Preservation of Function and Structure by ANX007 in Geographic Atrophy: Clinical Results from the Phase 2 ARCHER Trial

Joel Pearlman, MD, PhD, FASRS

On behalf of the ARCHER Investigators

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Financial Interests or Relationships to Disclose

- **4DMT: Principal Investigator; ANNEXON BIOSCIENCES, INC: Principal Investigator; BAYER: Principal Investigator; BOEHRINGER INGELHEIM: Principal Investigator; COGNITION THERAPEUTICS, Principle Investigator; EYEBIO: Principal Investigator; EYEPOINT PHARMA: Principal Investigator; GENENTECH, INC: Principal Investigator; KODIAK SCIENCES, INC: Principal Investigator; NOVARTIS PHARMACEUTICALS CORPORATION: Principal Investigator; OPTHEA LIMITED: Principal Investigator; OXURION: Principal Investigator; ROCHE USA: Principal Investigator; REGENERON PHARMACEUTICALS, INC: Principal Investigator; REZOLUTE BIO: Principal Investigator; SANDOZ PHARMACEUTICAL COMPANY: Principal Investigator; THROMBOGENICS: Principal Investigator.**

Summary of ARCHER Phase 2 Trial

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

ANX007, an anti-C1q Fab antibody administered IVT, **protected against the loss of visual acuity** in the Phase 2 ARCHER study

ANX007 also **demonstrated protection from photoreceptor loss**

ANX007 treatment was **generally well-tolerated;** no CNV increase; no reported cases of vasculitis

C1q Regulates the Health and Function of Neurons (Photoreceptors)

Modulates synaptic and neuronal activity normally, and as part of the neurodegenerative disease process

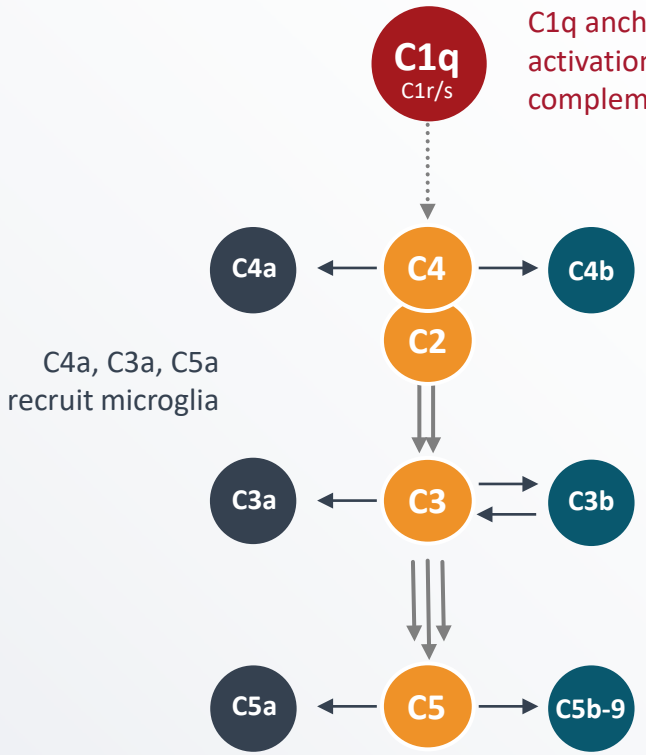
NORMAL ROLE IN CNS DEVELOPMENT

- **C1q recognizes excess functional synapses in development, activating complement and driving synapse elimination[1]**
- Highly regulated process allows stronger synapses to form appropriate circuits

PATHOGENIC ROLE IN NEURODEGENERATION

- **C1q recognizes functional synapses on stressed neurons, driving inflammation, synapse elimination and loss of neurons, such as photoreceptors**
- Inhibition of C1q protective in many neurodegenerative disease models, including:
  - Glaucoma[1]
  - Geographic Atrophy[6]
  - Alzheimer's disease[2]
  - Frontotemporal dementia[3]
  - Guillain-Barré Syndrome
  - Amyotrophic Lateral Sclerosis
  - Huntington's disease
  - Retinal ischemia[5]
  - Schizophrenia
  - Spinal muscular atrophy[4]
  - Traumatic brain injury

