

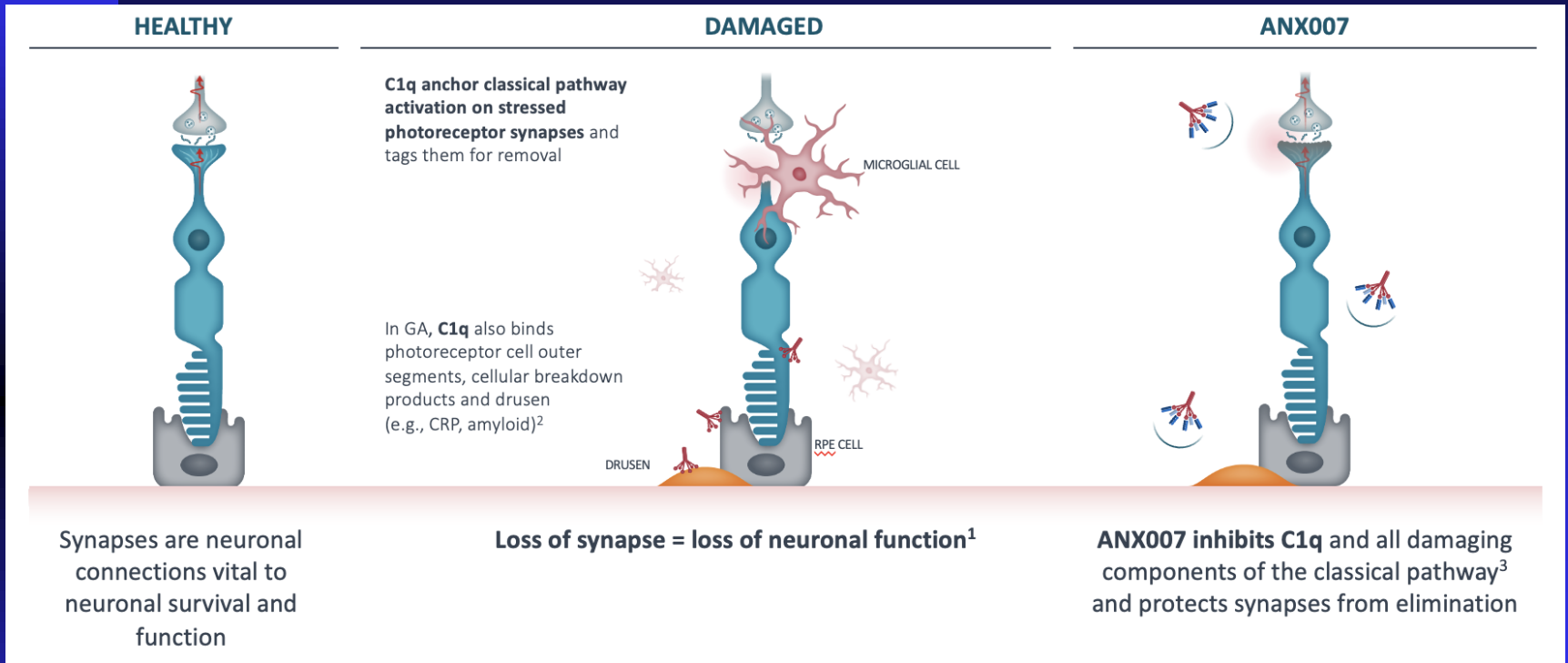
Prevention of Visual Acuity Loss and Preservation of Photoreceptors by ANX007 in Geographic Atrophy in the Phase 2 ARCHER Trial

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Karl Csaky, Jeffrey Heier, Charles Wykoff, Scott
Borland, Lori Taylor, Qing Chang and Donald Fong

