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ANX007: Preserving Vision through C1q Inhibition

Disruptive Innovations Symposia
Hawaiian Eye 2024
Lori Taylor, PhD

January 15, 2024

Forward-Looking Statements

This presentation contains “forward-looking” statements about Annexon, Inc. and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts, including statements regarding our clinical and preclinical programs, timing and commencement of future nonclinical studies and clinical trials and research and development programs, timing of clinical results, strategic plans for our business and product candidates, including additional indications which we may pursue, our financial position, runway and anticipated milestones, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “design,” “due,” “estimate,” “expect,” “focus,” “goal,” “intend,” “may,” “objective,” “plan,” “positioned,” “potential,” “predict,” “seek,” “should,” “target,” “will,” “would” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology.

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Overview: ARCHER Phase 2 Trial in Geographic Atrophy

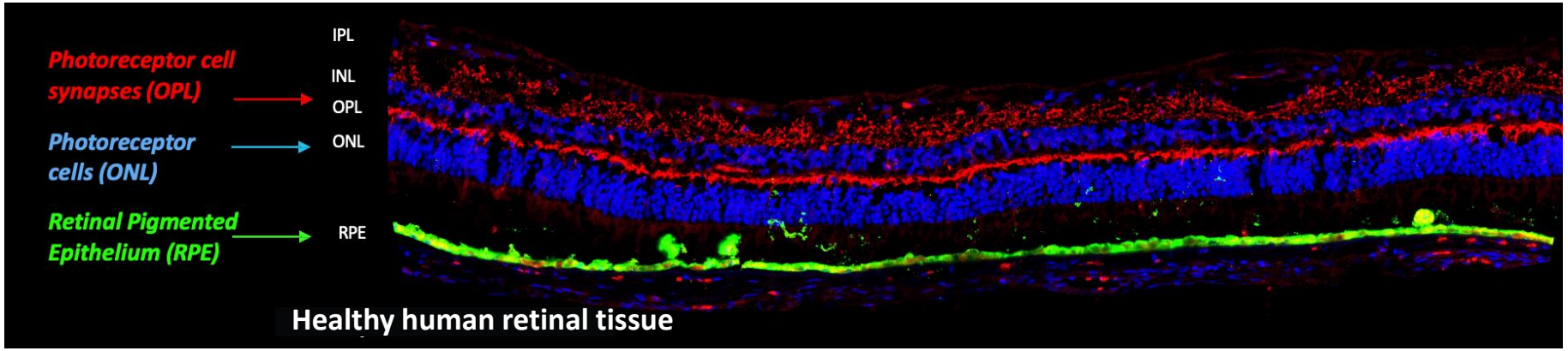
Pioneering upstream classical complement trial with demonstrated functional benefit

- ✓ Unique MOA **targeting classical complement inflammation where it starts**
- ✓ Preclinical classical complement inhibition **protected photoreceptor cell loss and function**
- ✓ **ARCHER 1st clinical demonstration of significant, dose & time-dependent vision preservation**
- ✓ **Vision preservation supported by multiple lines of evidence**, including: 12 months on-treatment and off-treatment analyses, and regardless of lesion location
- ✓ Clinical **impact consistently improved over time** on FAF lesion and BCVA ≥15-letter loss measures
- ✓ **ANX007 1st and only EMA PRIME Designation in GA** – based on preclinical & ARCHER data set
- ✓ Initiating **global Phase 3 program** to confirm ARCHER findings

Retinal Tissue from Patients with Geographic Atrophy (GA) Show Loss of Photoreceptor Synapses Prior to Neuronal Loss

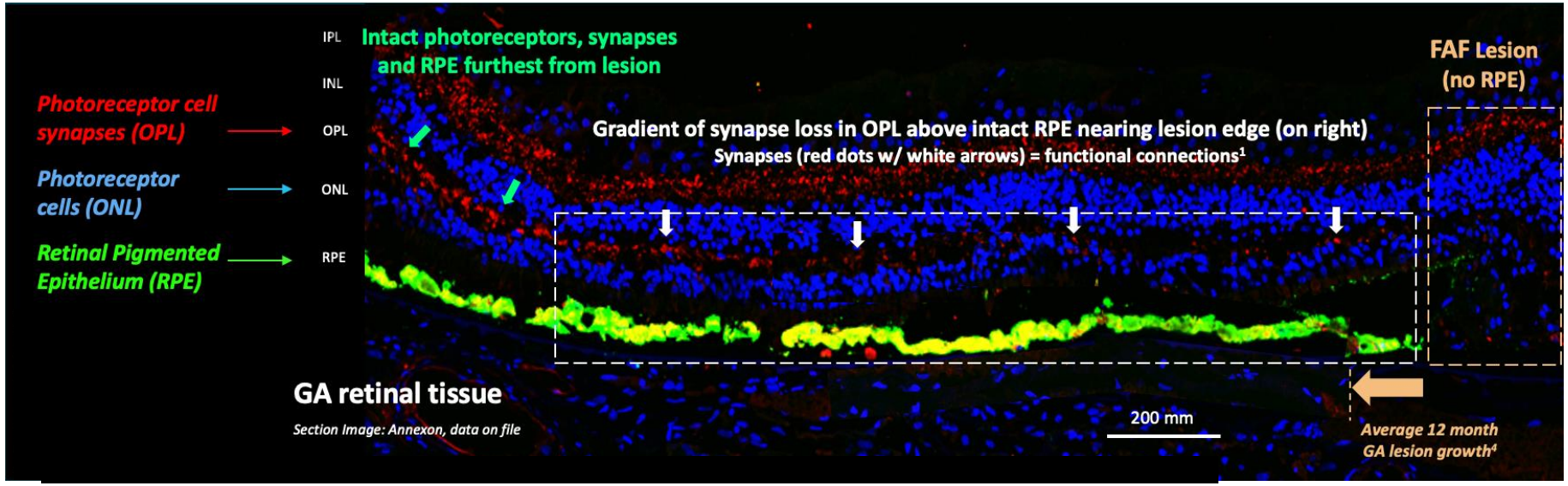
Healthy Human Retina (top)

