Preservation of Vision by ANX007: Clinical Results and Anatomical Changes from the Phase 2 ARCHER Trial

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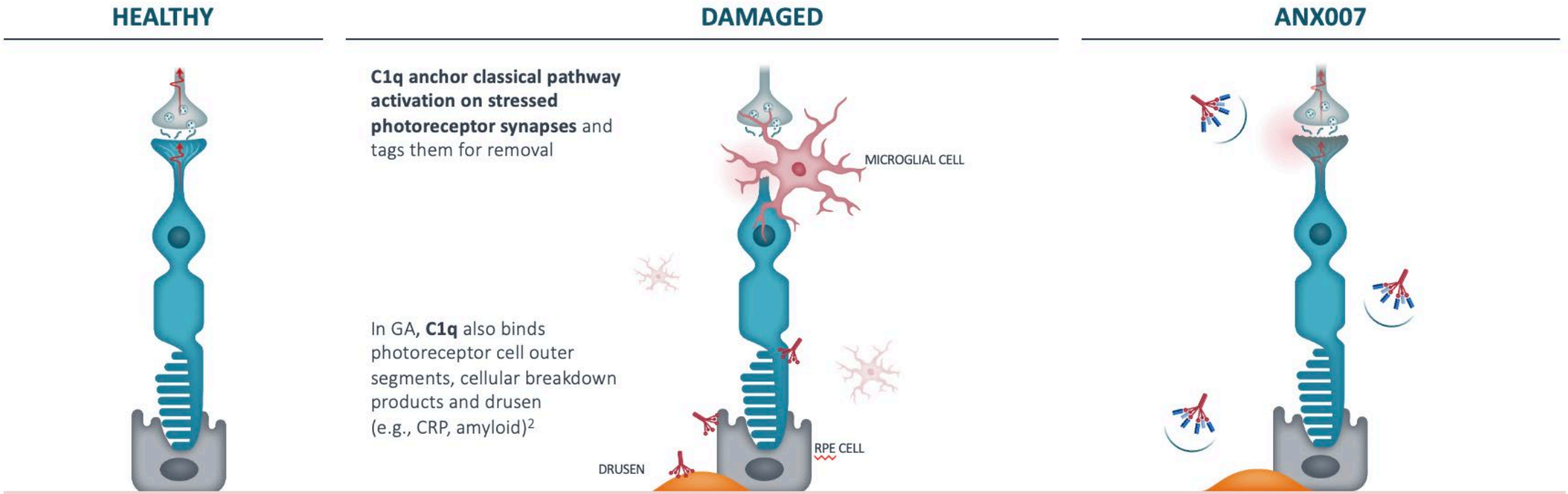
Disclosures

- Abbvie (Advisory Board: Honoraria)
- Annexon (Investigator: Grants)
- Apellis (Investigator: Grants)
- Clearside Biomedical (Advisory Board: Honoraria, Investigator: Grants)
- Genentech (Advisory Board: Honoraria, Investigator: Grants)
- Ophthea (Investigator: Grants)
- Regeneron (Advisory Board: Honoraria)
- RegenXBio (Investigator: Grants)

ANX007 MOA: Protecting Photoreceptor and Synapses via C1q Inhibition

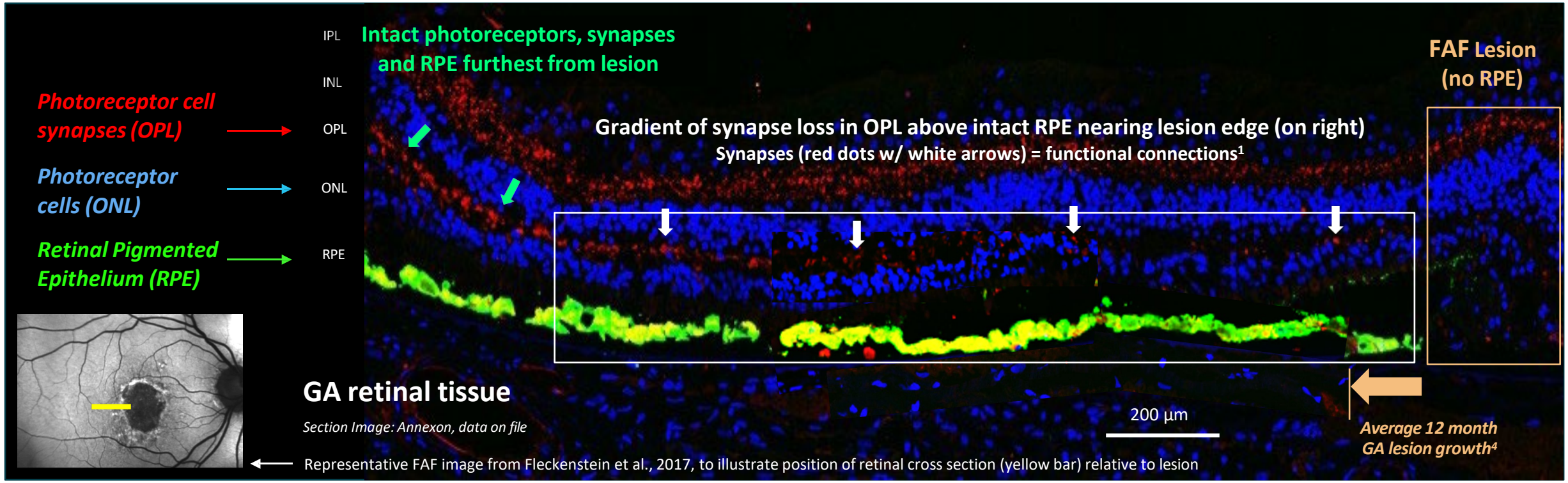
C1q inhibition neuroprotective in dry AMD / GA and other neurodegenerative diseases



