ARCHER II, a Phase 3, randomized clinical trial of Vonaprument (ANX007) in patients with dry AMD and GA: Study design and rationale

David Eichenbaum, MD

On Behalf of the ARCHER and ARCHER II Investigators

Presented at the American Society of Retinal Specialists, July 30 – August 2, 2025

Long Beach, California

Disclosures

Role Over Calendar Year: S: Speaker C: Consultant I: Investigator E: Equity/Stockholder/Options F: Founder

4DMT I,C,E
AbbVie C
Adverum I,C
Aerie/Alcon I
Akari C
Alexion I
Allegenesis I
Amaros C,E
ANI C
Annexon C,I
Apellis C,S
Astellas I,C,S
Aviceda I
Bitfount C
Bausch & Lomb C
Bayer I,C,S
Boehringer Ingelheim I,C
Boston Image Reading Center E
Complement Therapeutics C
CorEvitas/Vestrum C
EcoR1 C
EyeBio I
EyePoint I,C,E
Gemini I
Genentech C,I,S
Gyroscope I
Harrow C
Hemera E
Ionis I
Janssen I,E
Kodiak I,C
Kriya C
Kyowa Kirin I
Lexitas C
Nanoscope C
Neurotech C
Notal Vision C
Novartis I,C
Ocugen C
Ocular Therapeutix I,C
Oculis C
Ocuphire C
OcuTerra I
Ollin I,C,E
Opthea I,C
Orasis C
ONL I
Outlook C
Priovant I
Regeneron C,I,S
Regenxbio I,C
ReVive C,E
RetinAI I,C
Roche I,C
Samsara I,C
Stealth I,C
Tilak C
Unity I,C
US Retina E

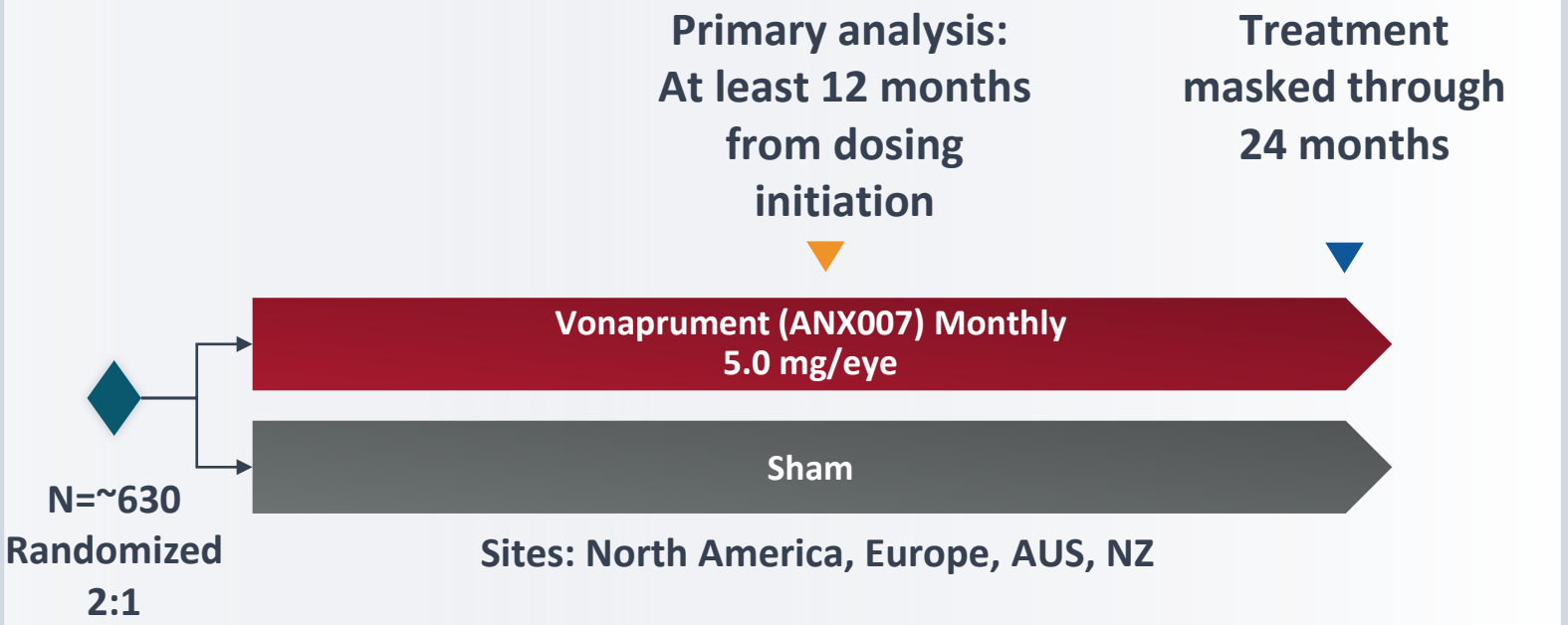
Key Take-Away Points:

- The Phase 3 ARCHER II program is now fully enrolled with a path to global registration
- ARCHER II is the only global pivotal program with vision preservation as the primary endpoint
- 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 (ANX007) has the potential to be the first pharmacologic treatment to preserve vision in patients with dry AMD with GA

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



PRIMARY ENDPOINT

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

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

SECONDARY ENDPOINTS

Safety, LLVA, EZ integrity

ARCHER: Phase 2 Trial Of The C1q Inhibitor ANX007 (vonaprument) 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 (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)

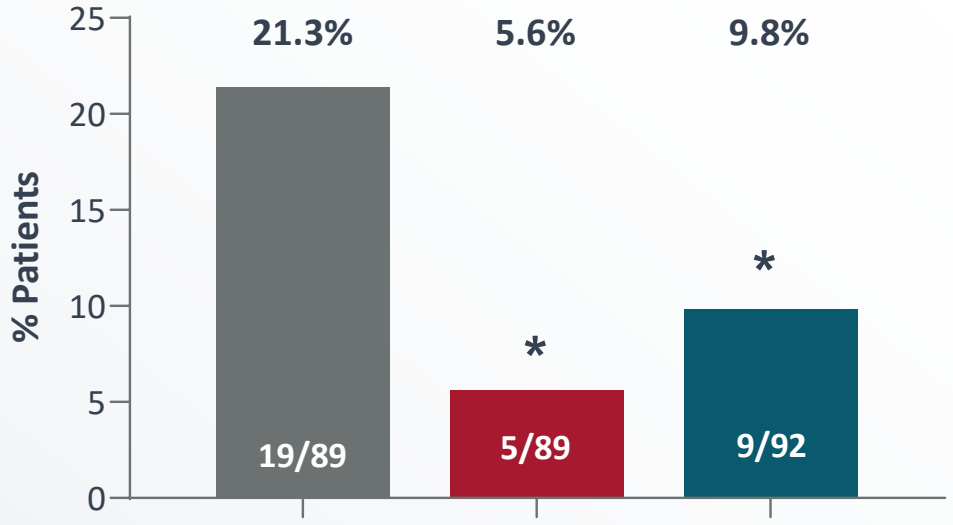
Off-treatment
(6 months)