- 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]



[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

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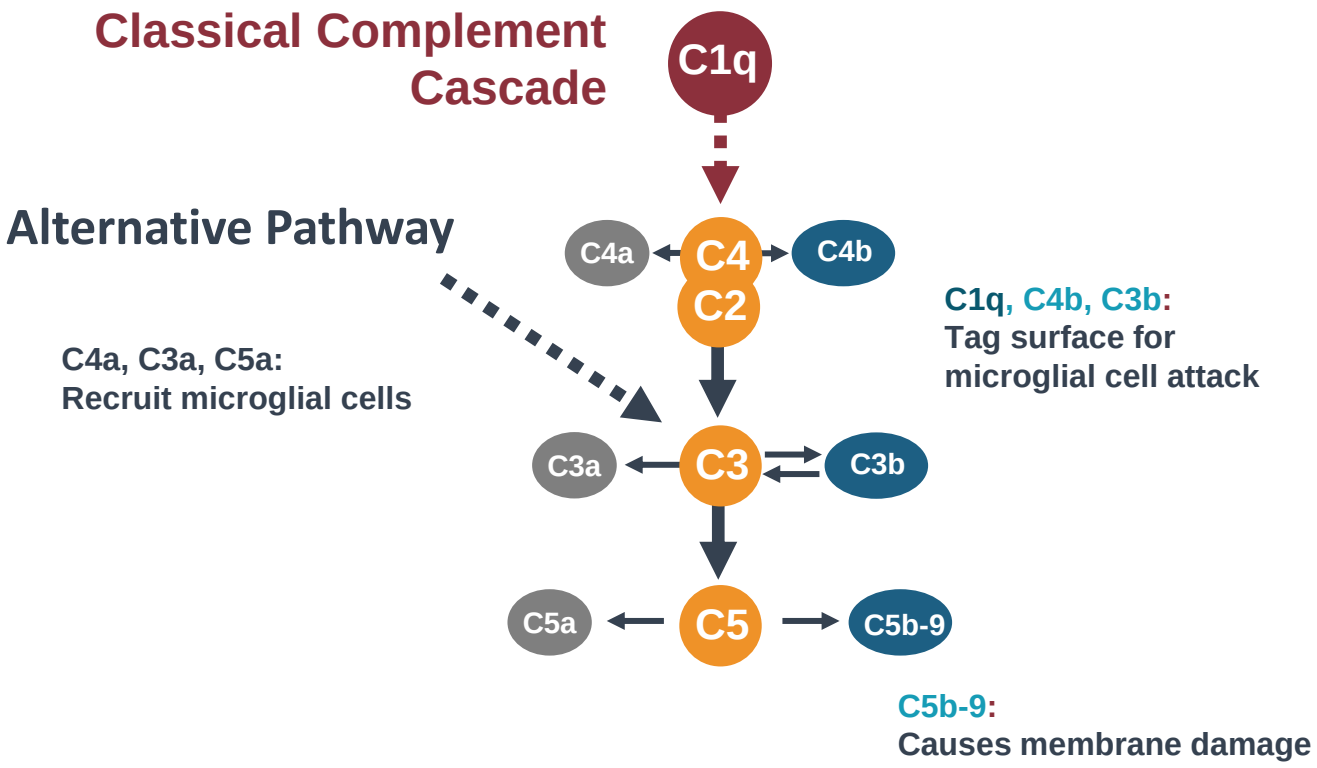
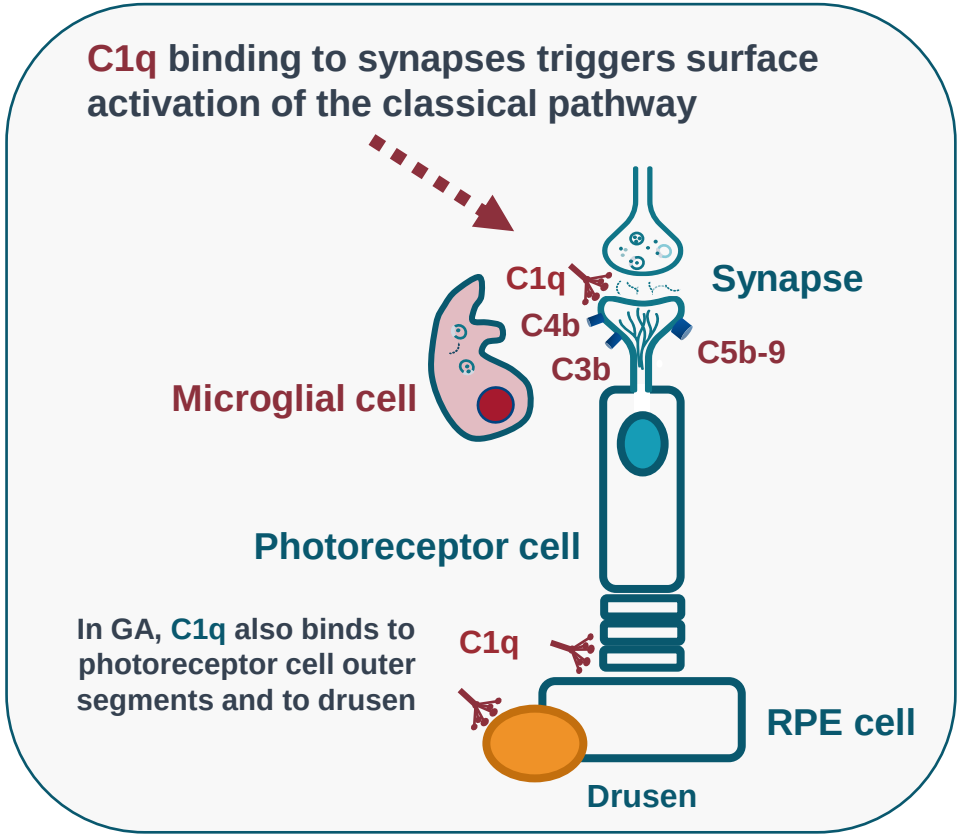
Targeting C1q and the Classical Complement Cascade for Neuroprotection is Distinct from Targeting C3 or C5