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

RPE Loss Occurs After Loss of Photoreceptor Cells, Synapses and Function in GA

- Photoreceptor cells and their synapses are lost over intact RPE (white box)
  - Decreasing gradient of red-labeled synapses (w/ white arrows) moving toward the lesion on right - loss of synapses is loss of function[1]
  - Also, decreasing gradient of blue-labeled photoreceptor cells toward lesion – photoreceptors are lost prior to RPE[2]
- FAF measures RPE loss/lesion growth, but not photoreceptor or synapse loss and correlates poorly w/ visual function[3]



[1]Selkoe, 2002 doi: 10.1126/science.1074069; Burger, et al., doi.org/10.1016/j.ydbio.2021.04.001; [2]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; [3]Heier, et al., 2020 Ophthalmology Retina **4**:673; [4]Shen, et al., 2020 *Ophthalmol Retina* **4**:899

ARCHER: Phase 2 Trial of C1q Inhibitor ANX007 in Dry AMD / GA

ANX007: non-pegylated IVT-administered Fab

Randomized, double-masked
Included **foveal and non-foveal** lesions
Stratified for lesion location and lesion size
12 months (n=270)

Sham monthly or every other month
(n=89)

ANX007 5mg monthly (EM)
(n=89)

ANX007 5mg every other month (EOM)
(n=92)

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)

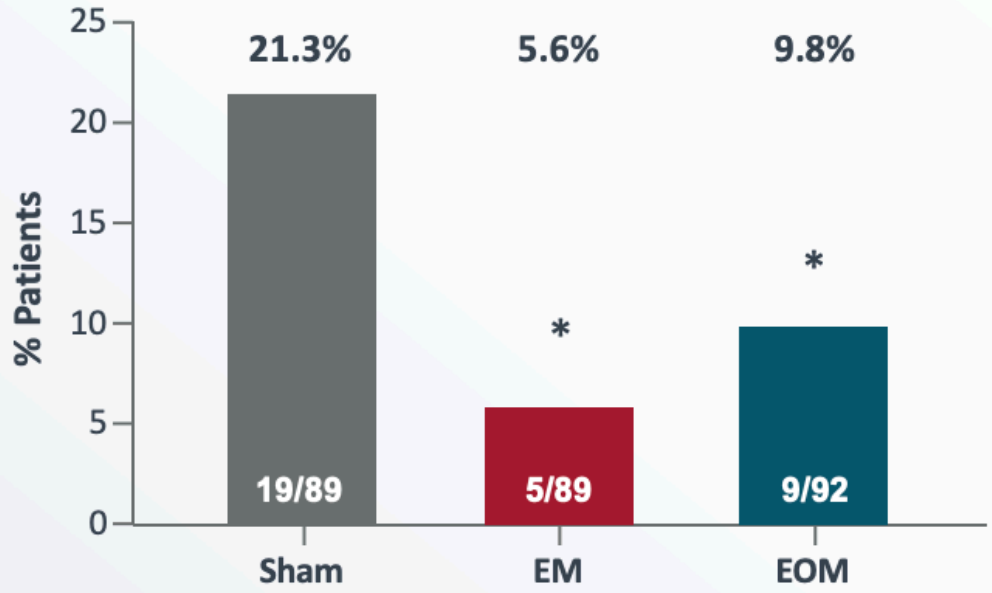
Off-treatment
(6 months)

END OF STUDY
Month 18

Consistent, Significant Protection from Vision Loss: BCVA and LLVA

First demonstration of consistent, dose dependent preservation across multiple measures of visual acuity

