

# Clinical Rationale for Loss of 15 or More ETDRS Letters in Eyes with Dry AMD and GA: Analysis of the Phase 2 ARCHER Visual Acuity Outcomes

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## INTRODUCTION

- Activation of the classical complement cascade has been implicated in the pathogenesis of geographic atrophy (GA) and other neurologic diseases
- C1q, the initiating molecule of the classical complement cascade, is a common driver of neurodegeneration
- Inhibition of C1q appears to convey neuroprotective effects across several neurodegenerative diseases
- Vonaprunent is an antibody fragment that inhibits C1q and is delivered intravitreally
- The Phase 2 ARCHER study (NCT04656561) compared vonaprunent (ANX007) 5mg monthly (EM), vonaprunent (ANX007) 5mg every other month (EOM), or sham (EM or EOM)

## BACKGROUND

### Vision-Based Primary Endpoints in Ophthalmology

- BCVA measures – particularly 15-letter changes – have been one of the “standard” visual acuity measures in ophthalmological pivotal studies historically

APPROVED PRODUCT	FUNCTIONAL PRIMARY ENDPOINT
Wet AMD	
Lucentis®	Trial 1 and 2: BCVA ≥15-letter change Trial 3 and 4: Mean BCVA change
Eylea®/Eylea HD®	BCVA ≥15-letter change/Mean BCVA change
Vabysmo®	Mean BCVA change
DME	
Lucentis®	BCVA ≥15-letter change
Eylea®/Eylea HD®	Mean BCVA change
Vabysmo®	Mean BCVA change
Iluvien®	BCVA ≥15-letter change
Ozurdex®	BCVA ≥15-letter change
GA	
No Approved Vision-Preserving Treatments	

### What is 15-Letter Loss?

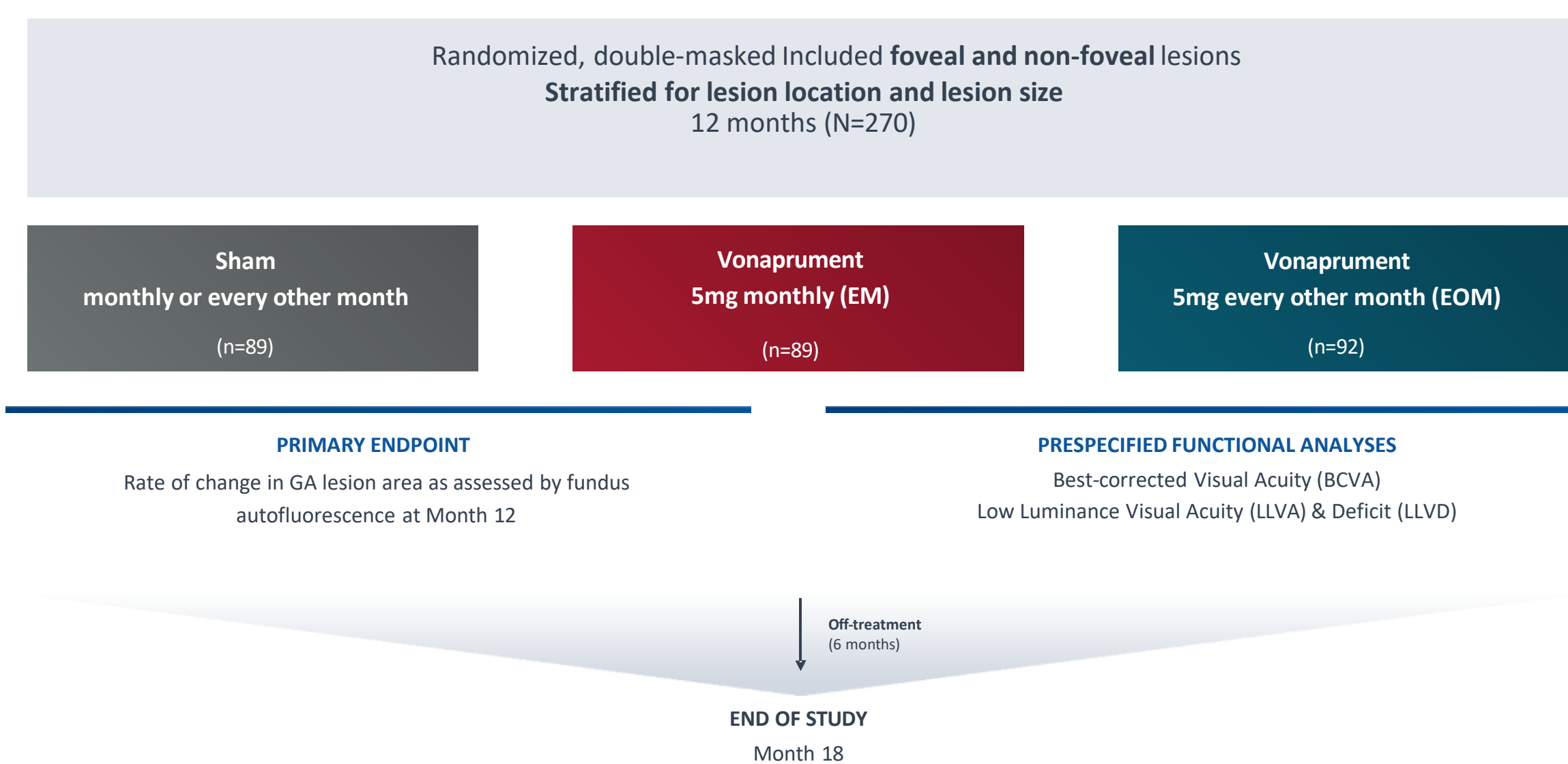
- Decline of 15 or more in BCVA letter score is relevant in GA because the measure represents:
  - 1) a Snellen equivalent of 3 line or greater loss on a standardized ETDRS chart
  - 2) a doubling (or more) of the visual angle
  - 3) a 0.3 or more logMAR change
  - 4) vision decline (for example):
    - 20/40 to 20/80 or worse
    - 20/63 to 20/125 or worse, etc.

