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Vonaprument: Only Geographic Atrophy Program to Show Significant Vision Preservation

Global Pivotal Program with Potential Blockbuster Market Opportunity



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Forward-Looking Statements

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 our clinical and preclinical programs, timing and commencement of future nonclinical studies and clinical trials and research and development programs, timing of clinical results, anticipated timing of submission of a Biologics Licensing Application, 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.

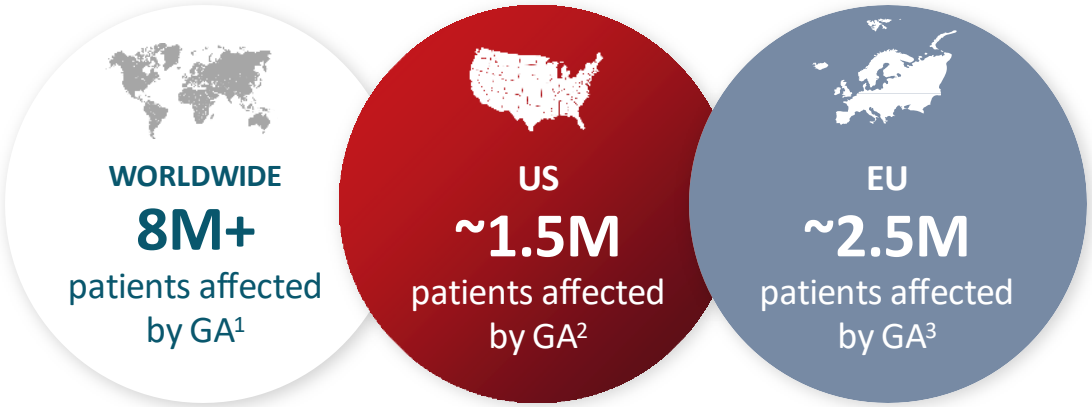
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Geographic Atrophy Remains a Significant Unmet Need

No approved treatments demonstrating vision preservation



GA SEVERELY LIMITS INDEPENDENCE AND IS A LEADING CAUSE OF BLINDNESS IN THE ELDERLY



- Avg. Age of GA Patient: 79 years
- GA greatly impacts quality of life, interfering with reading, driving, recognizing faces
- Incidence projected to increase due to aging population

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Vonaprument Overview
Only GA Program to Demonstrate Significant Vision Protection



Mechanistic Rationale for Functional Protection

Anti-C1q stops inflammation & damage on vision-required photoreceptors



Protected Key Retinal Structure Required For Central Vision

Preserved functional photoreceptors followed by RPEs



Protected BCVA Gold Standard Ophthalmology Outcome

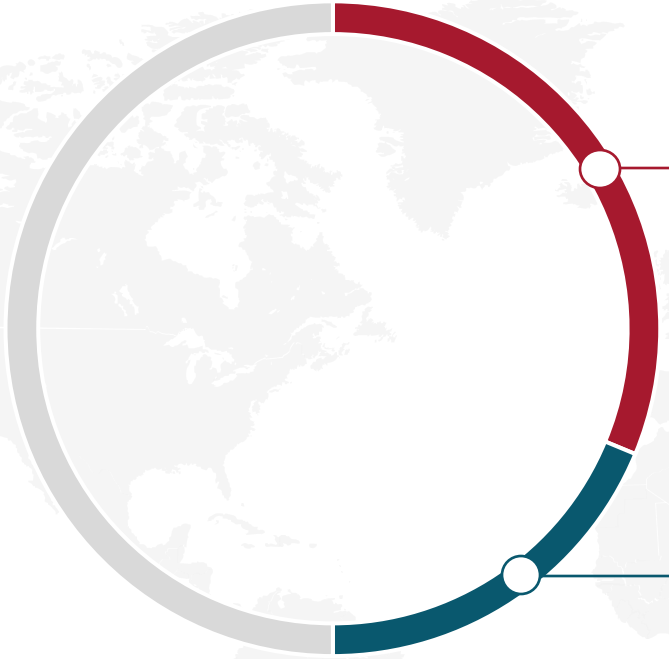
Dose dependent protection across multiple measures

First in Class Vision Protection as New Standard of Care in GA

WORLDWIDE

8M+

patients affected by GA[1]





EU

~2.5M

patients affected by GA[3]



US

~1.5M

patients affected by GA[2]

Less than

10%

of US patients receive treatment[4]

Lack of clear functional benefit of current GA therapies

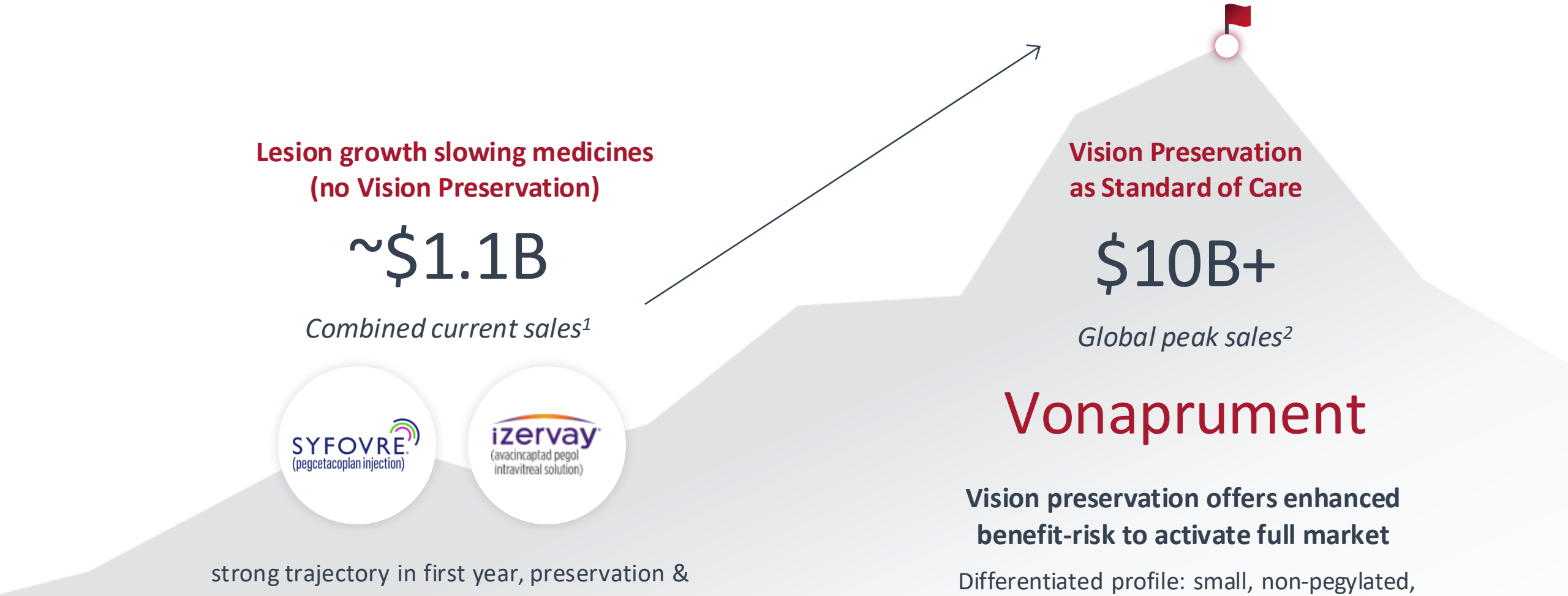
Vonaprument poised to capture and drive immense GA market

[1]Keenan et al, Ophthalmology. 2018 Jul 27;125(12):1913–1928; [2]Tufail A, et al. Presented at the 15th EURETINA Congress, Nice, France, September 17-20, 2015. Accessed November 21, 2019; [3]Based on Colijin JM, *et al.*, 2016; Wong WL, *et al.*, 2014; Rudnicka AR, *et al.*, 2014; Korb CA, *et al.*, 2014; Piermarocchi S, *et al.*, 2011; Fernandez-Arias C, *et al.*, 2011; Augood CA, *et al.*, 2006; Rudnicka AR et al., Ophthalmology. 2012;119(3):571-80. doi:10.1016/j.ophtha.2011.09.027 4 Based on market reports, approximately 75,000 patients are being actively treated with available therapies in the US, representing ~10% of the 800,000 people diagnosed with GA/under the care of retina specialists, but only about 5% of the 1.5M US population with GA.

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Vonaprument Poised to Build GA Market Similar to wet AMD

Vision preservation as standard of care to fundamentally transform GA diagnosis & treatment



Lesion growth slowing medicines (no Vision Preservation)

~$1.1B

Combined current sales[1]

SYFOVRE (pegcetacoplan injection)

izervay (avacincaptad pegol intravitreal solution)

strong trajectory in first year, preservation & safety concerns have plateaued market growth

Vision Preservation as Standard of Care

$10B+

Global peak sales[2]

Vonaprument

Vision preservation offers enhanced benefit-risk to activate full market

Differentiated profile: small, non-pegylated, low viscosity, limited conversion to CNV

1. Analyst estimates
2. ClearView Healthcare Partners analysis of 2037 worldwide sales and ANNX estimates

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Clinical Perspective of Dry AMD with GA



Geographic Atrophy is a Neurodegenerative Disease with Central Vision Loss and No Approved Vision-Preserving Treatments

GA is a progressive disease leading to:

- Gradual loss of central vision
- Difficulty seeing in low light
- Blurry or distorted vision

Average age of a GA patient: 79 years



Everyday activities like reading, driving, and recognizing faces become more challenging with more advanced disease

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GA is a Chronic Progressive Neurodegenerative Disease

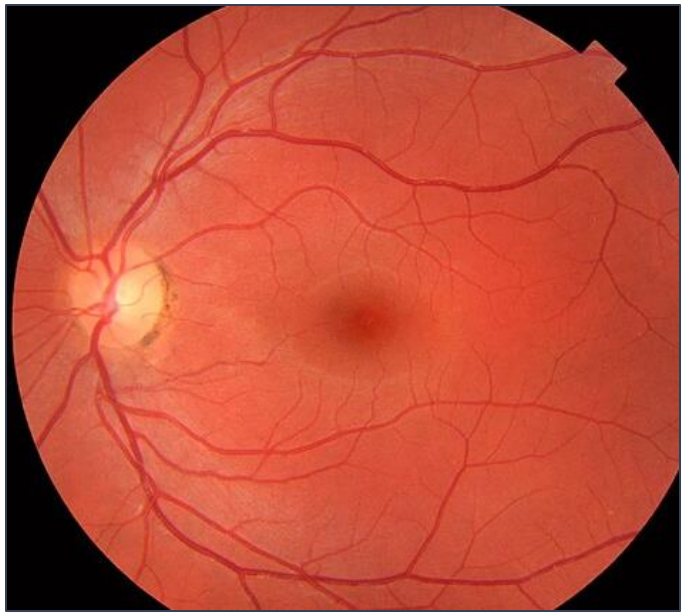
GA is Advanced Form of Dry AMD:

Loss of Photoreceptors –
neurons that sense light in the retina
leads to loss of vision

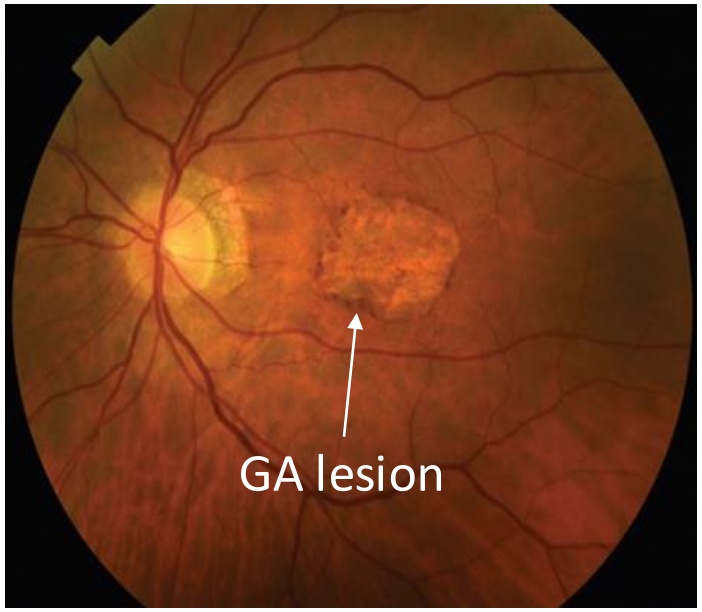
▼

Subsequent atrophy of Retinal Pigment Epithelium (RPE) –
cells that support the photoreceptors
shown in GA lesion growth

Normal retina



Retina with GA



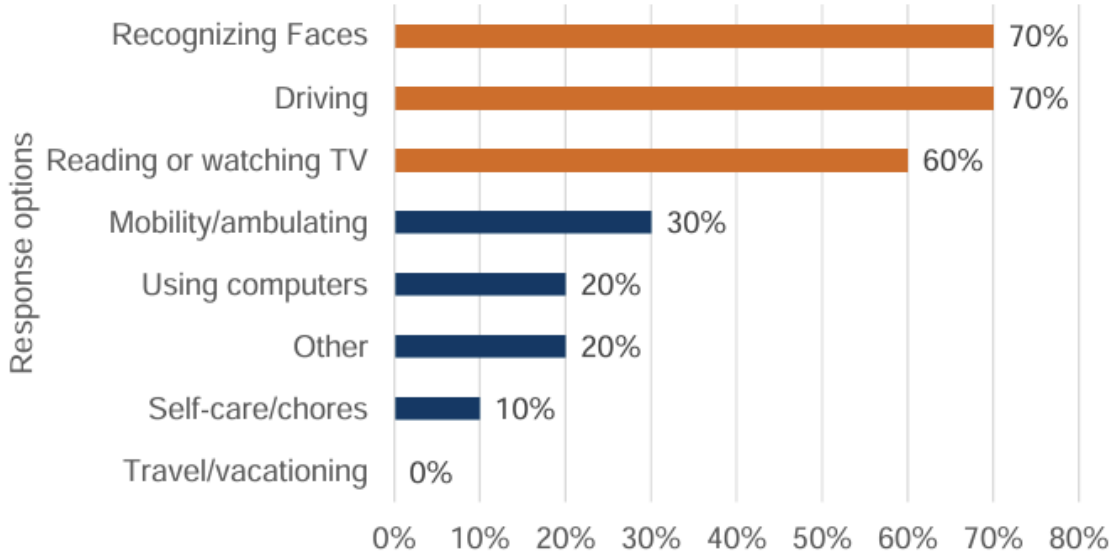
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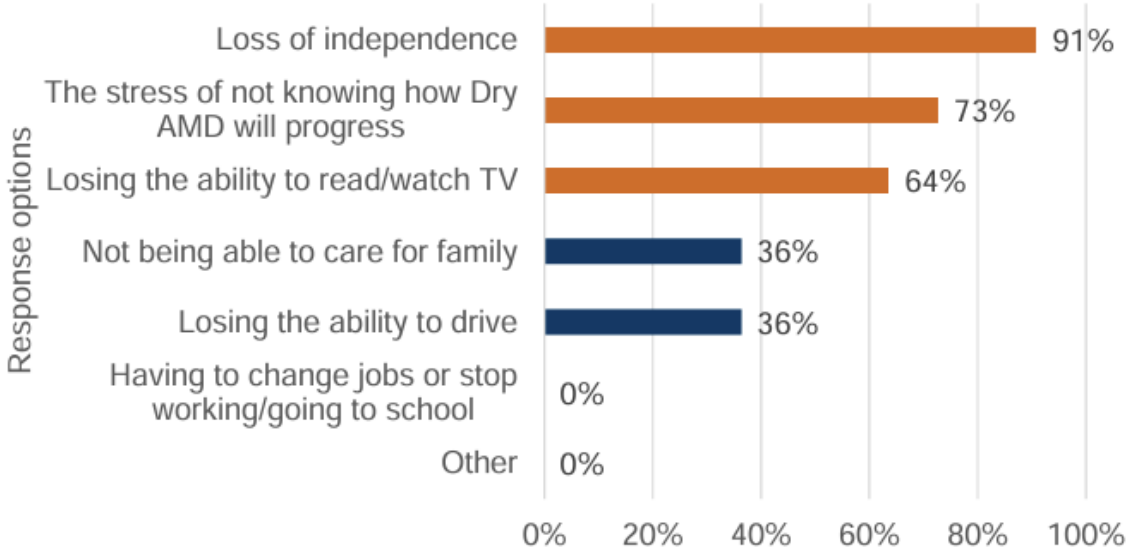
Vision Loss from GA Meaningfully Impacts Patients' Daily Lives

Recent survey results in patients with GA and their caregivers

ACTIVITIES GA PATIENTS ARE NOT ABLE TO DO, OR STRUGGLE WITH



WHAT WORRIES GA PATIENTS MOST ABOUT THEIR CONDITION IN THE FUTURE



From the Voice of the Patient Report; Dry Age-Related Macular Degeneration (AMD) Externally-Led Patient Focused Drug Development Meeting (EL-PFDD) Meeting; Report date: May 17, 2024

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ARCHER II Phase 3 Endpoint – BCVA 15 Letter Loss – is the Gold Standard Visual Acuity Endpoint in Retina Space

PRODUCT	FUNCTIONAL PRIMARY ENDPOINT
Wet AMD	
Lucentis	Proportion losing <15 letters BCVA
Eylea	Mean BCVA change
Vabysmo	Mean BCVA change
DME	
Lucentis	BCVA ≥15 letter
Eylea	Mean BCVA change
Vabysmo	Mean BCVA change
GA	
Syfovre	N/A
Izervay	N/A

BCVA 15 Letter Loss

- Represents 3 lines of letter loss
  - Loss of independence (e.g., inability to read, drive)
  - Impact on independent living

Clinically relevant, stable endpoint when confirmed at two consecutive visits

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Geographic Atrophy Treatment Landscape Rapidly Evolving