Disclosures

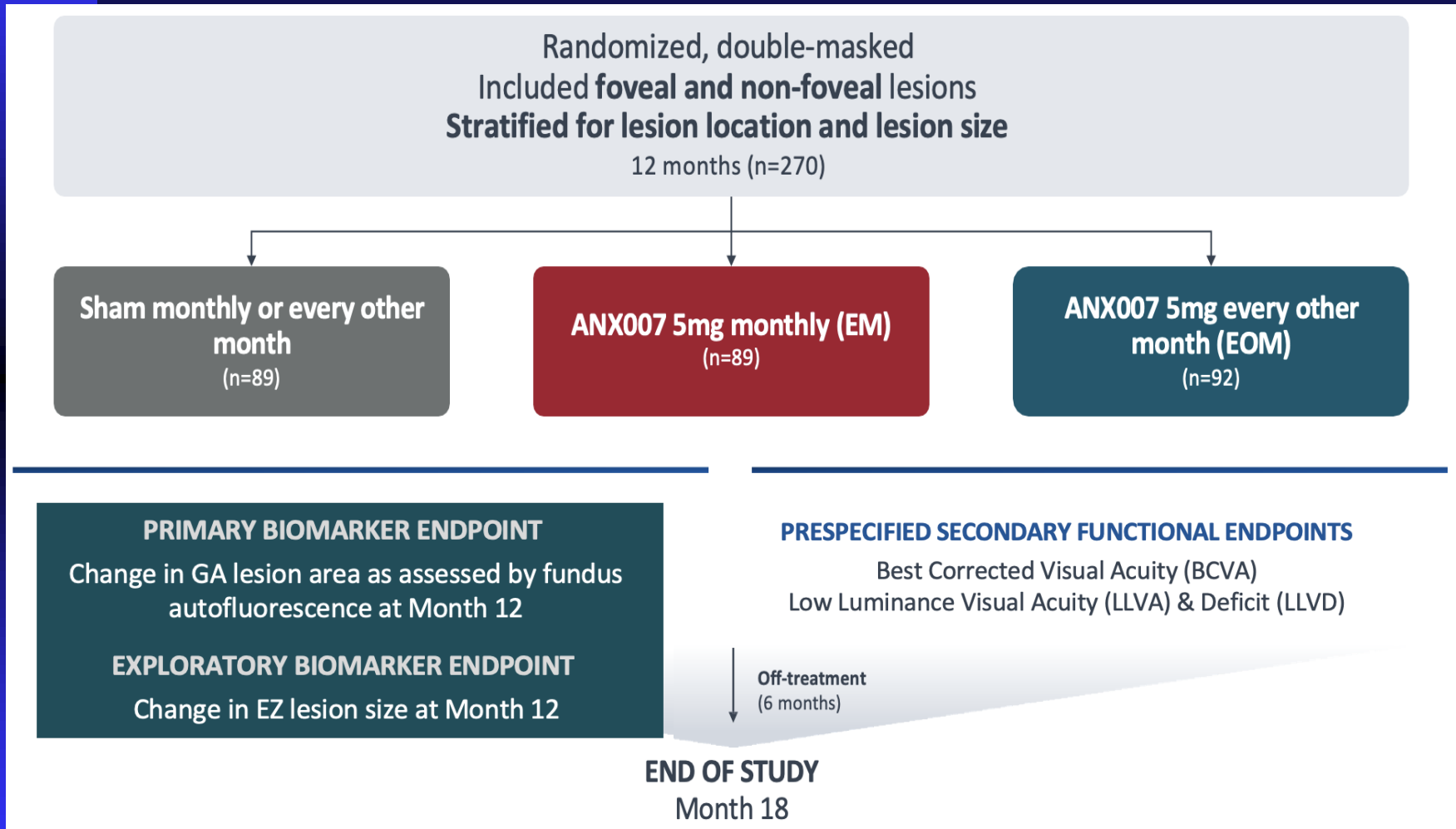
- 4D Molecular Therapeutics
- Annexon
- Regeneron
- Roche/Genentech
- Boehringer Ingelheim

ANX007 MOA: C1q Inhibitor



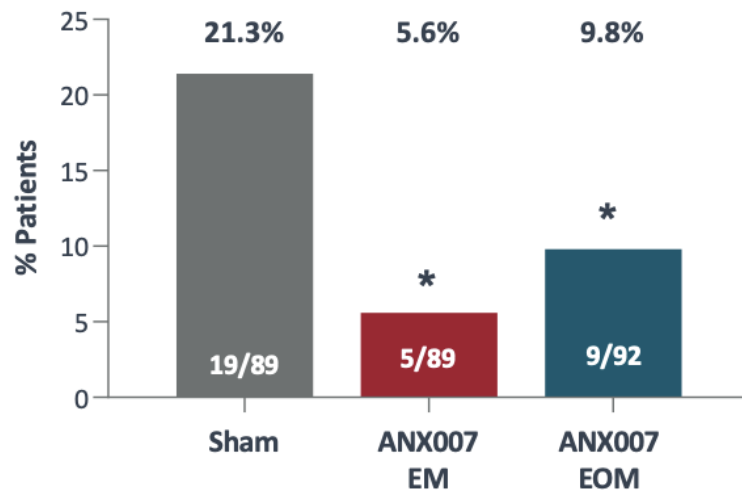
¹Stevens, 2007, *Cell* **131**:1164; Howell, et al., 2011 *J Clin Invest.* **121**:1429; Schafer, et al., 2012 *Neuron* **74**: 691; Stephan et al., 2012 *Annu Rev Neurosci* **35**:369; Hong, et al., 2016 *Science*. **352**:712; Lui, et al., 2016 *Cell* **165**:921; Dejanovic, et al., 2018 *Neuron* **100**:1322;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

ARCHER: Phase 2 Study of ANX007 in GA



ANX007: Statistically Significant Protection From BCVA and LLVA ≥ 15 -Letter Loss

PATIENTS WITH PERSISTENT BCVA ≥ 15 -LETTER LOSS THROUGH MONTH 12[#]



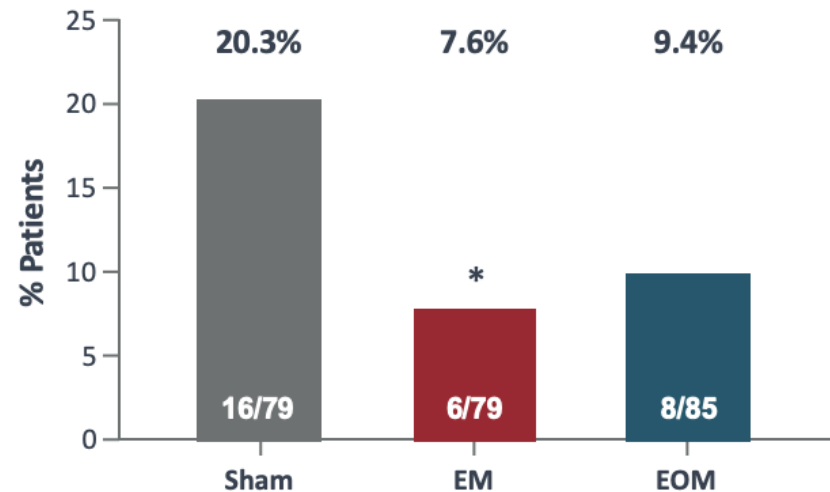
Nominal
p-value vs
sham[^]