Similar cohorts demonstrate ~25-35% of patients with BCVA ≥15-letter loss at two years<sup>1,2,3</sup>

- Loss of 15 or more ETDRS letters as measured by BCVA was a prespecified analysis in ARCHER (loss events defined as occurring at two consecutive study visits, including month 12)

## ARCHER METHODS & RESULTS

### ARCHER Phase 2 Study Design



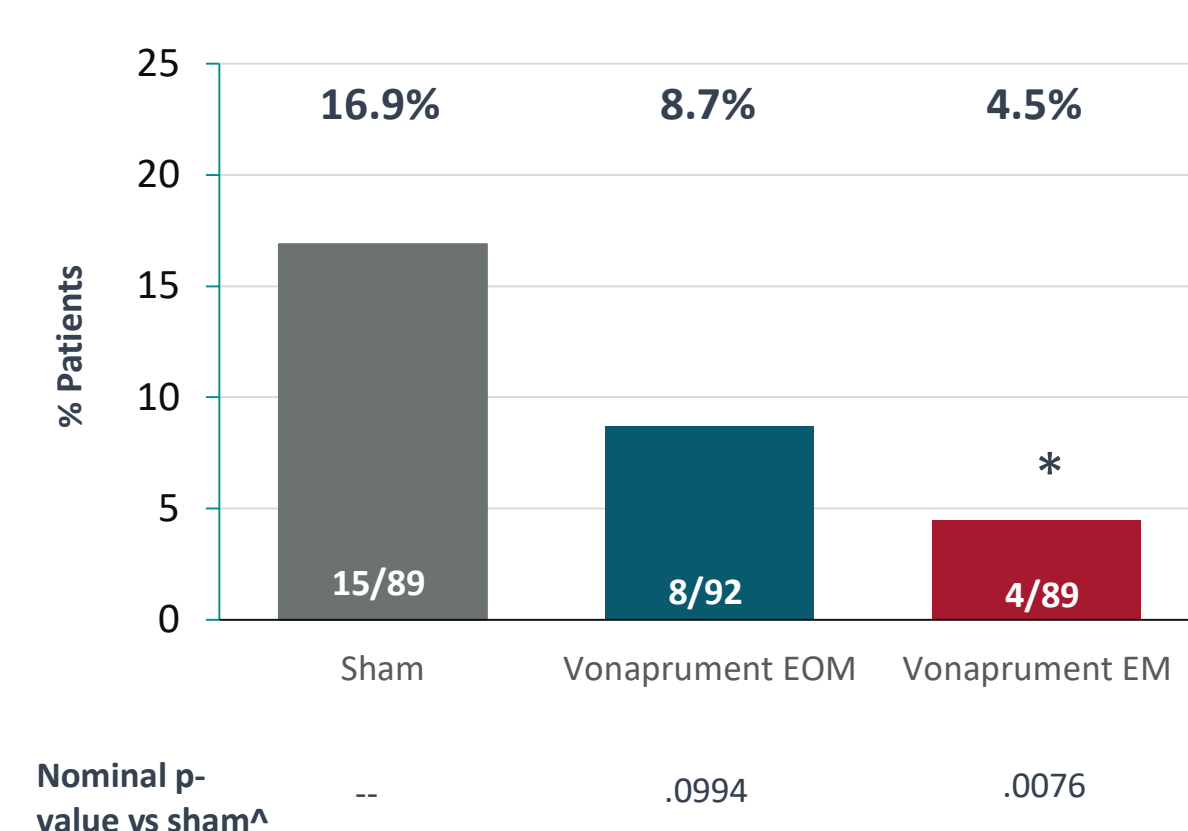
- 6.2% greater reduction in rate of change in GA lesion area from baseline with vonaprunent treatment at 12 months – did not reach statistical significance
- Consistent treatment effects observed across