C3/C5 therapies designed to stop RPE atrophy/lesions

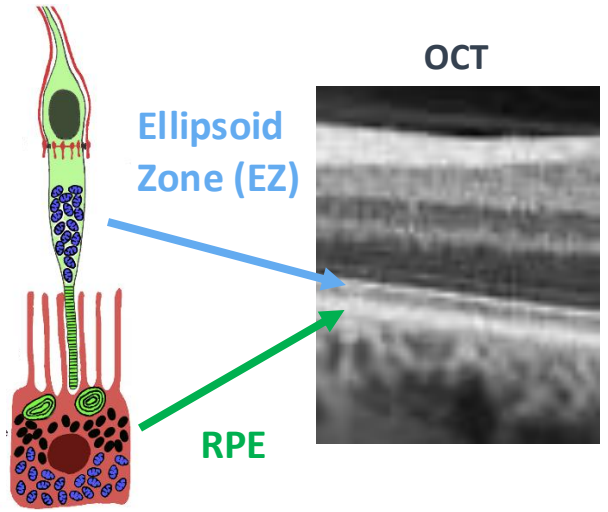
- Human genetics established complement inhibition as a therapeutic strategy for GA
- C3/C5 designed to target the alternative pathway to preserve RPE cells/reduce lesion growth
- Protection of RPE has not resulted in preservation of vision

SYFOVRE (pegcetacoplan injection)

izervay (avacincaptad pegol intravitreal solution)

Recent advances: PR neurons are increasingly understood as locus of disease based on OCT/EZ

- **GA is a neurodegenerative disease** resulting in photoreceptor and vision loss
- Loss of PRs via the classical pathway/C1q precedes RPE loss



Today's Opportunity

- Vision-preserving therapy will meaningfully improve patient lives

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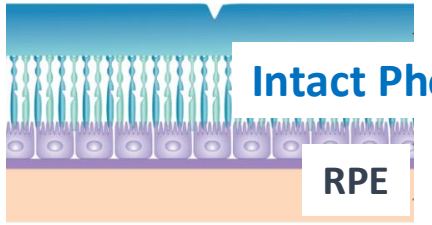
Anti-C1q Mechanism of Action



GA is a Neurodegenerative Disease that Starts at Photoreceptor Synapses and Cells Necessary for Vision

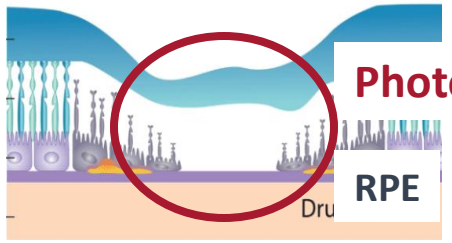
NORMAL RETINA

Photoreceptors convert to electrical signals



RETINA WITH GA

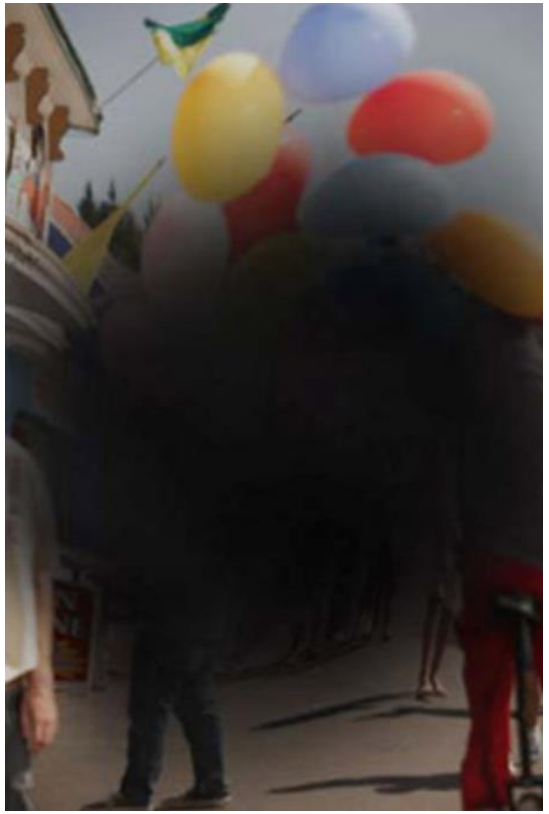
Loss of signals due to damaged or missing photoreceptors



Normal Vision



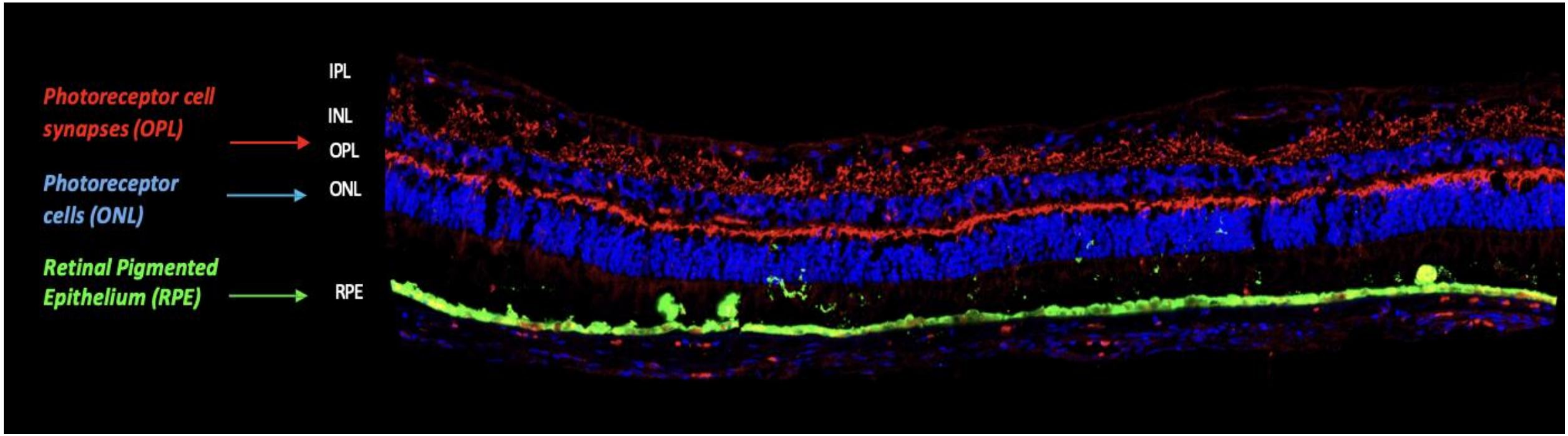
Reduced Vision



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Healthy Retina Has Uniform Layer of Photoreceptors and Synapses



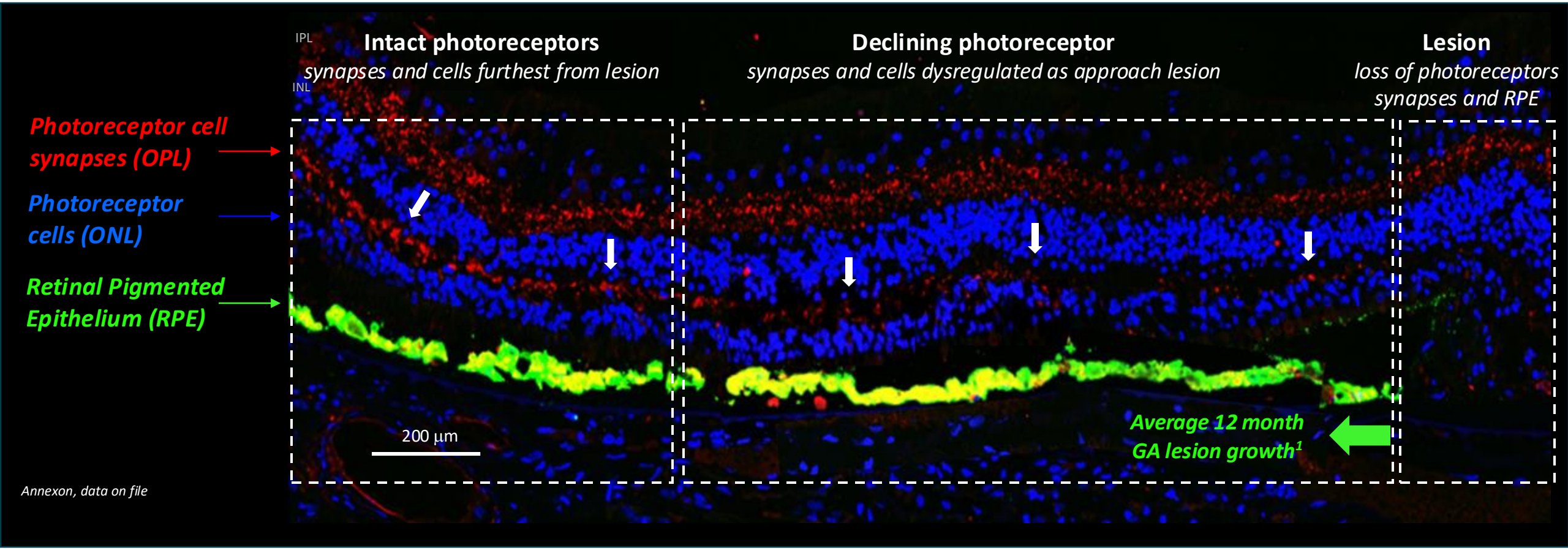
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[1]Bird et al., 2014 *JAMA Ophthalmol* doi:10.1001/jamaophthalmol.2013.5799; Li, et al., 2018 *Retina* 38:1937; Pfau, et al., 2020 10.1001/jamaophthalmol.2020.2914; Sarks, et al., 1988 *Eye* 2:552; [2]Selkoe, 2002 doi: 10.1126/science.1074069; Burger, et al., doi.org/10.1016/j.ydbio.2021.04.001; [3]Heier, et al., 2020 Ophthalmology Retina **4**:673; [4]Shen, et al., 2020 *Ophthalmol Retina* **4**:899

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In GA Photoreceptors and Synapses are Lost Before RPE Loss

Photoreceptors responsible for visual acuity. Photoreceptor loss = vision loss

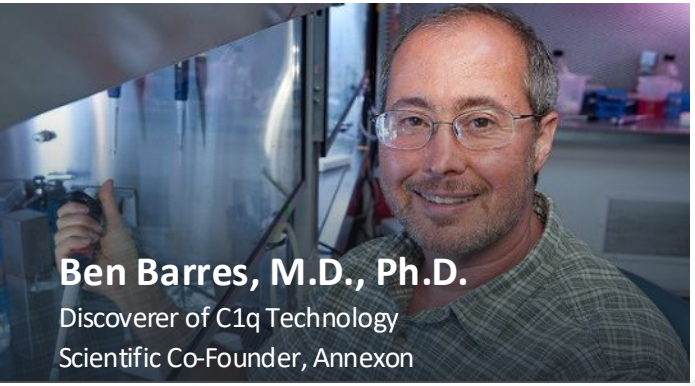


Photoreceptor Health	Functional retina	Reduced function	Lost function

[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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Anti-C1q is a Well-Researched & Differentiated Approach to Treating Neurodegeneration (protect synaptic / neuronal function)



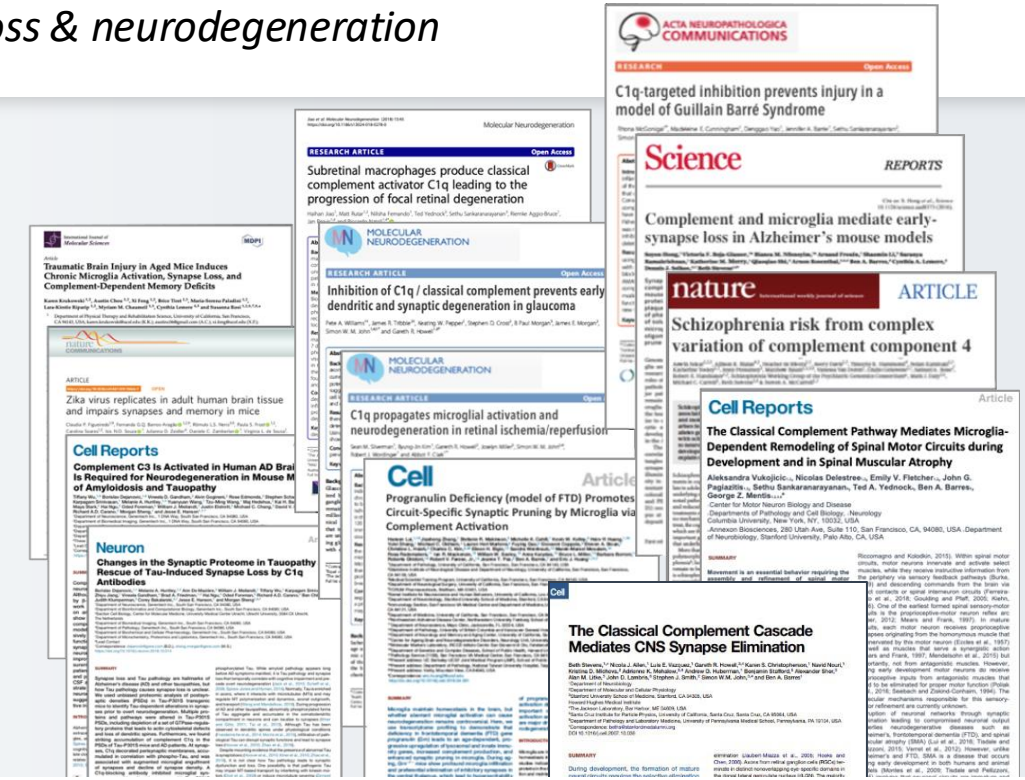
Ben Barres, M.D., Ph.D.
Discoverer of C1q Technology
Scientific Co-Founder, Annexon

C1q PLAYS KEY ROLE in NEURODEGENERATION PROCESS

- *Normal role for synapse elimination in development*
- *Pathogenic role in neurodegenerative diseases*
- *Anti-C1q protects against synapse loss & neurodegeneration*

Anti-C1q Protective in Neurodegenerative Diseases, Including:

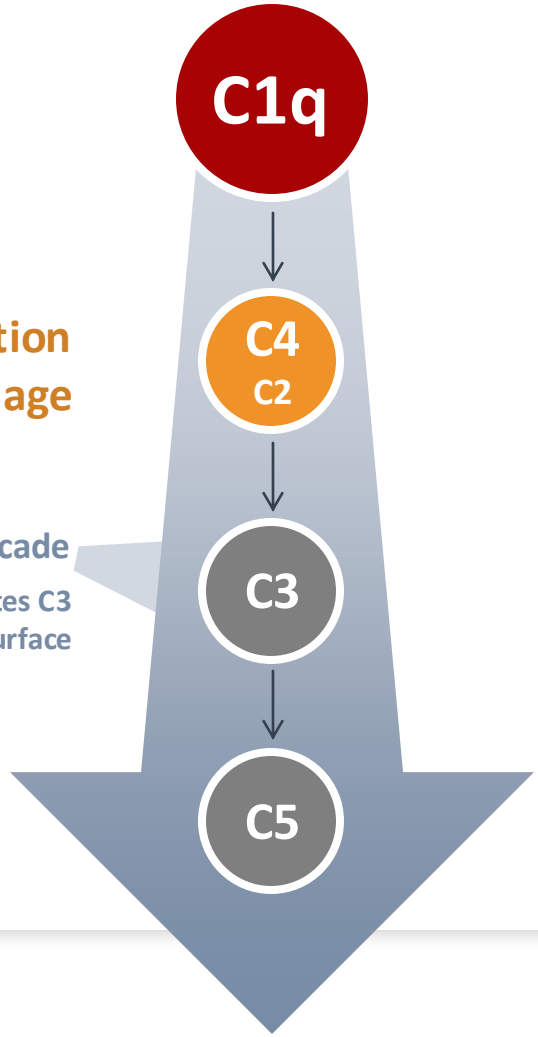
- Dry AMD (photoreceptor damage)
- Glaucoma
- Retinal ischemia
- Multiple Sclerosis/ Optic Neuritis
- Huntington's disease
- Guillain-Barré syndrome
- Alzheimer's disease
- Traumatic brain injury



[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]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

C1q and Classical Complement Plays Key Role in Neurodegeneration

Classical Complement Cascade



Amplifies inflammation and tissue damage

Alternative Complement Cascade

Non-selectively activates C3 on any surface

C1q tags functional synapses for removal in disease

- Activates classical pathway
- Attracts microglial cells
- Drives neuronal death
- Results in vision loss in AMD

C3/C5 removes dysfunctional cells at lesion edge

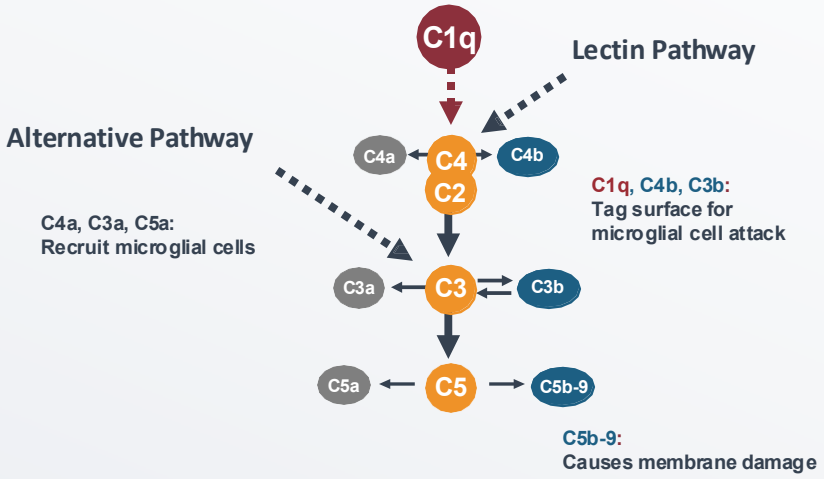
- Drives cell clearance (e.g., RPE) via alternative pathway
- Occurs after photoreceptor damage/loss
- Dysfunctional RPE cells secrete VEGF, increasing CNV risk

