

Baseline Characteristics Associated With Loss of BCVA ≥15 ETDRS Letters in Participants With Geographic Atrophy in the Phase 2 ARCHER Study

Margaret Chang MD, MS¹

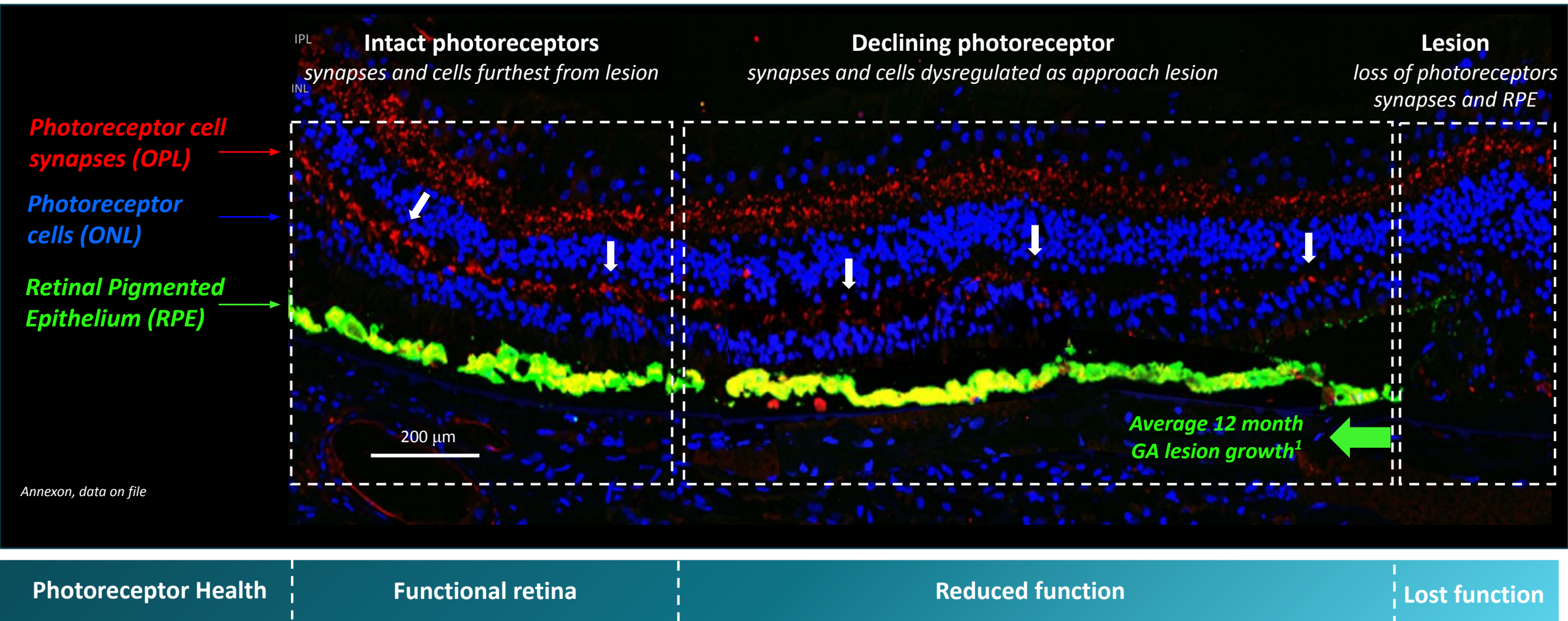
On behalf of the ARCHER and ARCHER II Investigators

¹Retina Consultants Medical Group, Sacramento, CA

Disclosures

- Speaker: Genentech, Annexon
- Consultant: Genentech, AbbVie/RegenXBio, Astellas, Ocular Therapeutix, Oculis, Eyepoint, Boehringer, Ollin, Outlook, Adverum, Annexon, RetinAI
- Research support: Novartis, Eyebio, OcuTerra, Alexion, Outlook, Kodiak, 4DMT, Perceive, Kalaris, ONL, Character Biosciences
- Stock Options: Ollin

