Prevention of Visual Acuity Loss and Preservation of Photoreceptors by ANX007 in Dry Age-Related Macular Degeneration (AMD)/Geographic Atrophy (GA) in the Phase 2 ARCHER Trial, Including in Patients with Less Advanced Disease

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Floretina Meeting 2024

Targeting C1q-Mediated Neurodegeneration – Preservation of Synapses & Neuronal Function

Dr. Ben Barres discovery of C1q's role in neurodegeneration (2007) › **Spawned entire fields and Validated in labs world-wide[1]** › **Anti-C1q protective in several disease models**

Ben Barres, M.D., Ph.D.
Discoverer of C1q Technology
Chair of Neurobiology at Stanford University
Scientific Co-Founder, Annexon

KEY DISCOVERIES:

1. C1q normally functions to eliminate excess synapses in development[1]
2. C1q-mediated synaptic pruning is common pathway of neurodegeneration
3. C1q inhibition protects against synapse loss and neurodegeneration in several disease models[2]

- Alzheimer's disease
- Amyotrophic Lateral Sclerosis
- Frontotemporal dementia
- Geographic Atrophy
- Glaucoma
- Guillain-Barré Syndrome
- Huntington's disease
- Retinal ischemia
- Schizophrenia
- Spinal muscular atrophy
- Traumatic brain injury

[1]Stevens, et al., 2007 DOI 10.1016/j.cell.2007.10.036; Schafer et al., 2012 DOI 10.1016/j.neuron.2012.03.026; Hong, et al., 2016 doi: 10.1126/science.aad8373; Lui et al., 2016 doi.org/10.1016/j.cell.2016.04.001; [2]Yednock, et al, 2022, doi.org/10.1186/s40942-022-00431-y

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

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

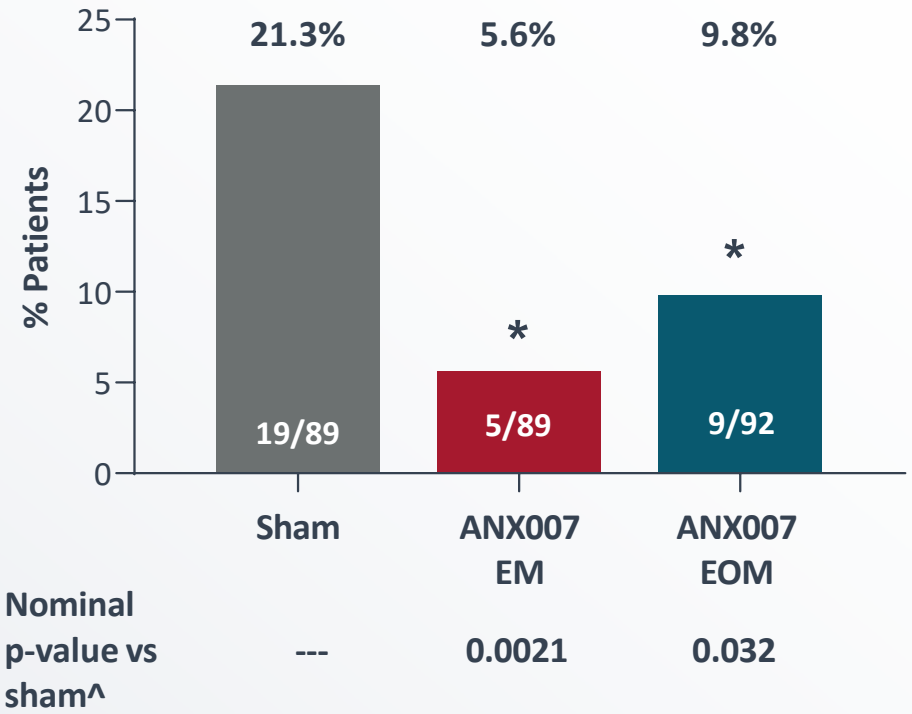
PRESPECIFIED SECONDARY FUNCTIONAL ENDPOINTS

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

Off-treatment
(6 months)

