ANNEXON biosciences

STOP THE START

of classical complement-driven diseases

ARCHER Trial Visual Acuity Results in Geographic Atrophy

18 December 2023

Forward-Looking Statements and Disclaimers

This presentation contains “forward-looking” statements about Annexon, Inc. and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts, including statements regarding topline data from the ARCHER Phase 2 trial and post-hoc analyses, our clinical and preclinical programs, timing and commencement of future nonclinical studies and clinical trials and research and development programs, timing of clinical results, strategic plans for our business and product candidates, including additional indications which we may pursue, our financial position, runway and anticipated milestones, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “design,” “due,” “estimate,” “expect,” “focus,” “goal,” “intend,” “may,” “objective,” “plan,” “positioned,” “potential,” “predict,” “seek,” “should,” “target,” “will,” “would” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology.

Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including, but not limited to, risks and uncertainties related to: the ongoing off-treatment follow-up portion of the ARCHER Phase 2 trial and final results from the ARCHER Phase 2 trial; our history of net operating losses; our ability to obtain necessary capital to fund our clinical programs; the early stages of clinical development of our product candidates; the effects of COVID-19 or other public health crises on our clinical programs and business operations; our ability to obtain regulatory approval of and successfully commercialize our product candidates; any undesirable side effects or other properties of our product candidates; our reliance on third-party suppliers and manufacturers; the outcomes of any future collaboration agreements; and our ability to adequately maintain intellectual property rights for our product candidates.

These and other risks are described in greater detail under the section titled “Risk Factors” contained in our Annual Report on Form 10-K and Quarterly Reports on Form 10-Q and our other filings with the Securities Exchange Commission (SEC)Quarterly Report on Form 10-Q filed with the Securities Exchange Commission (SEC) on March 31, 2023 and our other filings with the SEC from time to time. All forward-looking statements in this presentation speak only as of the date of this presentation. Except as required by law, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise.

This presentation concerns drug candidates that are under clinical investigation, and which have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). These are currently limited by federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates or statistical data. Neither we nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this presentation.

Comparisons to third-party studies are provided for illustrative purposes only. Differences exist between trial designs, study sites, subject populations and applicable products or candidates, and caution should be exercised when comparing outcomes across studies.

ANNEXON
biosciences

A bold mission to free the body, brain and eye from complement-mediated disease

Overview of ANX007 Geographic Atrophy Program

Pioneering upstream classical complement trial with demonstrated functional benefit

- ✓ Unique MOA targeting classical complement inflammation where it starts
- ✓ Preclinical classical complement inhibition protected photoreceptor cell loss and function
- ✓ ARCHER 1st clinical demonstration of significant, dose & time-dependent vision preservation
- ✓ Vision preservation supported by multiple lines of evidence, including: 12 months on-treatment, fellow-eye, foveal status and off-treatment analyses
- ✓ Clinical impact consistently improved over time on BCVA ≥15-letter loss measures
- ✓ 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 preclinical & ARCHER data set
- ✓ Robust global Phase 3 program to confirm ARCHER findings

ANNEXON
biosciences

Anti-C1q Mechanism of Action

Classical Complement-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

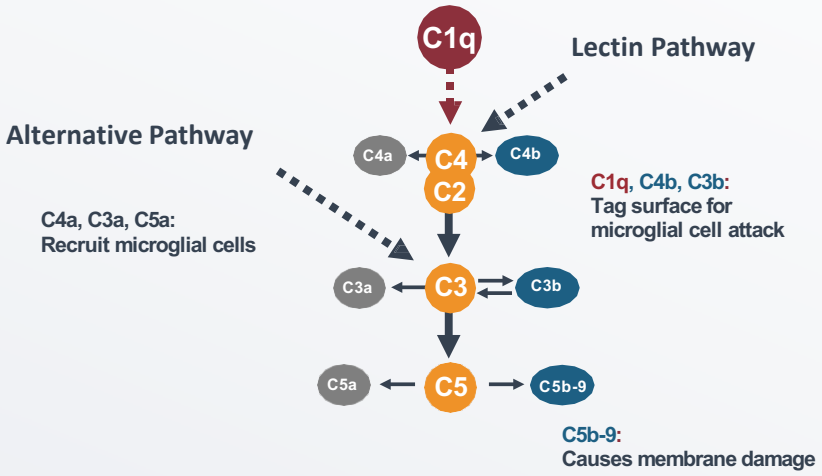
- Discovered by Annexon co-founder, Ben Barres, spawning an entire field and validated in multiple labs[1]
- Synapse loss correlates with functional decline[2]
- Synapse loss precedes neuronal loss[3]

[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

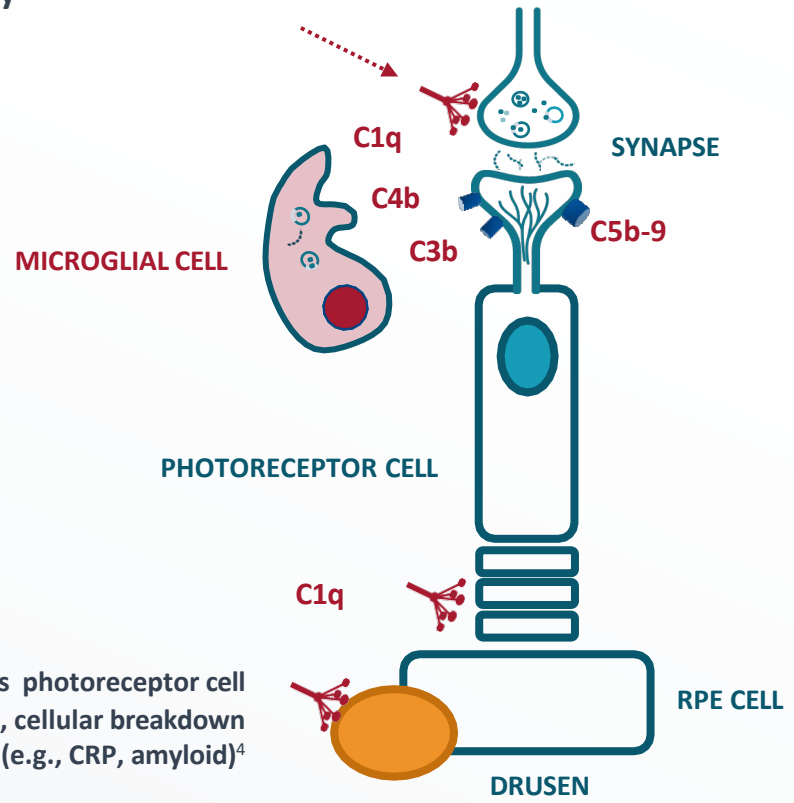
Anti-C1q: A Distinct Neuroprotective Mechanism

C1q initiates classical complement cascade to drive photoreceptor synapse & cell loss and neuroinflammation

- C1q is a **key driver of neurodegeneration**[1]
- C1q anchors classical pathway activation on **photoreceptor cells to cause inflammation and loss**[2]
- **ANX007 inhibits C1q** and all damaging components of the classical pathway[3]



C1q binds stressed photoreceptor synapses and activates the classical pathway



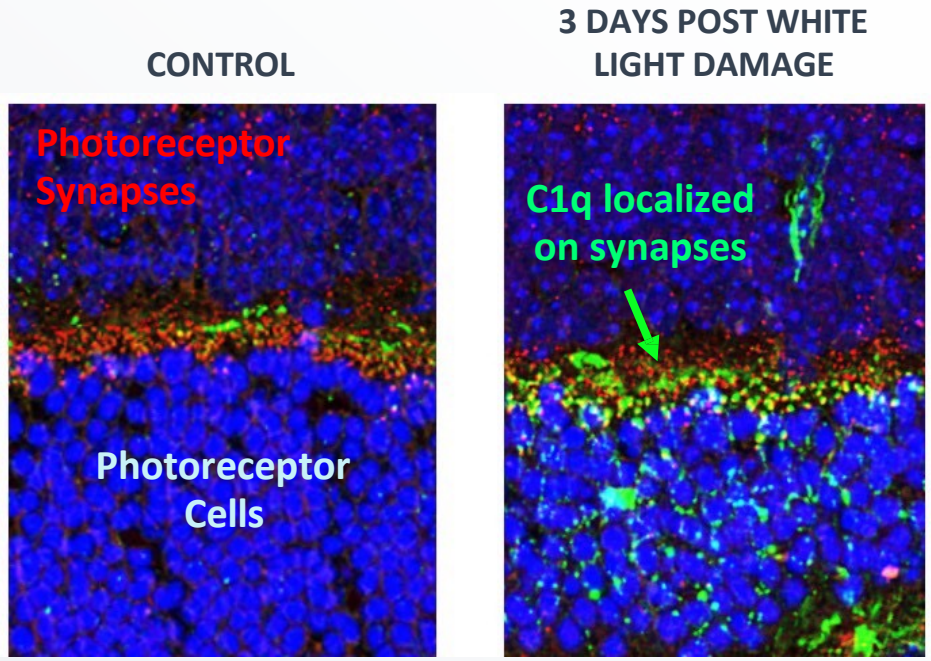
In GA, **C1q** also binds photoreceptor cell outer segments, cellular breakdown products and drusen (e.g., CRP, amyloid)[4]

