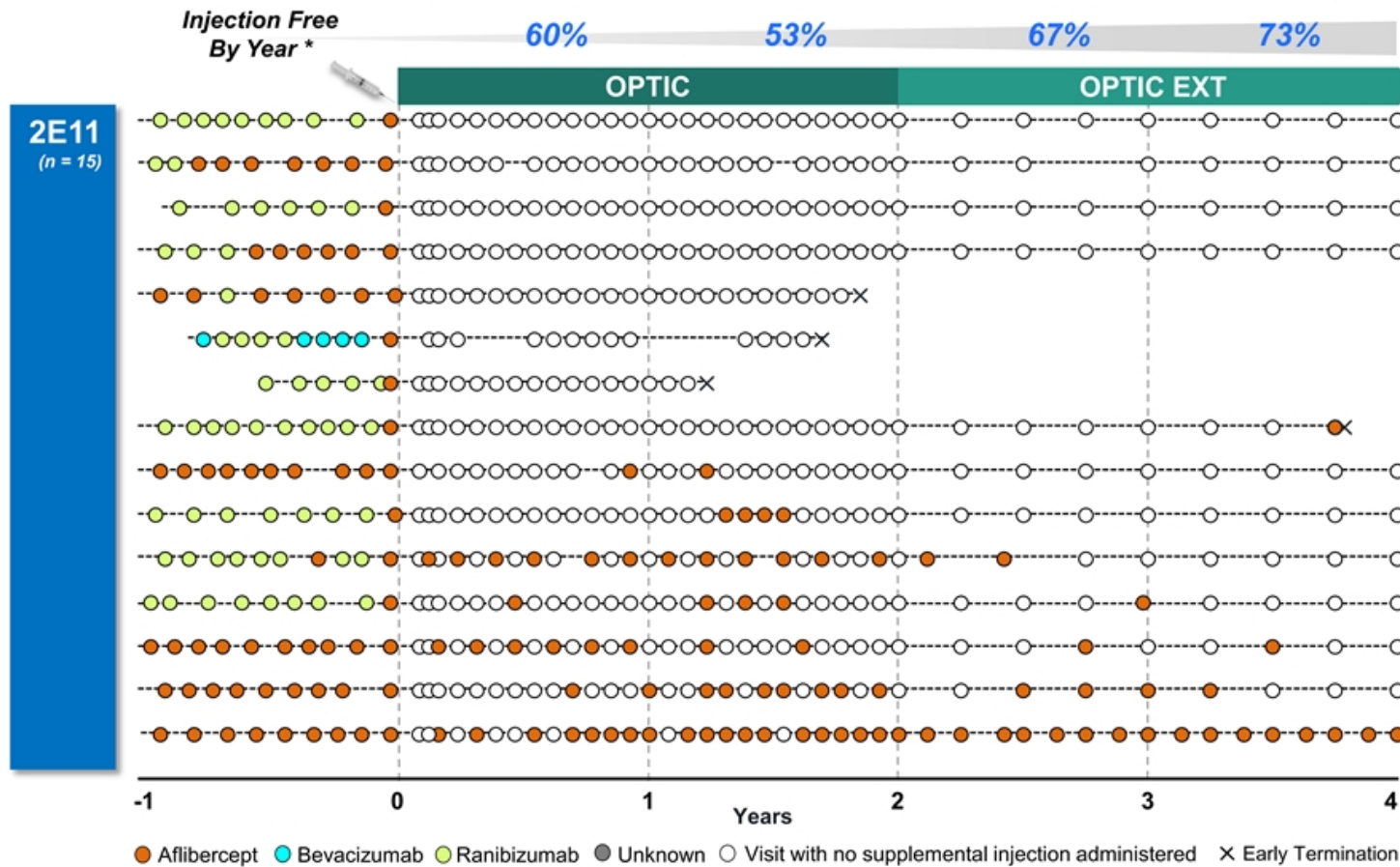
2E11 shows >80% reduction in annualized anti-VEGF injections in every year



27 Annualized rate (Prior) = (number of IVTs in 12 months prior to Ixo-vec) / (days from the first IVT in the past 12 months to Ixo-vec / 365.25).  
Annualized rate (Post) = (number of aflibercept IVTs since Ixo-vec) / (days from Ixo-vec to the last study follow-up / 365.25).  
Analysis includes all participants from the OPTIC study.

# Consistent Injection-Free Rates through 4 Years

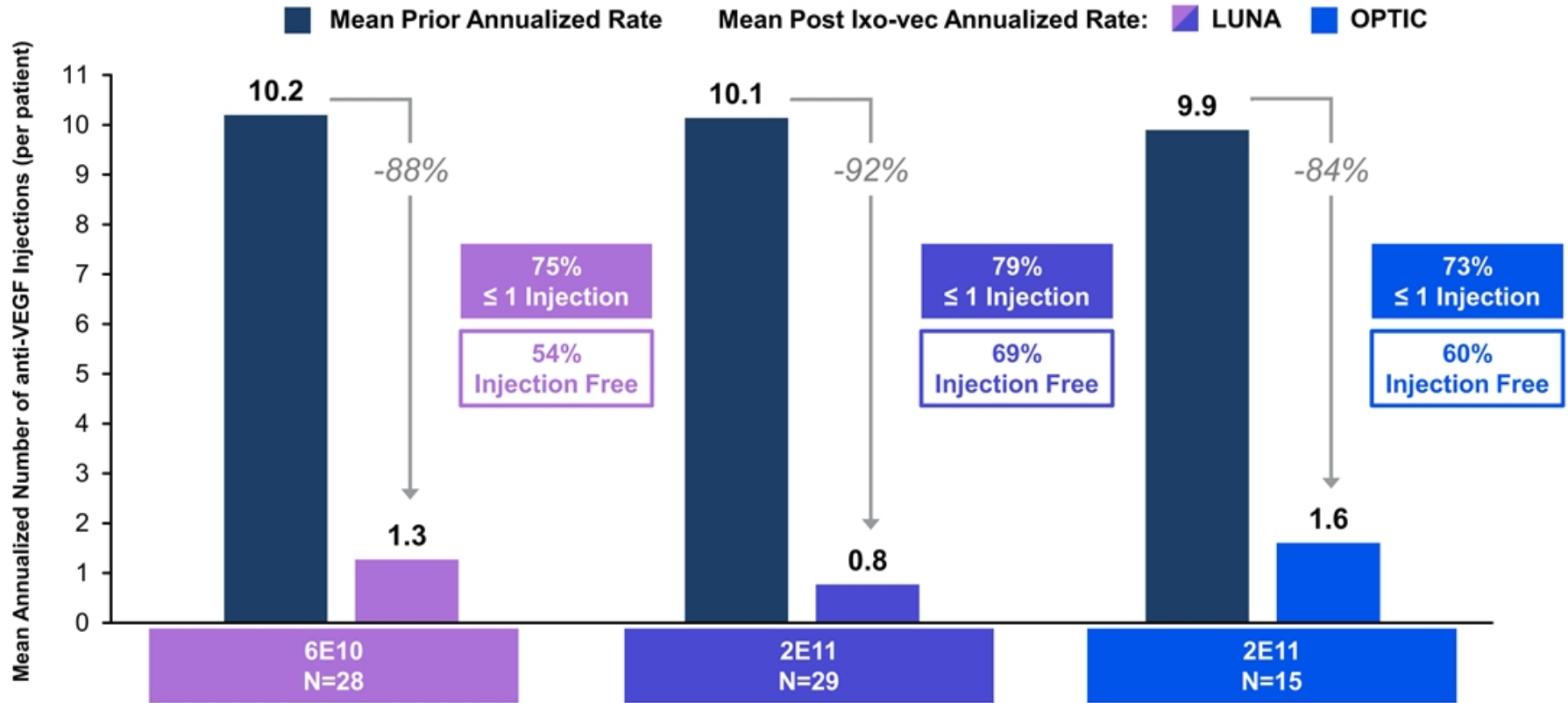
Proportion of injection-free patients consistent in each year of follow-up



\*Supplemental afibercept injections after the first one could be administered at physician's discretion. All patients terminated due to loss to follow up, death or other reasons included for calculations across all periods  
 [% Injection Free = (Total Cohort - Patients Rescued in Period) / (Total Cohort) \* 100]

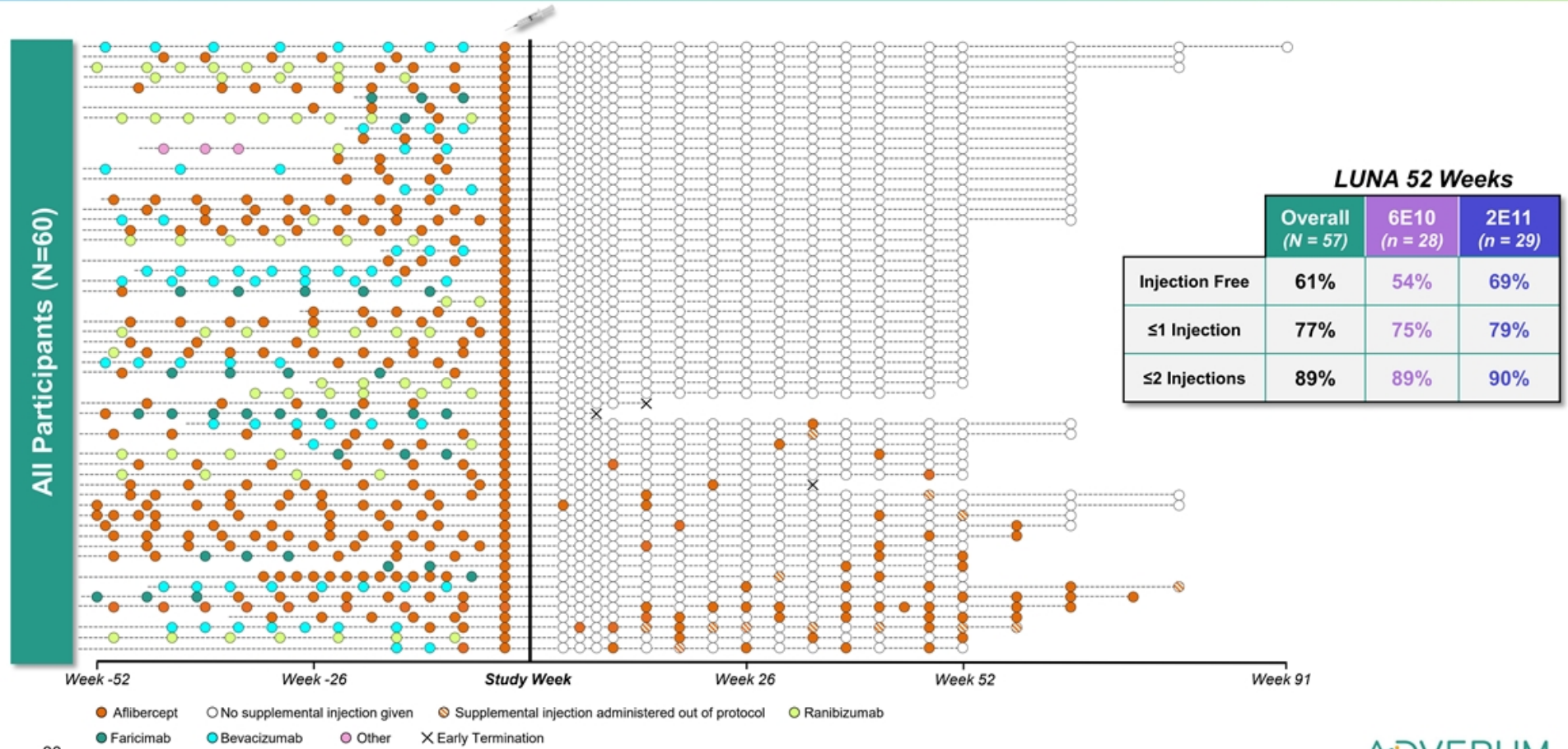
# 52-Week LUNA and OPTIC Injection Burden Reduction are Consistent

>80% reduction in annualized anti-VEGF injections, >50% injection free



# Potential Best-in-Class Injection-Free Rates

52-week LUNA data demonstrate >50% injection free in hard-to-treat patients



30

Doses pooled in swim lane plot to preserve investigator masking in an ongoing double masked study.