- Blocks C1q's ability to anchor classical complement activation to the synapse or photoreceptor cell surface
- Prevents C4b surface deposition, and subsequent C3 and / or C5 damage to the photoreceptor cell
- Leaves C3 and C5 activity in place for normal clearance and homeostatic functions via the lectin and alternative pathways





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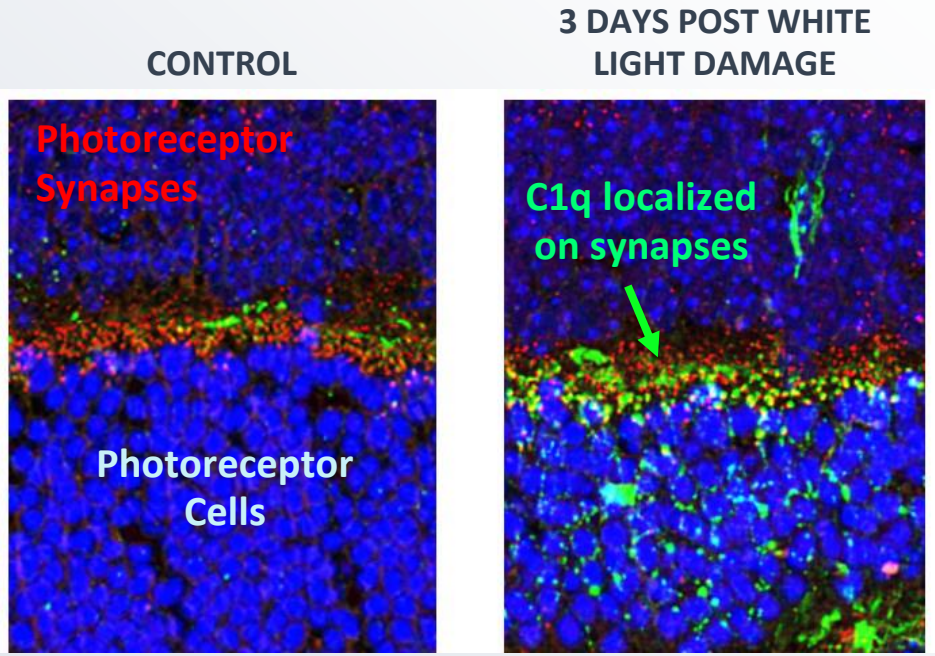
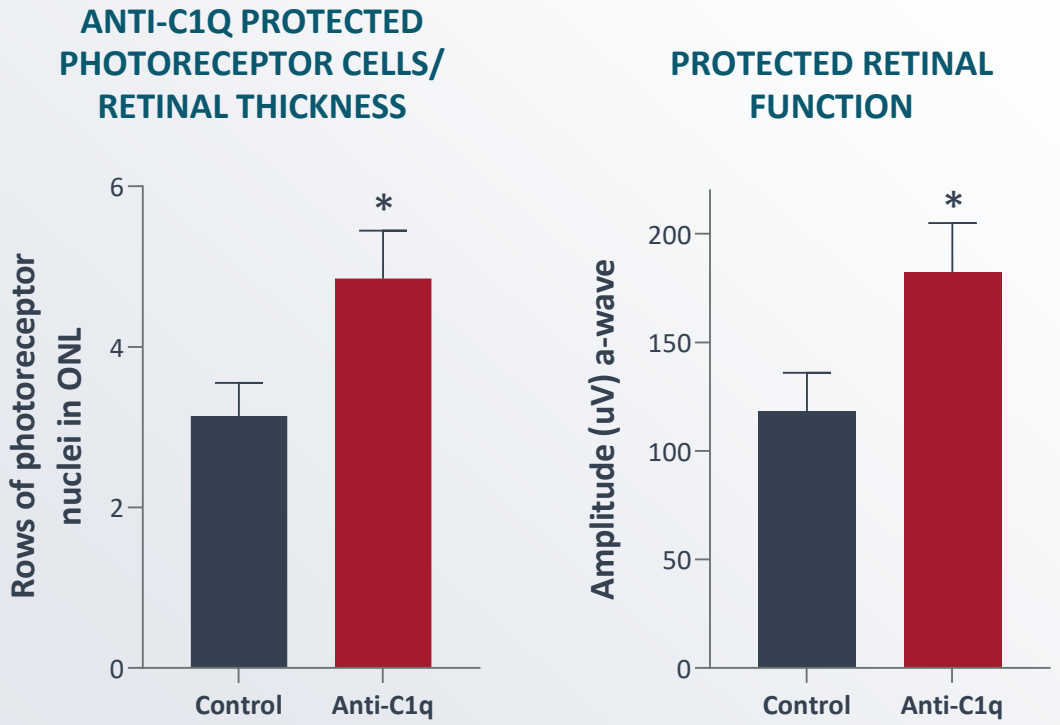
Anti-C1q Protected Photoreceptor Cells and Their Function in Models of Photoreceptor Damage