[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]Tassoni, et al., SFN 2022; Annexon data on file; Jiao, et al., 2018 *Mol Neurodegener* **13**:45; Katschke, 2018 Sci Rep. **8**:7348. [3]Lansita, et al., 2017 *International Journal of Toxicology*, **36**:449; [4]Yednock, et al., 2022 *Int J Retina Vitreous* **8**:79

ANNEXON biosciences

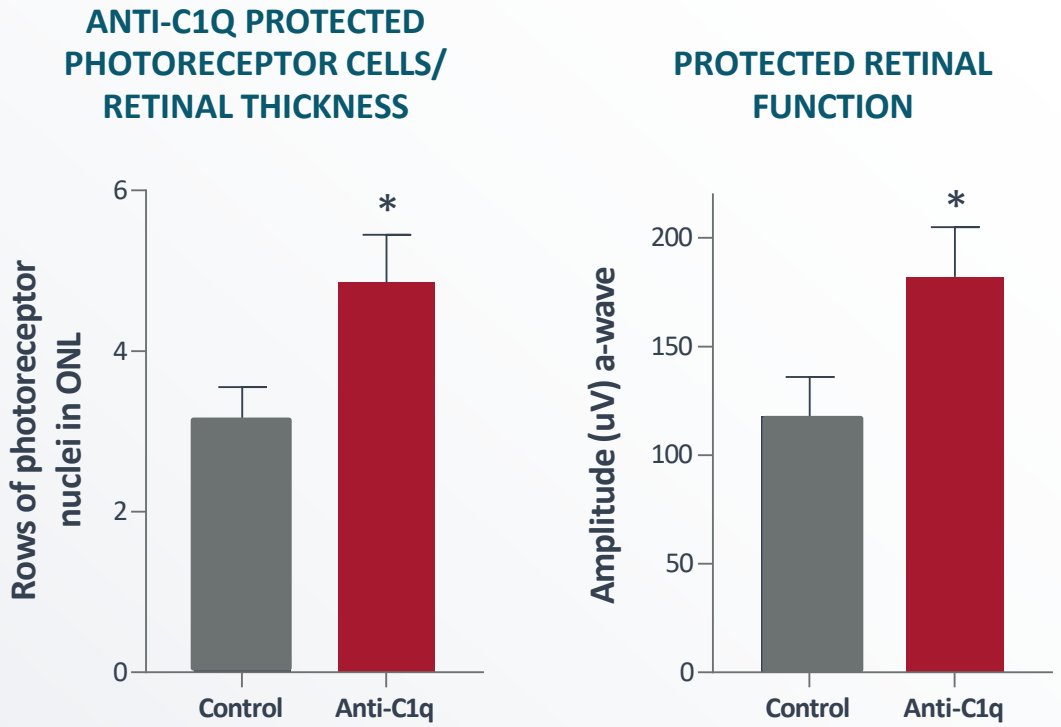
Anti-C1q Protected Photoreceptor Cells and Their Function in Models of Photoreceptor Damage

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



Annexon data on file

Anti-C1q Protected Photoreceptors and Function

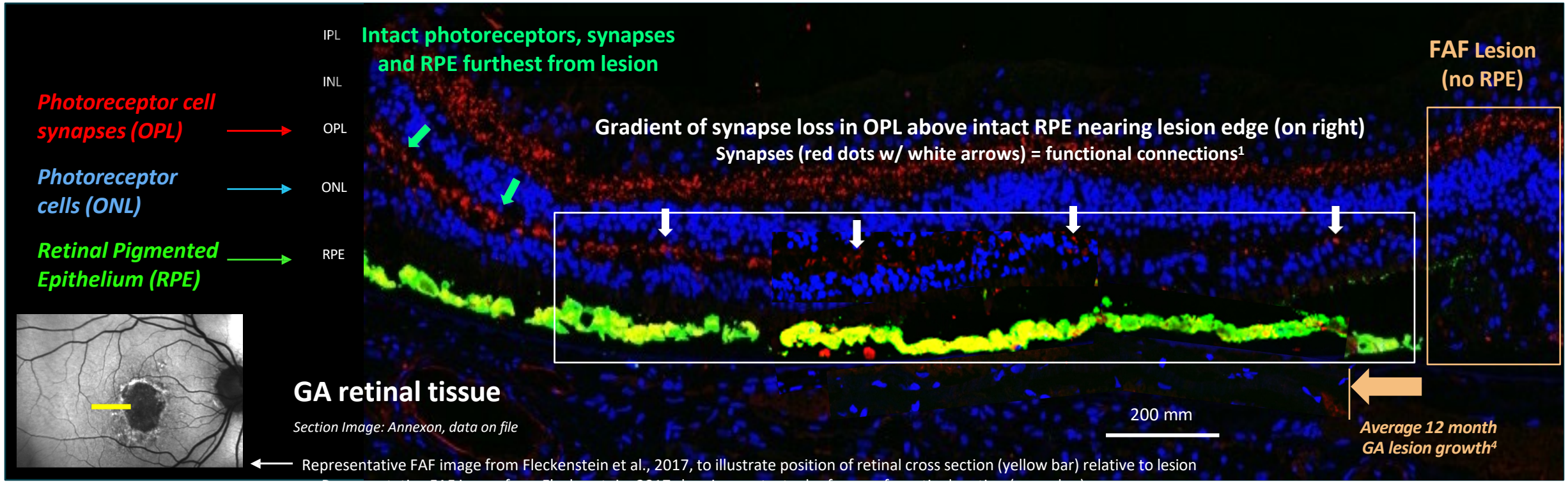


Jiao, et al., 2018 *Mol Neurodegener* 13(1):45

ANNEXON biosciences

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

ANNEXON biosciences

ANNEXON
biosciences

ARCHER Trial Overview

Geographic Atrophy (GA): Progressive and Life-altering Disease that Remains a Leading Cause of Blindness in Elderly People

- Advanced form of age-related macular degeneration (AMD)
- Chronic, progressive neurodegenerative disease of the eye with irreversible vision loss
- 1M people diagnosed in US; 2.5M in EU
- Diagnosis can be traumatic and impact the social and financial aspects of patients lives, including reading, daily activities and recognizing faces
- **No currently approved therapies have demonstrated preservation of visual function**
- **Urgent unmet need to protect against vision loss**

ANNEXON biosciences

ANX007: Differentiated Inhibitor of C1q and Classical Complement to Treat Geographic Atrophy

ANX007

IVT administered antigen-binding fragment (Fab)

KEY ATTRIBUTES

- ✓ **Design:** Modeled after established IVT-administered Fab antibodies
- ✓ **Profile:** 50kD Fab antibody; low viscosity / non-pegylated; <10 pM potency formulated for intravitreal administration
- ✓ **Dosing:** 5 mg / 100 microliters; PK in patient aqueous humor supports monthly/every other month dosing
- ✓ **Specificity:** Full target engagement / inhibition of classical complement pathway observed; lectin and alternative pathway in place for immune and homeostatic functions[1]

[1]Sun, et al., 2023 Ophthal Sci 3(2):100290

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

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

ANNEXON biosciences

Patient Demographics and Study Eye Characteristics Generally Well-Balanced Across Groups

CHARACTERISTIC	SHAM POOLED (N=89)	ANX007 EM (N=89)	ANX007 EOM (N=92)
Age, mean (SD)	79.8 (7.49)	79.7 (8.64)	80.5 (8.53)
Female, n (%)	59 (66.3%)	47 (52.8%)	60 (65.2%)
Caucasian, n (%)	87 (97.8%)	87 (97.8%)	89 (96.7%)
Mean BCVA, mean (SD)	**58.5 (16.2)**	**58.8 (17.2)**	**58.3 (15.0)**
Foveal Lesion	49.4%	57.3%	53.3%
GA Lesion Size (mm^2), mean (SD)	7.28 (3.99)	7.28 (3.96)	7.53 (4.10)
GA Lesion < 7.5 mm^2	61.8%	58.4%	57.6%
Fellow Eye CNV	22.5%	24.7%	17.4%
Multifocality, n (%)	65 (73.0%)	61 (68.5%)	67 (72.8%)

Discontinuations Consistent with Previous GA Studies

	SHAM POOLED (N=89)	ANX007 EM (N=89)	ANX007 EOM (N=92)
Discontinued treatment	**10 (11.2%)**	**13 (14.6%)**	**11 (12.0%)**
Withdrawal by subject			
Unrelated health issues	2	1	2
Moved / travel / time	1	2	2
Personal reasons / no reason given	2	3	2
Other	1	2	---
Death	2	2	3
Lost to follow-up	1	2	2
Physician decision	1	1	---

BCVA: Widely Accepted Functional Endpoint of Visual Acuity

BCVA 15-letter change or Mean BCVA change used in multiple sham-controlled pivotal trials

BEST CORRECTED VISUAL ACUITY (BCVA)