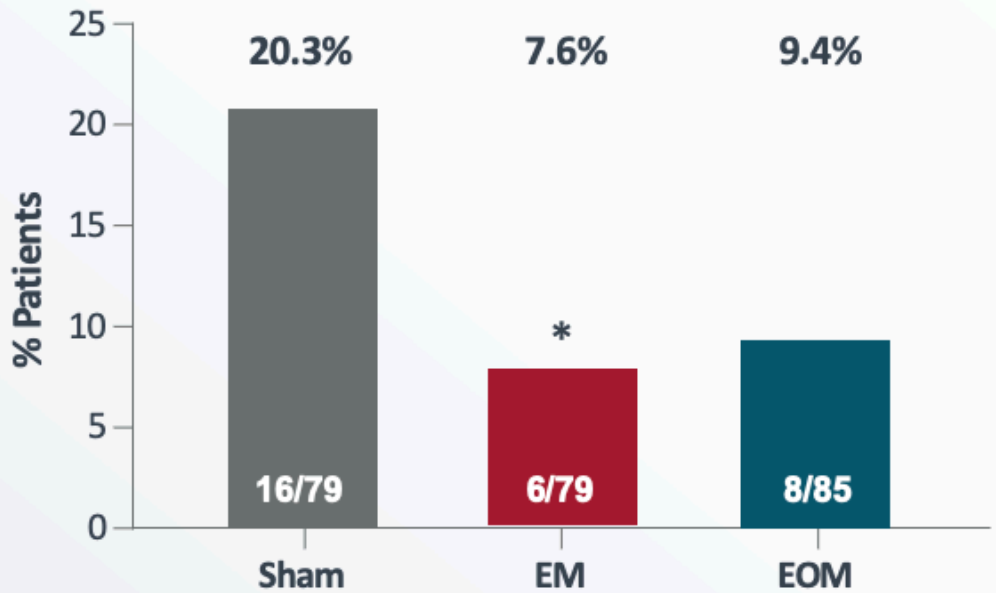
PATIENTS WITH PERSISTENT BCVA ≥15-LETTER LOSS THROUGH MONTH 12#



Nominal p-value vs Sham^	--	0.021	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#