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 Geographic Atrophy

FDA Fast Track status and EMA PRIME Designation granted for ANX007

ANX007

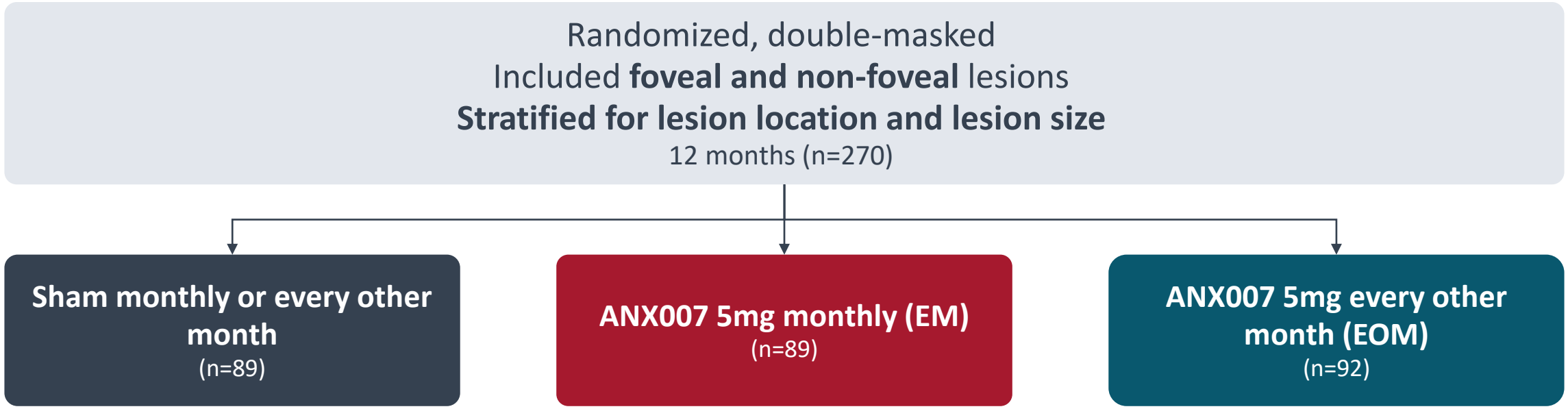
IVT administered antigen-binding fragment (Fab)

KEY ATTRIBUTES

- ✓ **Design:** Modeled after established IVT administered 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[1]

[1]Sun, et al., 2023 Ophthal Sci 3(2):100290

ARCHER: Phase 2 Trial of C1q Inhibitor ANX007 in GA Patients



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

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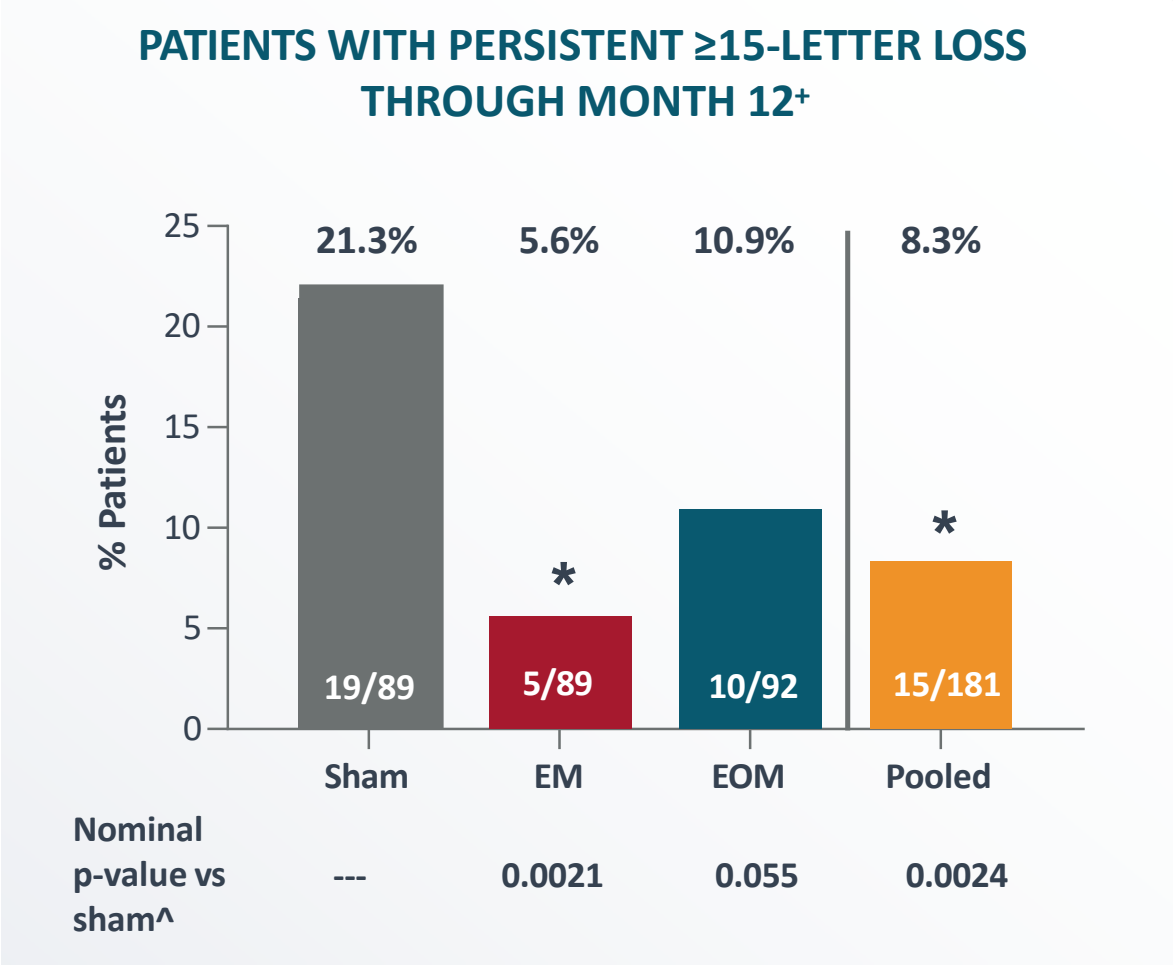
ANX007 Demonstrated Statistically Significant Protection From Vision Loss as Measured by BCVA ≥15-Letter Loss



