Efficacy and Safety of Intravitreal Injections of ANX007 in Patients With Geographic Atrophy: Results of the ARCHER Study

Jeffrey Heier, Charles Wykoff, Glenn Jaffe, David Lally, Roger A. Goldberg, Allen Hu, Carl Regillo, David Boyer, Karl Csaky, Wendy Murahashi, Harman Hansra, Scott Borland, Lori Taylor and Donald Fong

On behalf of the ARCHER Investigators

February 3, 2024

Key Takeaways

ANX007 has a unique neuroprotective mechanism of action targeting the C1q pathway

In the Phase 2 ARCHER study, while the primary endpoint of GA reduction was not met, GA area reduction was trending over time

Treatment with ANX007 resulted in consistent, dose dependent protection from vision loss, demonstrated across a broad range of GA patients

ANX007 was generally well tolerated

ANX007 global Phase 3 program is under development with first and only EMA PRIME designation in GA

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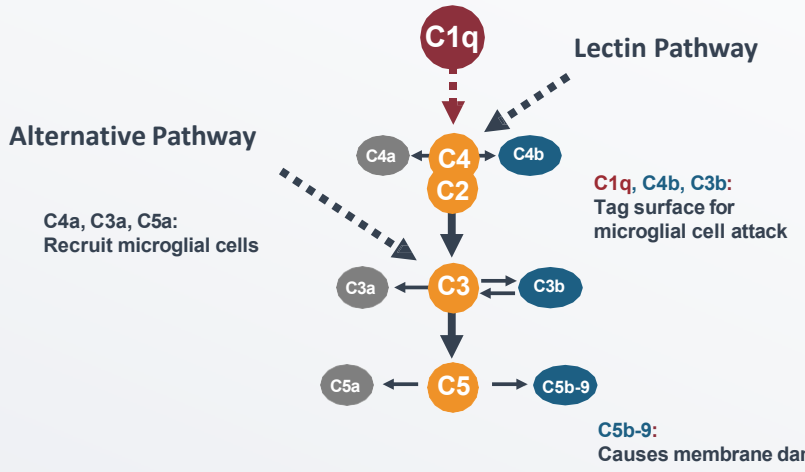
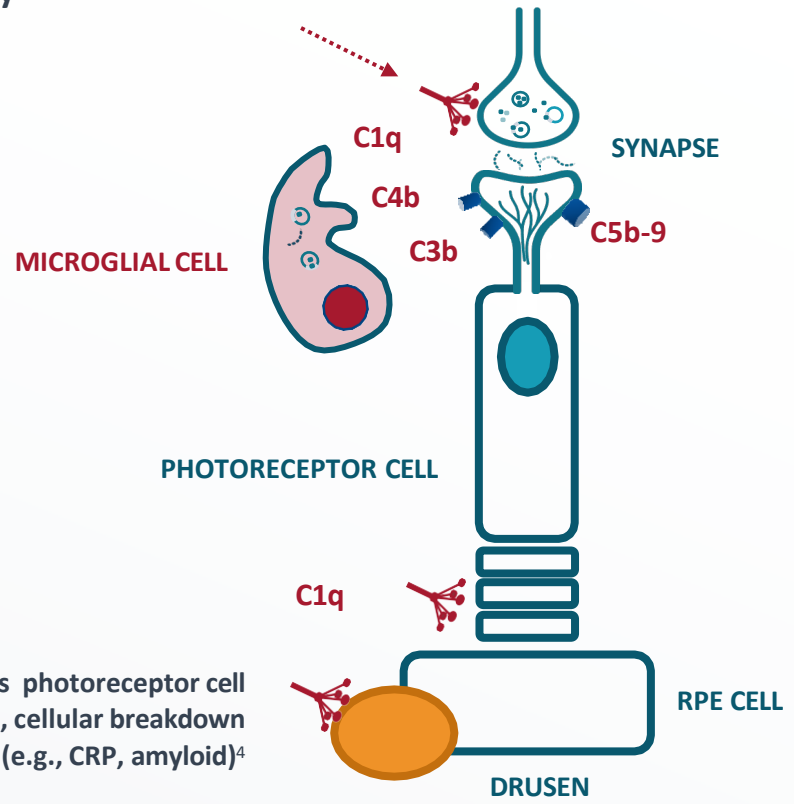
Anti-C1q: A Unique Neuroprotective Mechanism

C1q initiates classical complement cascade to drive photoreceptor synapse & cell loss and neuroinflammation

- C1q is a **key driver of neurodegeneration**[1]
- C1q anchors classical pathway activation on **photoreceptor cells to cause inflammation and loss**[2]
- **ANX007 inhibits C1q** and all damaging components of the classical pathway[3]



C1q binds stressed photoreceptor synapses and activates the classical pathway



In GA, **C1q** also binds photoreceptor cell outer segments, cellular breakdown products and drusen (e.g., CRP, amyloid)[4]

[1]Stevens, 2007, *Cell* **131**:1164; Howell, et al., 2011 *J Clin Invest*. **121**:1429; Schafer, et al., 2012 *Neuron* **74**: 691; Stephan et al., 2012 *Annu Rev Neurosci* **35**:369; Hong, et al., 2016 *Science*. **352**:712; Lui, et al., 2016 *Cell* **165**:921; Dejanovic, et al., 2018 *Neuron* **100**:1322; Vukojicic , et al., 2019, *Cell Rep.* **29**:3087; Williams, et al., 2016 *Mol Neurodegener* **11**:26; [2]Tassoni, et al., SFN 2022; Annexon data on file; Jiao, et al., 2018 *Mol Neurodegener* **13**:45; Katschke, 2018 Sci Rep. **8**:7348. [3]Lansita, et al., 2017 *International Journal of Toxicology*, **36**:449; [4]Yednock, et al., 2022 *Int J Retina Vitreous* **8**:79