END OF STUDY
Month 18

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

Regimen- and time-dependent protection of vision

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

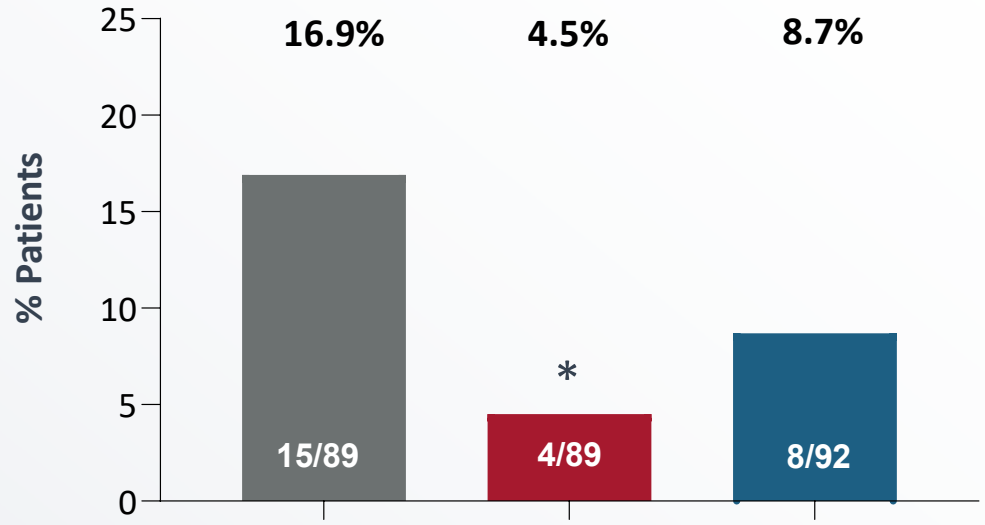


Nominal p-value vs Pooled Sham^	---	0.0021	0.032

#Persistent 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

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

Month 12 event confirmed at month 15

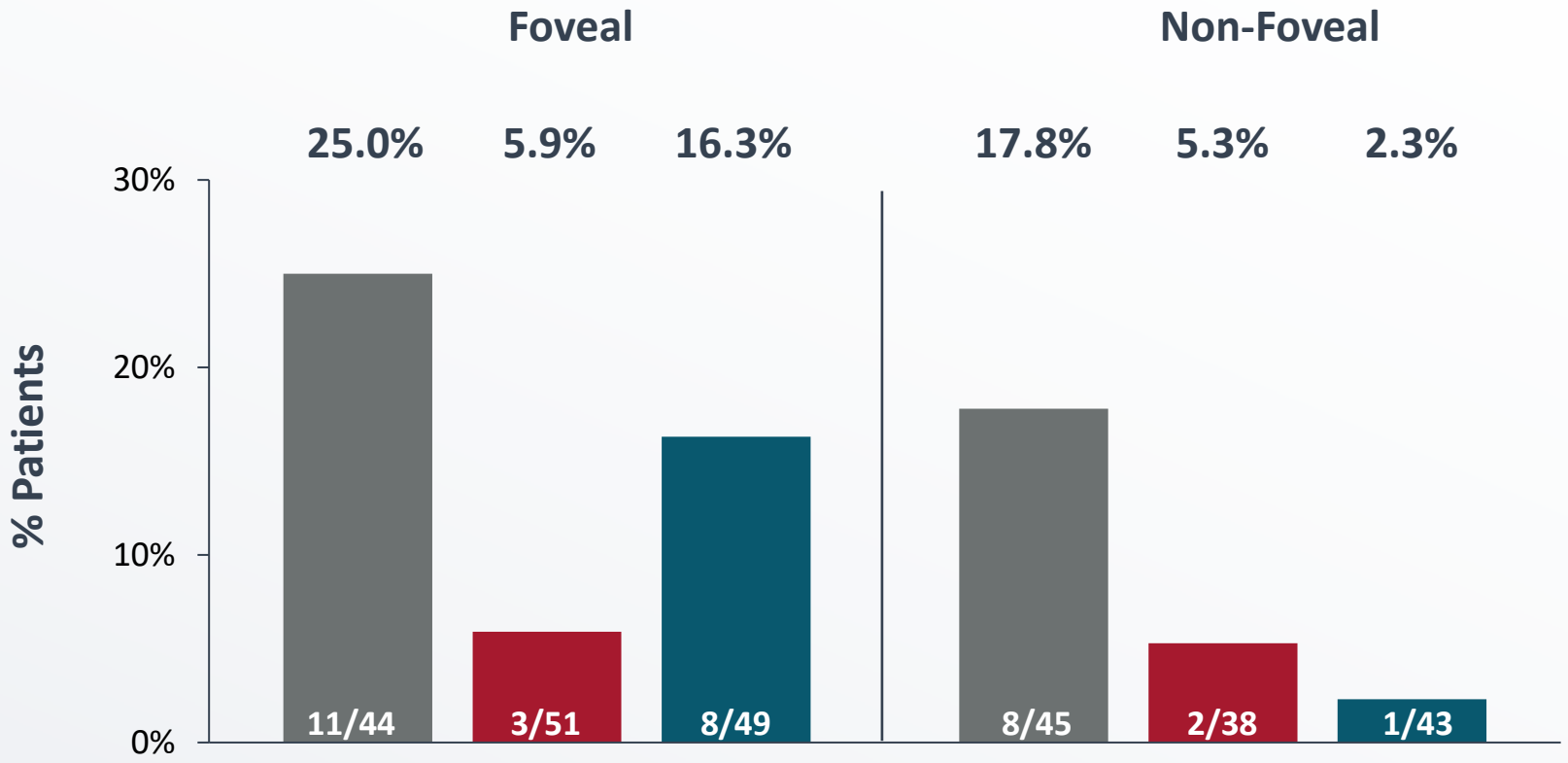


Nominal p-value vs Pooled Sham^	---	0.0076	0.0994

##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