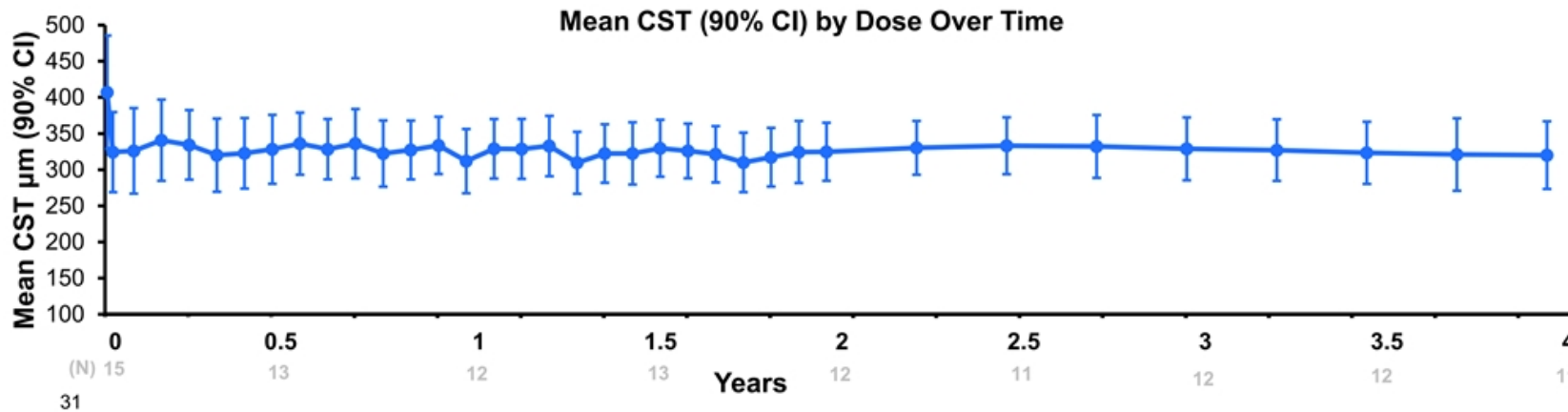
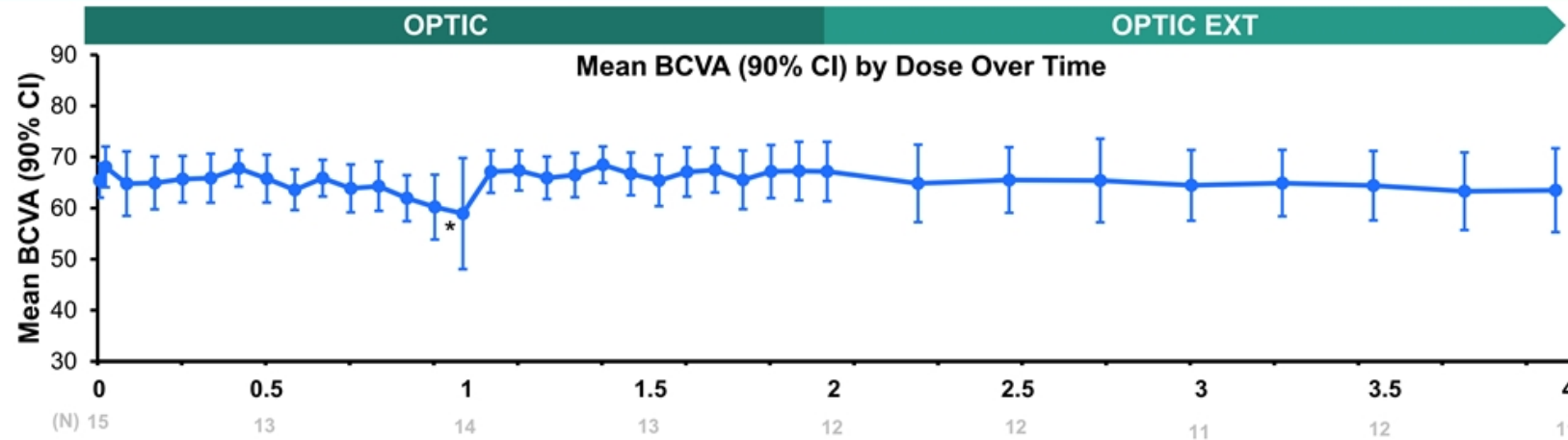
Early termination patients not included in injection calculations. [% Injection Free = (Total Cohort - Early Termination Patients - Rescued Patients) / (Total Cohort - Early Termination Patients) \* 100]

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Data cut: LUNA 29AUG2024

# Ixo-vec Maintains BCVA & CST

Demonstrated robust and durable activity through 4 years of follow up



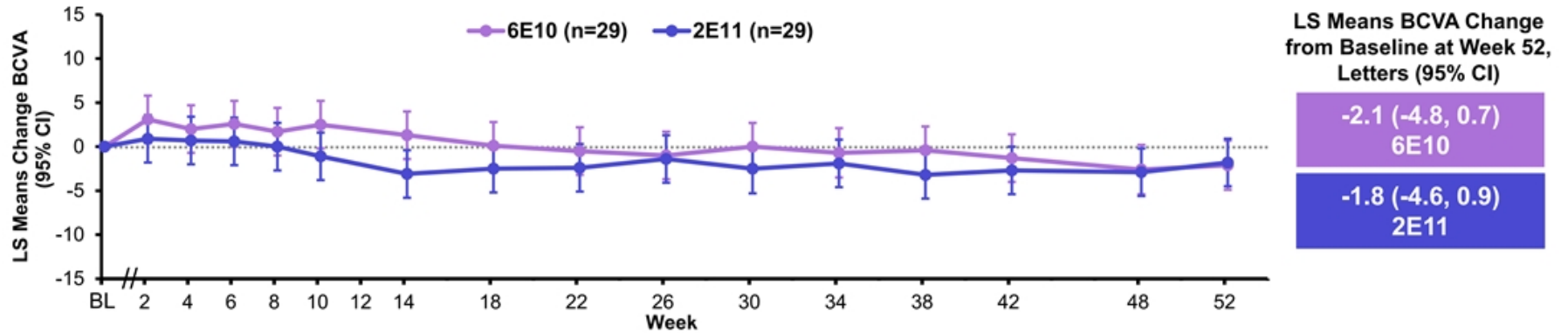
\*Cataract surgery

# Ixo-vec Maintains BCVA & CST

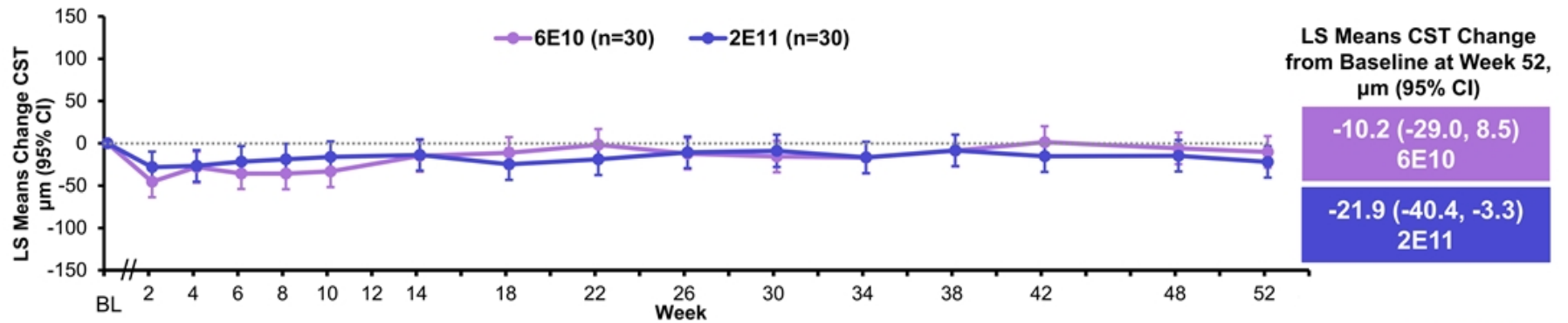
Both doses demonstrate robust and durable activity, consistent with OPTIC



Least Squares Means Change in Best Corrected Visual Acuity (BCVA) Over Time by Dose\*



Least Squares Means Change in Central Subfield Thickness (CST) Over Time by Dose



Least Squares Means are based on Mixed Model Repeated Measures (MMRM) including dose group, baseline value, visit and visit dose group. \*Excludes 1 participant at each dose with letter loss due to cataract



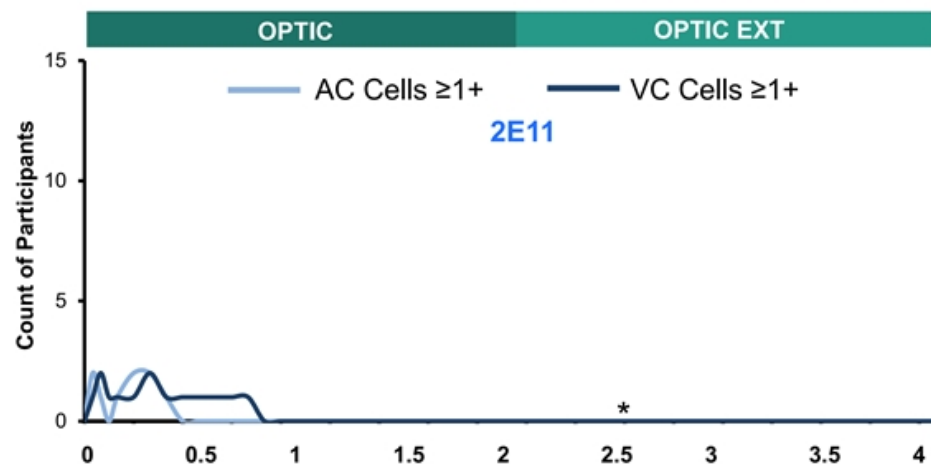
# OPTIC 2E11 Well Tolerated through 4 Years

100% of patients who had inflammation resolved by year 1



## OPTIC 2E11

- 2E11 was generally well tolerated through 4 years of follow up
- Inflammation was dose dependent, did not impact vision and, when present, was responsive to local corticosteroids
- Long-term safety data with 10-fold safety margin from highest dose tested in nAMD**



Short prophylactic regimen was 13 days oral prednisone or 6 weeks of topical drops

33 \*2E11 participant with inflammation at year 2.5 underwent a cataract surgery near the start of OPTIC EXT. At the next scheduled visit (3 months later—2.5 year visit), inflammation was detected that was responsive to topical corticosteroids. Cell grades as assessed by slit lamp. Grade categories are based on the Standardization of Uveitis Nomenclature (SUN) criteria for aqueous cells and National Institutes of Health guidelines for vitreous cells.

## Safety Summary: LUNA 52-Week

*Ixo-vec continues to be well tolerated, supporting potential best-in-class product profile*



### **Ixo-vec had a favorable safety profile and was well tolerated in total LUNA population**

- No Ixo-vec-related serious adverse events. All Ixo-vec-related adverse events (AEs) were either mild or moderate
  - No episcleritis, vasculitis, retinitis, choroiditis, vascular occlusion, or hypotony
- Most common Ixo-vec-related AEs were dose-dependent anterior inflammation responsive to local corticosteroid and anterior pigmentary changes with no impact on vision<sup>1</sup>
- 6E10 patients had no inflammation at week 52 and at any subsequent visit<sup>2</sup>

### **Local corticosteroids alone effectively minimized inflammation at both doses<sup>3</sup>**

- No patients had inflammation at week 52 and at any subsequent visit

### **6E10 + topical steroid eyedrops selected for pivotal program**

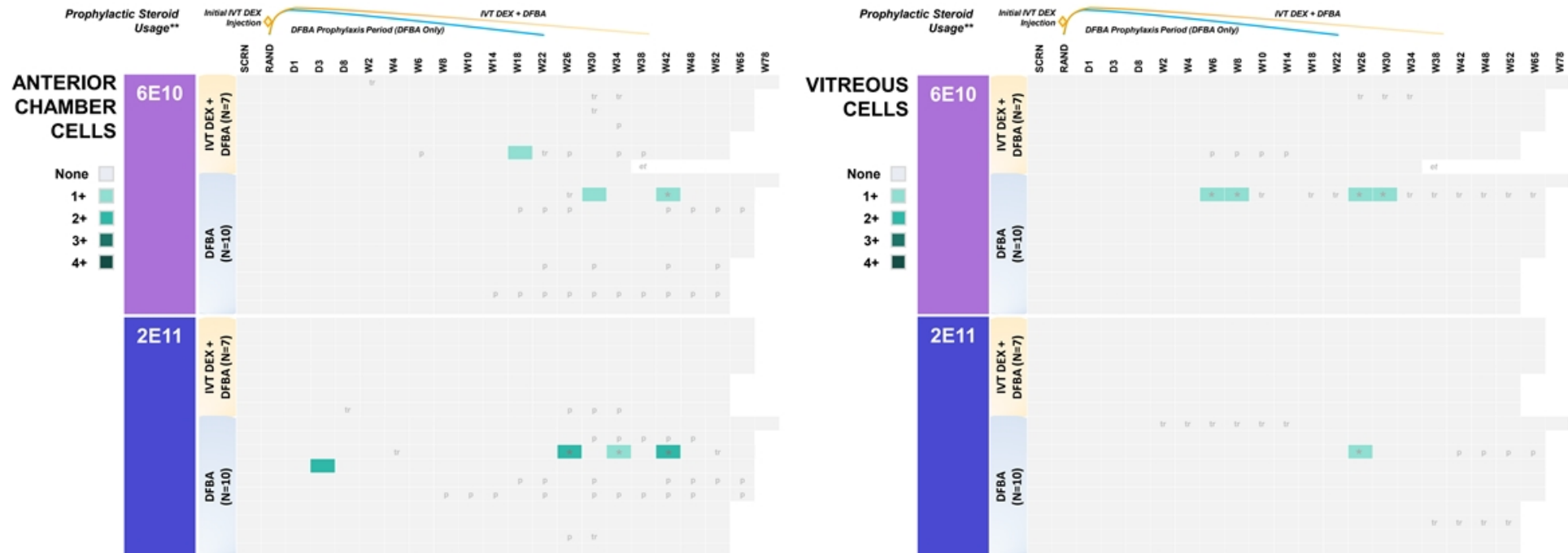
- No patients had inflammation at week 52 and at any subsequent visit<sup>4</sup>
- Only a single patient had inflammation at any timepoint, which resolved prior to week 52

34

<sup>1</sup>Anterior chamber cell, anterior chamber pigmentation, iris transillumination defect, iritis. <sup>2</sup>No inflammation: no  $\geq 1$  ACVC cells. <sup>3</sup>Topical difluprednate with or without IVT dexamethasone (N=34). <sup>4</sup>Topical difluprednate alone (N=10).

# Extended Local Prophylaxis Effective in Minimizing Inflammation

Inflammation responded to local corticosteroids and resolved over time



**No patients had inflammation at week 52 or at any subsequent visit**

35 No inflammation: no ≥ 1 AC/V cells. IVT DEX = Ozurdex, DFBA = difluprednate, tr = Trace, p = Pigmented Cells, \* = Mixed Pigmented / Non-Pigmented Cells, et – Early Termination. \*\*IVT DEX + DFBA: protocol amended early in study to include difluprednate starting at week 4 to match the taper in the difluprednate only regimen; if initiated after week 4 visit, difluprednate may be adjusted at the discretion of investigator in consult with medical monitors. Due to this, difluprednate prophylaxis with IVT DEX + DFBA may have lasted up to week 34.