END OF STUDY
Month 18

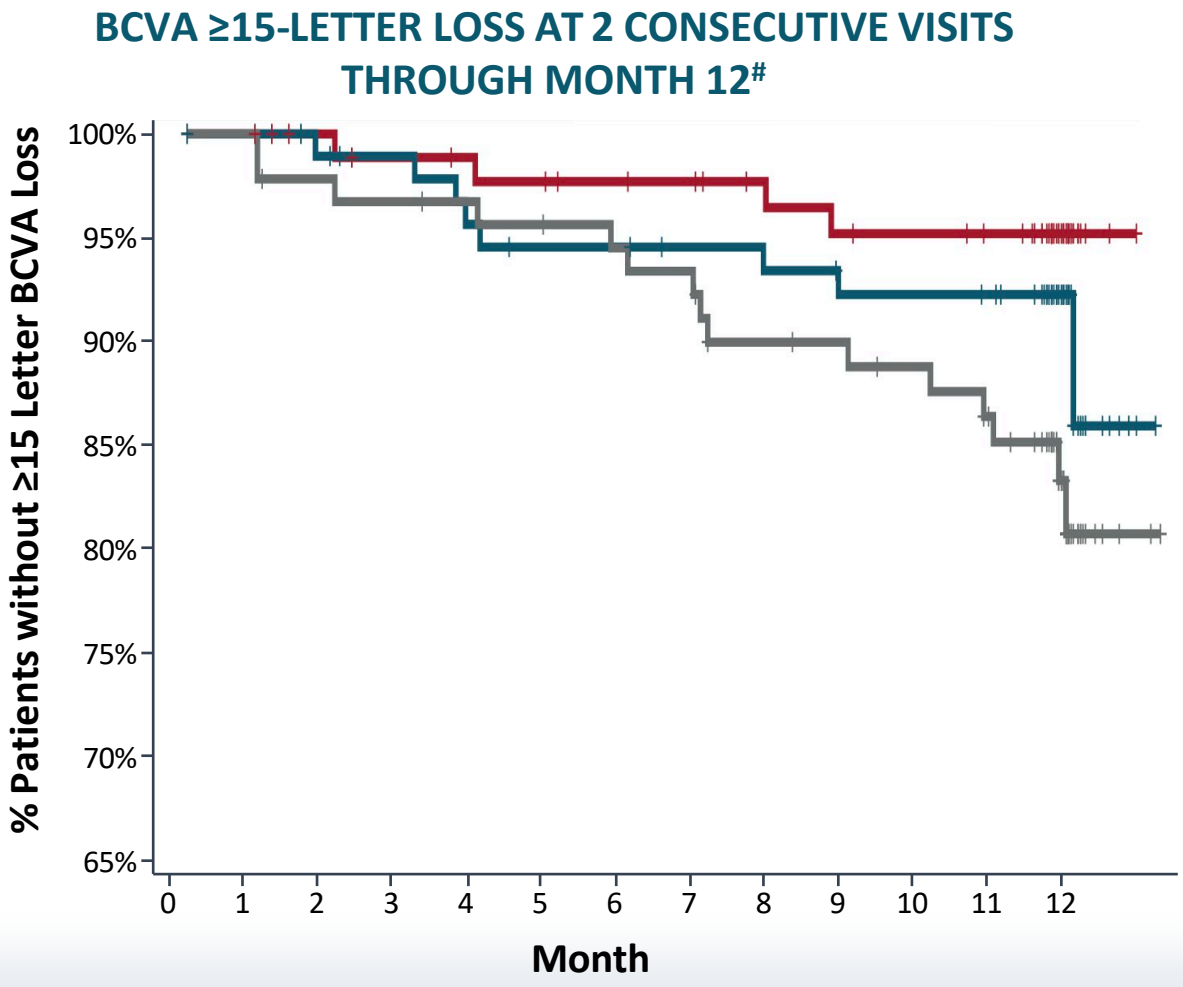
ANX007 Demonstrated Statistically Significant Protection From Vision Loss as Measured by BCVA ≥15-Letter Loss



- First known significant preservation of vision in GA
- Dose-dependent response
- BCVA ≥15-letter loss universally deemed clinically meaningful
- Persistent loss defined as two consecutive visits or last visit

#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

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



EM (n=89)

73% Risk Reduction ANX007 EM

HR (CI) = 0.272 (0.090 to 0.819); p = 0.0098

EOM (n=92)