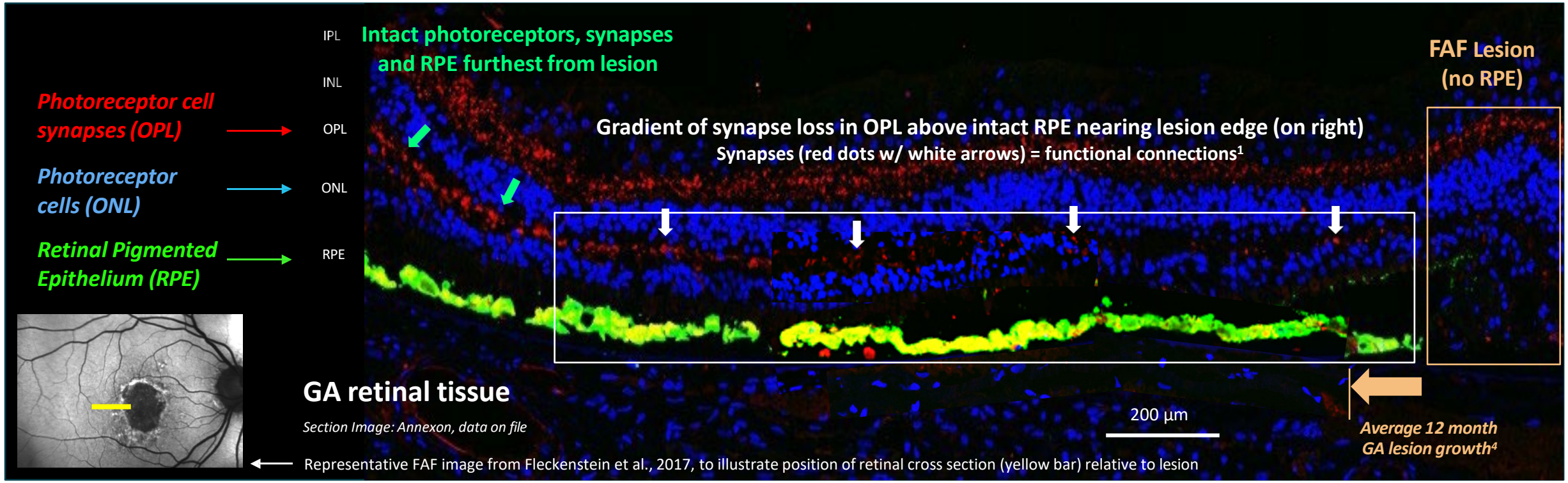
C1q: Initiating Molecule of the Classical Complement Cascade



[1]Stevens, 2007, *Cell* **131**:1164; Howell, et al., 2011 *J Clin Invest.* **121**:1429; Schafer, et al., 2012 *Neuron* **74**: 691; [2]Hong, et al., 2016 *Science*. **352**:712; Dejanovic, et al., 2018 *Neuron* **100**:1322; Yoshiyama et al., 2007 DOI 10.1016/j.neuron.2007.01.010; [3]Lui, et al., 2016 *Cell* 165:921; [4]Vukojicic, et al., 2019, *Cell Rep*. **29**:3087; [5]Williams, et al., 2016 *Mol Neurodegener* **11**:26; [6]Tassoni, et al., SFN 2022; Annexon data on file; Jiao, et al., 2018 *Mol Neurodegener* **13**:45; Katschke, 2018 *Sci Rep*. **8**:7348; Yednock, et al., 2022 *Int J Retina Vitreous* **8**:79; 3Lansita, et al., 2017 *International Journal of Toxicology*

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: ANX007 Phase 2 Trial in GA

ANX007: non-pegylated IVT-administered Fab, fully inhibits C1q

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

Sham	ANX007	ANX007
monthly or every other month	**5mg monthly (EM)**	**5mg every other month (EOM)**
(n=89)	(n=89)	(n=92)