0.0021

0.032

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

LLVA ≥ 15 -LETTER LOSS THROUGH MONTH 12[#]



Nominal
p-value vs
Sham[^]

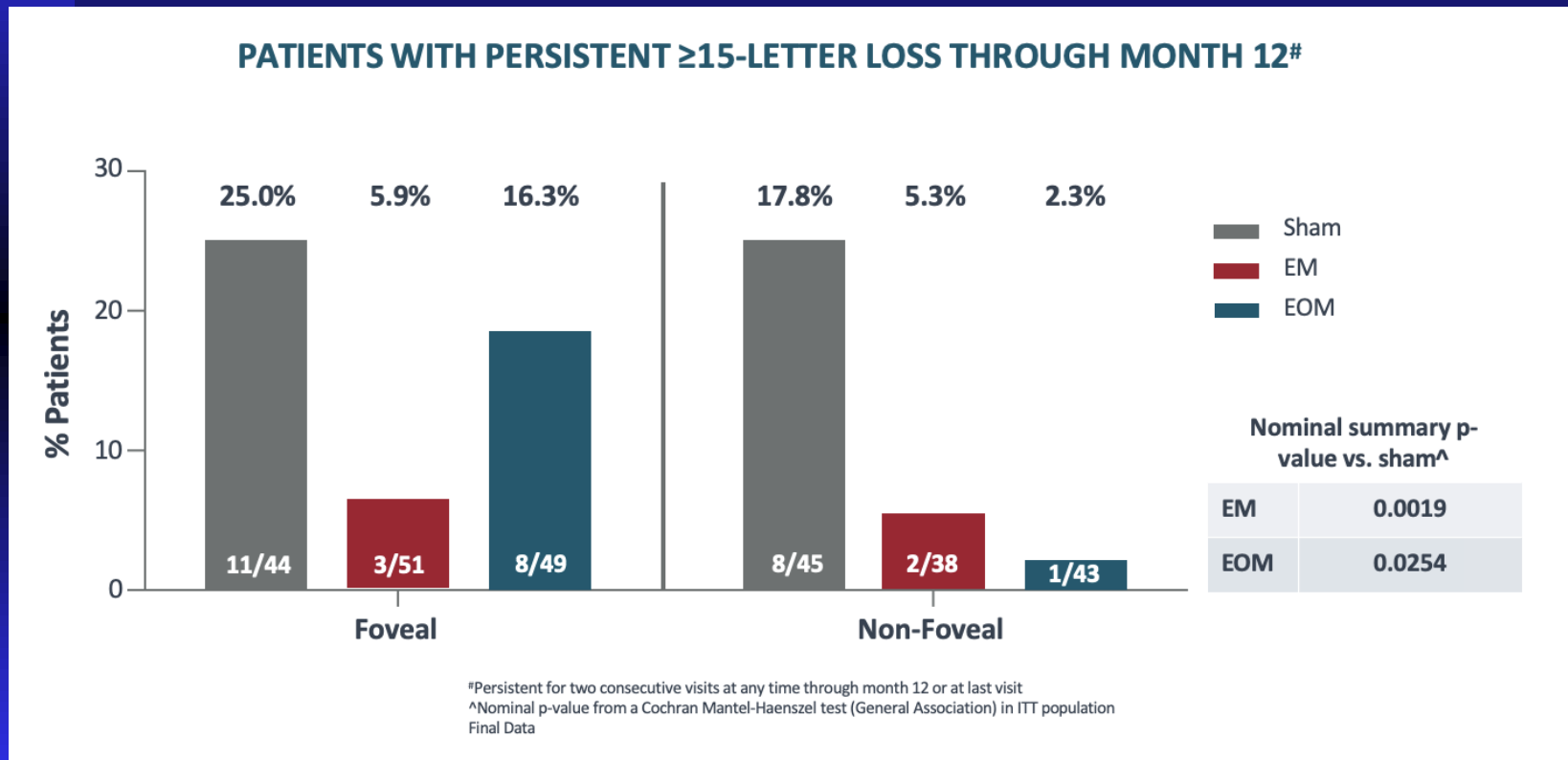
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0.022