50% Risk Reduction ANX007 EOM

HR (CI) = 0.504 (0.214 to 1.190); p = 0.0788

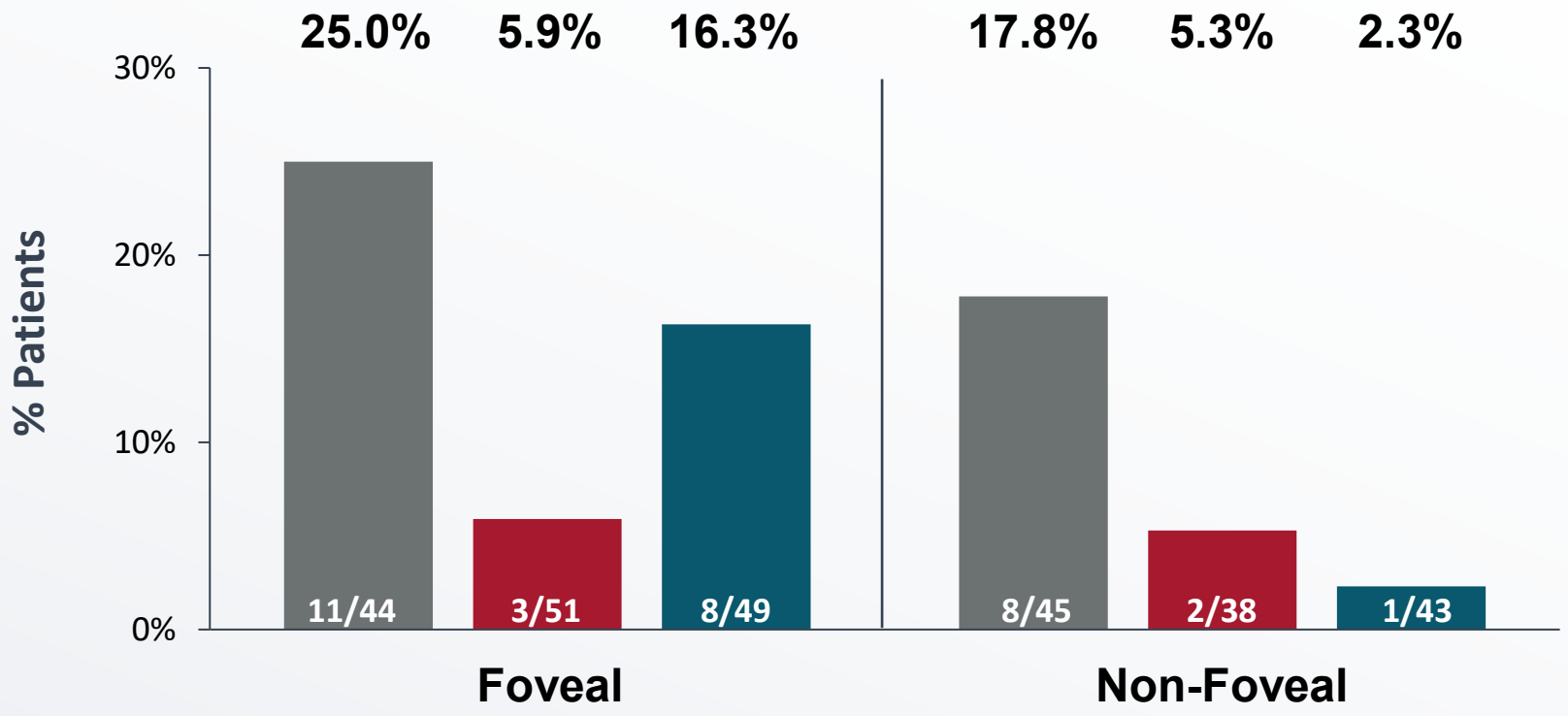
Sham (n=89)

INCREASING ANX007 IMPACT OVER TIME

HR, hazard ratio; Nominal log-rank test (versus sham) p-values are presented;
#Persistent BCVA 15-LL at two consecutive visits including month 12 supported by ensuing (off-treatment) visit
Final data

ANX007 BCVA Subgroup Analysis: Protection from Vision Loss Observed in Both Foveal and Non-Foveal Lesions