visual acuity measures (BCVA, LLVA) support vonaprunent effect in GA

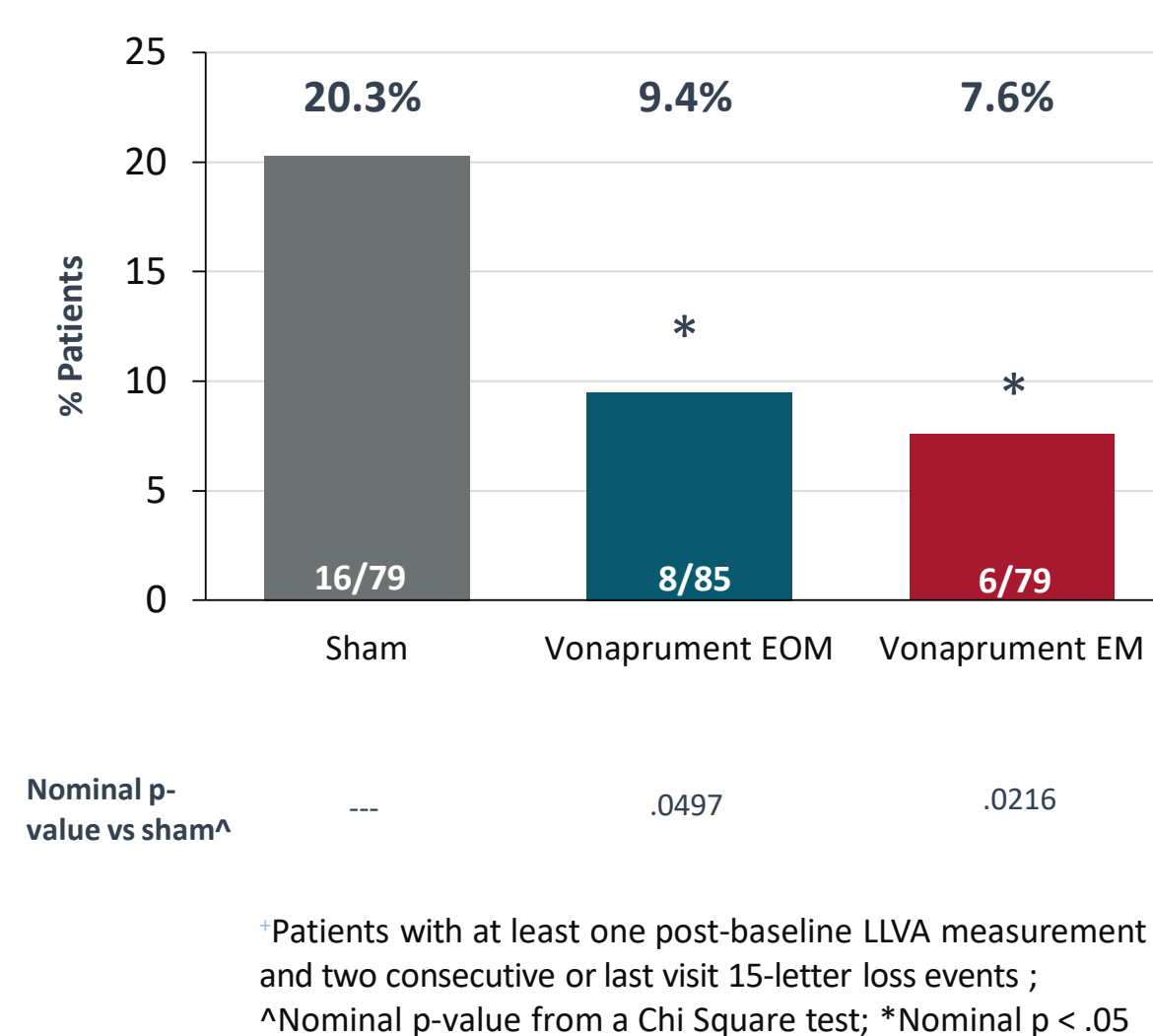
- Preservation of photoreceptor (EZ) structure across the full macular grid and subdomains is supportive of vonaprunent vision impact

