ARCHER II, a Phase 3, Randomized Clinical Trial of Vonaprument (ANX007) in Patients with Dry AMD and GA: Study Design and Rationale

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Disclosures

Consultant to: Abbvie, Adverum, **Annexon**, Apellis, Bayer, Boehringer & Ingelheim, RETINAI, Roche, Zeiss

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

Randomized, double-masked
Included **foveal and non-foveal** lesions
Stratified for lesion location and lesion size
12 months of Active Treatment (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 ENDPOINT

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

PRESPECIFIED FUNCTIONAL ANALYSES

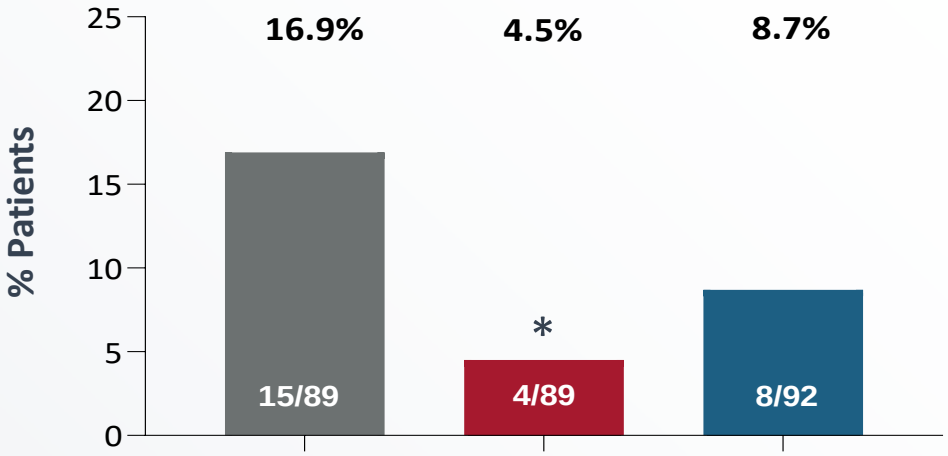
Best Corrected Visual Acuity (BCVA)
Low Luminance Visual Acuity (LLVA) & Deficit (LLVD)

Off-treatment
(6 months)

END OF STUDY
Month 18

Fewer Vonaprument-Treated Eyes Experienced BCVA ≥15-Letter Loss Compared to Sham

PROPORTION OF PATIENTS WITH CONFIRMED BCVA ≥15-LETTER LOSS AT TWO CONSECUTIVE VISITS THROUGH MONTH 12*

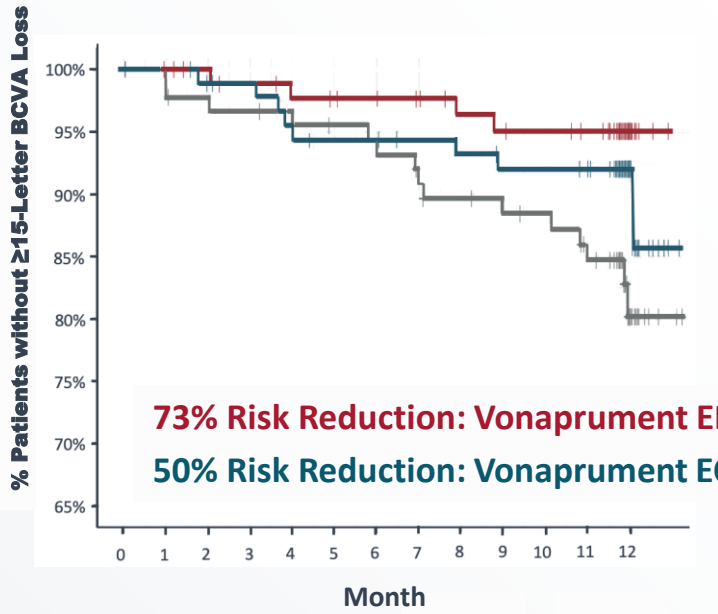


Nominal p-value vs Pooled Sham^	---	Vonaprument EM 0.0076	Vonaprument EOM 0.0994

*BCVA ≥15-Letter Loss at Month 12 was confirmed at the subsequent visit (Month 15). In ARCHER, visits were monthly through Month 12 and then at Months 15 & 18