Photoreceptor Cells, Synapses & Function Are Lost Prior to RPE in GA

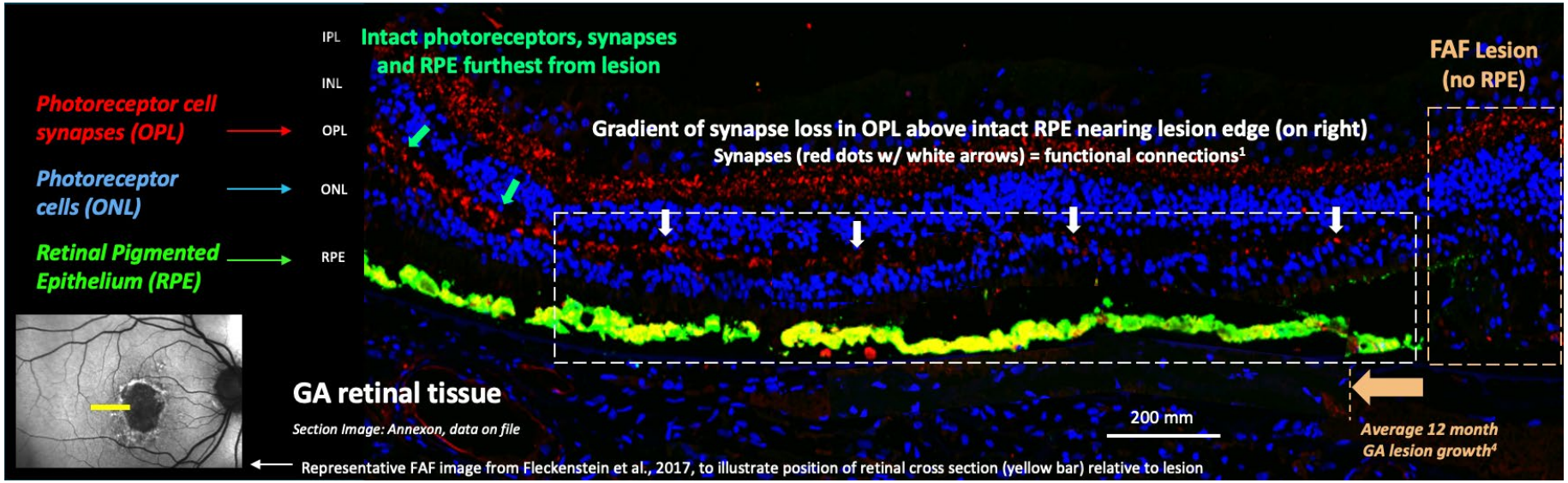
Blocking C1q protects photoreceptor cells and function upstream of RPE loss

Healthy Human Retina (top)

- Uniform layer of photoreceptor synapses (red) and photoreceptor neurons (blue)

GA Patient Retina (Bottom)

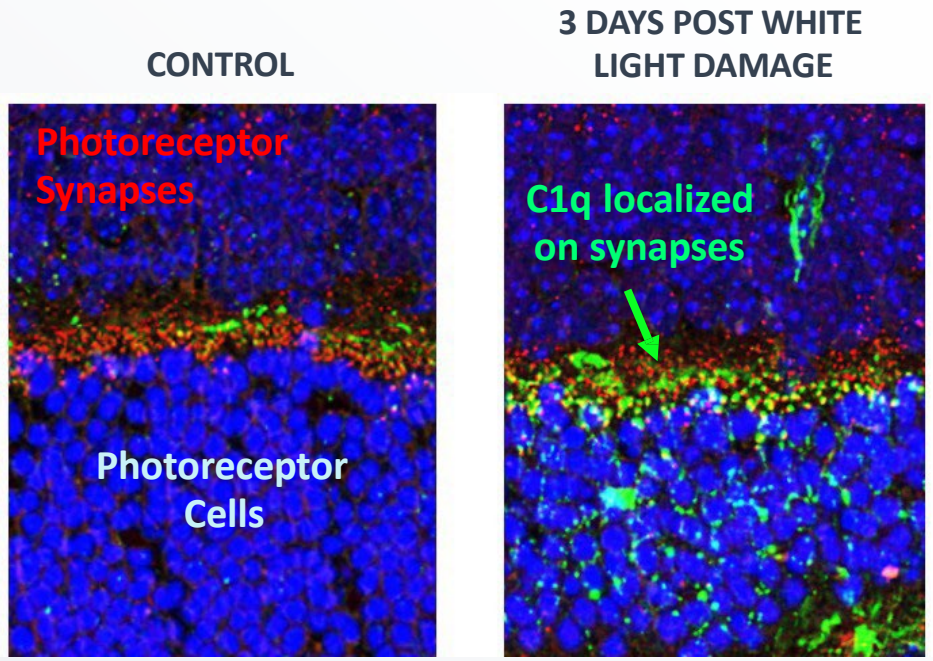
- Decreasing gradient of synapses and neurons (within white box) moving right toward lesion
- Photoreceptors are lost prior to RPE[1]
- Loss of synapses is loss of function[2]
- FAF lesion growth tracks RPE loss, not photoreceptors, and correlates poorly w/ visual function[3]



[1]Bird et al., 2014 *JAMA Ophthalmol* doi:10.1001/jamaophthalmol.2013.5799; Li, et al., 2018 *Retina* 38:1937; Pfau, et al., 2020 10.1001/jamaophthalmol.2020.2914; Sarks, et al., 1988 *Eye* 2:552; [2]Selkoe, 2002 doi: 10.1126/science.1074069; Burger, et al., doi.org/10.1016/j.ydbio.2021.04.001; [3]Heier, et al., 2020 Ophthalmology Retina **4**:673;

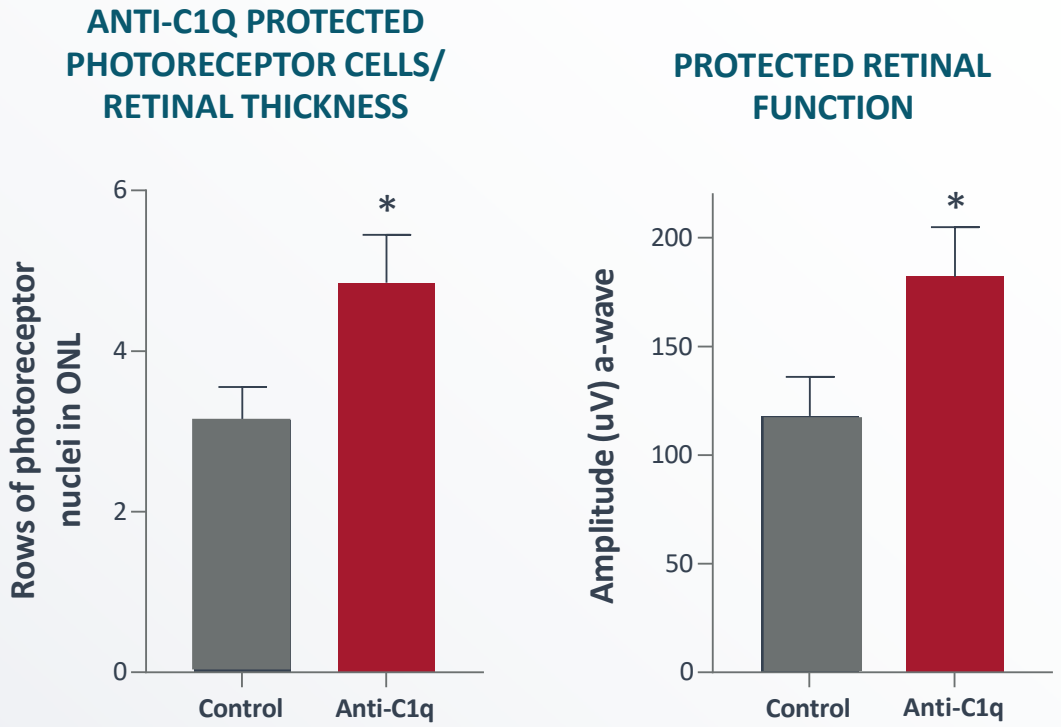
Anti-C1q Protected Photoreceptor Cells and Their Function in Models of Photoreceptor Damage