## ARCHER RESULTS

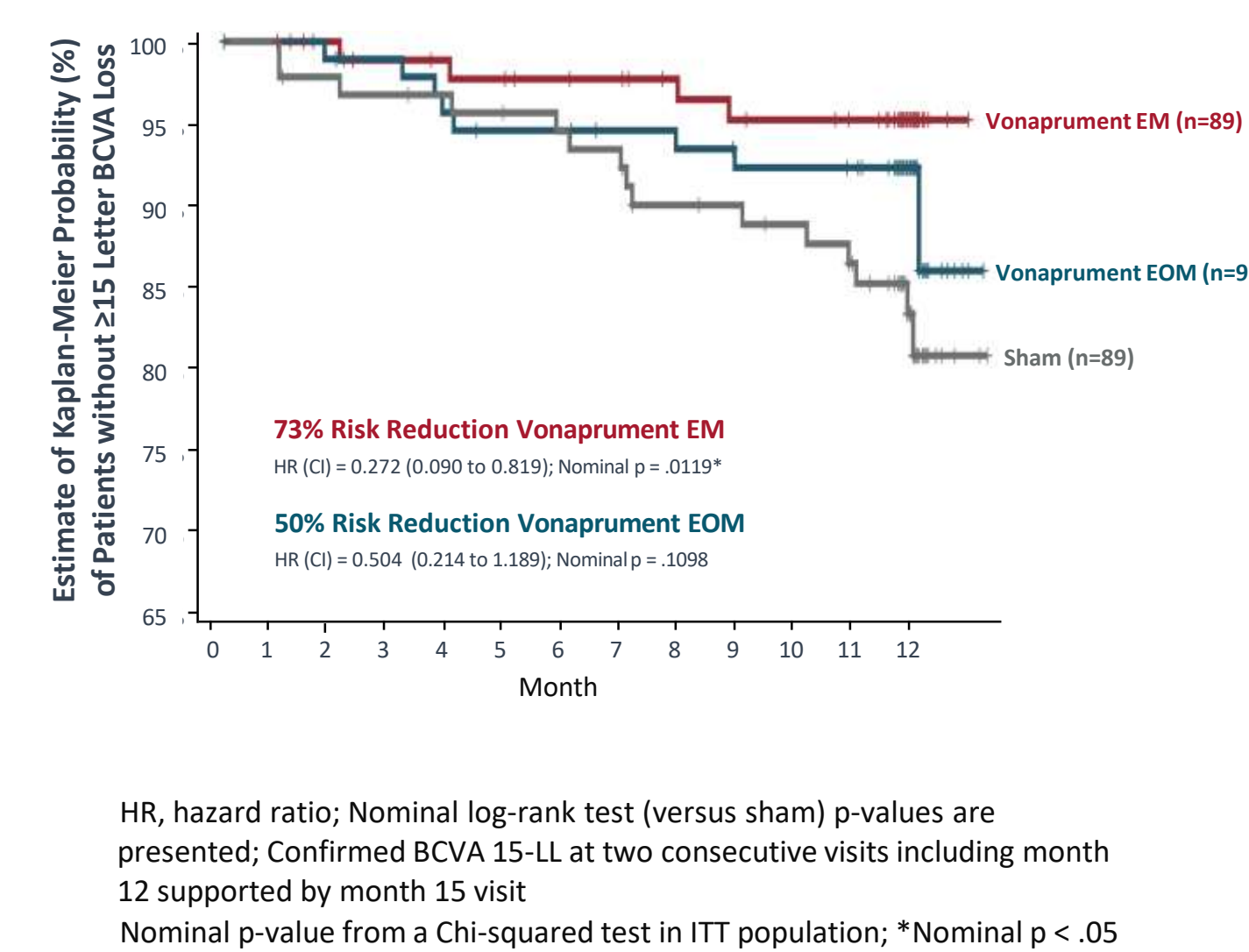
### Proportion of Patients With ≥15-letter BCVA Loss