# Both LUNA Steroid Regimens Result in Enhanced Safety Profile

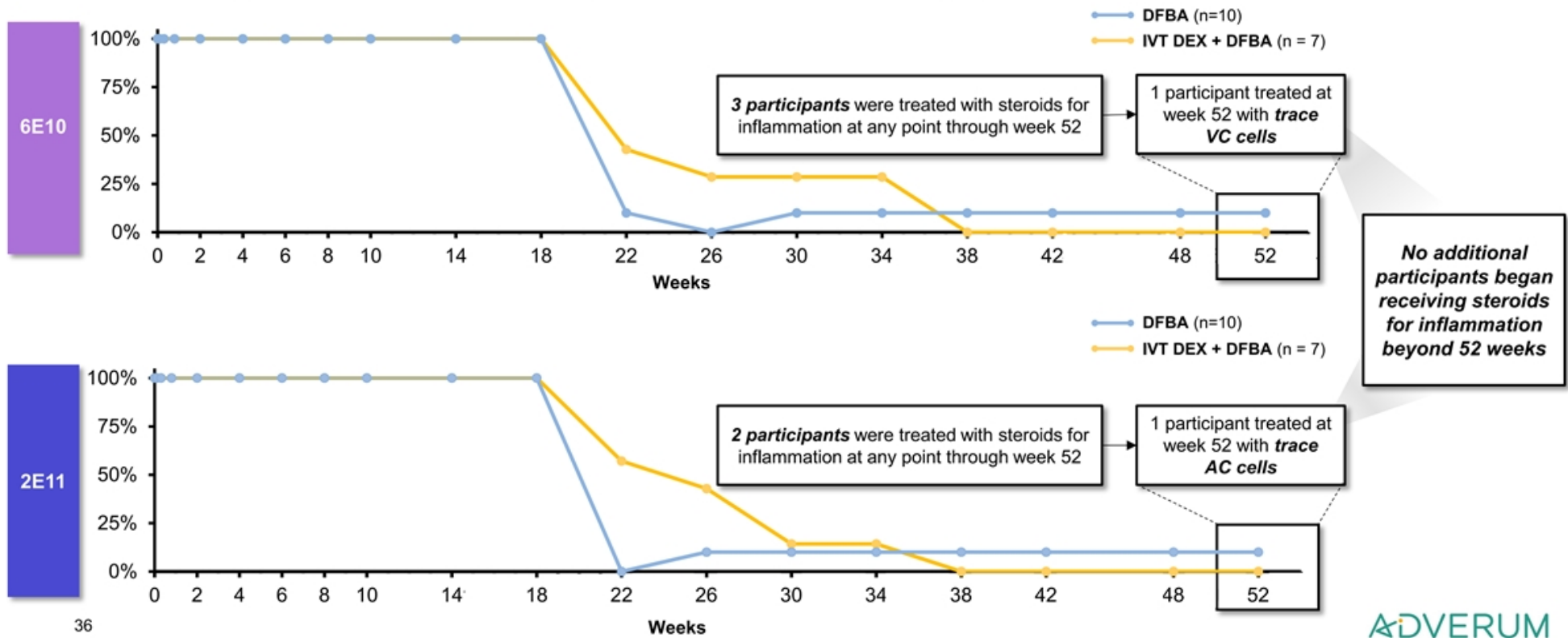
Topical eyedrops effective at minimizing inflammation & long-term steroid need



Prophylactic Regimens:  
Initial IVT DEX Injection



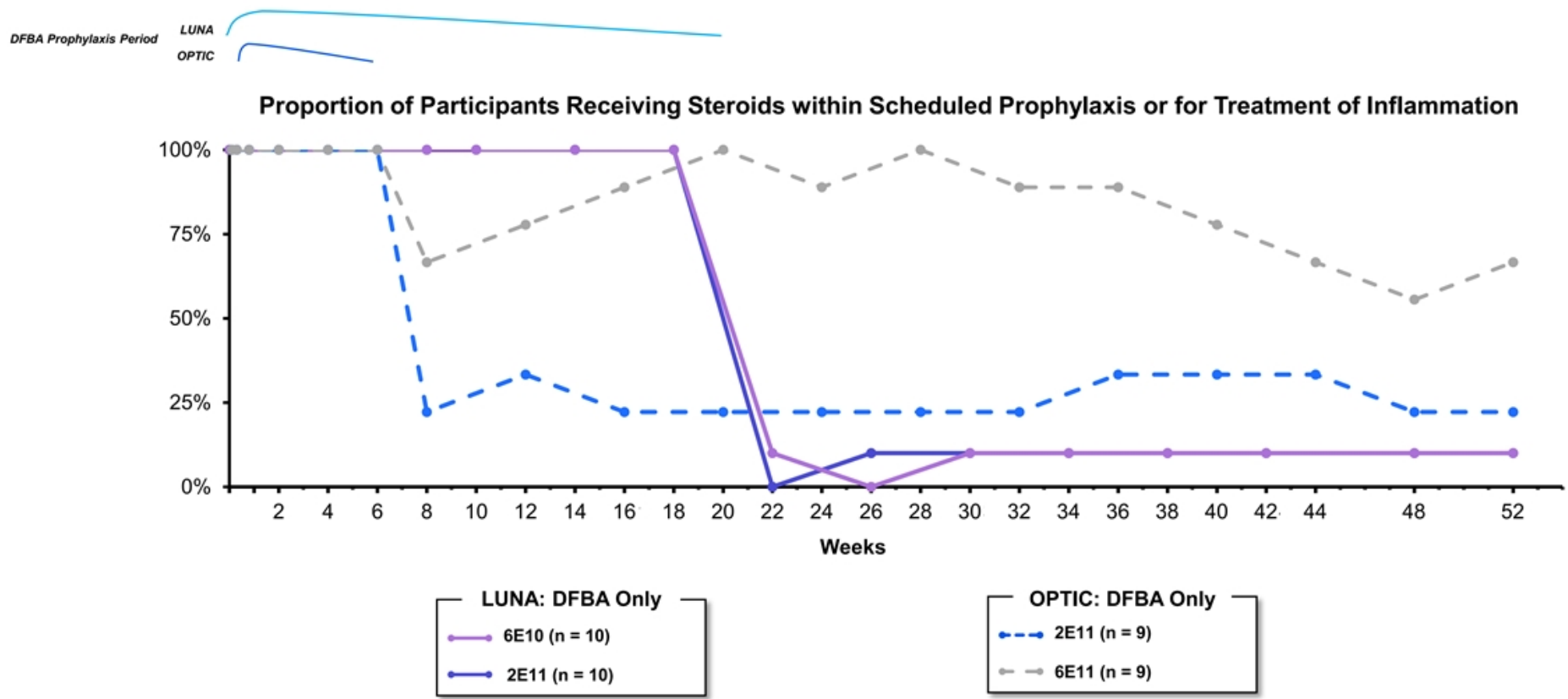
Proportion of Participants Receiving Steroids within Scheduled Prophylaxis or for Inflammation Treatment



Treatment of inflammation defined as non-pigmented or mixed pigmented ACV, including trace cells, or iritis, or vitritis. IVT DEX = Ozurdex, DFBA = difuprednate. Ozurdex injections are represented as 8 weeks of treatment.

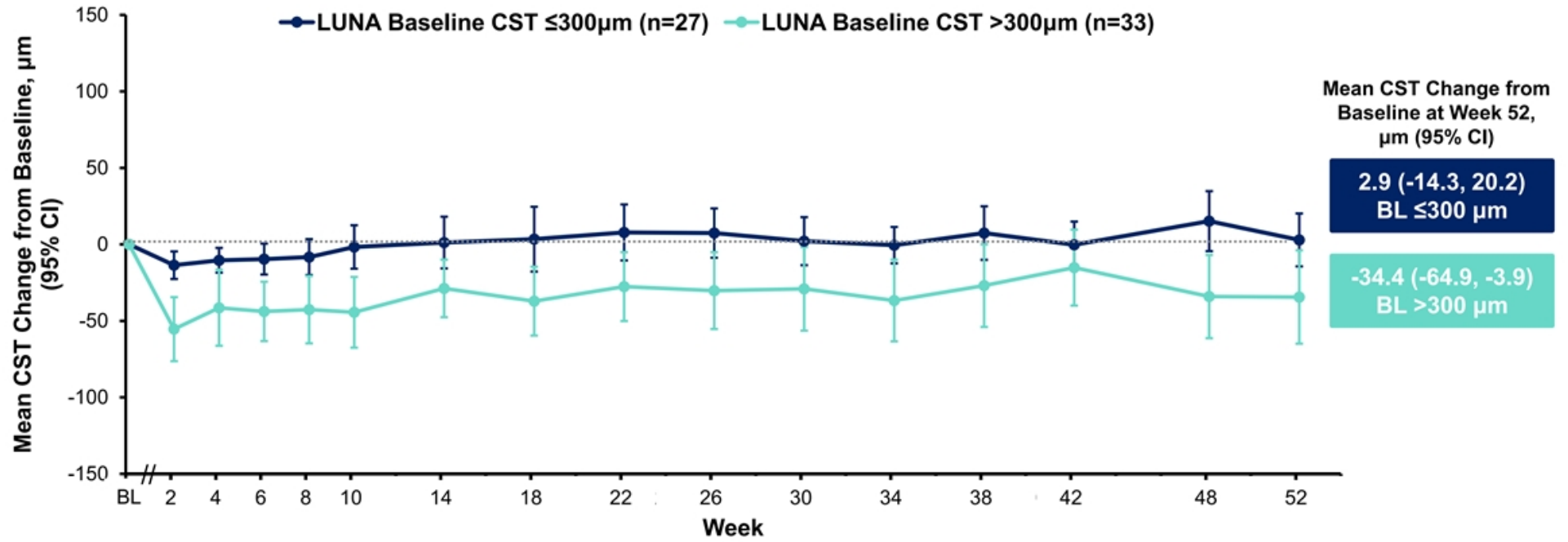
# Extended Prophylaxis in LUNA Improves Upon OPTIC Experience

Phase 3 regimen enhances overall safety profile & reduces long-term steroid need



# CST Maintained in Patients with High Disease Burden

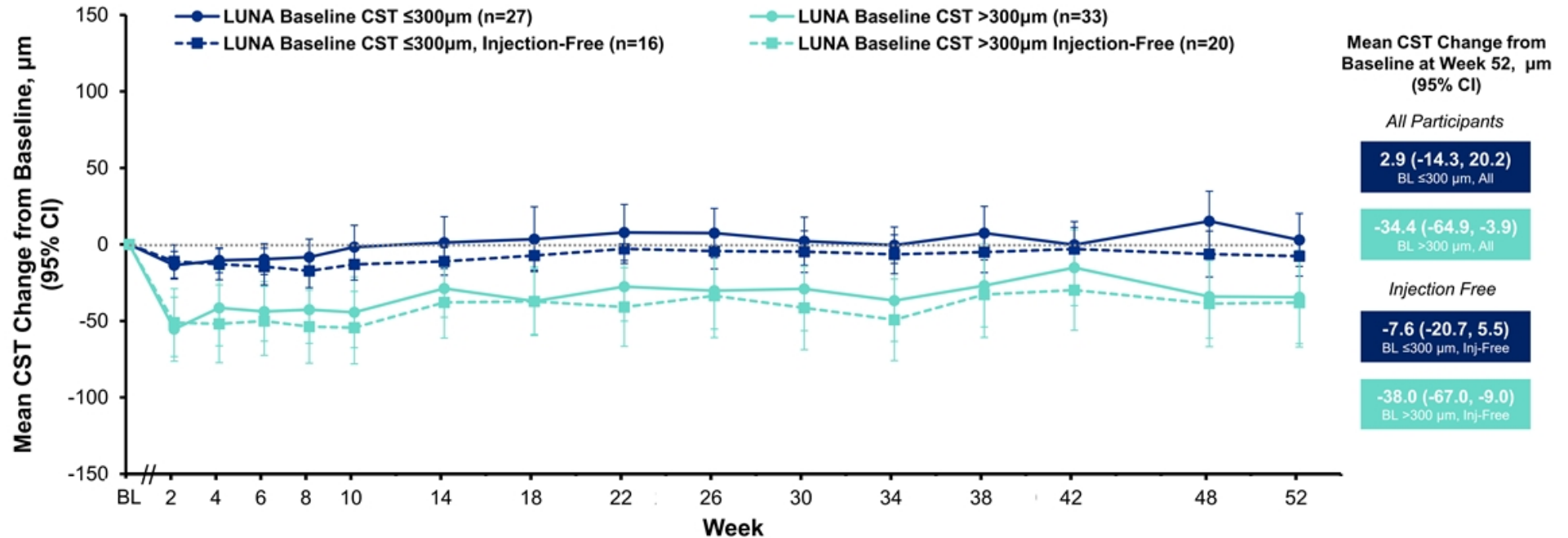
Fluid reduction in patients with baseline CST >300 μm; maintenance in ≤300 μm



Baseline Characteristic for Subgroup	CST ≤300 μm	CST >300 μm
Mean CST, μm (SD)	269.9 (18.7)	416.6 (119.1)

# Consistent Anatomic Benefit in Broad Population

Anatomic stability with reduction and maintenance of CST in injection-free patients



