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STOP THE START

of classical complement-driven diseases

ANX007 Update: ASRS Compilation

August 2024

Overview of ANX007 Geographic Atrophy Program

Structure-confirmed vision benefit in Phase 2 ARCHER study; Phase 3 ARCHER II ongoing

- ✓ Unique neuroprotective MOA, blocking C1q-mediated synapse and photoreceptor elimination
- ✓ Consistent, significant, dose & time-dependent vision protection across pre-specified endpoints
  - — Multiple lines of evidence, including: 12 months on-treatment, fellow-eye and off-treatment analyses
  - — Benefits demonstrated on multiple visual acuity measures (e.g., BCVA, LLVA)
- ✓ First-in-kind visual function benefit supported by protection of structures correlated with visual function
  - — Significant protection of photoreceptors across retina
  - — Enhanced protection of photoreceptors and RPE specifically in the foveal center subdomains – structures correlated with visual acuity
- ✓ Generally well tolerated; no CNV increase in treated vs. sham; no reported cases of vasculitis
- ✓ ANX007 1st and only EMA PRIME Designation in GA – based on functional benefit
- ✓ Global Phase 3 program to confirm ARCHER findings **NOW ENROLLING**

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Overview of ANX007 ASRS Presentations

Visual acuity and structural protection in Phase 2 ARCHER study

C1q-Mediated Neurodegeneration Extensively Researched in Ophthalmic and Neurological Diseases

Functional clinical benefit previously demonstrated in Huntington's disease and ALS, and now in GA

Ben Barres, M.D., Ph.D.
Discoverer of C1q Technology
Scientific Co-Founder, Annexon

Anti-C1q protective in several models, including:

- Geographic atrophy (photoreceptor damage)
- Glaucoma
- Retinal ischemia
- Huntington's disease
- Amyotrophic lateral sclerosis
- Alzheimer's disease
- Frontotemporal dementia
- Spinal muscular atrophy
- Traumatic brain injury

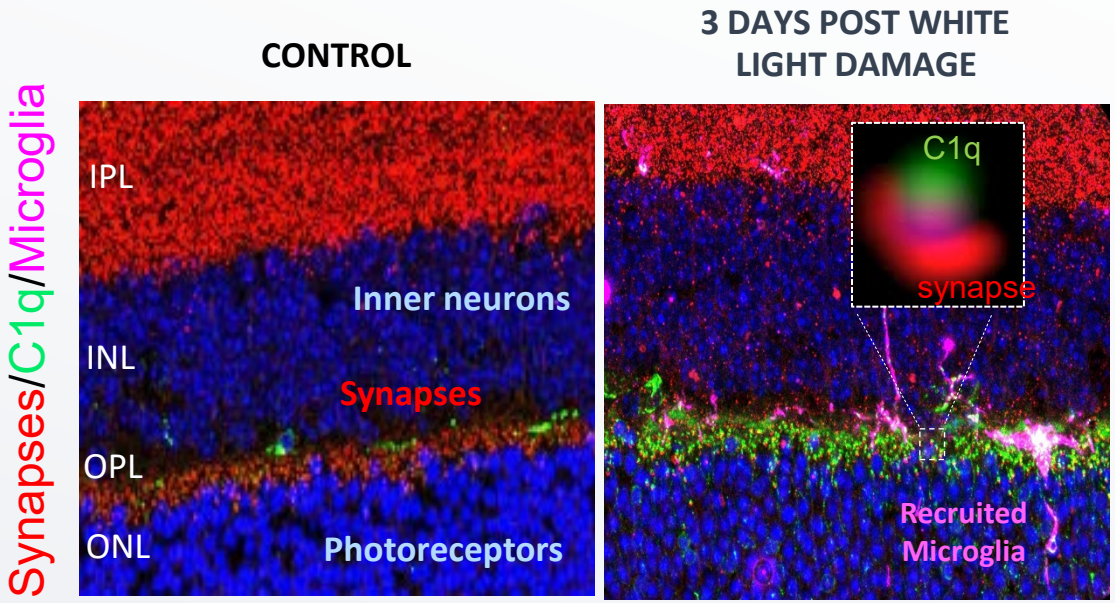
ANTI-C1q PROTECTS AGAINST SYNAPSE LOSS AND NEURODEGENERATION

- Discovered by Annexon co-founder, Ben Barres, spawning an entire field and validated in multiple labs[1]
- Synapse loss correlates with functional decline[2]
- Synapse loss precedes neuronal loss[3]

[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]Davies et al., 1987 *J Neurological Sci* **78**:151; Terry, et al., 1991 *Ann Neurol* **30**:572; [3]Yoshiyama et al., 2007 DOI 10.1016/j.neuron.2007.01.010

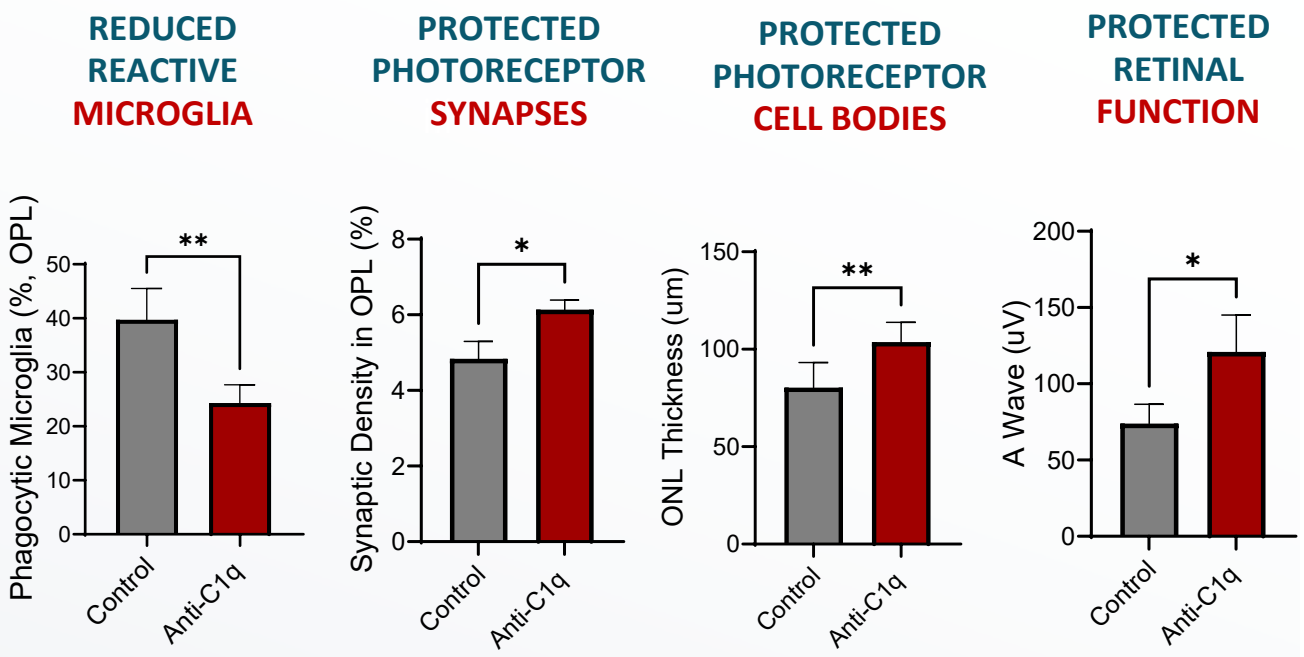
Anti-C1q Protected Photoreceptor Cells and Their Function in Models of Photoreceptor Damage