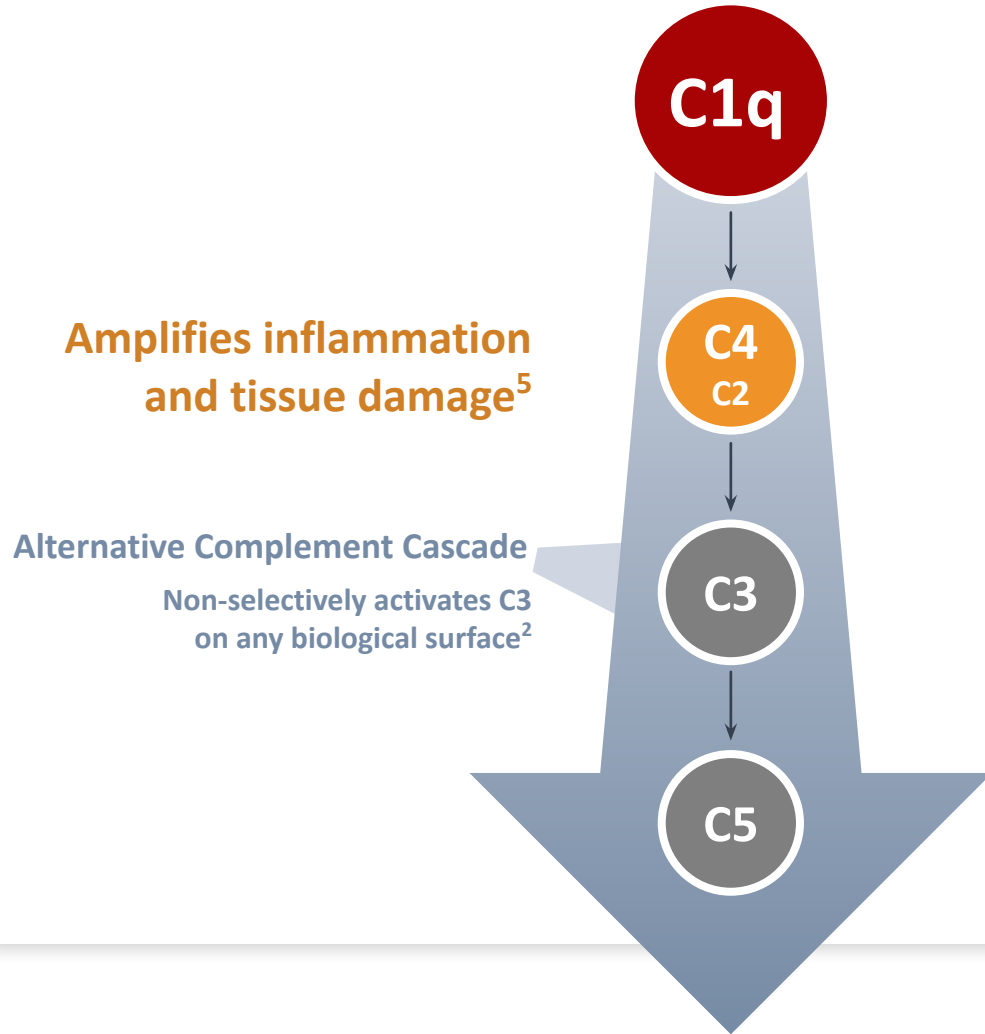
GA is a Neurodegenerative Disease; Photoreceptor (PR) Synapses and Cells are Lost Before RPE



¹Selkoe, 2002 doi: 10.1126/science.1074069; Burger, et al., doi.org/10.1016/j.ydbio.2021.04.001; ²Bird 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; ³Heier, et al., 2020 Ophthalmology Retina 4:673; ⁴Shen, et al., 2020 Ophthalmol Retina 4:899