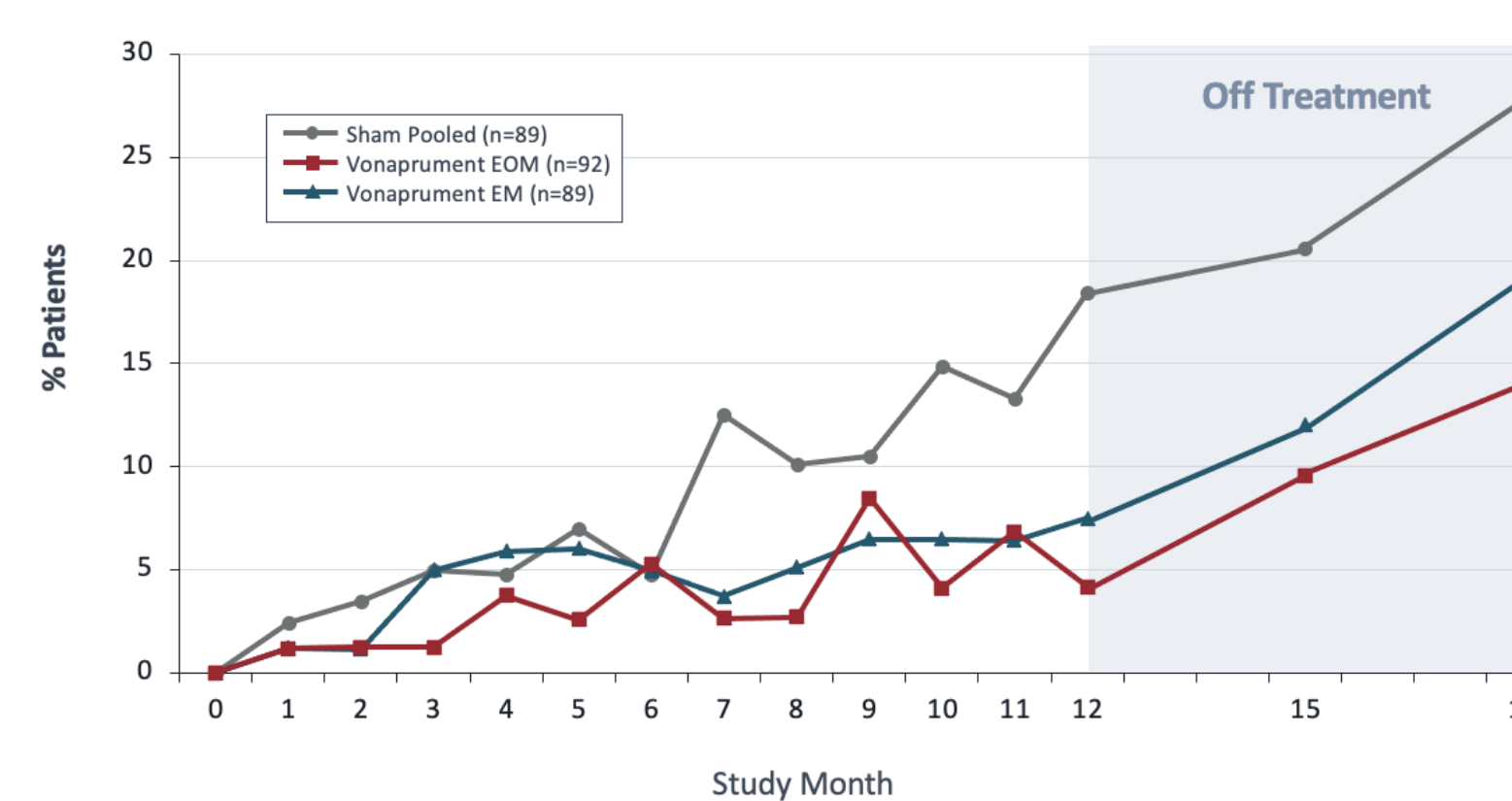
### Proportion of Patients With ≥15-letter LLVA Loss