C1q Deposition on Photoreceptor Cells and Synapses with Light-Induced Damage



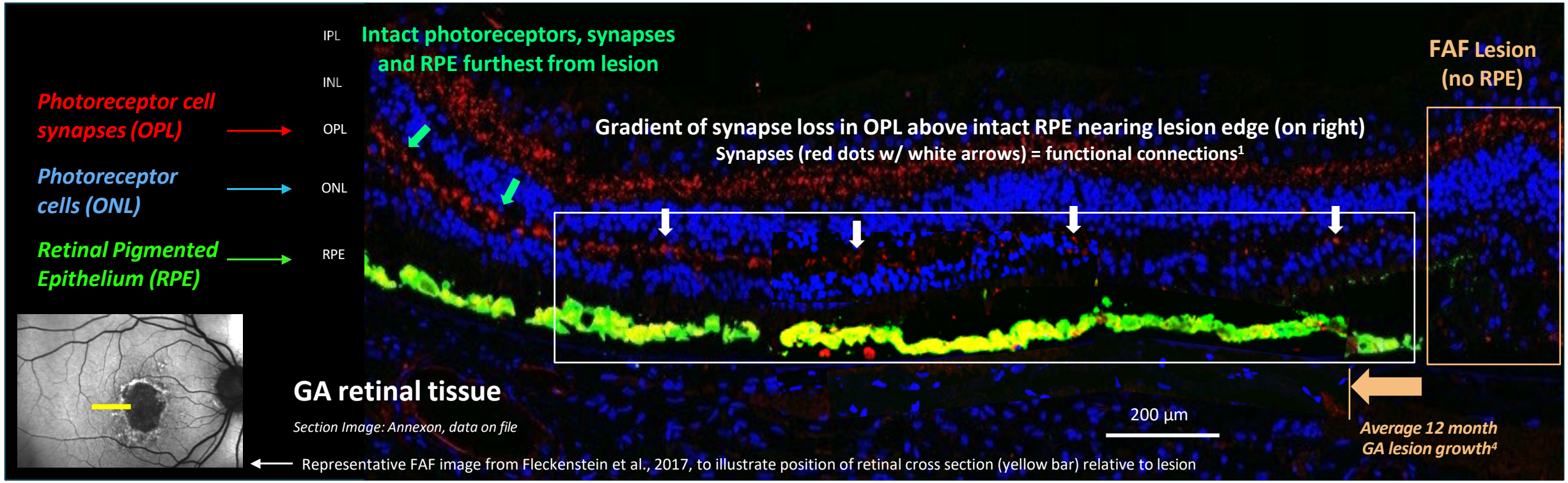
Tassoni, et al., Annexon on file

Anti-C1q Protected Photoreceptors and Function



Photoreceptor Cells, Synapses & Function Lost Prior to RPE 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

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ANX007 Impact on Visual Acuity

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

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 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

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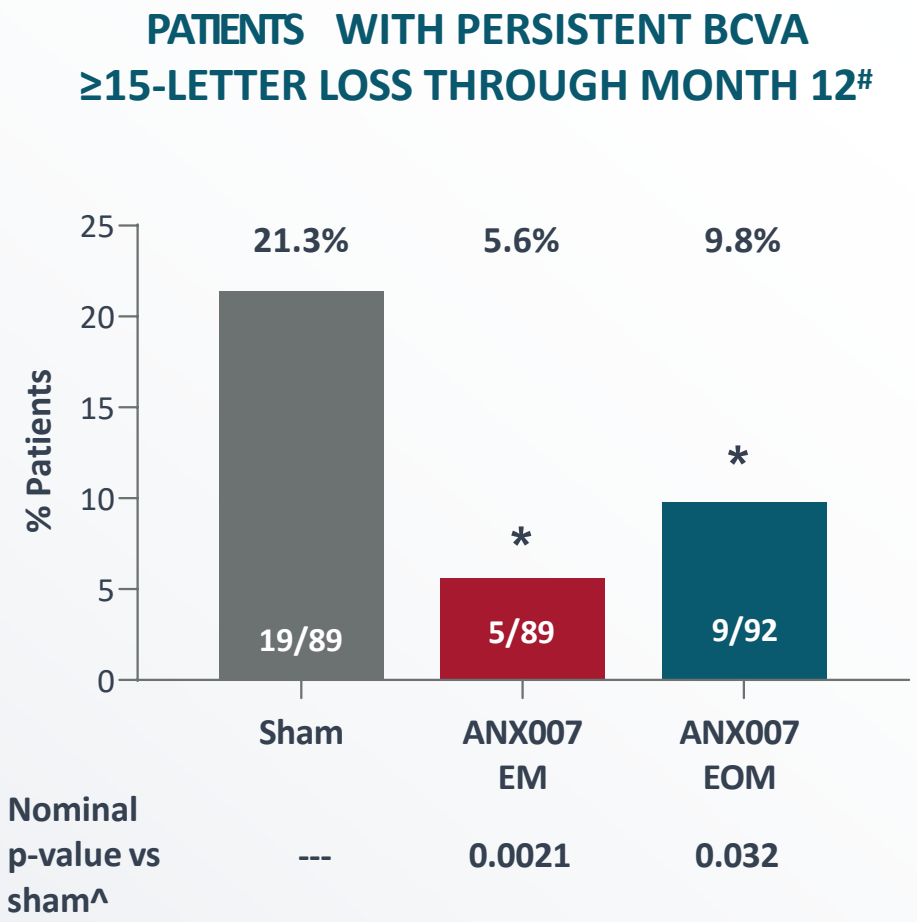
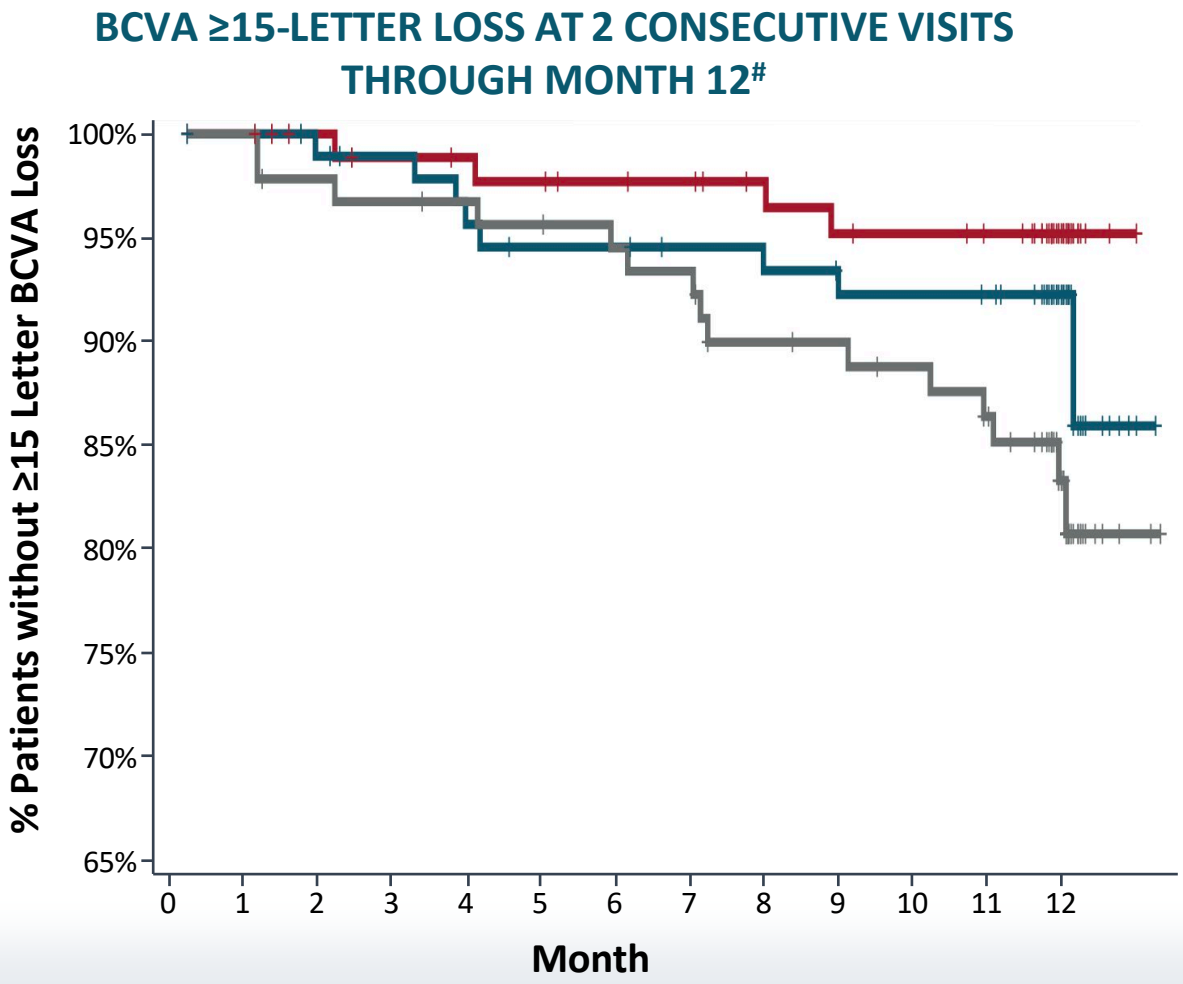
ANX007 Demonstrated Statistically Significant Protection From Vision Loss as Measured by BCVA ≥15-Letter Loss