C1q Plays a Key Role in Neurodegeneration

Classical Complement Cascade



C1q tags functional synapses for removal in disease¹

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

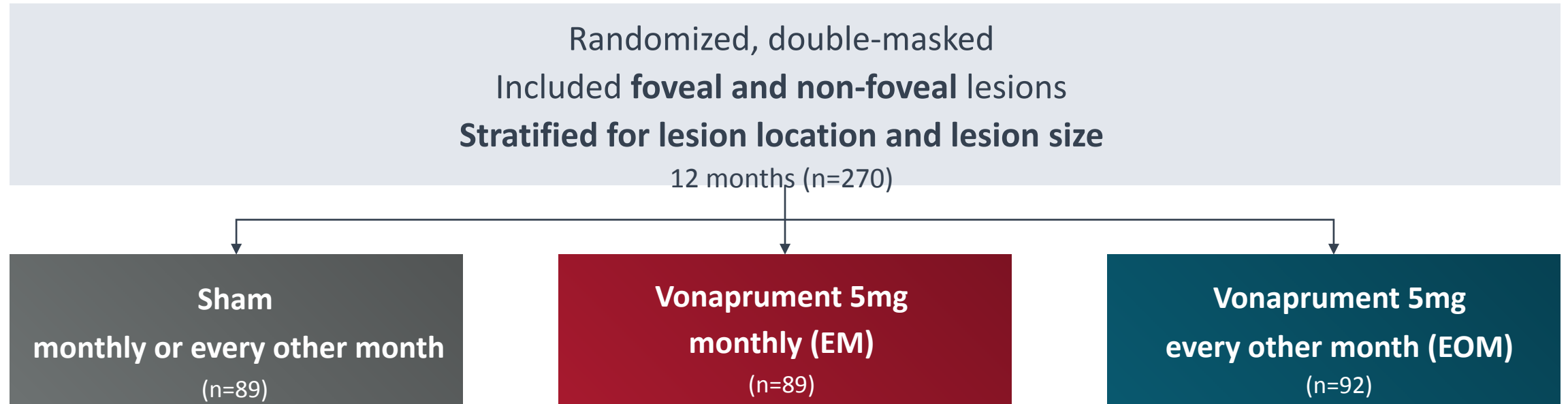
C3/C5 removes dysfunctional cells at lesion edge

- Drives cell clearance (e.g., RPE) via alternative pathway²
- Occurs after photoreceptor damage/loss⁴
- Dysfunctional RPE cells secrete VEGF, increasing CNV risk³

¹Yednock, et al, 2022 *International J Retin and Vitreous* 8:79; ²Merle, et al., 2015 *Front Immunol* 6:262; ³Paterson, et al., 2023 *Molecular Vision* 29:87-101; Farjood et al. 2020 *J Biol Eng* 14:13;

⁴Ehlers and Wykoff *Retina Today* Nov/Dec 2024; Pfau, et al., 2020 10.1001/jamaophthalmol.2020.2914; ⁵Mannes, et al., *Blood*. 2021;137(4):443-455

ARCHER: Phase 2 Trial Of The C1q Inhibitor Vonaprument (ANX007) in Patients with Dry AMD and GA