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

+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*

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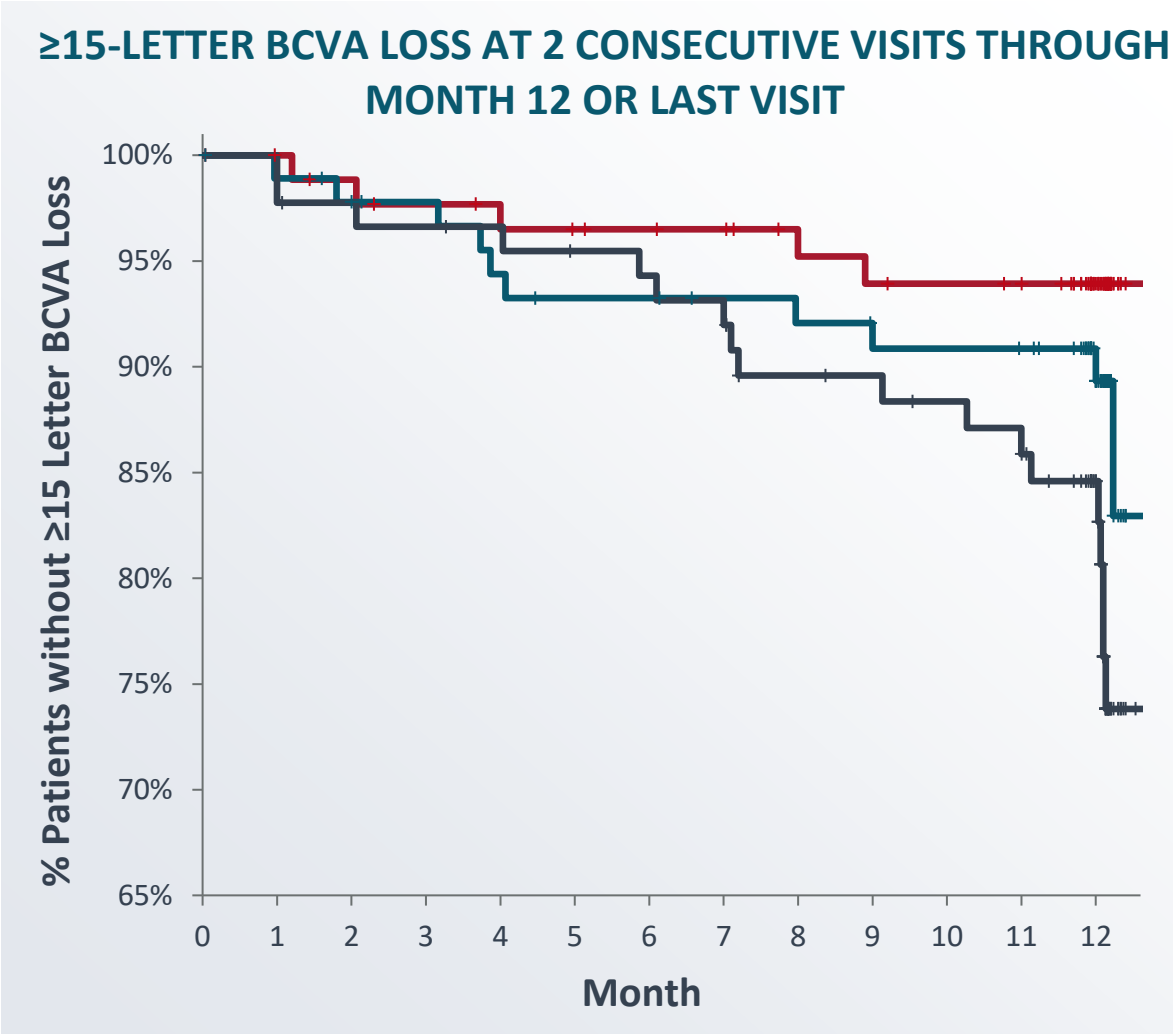
Significant, Time-Dependent Protection From BCVA ≥15-Letter Vision Loss with ANX007 Monthly Treatment



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)