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

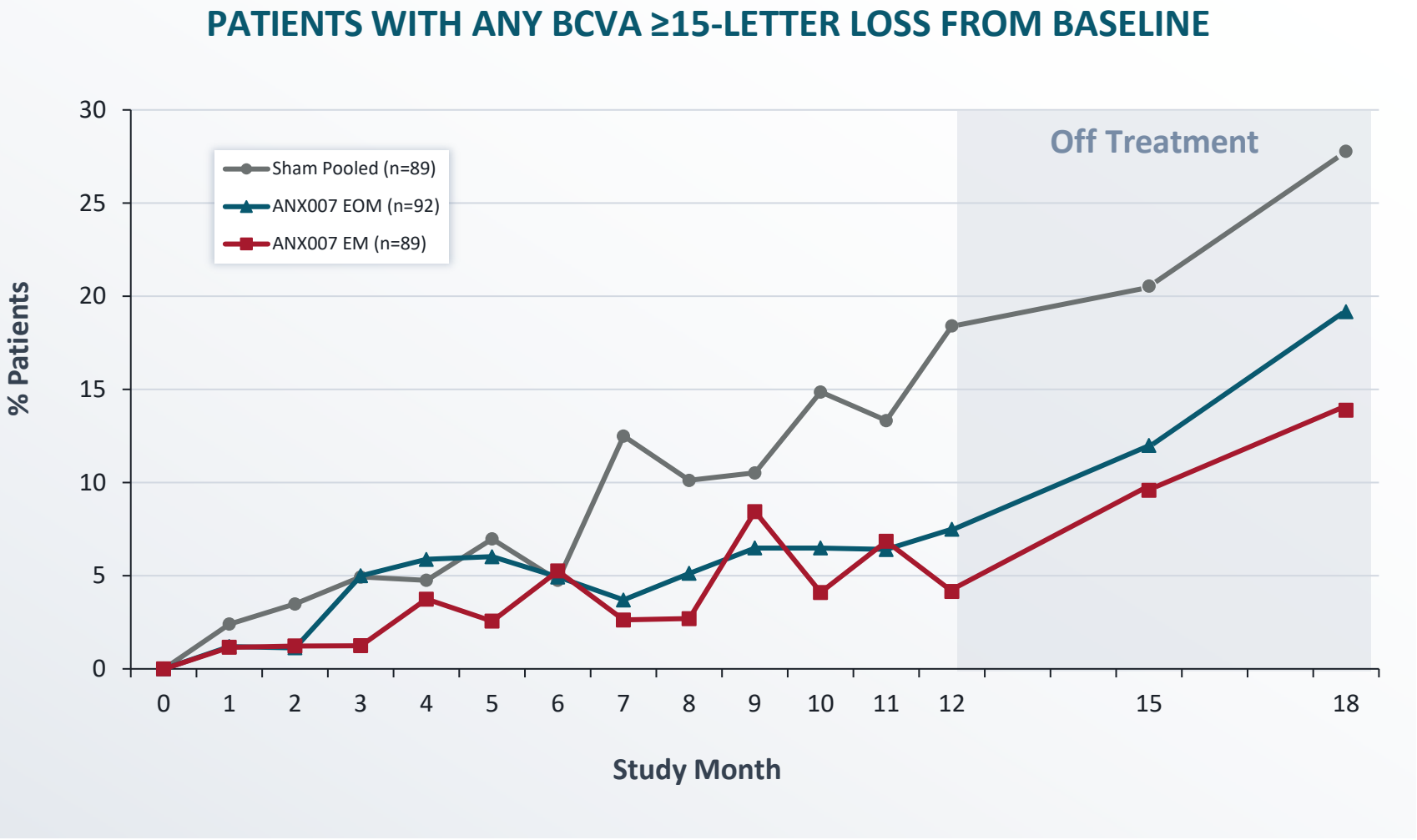


Nominal summary p-value vs. sham^	
ANX007 EM	0.0019
ANX007 EOM	0.0254

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

BCVA ≥15-Letter Loss Accelerated After Cessation of Treatment

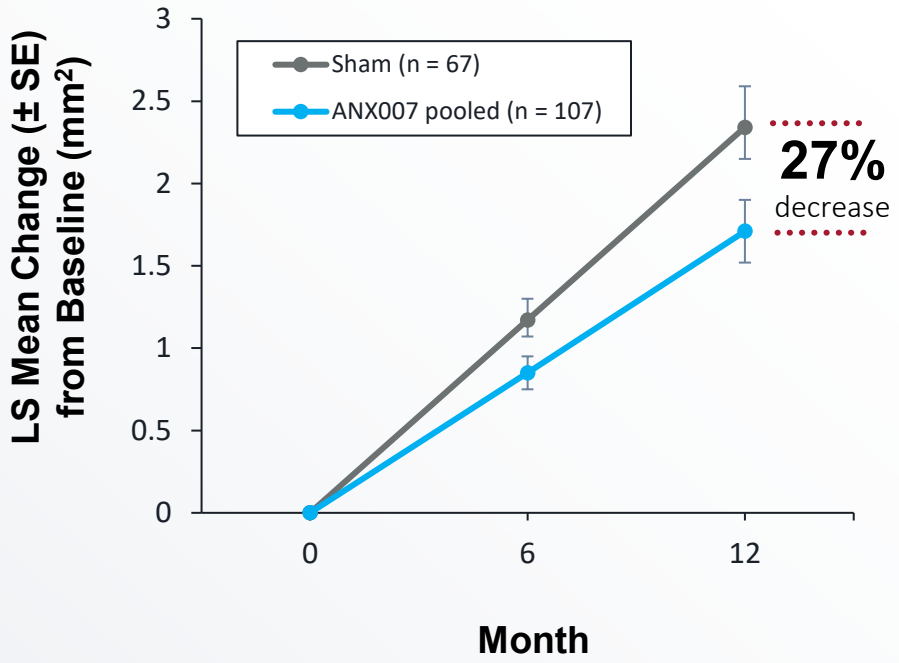
Consistent with true on-treatment drug effect and disease-modifying mechanism of action



- 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 LL increased to parallel that of sham (>1.6% per month)