PRIMARY ENDPOINT

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

PRESPECIFIED FUNCTIONAL ANALYSES

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

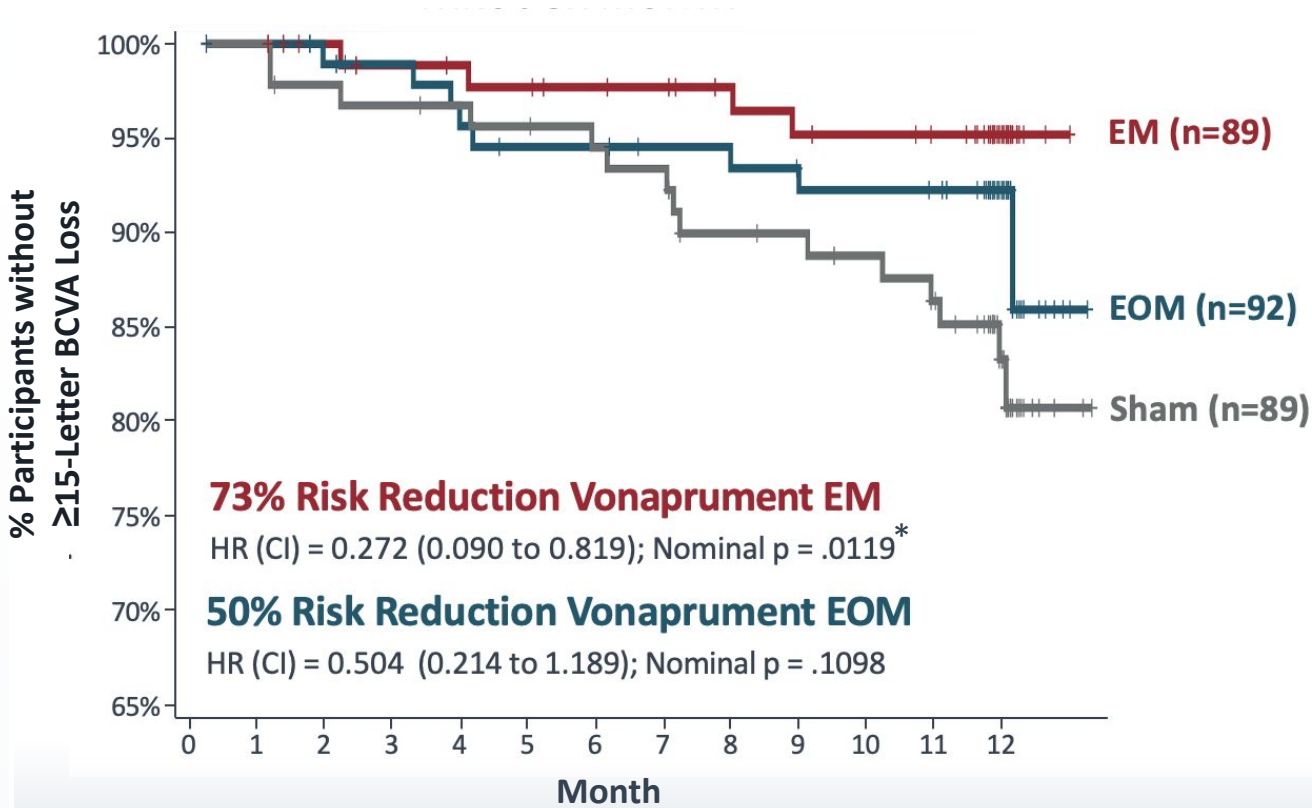
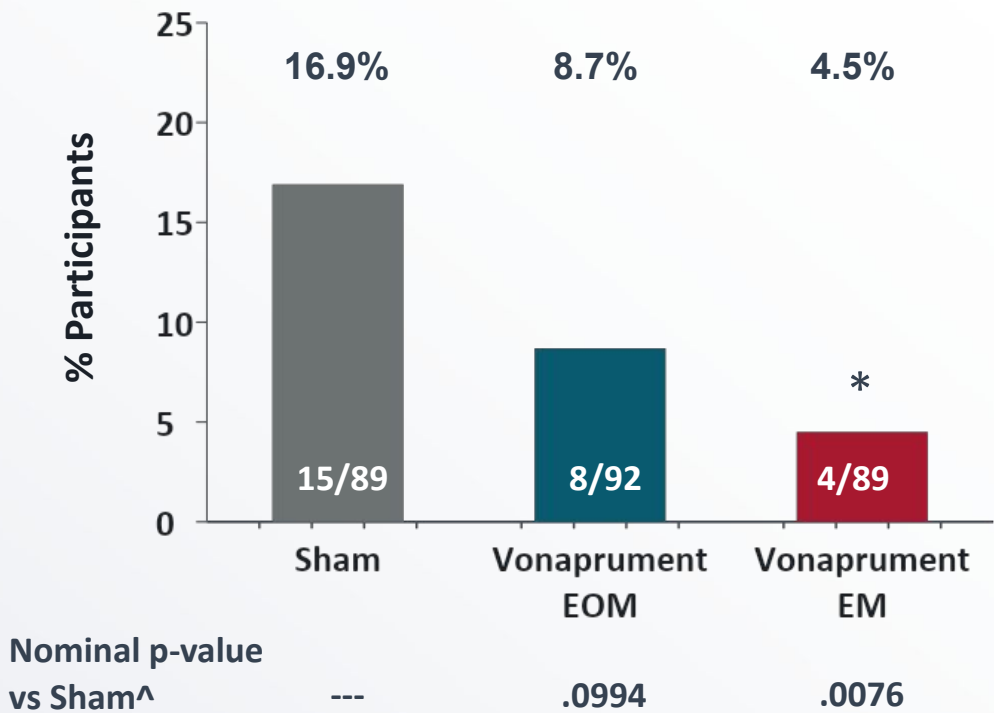
Off-treatment
(6 months)