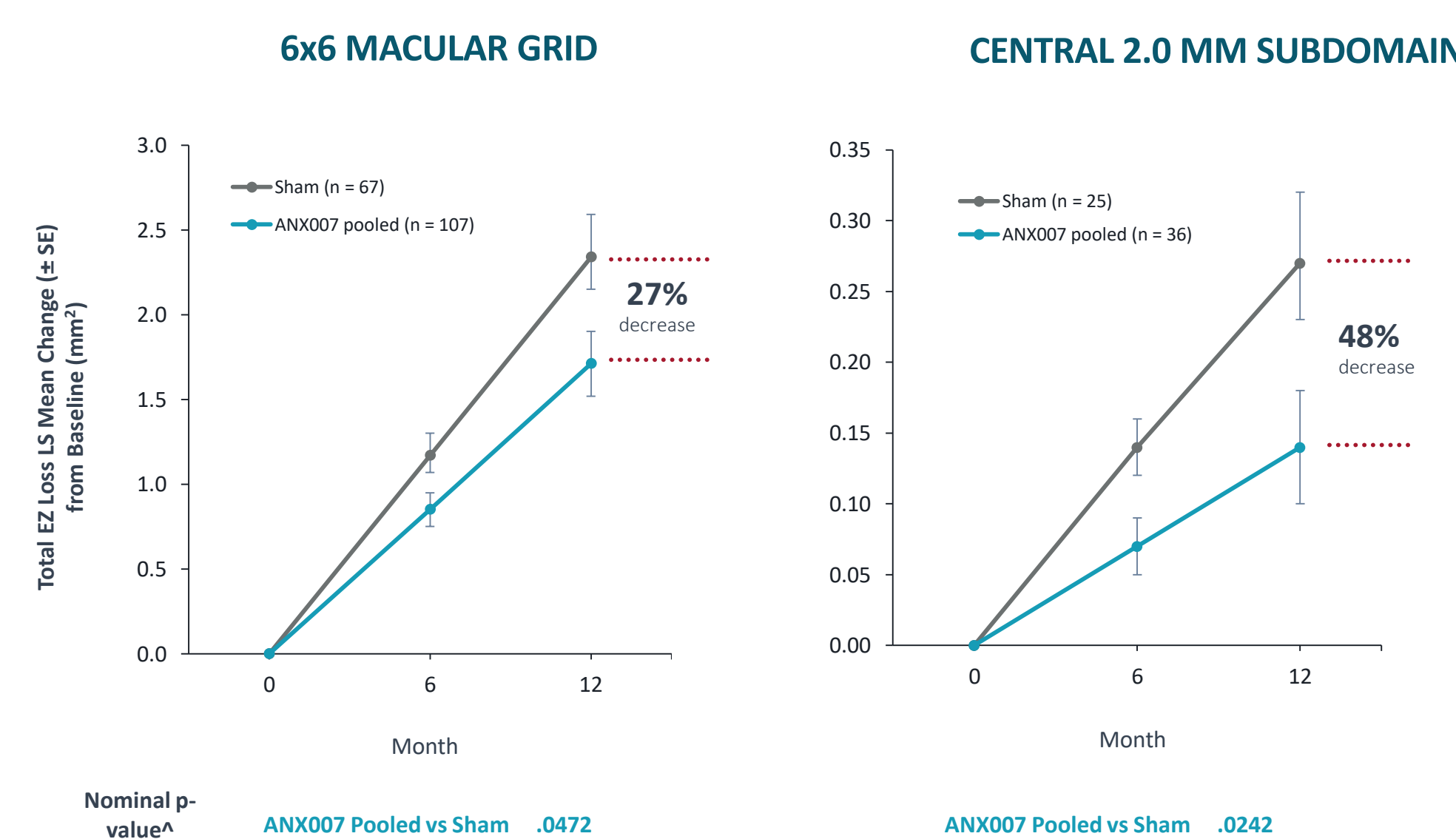
### Proportion of Patients Without ≥15-letter BCVA Loss at 2 Consecutive Visits Through Month 12