PRIMARY BIOMARKER ENDPOINT

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

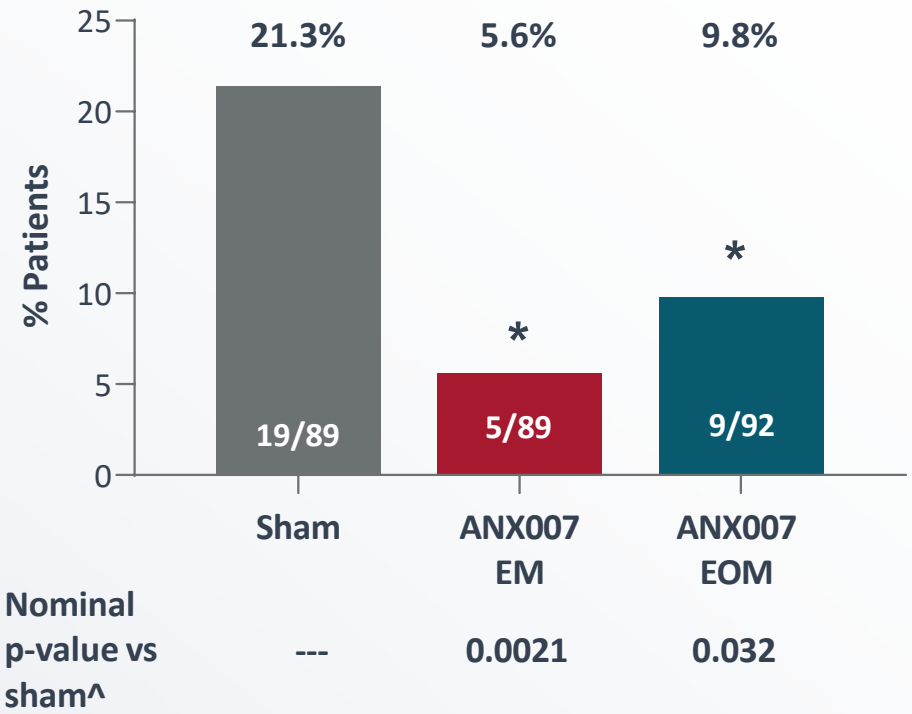
PRESPECIFIED SECONDARY FUNCTIONAL ENDPOINTS

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

Off-treatment
(6 months)

END OF STUDY
Month 18

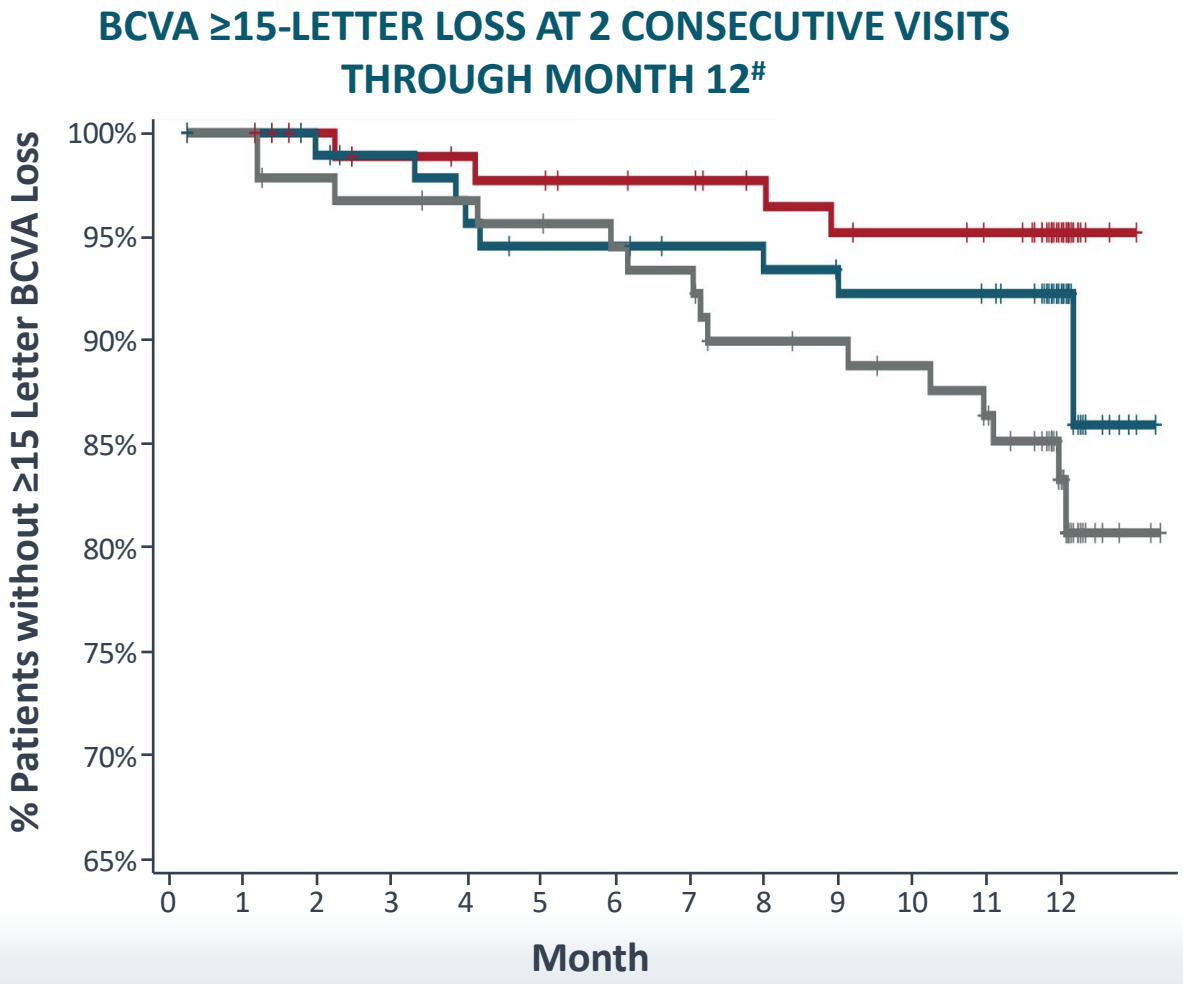
ANX007 Demonstrated Statistically Significant Protection From Vision Loss as Measured by BCVA ≥15-Letter Loss