0.050

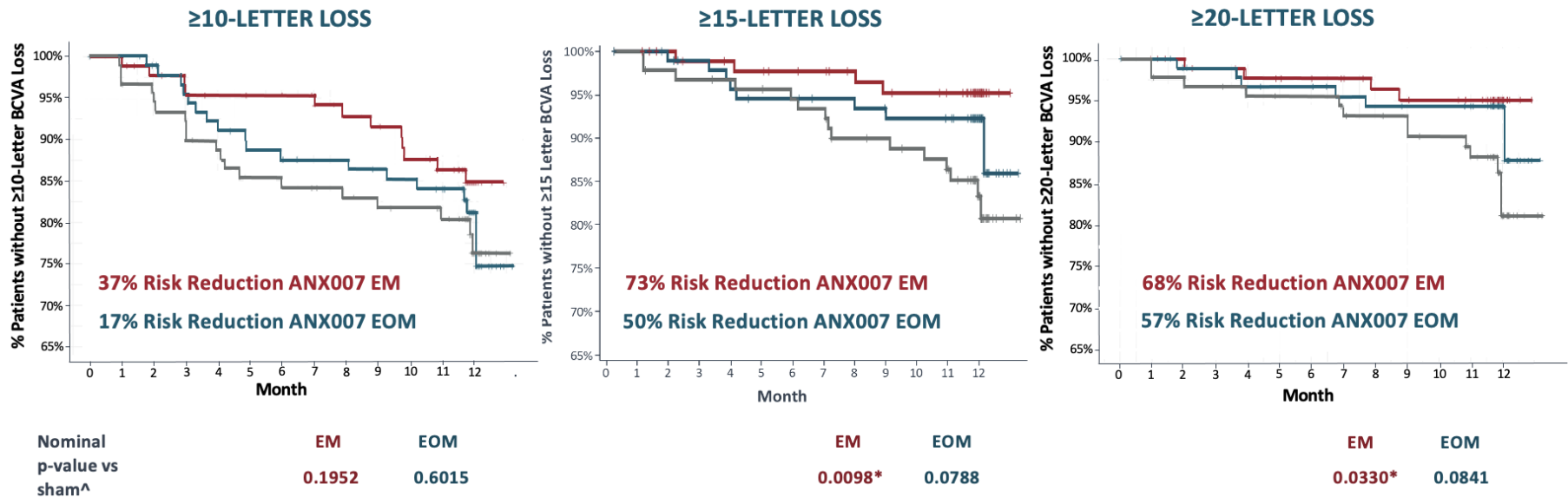
[#]Patients with single LLVA ≥ 15 -letter loss event and at least one post-baseline LLVA measurement
[^]Nominal p-value from a Chi-square test; * Nominal p < 0.05
 Final data

ANX007 BCVA Subgroup Analysis: Protection from VA Loss in Foveal and Non-Foveal Eyes



ANX007: Consistent Protection from Vision Loss with BCVA ≥ 10 -, ≥ 15 - and ≥ 20 -Letter Assessments

Persistent BCVA Vision Loss Through Month 12[#]

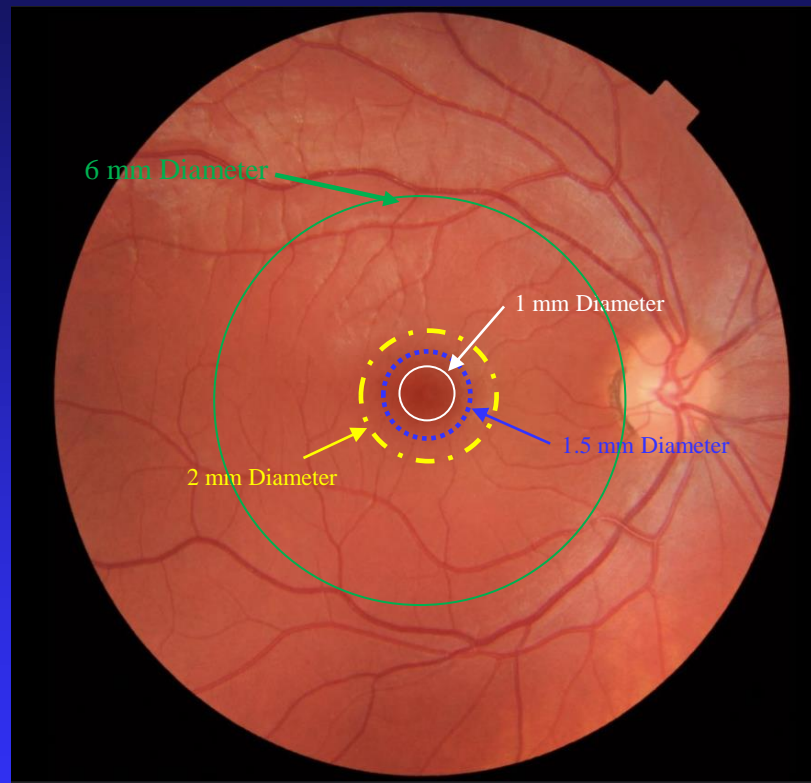


[#]Persistent for two consecutive visits through month 12, with month 12 confirmed at month 15 visit