C1q Deposition on Photoreceptor Cells and Synapses with Light-Induced Damage



Annexon data on file

Anti-C1q Protected Photoreceptors and Function



Jiao, et al., 2018 *Mol Neurodegener* 13(1):45

ANX007: Differentiated Inhibitor of C1q and Classical Complement to Treat GA

Design

- Constant region framework modeled after established IVT Fab antibodies

Profile

- 50kD Fab antibody
- **Low viscosity/non-pegylated**
- <10 pM potency formulated for intravitreal administration

Dosing

- 5 mg/100 microliter
- PK in patient aqueous humor supports monthly/every other month dosing

Specificity

- **Full target engagement/inhibition of classical complement pathway**
- Lectin and alternative pathways in place for immune and homeostatic functions

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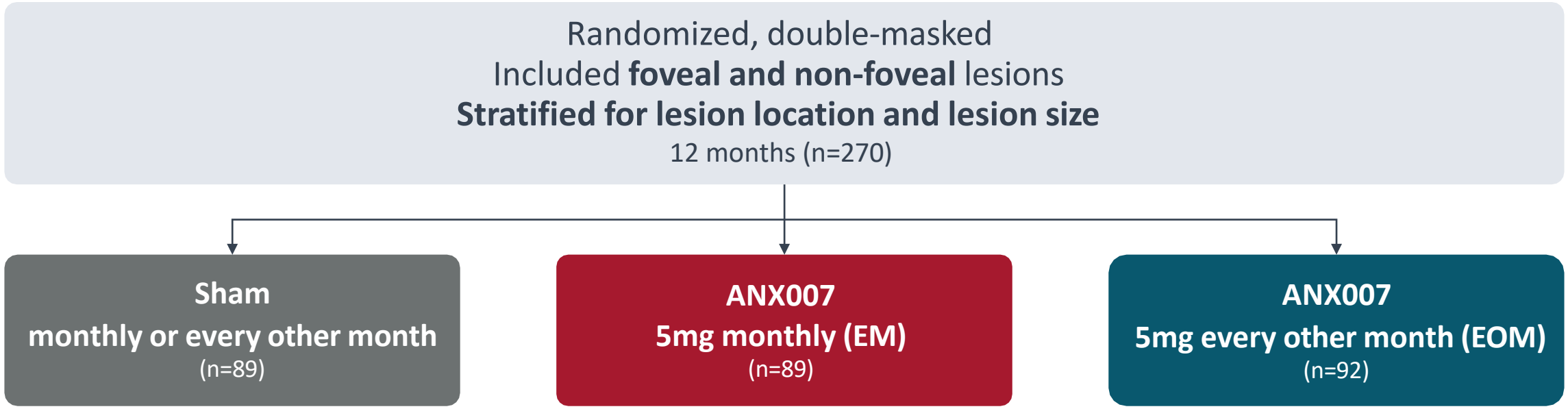
ARCHER: Phase 2 Trial ANX007 in GA



PRIMARY BIOMARKER ENDPOINT

Change in GA lesion area as assessed by fundus autofluorescence at Month 12

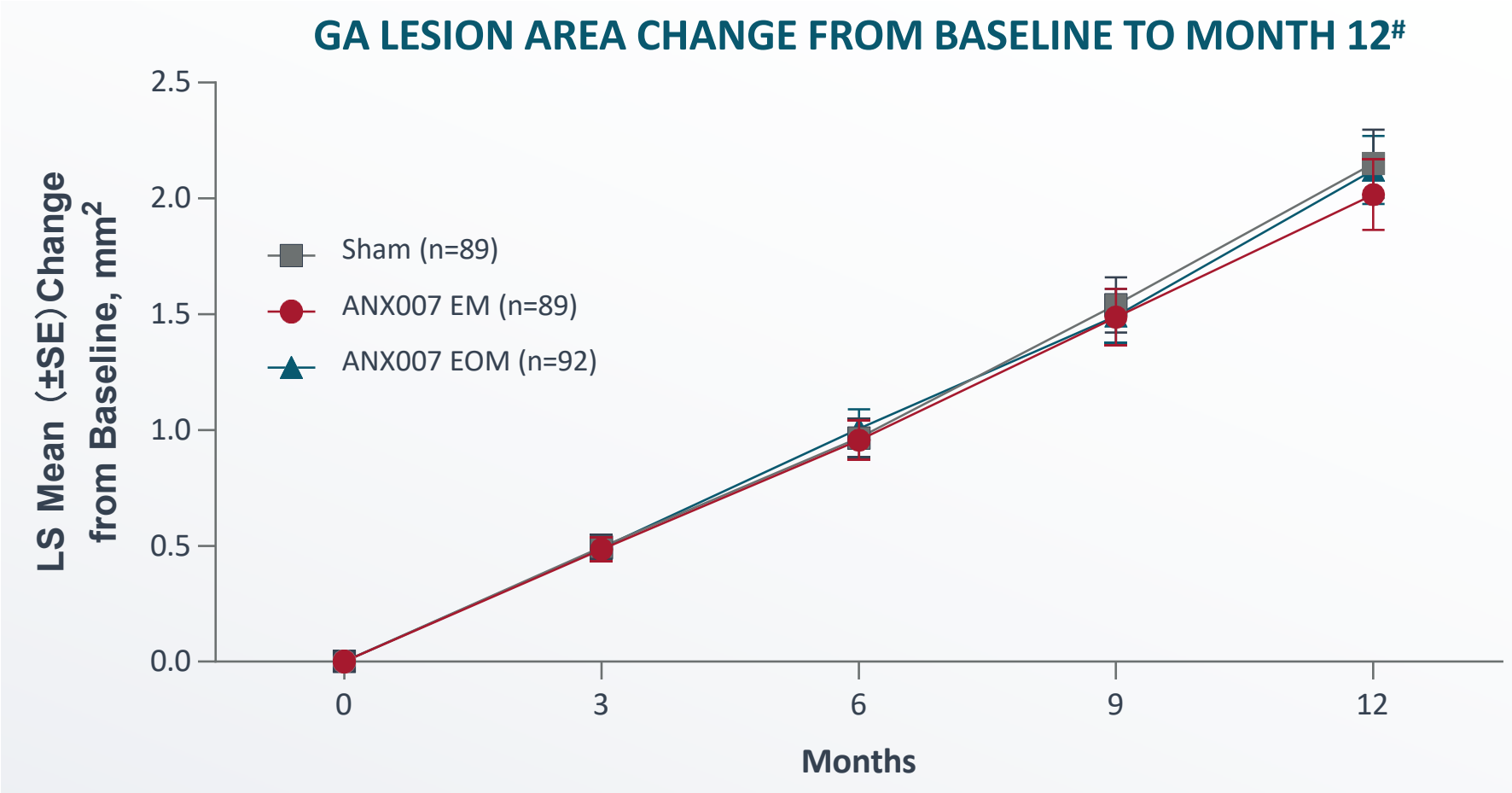
PRESPECIFIED SECONDARY FUNCTIONAL ENDPOINTS