- First known significant preservation of vision in GA
- Dose-dependent response
- 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 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)

53% Risk Reduction ANX007 EOM

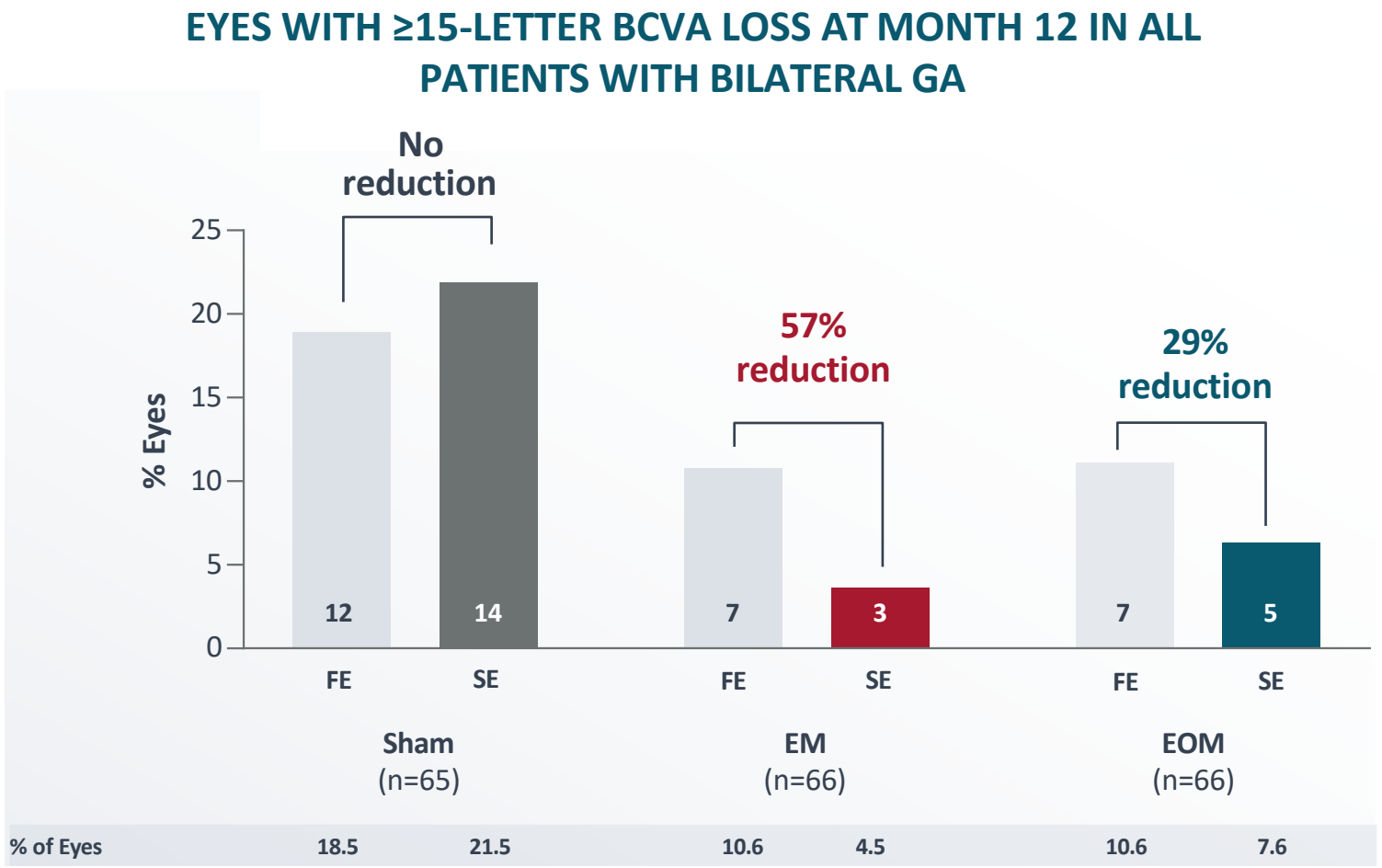
HR (CI) = 0.504 (0.214 to 1.190); p = 0.0788