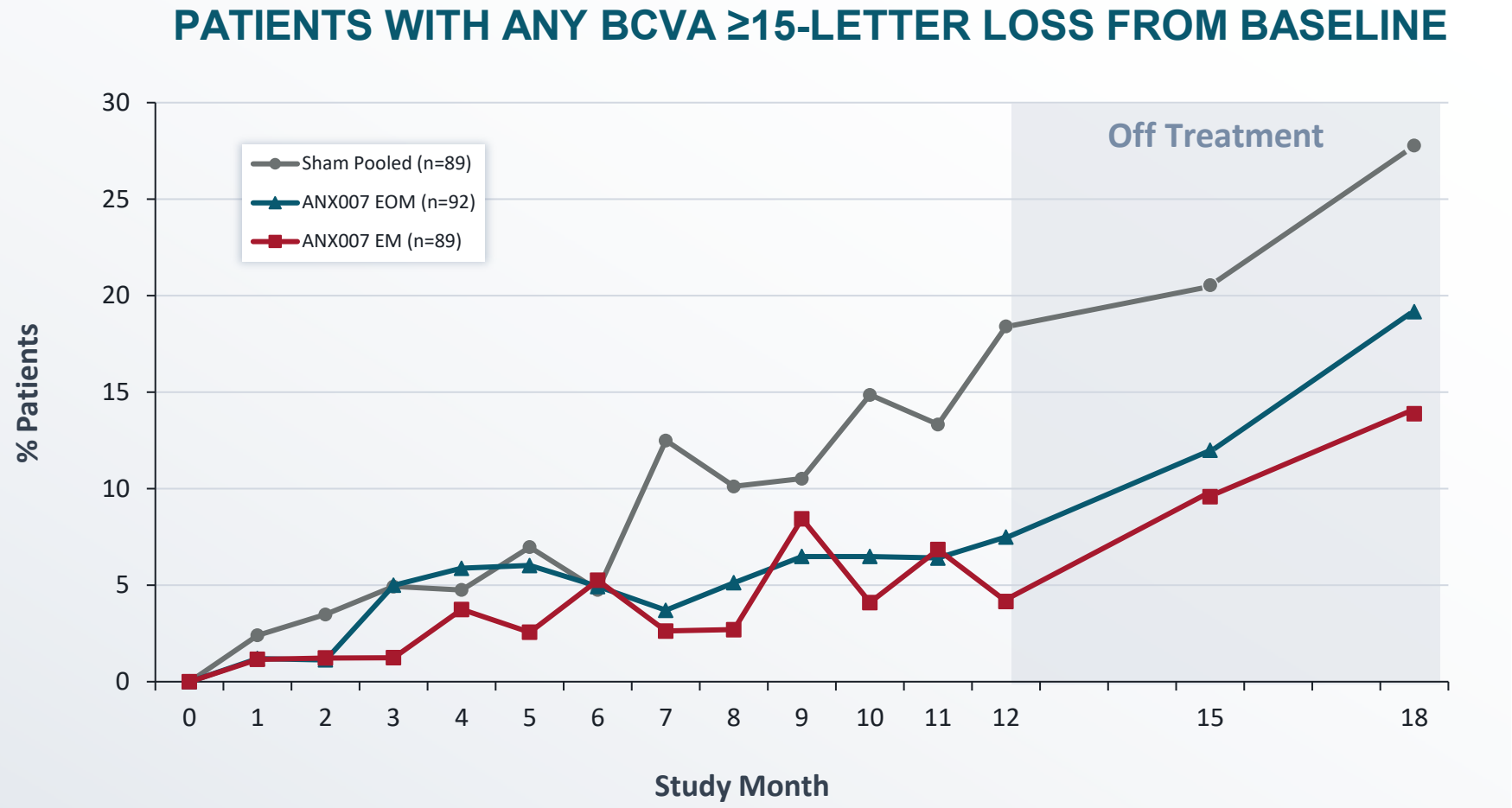


Nominal p-value vs Sham^	--	0.022	0.050

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

BCVA ≥15-Letter Loss Accelerated After Cessation of Treatment

Consistent with true on-treatment drug effect and disease-modifying mechanism of action

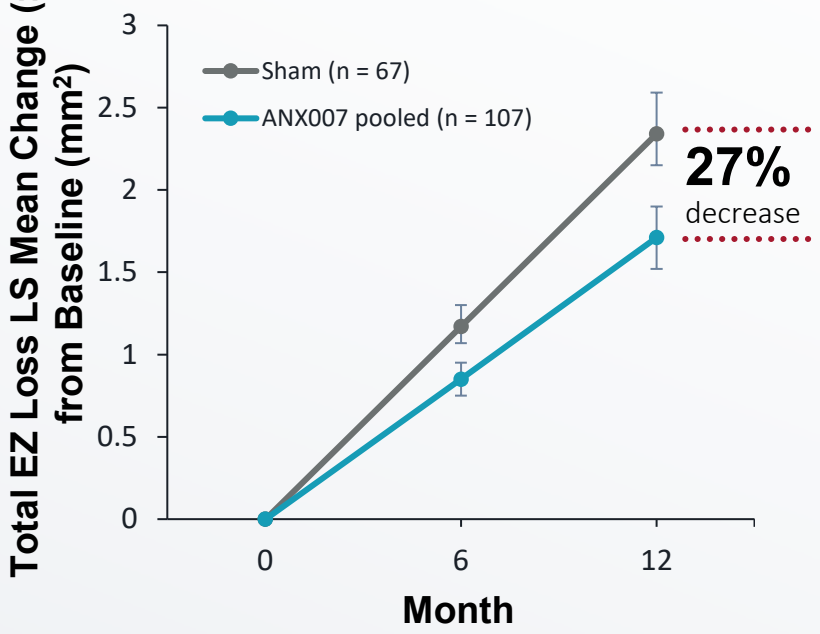


- Low frequency (<0.6% per month) of single BCVA ≥15-letter losses in EM- and EOM-treated groups during 12-month treatment period
- While benefit was maintained after treatment cessation the rate of BCVA≥15-letter loss increased to parallel that of sham (>1.6% per month)

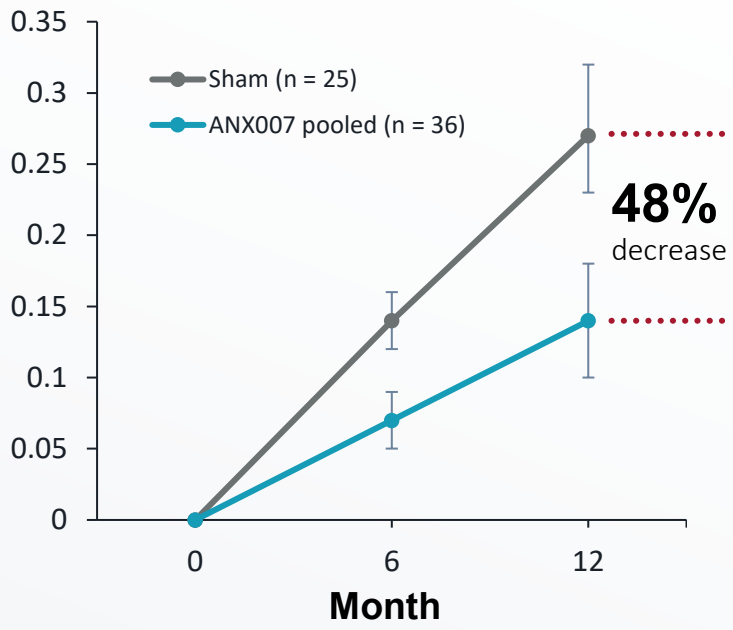
Significant Photoreceptor Protection Through 12 Months

More robust protection with ANX007 in center, area best associated with vision, compared to pan-macula