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

#Persistent 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 ≥15 Letter Vision Loss with ANX007 Monthly Treatment (All Patients)



EM (n=89)

73% Risk Reduction ANX007 EM

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

EOM (n=92)

53% Risk Reduction ANX007 EOM

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

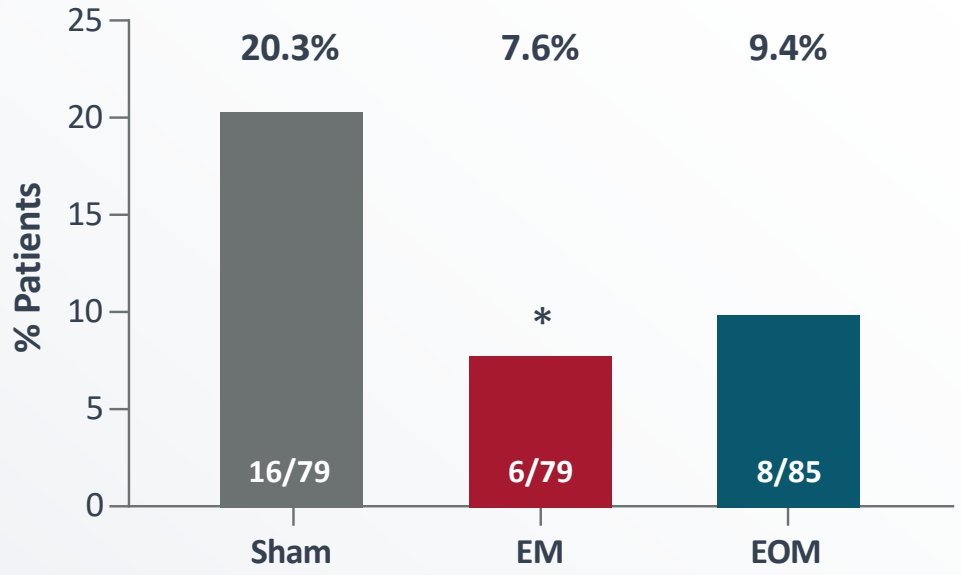
Sham (n=89)

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

Consistent Protection From Vision Loss with ANX007 Treatment Also Demonstrated with LLVA (All Patients)