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

Protection From Vision Loss Supported by Fellow Eye Analysis

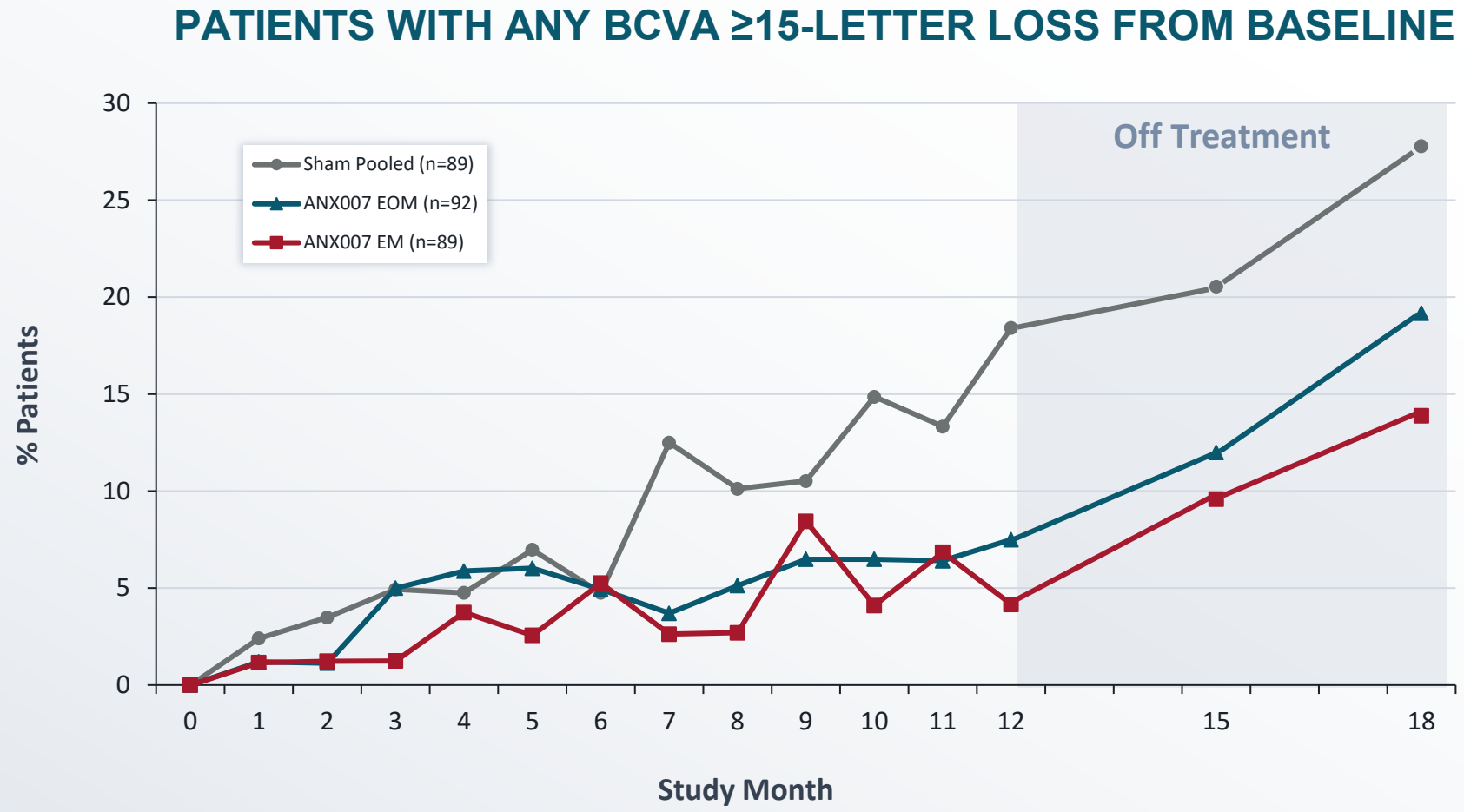


EM, every month; EOM, every other month; Pooled: EM+EOM; FE, fellow eye; SE, study eye
All patients with bilateral GA were included due to small sample size

- Sham: No reduction in BCVA vision loss study vs. fellow eye
- Dose dependent protection from vision loss in ANX007 treated study eyes relative to fellow eyes
  - EM: 57% reduction in 15-letter loss
  - EOM: 29% reduction in 15-letter loss

BCVA ≥15-Letter Loss Accelerated After Cessation of Treatment

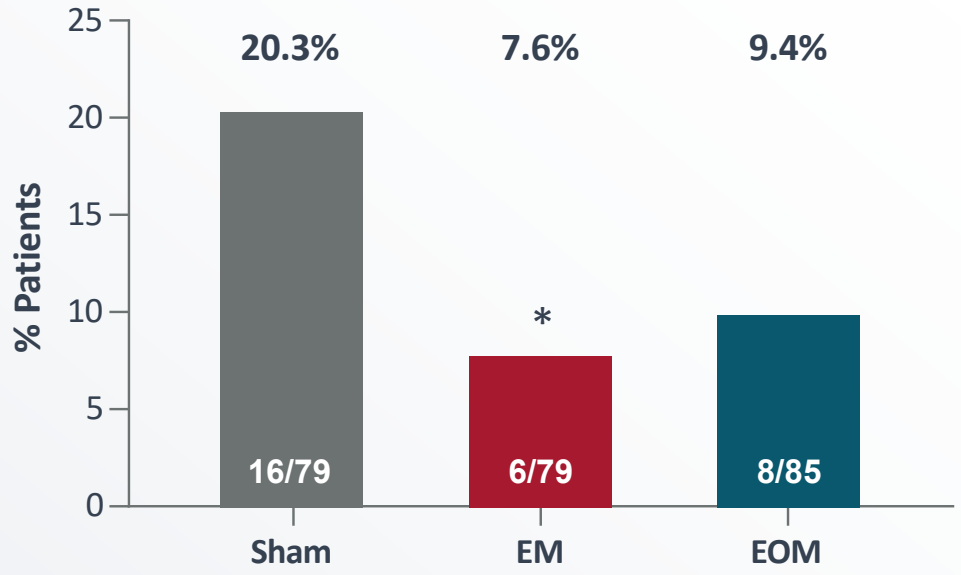
Visual Function Loss Paralleled Sham in Off-Treatment Period; Disease-modification with ANX007 treatment



- 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

Consistent Protection From Vision Loss with ANX007 Treatment Also Demonstrated with LLVA