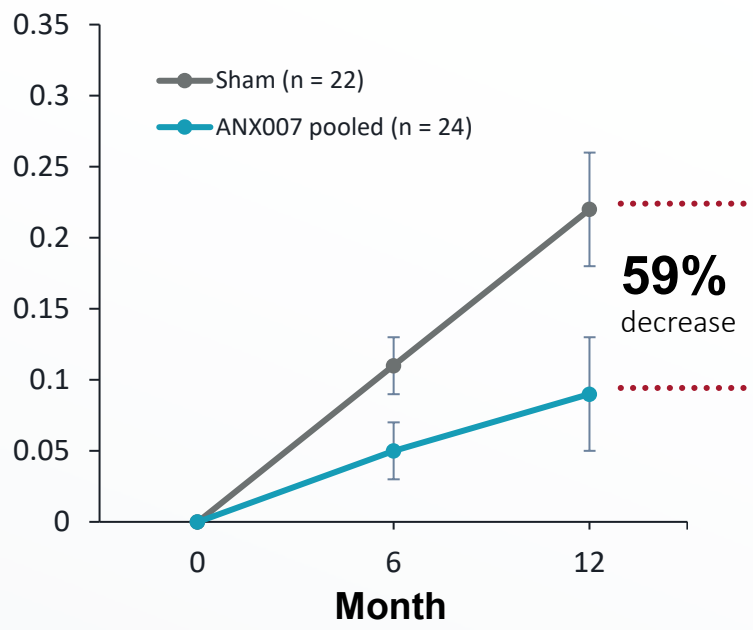
PAN-MACULA



CENTRAL 2.0 MM



CENTRAL 1.5 MM

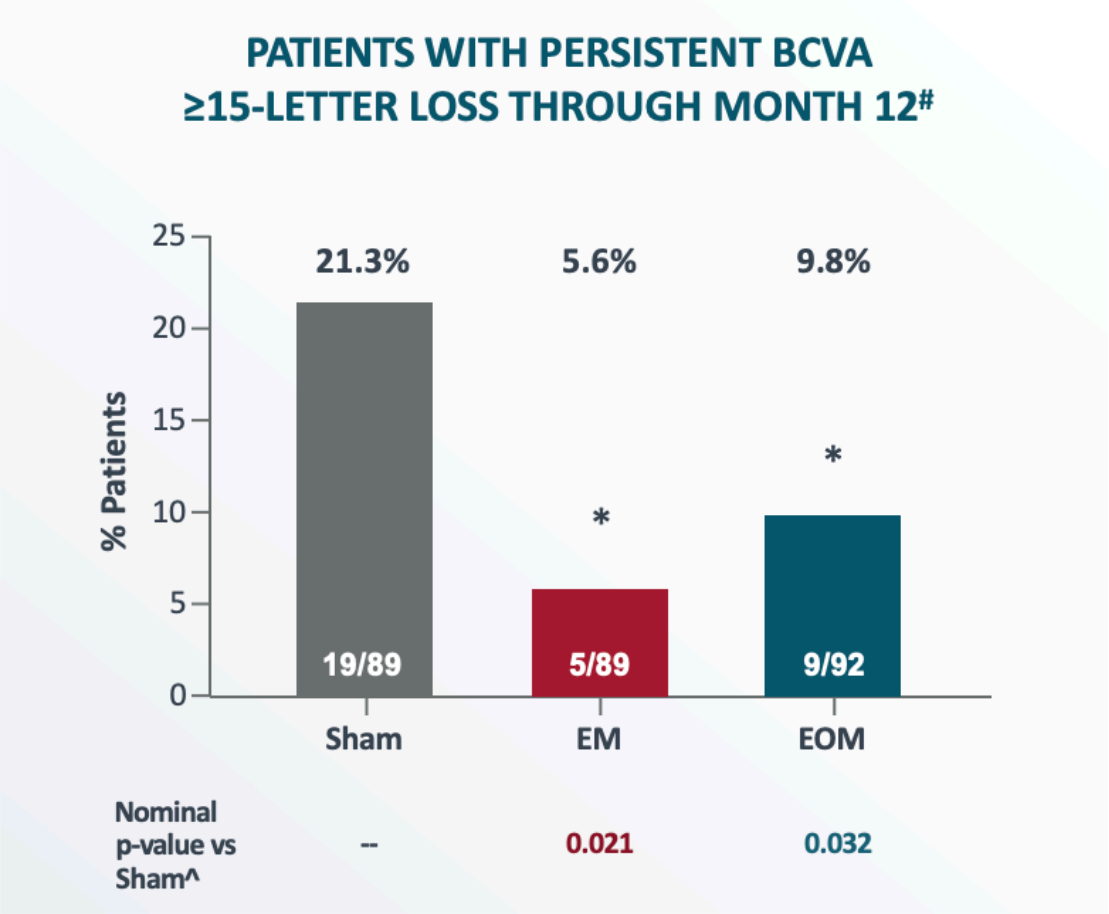


Nominal p-value^		
ANX007 Pooled vs Sham	0.0457	
ANX007 Pooled vs Sham	0.0218	
ANX007 Pooled vs Sham	0.0319	