^Nominal p-value from a Chi-square test in ITT population: *Nominal p < 0.05

PROBABILITY OF CONFIRMED## BCVA ≥15-LETTER LOSS THROUGH MONTH 12



Nominal p-value vs sham^	EM	EOM
	0.0119*	0.1098

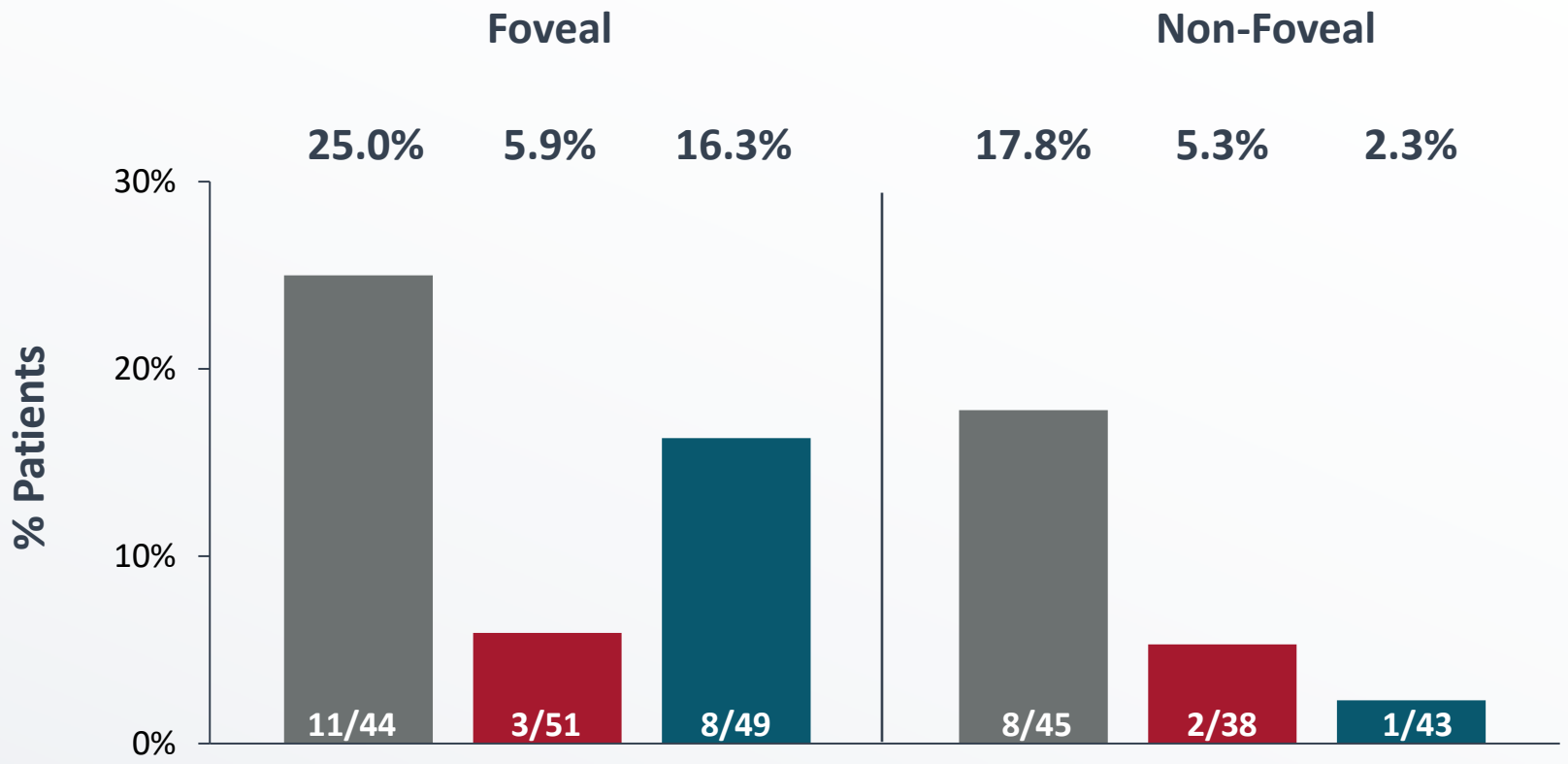
##Confirmed for two consecutive visits through month 12; month 12 confirmed at month 15 visit