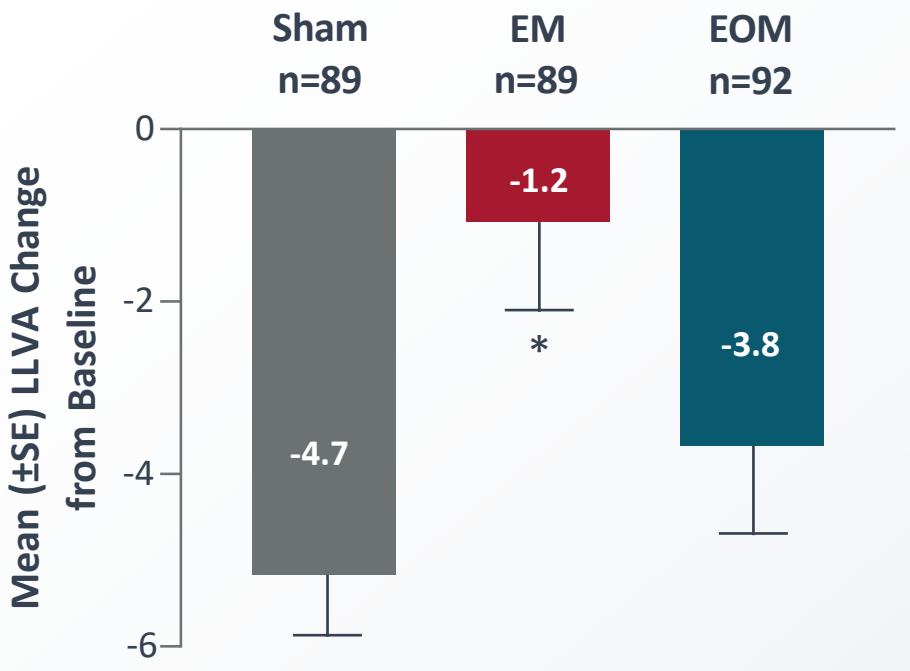
LLVA ≥15-LETTER LOSS THROUGH MONTH 12#



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

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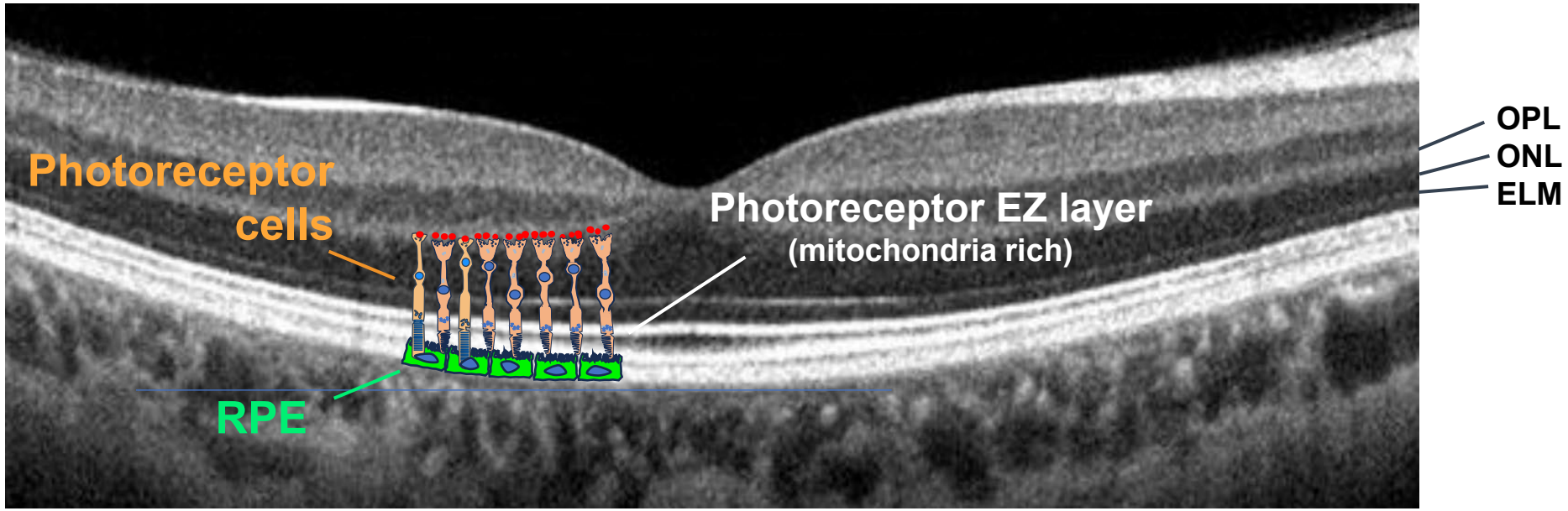
ANX007 Impact on Retinal Structure

Change in OCT Ellipsoid Zone (EZ) Directly Measures Photoreceptor Anatomy



octscans.com

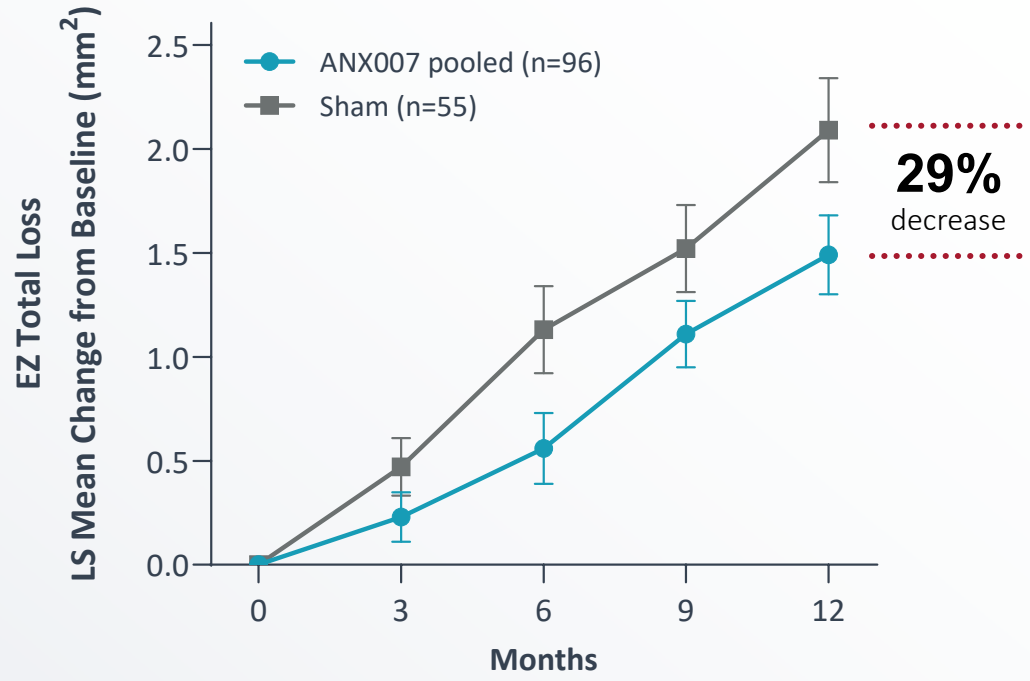
ARCHER EZ Population

Sham	ANX007 EM	ANX007 EOM	Total
71	60	62	193

- 193 patients with OCT scans from Heidelberg Spectralis
- Patient demographics and study eye characteristics were generally well balanced across groups
- Same treatment effect between sham, EM and EOM groups as in whole study population

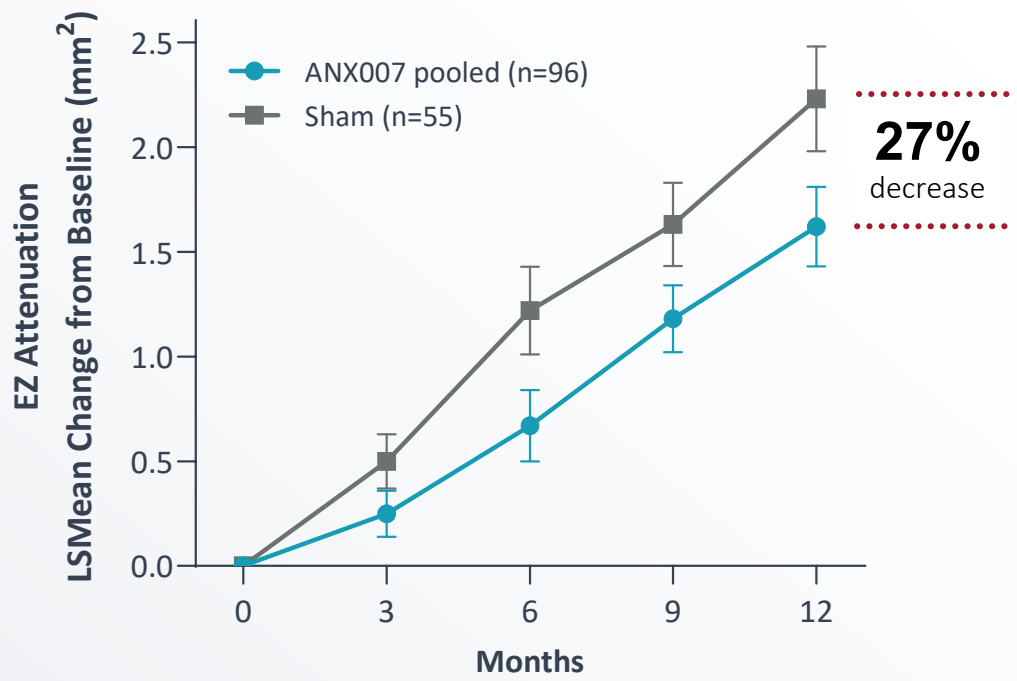
ANX007 Significantly Protected Photoreceptors Across Retina Through 12 Months