15-Letter Loss

20/60 to 20/120 vision

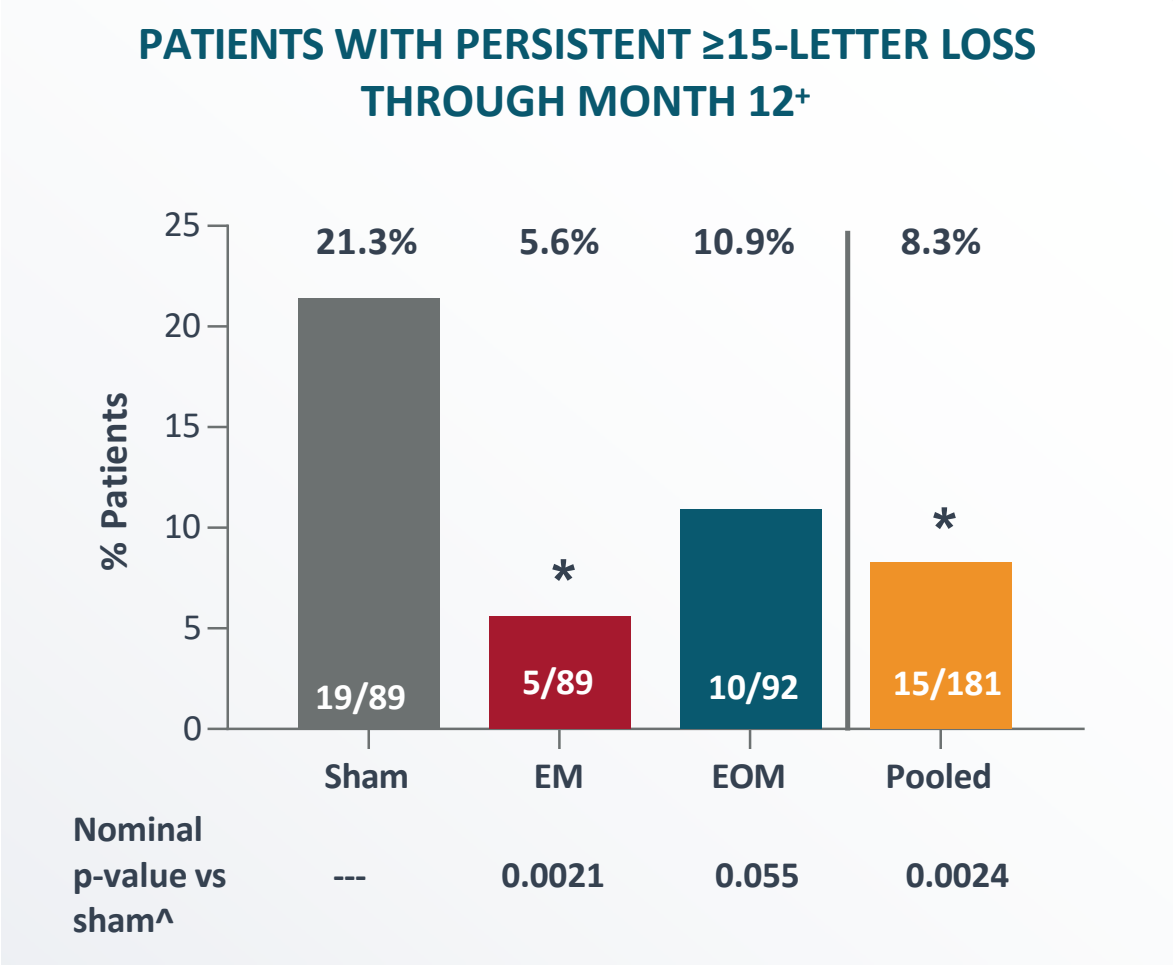
PRODUCT	PRIMARY ENDPOINT MEASURE
Wet AMD	
Lucentis	Trial 1 & 2: BCVA ≥15 letter Trial 3 & 4: mean BCVA change
Eylea	BCVA ≥15 letter
Vabysma	Mean BCVA change
DME	
Lucentis	BCVA ≥15 letter
Eylea	Mean BCVA change
Vabysma	Mean BCVA change
Iluvien	BCVA ≥15 letter
Retinal Vascular Occlusion (BRVO/CRVO)	
Lucentis	BCVA ≥15 letter
Eylea	BCVA ≥15 letter
Ozurdex	BCVA ≥15 letter

ANNEXON biosciences

ANNEXON
biosciences

ARCHER Trial
Visual Acuity Results

Prespecified Secondary Endpoint (BCVA): ANX007 Demonstrated Significant, Dose-Dependent Protection From Vision Loss

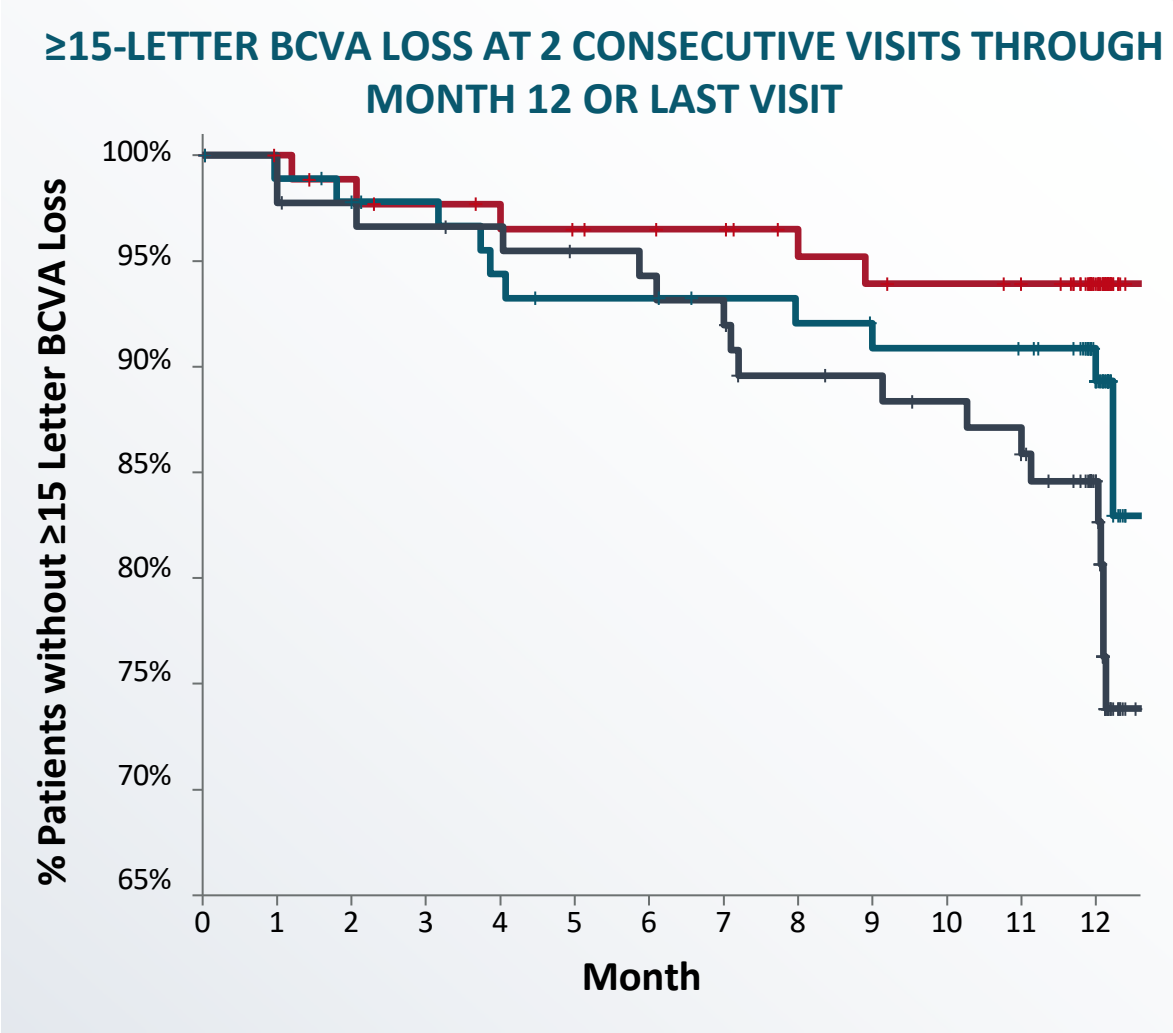


- Dose-dependent response
- 15-letter loss clinically meaningful
- Widely accepted endpoint

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

ANNEXON biosciences

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



EM (n=89)

72% Risk Reduction ANX007 EM

HR (CI) = 0.28 (0.11 to 0.76)

p = 0.006

EOM (n=92)

48% Risk Reduction ANX007 EOM

HR (CI) = 0.52 (0.24 to 1.13)

p = 0.064

Sham (n=89)

Sensitivity analysis confirmed treatment effect:

Significant 66% reduction in risk in EM group when excluding patients with vision loss only at month 12