[^]Nominal p-value from a Chi-square test in ITT population

* $p < 0.05$

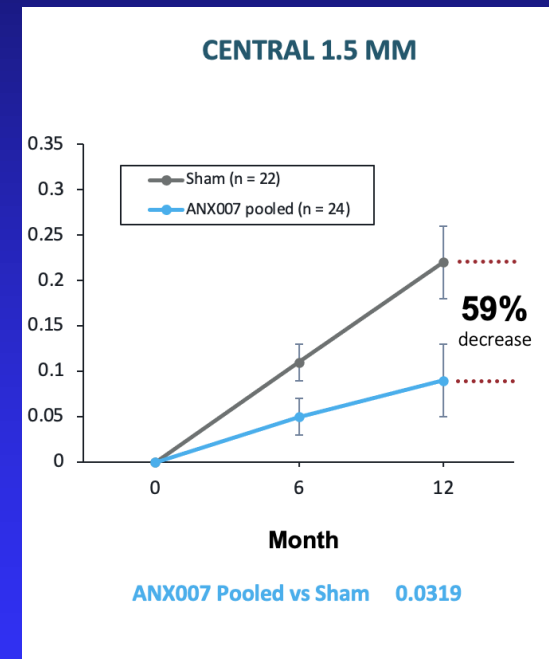
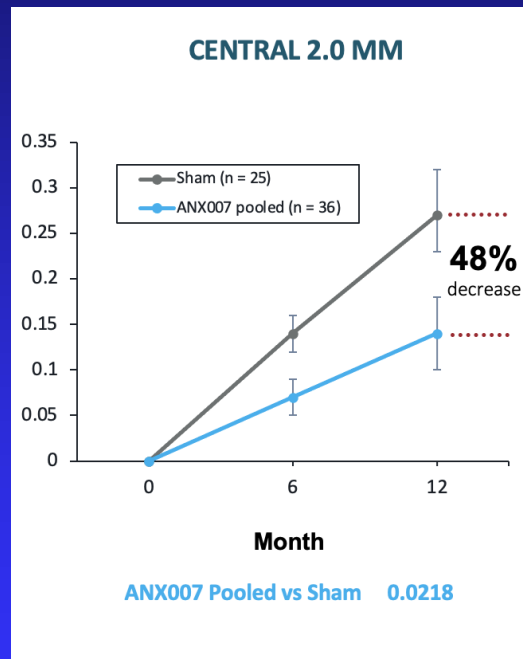
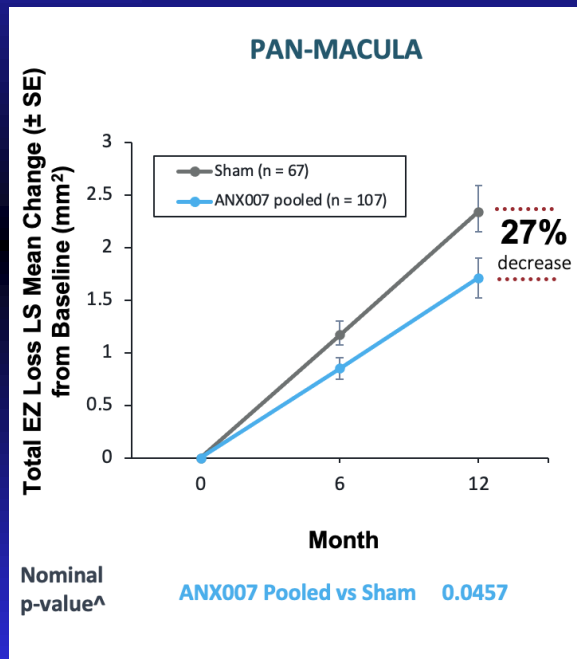
ANX007: Assessment of Drug Effect by Macular Location



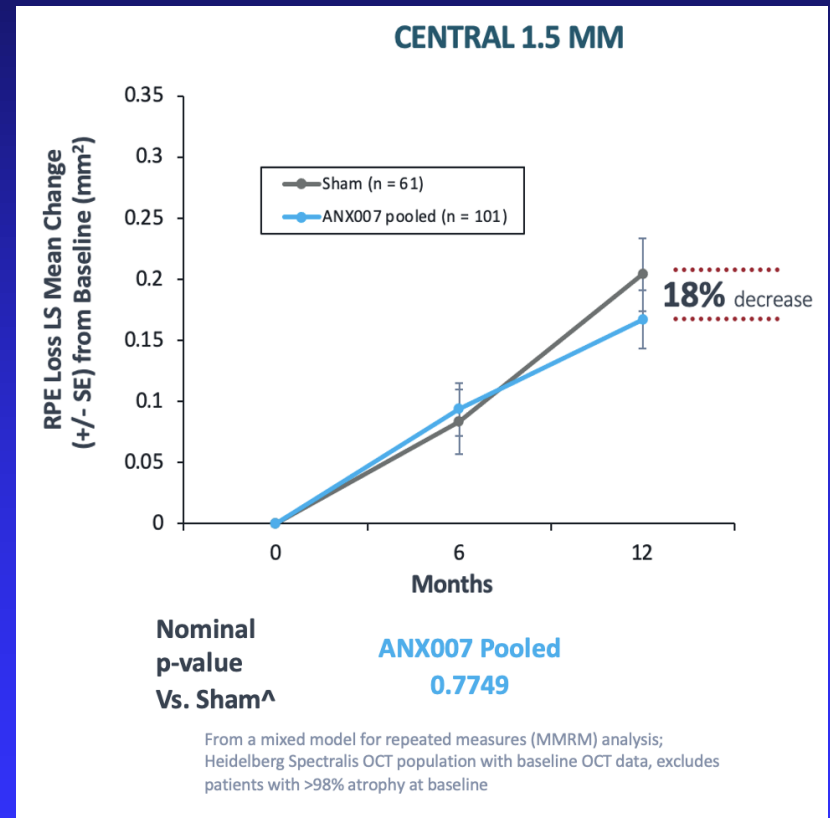
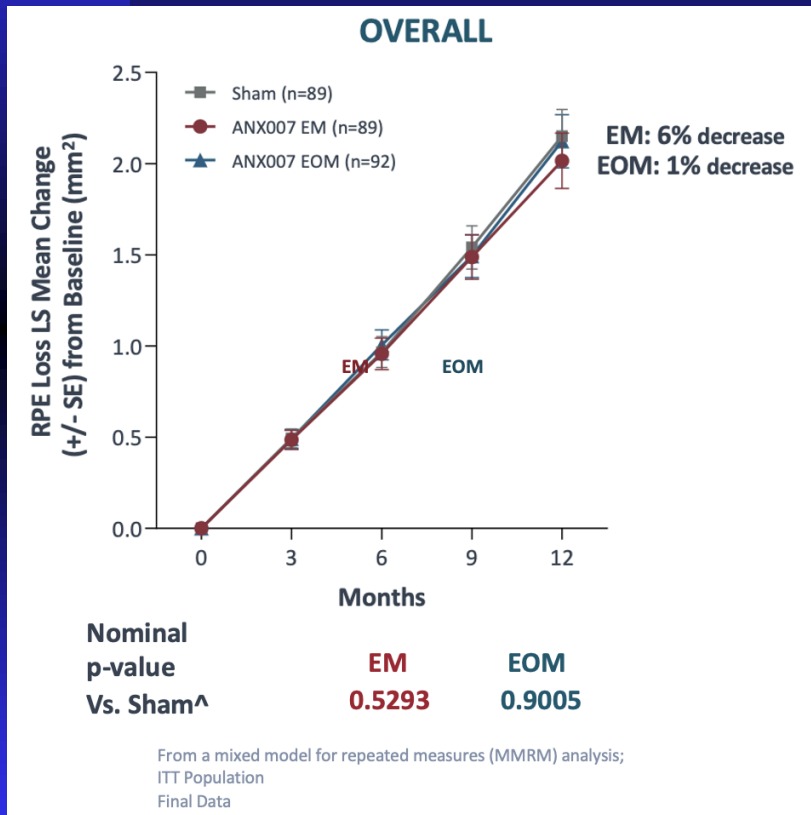
Dimensions are approximate