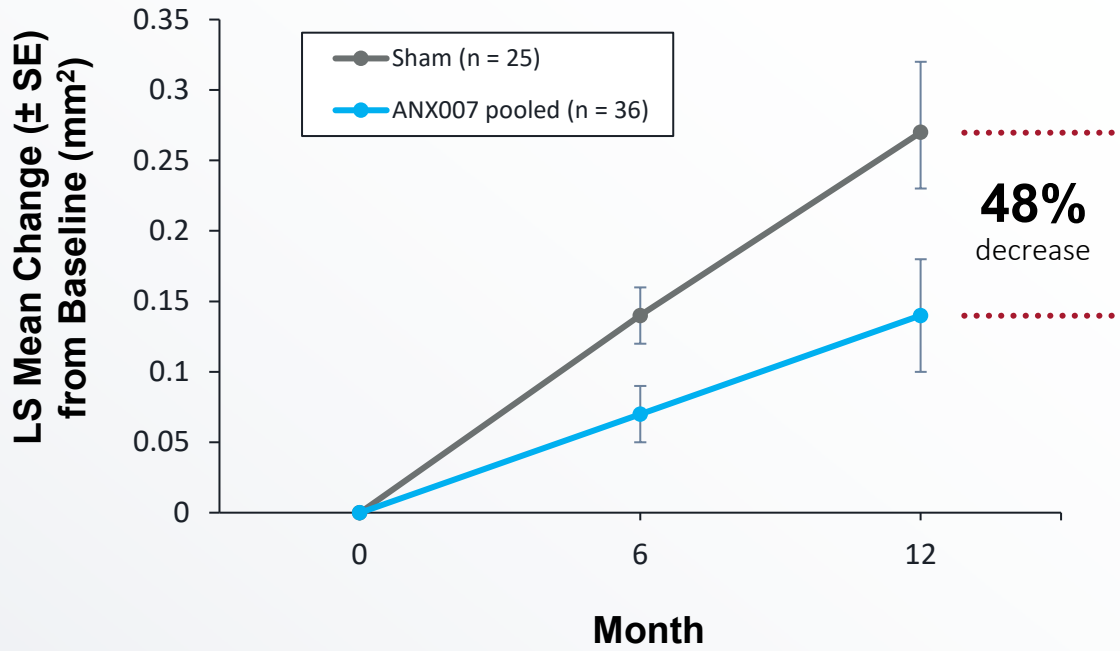
ANX007 Significantly Protected Photoreceptors Across Retina and in Central Subdomain Region Through 12 Months

TOTAL EZ LOSS (EZ = 0 µm thickness)



Nominal p-value^ ANX007 Pooled vs Sham 0.0457

TOTAL EZ LOSS (EZ = 0 µm thickness) CENTRAL 2.0 mm SUBDOMAIN



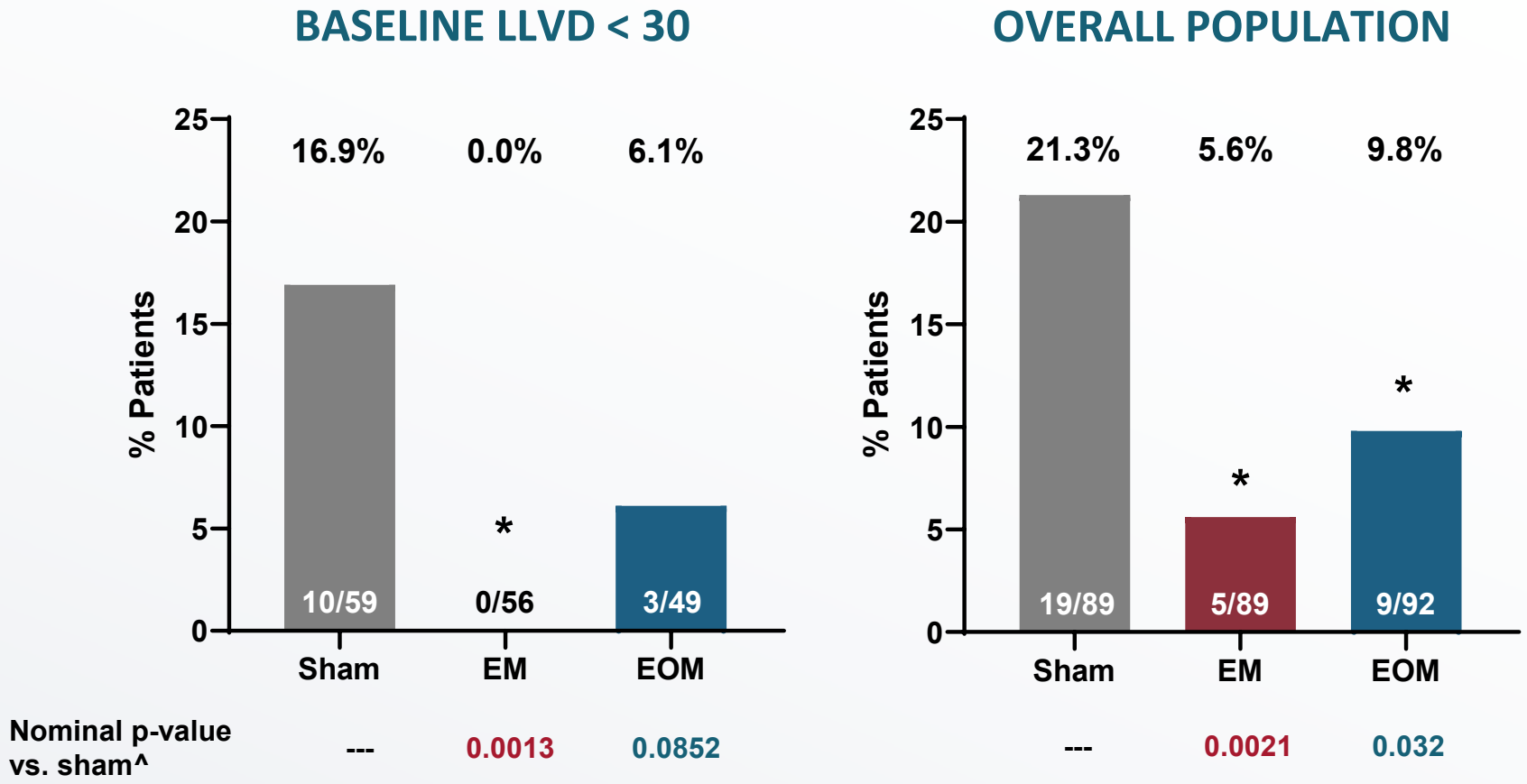
Nominal p-value^ ANX007 Pooled vs Sham 0.0218