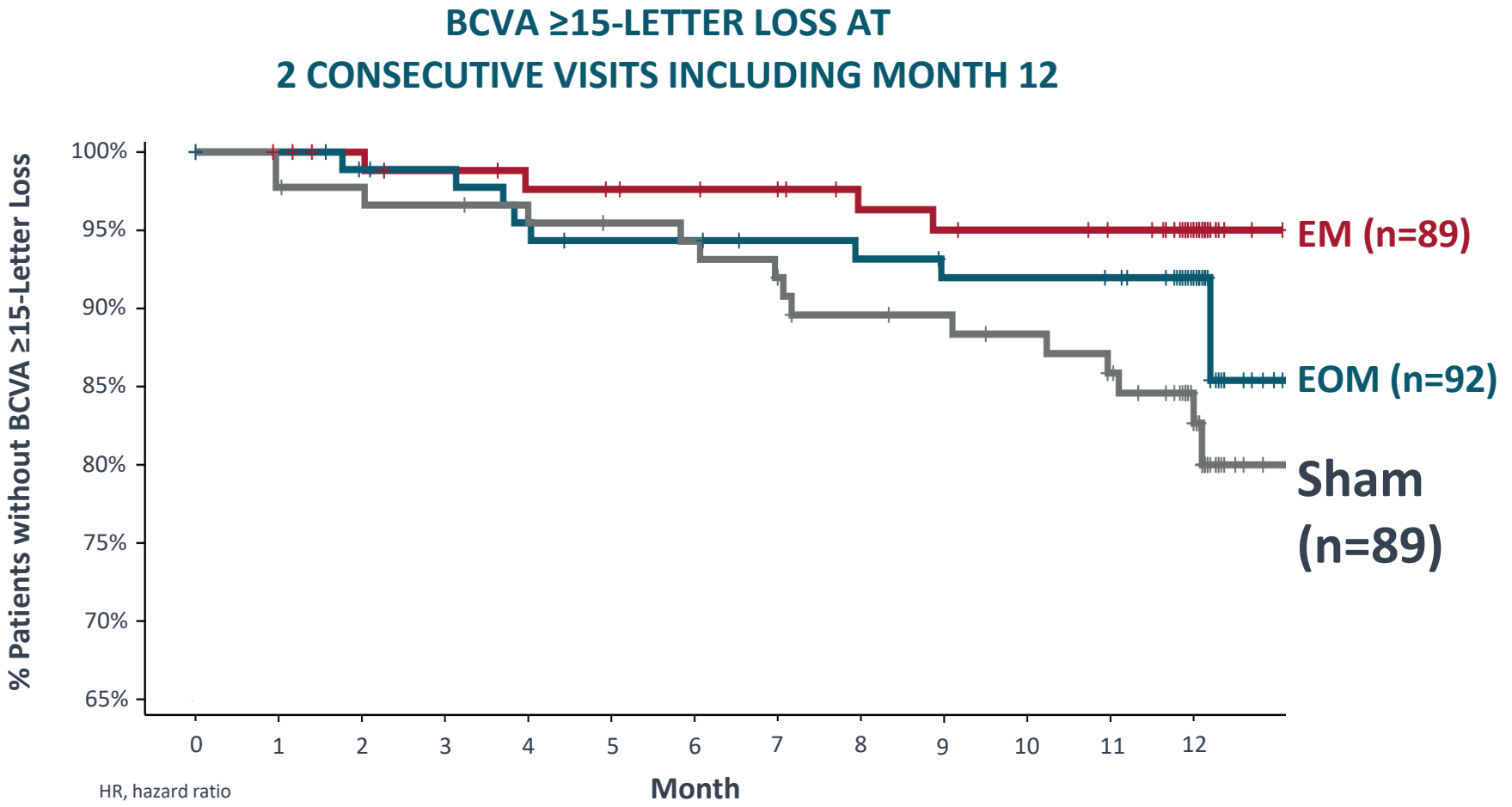
HR, hazard ratio.

Nominal log-rank test (versus Sham) p-values are presented

Increasing ANX007 Impact Over Time

ANNEXON biosciences

Significant, Time-Dependent Protection From BCVA ≥15-Letter Vision Loss Supported by Off-Treatment Data (includes month 15 visit)



HR, hazard ratio
Nominal log-rank test (versus sham) p-values are presented

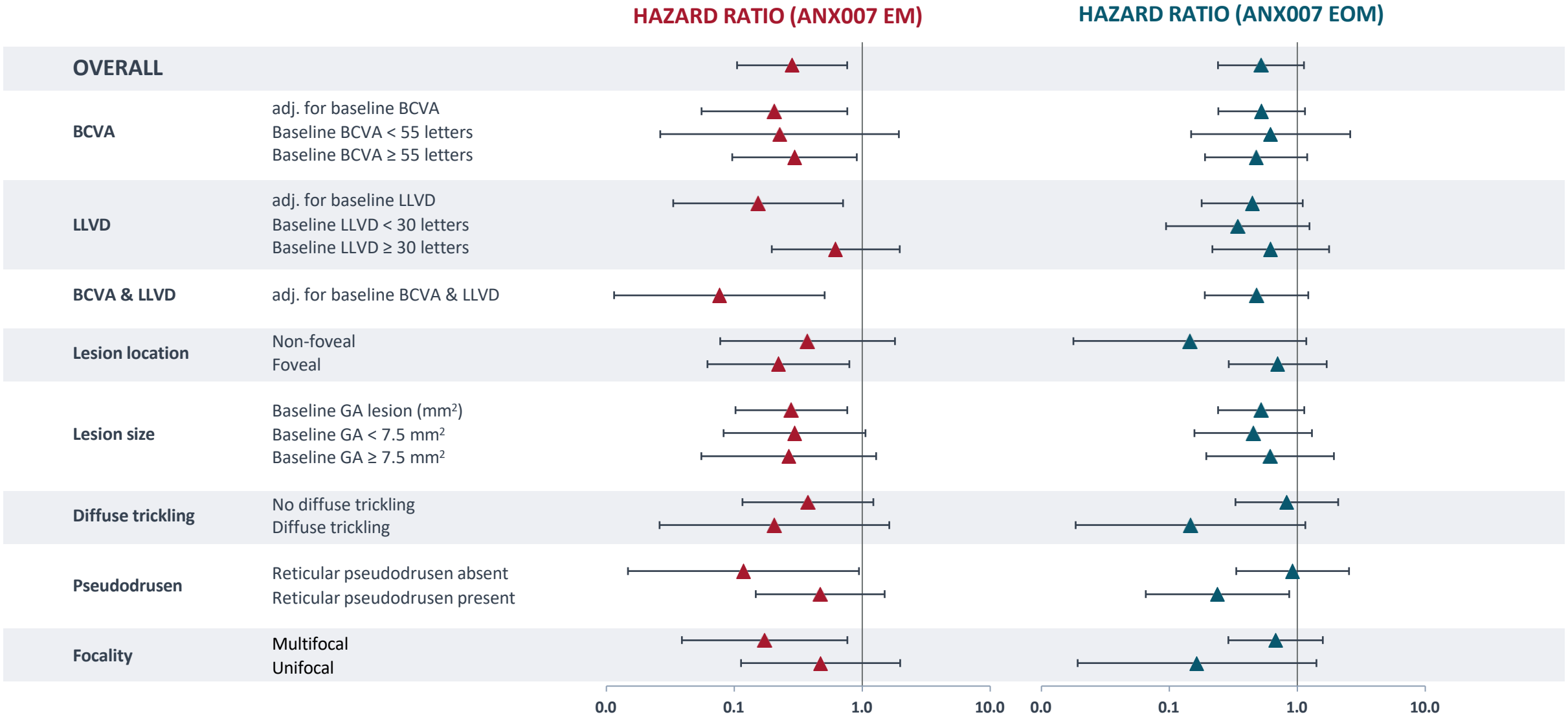
ANX007 EM 73% Risk Reduction
HR (CI) = 0.272 (0.090 to 0.819)
p = 0.0207

ANX007 EOM 50% Risk Reduction
HR (CI) = 0.504 (0.214 to 1.190)
p = 0.1181

Increasing ANX007 Impact Over Time

ANNEXON biosciences

ANX007 Protection from Vision Loss Consistent Across Baseline Characteristics



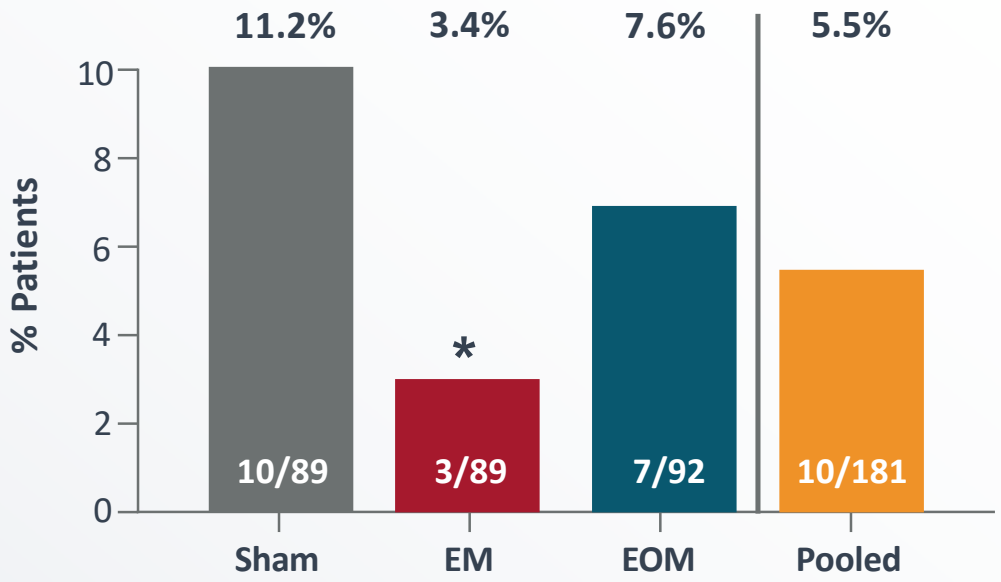
*persistent for two consecutive visits through month 12 or at last visit; Hazard ratios are from Cox regressions accounting for event time and censorship
NOTE: Hazard ratio not estimated for ANX007 EM vs Sham with baseline LLVD < 30 due to zero (0) event in ANX007 EM group for the subgroup.