END OF STUDY

Month 18

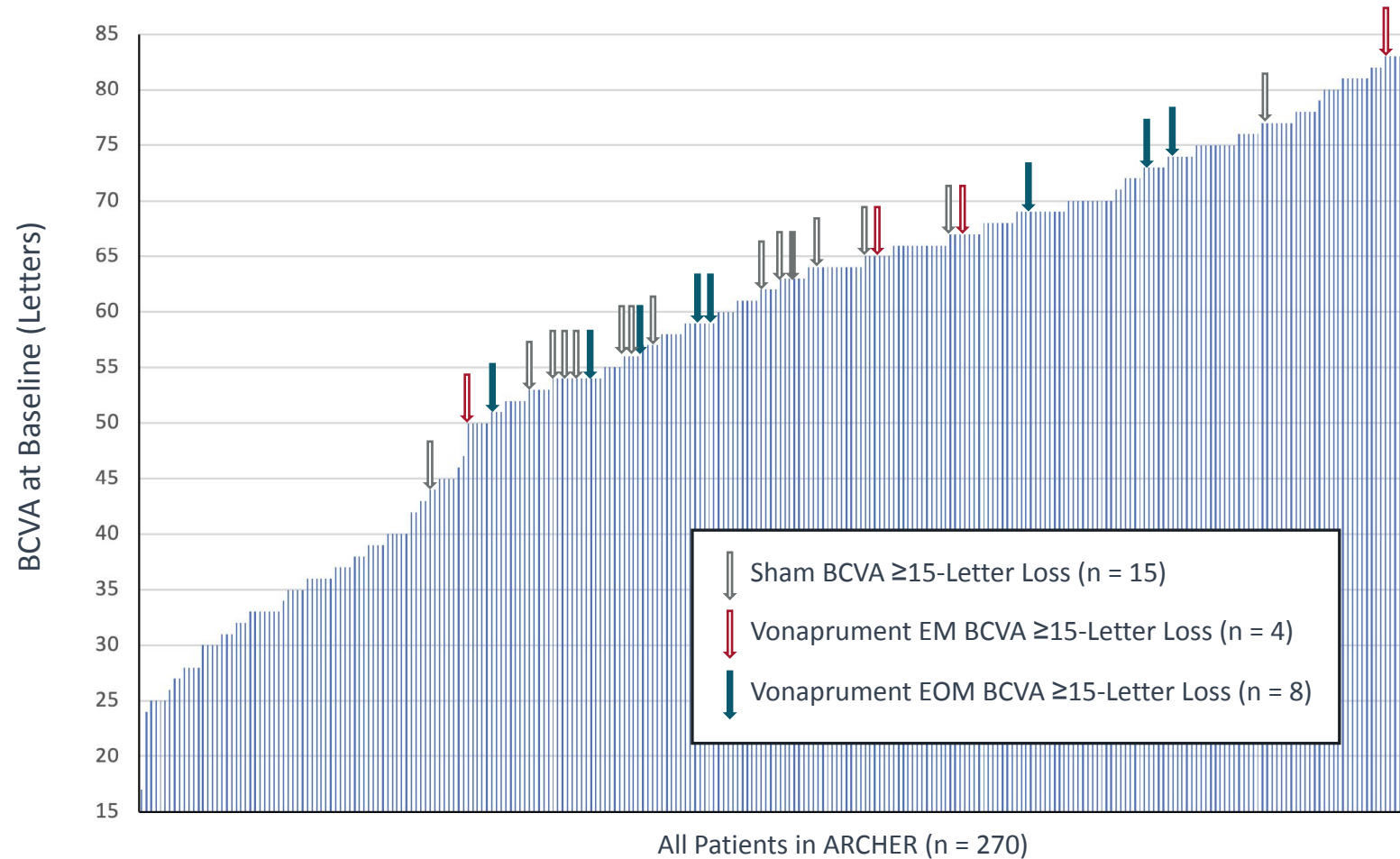
Vonaprument Demonstrated Dose-Dependent Protection From Vision Loss as Measured by BCVA ≥ 15 -Letter Loss