Best Corrected Visual Acuity (BCVA)
Low Luminance Visual Acuity (LLVA) & Deficit (LLVD)

Off-treatment
(6 months)

END OF STUDY
Month 18

ANX007 Did Not Significantly Reduce Lesion Area, a Surrogate Biomarker of Functional Change in GA



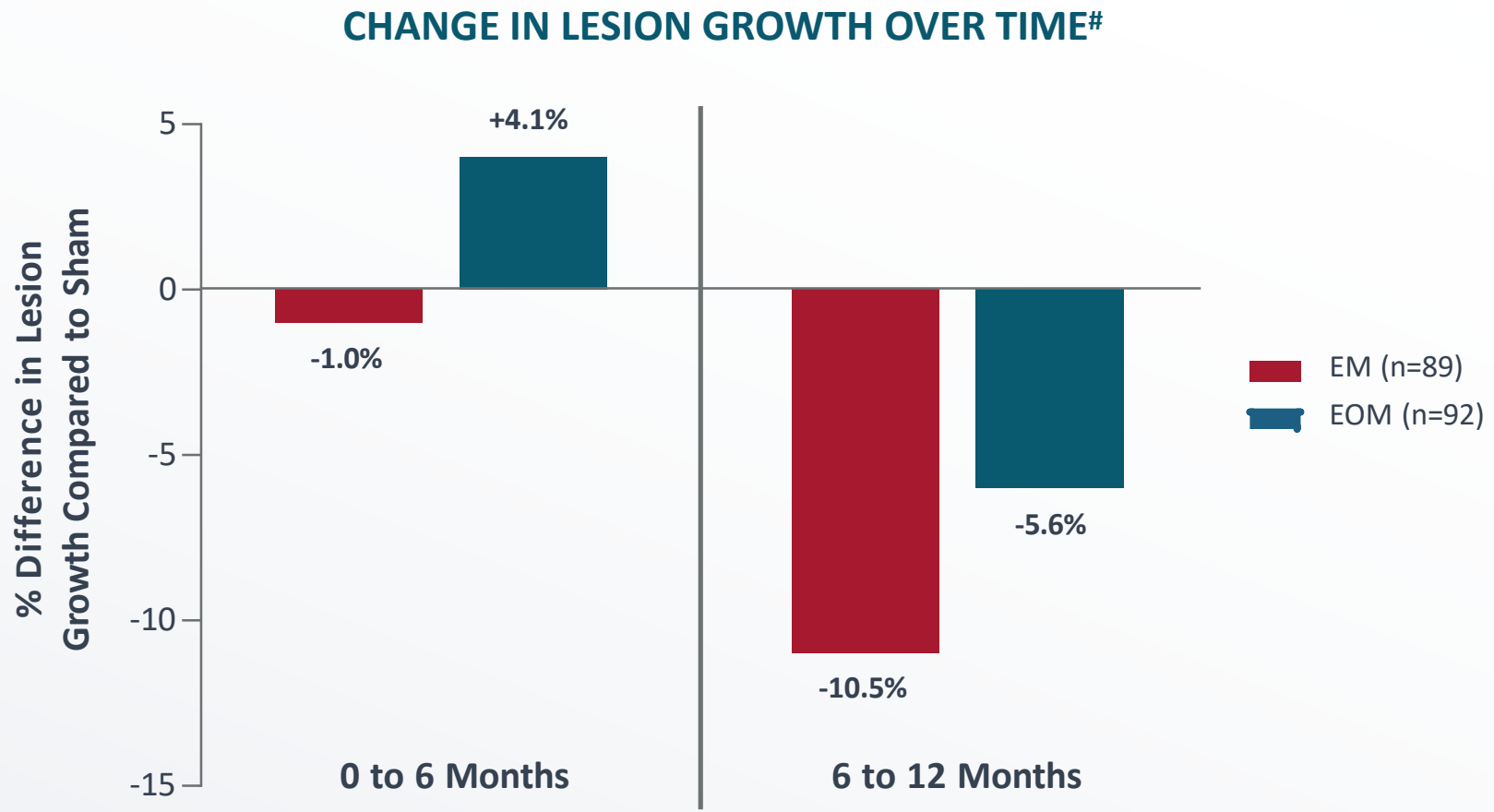
GA Area Change from Baseline at 12 Months

Arm	mm²	%	p-value
Sham	2.15	---	---
EM^	2.02	-6.2%	0.526
EOM^	2.12	-1.3%	0.896

^2-arm MMRM model

#The least-square (LS) mean, its standard error (SE), and p-value are based on a mixed-effect model for repeated measures (MMRM) adjusting for baseline lesion location, lesion focality, baseline GA lesion, and the baseline GA lesion by visit interaction.

ANX007 Effect on Lesion Growth Improves with Longer Treatment



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Increasing ANX007 Impact Over Time