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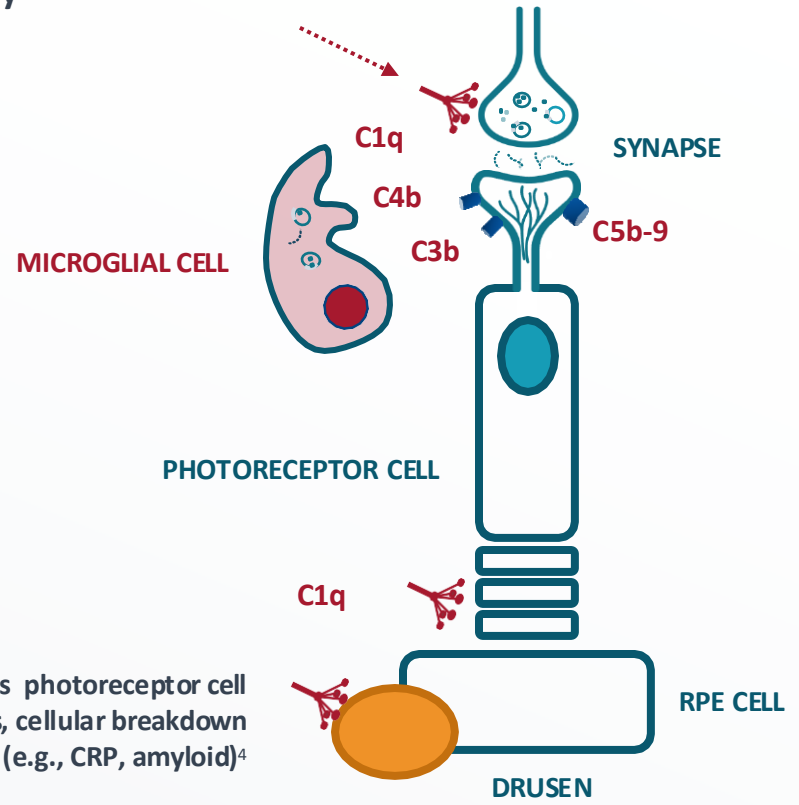
Anti-C1q: A Distinct Neuroprotective Mechanism

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]
- **Vonaprument 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]

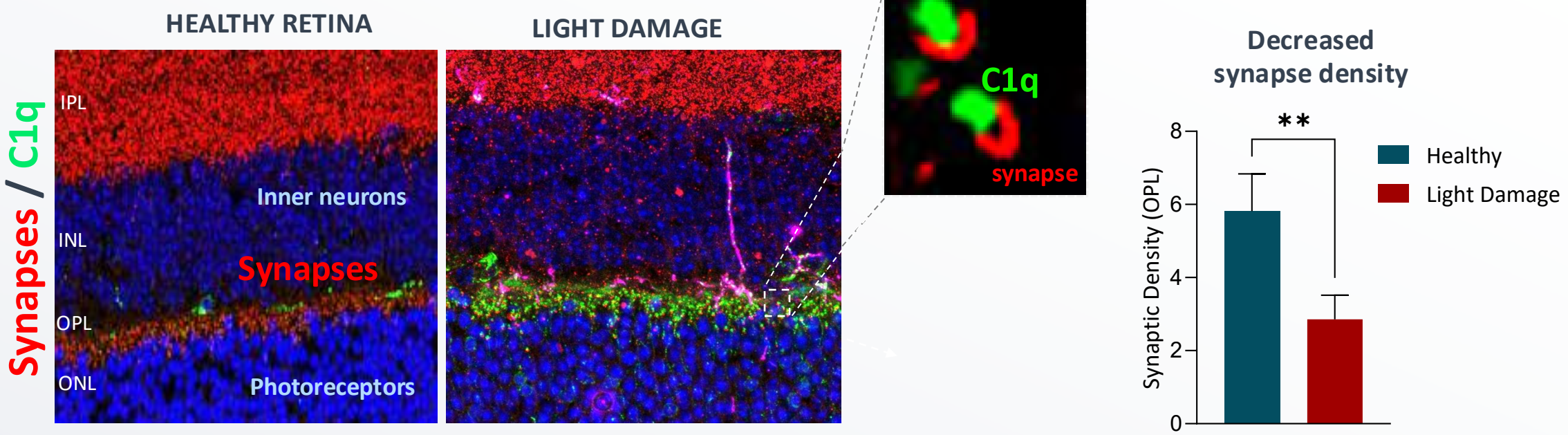
[1]Stevens, 2007, *Cell* **131**:1164; Howell, et al., 2011 *J Clin Invest*. **121**:1429; Schafer, et al., 2012 *Neuron* **74**: 691; Stephan et al., 2012 *Annu Rev Neurosci* **35**:369; Hong, et al., 2016 *Science*. **352**:712; Lui, et al., 2016 *Cell* **165**:921; Dejanovic, et al., 2018 *Neuron* **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

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C1q Recognizes and Aberrantly Eliminates Photoreceptor Synapses

Light-Induced Damage Model of Photoreceptor Degeneration

C1Q SELECTIVELY BINDS SYNAPSES ON DAMAGED PHOTORECEPTORS



Tassoni, et al., ARVO, 2024 and Annexon on file

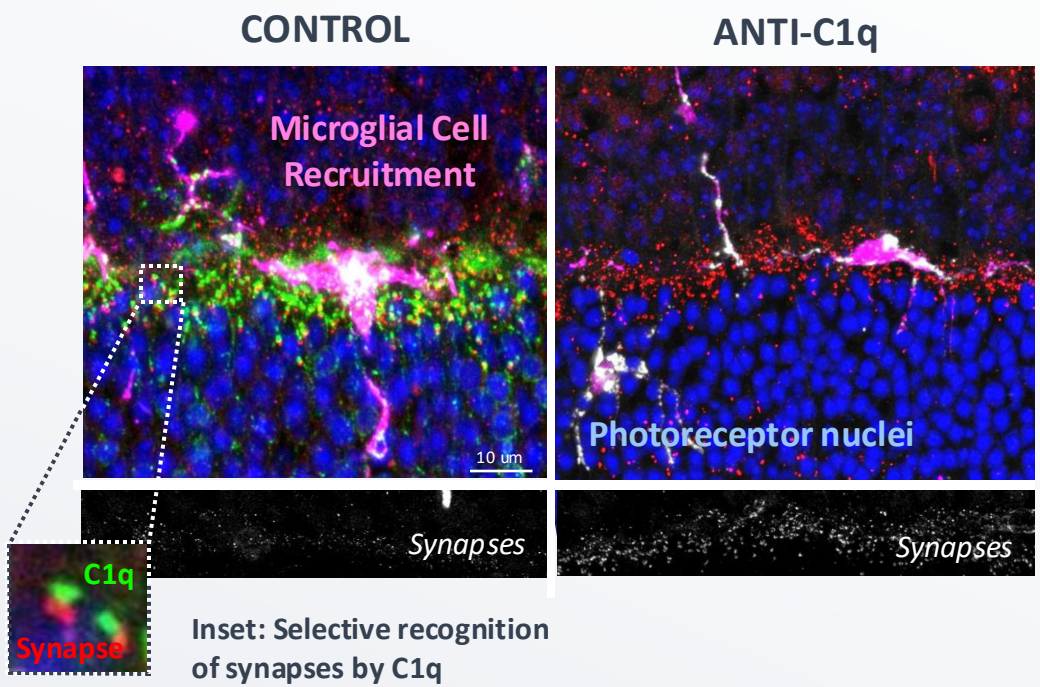
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C1q Inhibition Protected Photoreceptor Cells and Function

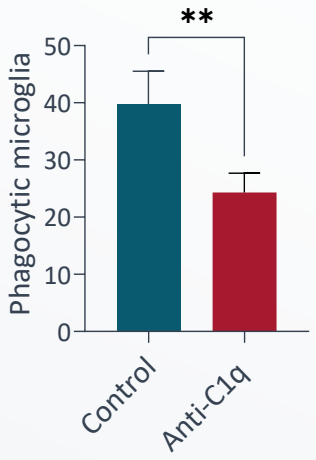
Light-Induced Damage Model of Photoreceptor Damage

VONAPRUMENT REDUCED INFLAMMATION AND PRESERVED PHOTORECEPTOR SYNAPSES AND CELL BODIES

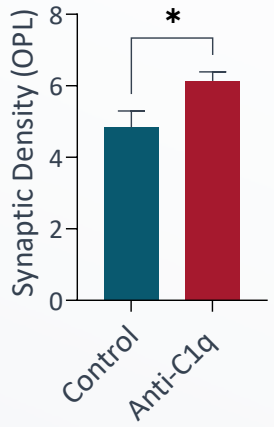


Inset: Selective recognition of synapses by C1q

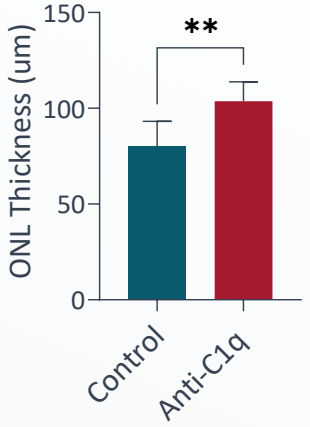
Reduced reactive microglia



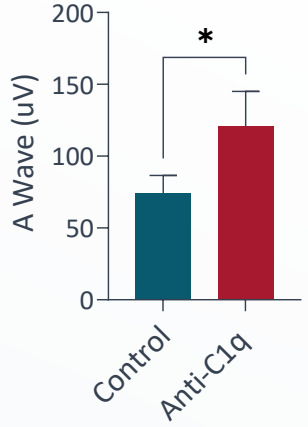
Protected photoreceptor synapses



Protected photoreceptor cell bodies



Protected retinal function



*p < 0.05
**p < 0.01

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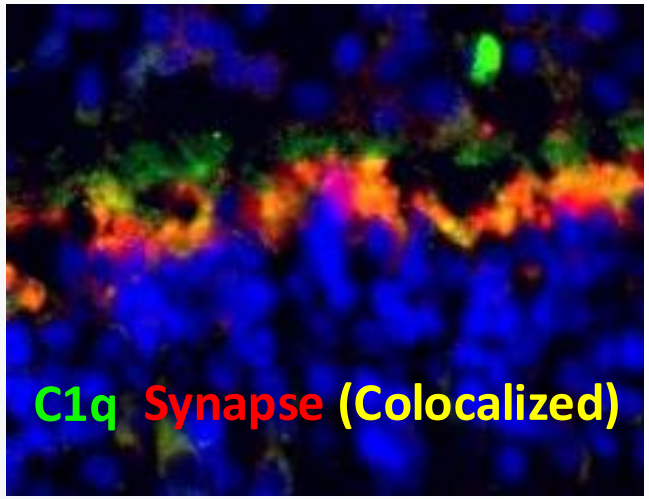
Tassoni, et al., ARVO 2024; Annexon data on file; Jiao, et al., 2018 *Mol Neurodegener* **13**:45;.

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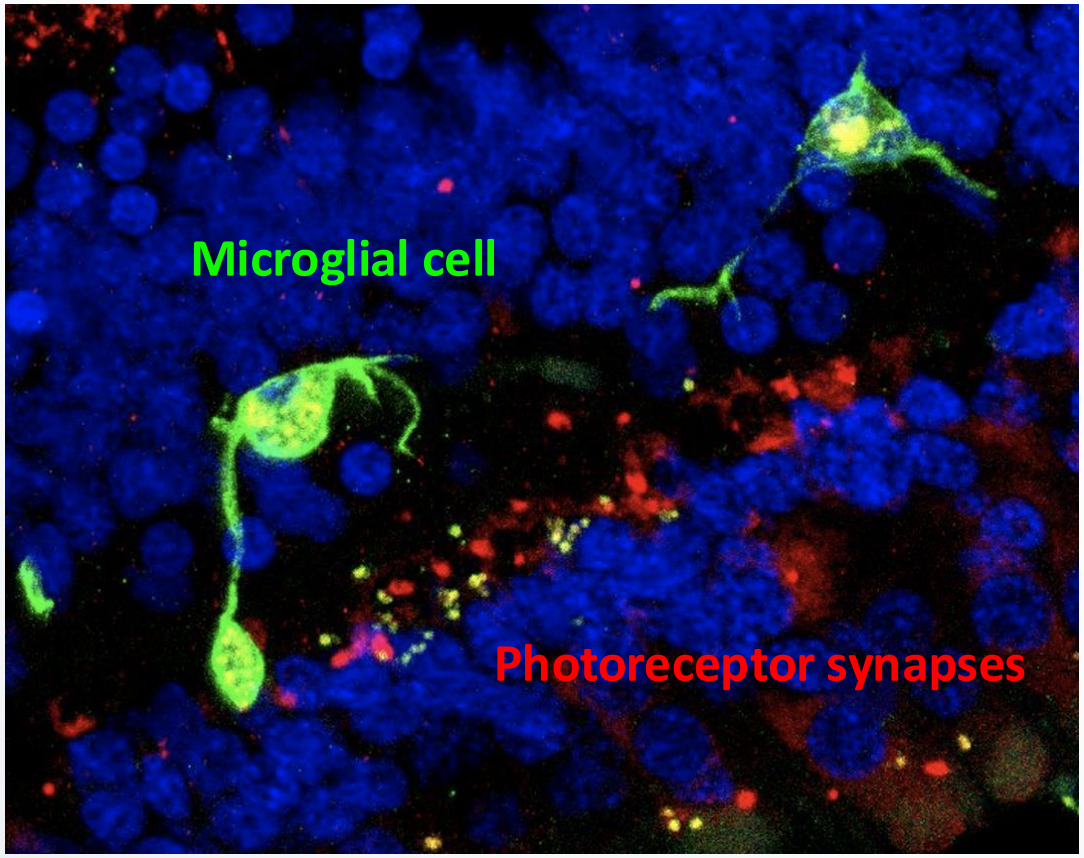
C1q Deposition and Synapse Loss in GA

Human postmortem GA retina tissue

C1q DEPOSITION ON PHOTORECEPTOR SYNAPSES



MICROGLIAL CELL RECRUITMENT AND PHOTORECEPTOR SYNAPSE LOSS



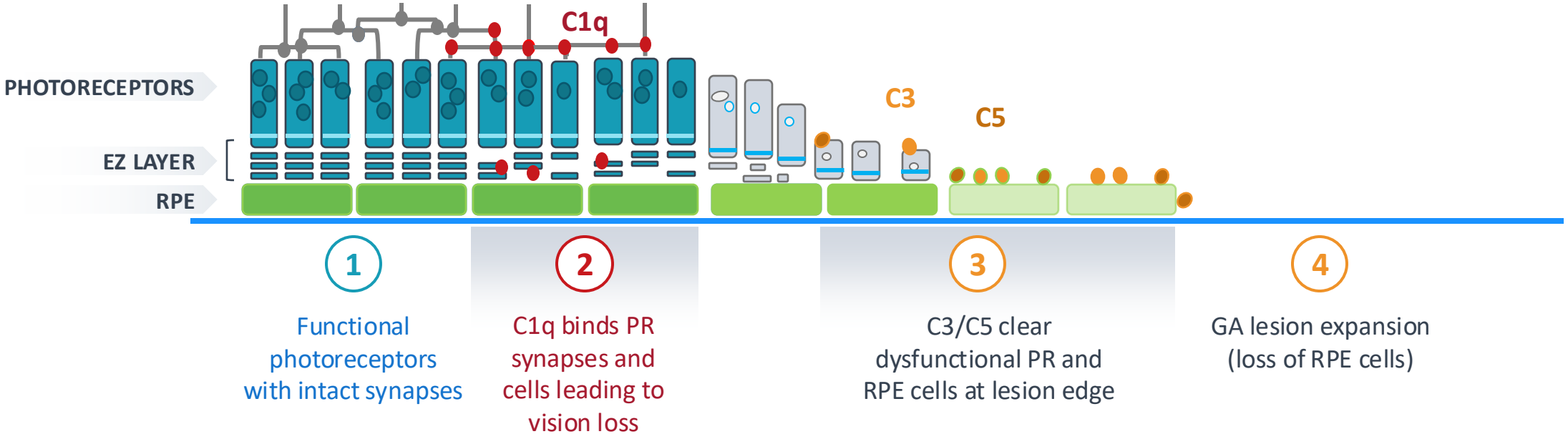
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Tassoni, et al., ARVO 2024; Annexon data on file;

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Sequence of GA Progression: C1q Binds and Removes Functional Photoreceptors Prior to RPE Atrophy and Lesion Growth

C3/C5 clears dysfunctional photoreceptors and RPE at lesion edge

Depiction of Photoreceptor and RPE Layers in GA Retina



C1q inhibition
targets functional photoreceptors
Preserving vision

C3/C5 inhibition
targets dysfunctional cells
At lesion edge after photoreceptor damage/loss

[1]Yednock, et al, 2022 International *J Retin and Vitreous* **8**:79; [2]Heier et al, Vision Protection in Dry Age-related Macular Degeneration: Randomized Clinical Trial of Vonaprument, submitted 2025; [3]Merle, et al., 2015 *Front Immunol* **6**:262; [4]Paterson, et al., 2023 *Molecular Vision* **29**:87-101; Farjood et al. 2020 *J Biol Eng* **14**:13; [5]Ehlers and Wykoff *Retina Today* Nov/Dec 2024; Pfau, et al., 2020 10.1001/jamaophthalmol.2020.2914; [6]Katschke, et al, 2018 *Sci Rep* **8**:7348

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Summary of GA and Vonaprument's Role in Protecting Vision Loss

Blocks C1q to stop photoreceptor damage where it starts

Vision loss in GA is driven by photoreceptor synapse and cell loss

- Neurodegeneration, photoreceptor damage, and vision loss precedes RPE atrophy

C1q is the aberrant upstream trigger of this neurodegenerative process in GA

- Tags functional photoreceptor synapses and cells in disease for removal
- Activates classical complement cascade, with microglial recruitment and neuroinflammation
- Synapse loss → photoreceptor damage → irreversible vision loss

Clear mechanistic differentiation vs. downstream complement inhibitors

- Upstream C1q: protects photoreceptors necessary for visual acuity
- Allows for normal clearance functions of alternative pathway
- Downstream C3/C5: slows RPE lesion growth but does not slow vision loss

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Vonaprument (ANX007) – a Unique Neuroprotective Drug Candidate



Vonaprument (ANX007): Differentiated IVT Inhibitor of C1q and Classical Complement to Treat Geographic Atrophy

DESIGN



- **Modeled on established IVT Fab antibodies**
- **Same anti-C1q structure as tanruprubart** – well tolerated IV treatment in GBS, HD, and ALS

PROFILE



- **Small 50 kD Fab antibody**
- **Non-pegylated, with low viscosity and high potency** (<10 pM)

DOSING



- 5 mg administered in **25 microliter dose (in ongoing Phase 3 ARCHER II trial)**