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



[^]Nominal p-value from a Chi-Square test in ITT population ; *Nominal p < .05

ARCHER: BCVA ≥ 15 -Letter Loss Occurred in Patients with Compromised BCVA Vision at Baseline, but Still With Vision to Lose

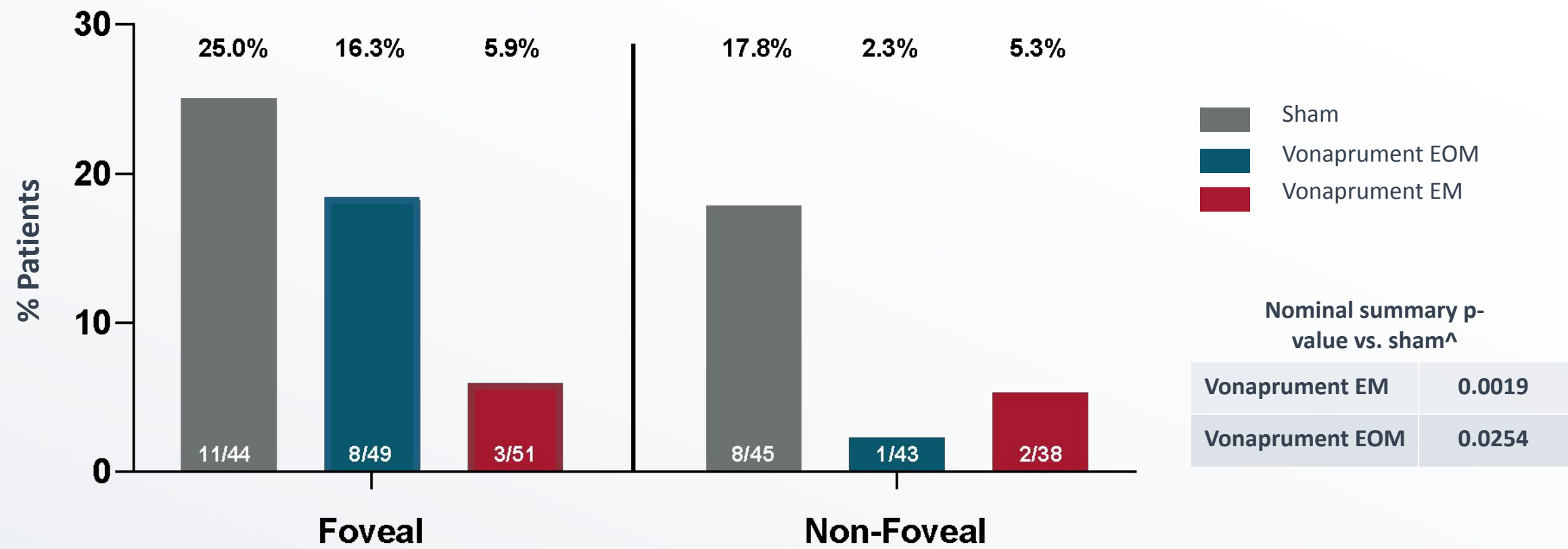


- BCVA ≥ 15 -letter loss did not occur in participants with baseline BCVA < 44 letters
- BCVA ≥ 15 -letter loss less frequent in participants with baseline BCVA > 69 letters