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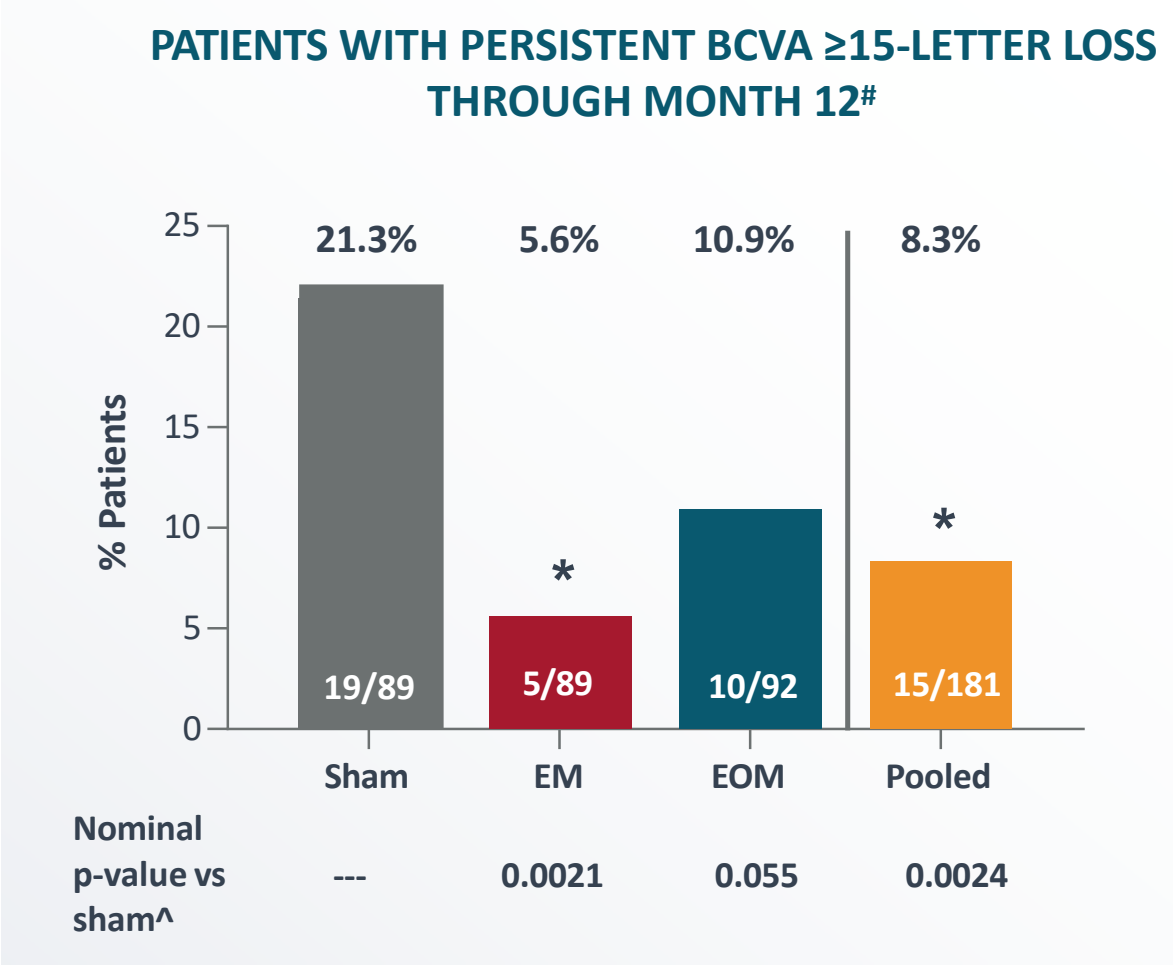
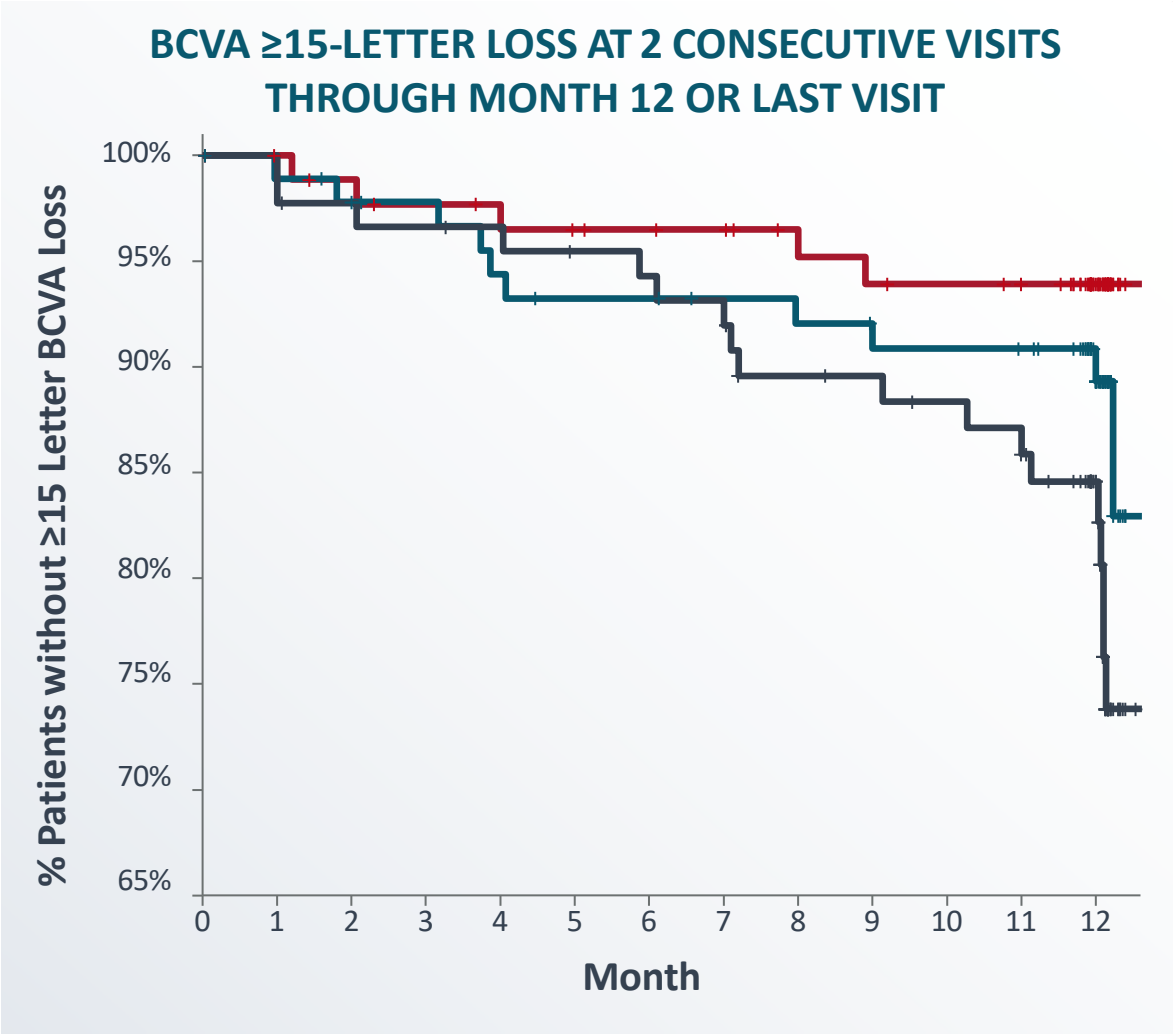
ANX007 Demonstrated Statistically Significant Protection From Vision Loss as Measured by BCVA ≥15-Letter Loss



#Persistent for two consecutive visits through month 12 or at last visit
^Nominal p-value from a Chi-square test in ITT population
** Nominal P < 0.05*

- First known significant preservation of vision in GA
- Dose-dependent response informative
- BCVA ≥15-letter loss universally deemed clinically meaningful

Significant, Time-Dependent Protection From ≥15 Letter Vision Loss with ANX007 Monthly Treatment



EM (n=89)

72% Risk Reduction ANX007 EM

HR (CI) = 0.28 (0.11 to 0.76)

p = 0.006

EOM (n=92)

48% Risk Reduction ANX007 EOM

HR (CI) = 0.52 (0.24 to 1.13)

p = 0.064

Sham (n=89)

Sensitivity analysis confirmed treatment effect:

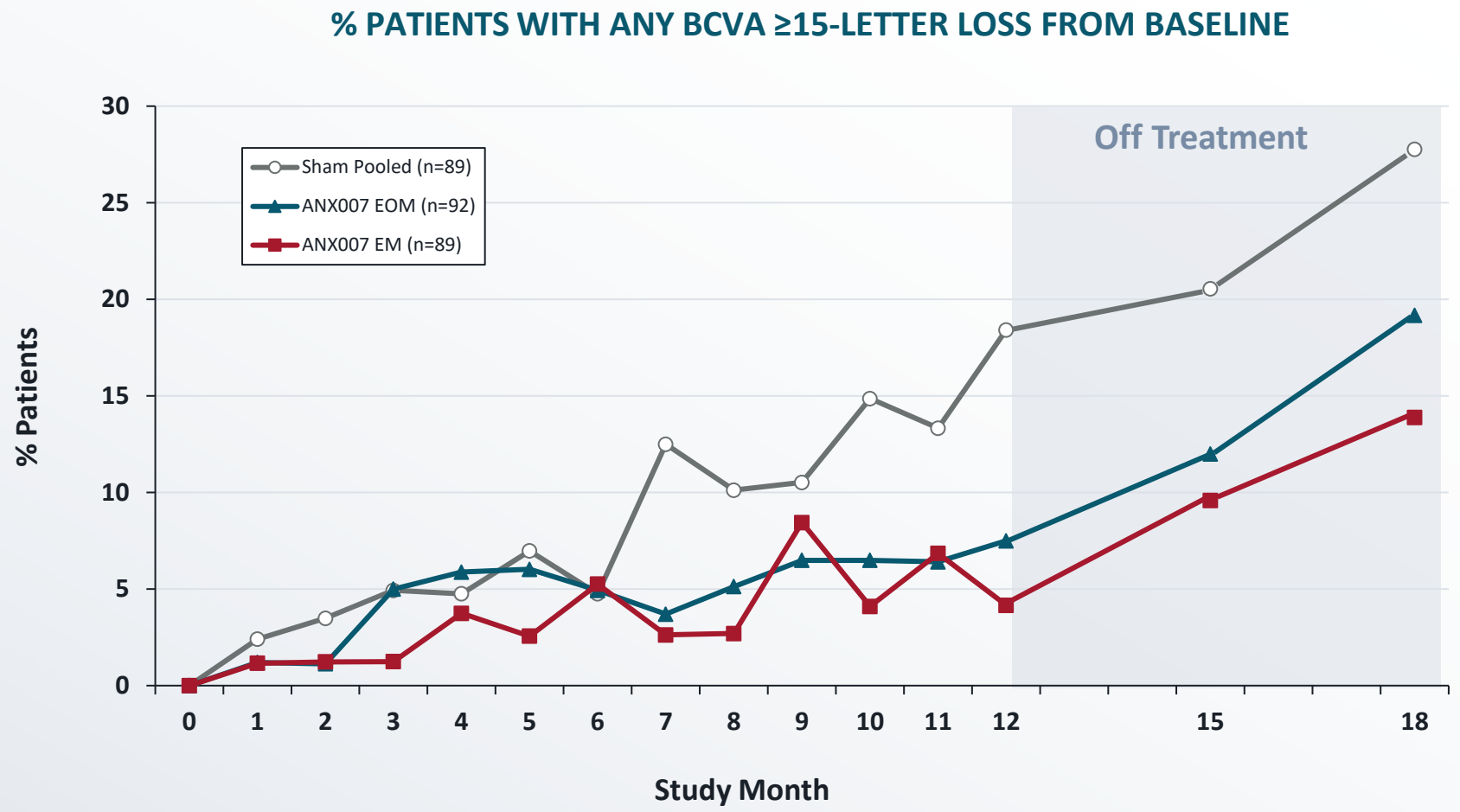
Significant 66% reduction in risk in EM group when excluding patients with vision loss only at month 12

HR, hazard ratio; Nominal log-rank test (versus Sham) p-values are presented

Increasing ANX007 Impact Over Time

BCVA ≥15-Letter Loss Accelerates After Cessation of Treatment

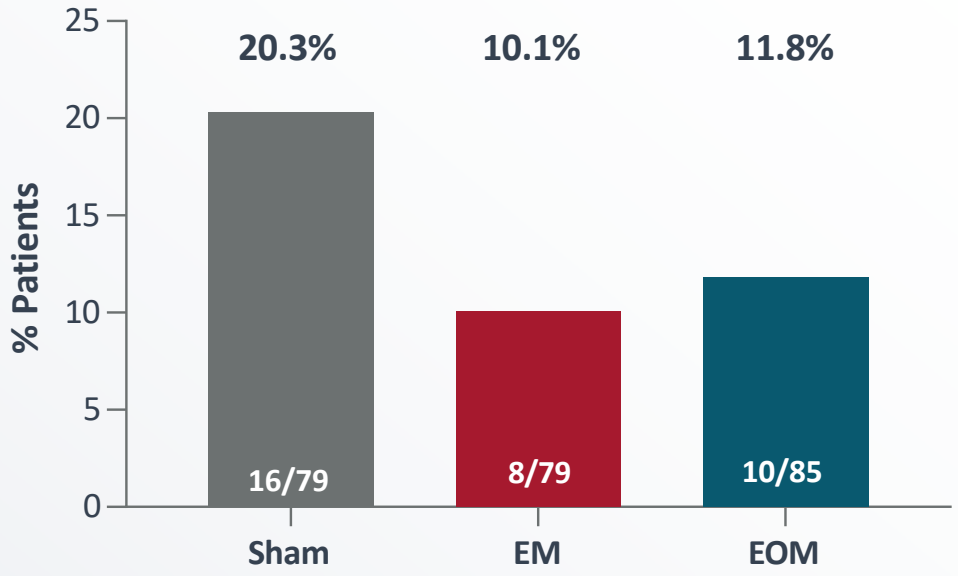
Visual Function Loss Parallels Sham in Off-Treatment Period



- Low frequency (<10% per timepoint) of single BCVA ≥15-letter losses in EM- and EOM-treated groups during 12-month treatment period
- BCVA ≥15-letter loss frequency increased (10% or greater) in off-treatment period for EM and EOM groups, paralleling sham behavior

Prespecified Secondary Analyses: ANX007 Provided Consistent Protection from Vision Loss on Additional Measures—LLVA & LLVD

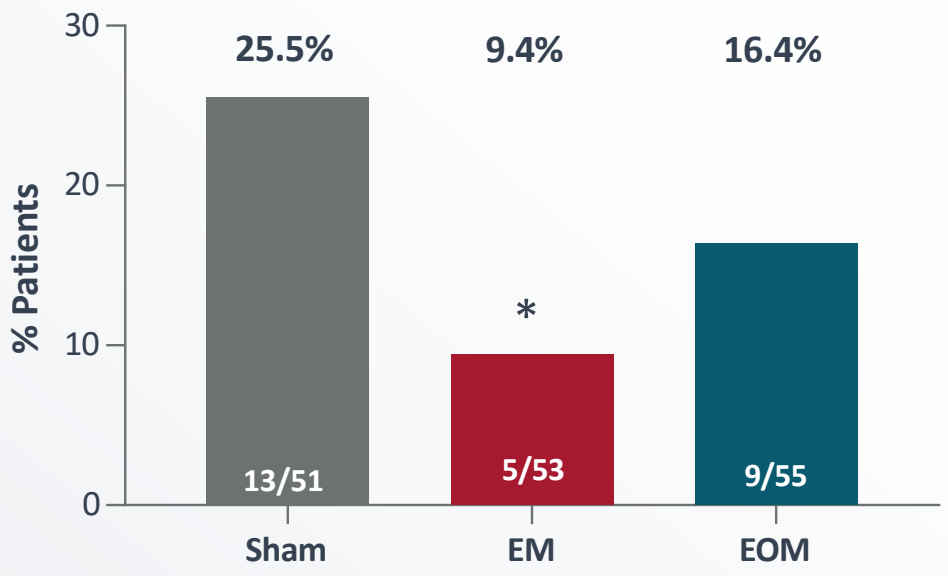
LLVA ≥15-LETTER LOSS THROUGH MONTH 12#



	Sham	EM	EOM
Nominal p-value vs Sham^	--	0.076	0.14

#Patients with at least one post baseline LLVA measurement
^Nominal p-value from a Chi-square test