BCVA Subgroup Analysis: Protection from Vision Loss Observed in Both Foveal and Non-Foveal Lesions with Vonaprument vs Sham

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



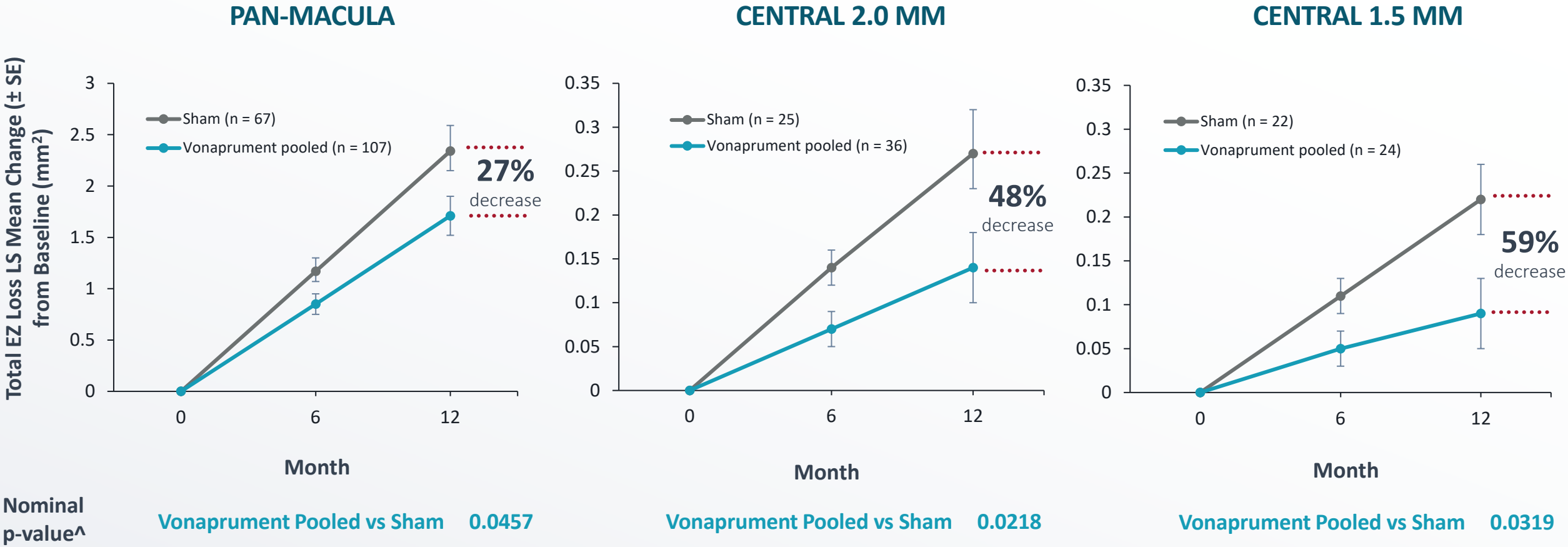
Nominal summary p- value vs. Pooled Sham^

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

Numerically Greater Photoreceptor Protection in Central Macula with Vonaprument

Comparison of Vonaprument effect on Ellipsoid Zone (EZ) across macula and in central subdomains through 12 months



^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, regimen- 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