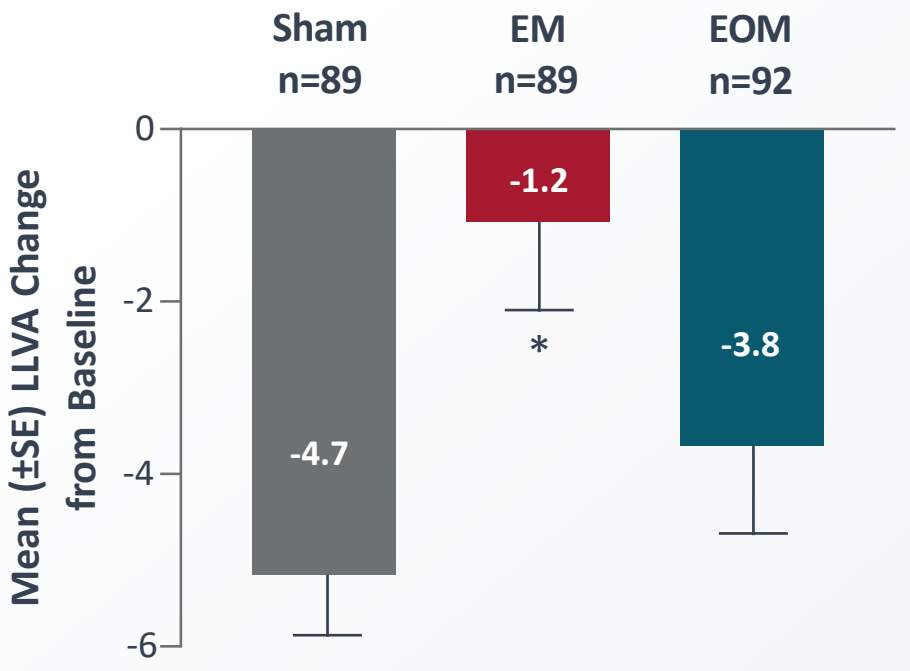
LLVA ≥15-LETTER LOSS THROUGH MONTH 12#



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

MEAN CHANGE IN LLVA AT MONTH 12+

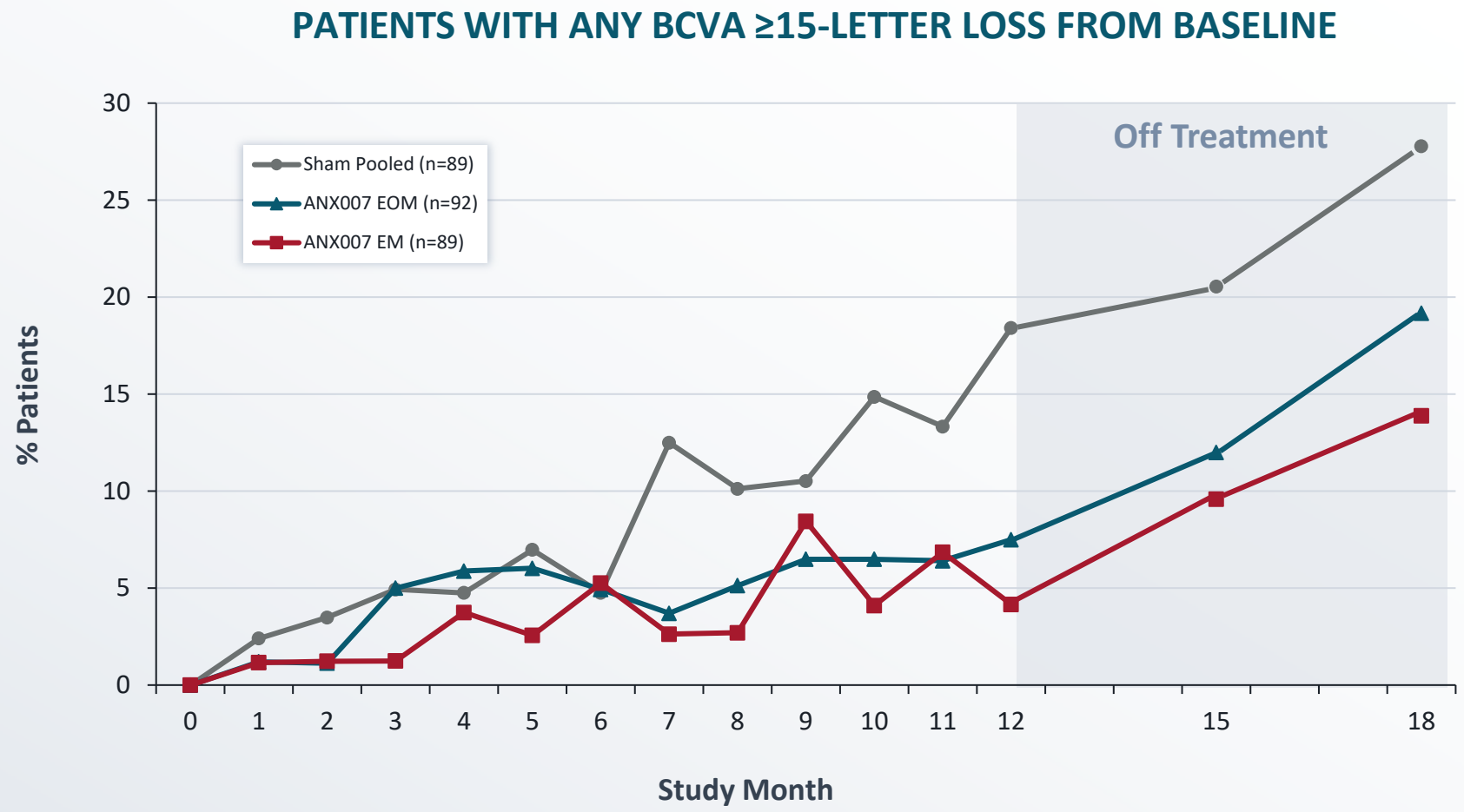


Nominal p-value vs sham^	---	0.0354	0.5890

+Mean, standard error (SE), and p-value based on MMRM