^Nominal p-value from a Chi-square test in ITT population

* P < 0.05

Subgroup Analysis: Visual Acuity Outcomes in Subfoveal and Non-Subfoveal Lesions

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



Nominal summary p- value vs. Pooled Sham^

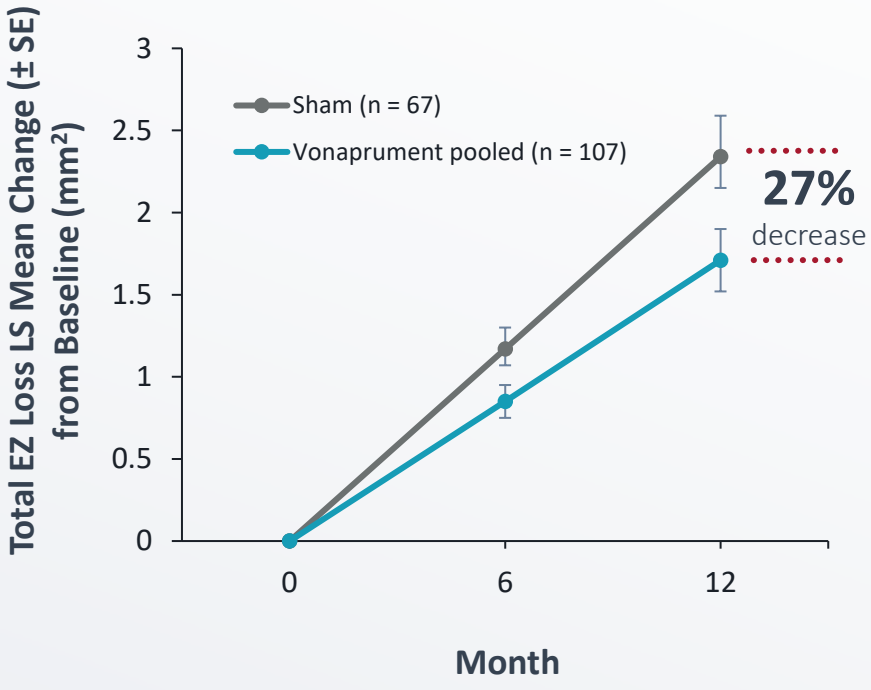
Vonaprument EM (pooled)	0.0019
Vonaprument EOM (pooled)	0.0254

#Confirmed 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

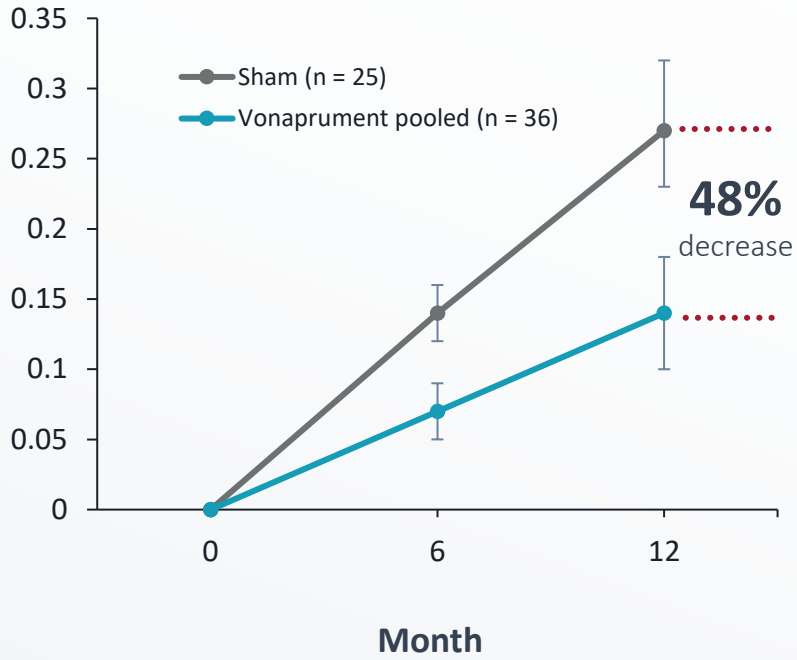
EZ Preservation with Vonaprument Observed Across Macula; Numerically Greater in Central Macular Regions