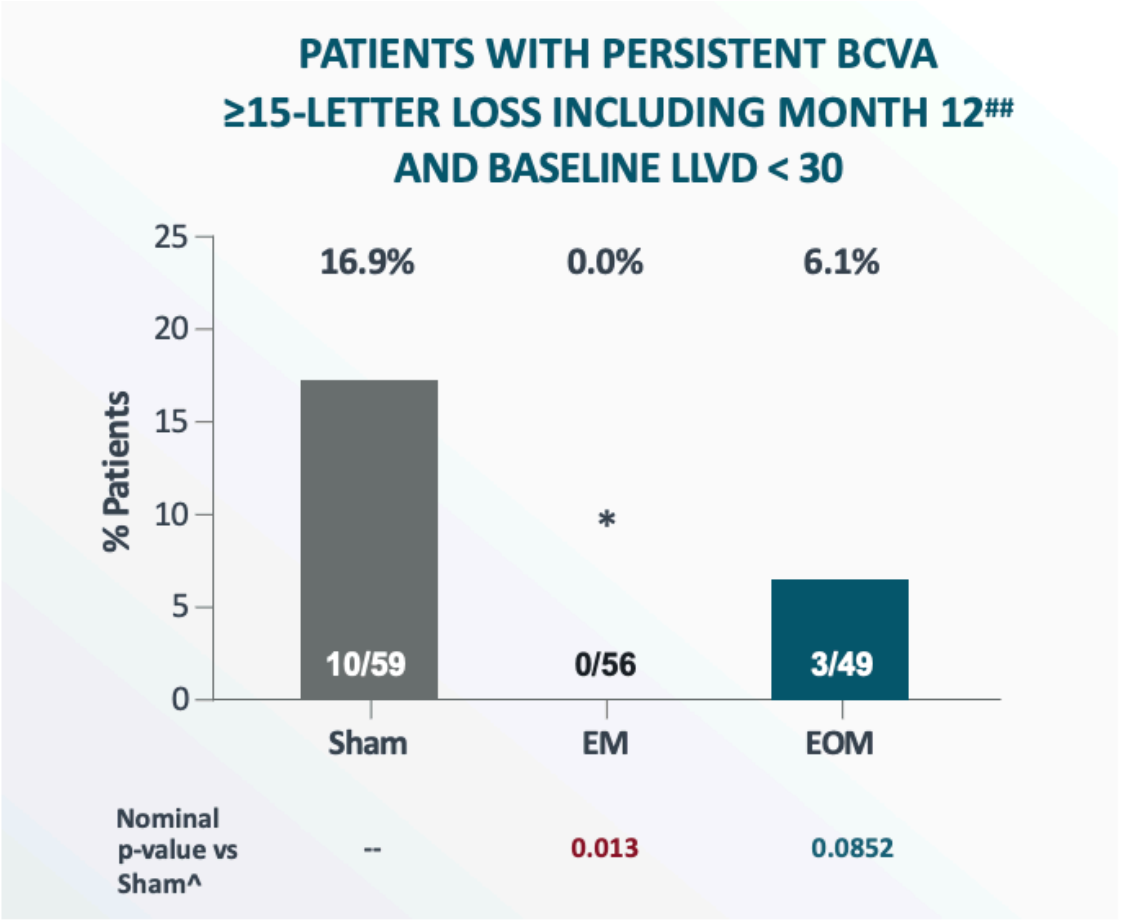
^Nominal p-values from a linear mixed model for repeated measures model (slope) analysis; Heidelberg Spectralis OCT population with baseline OCT data, excludes patients with >98% atrophy/attenuation at baseline

Profound Effect of ANX007 in Eyes with Less Advanced Disease

Protection from vision loss (BCVA ≥15-letter) based on retina health at baseline (LLVD < 30)