ANNEXON biosciences

ANX007 Effect on BCVA ≥15-Letter Loss Improves with Longer Treatment

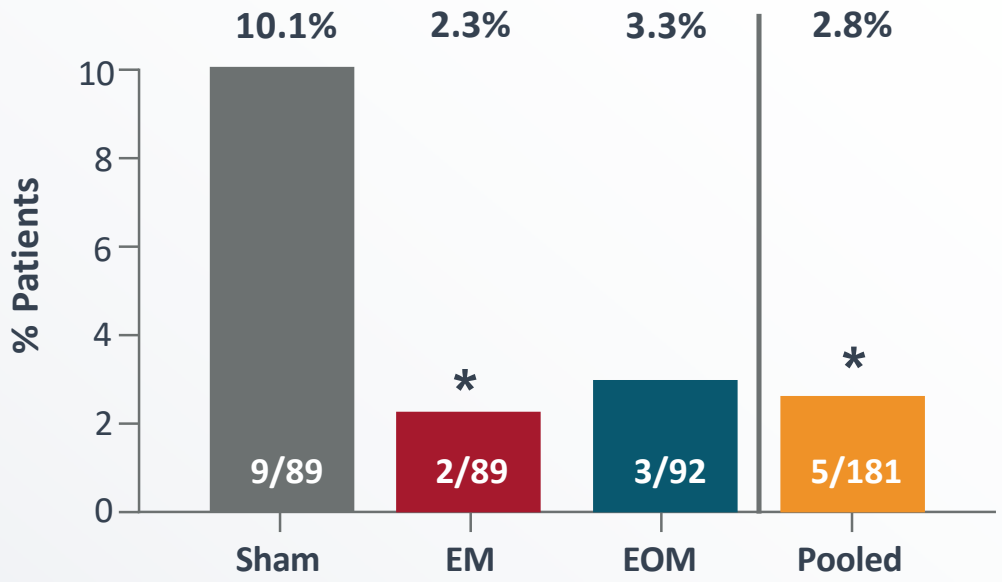
PATIENTS WITH PERSISTENT BCVA ≥15-LETTER LOSS

STUDY MONTHS 0-6



Nominal p-value vs sham^	---	0.0437	0.403	0.0921

STUDY MONTHS 6-12



Nominal p-value vs sham^	---	0.0293	0.064	0.0105

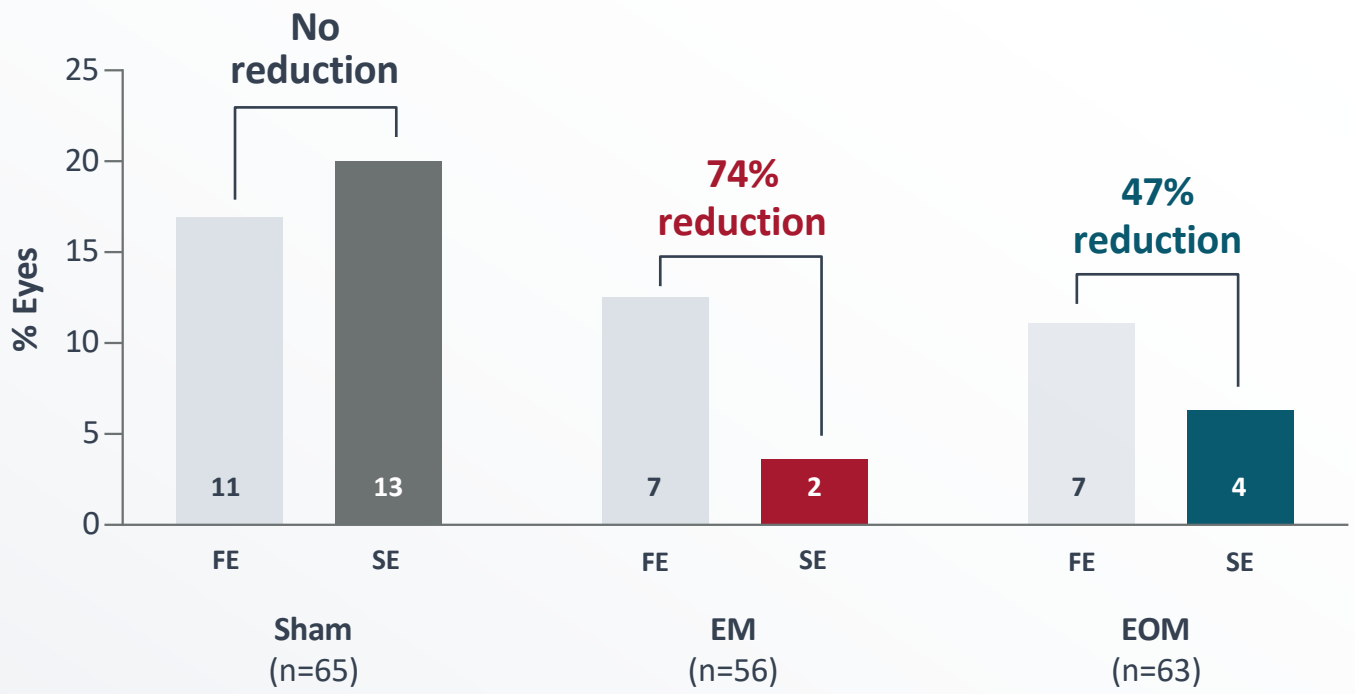
⁺Persistent for two consecutive visits through month 12 or at last visit; ^Nominal p-value from a Chi-square test in ITT population; Nominal P < 0.05*

Increasing ANX007 Impact Over Time

ANNEXON biosciences

Protection From Vision Loss Supported by Fellow Eye Analysis

EYES WITH ≥15-LETTER BCVA LOSS AT MONTH 12 IN ALL PATIENTS WITH BILATERAL GA



	Sham (n=65)		EM (n=56)		EOM (n=63)	
% of Eyes	16.9	20.0	12.5	3.6	11.1	6.3
Odds Ratio vs Fellow Eyes (within treatment arm)		1.25		0.26		0.53

- 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: 74% reduction in 15-letter loss
  - EOM: 47% reduction in 15-letter loss

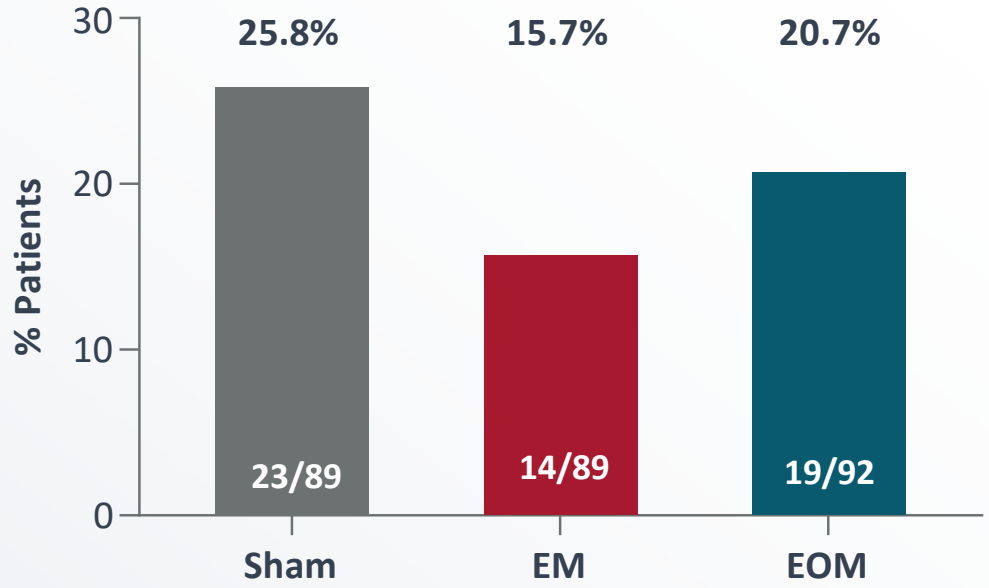
BCVA, best-corrected visual acuity; CI, confidence interval; OR, odds ratio;
EM, every month; EOM, every other month; Pooled: EM+EOM; FE, fellow eye; SE, study eye
All patients with bilateral GA were included due to small sample size