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

Increasing ANX007 Impact Over Time

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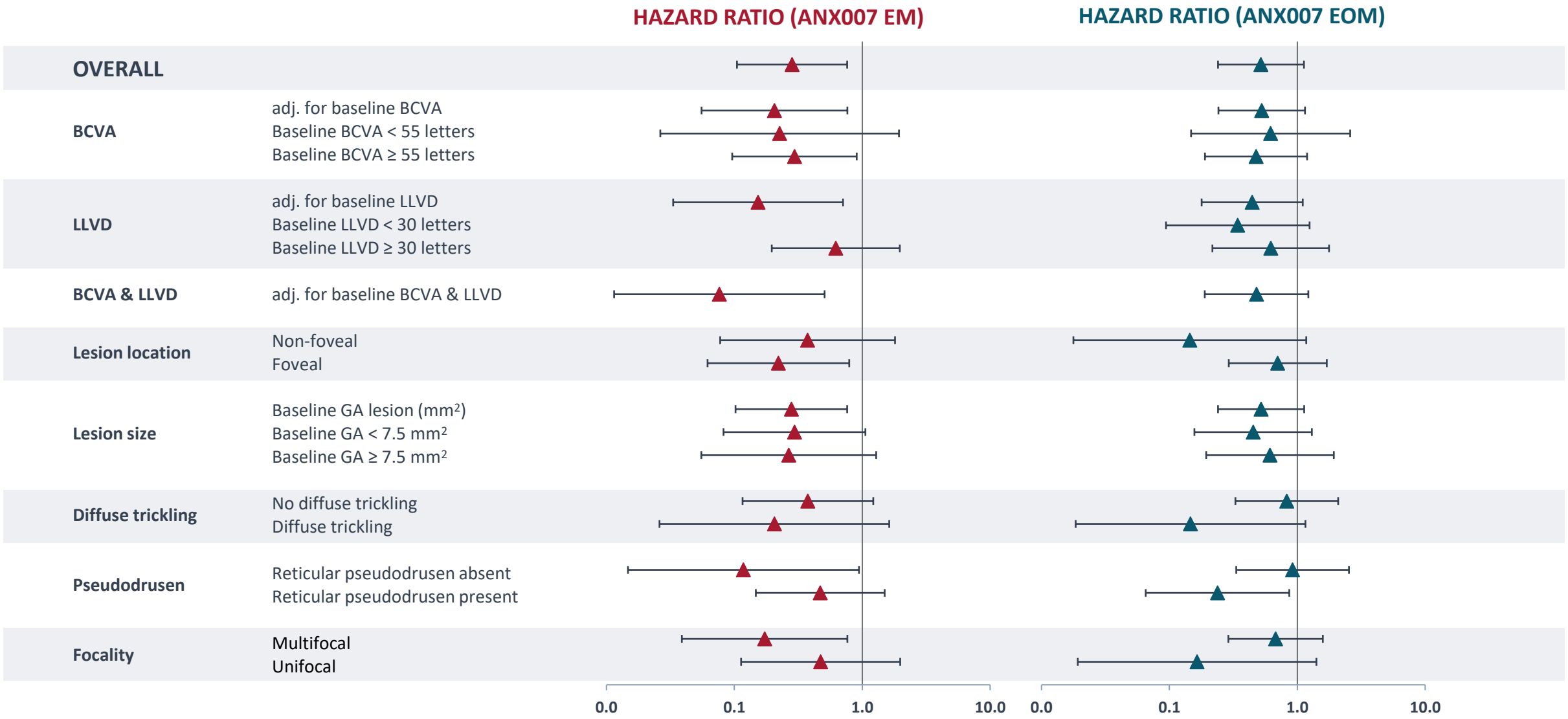
ANX007 Protection from Vision Loss Consistent Across Baseline Characteristics

NEW ANALYSIS



*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.

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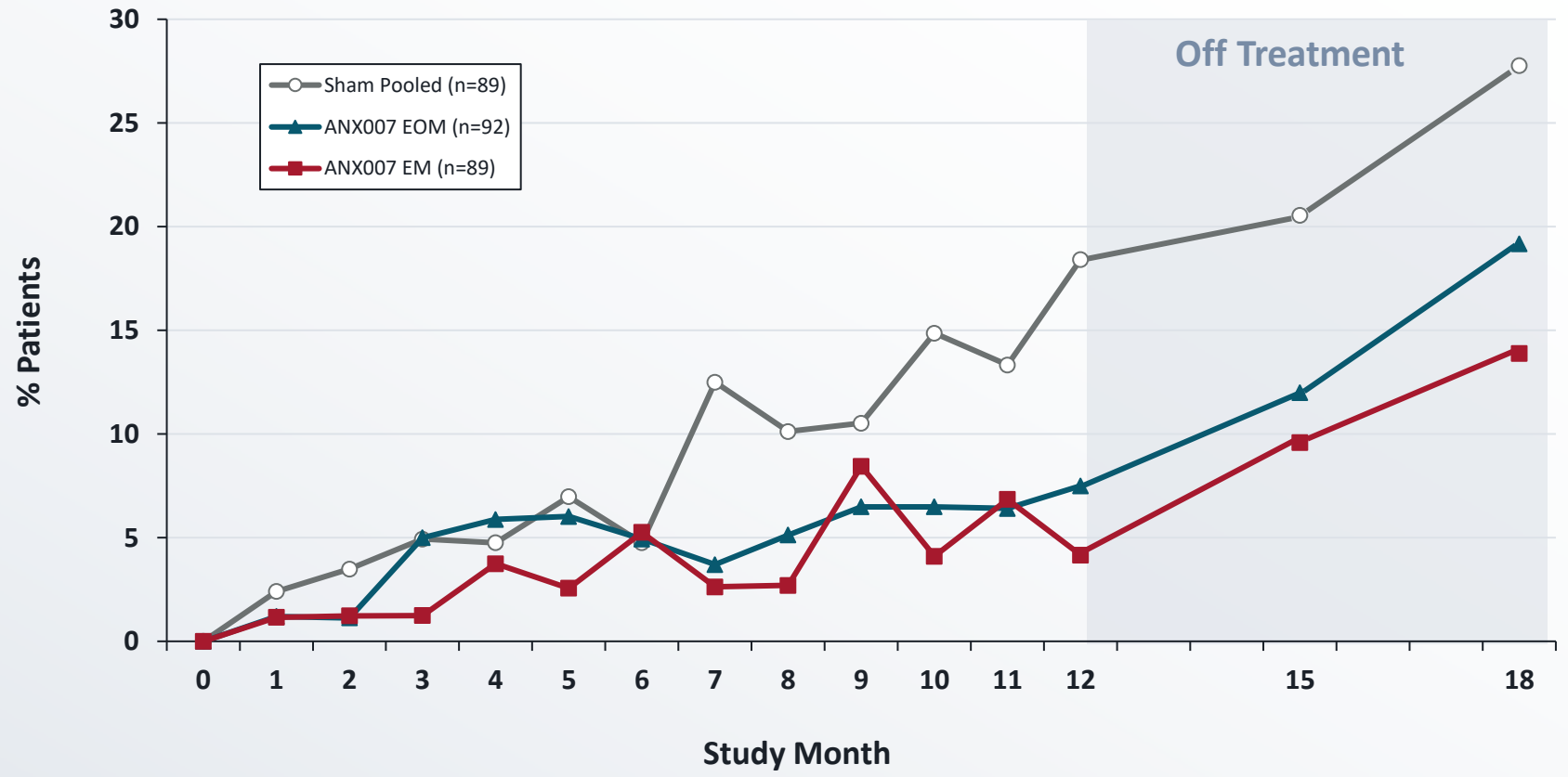
BCVA ≥15-Letter Loss Accelerates After Cessation of Treatment