ANX007: Significant Photoreceptor (EZ) Protection Through Month 12

Central Foveal Region Effect > Pan Macula Effect



ANX007: Reduced RPE Loss (FAF) in Foveal Center (1.5mm Diameter) Through 12 Months

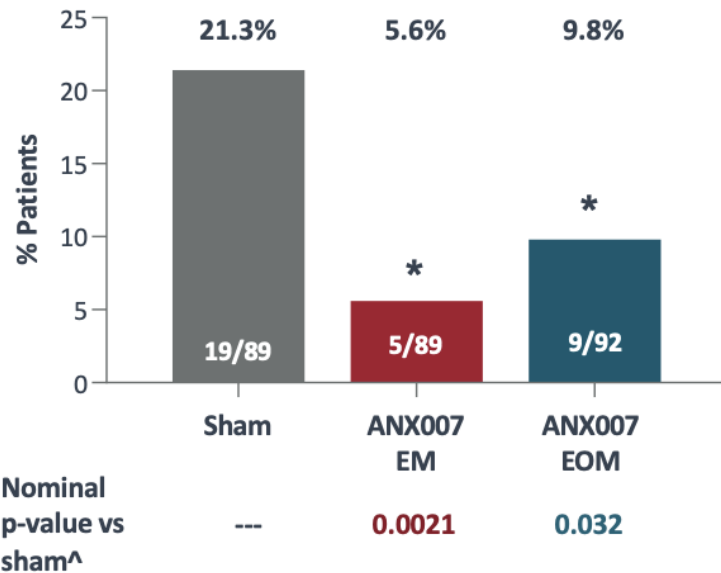


ANX007: Assessment of Drug Effect in Patients with Less Advanced Disease

- At Study Baseline:
 - Smaller LLD (Baseline LLD < 30)
 - Low light VA (LLVA) lost first in GA
 - $LLD = BCVA - LLVA$
 - Lower EZ loss (< 80% in central 2.0mm)
 - Smaller lesions (< 4mm²)

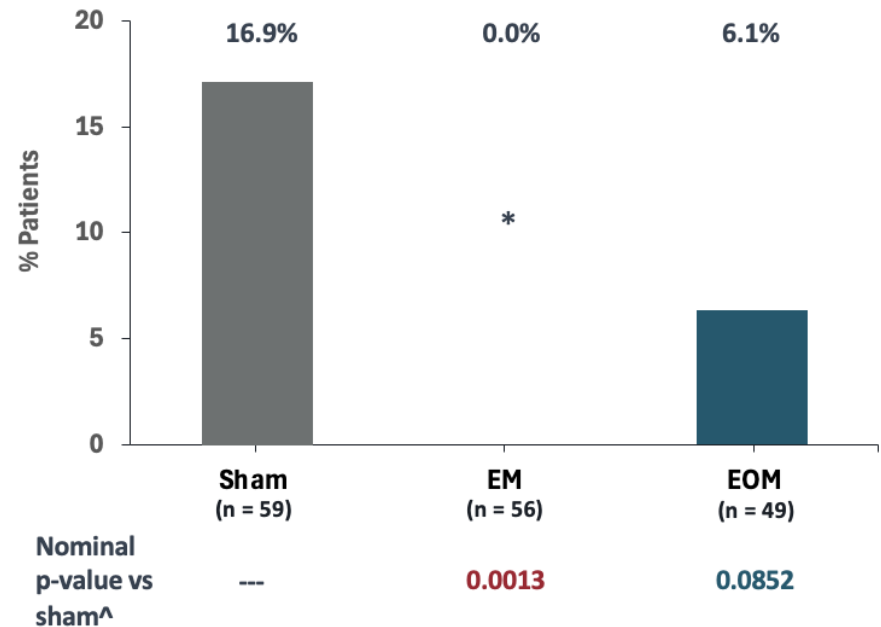
ANX007: Larger Effect in Less Advanced Disease – BCVA