ANNEXON biosciences

Consistent Protection from Vision Loss with BCVA ≥10 and ≥20-Letter Assessments

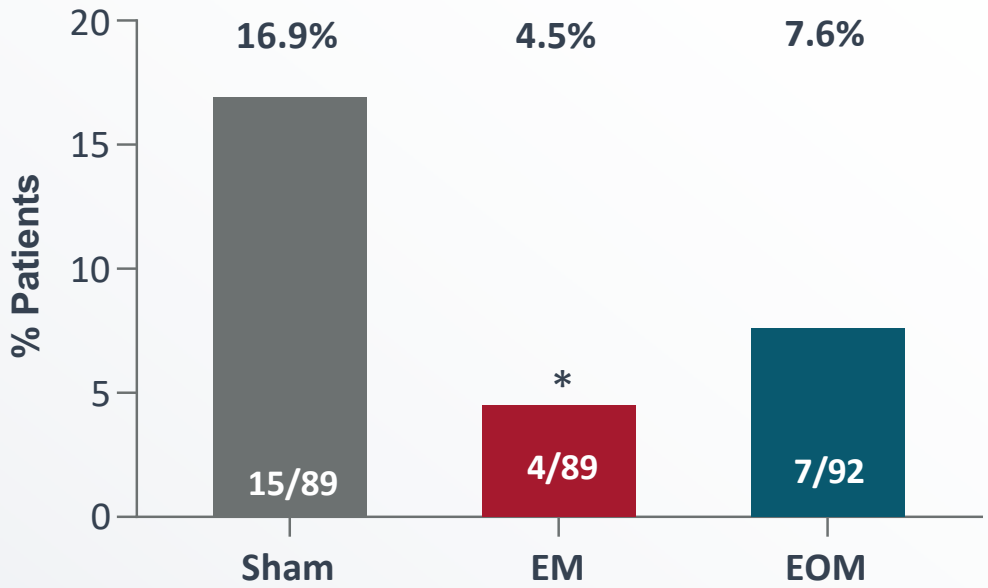
Persistent BCVA Vision Loss Through Month 12[+]

≥10-LETTER LOSS



Nominal p-value vs sham^	---	0.096	0.408

≥20-LETTER LOSS

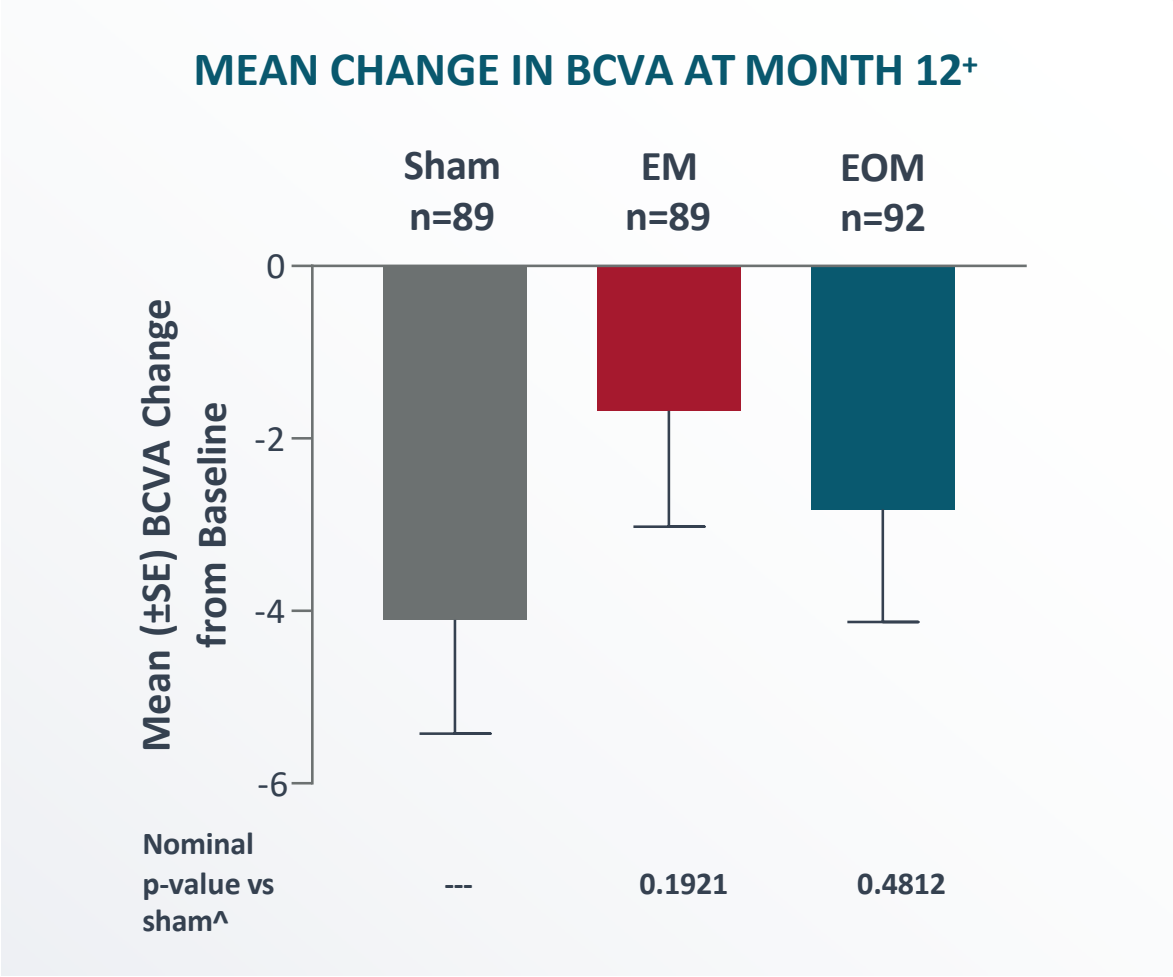


Nominal p-value vs sham^	---	0.0076	0.57

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

ANNEXON biosciences

Mean Change in BCVA at Month 12 Further Supports Consistent Protection From Vision Loss with ANX007 Treatment



- Trend for dose-dependent response in ANX007 treated groups
- BCVA loss in sham through 12 months consistent with previous GA trials[1,2,3]

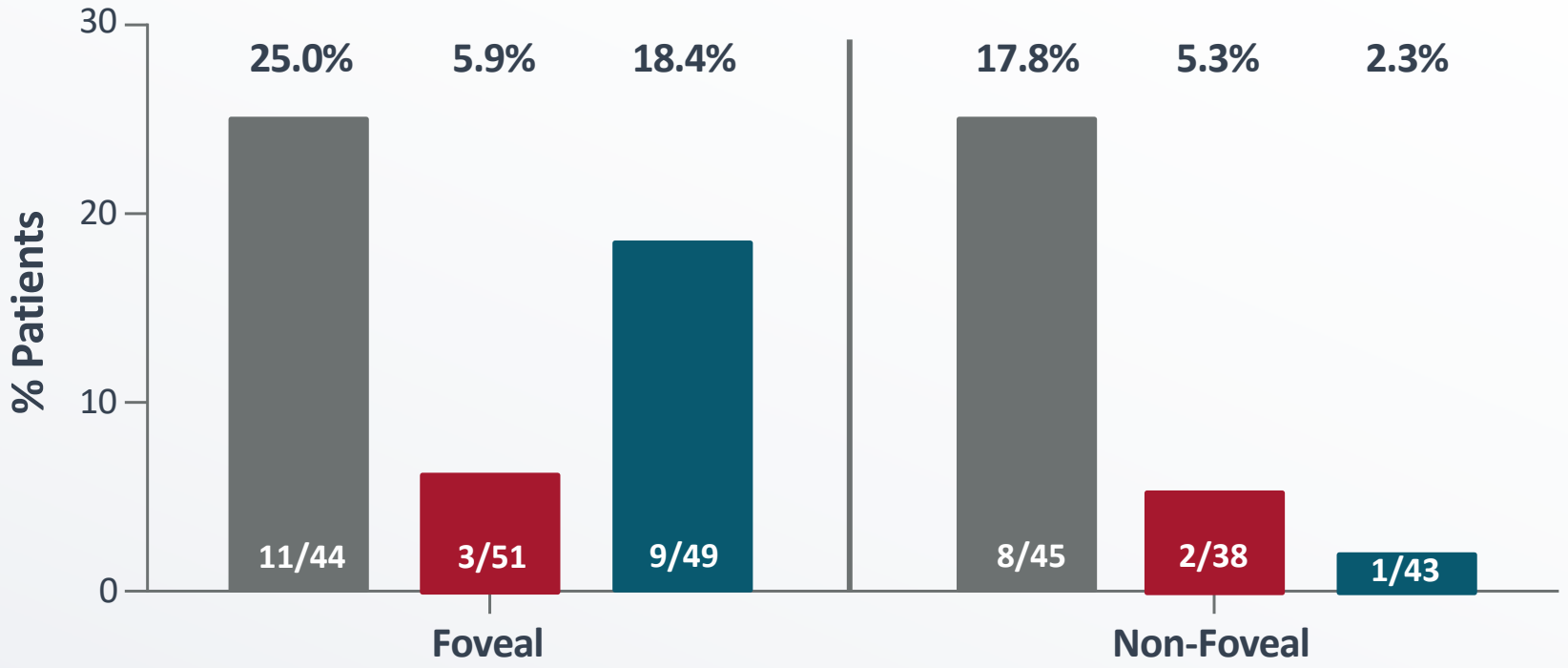
+Mean, standard error (SE), and p-value based on MMRM adjusting for baseline lesion location, lesion focality, baseline GA lesion, and the baseline GA lesion by visit interaction.
^Nominal p-value from MMRM adjusting for baseline lesion location, lesion focality, baseline GA lesion, and the baseline GA lesion by visit interaction in ITT population

[1]Liao et al (2020) *Ophthalmology* 127: 186-195; [2]Holtz et al (2018) *JAMA Ophthalmology* 136:666-677;
[3]Heier et al, *Retina Society* 2022

ANNEXON biosciences

ANX007 BCVA Subgroup Analysis: Protection from Vision Loss in Foveal and Non-Foveal Patients