EZ TOTAL LOSS (EZ = 0 μm)*



Nominal p-value vs sham^ ANX007 0.017

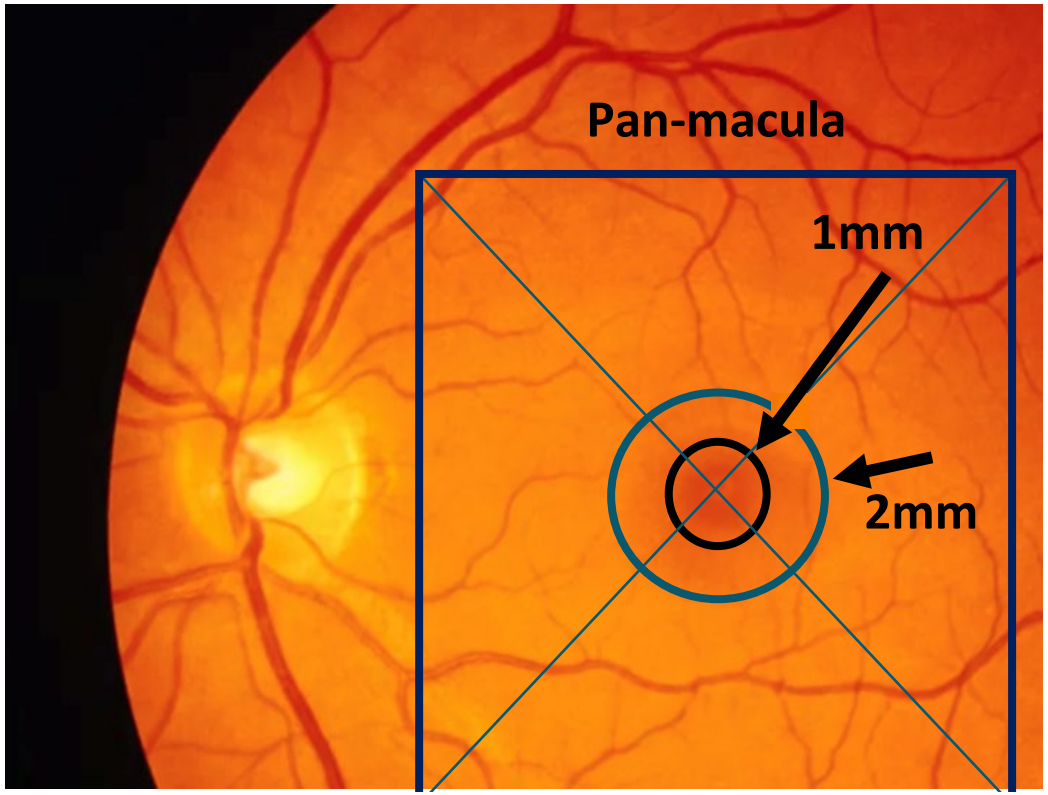
EZ ATTENUATION (EZ < 20 μm)*



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

EZ Disruption in Central Fovea, Not Across Full Retina, Correlates with BCVA in GA Patients^



Parameter	Region	Correlation with GA Eyes (Pearson r value)
EZ Loss	1mm	**-0.49***
	2mm	**-0.54***
	Pan-macula	-0.34 (ns)

*p≤0.05

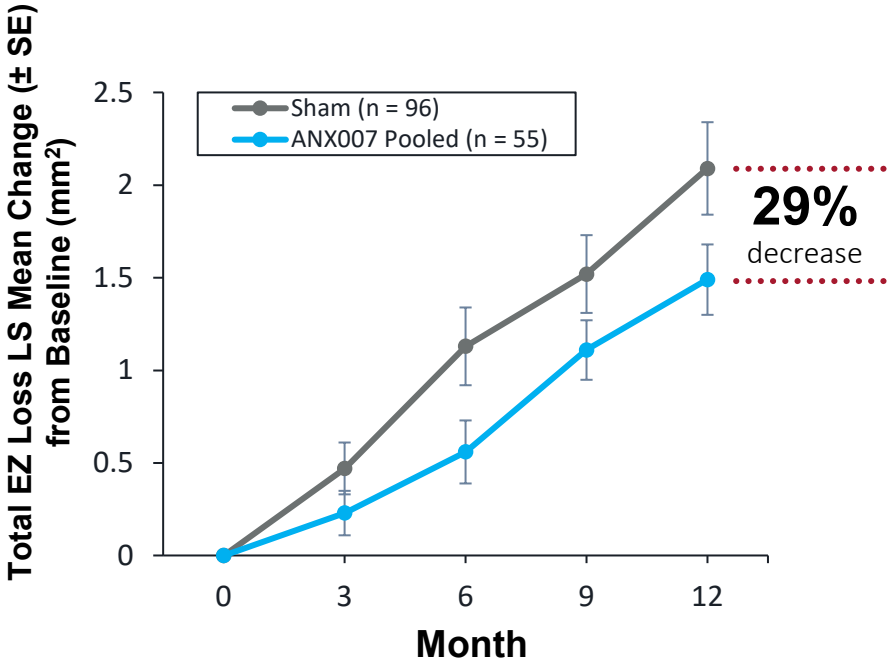
^From Yordi et al (2024) J Pres Med 14: 543

Photoreceptor Protection Through 12 Months in Central Fovea

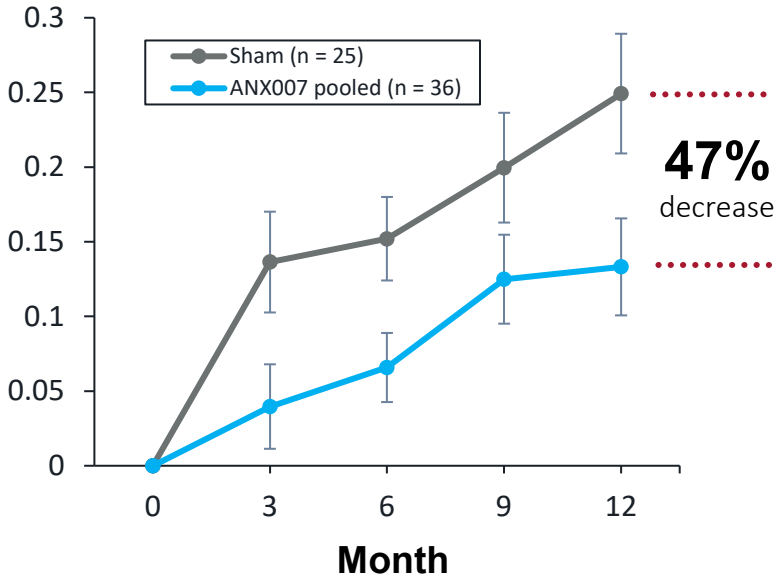
More robust protection with ANX007 in center, area most closely associated with visual acuity, compared to pan-macula