**PATIENTS WITH PERSISTENT BCVA
≥15-LETTER LOSS THROUGH MONTH 12[#]**



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

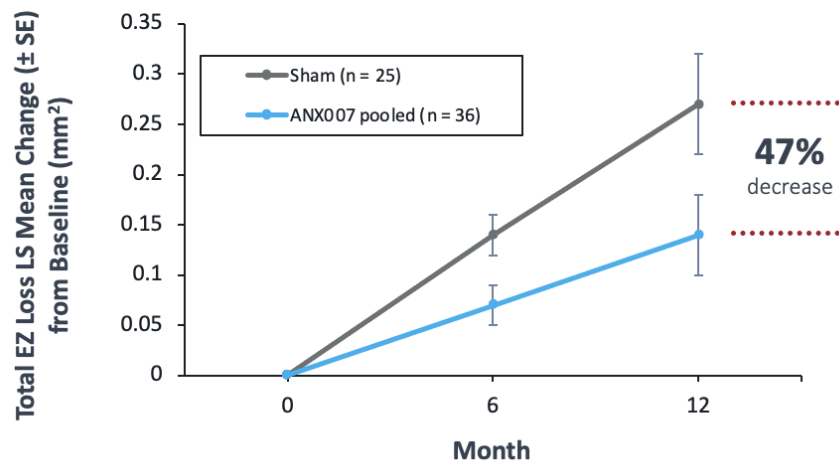
**PERSISTENT ≥15-LETTER LOSS INCLUDING MONTH 12[#]
IN PATIENTS WITH BASELINE LLVD <30**



[#]Persistent for two consecutive visits including month 12
[^]Nominal p-value from a Chi-square test in ITT population
 * Nominal P < 0.05
 Final Data

ANX007: Larger Effect in Less Advanced Disease – EZ Loss

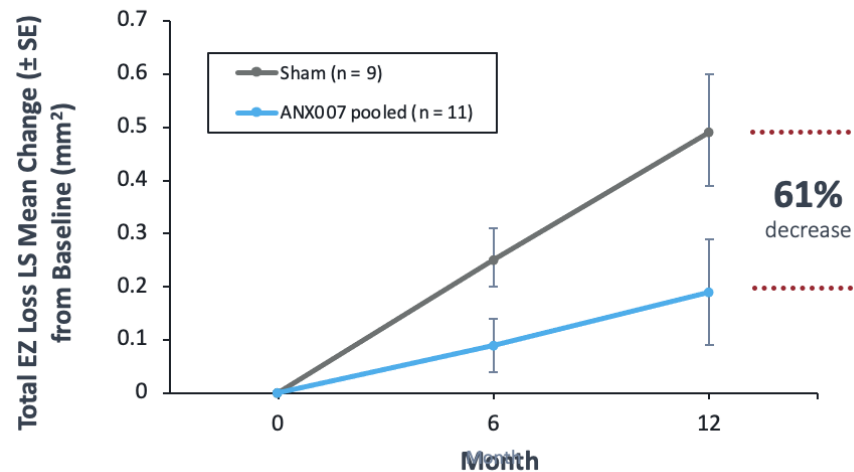
**TOTAL EZ LOSS (EZ = 0 μ m)
CENTRAL 2.0 MM - < 98% LOSS @ BASELINE**



Nominal p-value vs sham[^] ANX007 0.0242

[^]Nominal p-values from a linear mixed model for repeated measures model (slope) analysis; Heidelberg Spectralis OCT population with baseline OCT data, excludes patients with >98% atrophy at baseline

**TOTAL EZ LOSS (EZ = 0 μ m)
CENTRAL 2.0 MM - < 80% LOSS @ BASELINE**

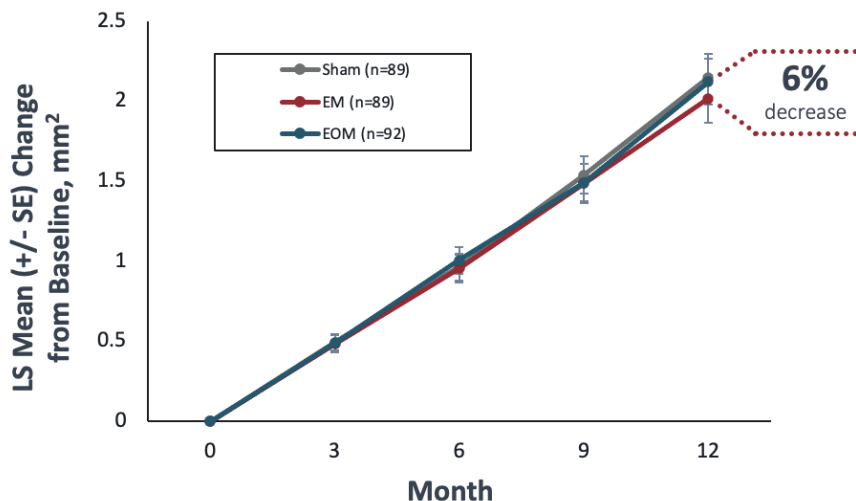


Nominal p-value vs sham[^] ANX007 0.0575

[^]Nominal p-values from a linear mixed model for repeated measures model (slope) analysis; Heidelberg Spectralis OCT population with baseline OCT data, excludes patients with >80% atrophy at baseline