adjusting for baseline lesion location, lesion focality, baseline GA lesion, and the baseline GA lesion by visit interaction.
^Nominal p-value from a Chi-square test in ITT population
* Nominal P < 0.05
Final data

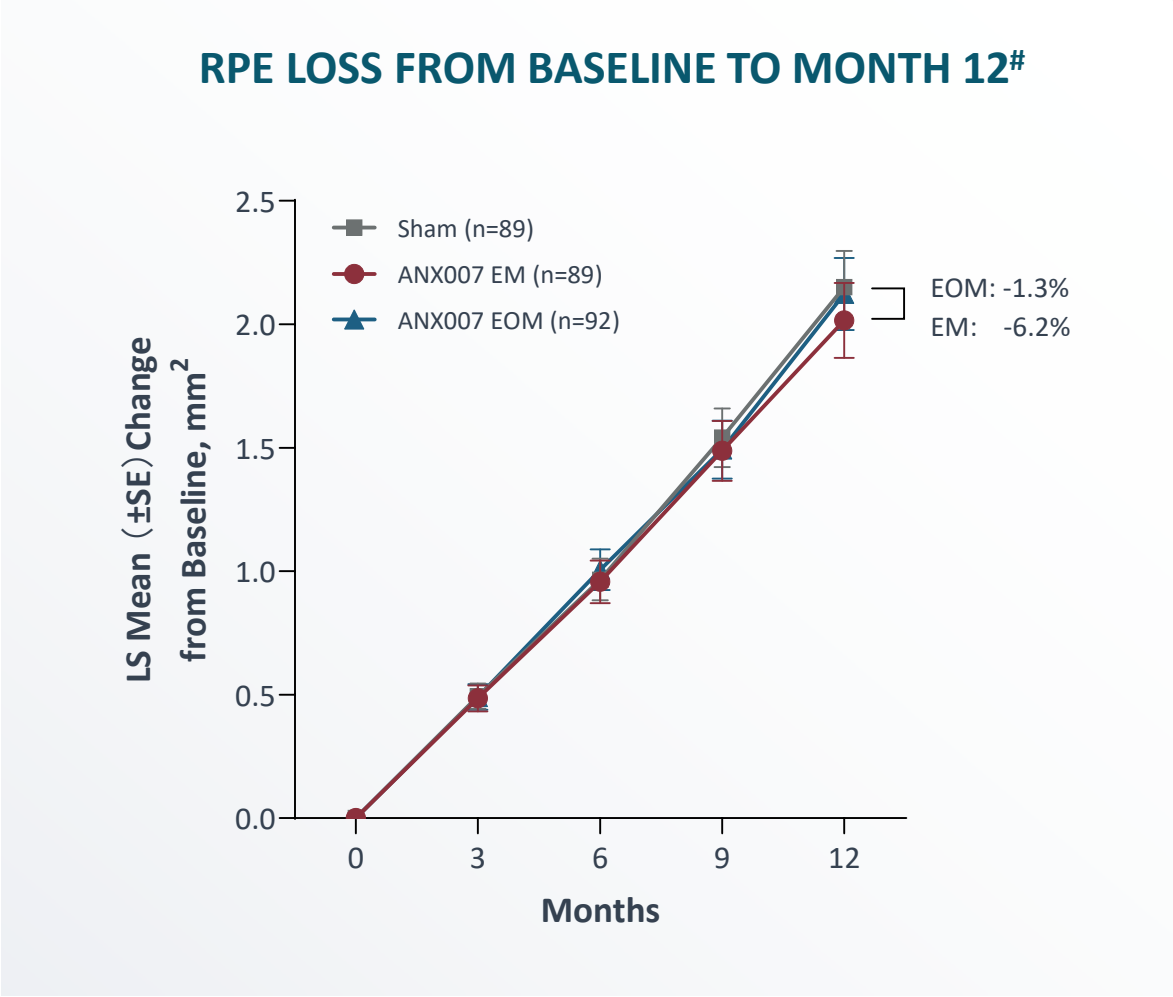
BCVA ≥15-Letter Loss Accelerated After Cessation of Treatment