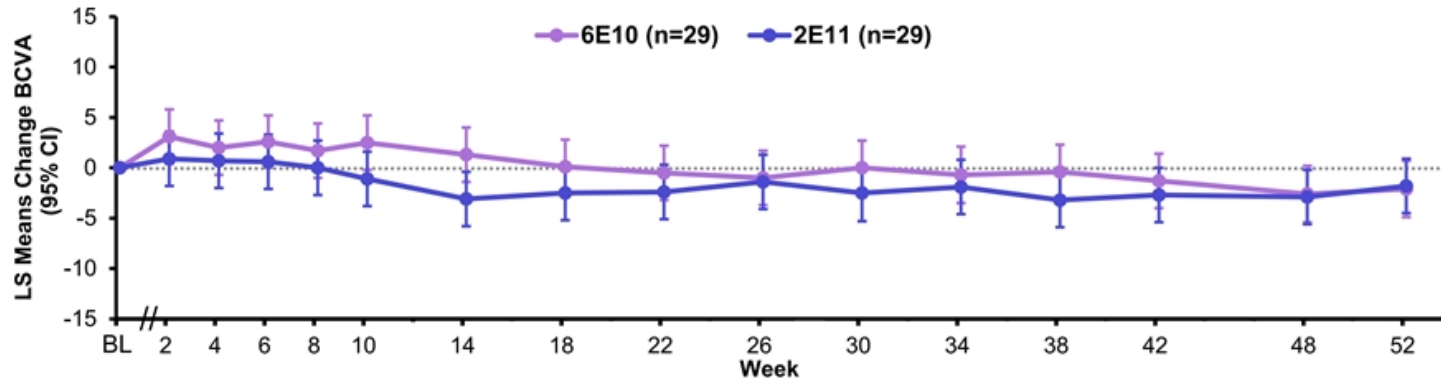
Baseline Characteristic for Subgroup	CST $\leq 300 \mu\text{m}$ All Participants	CST $> 300 \mu\text{m}$ All Participants	CST $\leq 300 \mu\text{m}$ Injection Free	CST $> 300 \mu\text{m}$ Injection Free
Mean CST, $\mu\text{m}$ (SD)	269.9 (18.7)	416.6 (119.1)	273.8 (16.7)	417.6 (142.0)

# Ixo-vec Maintained Visual & Anatomic Outcomes

BCVA maintenance demonstrated in overall population and injection-free patients



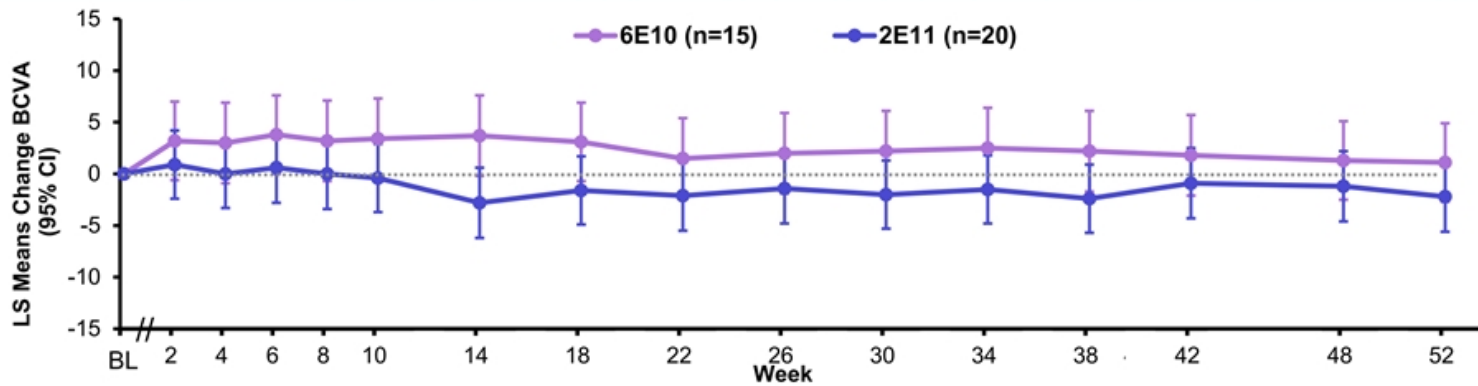
Least Squares Means Change in Best Corrected Visual Acuity (BCVA) Over Time by Dose\*



LS Means BCVA Change from Baseline at Week 52, Letters (95% CI)

-2.1 (-4.8, 0.7)	6E10
-1.8 (-4.6, 0.9)	2E11

Least Squares Means Change in Best Corrected Visual Acuity (BCVA) Over Time by Dose in Supplemental Injection Free Participants\*\*



LS Means BCVA Change from Baseline at Week 52, Letters (95% CI)

+1.1 (-2.7, 4.9)	6E10
-2.2 (-5.5, 1.2)	2E11

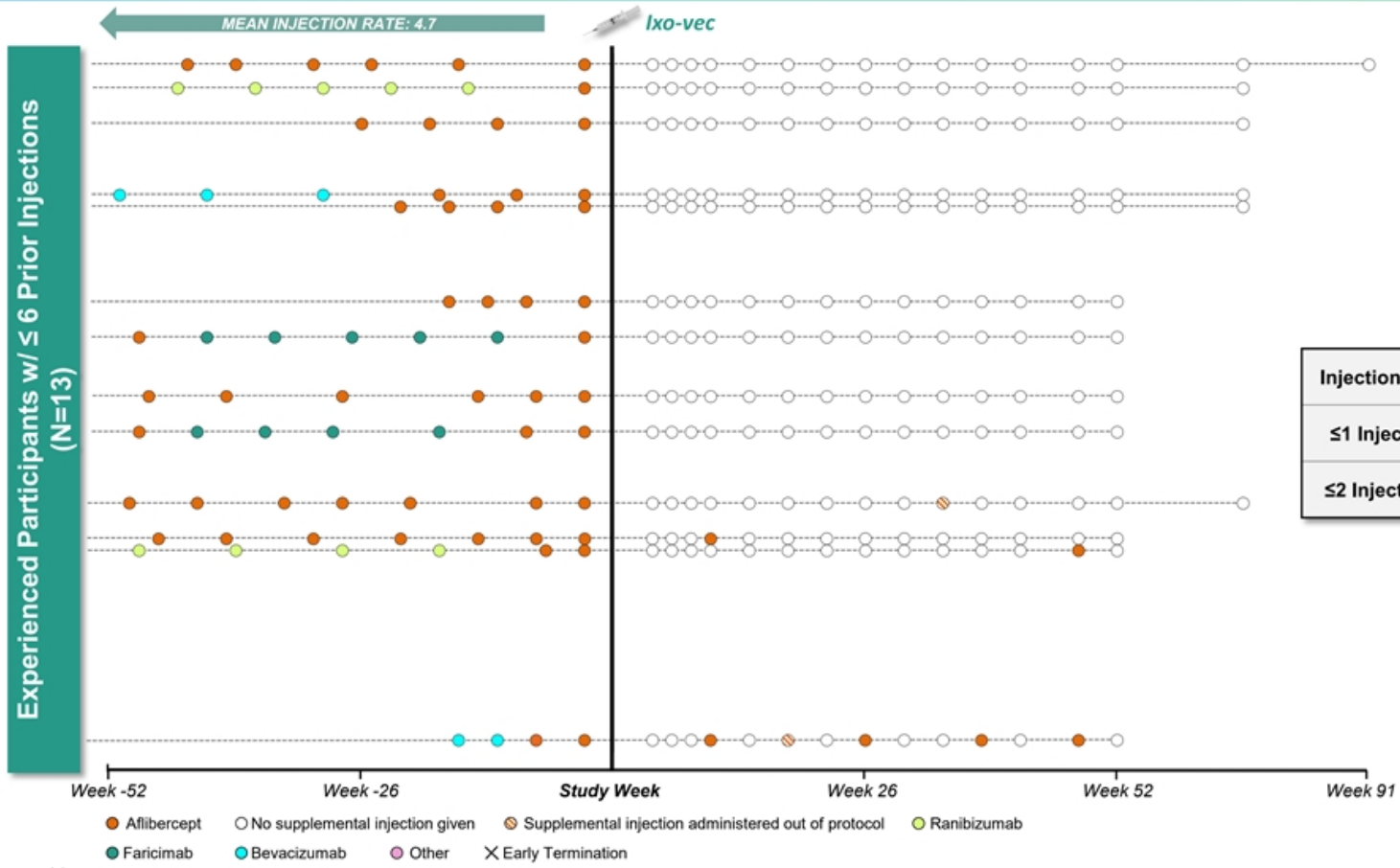
40

Least Squares Means are based on Mixed Model Repeated Measures (MMRM) including dose group, baseline value, visit and visit dose group  
 \*Excludes 1 participant at each dose with letter loss due to cataract. \*\* Excludes 1 participant with letter loss due to cataract



# 75% Injection Free in 6E10 Patients with Less Treatment Burden

Treatment-experienced patients with  $\leq 6$  injections in year prior



**LUNA 52 Weeks**

	Overall (N = 13)	6E10 (n = 4)	2E11 (n = 9)
Injection Free	69%	75%	67%
$\leq 1$ Injection	92%	100%	89%
$\leq 2$ Injections	92%	100%	89%

Only one patient required supplemental injection through their Week 52 visit.

41

Doses pooled in swim lane plot to preserve investigator masking in an ongoing double masked study. Early termination patients not included in injection calculations. % Injection Free = (Total Cohort - Early Termination Patients - Rescued Patients) / (Total Cohort - Early Termination Patients) \* 100. Experienced patients: diagnosed at least one year prior to administration of Ixo-vec.

- **Potential best-in-class product profile**  
Maintenance of visual and anatomic endpoints with over 80% reduction in injection burden and greater than 50% injection freedom
- **10X safety margin with >4 years follow-up**
- **No OPTIC 2E11 patients had inflammation at Year 1 and through Year 4**
- **No LUNA 6E10 patients had inflammation at 52 weeks or any subsequent visit**  
Favorable safety profile with local prophylaxis

**De-risked dose & prophylactic regimen for registrational trials**

# Ixo-vec Pivotal Program

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# Ixo-vec Pivotal Program for Wet AMD in Broad Patient Population

*Designed to maximize probabilities of clinical, regulatory, and commercial success*

## Ixo-vec Global Pivotal Program

- Two double-masked randomized Phase 3 trials
- Noninferiority design vs. on-label aflibercept
- ARTEMIS U.S. study based on EOP2 feedback
- 2<sup>nd</sup> study to be conducted in the U.S. and Ex-U.S.



# ARTEMIS Phase 3 Wet AMD Study Design

*Noninferiority trial designed to enable regulatory approval and drive commercial success*

**Randomized, Double Masked, On-Label Aflibercept-Controlled Phase 3 Trial in Broad Population**

## Objective

**To demonstrate that a single intravitreal injection of Ixo-vec 6E10 achieves comparable visual outcomes to on-label aflibercept, while significantly reducing the treatment burden**

## Trial Design

- **Two-arm noninferiority trial in US**
  - Ixo-vec 6E10
  - Aflibercept control 2mg q8W
- 284 treatment-naïve and previously treated patients with wet AMD
- Sham injections for masking
- One-year primary endpoint with -4.5 letter noninferiority margin

## Endpoints

### Primary Endpoint

Mean change in BCVA from Baseline to average of Weeks 52 and 56

### Secondary Endpoint

Treatment burden reduction

# ARTEMIS Phase 3 Wet AMD Study Design

Broad target patient population enriched for anti-VEGF response

## Key Inclusion Criteria

Treatment-naïve and previously treated wet AMD

**BCVA:**  
35 – 78 letters

**Anti-VEGF responsive:**  
After two aflibercept loading doses

Week	-8	-4	D1
Ixo-vec 6E10 n = 142	●	●	●
Aflibercept 2mg (Q8w) n = 142	●	●	●

Baseline      Response

- Ixo-vec IVT
- Aflibercept IVT
- Sham
- Sham or supplemental injection if criteria met
- Supplemental injection if criteria met

# ARTEMIS Phase 3 Wet AMD Study Design

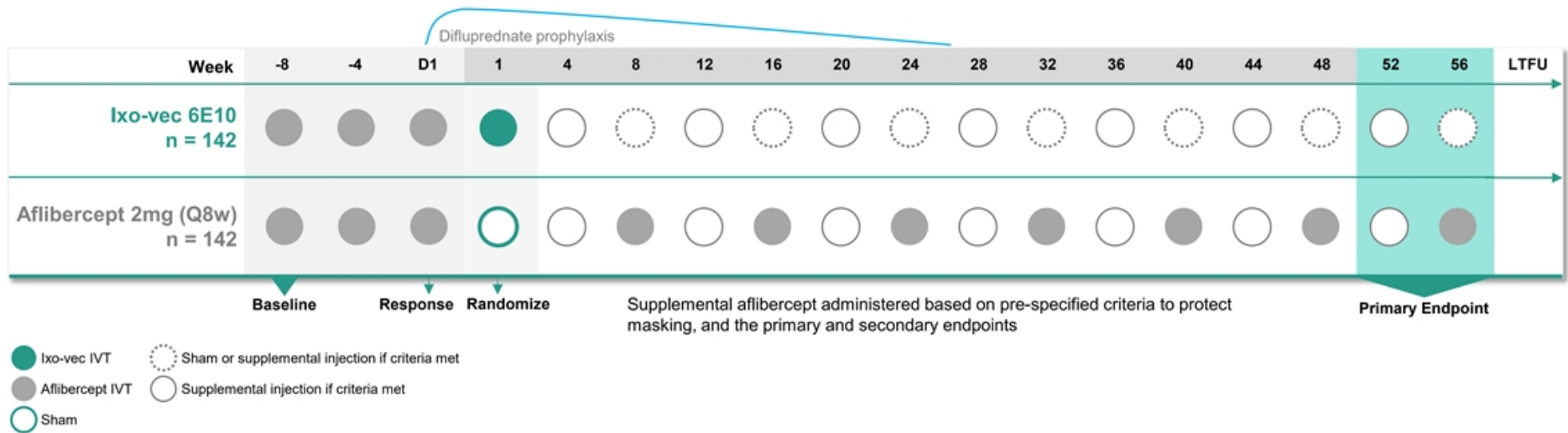
Patients randomized after 3 aflibercept loading doses and assessed every 4 weeks for disease activity

## Key Inclusion Criteria

Treatment-naïve and previously treated wet AMD

**BCVA:**  
35 – 78 letters

**Anti-VEGF responsive:**  
After two aflibercept loading doses



Designed to Maximize Probability of Clinical, Regulatory, and Commercial Success

# Patient Preference Survey

---





## Pre-specified Patient Preference Survey

*Designed to understand patient needs & commercial potential*



*“...Patient preference refers to a **patient’s perspective, expectations, and goals for health**, as well as the processes involved in **evaluating the potential benefits, harms, and costs of each treatment option offered to the patient...**”*

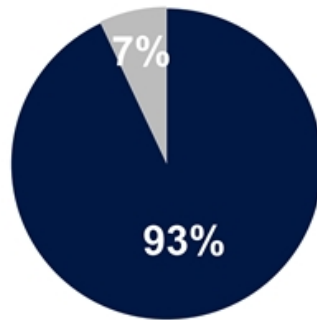
- Patient preference and DTC advertising has begun to drive adoption of novel therapies for wet AMD, with Vabysmo’s “*Open up your World*” campaign contributing to >\$4B in annualized sales.
- In LUNA, Adverum’s pre-specified patient preference survey asked whether patients prefer Ixo-vec over their prior treatment with IVT injections, whether the prophylaxis was easy to manage and if patients would recommend Ixo-vec to family or friends.