SPECIFICITY



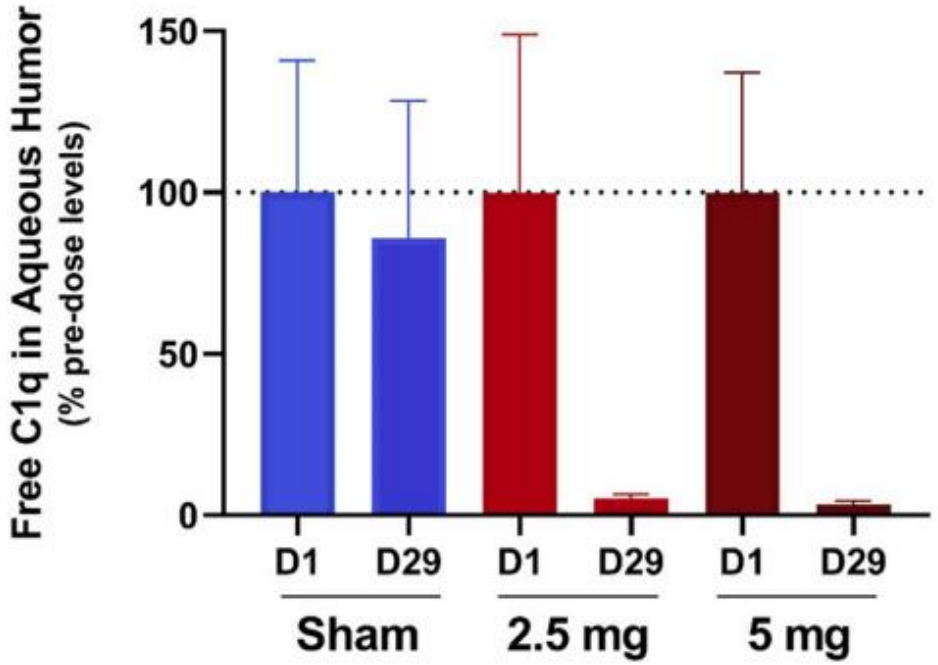
- **Full target engagement** of classical pathway
- **Lectin and alternative pathway left in place** for immune and homeostatic functions [1]

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

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Dose Ranging Trial: Vonaprument Demonstrated Full C1q Target Engagement

Significant Reduction in Free C1q through 4 Weeks after Single Vonaprument Dose



Patient aqueous humor PK/PD supports 5mg at least monthly intravitreal injection

Well-tolerated, good safety profile

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Sun et al, Ophthalmology Science (2023)

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ARCHER Phase 2 Trial Overview



ARCHER: Phase 2 Trial of C1q Inhibitor Vonaprument 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)
- **Vonaprument 5mg monthly (EM)** (n=89)
- **Vonaprument 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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Patient Demographics and Study Eye Baseline Characteristics Generally Well-Balanced Across Groups

CHARACTERISTIC	SHAM POOLED (N=89)	VONAPRUMENT EM (N=89)	VONAPRUMENT 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 (%)	86 (96.6%)	88 (98.9%)	89 (96.7%)
Mean BCVA, mean (SD)	**58.5 (16.2) ~20/70**	**58.8 (17.2) ~20/70**	**57.9 (15.3) ~20/70**
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%)

Proportion of Study Discontinuations Similar Among Treatment Arms and Consistent with Previous GA Studies (Through 12 Months)

	SHAM POOLED (N=89)	VONAPRUMENT EM (N=89)	VONAPRUMENT 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	---

ARCHER POC: Key Safety Data

ADVERSE EVENTS OF SPECIAL INTEREST n (%)	SHAM (N=89)	VONAPRUMENT EM (N=89)	VONAPRUMENT 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	0	0	0
Intraocular Inflammation+	0	2 (2.2%)	1 (1.1%)
Ischemic Optic Neuropathy+	0	0	0

CNV rate generally similar across sham and treatment arms

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

Vonaprument, formerly ANX007

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ARCHER Phase 2 Trial: Vonaprument Impact on Retinal Structure Associated with Visual Acuity

Importance of Ellipsoid Zone and Central Photoreceptors in Visual Function



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ARCHER: Phase 2 Clinical Trial Structural Outcomes

Retinal Pigment Epithelium/GA Lesion Size

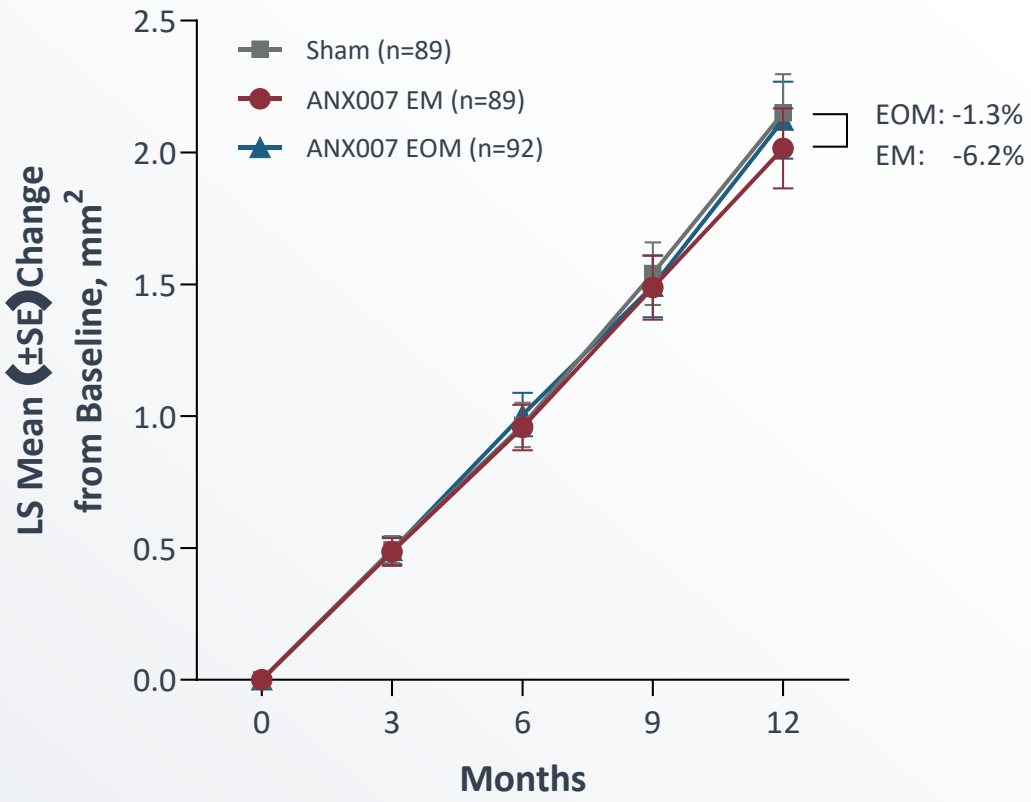
- Loss After Photoreceptor Synapses / Cells

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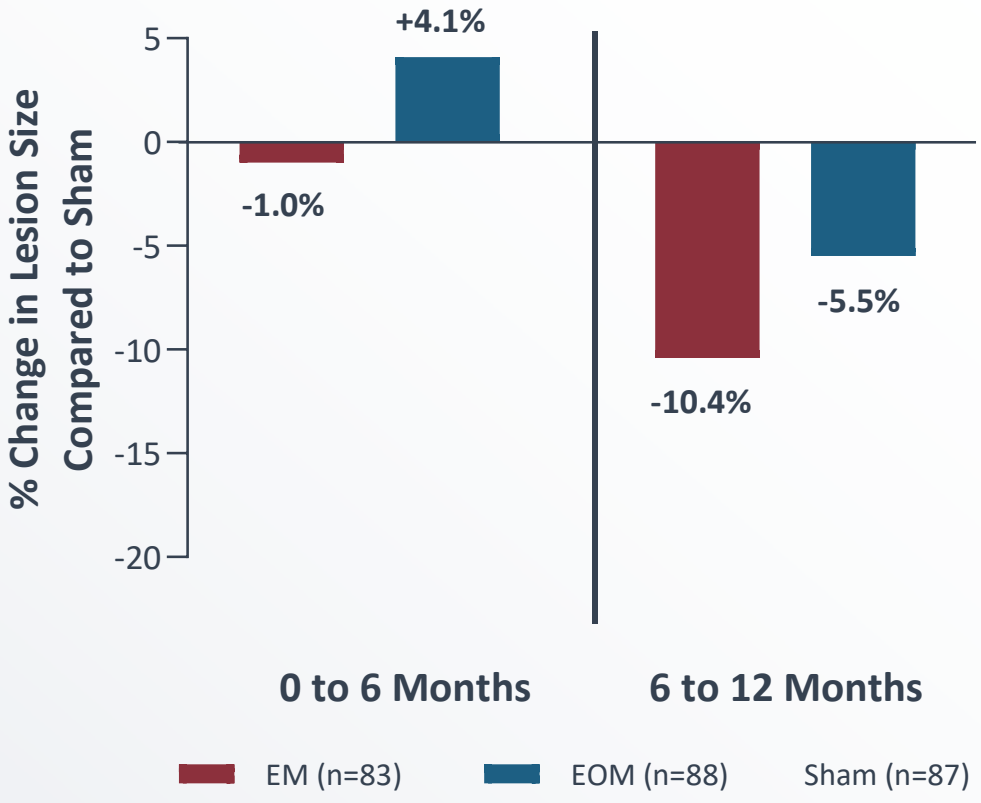
Vonaprument Treatment Effect on RPE Loss through 12 Months

No significant reduction at month 12, but effects increased over 2nd half of study

RPE LOSS FROM BASELINE TO MONTH 12#



CHANGE IN RPE LOSS OVER TIME#



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#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.

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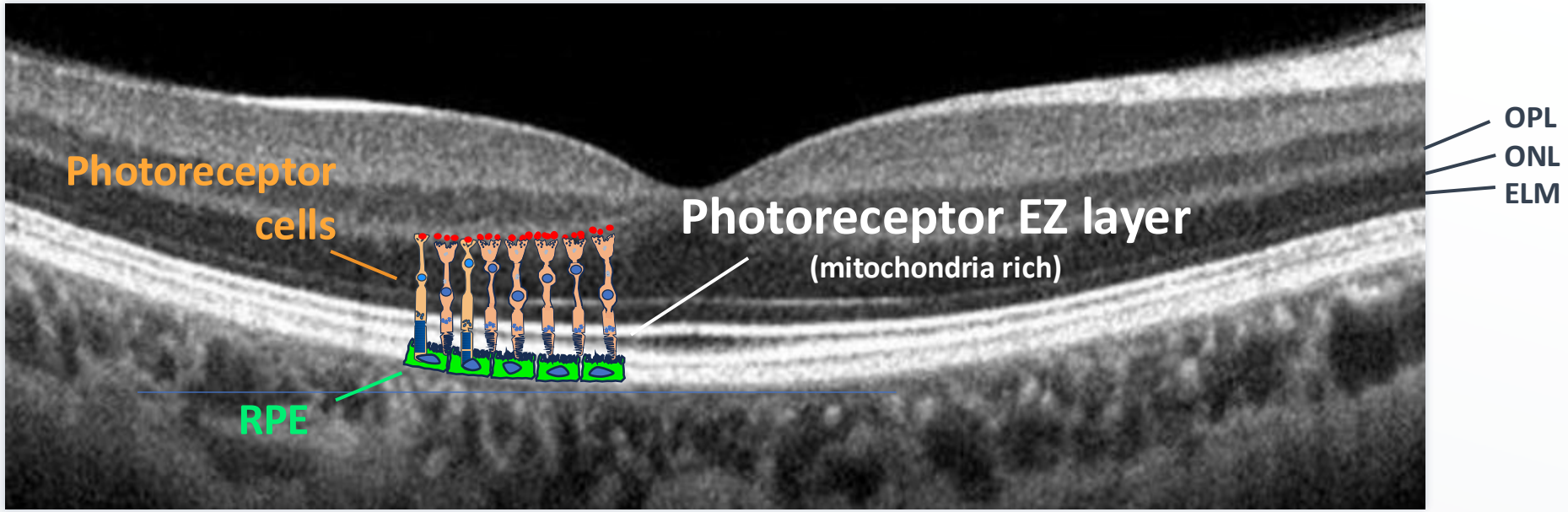
ARCHER: Phase 2 Clinical Trial Structural Outcomes

Ellipsoid Zone

- Demonstrating Protection of Photoreceptor Health

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Ellipsoid Zone (EZ) is a Key Anatomic Measure of Photoreceptor Health and Function



octscans.com

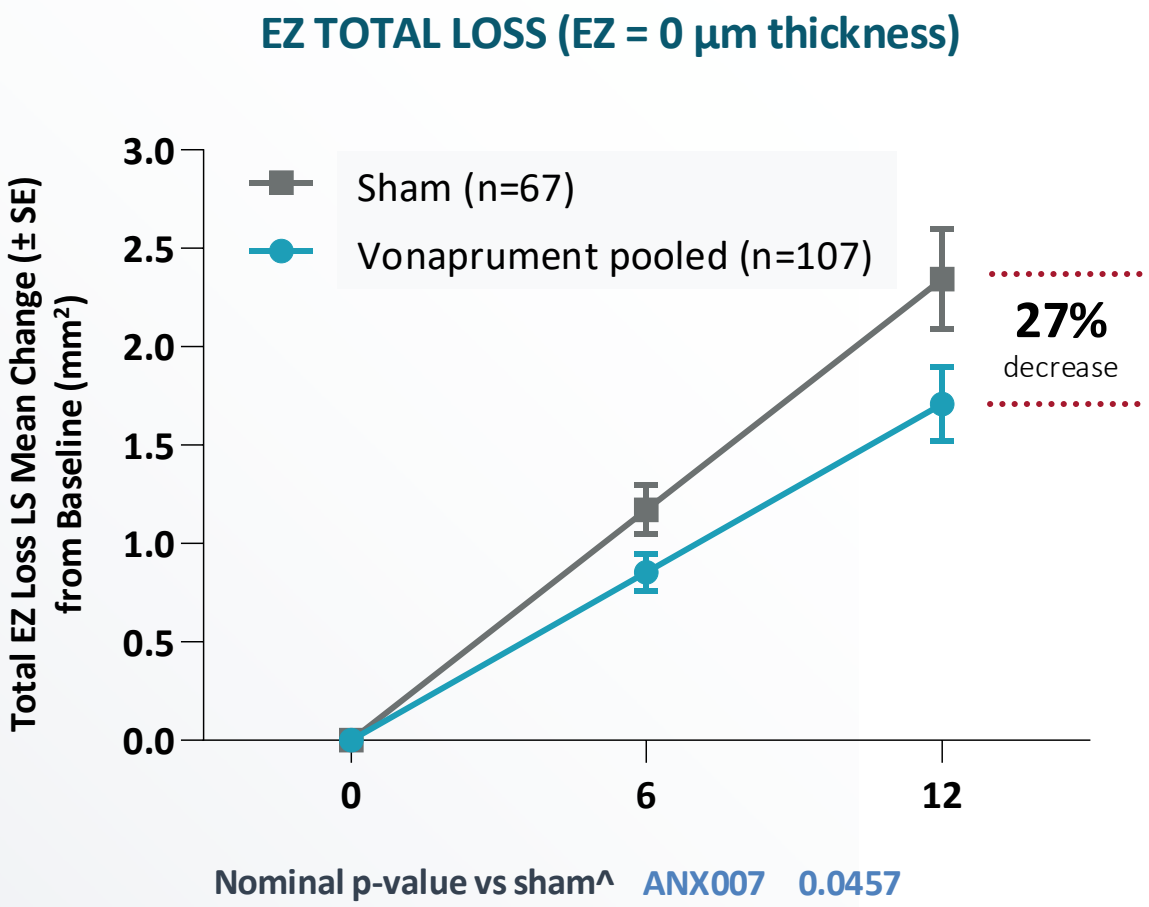
- Hyperreflective band on spectral domain optical coherence tomography (SD-OCT)
- Represents photoreceptor inner segments, contains densely packed mitochondria
- Physiologic link to photoreceptor activity and viability

Ehlers JP et al Retina Today; Dec 2024: 53-55

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Protection Against Total EZ Loss Through 12 Months



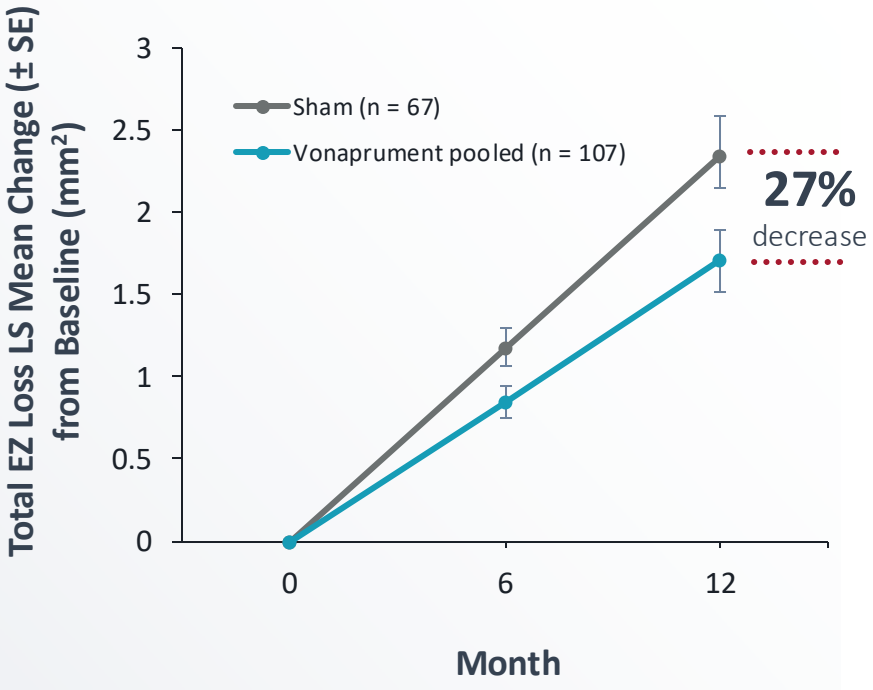
Vonaprument showed protection of functioning photoreceptors measured by EZ across pan-macula

^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
Vonaprument treatment arms were not statistically different
Final data