EZ is an imaging biomarker for photoreceptor integrity

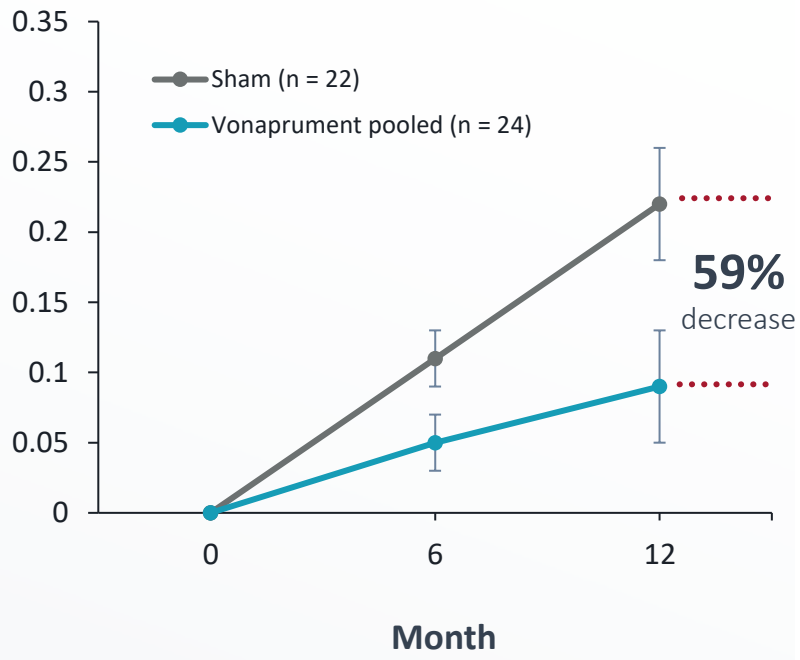
PAN-MACULA



CENTRAL 2.0 MM



CENTRAL 1.5 MM



Nominal p-value^		
Vonaprument Pooled vs Sham	0.0457	
Vonaprument Pooled vs Sham	0.0218	
Vonaprument Pooled vs Sham	0.0319	

^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

ARCHER: 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

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

ARCHER: Outcomes Informing ARCHER II Phase 3 Study Design

Prespecified and post-hoc analyses revealed important trends

VISUAL ACUITY:

Consistent, dose- and time-dependent trends favoring vonaprument across various measures and subgroup analyses

RETINAL STRUCTURE:

Ellipsoid Zone - a biomarker of photoreceptor integrity: Reduced total EZ loss with vonaprument vs sham, with this trend increasing in subdomains nearer the center of the macula