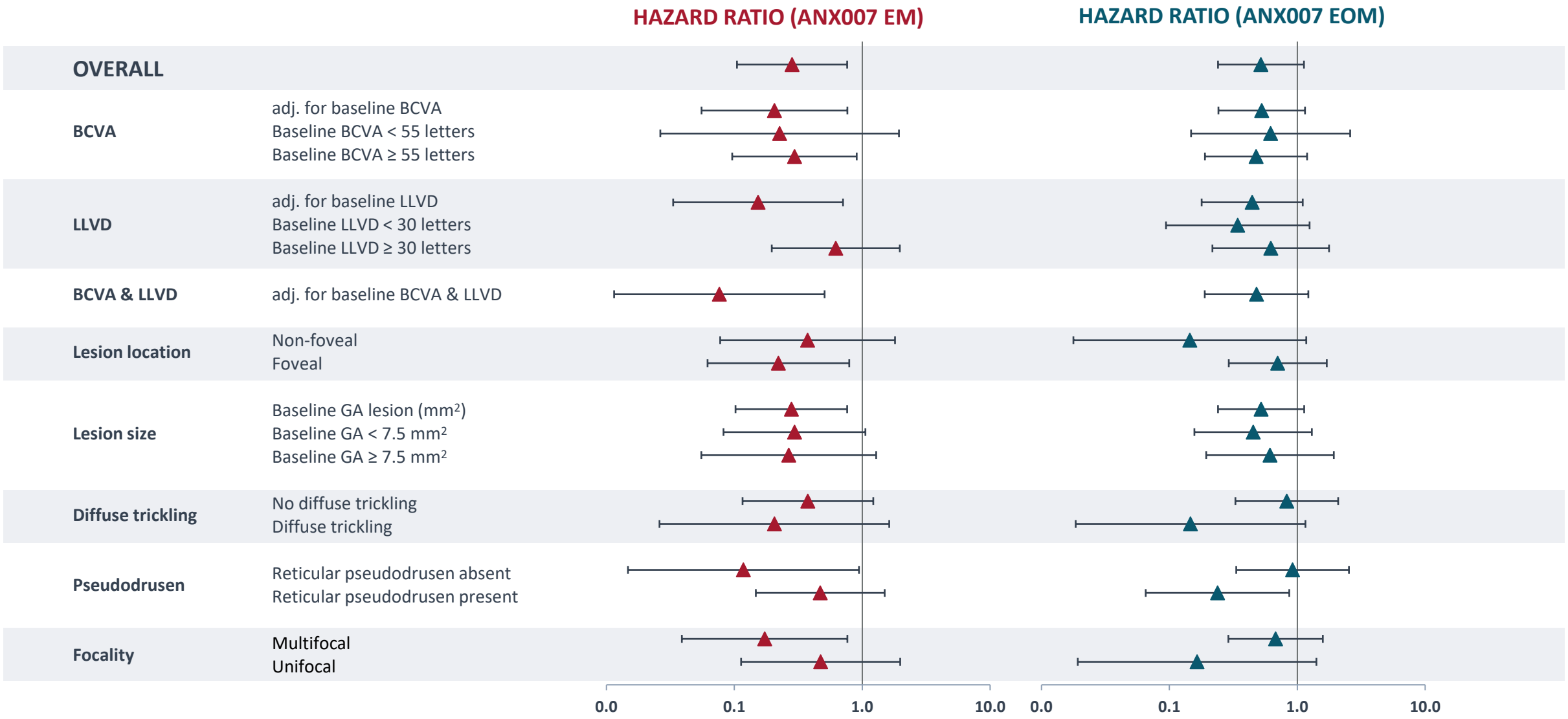
LLVD ≥15-LETTER WORSENING THROUGH MONTH 12#



	Sham	EM	EOM
Nominal p-value vs sham^	--	0.0305	0.2470

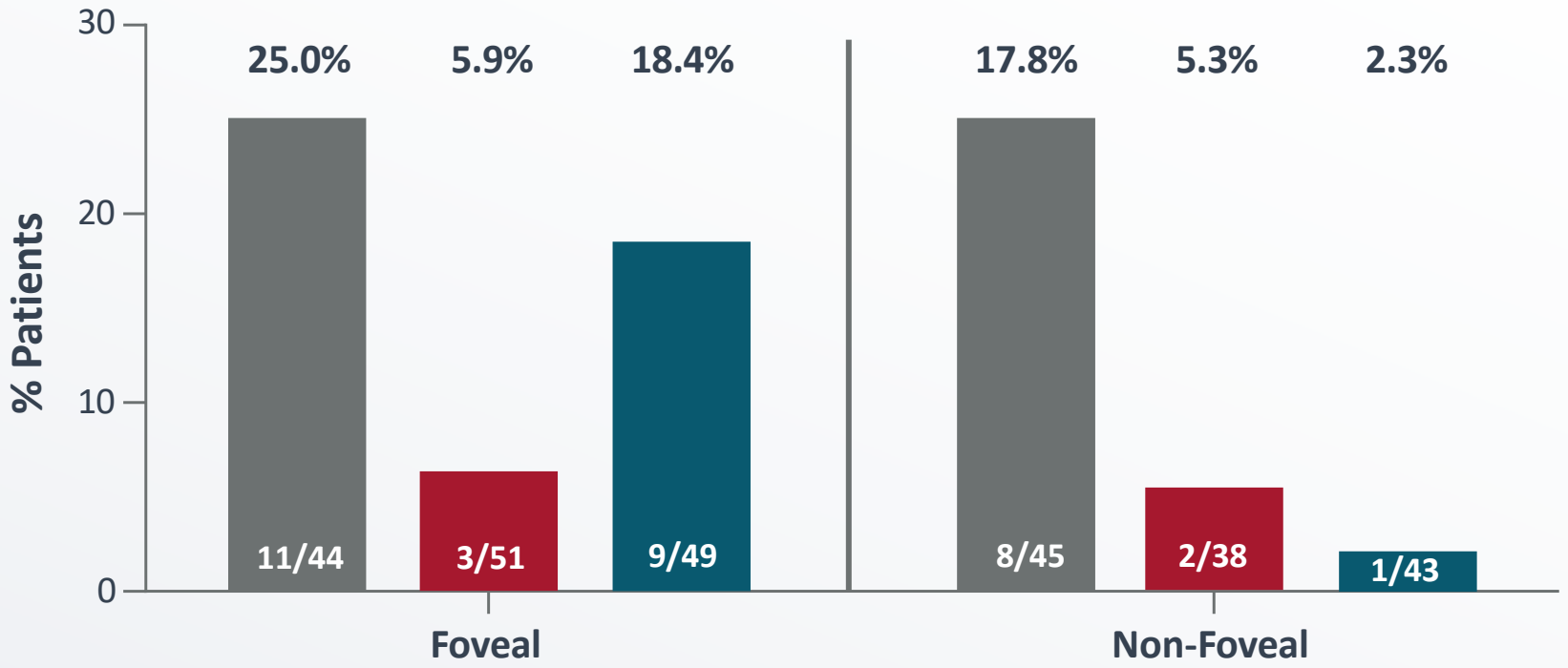
#In subjects with BCVA ≥55
^Nominal p-value from a Chi Square test
*p<0.05