Visual Function Loss Paralleled Sham in Off-Treatment Period (All Patients)



- 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

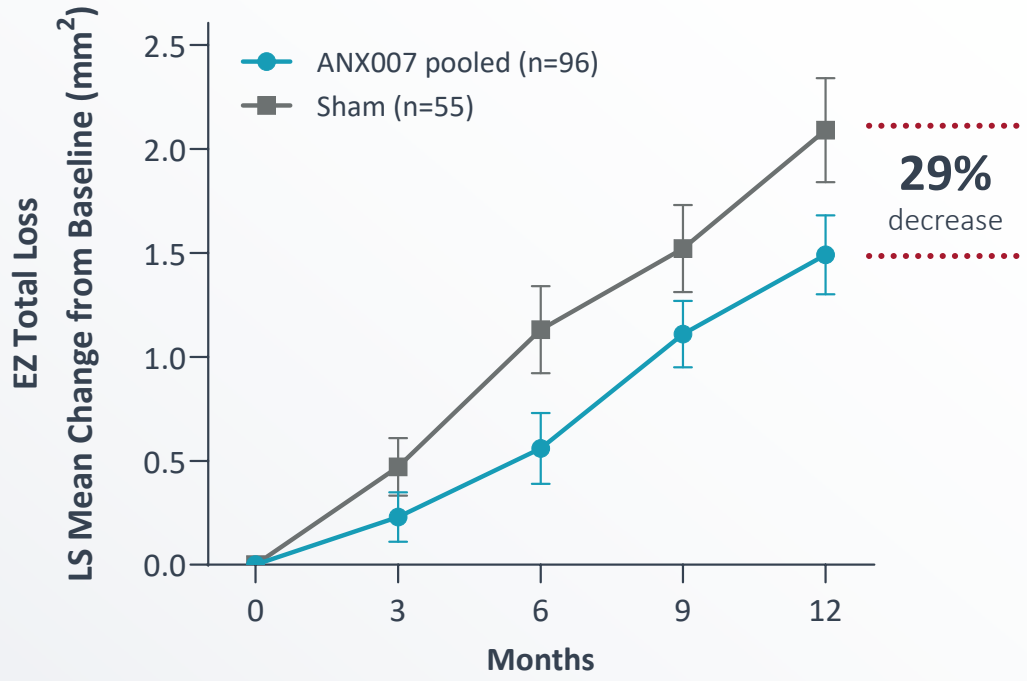
ANX007 Did Not Significantly Reduce Overall RPE Loss, but Effects Increased Over Time



#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.

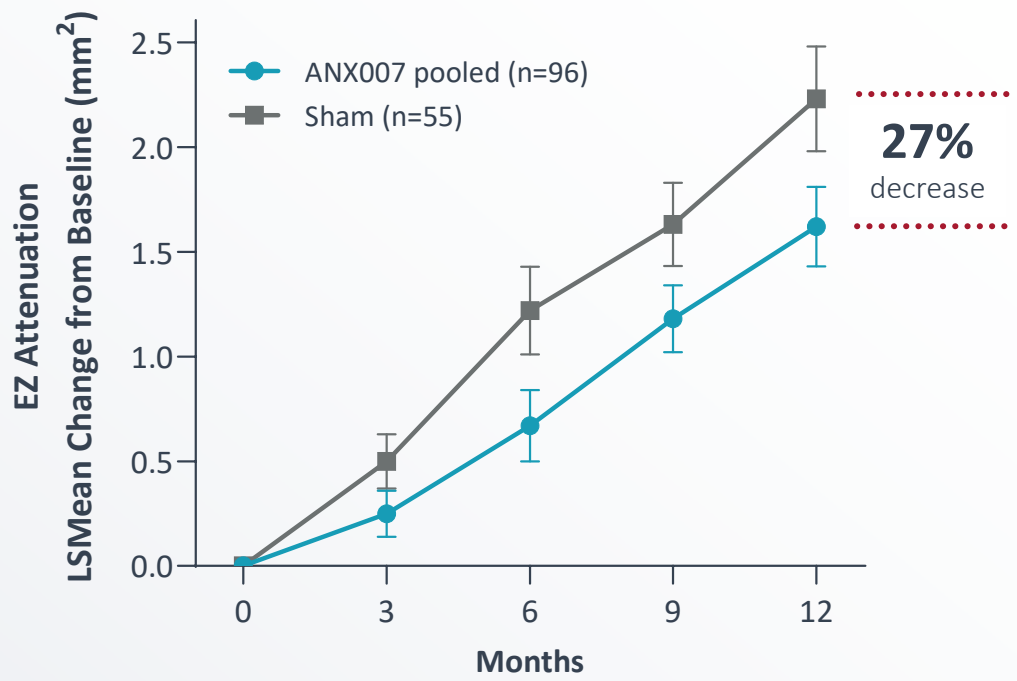
ANX007 Significantly Protected Photoreceptors Through 12 Months