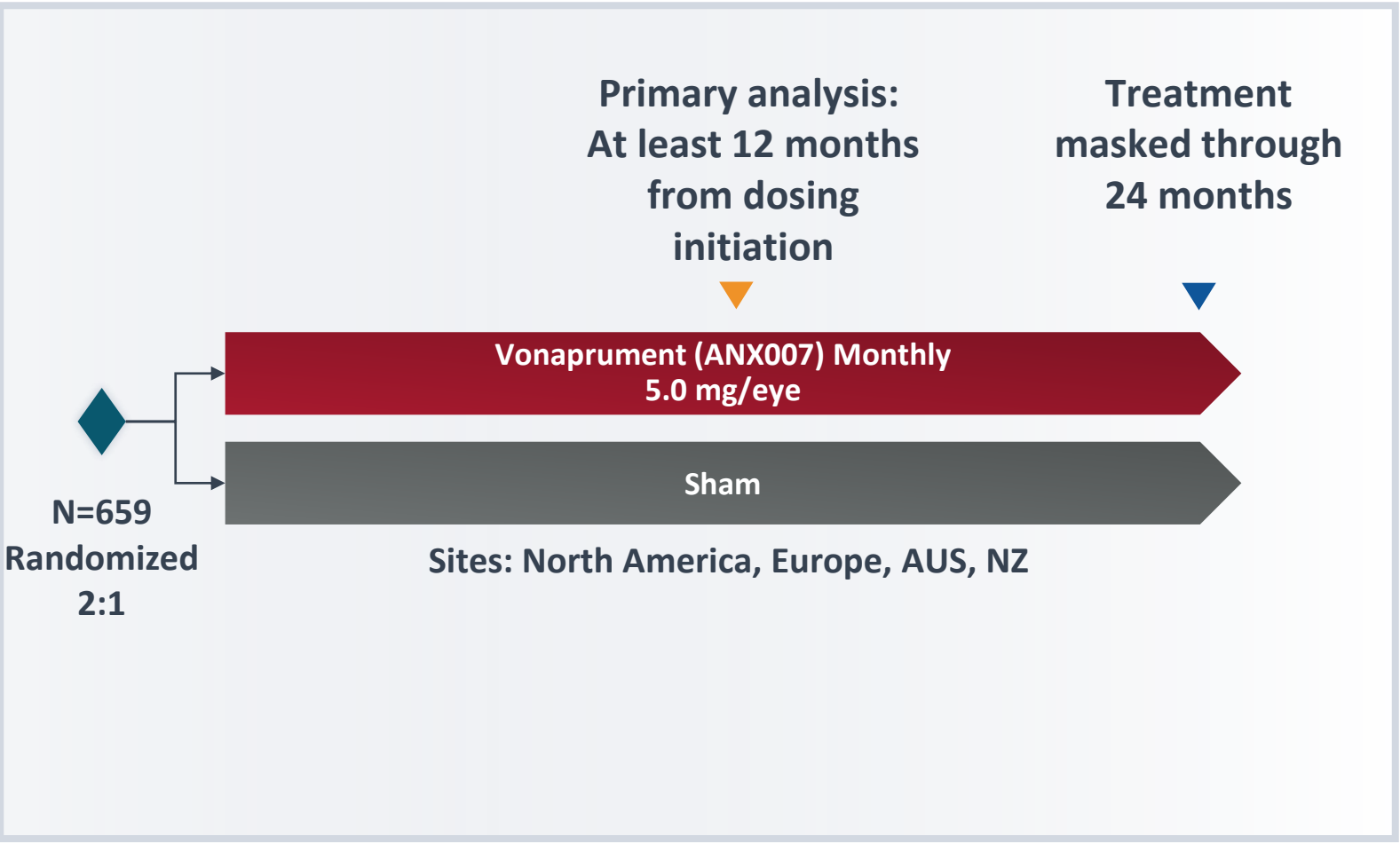
GENERALLY WELL-TOLERATED:

No CNV increase; no reported cases of vasculitis or Ischemic Optic Neuropathy

ARCHER II Phase 3 Program – Now Fully Enrolled

POPULATION FOR ARCHER II: Similar to ARCHER population, including foveal and non-foveal lesions and enriched for BCVA to exclude those with <45 ETDRS letters at baseline

PRIME designation from EMA; Fast Track from FDA



PRIMARY ENDPOINT

Confirmed* BCVA ≥15-letter loss through primary analysis timepoint

** ≥15-letter loss confirmed at two consecutive visits*

SECONDARY ENDPOINTS

Safety, LLVA, EZ integrity

Key Take-Away Points:

- Phase 3 ARCHER II trial of vonaprument (ANX007) in Dry AMD with GA:
  - Has completed enrollment; Data Expected 2H 2026
  - Is the only global pivotal program with vision preservation as the primary endpoint
  - Has a path to global registration
    - EMA: PRIME designation; Selected to Participate in Product Development Coordinator Pilot
    - FDA: Fast Track Designation
- Learnings from the Phase 2 ARCHER study informed the ARCHER II design
  - As in ARCHER, eyes with foveal and non-foveal lesions are included
  - Eyes with <45 ETDRS letters at baseline are excluded
- Vonaprument has the potential to be the first biologic treatment to preserve vision in patients with dry AMD with GA