ANX007 Protection from Vision Loss Consistent Across Baseline Characteristics



*persistent for two consecutive visits through month 12 or at last visit; Hazard ratios are from Cox regressions accounting for event time and censorship
NOTE: Hazard ratio not estimated for ANX007 EM vs Sham with baseline LLVD < 30 due to zero (0) event in ANX007 EM group for the subgroup.

ANX007 BCVA Subgroup Analysis: Protection from Vision Loss in Foveal and Non-Foveal Patients



Nominal summary p-value vs. sham^

EM	0.0019
EOM	0.0439

#Persistent for two consecutive visits at any time through month 12 or at last visit
^Nominal p-value from a Cochran Mantel-Haenszel test (General Association) in ITT population

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ANX007 Generally Well-Tolerated

ADVERSE EVENTS OF SPECIAL INTEREST n (%)	SHAM (N=89)	ANX007 EM (N=89)	ANX007 EOM (N=92)
Choroidal Neovascularization	3 (3.4%)	4 (4.5%)	4 (4.3%)
Endophthalmitis	0	1 (1.1%)	2 (2.2%)
Retinal Vascular Occlusion	0	0	1^ (1.1%)
Retinal Vasculitis – No Cases Reported			
Intraocular Inflammation+	0	2 (2.2%)	1 (1.1%)
Ischemic Optic Neuropathy+ - No Cases Reported			

^Isolated cilioretinal artery occlusion; no vasculitis confirmed by DSMC and reading center
+Not AESI, included because of current interest

INTRAOCULAR INFLAMMATION DETAILS* n

Iritis – 1
Resolved with topical steroids in 2 days
No Vasculitis

Vitritis – 1
Resolved with topical steroids in 9 days
No Vasculitis

Vitreous Debris – 1
KP on endothelium, prior treatment with topical steroids
No Vasculitis

*Event Verbatim term listed

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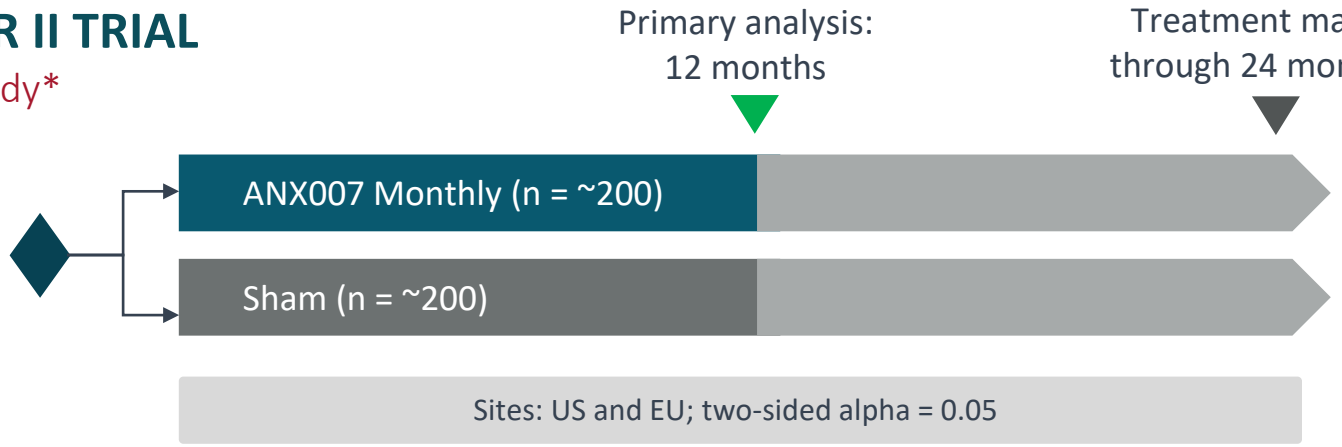
ANX007 Global GA Pivotal Program to begin Mid-2024

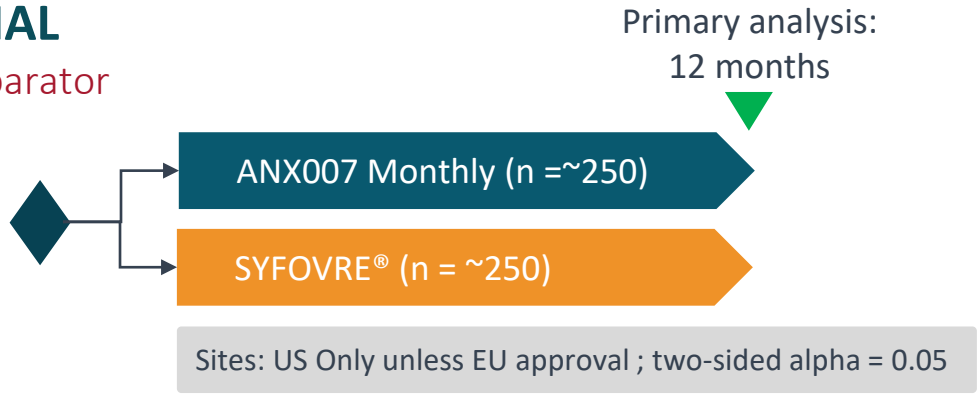
Replicate ARCHER and support global approvals

PRIME Designation from EMA

ARCHER II TRIAL
Sham Study*



ARROW TRIAL
Injection Comparator



Primary Endpoint

Persistent ≥15-Letter BCVA Loss through 12 months, or accumulation of appropriate number of events – Aligned with FDA

Key Secondary Endpoints

Safety, Low Luminance VA (LLVA), Low Luminance Visual Deficit (LLVD)

*ARCHER n=270 GA patients. **24 months total treatment per regulatory direction

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