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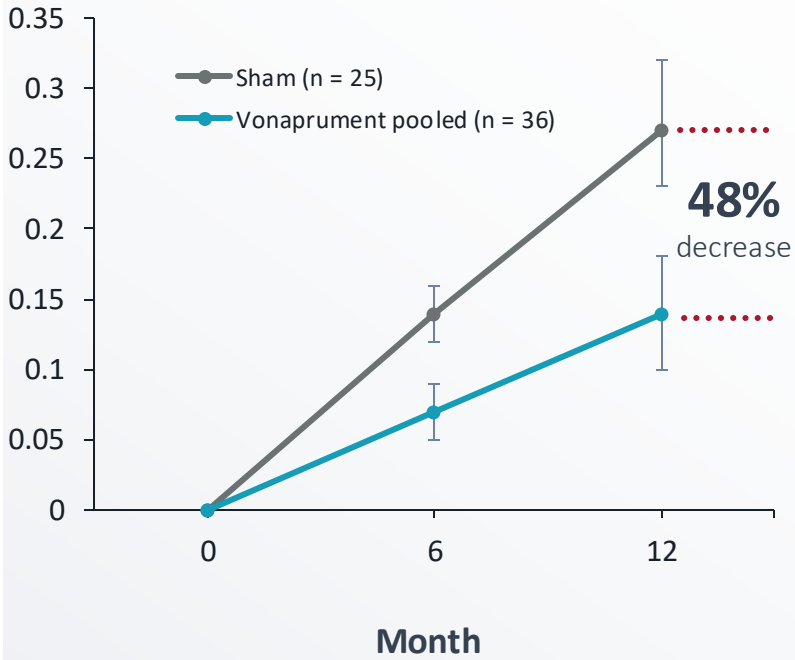
Greater Protection Against EZ Loss in Central Retina Necessary for Visual Acuity

PAN-MACULA



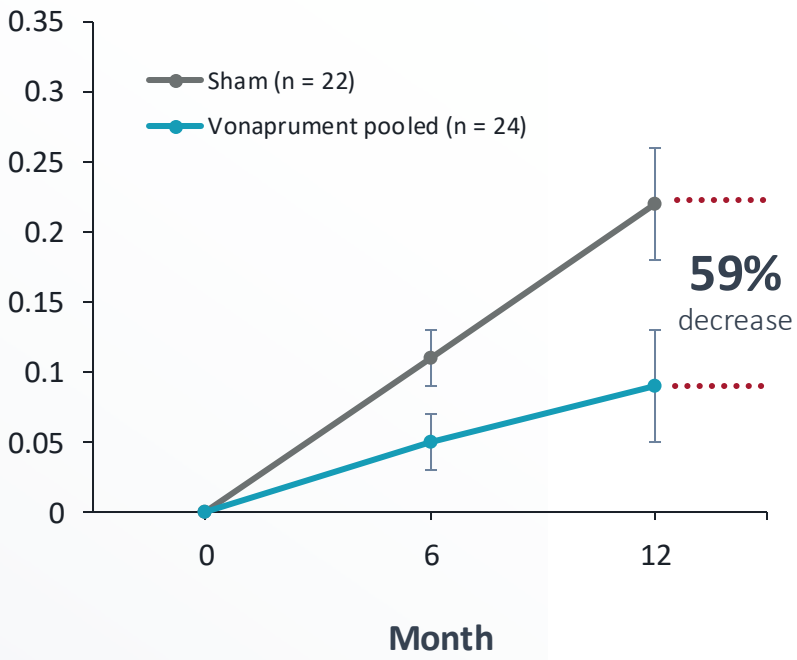
Nominal p-value^ Vonaprument Pooled vs Sham 0.0457

CENTRAL 2.0 MM



Vonaprument Pooled vs Sham 0.0218

CENTRAL 1.5 MM



Vonaprument Pooled vs Sham 0.0319

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^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

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ARCHER Phase 2 Sham Subject: 15-Letter and Ellipsoid Zone Loss

Baseline

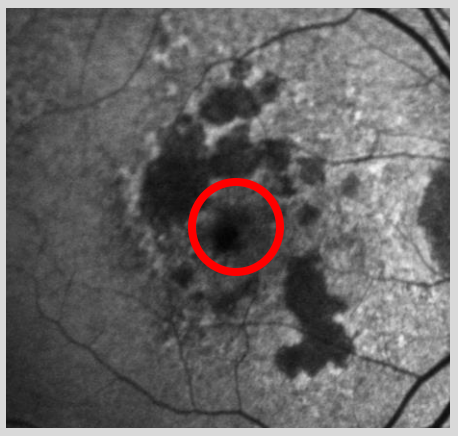
BCVA: 66 Letters



Intact Ellipsoid Zone (EZ)

EZ Loss

EZ Atrophy: 12.39 mm²



RPE Atrophy/GA Lesion

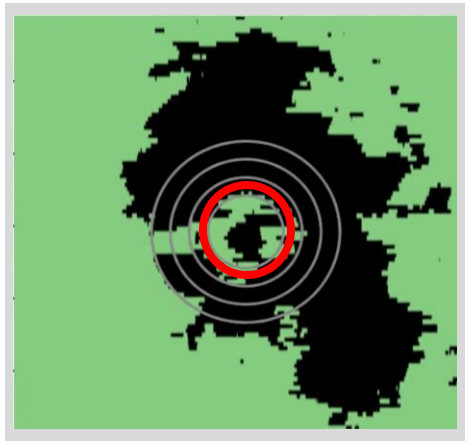
RPE Lesion: 4.90 mm²

- EZ is a key anatomic measure of photoreceptor health & function
- Visual acuity is dependent on photoreceptor status:
  - Amount lost
  - Location of EZ loss (central)
- EZ loss is always larger and precedes RPE loss

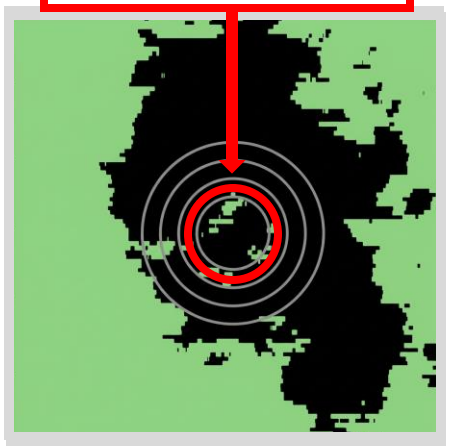
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ARCHER Phase 2 Sham Subject: 15-Letter and Ellipsoid Zone Loss

Baseline	Month 12
BCVA: 66 Letters	BCVA: 51 Letters



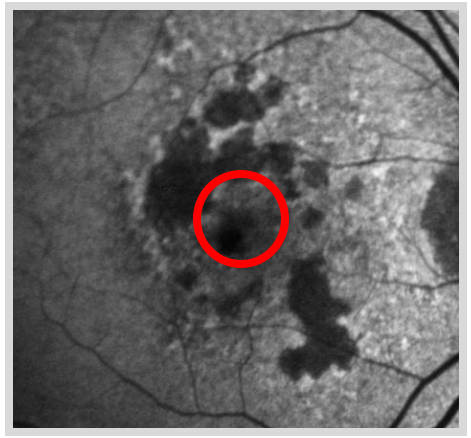
EZ Atrophy: 12.39 mm²



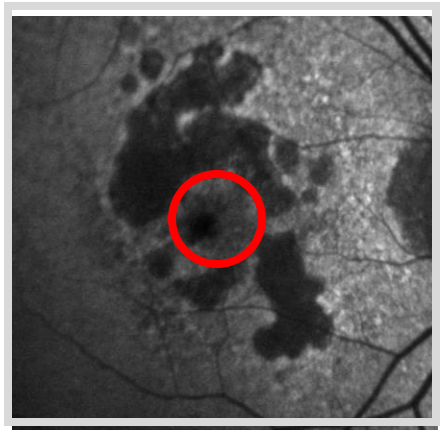
EZ Atrophy: 15.03 mm²

Intact EZ

EZ Loss



RPE Lesion: 4.90 mm²



RPE Lesion: 7.74 mm²

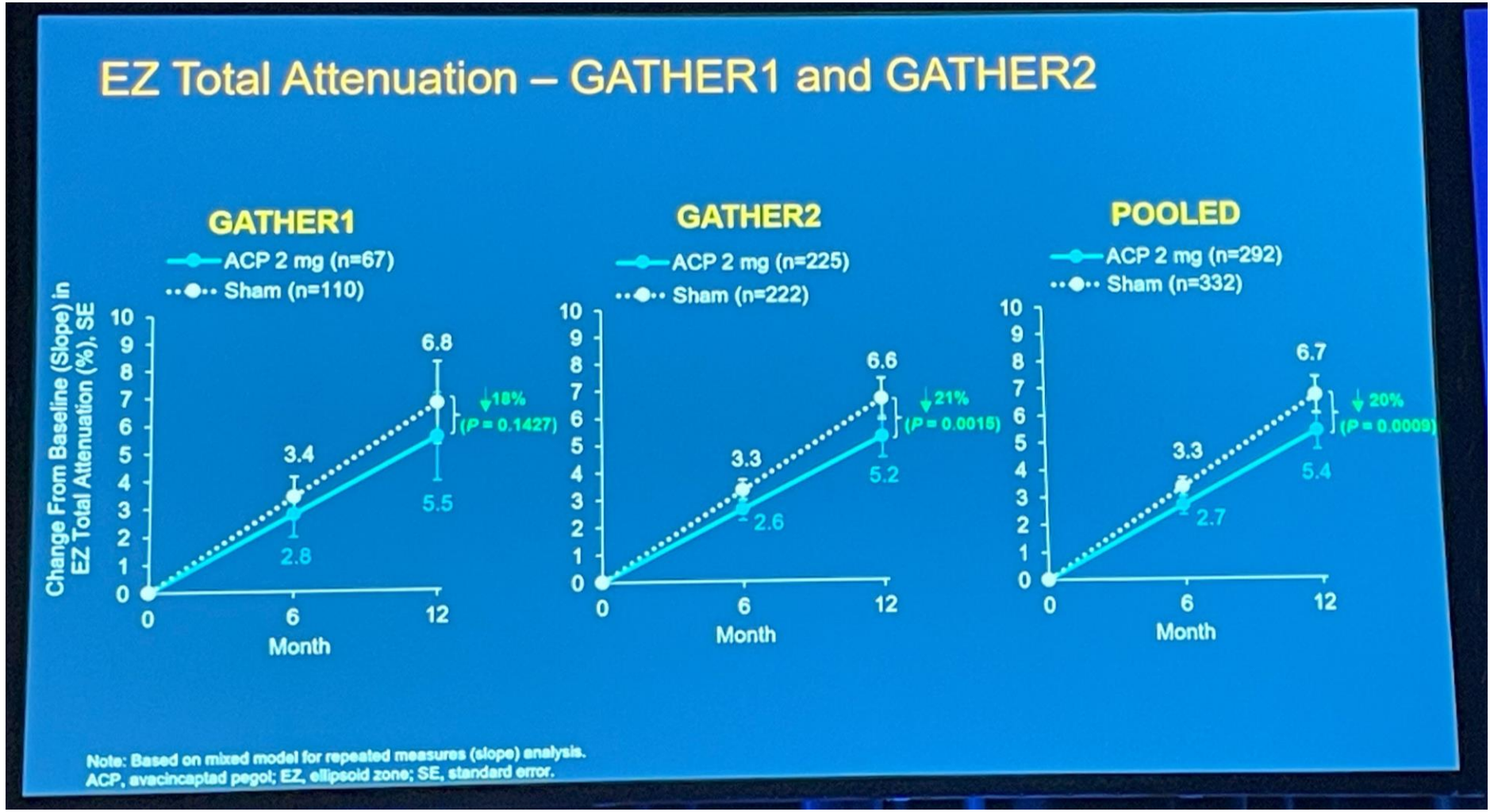
RPE Atrophy

- Visual Acuity loss associated with near total EZ loss in central retina, not changes in RPE lesion
- Photoreceptor loss drives disease progression, with RPE atrophy lagging

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GATHER 1/2: Izervay EZ Analysis Across Pan Macula

Only studied non-foveal patients; No data available on central retinal domains

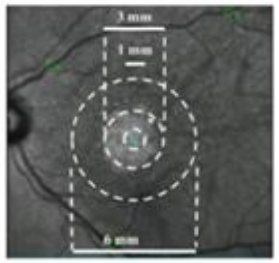


Ehlers J ARVO 2024

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DERBY/OAKS: Syfovre Post-hoc Photoreceptor Protection Analysis

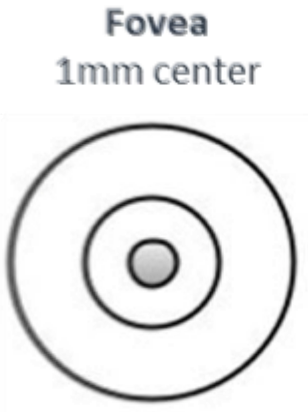
Photoreceptor protection diminishes in central subfields, area critical for visual acuity

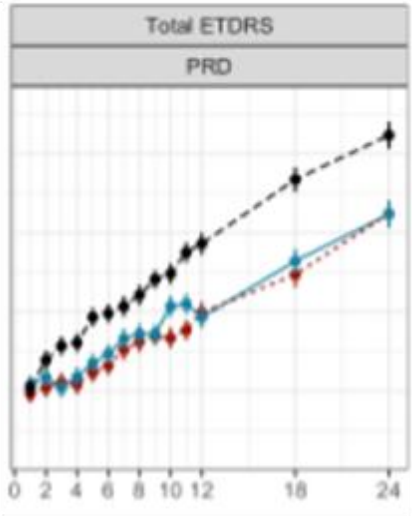


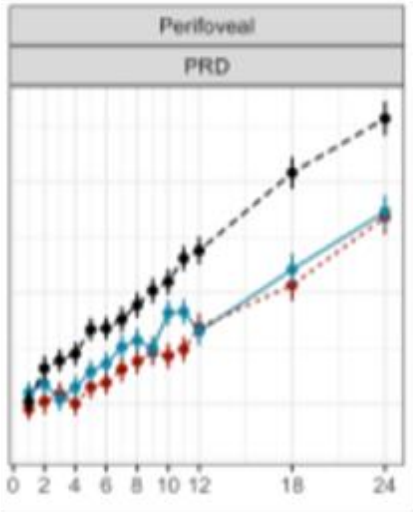


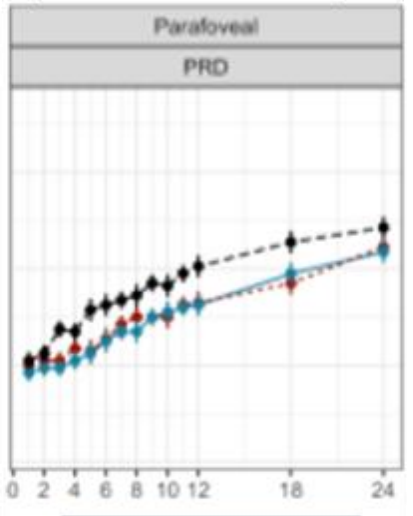


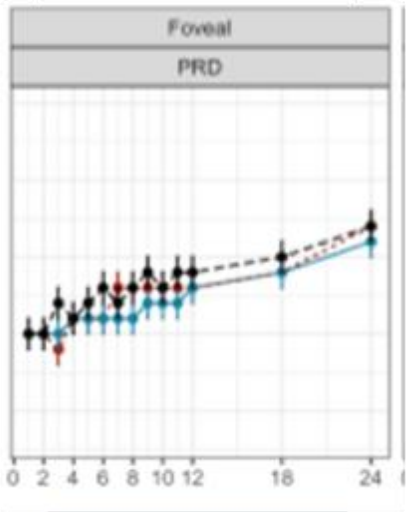












	12M	18M	24M
% change	-46.5%	-45.1%	-30.8%
P-value	<0.001	<0.001	<0.001

	24M
% change	-34.6%
P-value	<0.0001

	24M
% change	-13.6%
P-value	0.14

	24M
% change	-8.5%
P-value	0.56

Sham combined Peg EOM Peg Monthly

Fu DJ eta al, JAMA Opthalmology 2024

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ARCHER Phase 2: Vonaprument Protected Key Retinal Structures Important for Vision Preservation

Vonaprument Protected Functional Photoreceptors Across the Entire Macula

- OCT-based Ellipsoid Zone measurements provide objective measure of photoreceptor health
- Central retinal structures are critical for visual acuity and are key therapeutic target
- Photoreceptor preservation greatest in central retina, key for vision preservation

RPE Atrophy (GA Lesion) is Lagging Indicator of Disease Progression

- RPE loss occurs after loss of photoreceptors necessary for visual acuity
- Primary RPE protection (C3/C5) not associated with any functional benefit
- Vonaprument did not significantly protect RPE loss at month 12. RPE protection increased over 2nd half of study, suggesting increased RPE protection with longer treatment

Ellipsoid Zone (EZ) Analysis is Best Measure of Disease Progression in Dry AMD with GA

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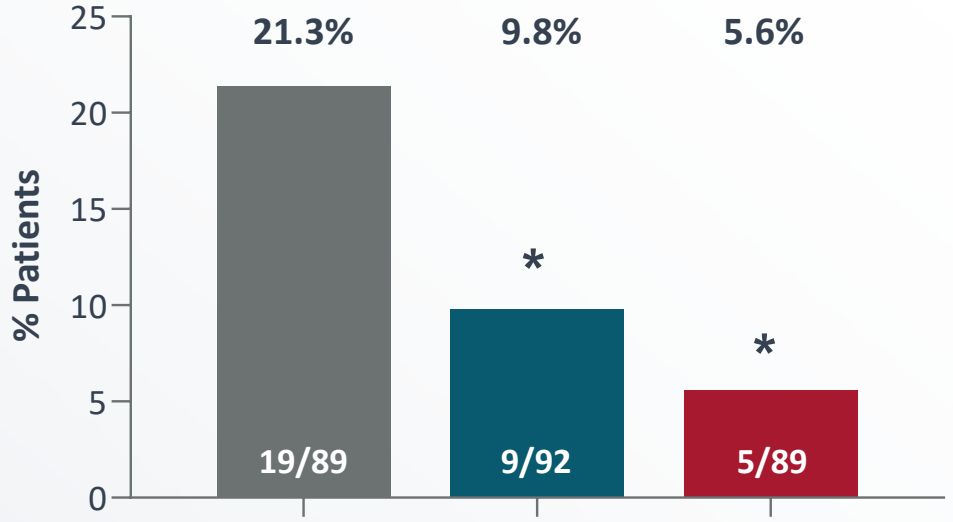
ARCHER Phase 2 Trial: Vonaprument Significant Protection of Vision Loss



Vonaprument Demonstrated Dose-Dependent Protection From Vision Loss as Measured by BCVA ≥15-Letter Loss