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

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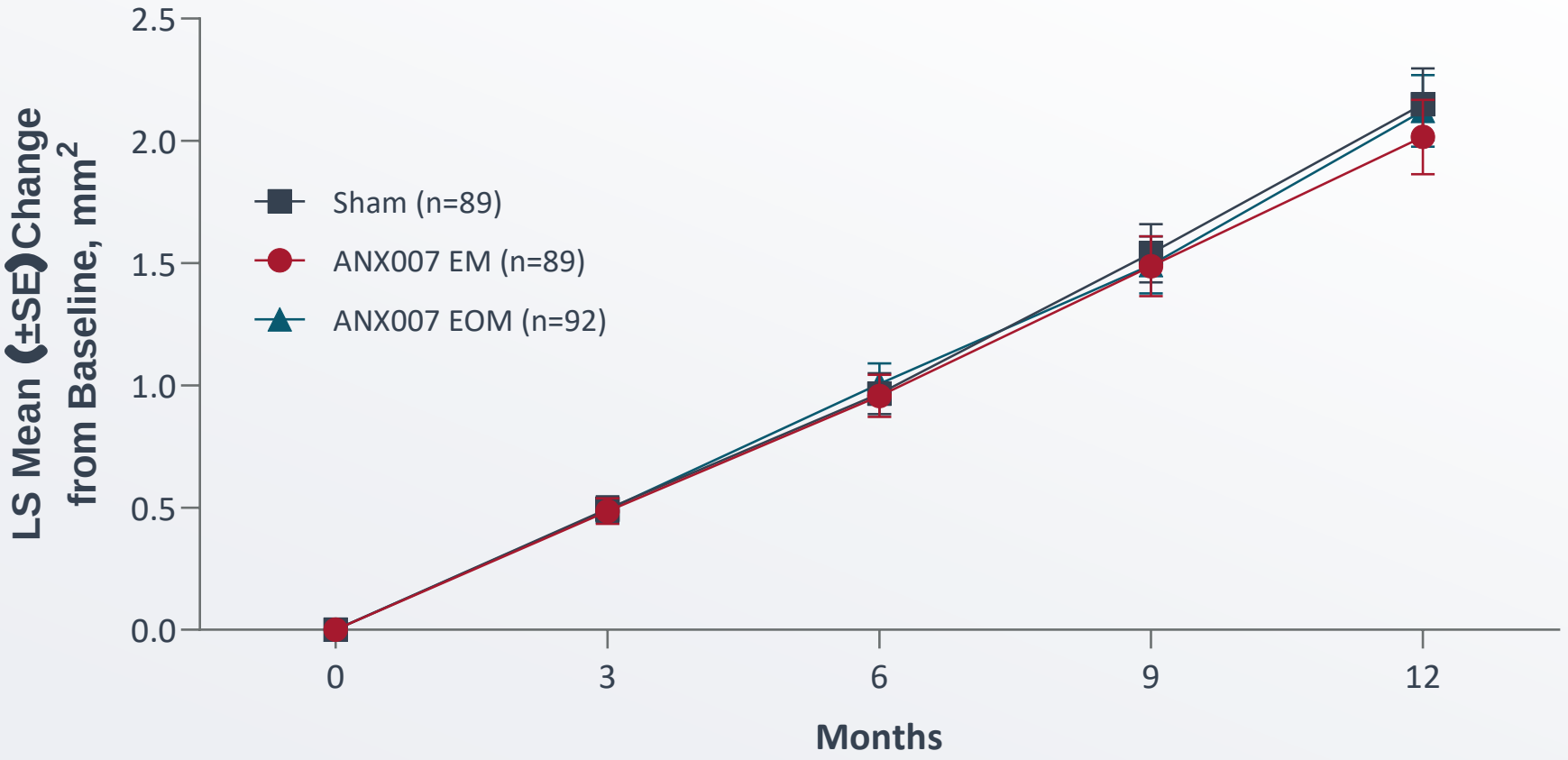
ANX007 Did Not Significantly Reduce Lesion Area, the Primary Endpoint and a Surrogate Biomarker for Vision Loss in GA

GA LESION AREA CHANGE FROM BASELINE TO MONTH 12⁺



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.

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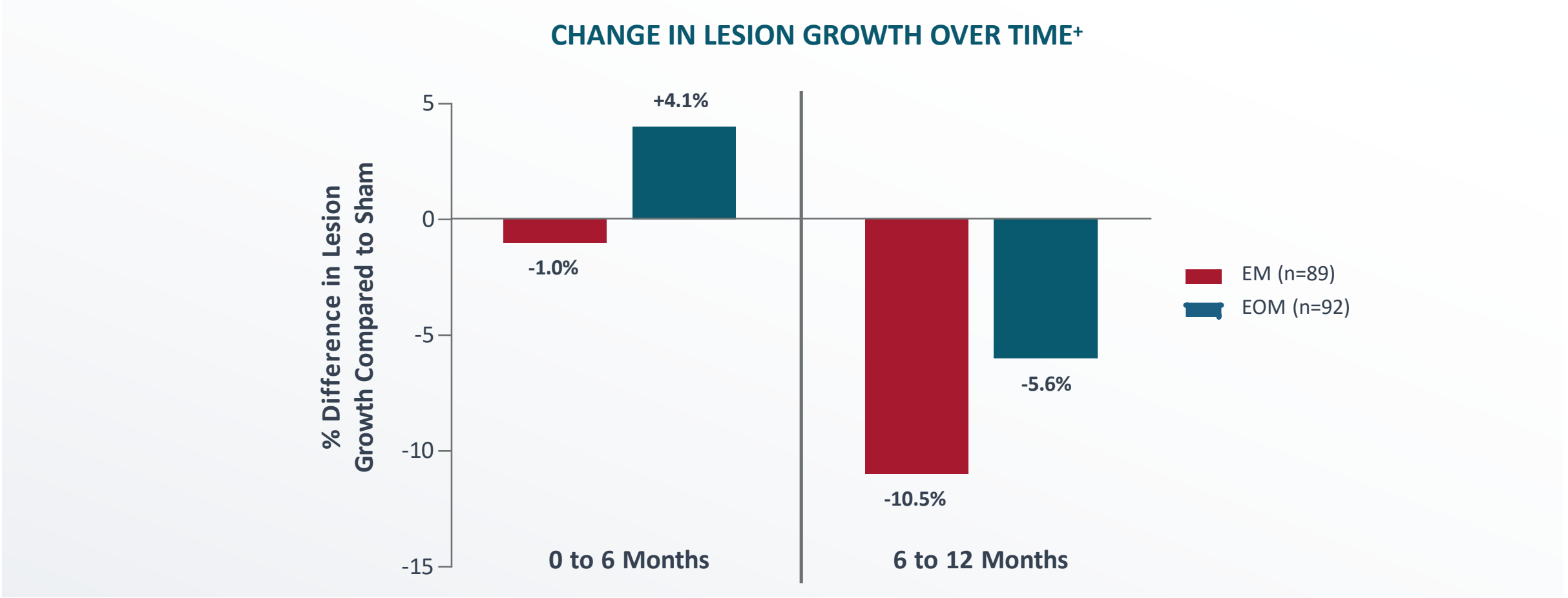
ANX007 Effect on Lesion Growth Improves with Longer Treatment