### Proportion of Patients With Single Visit ≥15-letter BCVA Loss Through Month 18, Including Off Treatment Period

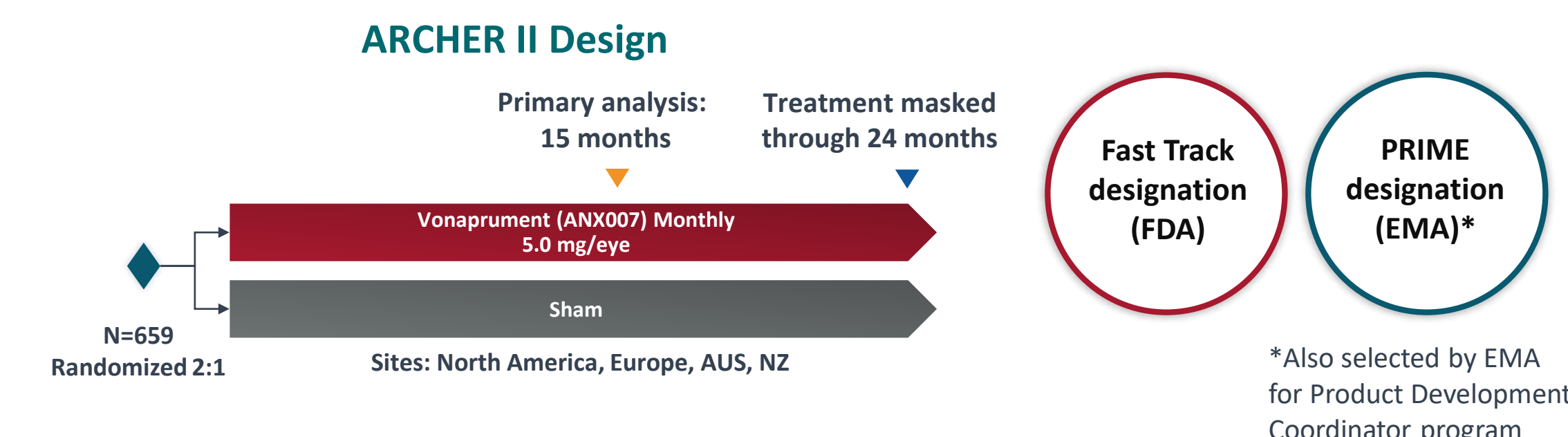


### LS Mean Change from Baseline in Total Ellipsoid Zone (EZ) Loss Through 12 Months



<sup>a</sup>Nominal p-values from a linear mixed model for repeated measures model (slope) analysis; Heidelberg Spectralis OCT population with baseline and at least one post-baseline OCT image, excludes patients with >98% atrophy at baseline

## ARCHER II PHASE 3 PROGRAM



- Primary endpoint: Proportion of eyes with confirmed BCVA ≥15-letter loss through primary analysis timepoint
  - Confirmed defined as: 15-letter or greater loss in BCVA observed at two consecutive study visits
- Secondary endpoints: Safety, LLVA, LLVD, EZ integrity
- Study population: Comparable to ARCHER; foveal and non-foveal lesions included; history of CNV in fellow eye permitted; eyes with <45 BCVA letters at baseline excluded
- ARCHER II is fully enrolled; data expected 4Q 2026

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## CONCLUSIONS

- ARCHER results suggest that C1q inhibition with vonaprunent conveys a drug-related photoreceptor protective effect that may explain associated prevention of visual acuity loss
- ARCHER BCVA ≥15-letter loss incidence rate consistent with larger prior datasets
- Data from inhibition with C1q suggest that the anti-C1q approach may provide neuroprotection against inflammation and neuronal damage and loss induced by downstream complement components
- Vonaprunent has the potential to be the first pharmacologic treatment to preserve vision in patients with GA

## ACKNOWLEDGMENTS

- DCY:** Serves as a consultant/speaker for Apellis, Astellas, Eyepoint, Roche, Regeneron, Alcon, Ani Pharmaceuticals, 4D Molecular Therapeutics
- SB, LT, RD, XT, WLC:** Employment with and equity ownership in Annexon Biosciences, Inc.
- These studies sponsored by Annexon Biosciences (Brisbane, California, USA)