^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

ANX007 Functional and Structural Benefits Greatest in Eyes with Less Advanced Dry AMD / GA

Lower low luminance visual deficit = more robust ANX007 response

PERSISTENT BCVA 15-LETTER THROUGH MONTH 12#



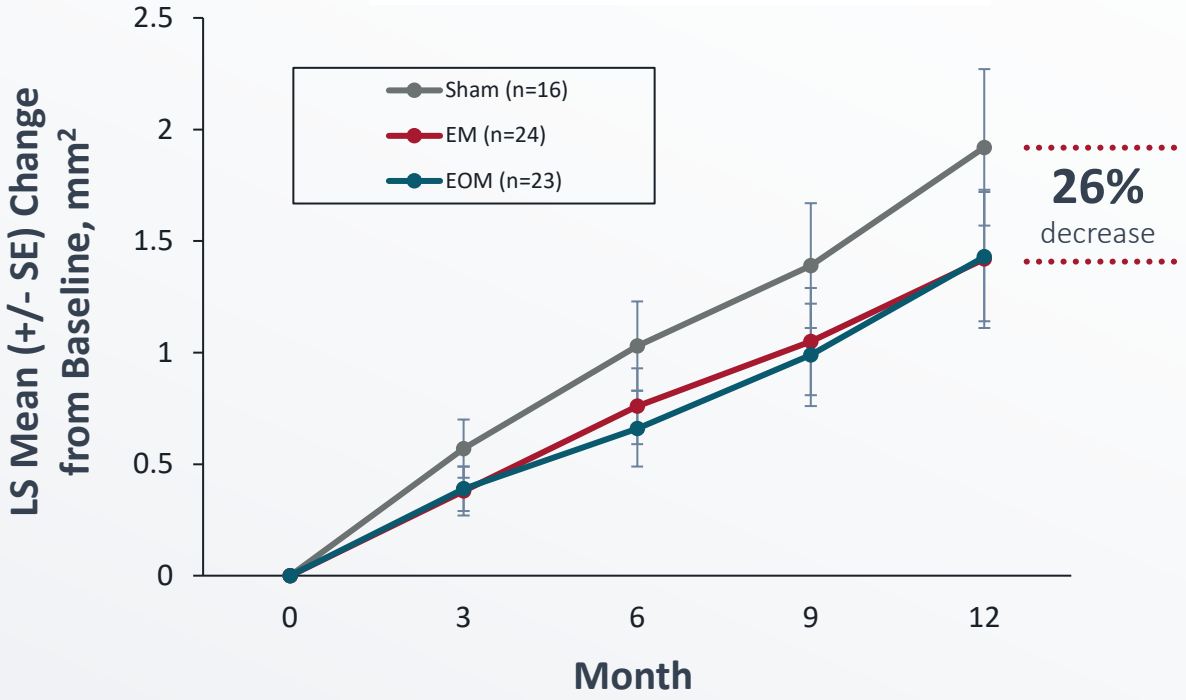
#Persistent BCVA 15-letter loss for two consecutive visits thought month 12 or at last study visit
^Nominal p-value from a Chi-square test in LLVD<30 at baseline and ITT populations ; Final data