# >90% of Patients Preferred Ixo-vec over Today's Standard of Care

52-week results from LUNA pre-specified patient preference survey

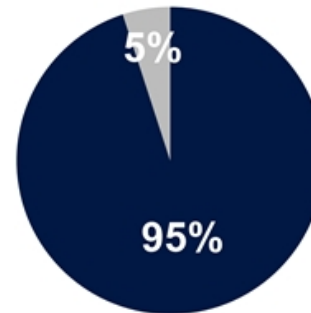


Would you prefer Ixo-vec therapy over the prior treatment(s) you received to treat your wet AMD?



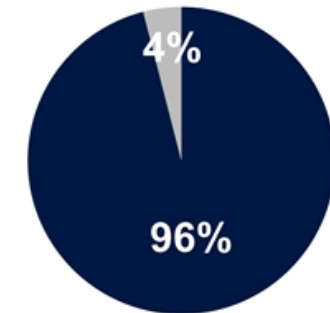
Total Study  
(n=56)

Would you want to receive Ixo-vec therapy in your other eye if you had wet AMD in both eyes?



Total Study  
(n=56)

Would you recommend Ixo-vec to your family or friends if they had wet AMD?



Total Study  
(n=56)

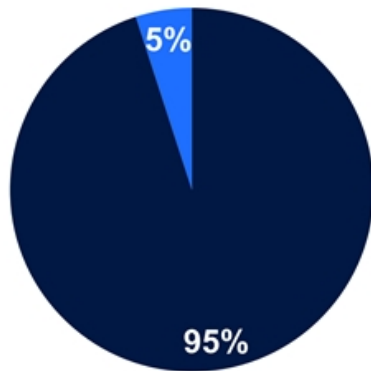
■ Yes ■ No

# Topical Steroid Eyedrops were Easy or Very Easy to Manage

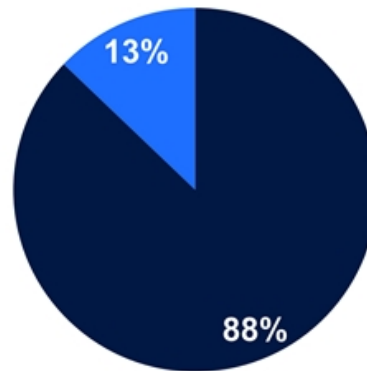
52-week results from LUNA pre-specified patient preference survey



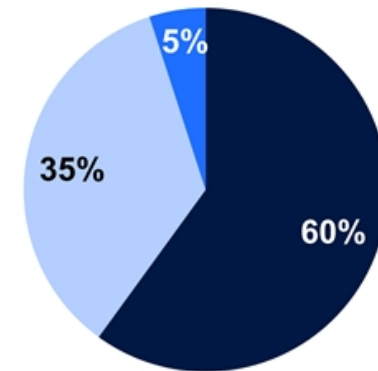
## Was the steroid treatment you received easy to manage?



**Difluprednate Only**  
(n=20)



**Ozurdex + Difluprednate**  
(n=16)



**Oral Prednisone + Difluprednate +/- Ozurdex**  
(n=20)

- Easy or Very Easy to Manage
- Undecided
- Difficult or Very Difficult to Manage

51

Adverum conducted a pre-specified Patient Preference Survey in LUNA

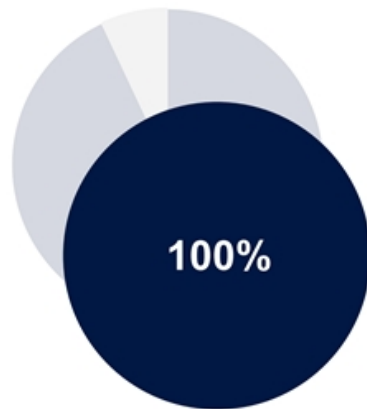
ADVERUM  
Data cut: LUNA 29AUG2024

# 100% of Ixo-vec 6E0 + Steroid Drops Preferred it over Standard of Care

52-week results from LUNA pre-specified patient preference survey

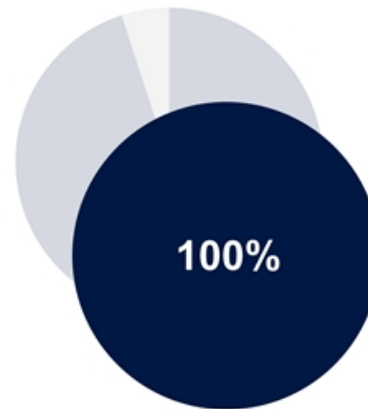


Would you prefer Ixo-vec therapy over the prior treatment(s) you received to treat your wet AMD?



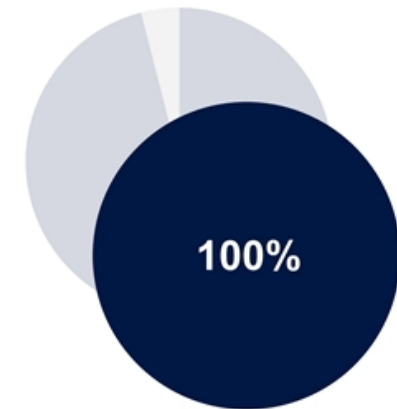
6E10 +  
Difluprednate  
(n=10)

Would you want to receive Ixo-vec therapy in your other eye if you had wet AMD in both eyes?



6E10 +  
Difluprednate  
(n=10)

Would you recommend Ixo-vec to your family or friends if they had wet AMD?



6E10 +  
Difluprednate  
(n=10)

■ Yes ■ No

# Commercial Opportunity

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# Large and Growing Global Market Opportunity

*Wet AMD physicians and patients embrace innovation*

## Wet Age-Related Macular Degeneration

*A leading cause of vision loss among older adults*

**1.5M**  
US Patients

**20M**  
Worldwide

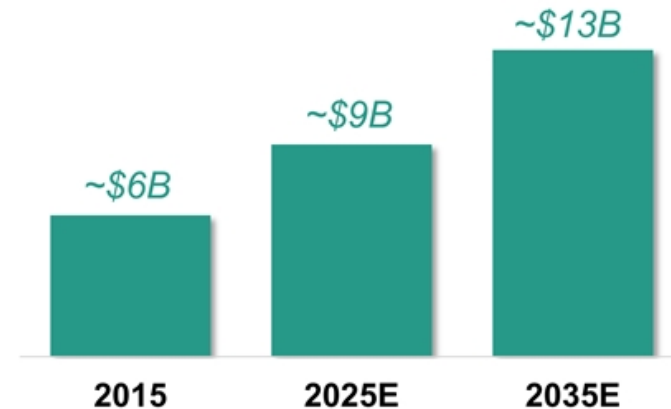
*~200k US patients diagnosed annually*

**Up to 42% of patients develop bilateral disease within 2-3 years of initial diagnosis**

## Multi-Billion Dollar Market Opportunity





*Growth driven by aging population and product innovation*

Global Wet AMD Sales

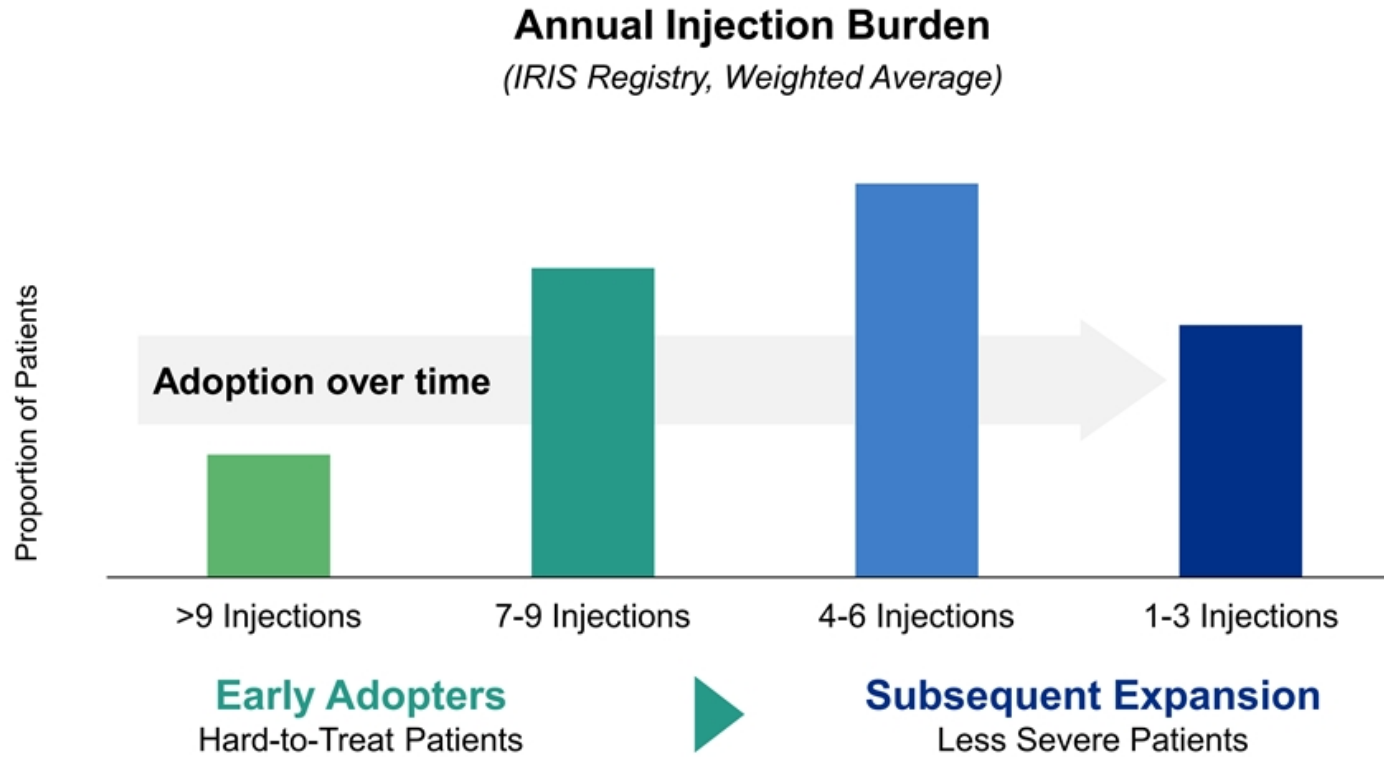


# Ixo-vec is Poised to Transform How wAMD is Treated

Potential product profile designed to fit needs of key stakeholders

Emerging Product Profile	 <b>Powerful and Durable Efficacy Profile</b>	 <b>Predictable Safety Profile</b>	 <b>Seamless Practice Integration</b>	 <b>Patient Preference &amp; Impact</b>
<b>Providers</b>	<ul style="list-style-type: none"> <li>• Sustained vision</li> <li>• Durable anatomic improvements</li> <li>• Substantial reduction in treatment burden</li> </ul>	<ul style="list-style-type: none"> <li>• No new onset of inflammation past week 30</li> <li>• Inflammation is infrequent, resolves and does not impact vision</li> </ul>	<ul style="list-style-type: none"> <li>• IVT administration</li> <li>• Integrates into clinical practice, operations, and economic model</li> </ul>	<ul style="list-style-type: none"> <li>• Reduced patient drop off</li> <li>• Sustained long-term vision for patients</li> </ul>
<b>Patients &amp; Caregivers</b>	<ul style="list-style-type: none"> <li>• &gt;50% chance of injection freedom</li> <li>• Sustained vision for life with few injections</li> </ul>	<ul style="list-style-type: none"> <li>• Easy to manage steroid eye drops</li> </ul>	<ul style="list-style-type: none"> <li>• Fewer office visits</li> <li>• Routine retina visit</li> </ul>	<ul style="list-style-type: none"> <li>• 93% preference over prior IVT injections</li> <li>• 100% said topical steroids were Easy or Very Easy to manage</li> </ul>
<b>Payers</b> <ul style="list-style-type: none"> <li>• Potential to reduce healthcare system burden in a cost-effective manner</li> <li>• Maximize payer return on investment through preserving long-term vision with as little as one injection</li> </ul>				

# Market Leadership in Wet AMD May Require Best-in-Class Profile that First Demonstrates Success in Hard-to-Treat Patients





# Wet AMD May be the First Large-Market Indication for Gene Therapy

## Epidemiology

### HIGH PREVALENCE

Large addressable market at launch



### LARGE ANNUAL INCIDENCE

New patients, bilateral disease, growing with population ages



## Economics

### MASS MARKET PRICING

Lower cost per patient than orphan diseases



### LOWER COGS

>1000x lower dose than systemic gene therapies



## Market Environment

### URGENCY FOR ADOPTION

Lack of maintained vision in the real-world suggest early adoption after initial vision gain



### VALIDATED TREATMENT

Aflibercept sustained delivery, a mega-blockbuster anti-VEGF used in over 70M injections<sup>1</sup>