ANX007: Larger Effect in Less Advanced Disease – Lesion Growth

RPE LOSS/LESION GROWTH OVERALL



Nominal p-value
vs. sham[^]

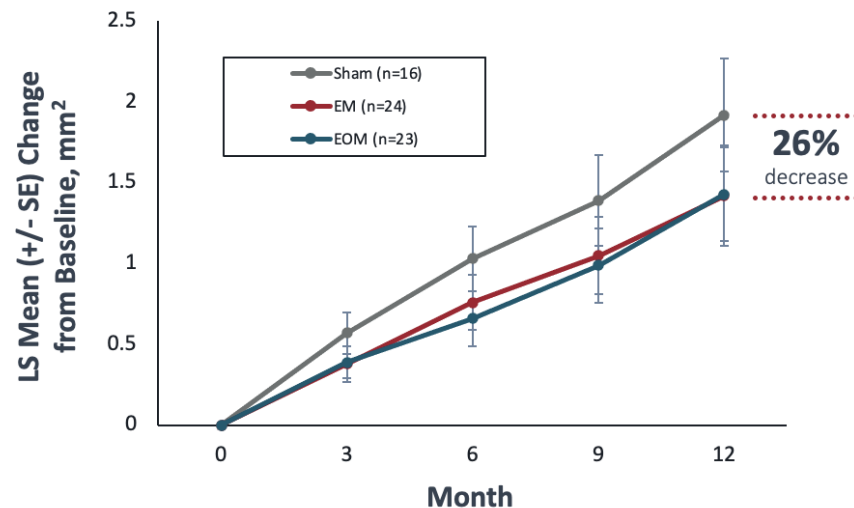
EM **EOM**
0.5293 **0.9005**

	SHAM	EM	EOM
Mean Change in Lesion Size (mm ²)	2.15	2.02	2.12

From a mixed model for repeated measures (MMRM) analysis;

[^]Nominal p-value from a Chi-square test in ITT population; Final Data

RPE LOSS/LESION GROWTH GA LESIONS < 4.0 MM² AT BASELINE



Nominal p-value
vs. sham[^]

EM **EOM**
0.46 **0.46**

	SHAM	EM	EOM
Mean Change in Lesion Size (mm ²)	1.92	1.42	1.43

From a mixed model for repeated measures (MMRM) analysis; [^]Nominal p-value from a Chi-square test in population with baseline lesion size < 4.0mm²; Final Data

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

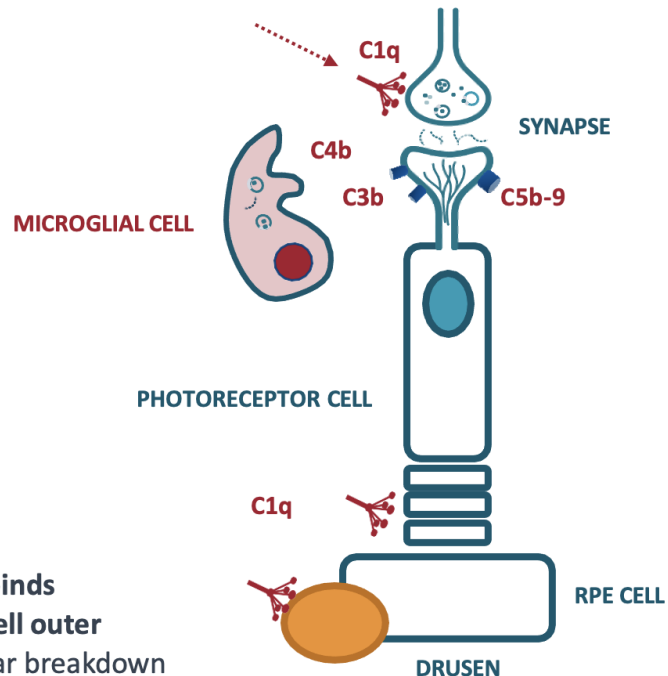
Key Takeaways

- ANX007:
 - Protected against VA loss in ARCHER
 - Impacts on PR/RPE most pronounced in central region
 - Structure protection aligns with function protection
 - Effects larger with less advanced disease
- Findings support PR synapse protection MOA
- Informs ARCHER II phase 3 study now underway

Back-Up

ANX007 MOA: C1q Inhibitor

C1q is a key driver of neurodegeneration¹ and binds stressed photoreceptor synapses and activates the classical pathway



ANX007 inhibits C1q and all damaging components of the classical pathway³ and **protects synapses from elimination**

In GA, **C1q** also binds **photoreceptor cell outer segments**, cellular breakdown products and drusen (e.g., CRP, amyloid)²

¹Stevens, 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; ²Yednock, et al., 2022 *Int J Retina Vitreous* **8**:79; ³Lansita, et al., 2017 *International Journal of Toxicology*, **36**:449