Consistent treatment effect when month 12 loss is confirmed at month 15

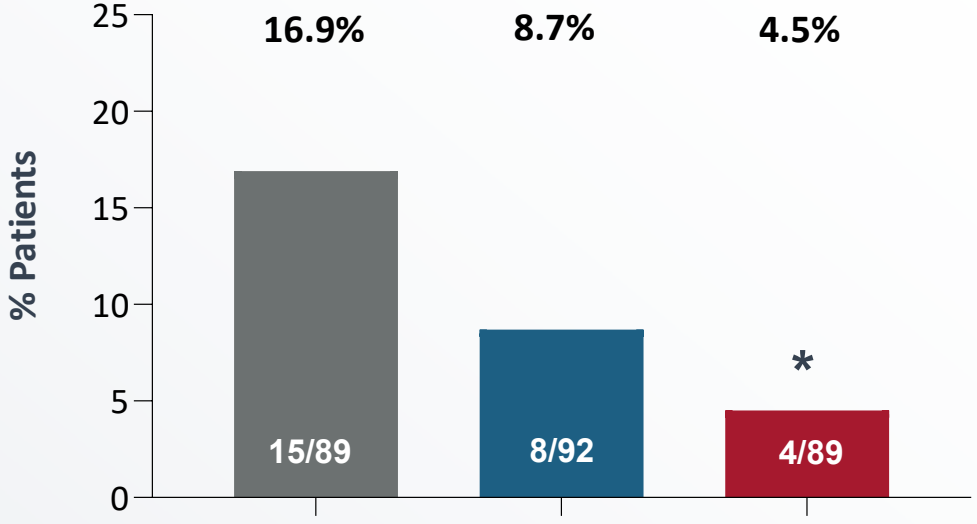
PATIENTS WITH CONFIRMED BCVA ≥15-LETTER LOSS THROUGH MONTH 12 OR LAST VISIT#



Nominal p-value vs Pooled Sham^	---	0.032	0.0021

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

Month 12 event confirmed at month 15



Nominal p-value vs Pooled Sham^	---	0.0994	0.0076

#Confirmed 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

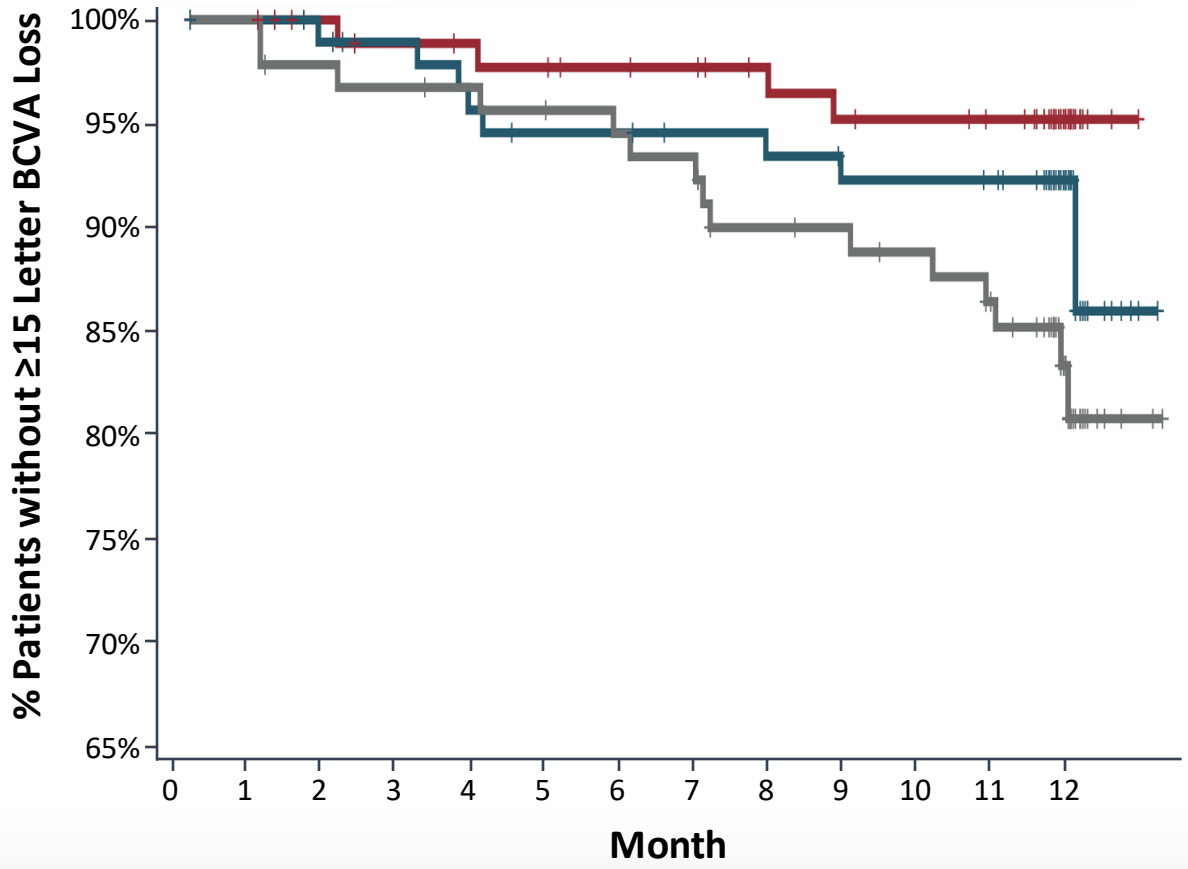
##Confirmed at two consecutive visits through month 12; month 12 event confirmed at month 15
^Nominal p-value from a Chi-square test in ITT population: *Nominal p < 0.05

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Vonaprument Monthly Treatment Provided 73% Reduced Risk of ≥15-Letter Vision Loss at Month 12

BCVA ≥15-LETTER LOSS CONFIRMED AT 2 CONSECUTIVE VISITS THROUGH MONTH 12#



Vonaprument EM	88	87 (0)	85 (0)	83 (1)	81 (2)	80 (2)	79 (2)	77 (2)	74 (3)	73 (4)	72 (4)	70 (4)	39 (4)
Vonaprument EOM	91	91 (0)	88 (1)	87 (1)	84 (4)	82 (5)	82 (5)	80 (5)	79 (6)	77 (7)	77 (7)	76 (7)	50 (7)
Sham	89	87 (2)	86 (2)	85 (3)	83 (4)	82 (4)	81 (5)	77 (7)	74 (9)	73 (9)	71 (10)	68 (12)	41 (14)

EM (n=89)

73% Risk Reduction Vonaprument EM

HR (CI) = 0.272 (0.090 to 0.819); Nominal p = 0.0119

EOM (n=92)

50% Risk Reduction Vonaprument EOM

HR (CI) = 0.504 (0.214 to 1.189); Nominal p = 0.1098

Sham (n=89)

INCREASING VONAPRUMENT IMPACT OVER TIME

HR, hazard ratio; Nominal log-rank test (versus sham) p-values are presented; Note: vertical tick marks represent patients that have exited the study without 15-letter loss event

Confirmed BCVA 15-LL at two consecutive visits including month 12 supported by ensuing (off-treatment) visit

Final data

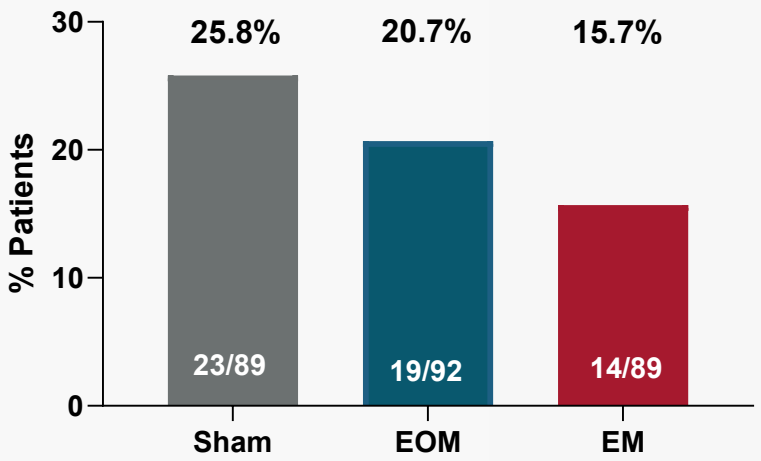
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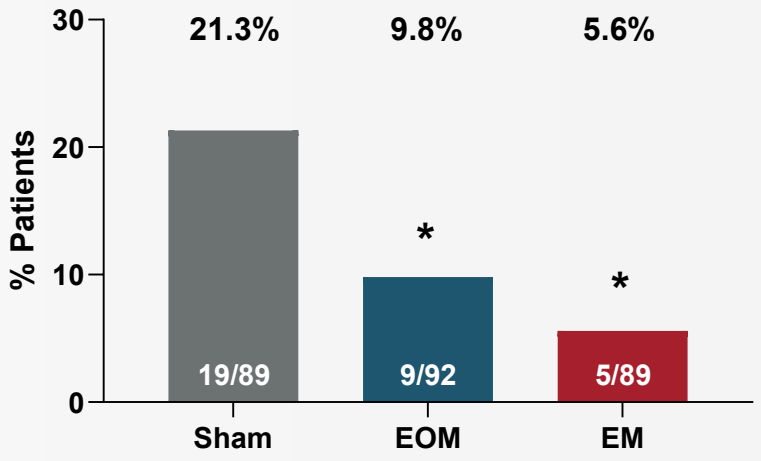
Sensitivity Analysis: Consistent Dose-Dependent Protection from Vision Loss with BCVA ≥10, ≥15 and ≥20- Letter Assessments

CONFIRMED BCVA VISION LOSS THROUGH MONTH 12#

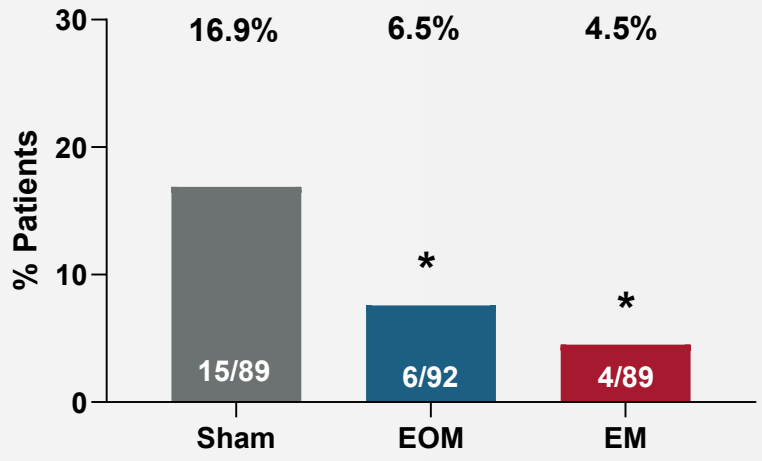
≥10-LETTER LOSS



≥15-LETTER LOSS



≥20-LETTER LOSS



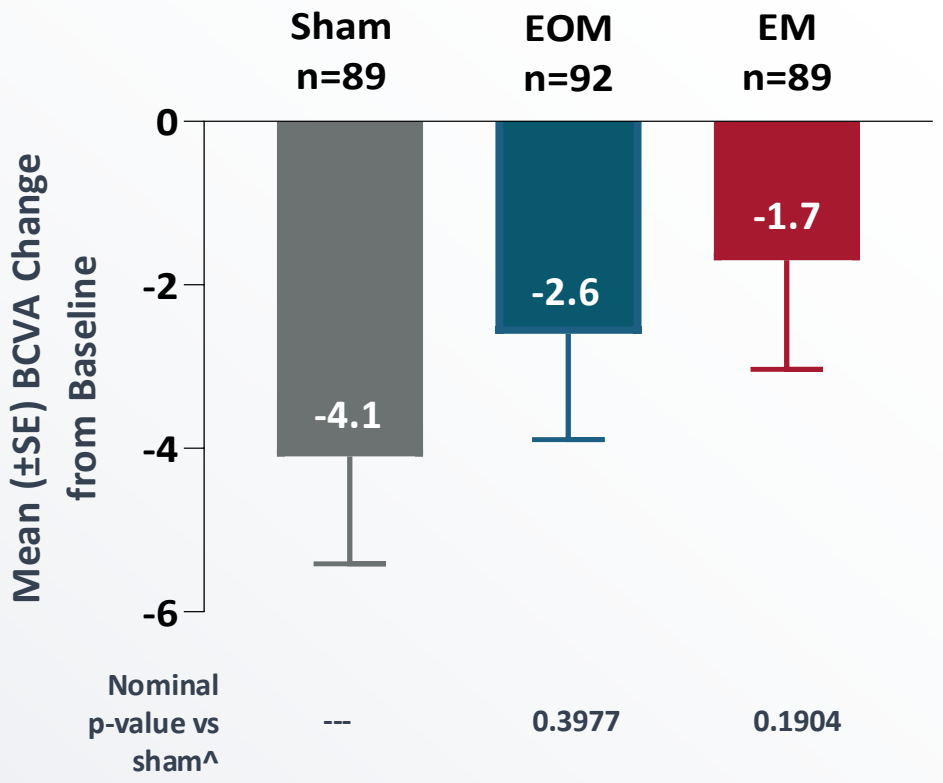
	Sham	EOM	EM
Nominal p-value vs sham^	---	0.408	0.096
	---	0.032	0.002
	---	0.030	0.008

#Confirmed 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
Final data

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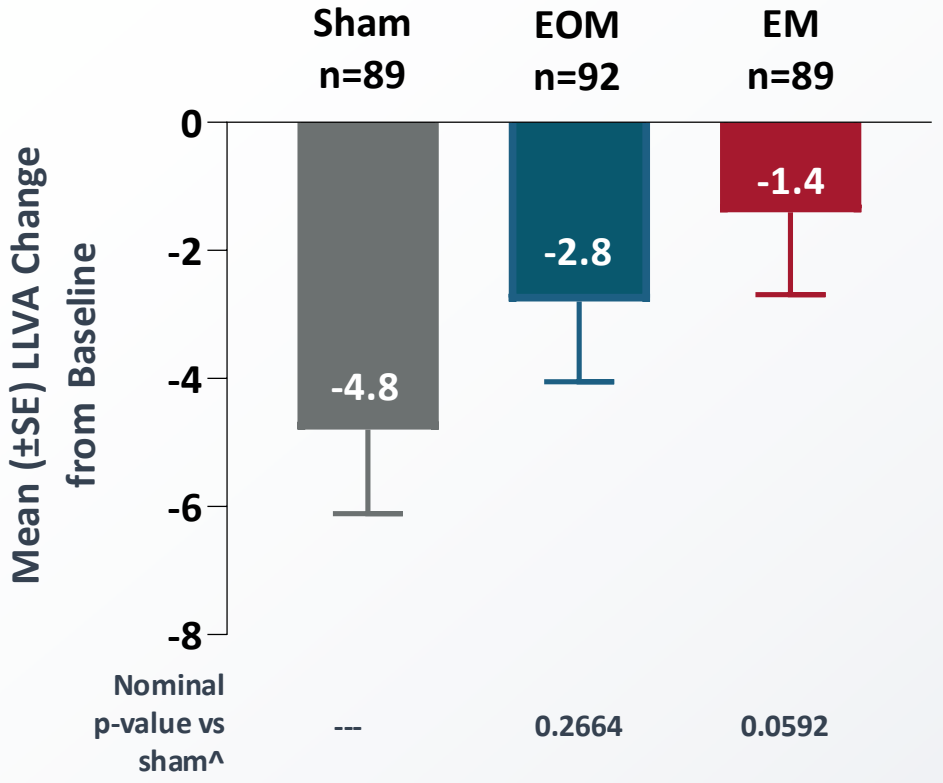
Vonaprument Consistent Dose-Dependent Vision Protection on Mean Change in BCVA & LLVA

MEAN CHANGE FROM BASELINE IN BCVA AT MONTH 12#



#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
Final data

MEAN CHANGE FROM BASELINE IN LLVA AT MONTH 12#



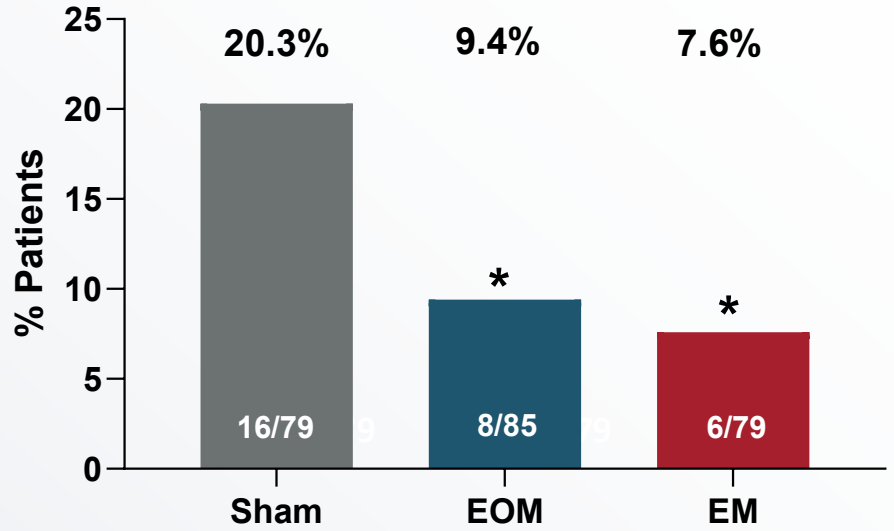
#Mean, standard error (SE), and p-value based on MMRM adjusting for baseline lesion location, lesion focality, baseline GA lesion, and the baseline GA lesion by visit interaction.
^Nominal p-value from a Chi-square test in ITT population
* Nominal P < 0.05
Final data

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Vonaprument Consistent Dose-Dependent Vision Protection Measured by LLVA and LLVD

LLVA ≥15-LETTER LOSS THROUGH MONTH 12#

Low Luminance Visual Acuity (LLVA): visual acuity assessed in low light conditions