# CMC Positioned to Support Pivotal Program and Commercial Scale Up

*Ixo-vec currently manufactured at commercial scale*



**Commercial-scale manufacturing in place at global CDMO**



**Supported by robust regulatory CMC input**



**All Ixo-vec Phase 3 material has been manufactured**



**Cost-efficient Sf9 suspension process enables biologics-like COGS**



# KOL Panel

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# KOL Panel with Leading Retinal Specialists

## Discussing LUNA and OPTIC Results, and Pivotal Trial Design

MODERATOR



**Star Seyedkazemi, PharmD**  
*Chief Development Officer*



**Charles C. Wykoff, MD, PhD**  
*Director of Research,  
Retina Consultants of Texas*



**Mark Barakat, MD**  
*Director of Clinical Research  
Macula Institute of Arizona*



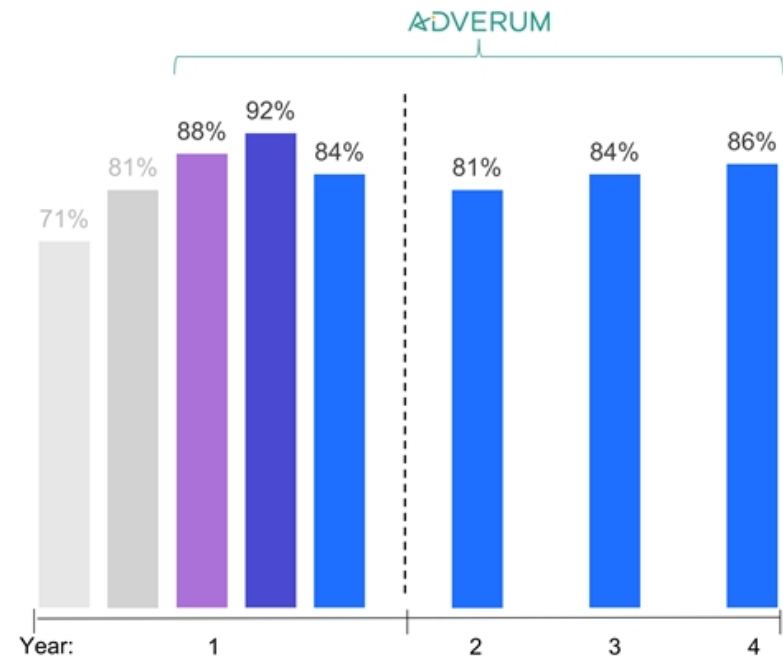
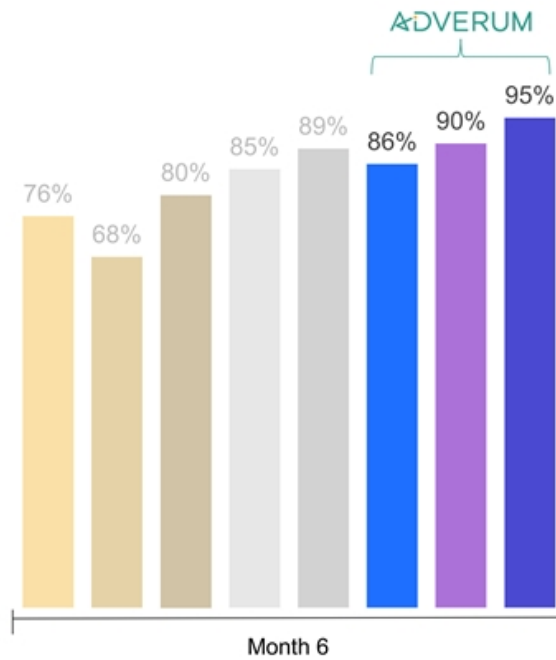
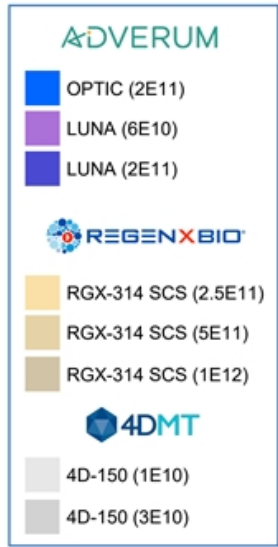
**Szilárd Kiss, MD**  
*Distinguished Professor of Ophthalmology,  
Director of Retina Service  
Cornell University  
Adverum Board Member*

# Conclusion & Takeaways

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# Largest Treatment Burden Reduction in Hard-to-Treat Patients from 6 Months to > 4 Years

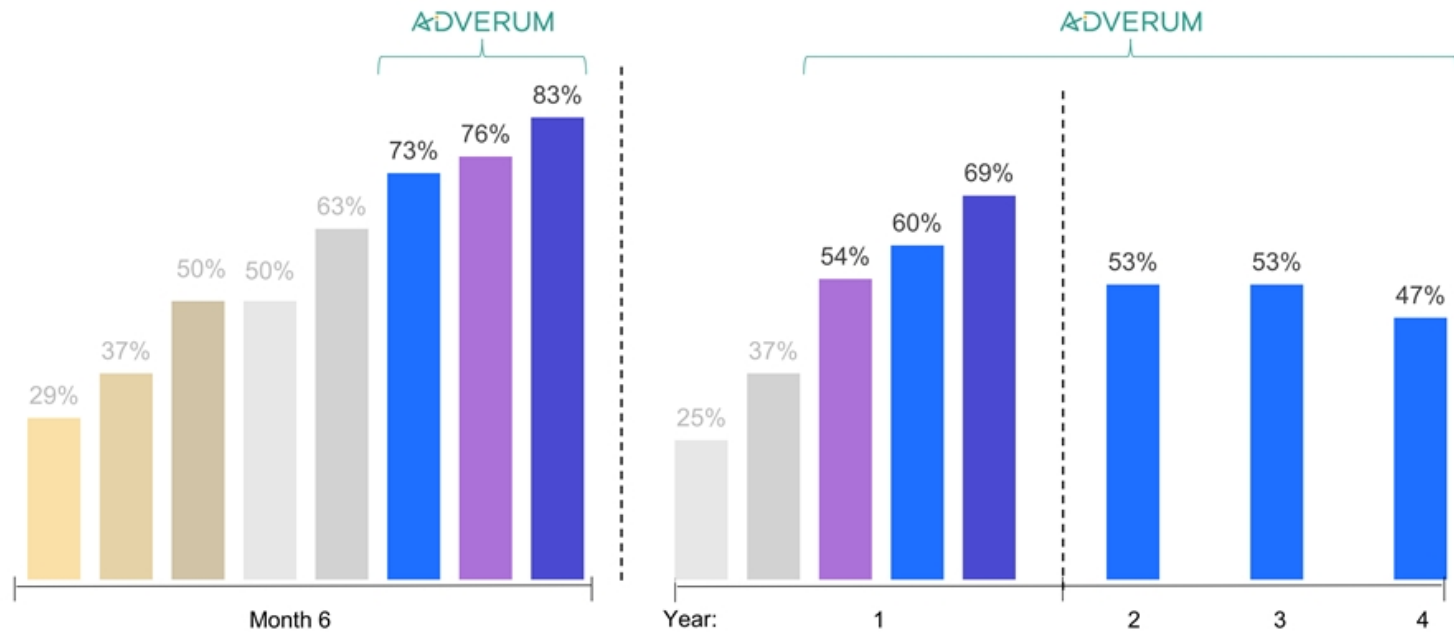
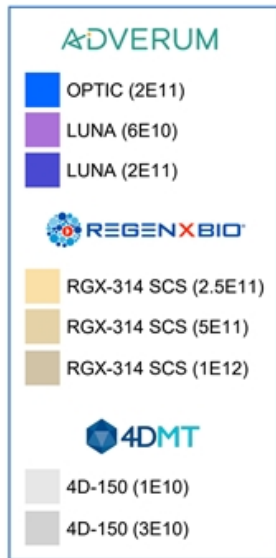
## % Annualized Reduction in Injection Burden



62 Among IVT and suprachoroidal gene therapy for wet AMD; excludes ABBV-RGX-314 subretinal. ABBV-RGX-314 SCS in AAVIATE (NB: 21 of 56 subjects at 1E12 dose received booster shot at wk 4, not included in post RGX-314 mean annualized injections). RGX-314 data as of 3Feb2024. Latest available 4D-150 PRISM Phase 2a Dose Expansion Cohort data as of 18Sep2024 (Phase 1/2a for 1E10 dose as Phase 2a wasn't reported separately). Data are based on a cross-trial comparison and are not based on head-to-head clinical trials. Cross-trial comparisons are inherently limited and may suggest misleading similarities or differences in outcomes. Results of head-to-head comparisons may differ significantly from those set forth herein.

# Highest Injection-Free Rates in Hard-to-Treat Patients from 6 Months to > 4 Years

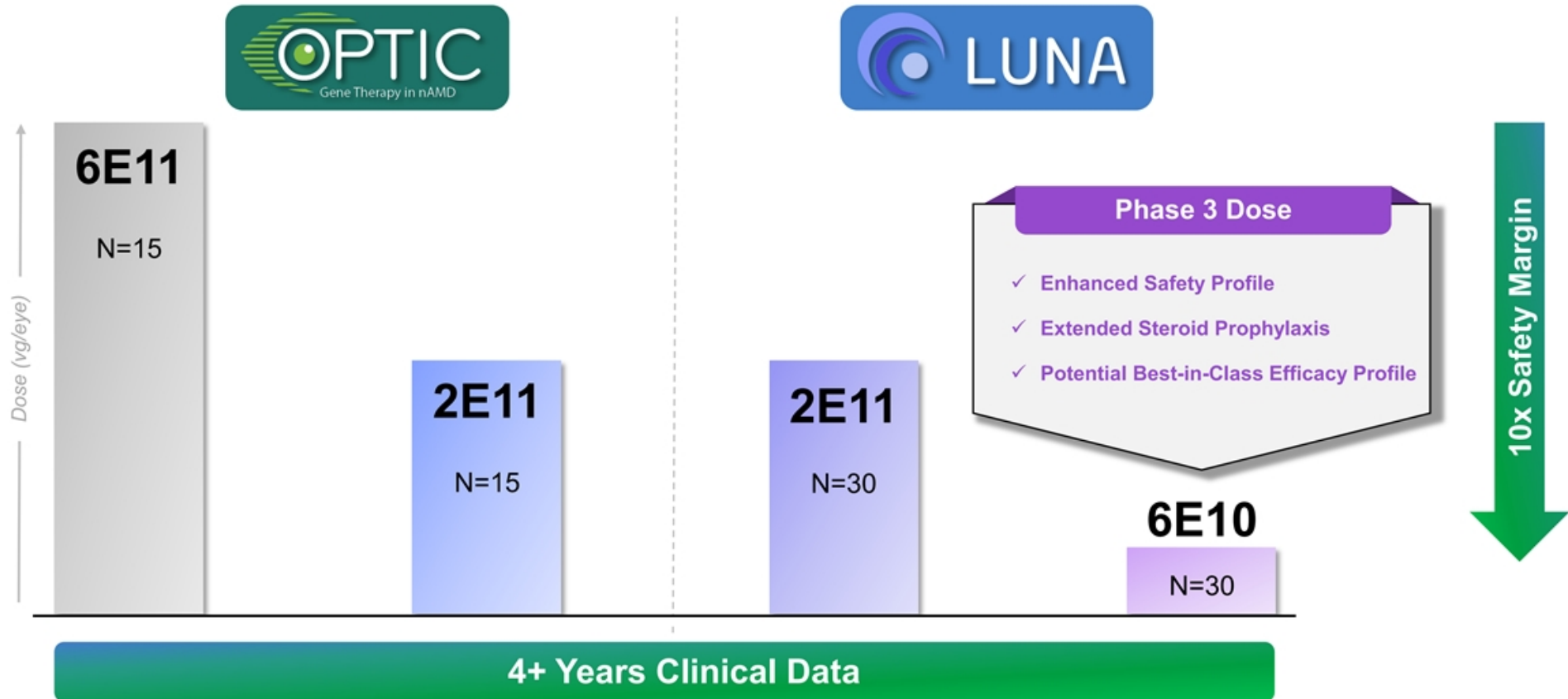
## % Injection-Free



63 Among IVT and suprachoroidal gene therapy for wet AMD; excludes ABBV-RGX-314 subretinal. ABBV-RGX-314 SCS in AAVIATE (NB: 21 of 56 subjects at 1E12 dose received booster shot at wk 4, not included in post RGX-314 mean annualized injections). RGX-314 data as of 3Feb2024. Latest available 4D-150 PRISM Phase 2a Dose Expansion Cohort data as of 18Sep2024 (Phase 1/2a for 1E10 dose as Phase 2a wasn't reported separately; calculated from swim lane plot). Data are based on a cross-trial comparison and are not based on head-to-head clinical trials. Cross-trial comparisons are inherently limited and may suggest misleading similarities or differences in outcomes. Results of head-to-head comparisons may differ significantly from those set forth herein.