PATIENTS WITH PERSISTENT ≥15-LETTER LOSS THROUGH MONTH 12+



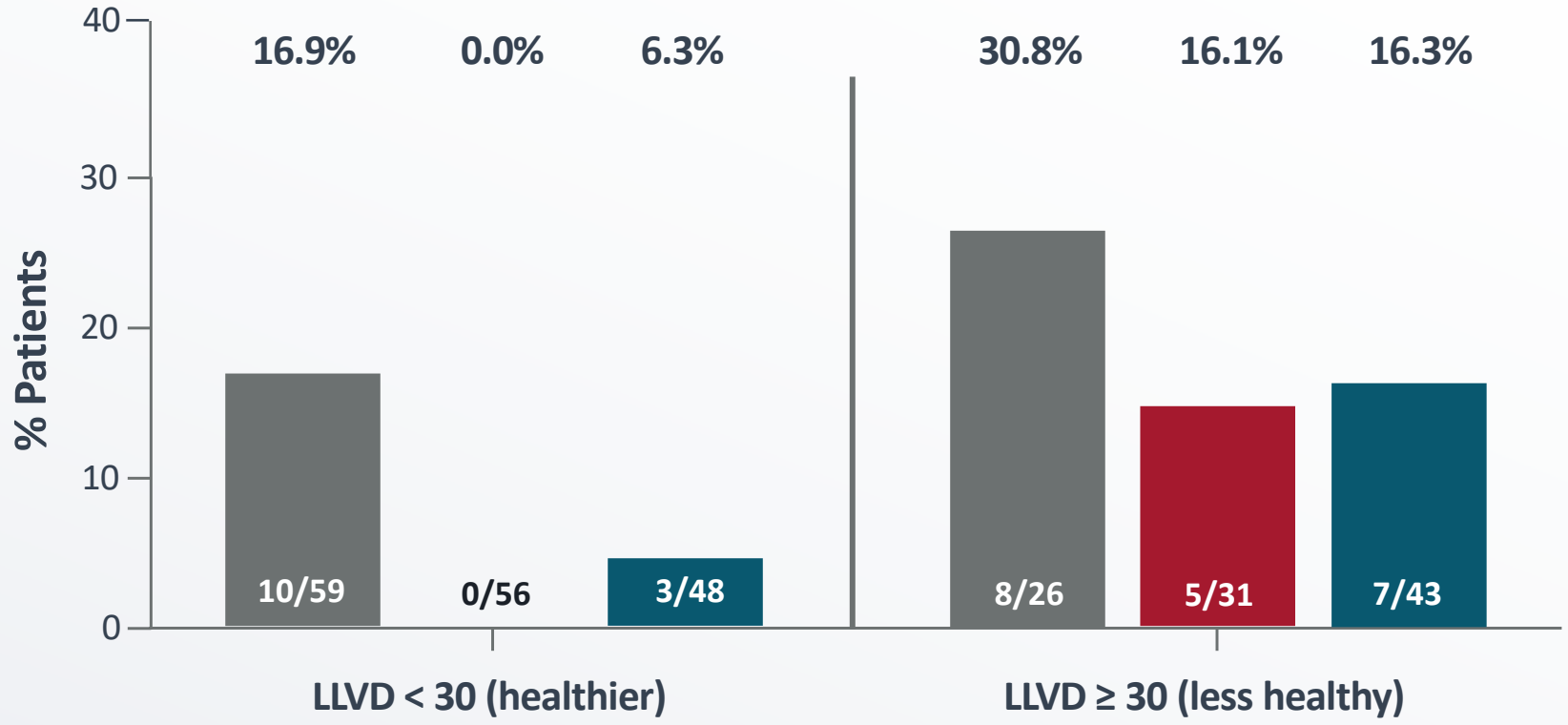
Nominal summary p-value vs. sham^

EM	0.0019
EOM	0.0439

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

ANNEXON biosciences

ANX007 Protected Against Vision Loss BCVA ≥15-Letter Loss Regardless of Retina Health at Baseline



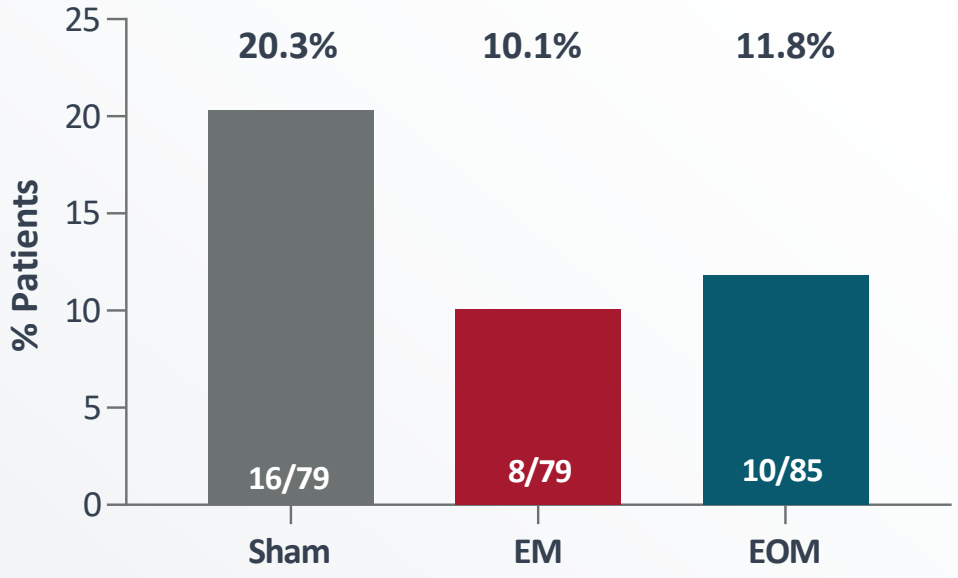
Nominal summary p-value vs. sham^	
EM	0.0016
EOM	0.029

#Persistent for two consecutive visits including month 12
^Nominal p-value from a Cochran Mantel-Haenszel test (General Association) in ITT population

ANNEXON biosciences

Prespecified Secondary Analyses: ANX007 Provided Consistent Protection from Vision Loss on Additional Measures—LLVA & LLVD

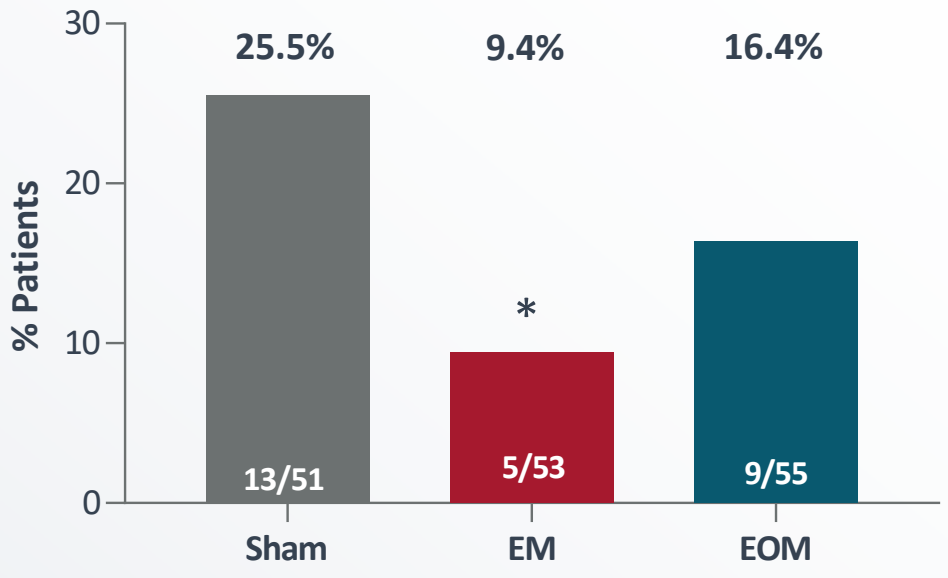
LLVA ≥15-LETTER LOSS THROUGH MONTH 12+^



	Sham	EM	EOM
Nominal p-value vs Sham^	--	0.076	0.14

+Patients with at least one post baseline LLVA measurement
^Nominal p-value from a Chi-square test