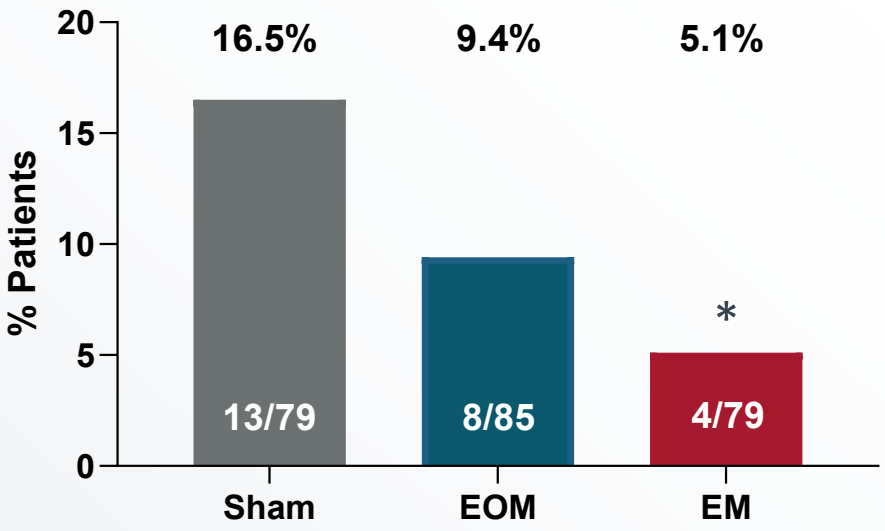


Nominal p-value vs sham^	--	0.0497	0.0216

#Patients with at least one post-baseline LLVA measurement and two consecutive or last visit 15-letter loss events
^Nominal p-value from a Chi Square test; *p<0.05
Final data

LLVD ≥15-LETTER WORSENING THROUGH MONTH 12#

Low Luminance Visual Deficit (LLVD): difference between BCVA and LLVA to assess disease progression



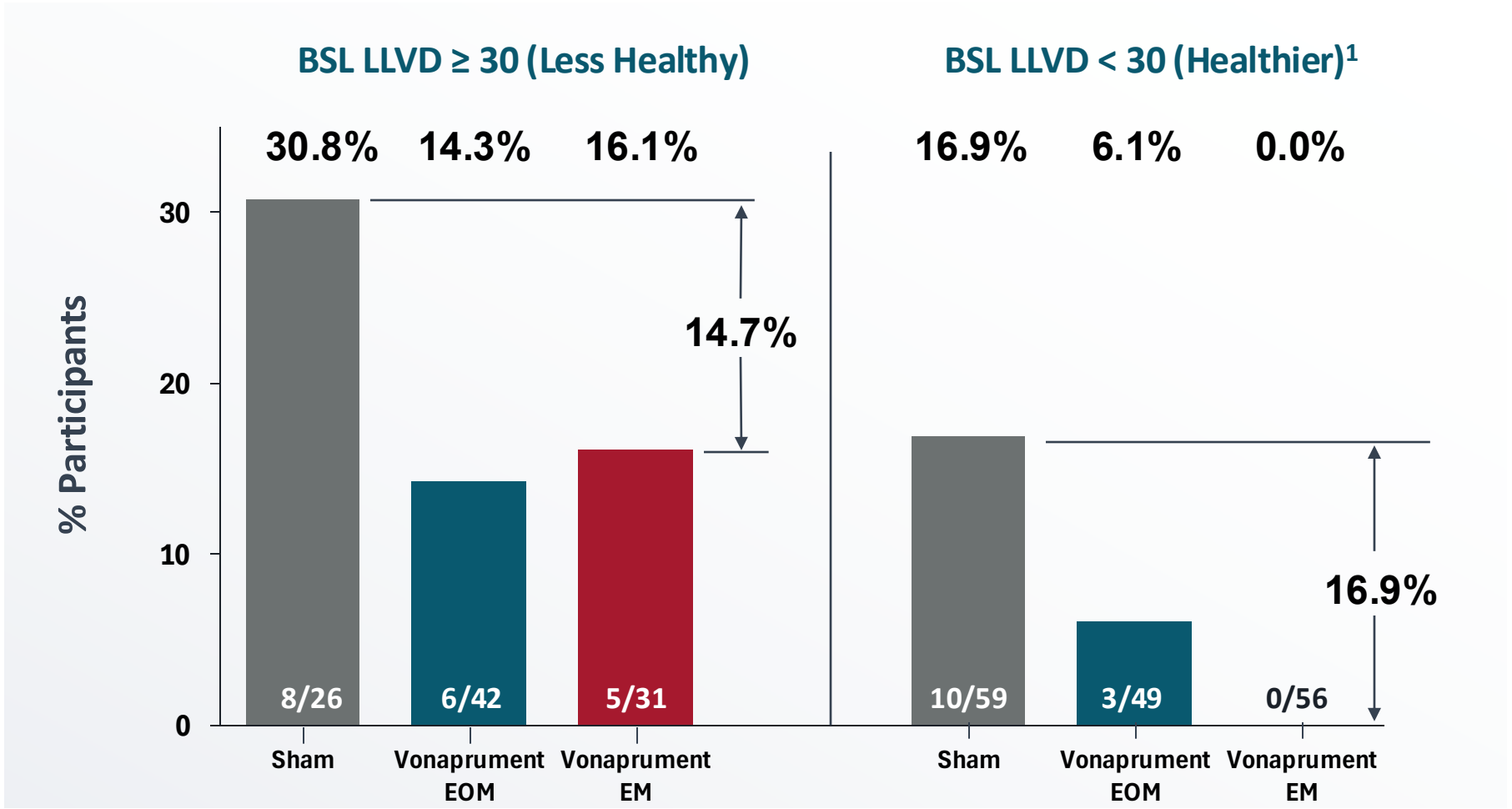
Nominal p-value vs sham^	--	0.1774	0.0209

#≥15-letter worsening in LLVD was defined as a change from Baseline of ≥15-letters across 2 consecutive visits, or at the last visit, through month 12
^Nominal p-value from a chi-square test in the ITT set
*p<0.05

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Vonaprument Demonstrated Dose-Dependent Vision Protection in Both Healthier and Less Healthy Eyes

Broad treatment effect across severity of photoreceptor dysfunction



Review of Subgroup based on Visual Acuity Measures

Participants with confirmed BCVA ≥15-letter loss through month 12[#]

Nominal summary p-value vs. sham^	
ANX007 EM	0.0016
ANX007 EOM	0.0183

[1]LLVD <30 at baseline were designated as eyes with less advanced disease, based on mean baseline values in lampalizumab Phase 3 studies. Holz FG, et al. Efficacy and Safety of Lampalizumab for Geographic Atrophy Due to Age-Related Macular Degeneration: Chroma and Spectri Phase 3 Randomized Clinical Trials. JAMA Ophthalmol. 2018;136(6):666–677.

[#]Confirmed for two consecutive visits at any time through month 12 or at last study visit

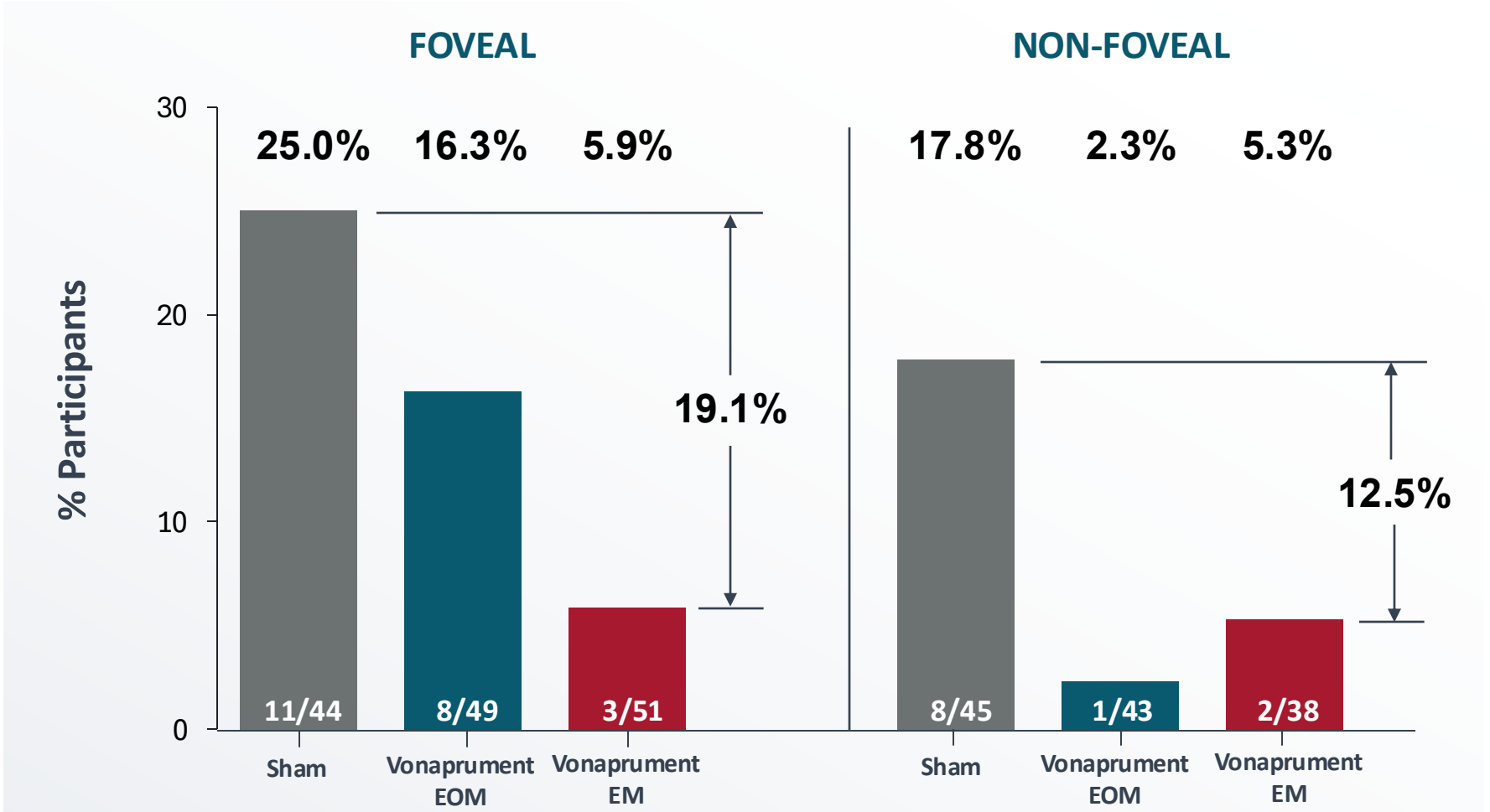
^Nominal p-value from a Cochran Mantel-Haenszel test (General Association) in ITT population

Final data

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Vonaprument Demonstrated Dose-Dependent Vision Protection in Participants with Foveal and Non-Foveal Lesions

Vonaprument treatment effect across the disease spectrum



Review of Subgroup based on Structural Characteristics

Participants with confirmed BCVA ≥15-letter loss through month 12#

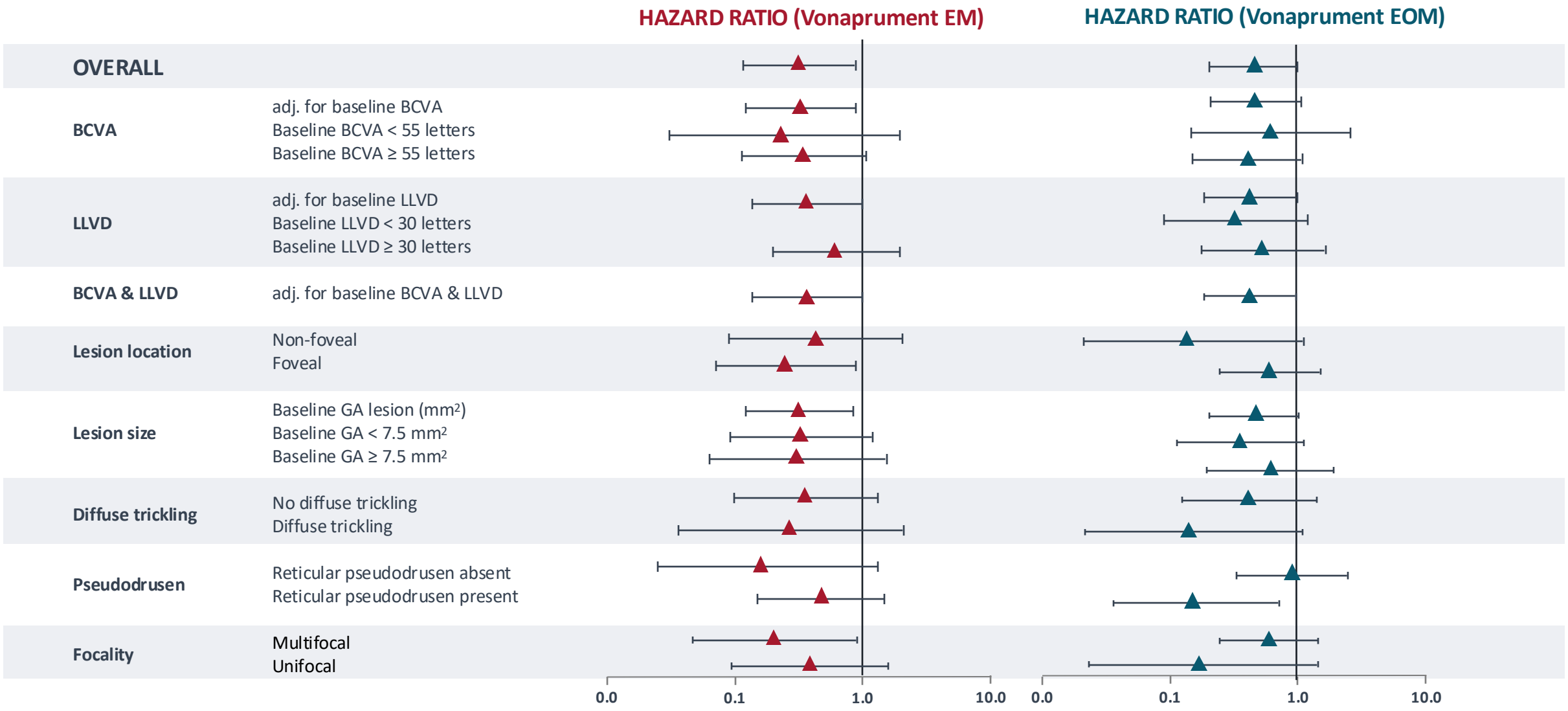
Nominal summary p-value vs. sham^	
ANX007 EM	0.0019
ANX007 EOM	0.0254

#Confirmed 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

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Vonaprument Protection from Vision Loss Consistent Across Baseline Characteristics#

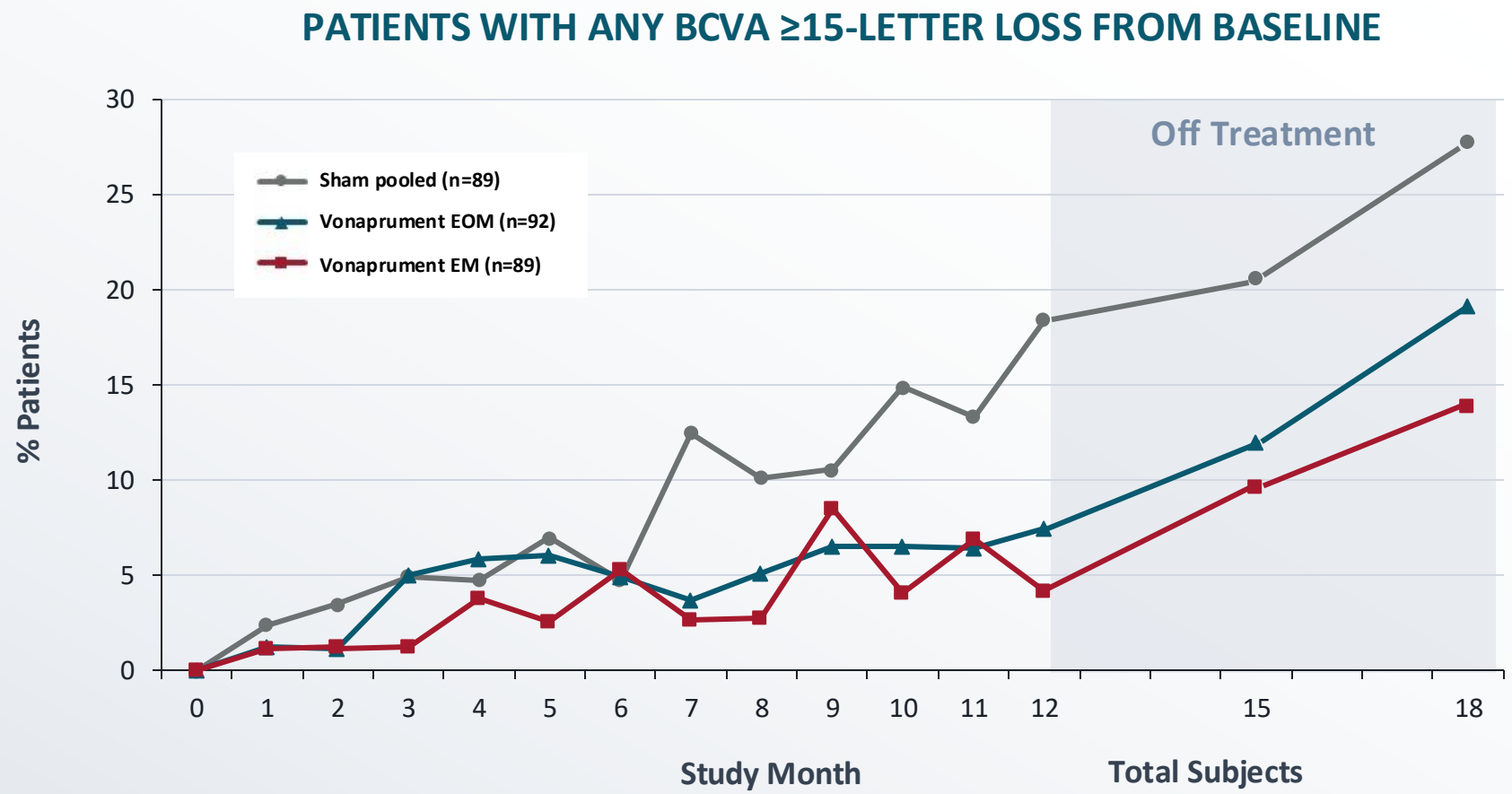


#Persistent for two consecutive visits through month 12 or at last visit; Hazard ratios are from Cox regressions accounting for event time and censorship
NOTE: Hazard ratio not estimated for ANX007 EM vs Sham with baseline LLVD < 30 due to zero (0) event in Vonaprument EM group for the subgroup.