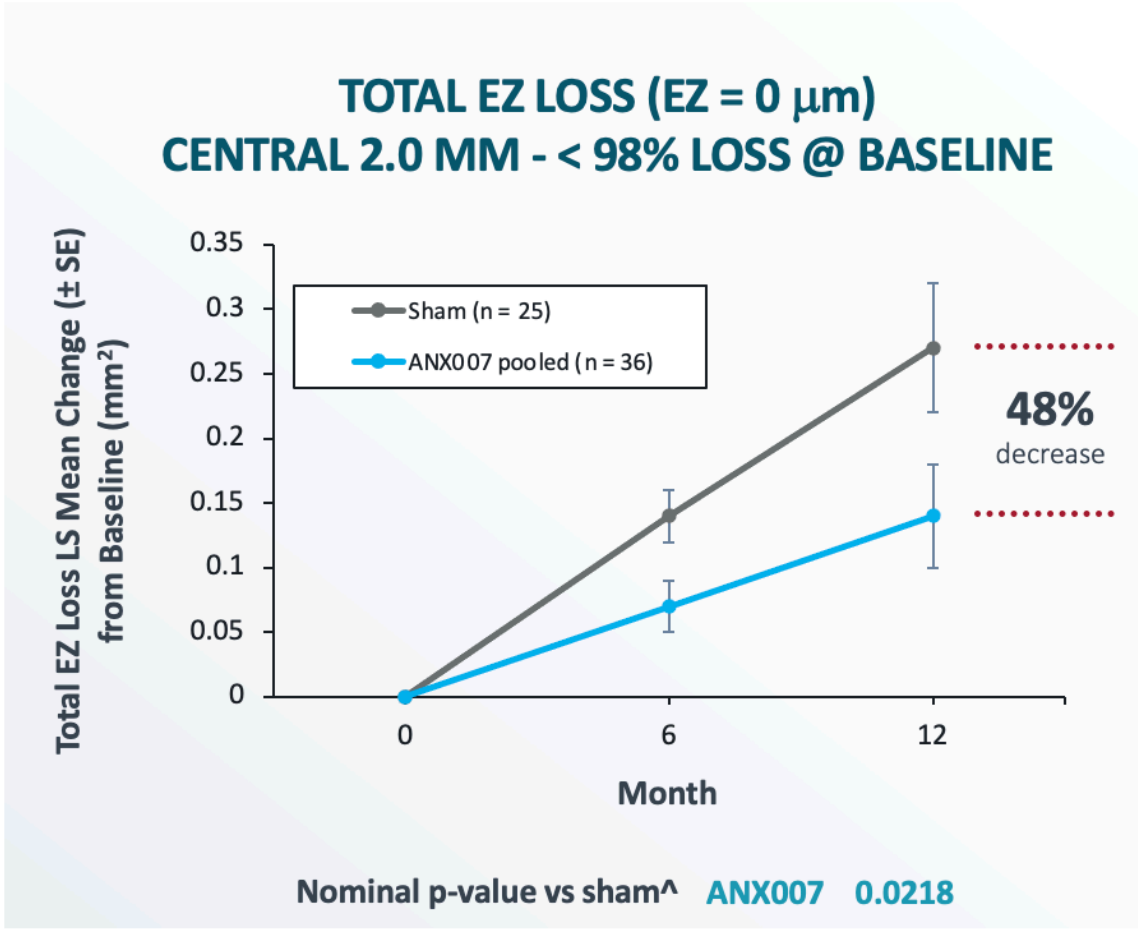
#Persistent for two consecutive visits through month 12 or at last study visit
^Nominal p-value from a Chi-square test in ITT population: * Nominal p < 0.05
Final data



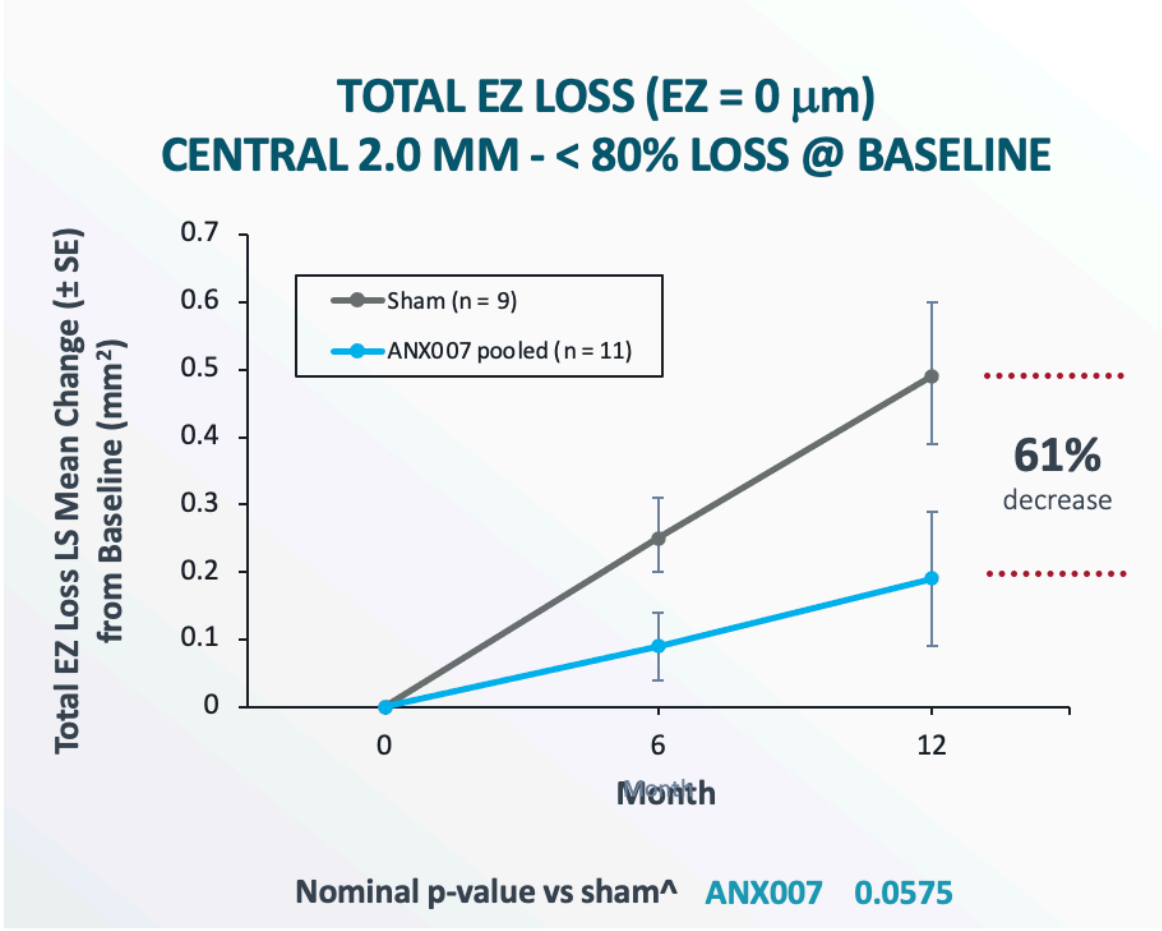
##Persistent for two consecutive visits including month 12 supported by month 15
^Nominal p-value from a Chi-square test in ITT population: * Nominal p < 0.05
Final data