TOTAL EZ LOSS (EZ = 0 μm)*

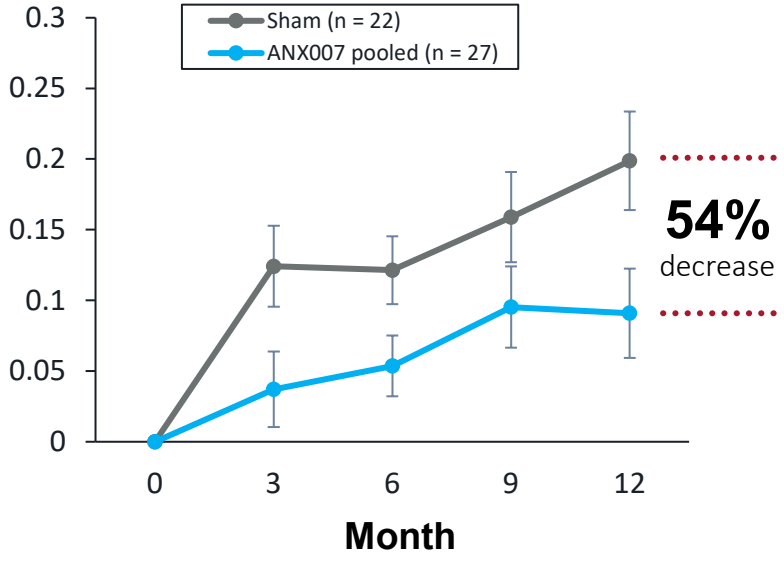
PAN-MACULA



CENTRAL 2.0 MM



CENTRAL 1.5 MM

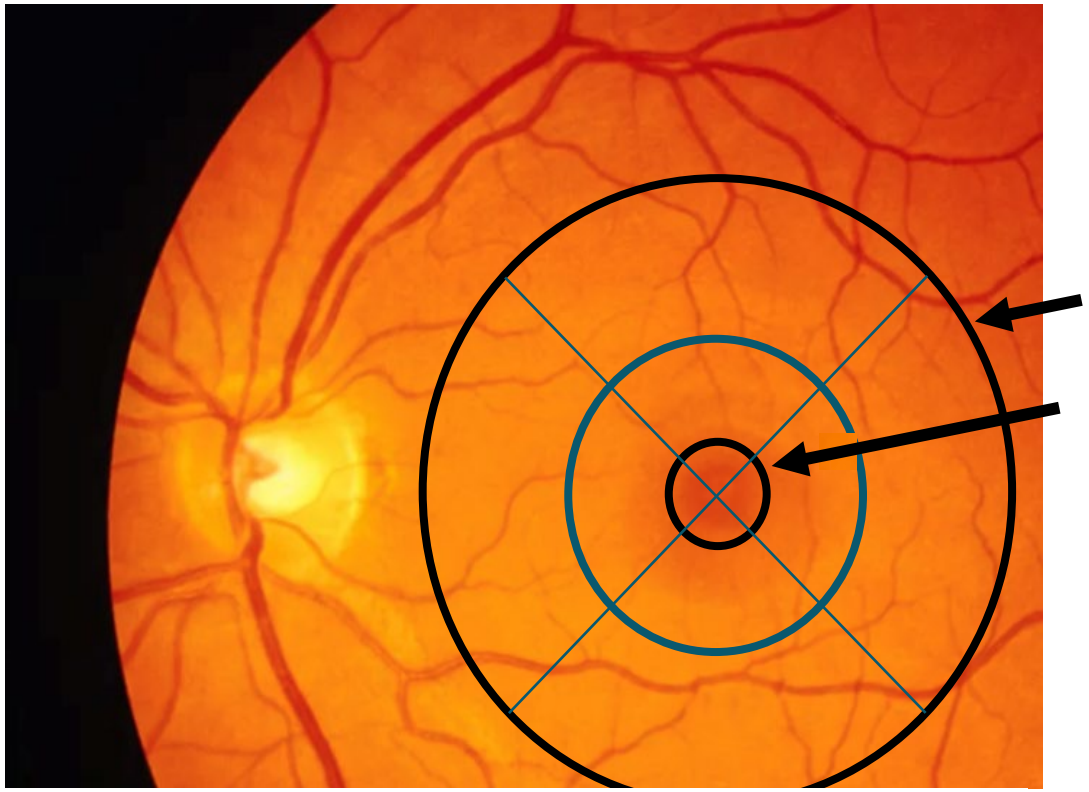


Nominal p-value vs sham^		
	ANX007 0.017	ANX007 0.0203	ANX007 0.017

^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

RPE Loss within the Central Fovea Correlates with BCVA Loss[1]

Correlation in central 1mm seen as early as 6 months; RPE loss across full retina not well correlated with BCVA loss



Spearman Correlation Coefficients Comparing the Changes in RPE Area with BCVA Change Over Time

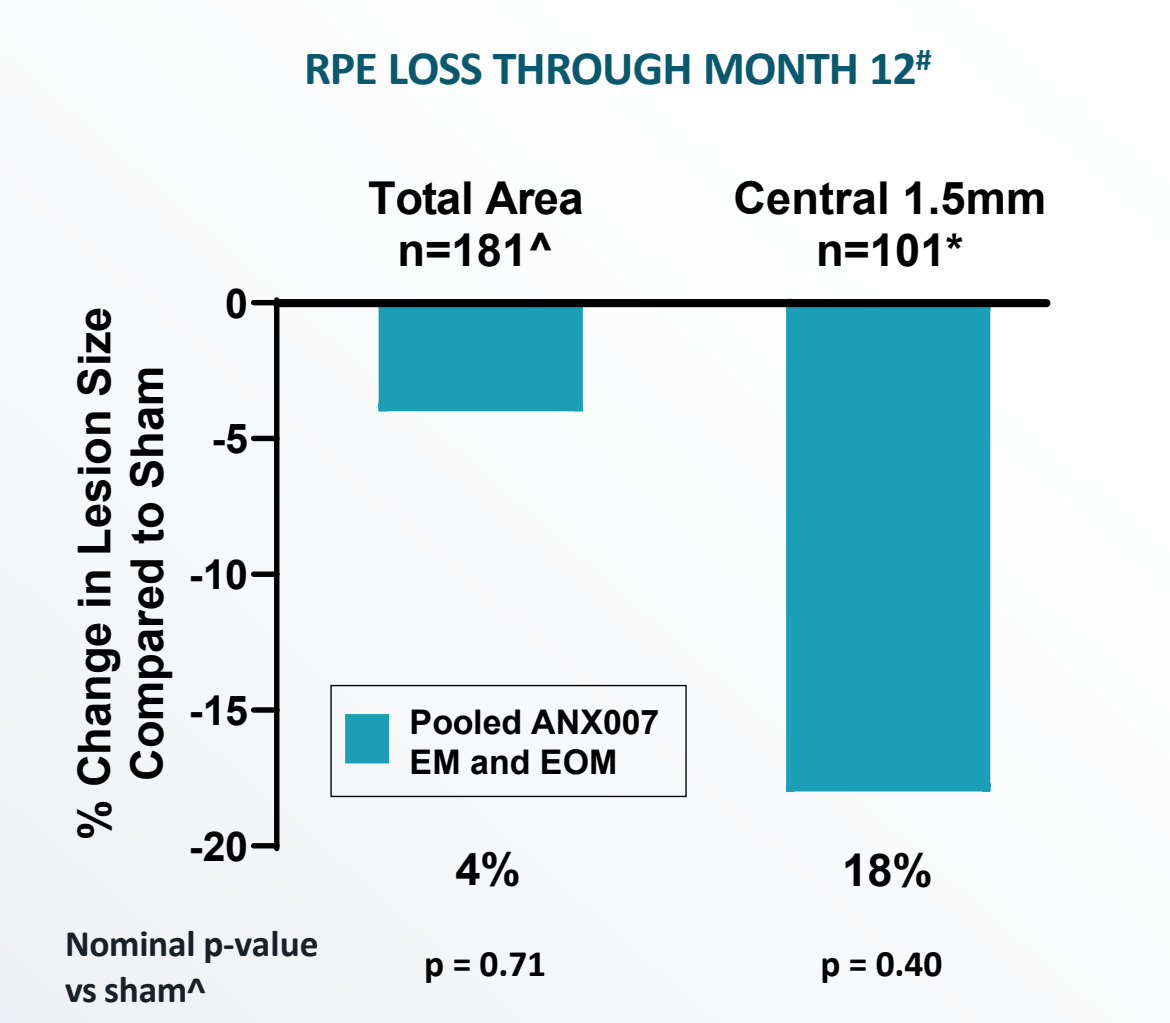
Location	Month 6	Month 12	Month 18
Full 6 mm diameter	p=0.59	p=0.15	**p=0.03**
1mm foveal center	**p=0.03**	**p=0.001**	**p<0.0001**

- Correlation in central 1mm as early as 6 months
- Overall lesion growth correlates after 18 months