ANX007 Functional and Structural Benefits Greatest in Eyes with Less Advanced Dry AMD / GA

Smaller lesions = more robust ANX007 response

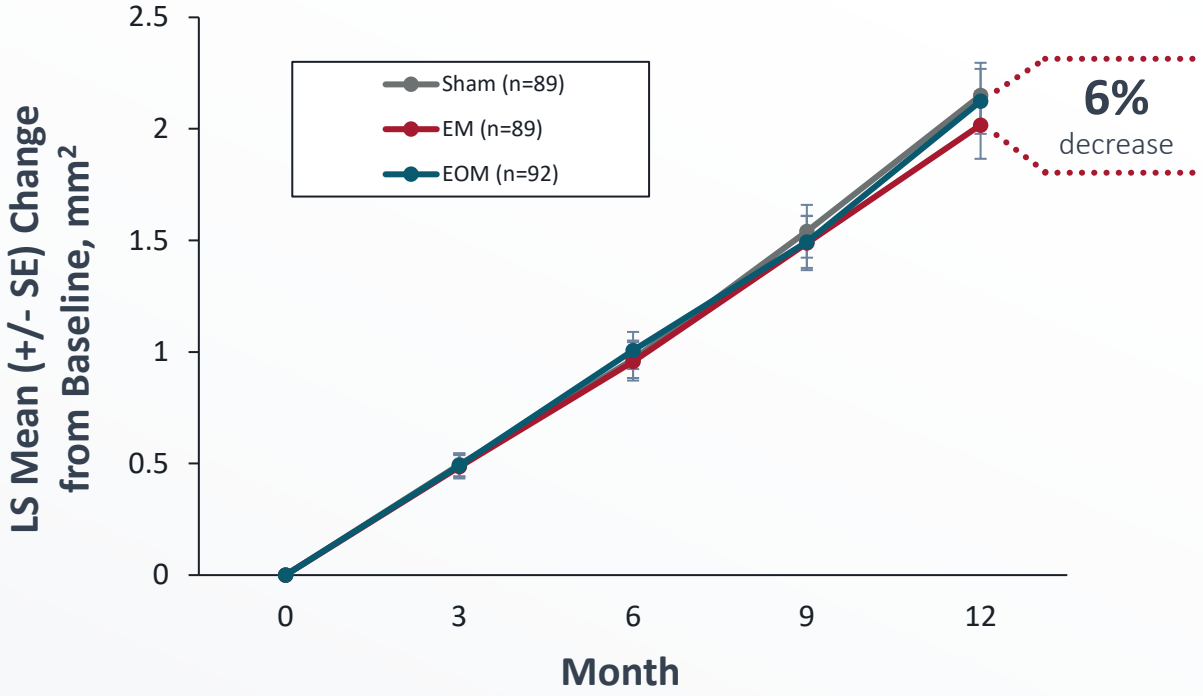
GA LESION GROWTH / RPE LOSS

GA LESIONS < 4.0 mm²



Nominal p-value vs. sham^	EM
	0.46

ALL GA LESIONS



Nominal p-value vs. sham^	EM
	0.53

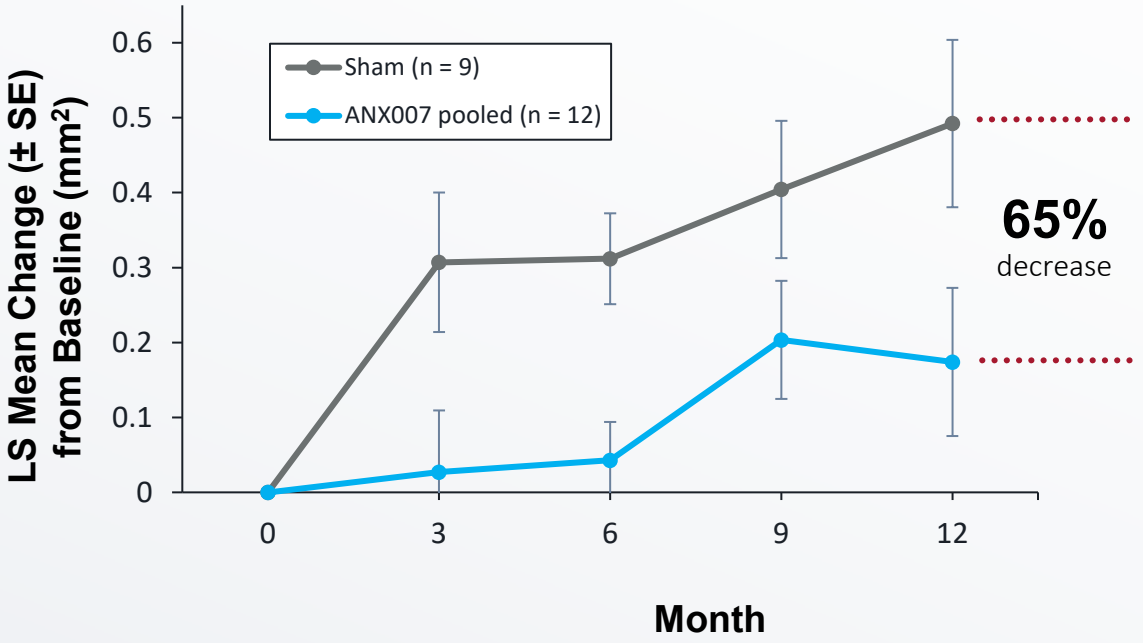
From mixed model for repeated measures;
^Nominal p-value from a Chi-square test in population with baseline lesion size < 4.0 mm² and ITT population; Final Data