EZ TOTAL LOSS (EZ = 0 μm)*



Nominal p-value vs sham^ ANX007 0.017

EZ ATTENUATION (EZ < 20 μm)*



Nominal p-value vs sham^ ANX007 0.021

^Nominal p-values from a mixed model for repeated measures (MMRM) analysis; Heidelberg Spectralis OCT population with baseline OCT data (n=151)
*Two treatment groups (EM and EOM) were not different statistically

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

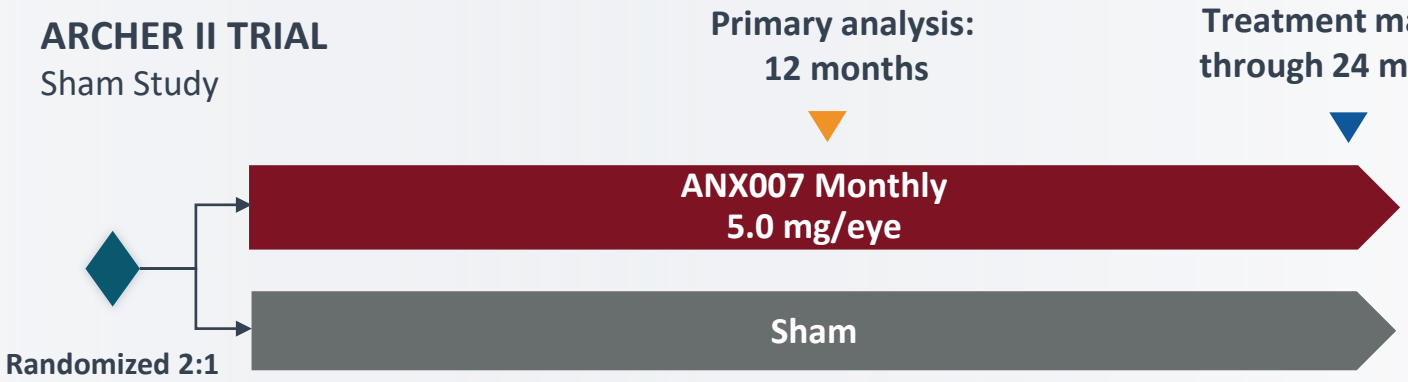
Vitreous Debris – 1
KP on endothelium, prior treatment with topical steroids
No Vasculitis

*Event Verbatim term listed

ANX007 Global GA Pivotal Program to begin Mid-2024

ARCHER II initiation in mid-2024; ARROW trial initiation in late-2024

ARCHER II TRIAL
Sham Study



Sites: NA, EU, UK, AU, NZ

ARROW TRIAL
Injection Comparator

Sites: US Only unless EU approval of Syfovre

PRIME Designation from EMA

PRIMARY ENDPOINT

Persistent BCVA ≥15-Letter Loss through 12 months*

KEY SECONDARY ENDPOINTS

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

*Event-based study endpoint

ANX007: A Novel Neuroprotective Agent Demonstrating Benefit on Visual Acuity and Photoreceptor Structure in GA

- **BLOCKS C1Q FOR NEUROPROTECTION:** Protected synapses and photoreceptors
- **PRESERVED VISUAL FUNCTION:** Reduced risk of BCVA 15-letter loss by 73%
- **PROTECTED RETINAL STRUCTURE:** Photoreceptors and foveal RPE, most closely associated with vision
- **GENERALLY WELL-TOLERATED:** No CNV increase; no reported cases of vasculitis

INITIATING PHASE 3