Enhanced EZ Protection in Central Fovea in Less Advanced Disease

Protection from structural loss (EZ Loss) based on EZ health at baseline (< 80% loss)



^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



^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 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

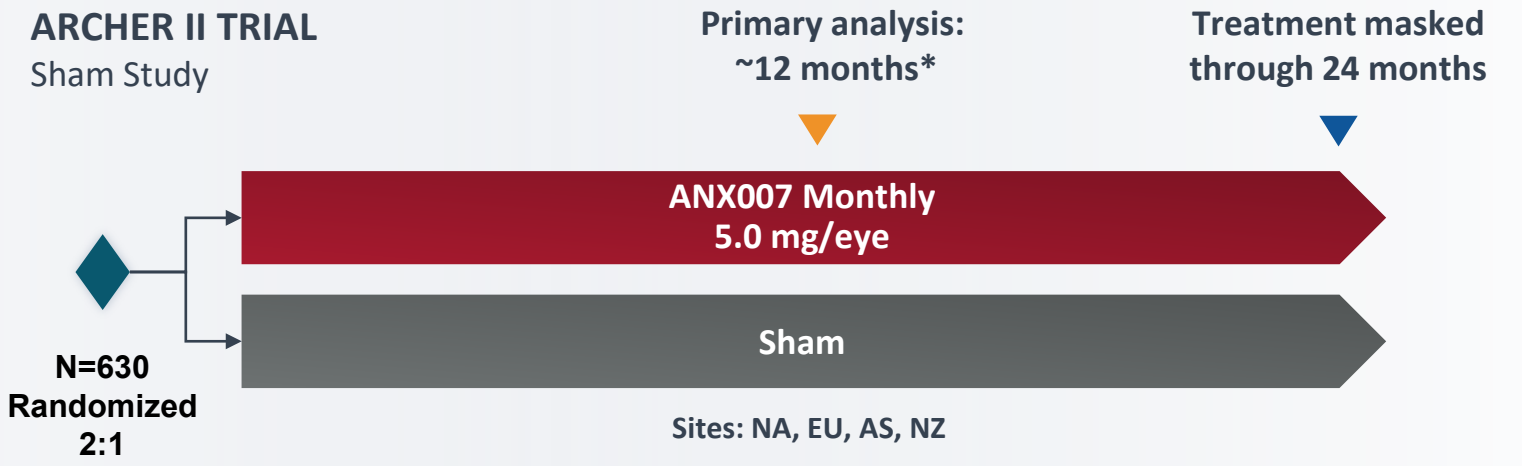
Vitritis – 1
Resolved with topical steroids in 9 days
No Vasculitis

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

*Event Verbatim term listed

ANX007 Global Phase 3 Program Ongoing in Dry AMD / GA

PRIME designation from EMA; Fast Track from FDA



PRIMARY ENDPOINT

Persistent BCVA ≥15-Letter Loss through ~12 months*

*Primary analysis based on accumulation of BCVA ≥15-letter loss target events assessed between months 12-18 from initiation of dosing

SECONDARY ENDPOINTS

Safety, Low Luminance VA (LLVA), Ellipsoid zone (EZ)

ANX007: Vision and Structure Protection via a Novel Neuroprotective Mechanism

ANX007 consistently protected against the loss of visual acuity in the Phase 2 ARCHER study

Protection of photoreceptors, with greatest impact in central subdomains that better correlate with visual function

Greater effects of ANX007 on function and structure in eyes with less advanced AMD characteristics

ANX007 treatment was generally well-tolerated; no CNV increase; no reports of vasculitis

Global, regulatory-aligned Phase 3 program initiated July 2024