# 5+ Years of Clinical Experience Establish 10x Safety Margin

*Ixo-vec 6E10 with extended prophylaxis de-risks Phase 3 & commercialization*

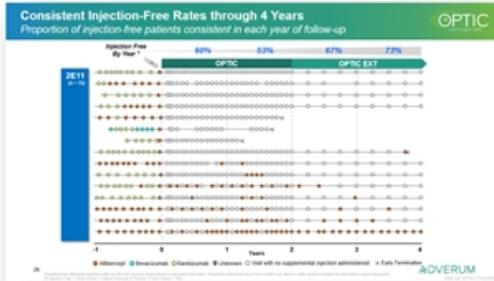




# Reliable Benefit & Predictable Safety Enable True Paradigm Shift

4-year OPTIC & 52-week LUNA data underscore Ixo-vec's profile

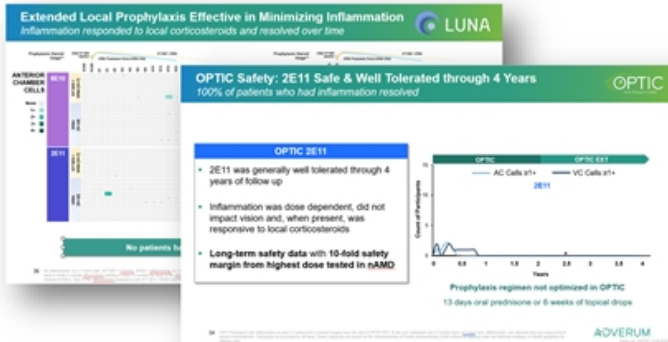
## Demonstrated Reliable Long-Term Benefit



**78%** of patients who were injection free through year 1 remained injection free through year 4

**88%** of patients who were injection free through year 2 remained injection free through year 4

## Demonstrated Predictable Safety Profile with Local Prophylaxis



**NO** new onset of inflammation after week 30

**100%** of inflammation resolved by year 1

# Ixo-vec's Derisked Phase 3 and Commercial Profile

Clinical updates underscore Ixo-vec's potential best-in-class product profile



- **Potential best-in-class product profile**  
>50% injection free and >80% treatment burden reduction in hard-to-treat patients
- **10X safety margin with >4 years follow-up**
- **No OPTIC 2E11 patients had inflammation at Year 1 and through Year 4**
- **No LUNA 6E10 patients had inflammation at 52 weeks or any subsequent visit**  
Favorable safety profile with local prophylaxis
- **LUNA patient survey demonstrates strong patient preference for Ixo-vec**

**ARTEMIS**  
Phase 3 Trial

**6E10**

With topical  
steroid eyedrops

**EOP2**

US study, incorporates  
FDA feedback

**284**

Patients

**Broad**

Patient population

**1H25**

Expected Phase 3  
initiation

# Q&A

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# Question & Answer Session



**Laurent Fischer, MD**  
*President and  
Chief Executive Officer*



**Rabia Gurses Ozden, MD**  
*Chief Medical Officer*



**Star Seyedkazemi, PharmD**  
*Chief Development Officer*



**Jason Mitchell**  
*Chief Commercial Officer*



**Peter Soparkar**  
*Chief Operating Officer*



**Linda Rubinstein**  
*Chief Financial Officer*



**Mike Zaroni**  
*Head of Investor Relations*



**Charles C. Wykoff, MD, PhD**  
*Director of Research,  
Retina Consultants of Texas*



**Mark Barakat, MD**  
*Director of Clinical Research  
Macula Institute of Arizona*



**Szilárd Kiss, MD**  
*Distinguished Professor of Ophthalmology,  
Director of Retina Service  
Cornell University  
Adverum Board Member*

# ADVERUM

[www.adverum.com](http://www.adverum.com)

For additional questions reach out to:

[IR@adverum.com](mailto:IR@adverum.com)

Preserving Sight for Life®

# Appendix

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IVT Gene Therapy for the  
Treatment of wet AMD

# LUNA & OPTIC Study Disposition

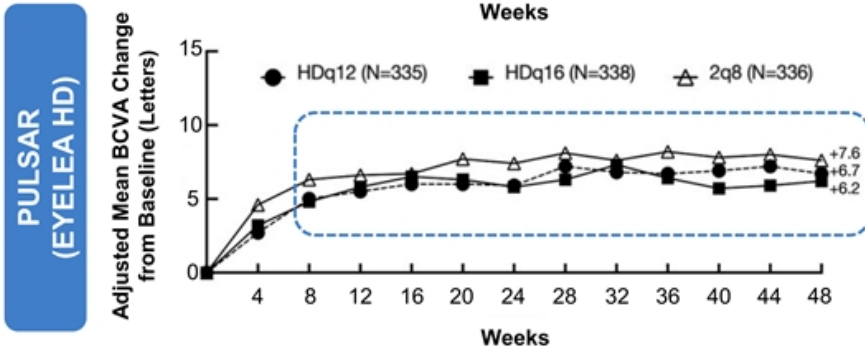
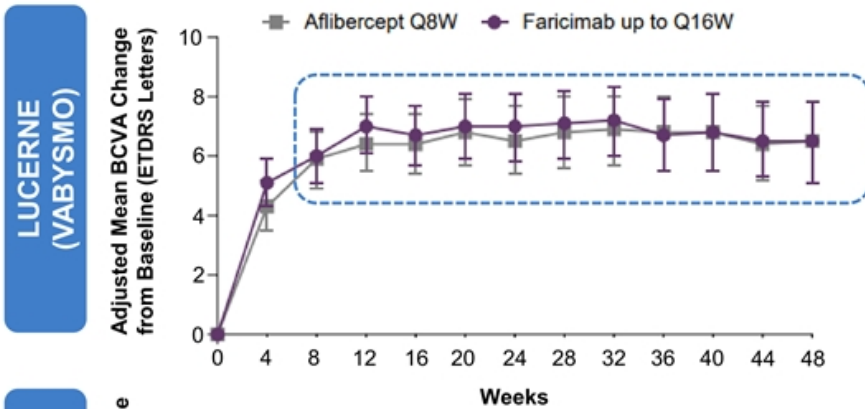
90 patients enrolled across LUNA & OPTIC trials



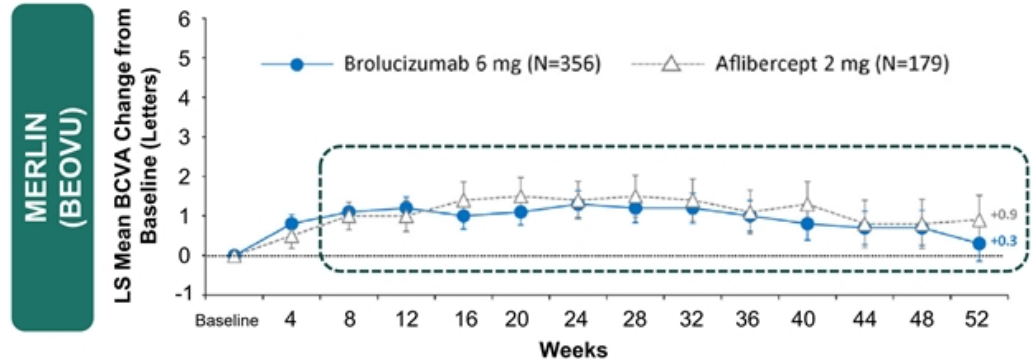
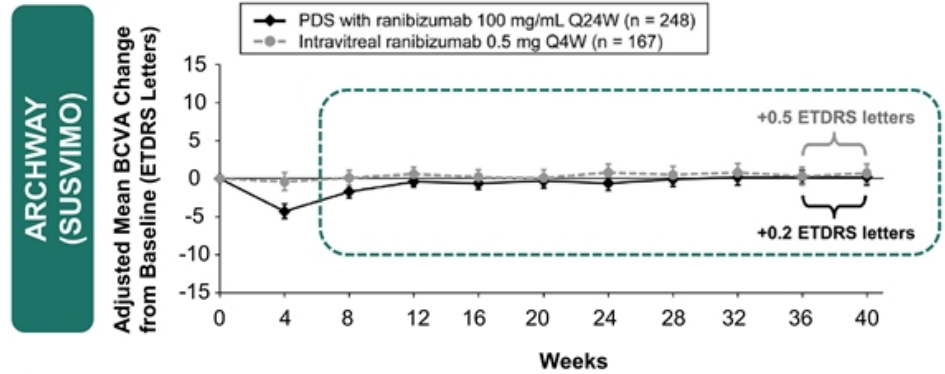
PARTICIPANT DISPOSITION	LUNA Total	OPTIC Total
<b>Number of participants enrolled and dosed with Ixo-vec</b>	60	30
Number of participants who completed 52-week visit	57	30
Number of participants enrolled in open-label extension	-	23
Number of participants who completed year 4 visit	-	21
<b>Number of participants who discontinued after Ixo-vec dosing</b>	3	7
By week 52 visit	3	0
By year 4 visit	-	7
<b>Reason for discontinuation (not related to Ixo-vec)</b>		
Unrelated adverse event (incl. death)	3	3
Lost to follow-up / withdrew consent	-	4

# Response to Anti-VEGF in Treatment Naïve vs Treatment Experienced Wet AMD: Similar BCVA Trajectories After Initial 2 Loading Doses

## Treatment Naïve



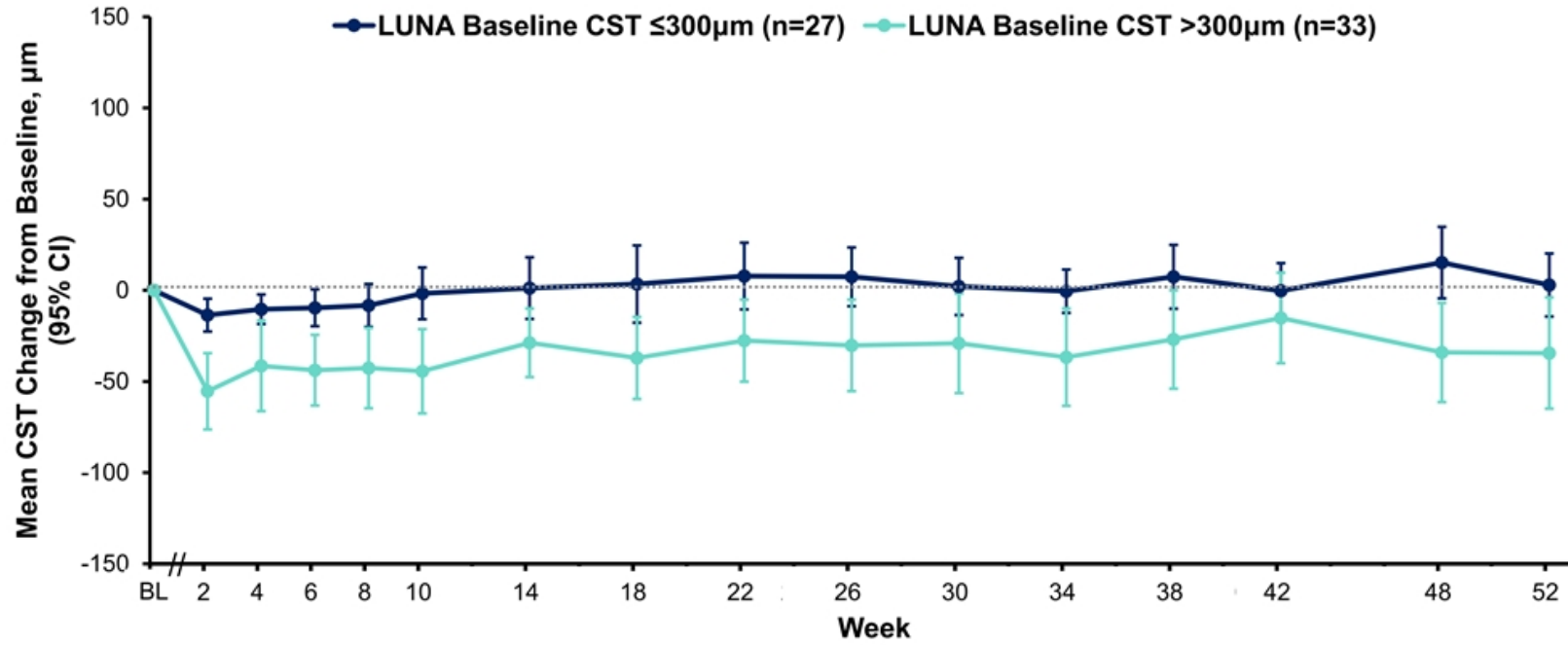
## Treatment Experienced





# CST Maintained in Patients with High Disease Burden

Fluid reduction in patients with baseline CST >300 μm; maintenance in ≤300 μm



Mean CST Change from Baseline at Week 52, μm (95% CI)

2.9 (-14.3, 20.2) BL ≤300 μm
6E10 9.2 (-24.6, 43.0) BL ≤300 μm
2E11 -3.4 (-17.9, 11.1) BL ≤300 μm