ANX007 Functional and Structural Benefits Greatest in Eyes with Less Advanced Dry AMD / GA

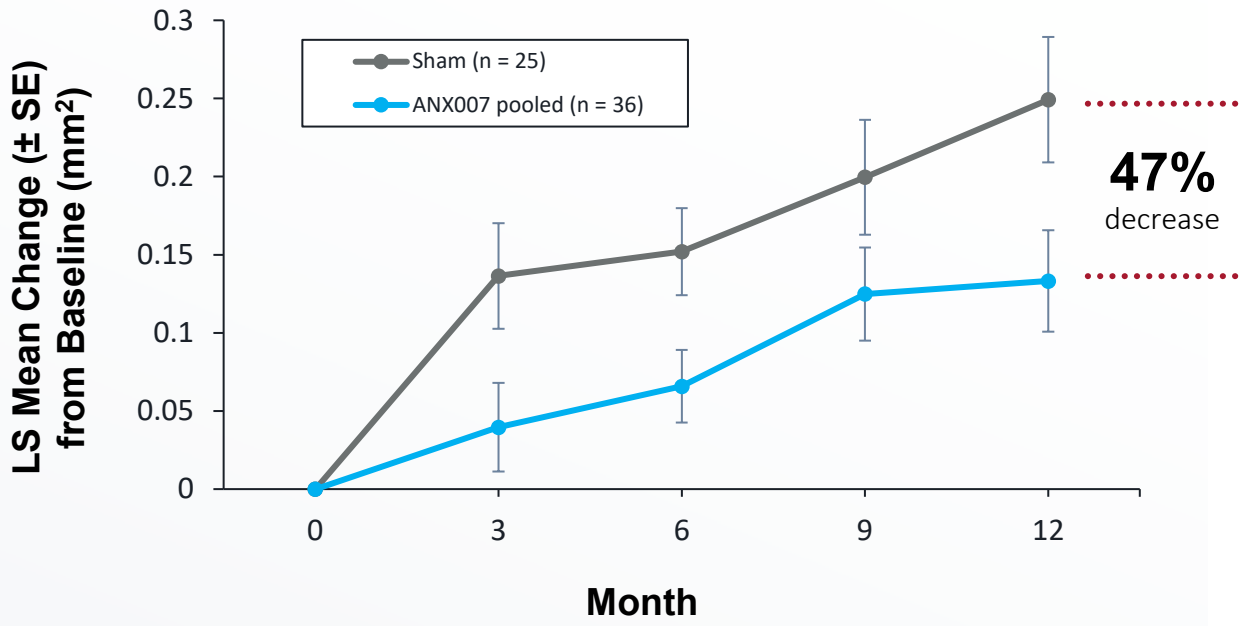
More EZ remaining = more pronounced ANX007 response

TOTAL EZ LOSS (EZ = 0 µm thickness)
CENTRAL 2.0 mm SUBDOMAIN

< 80% EZ LOSS @ BASELINE



< 98% EZ LOSS @ BASELINE



Nominal p-value vs sham^		
	ANX007 Pooled vs Sham	0.0259
	ANX007 Pooled vs Sham	0.0203

^Nominal p-values from a mixed model for repeated measures analysis; Heidelberg Spectralis OCT population with baseline OCT data; excludes patients with >80% and >98% loss 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			

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

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

ANX007: A Novel Neuroprotective Agent Demonstrating Consistent Vision Protection Now in Phase 3

Blocking C1q for neuroprotection, prevented synapse loss and protected photoreceptors from elimination in animal models

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

ANX007 has even greater effect in eyes with less advanced disease – lower LLVD, smaller GA lesions, more intact EZ

ANX007 was generally well-tolerated with strong benefit / risk profile

Global Phase 3 program NOW ONGOING