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Vonaprument Demonstrated Clear Protection of Vision During On-Treatment vs Off-Treatment Period



Total Subjects

	Month 12	Month 15	Month 18
Sham	76	73	72
EOM	80	75	73
EM	72	73	72

Reinforces on-treatment drug effect and disease-modifying mechanism of action

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ARCHER Phase 2: Vonaprument Protected Vision Across Multiple Functional Measures

Best Corrected Visual Acuity (BCVA) is Gold Standard Outcome in Ophthalmology

- 15 letter loss is benchmark primary measure in landmark development programs (e.g., Lucentis, Eylea)
- Measured at two consecutive visits adds veracity and minimizes subjectivity
- Clinically relevant to patients and regulators

Vonaprument Treatment Provides Disease-Modifying Preservation of Vision

- BCVA, LLVA, LLVD
- 73% Risk Reduction of 15-letter loss compared to natural history
- Off-treatment disease progression supports MOA
- Greatest protection in patients at highest risk of vision loss (foveal lesions)

Safety Enhances Favorable Benefit/Risk Profile

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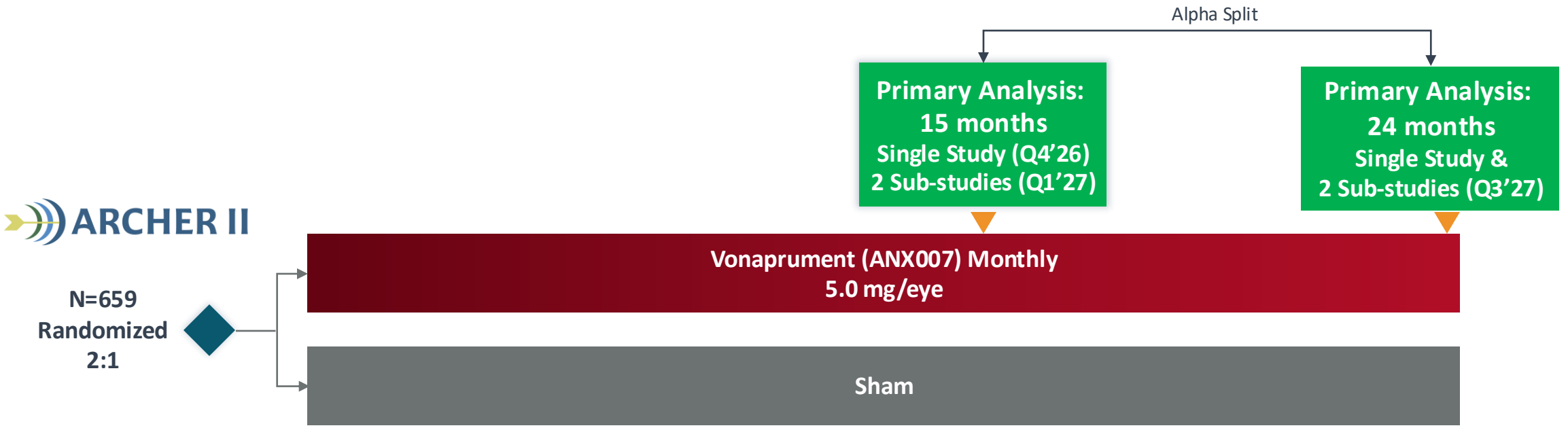
Strategically Designed ARCHER II Phase 3 Trial



ARCHER II Phase 3: Designed and Executed for Success

KEY ATTRIBUTES	DESIGNED TO INCREASE PROBABILITY OF SUCCESS
Larger, Longer Study	• Over-enrolled (n=659), powered to ≥90% • Higher patient retention increased power to ≥90%
Dual Endpoint Strategy to Show Vision Outcomes	• Powered to show positive treatment effect at Month 15 or Month 24 • Alpha allocated between Month 15 (majority) and Month 24 for efficacy in label
Global Regulatory Strategy	• Two pre-defined, well-powered sub-studies for US filing • PRIME designation and Product Development Coordinator for EU filing
Controlled for Disease Heterogeneity	• Enrolled patients at risk for vision loss but with enough vision to protect • Consistent treatment effect across broad spectrum of disease • Longer timepoints for more vision loss events and widening treatment delta

ARCHER II Phase 3: Designed and Powered to Confirm Vision Protection



Sites: North America, Europe, AUS, NZ

GLOBAL REGISTRATION PATH

EMA Prime and FDA Fast Track designations

Single protocol for EU filing

Single protocol analyzed as 2 sub-studies for US filing (powered at sub-study level)

DUAL PRIMARY ENDPOINTS

Landmark analysis of proportion of patients with confirmed BCVA ≥15-Letter Loss at Month 15 or Month 24

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ARCHER II Baseline Characteristics Well-Positioned to Successfully Replicate Phase 2 Vision Protection Outcomes

BASELINE VISUAL ACUITY MEASURES	ARCHER P2 (N = 270)	ARCHER II P3 (N = 659)
Mean BCVA (SD)	58.4 (16.2)	65.8 (10.5)
Baseline BCVA <45 Letters	23.3%	0.0%*
Mean LLVA (SD)	33.0 (16.9)	38.3 (17.2)
Mean LLVD (SD)	25.7 (16.9)	27.6 (15.6)
LLVD < 30 Letters	62.4%	60.7%

STRUCTURAL CHARACTERISTICS	ARCHER P2	ARCHER II P3
GA Lesion Size (mm^2), mean (SD)	7.36 (4.01)	7.23 (3.49)
GA Lesion Location (% Subfoveal)	51.9%	54.8%
Total EZ Loss, mm^2 (% of Total Area Lost)	12.7 (35.3%)	12.3 (34.3%)

Excluded subjects VA<20/100, no vision loss events

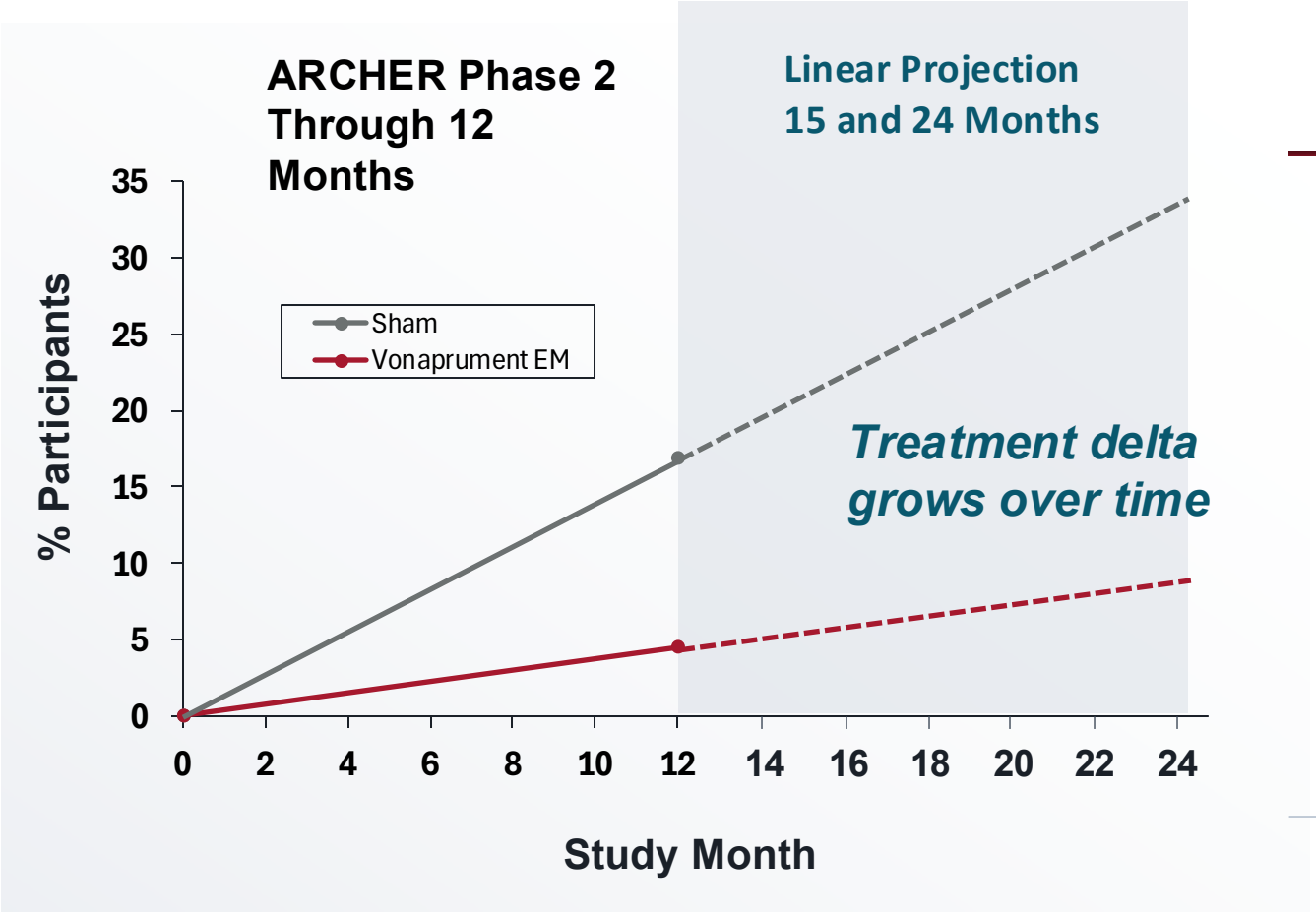
No 15-LL events (0/56) in P2 monthly arm

20% treatment delta in P2 ARCHER

*Individuals with baseline BCVA <45 letters not enrolled in ARCHER II due to very low incidence of BCVA 15-letter loss in ARCHER

Illustration of Event Based Analysis Which Gets Stronger Over Time

Why we like month 15 as our base case and month 24 with growing treatment delta



ARCHER II Key Features for Success

- ✓ **Larger** sample size (N=659; n~330/substudy)
- ✓ Prior GA trials[1] informed masked event rate projections, which have held during study
- ✓ Linear progression of vision loss events in GA
- ✓ **Longer** timepoints to accumulate more sham events
- ✓ Result: Both 15 & 24 month primary endpoints **de-risked with trial design and execution**

[1]Anegondi et al (2025) Ophthalmology

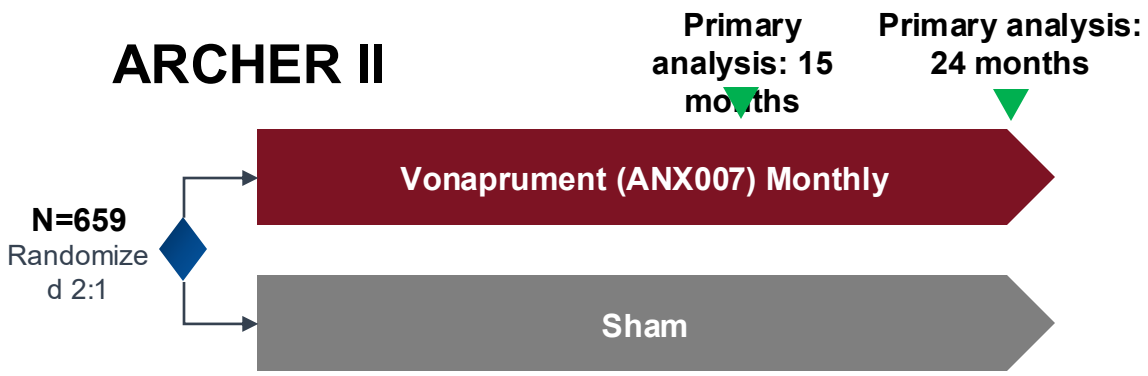
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ARCHER II: One Protocol Supporting Both EMA and FDA Filings

Phase 3 powered at Sub-study level

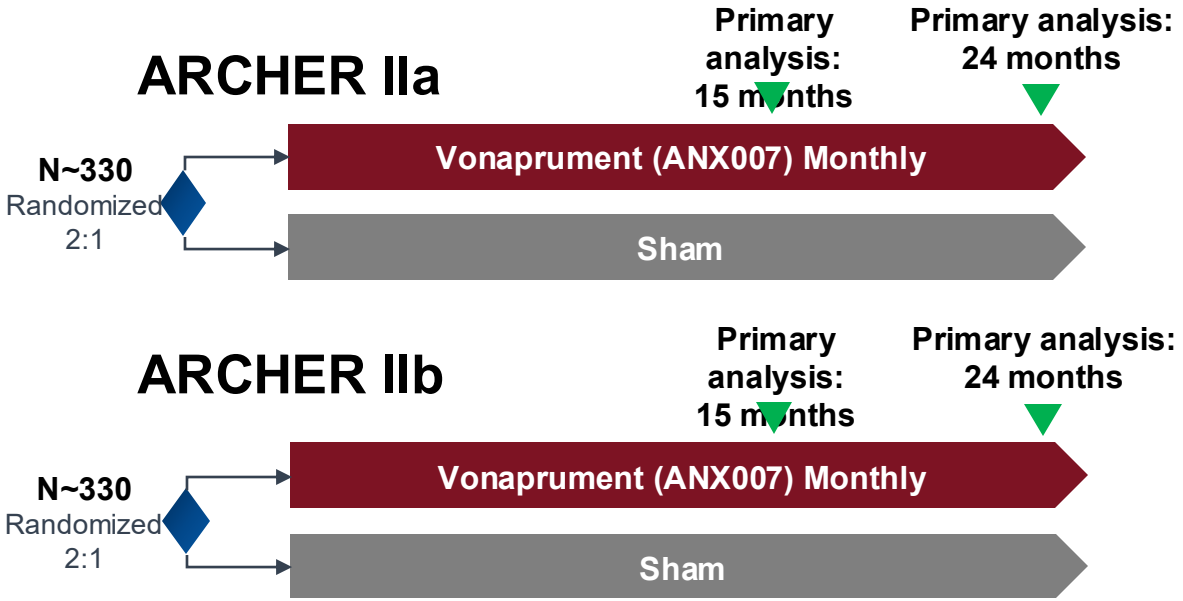
EMA

Single Study



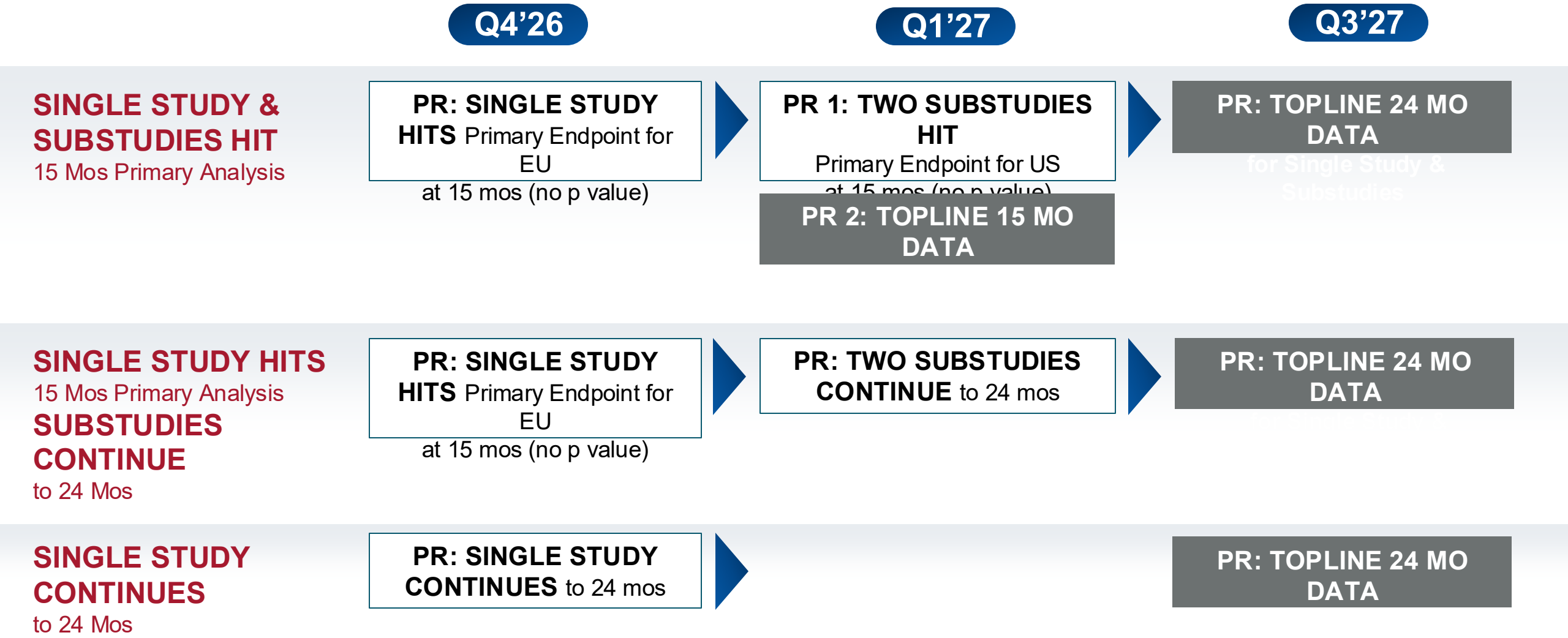
FDA

2 Sub-studies



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ARCHER II Phase 3: Potential Outcomes Scenarios & Expected Timing



**Futility – assessed by Data Monitoring Committee*

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Summary of Vonaprument Program



Building a Leading Ophthalmology Franchise

Recent organization enhancements with proven record of blockbuster commercialization in AMD space

Board of Directors



Mark Blumenkranz, MD, MMS
H.J. Smead Professor Emeritus in the Department of Ophthalmology Stanford University

Scientific Advisory Board



Eleonora Lad, MD, PhD
Vice Chair of Ophthalmology Clinical Research, Duke University Medical Center

Clinical Development



Donald Fong, MD
SVP, Clinical Development - Ophthalmology

Commercialization



Jake Schumacher, MBA
SVP, Head of Ophthalmology Franchise

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Vonaprument GA Program Designed & Executed for Success

Demonstrated Functional Outcomes

Vision Protection in Phase 2 across Broad Patient Population

Exceptional Pivotal Design & Execution

Targeted Patient Population in Larger, Longer, Well-Powered Phase 3

First in Class Product for Vision Protection

8M+ patients with global unmet need