1. Sayegh et al, Am J Ophthalmology 2017 179:118-128

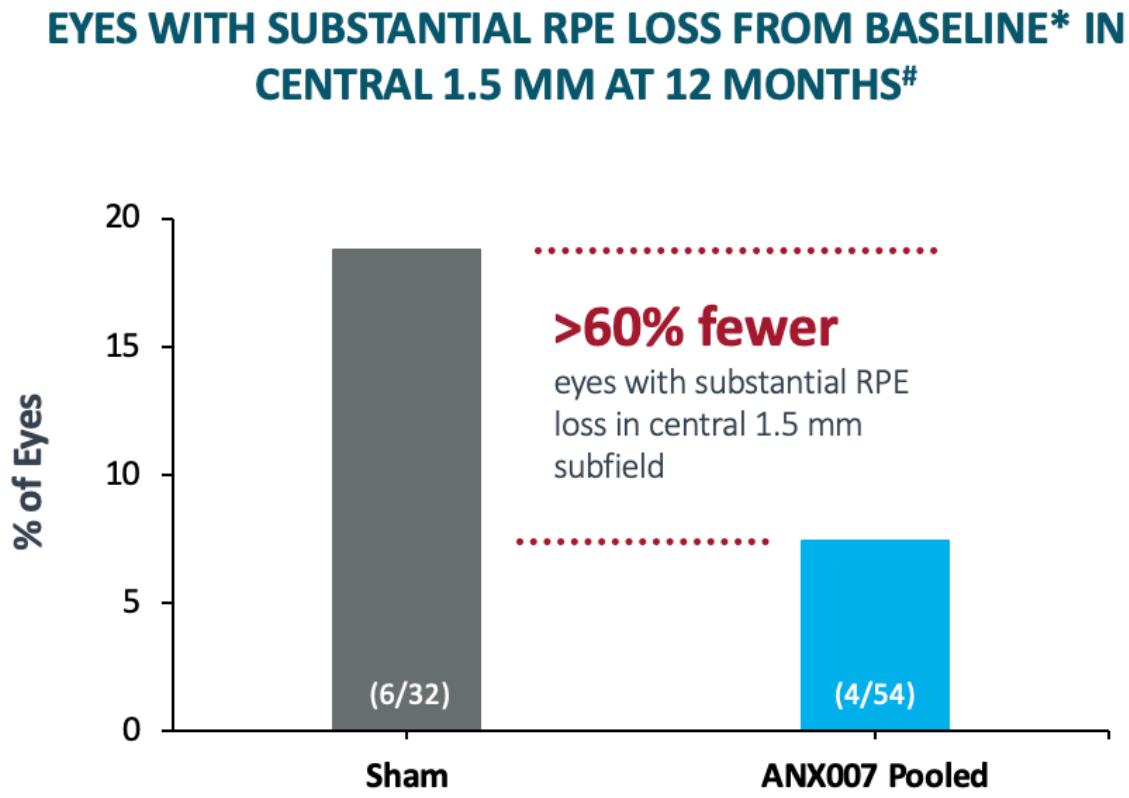
ANX007 Protection from RPE Loss More Robust in 1.5 mm Foveal Center

Consistent with treatment that protects from vision loss



#From a mixed model for repeated measures (MMRM) analysis; ^ITT population
*Heidelberg Spectralis OCT population with baseline OCT data, excludes patients with >98% atrophy at baseline

In Patients with Foveal Center RPE Remaining, ANX007 Reduced Substantial RPE Loss by 60%



#Eyes with at least 25% of RPE intact in the central 1.5mm at baseline (n = 86) in patients with Heidelberg Spectralis OCT scans (overall total n=193)
*Substantial RPE loss defined as 25% absolute loss of RPE

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

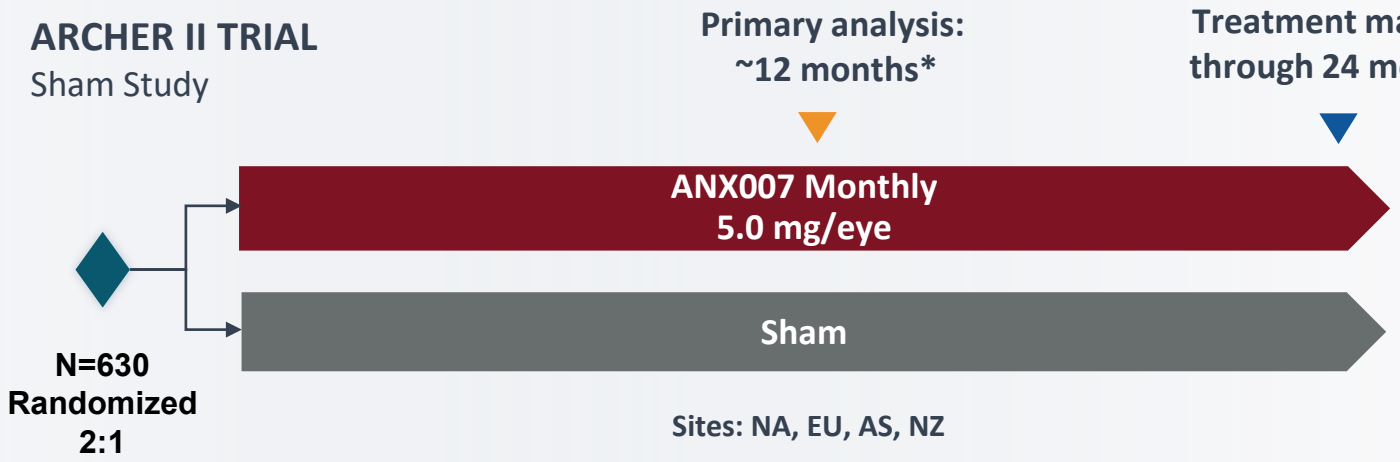
Vitreous Debris – 1
KP on endothelium, prior treatment with topical steroids
No Vasculitis

*Event Verbatim term listed

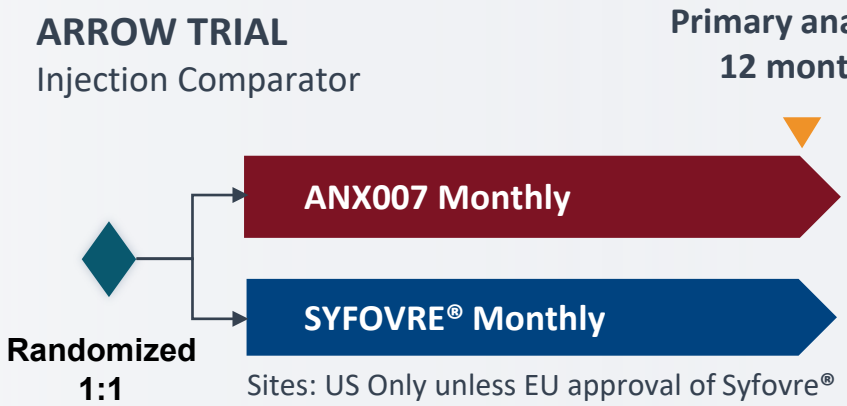
ANX007 Global GA Pivotal ARCHER II Trial INITIATED

ARCHER II enrollment ongoing; ARROW trial initiation in late-2024

ARCHER II TRIAL
Sham Study



ARROW TRIAL
Injection Comparator



PRIME Designation from EMA

PRIMARY ENDPOINT

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

*Primary analysis will occur between 12-18 months from dosing initiation based on accumulation of target events (patients experiencing BCVA ≥15-letter loss on consecutive visits)

SECONDARY ENDPOINTS

Safety, Low Luminance VA (LLVA), Anatomic assessments

ANX007: A Novel Neuroprotective Agent Demonstrating Vision Protection Supported by Structure Protection Now in Phase 3

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

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

Visual function benefit **supported by protection of retinal structures,** particularly those structures closely associated with visual function – **photoreceptors and foveal RPE**

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

Regulatory-aligned Phase 3 program NOW ONGOING