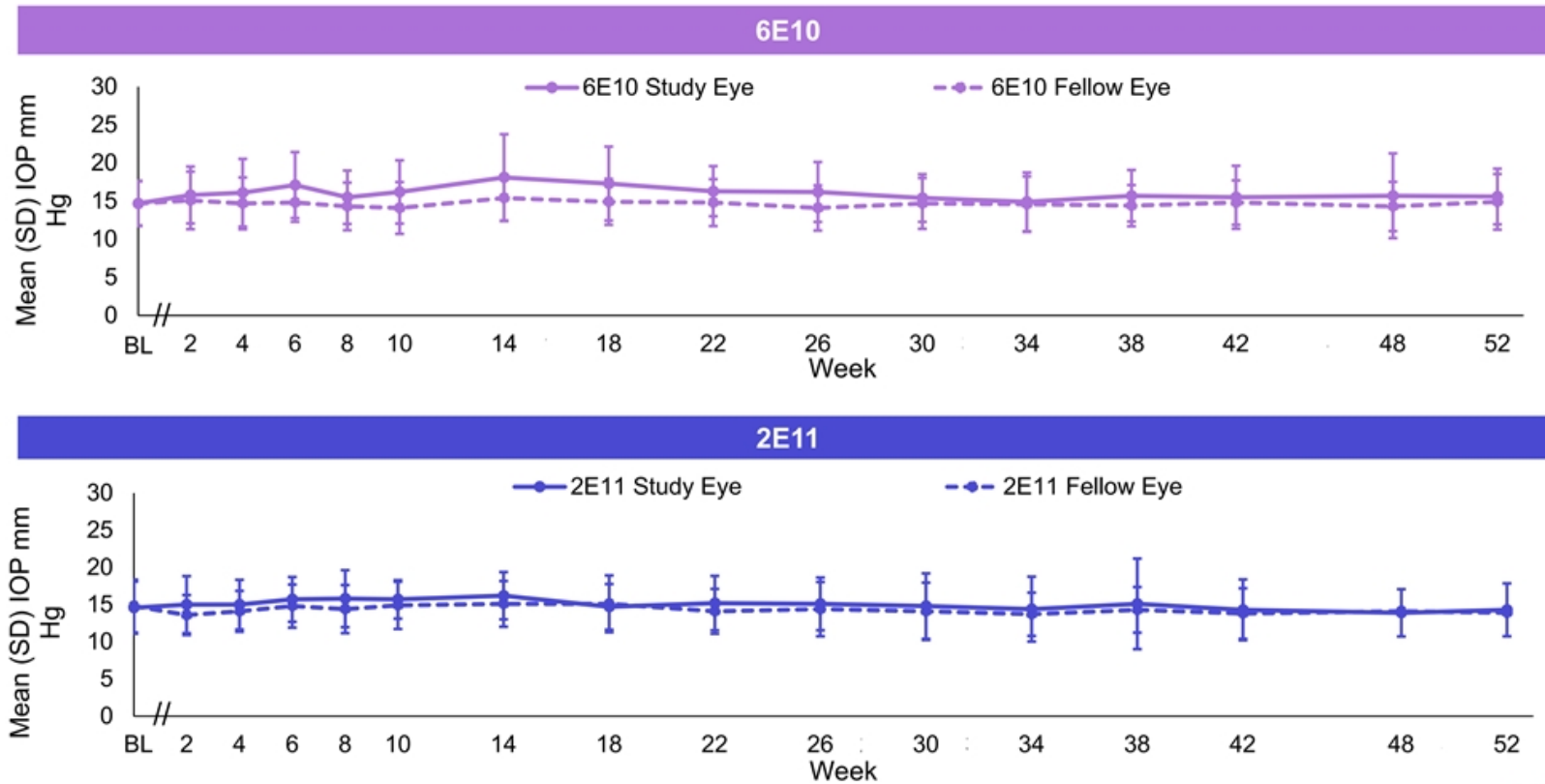
-34.4 (-64.9, -3.9) BL >300 μm
6E10 -35.5 (-83.3, 12.3) BL >300 μm
2E11 -33.3 (-77.6, 10.9) BL >300 μm

Baseline Characteristic for Subgroup	CST ≤300 μm	CST >300 μm
Mean CST, μm (SD)	269.9 (18.7)	416.6 (119.1)

# Stable Intraocular Pressure at Both Doses



### Mean IOP Over Time by Dose

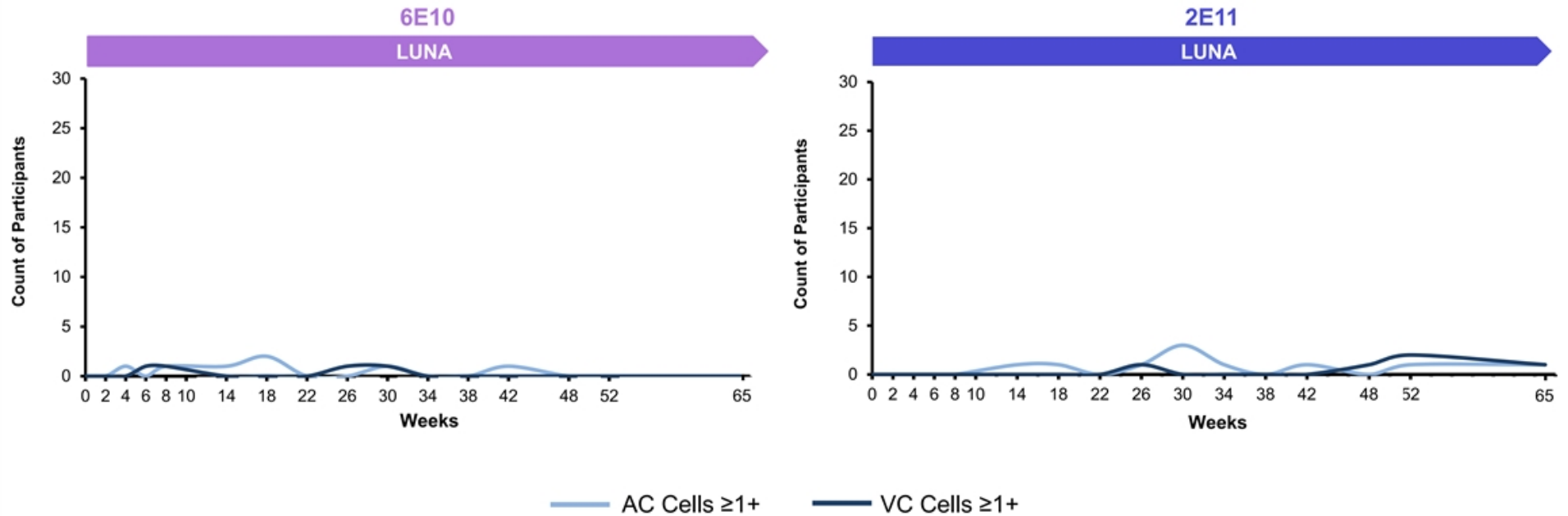


# LUNA Overall Population: Frequency of Inflammation

No patients at 6E10 had inflammation at week 52 or at any subsequent visit



## Frequency of Inflammation Over Time by Dose

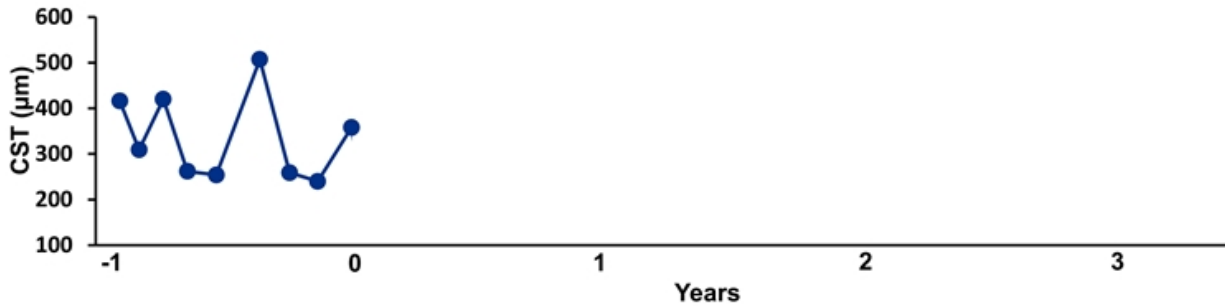
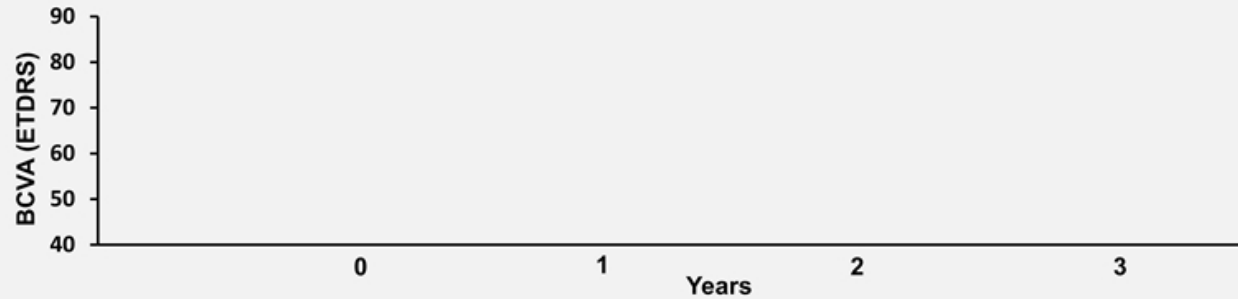


75 AC, aqueous cells; VC, vitreous cells. Cell grades as assessed by slit lamp. Grade categories are based on the Standardization of Uveitis Nomenclature (SUN) criteria for aqueous cells and National Institutes of Health guidelines for vitreous cells. AC: 0.5+; 1-5 cells 1+; 6-15 cells 2+; 16-50 cells 3+; 26-50 cells 4+; >50 cells; VC: 0.5+; 1-10 cells 1+; 11-20 cells 2+; 21-30 cells 3+; 31-100 cells 4+; >100 cells; Rare cells are captured as 0.5+ for analysis. \* Protocol amended early in study to include difluprednate starting at week 4 to match the taper in difluprednate regimens; if initiated after week 4 visit, difluprednate may be adjusted at the discretion of investigator in consult with medical monitors (6 participants did not receive difluprednate as part of prophylaxis)

# Case Study: Ixo-vec 2E11 Reduces Fluctuations in Fluid and Central Subfield Thickness (CST)

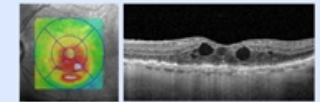
90-Year-Old Female with 9 IVTs in the 12 Months Prior to Ixo-vec

Aflibercept Q5W prior to Ixo-vec



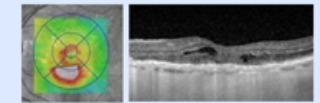
76 ● Anti-VEGF injection ○ Study visit, no supplemental injection ..... Baseline

-56 weeks



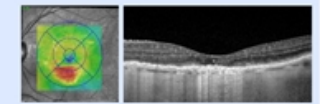
-2 wks (baseline)

BCVA: 53 letters  
CST: 358 µm



Day 0

Ixo-vec  
administration

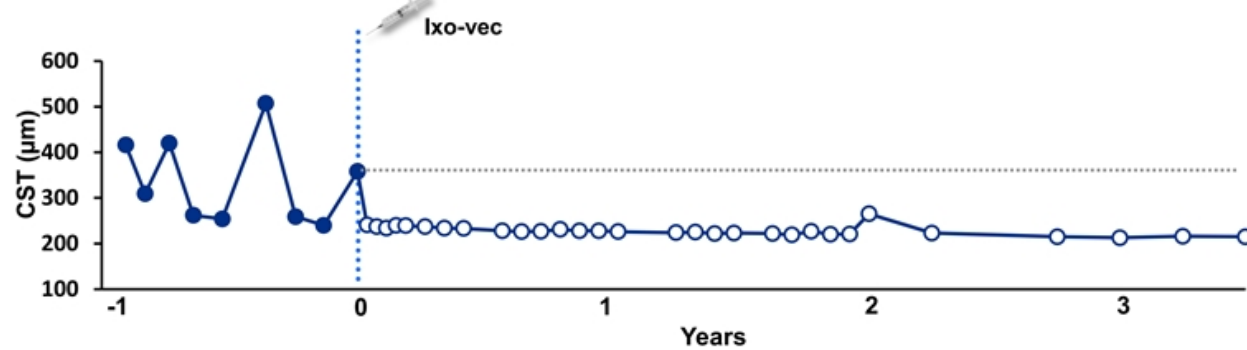
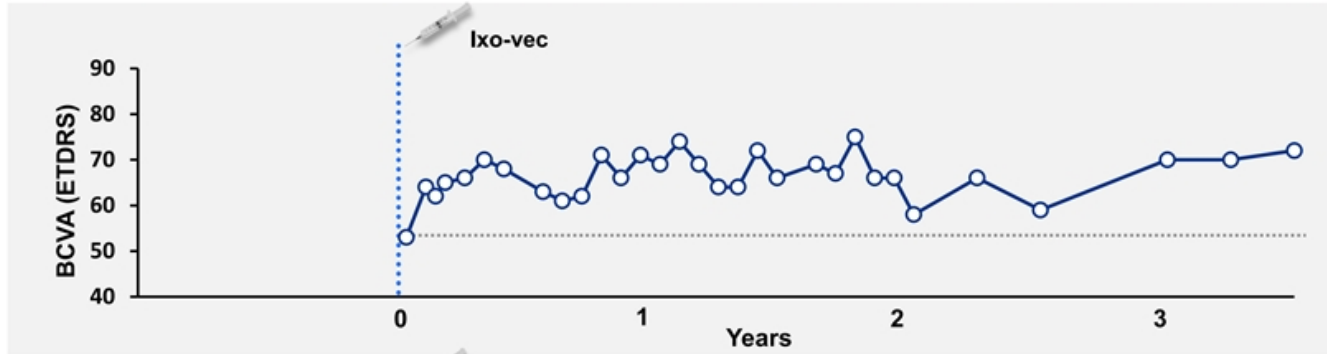


# Case Study: Ixo-vec 2E11 Reduces Fluctuations in Fluid and Central Subfield Thickness (CST)

90-Year-Old Female with 9 IVTs in the 12 Months Prior to Ixo-vec

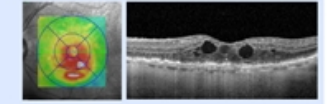
Aflibercept Q5W prior to Ixo-vec

100% anti-VEGF injection free following Ixo-vec



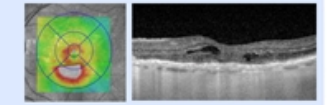
77 ● Anti-VEGF injection ○ Study visit, no supplemental injection ..... Baseline

-56 weeks



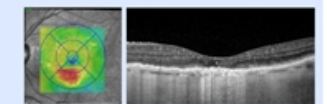
-2 wks (baseline)

BCVA: 53 letters  
CST: 358 µm



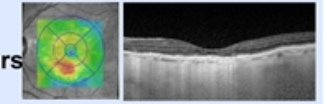
Day 0

Ixo-vec administration



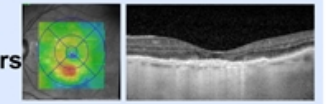
9 Months

BCVA Δ: +18 letters  
CST Δ: -127 µm



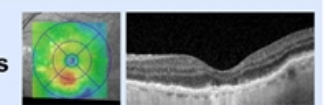
1 Year

BCVA Δ: +16 letters  
CST Δ: -132 µm



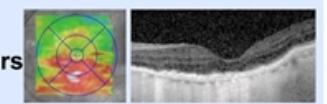
2 Years

BCVA Δ: +5 letters  
CST Δ: -93 µm



2.2 Years

BCVA Δ: +13 letters  
CST Δ: -135 µm



ADVERUM