15-LL Event Definition – confirmed loss of 15 or more letters by BCVA at two consecutive visits including month 12 supported by month 15
Events: n = 27

ARCHER: BCVA ≥ 15 -Letter Loss Is Related to Baseline Lesion Location

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

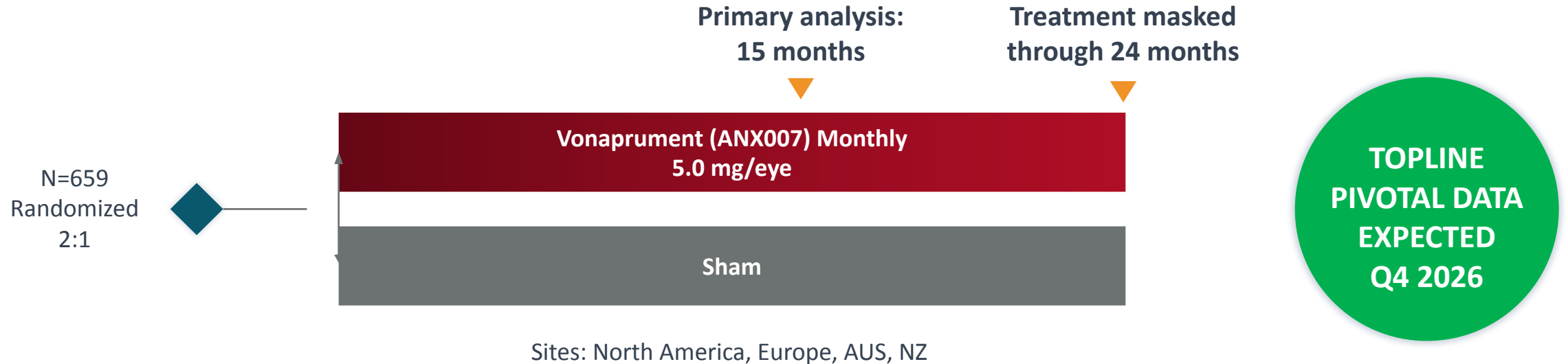


[^]Nominal p-value from a Cochran Mantel-Haenszel test (General Association) in ITT population

15-LL Event Definition – confirmed loss of 15 or more letters by BCVA at two consecutive visits through month 12 or at last study visit
Events: n = 33

Phase 3 Pivotal Program: Well-Informed Design and Powering

Leverages Phase 2 learnings and enriched for patients with higher risk of vision loss



GLOBAL REGISTRATION PATH¹

Prime designation in EU
Selected by EMA for PDC² program
FDA Fast Track designation

PRIMARY ENDPOINT

Proportion of patients who experience
a BCVA ≥ 15 -Letter Loss confirmed at
two consecutive visits

SECONDARY ENDPOINTS

Safety, LLVA, EZ integrity

¹Single protocol analyzed as two sub-studies addresses FDA two-trial recommendation

²Product Development Coordinator

Key Take-Away Points: Vonaprument in ARCHER and ARCHER II

Vision loss in GA is driven by photoreceptor synapse and cell loss, which precede RPE atrophy

C1q is an aberrant trigger for neurodegeneration in GA

- C1q aberrantly activates classical complement to drive removal of photoreceptor synapses and cells necessary for visual function

By targeting C1q, Vonaprument is mechanistically differentiated vs. downstream complement inhibitors

Confirmed loss of 15 or more BCVA letters was associated with:

- Baseline visual acuity (BCVA) above 45 letters (20/100)
- All lesion types – more strongly associated in those with subfoveal lesions

ARCHER II is the only global pivotal program in dry AMD with vision preservation as the primary endpoint

- Learnings from the Phase 2 ARCHER study informed the ARCHER II design