LLVD ≥15-LETTER WORSENING THROUGH MONTH 12+^



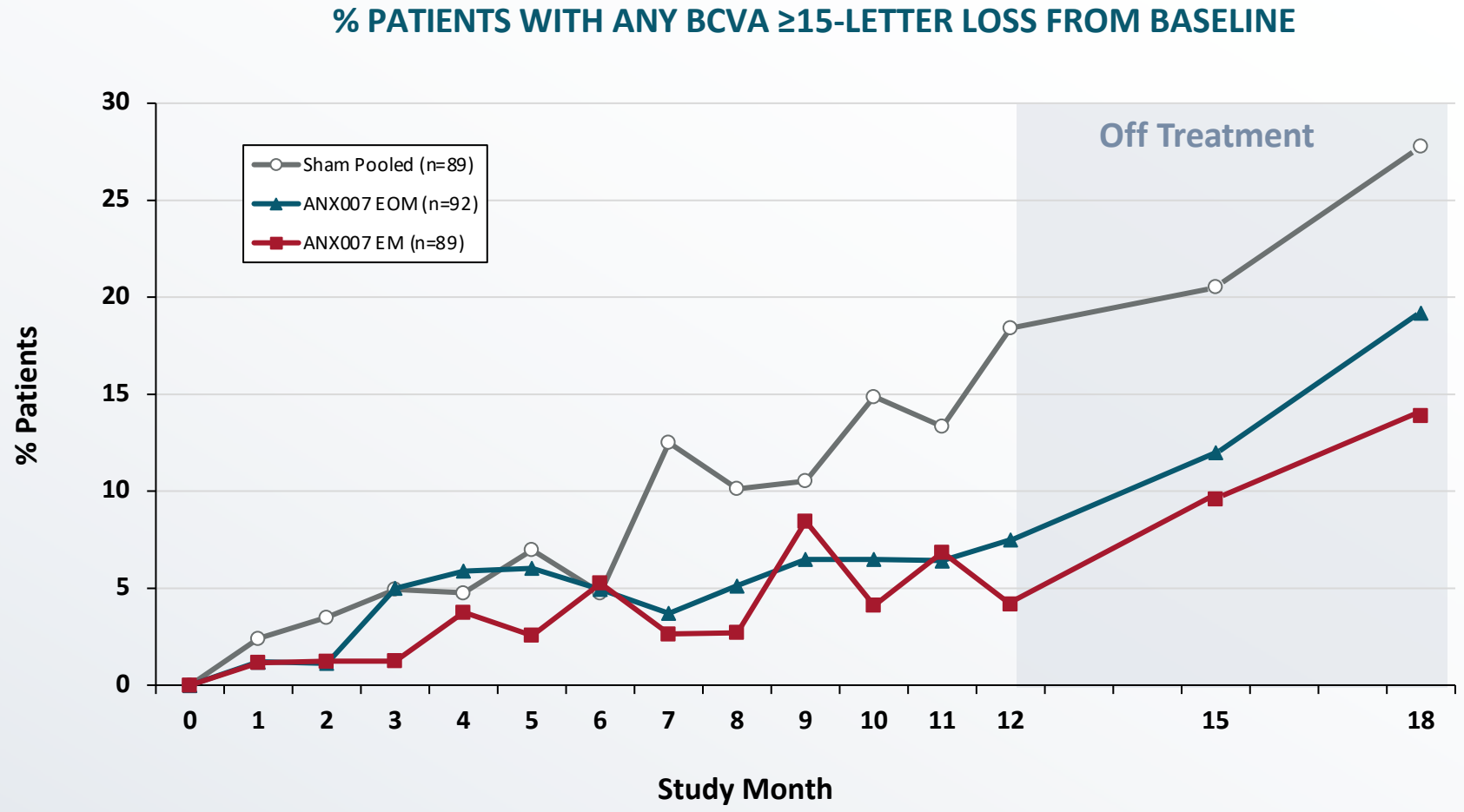
	Sham	EM	EOM
Nominal p-value vs sham^	--	0.0305	0.2470

+in subjects with BCVA ≥55
^Nominal p-value from a Chi Square test
*p<0.05

ANNEXON biosciences

BCVA ≥15-Letter Loss Accelerates After Cessation of Treatment

Visual Function Loss Parallels Sham in Off-Treatment Period



- 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

ANNEXON biosciences

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

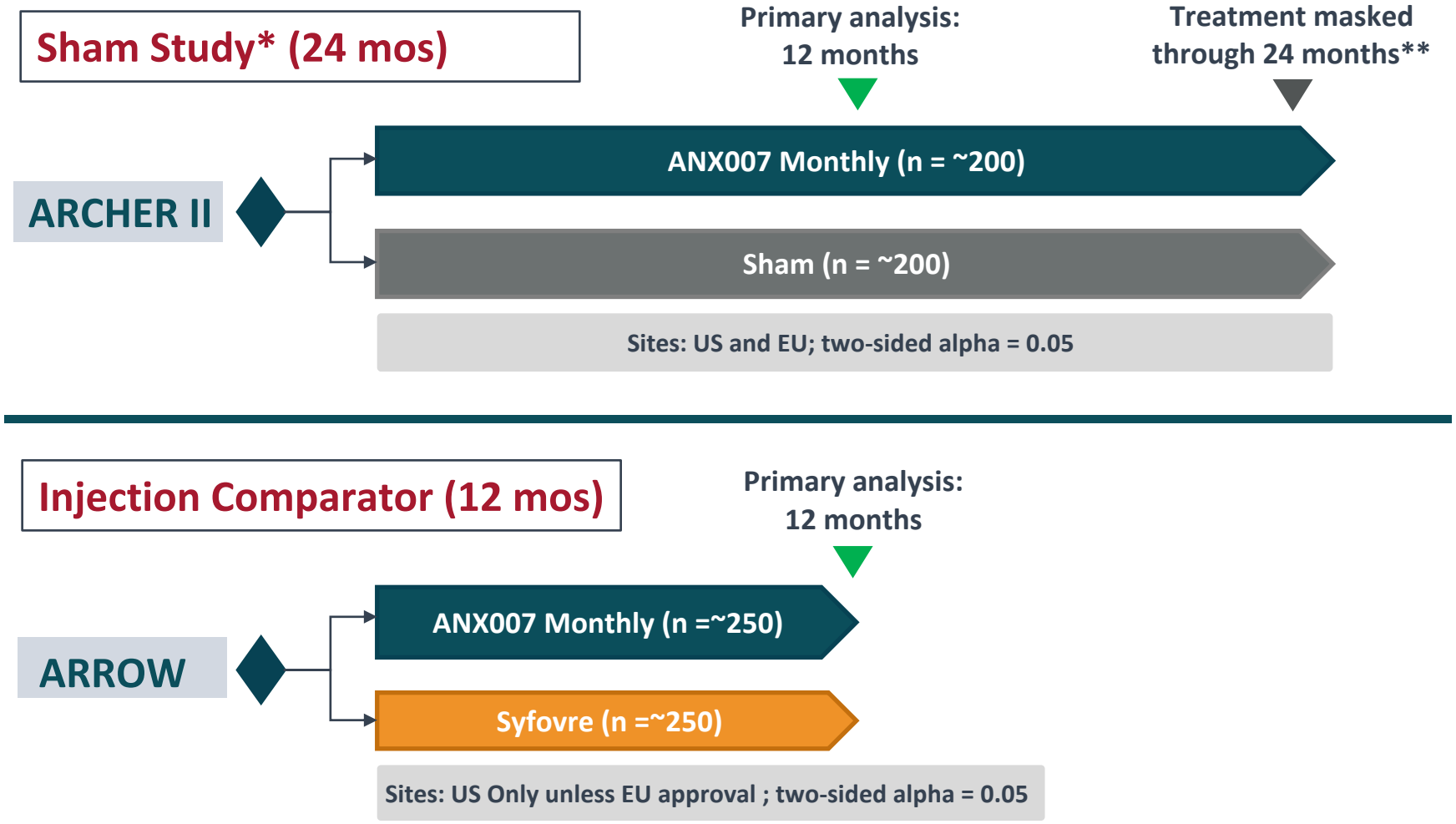
Vitreous Debris – 1
KP on endothelium, prior treatment with topical steroids
No Vasculitis

*Event Verbatim term listed

ANNEXON
biosciences

Phase 3 Program Overview

ANX007 GA P3 Trials Overview: Replicate ARCHER & Support Global Approvals



Primary Endpoint

- Persistent ≥15-Letter BCVA Loss through 12 months, or accumulation of appropriate # of events

POTENTIAL SECONDARY / EXPLORATORY ENDPOINTS

- LLVA / LLVD
- Ellipsoid Zone (EZ) attenuation / lesion growth

Study Design Elements

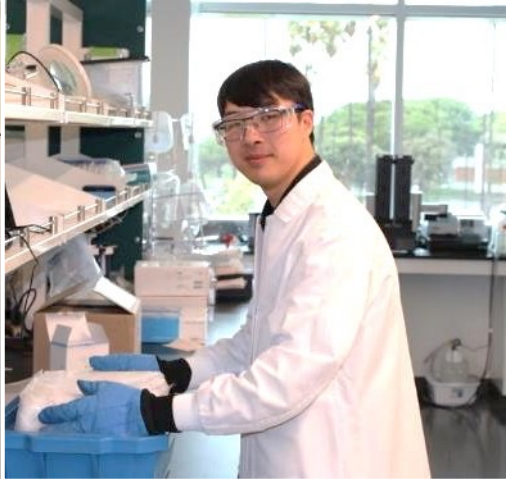
- Replicate ARCHER (e.g., inclusion/ exclusion, assessments etc.)
- Possible enrichment criteria for sham study (based on ARCHER data)

*Archer was a 270 patient trial

**24 mos. total treatment per regulatory direction

ANX007: A Novel Neuroprotective Agent Demonstrating Benefit in Vision in the ARCHER Trial

- ✓ C1q inhibition: distinct neuroprotective MOA
- ✓ ANX007 treatment demonstrated:
  - ✓ Consistent visual function benefits
  - ✓ Highly statistically significant effect on visual acuity endpoints
  - ✓ Dose- and time-dependent effect
  - ✓ Growing effect on both vision protection over time
- ✓ Vision loss accelerates after treatment cessation
- ✓ ANX007 generally well-tolerated
- ✓ Phase 3 clinical and regulatory preparations are underway, including PRIME program guidance and other FDA/EMA interactions



To the patients, families, caregivers, physicians and medical teams who participated in our trial, we are eternally grateful for your support and contributions!

To our employees, collaborators and advisors, thank you for your Warrior Spirit and All For One commitment!