+The least-square (LS) mean and its standard error (SE) 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

Increasing ANX007 Impact Over Time

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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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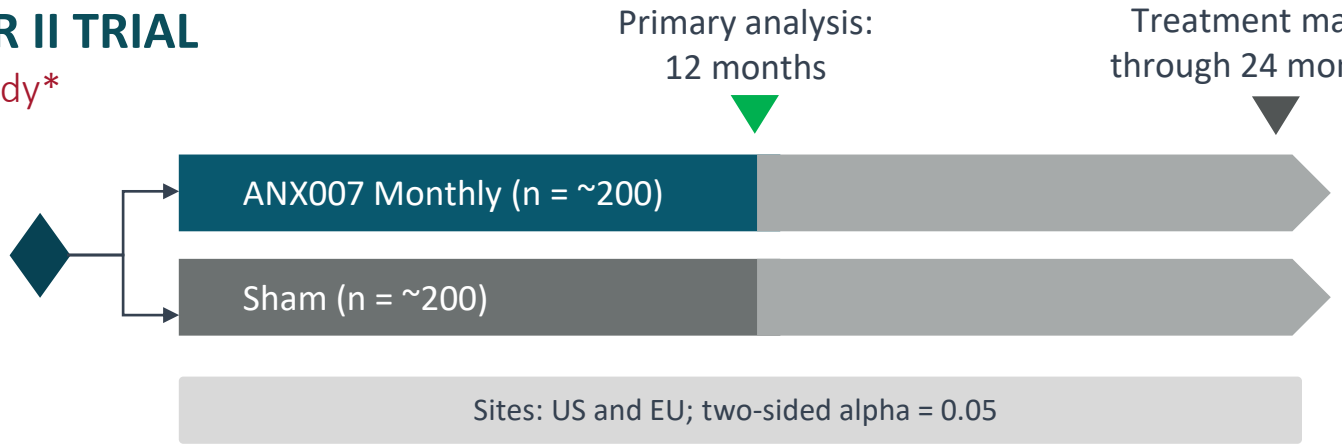
ANX007 Global GA Pivotal Program to begin Mid-2024

Repeat ARCHER and support global approvals

PRIME Designation from EMA

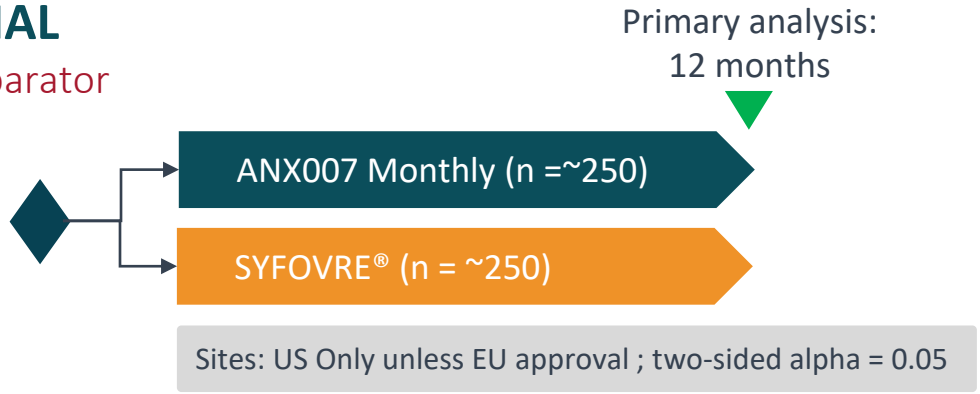
ARCHER II TRIAL

Sham Study*



ARROW TRIAL

Injection Comparator



Primary Endpoint

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

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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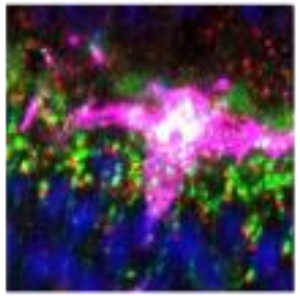
Closer to Achieving Our Mission with Differentiated GA Program



Distinctive scientific approach

to stop all complement mediated inflammation and tissue damage before it starts

ANX007 showed consistent preservation of vision across multiple measures

Consistent, robust effects on vision; Generally well-tolerated

Preparing for Global Phase 3 program

FDA alignment on primary endpoint; PRIME / EMA discussions ongoing; Phase 3 initiation mid-2024

On a Mission to Provide Functional Benefit to Patients Suffering From Complement-Mediated Disease

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Thank You!