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# STOP THE START

of classical complement-driven diseases



INVESTOR PRESENTATION | NOVEMBER 2026
Nasdaq: ANNX

# 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.

Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including, but not limited to, risks and uncertainties related to: our history of net operating losses; our ability to obtain necessary capital to fund our clinical programs; the early stages of clinical development of our product candidates; the effects of COVID-19 or other public health crises on our clinical programs and business operations; our ability to obtain regulatory approval of and successfully commercialize our product candidates; any undesirable side effects or other properties of our product candidates; our reliance on third-party suppliers and manufacturers; the outcomes of any future collaboration agreements; and our ability to adequately maintain intellectual property rights for our product candidates. These and other risks are described in greater detail under the section titled “Risk Factors” contained in our Annual Report on Form 10-K filed with the Securities Exchange Commission (SEC) on November 9, 2026 and our other filings with the SEC from time to time. All forward-looking statements in this presentation speak only as of the date of this presentation. Except as required by law, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise .

This presentation concerns drug candidates that are under clinical investigation, and which have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). These are currently limited by federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates or statistical data. Neither we nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this presentation.

# OUR FOCUS:

**Protecting function** for patients with devastating neuroinflammatory diseases

**The future of medicine isn't simply extending life. It's ...**

**Protecting the ability to live life.**

**Annexon is pioneering a new class of targeted therapies** designed to stop inflammation at its source in the body, brain, and eye before damage becomes irreversible.

# Potential Groundbreaking Lead Therapies for Patients in Large Underserved Global Markets



## Tanruprubart for GBS

First potential targeted rapid-acting therapy

- Comprehensive EU MAA filed
- Positive FORWARD study data to support planned US BLA



## Vonaprument for GA

First potential vision-protection treatment

- 1st significant vision-sparing data in Phase 2 evaluating vision
- 1st Phase 3 trial evaluating vision - Mo 15 primary outcome Q4 2026

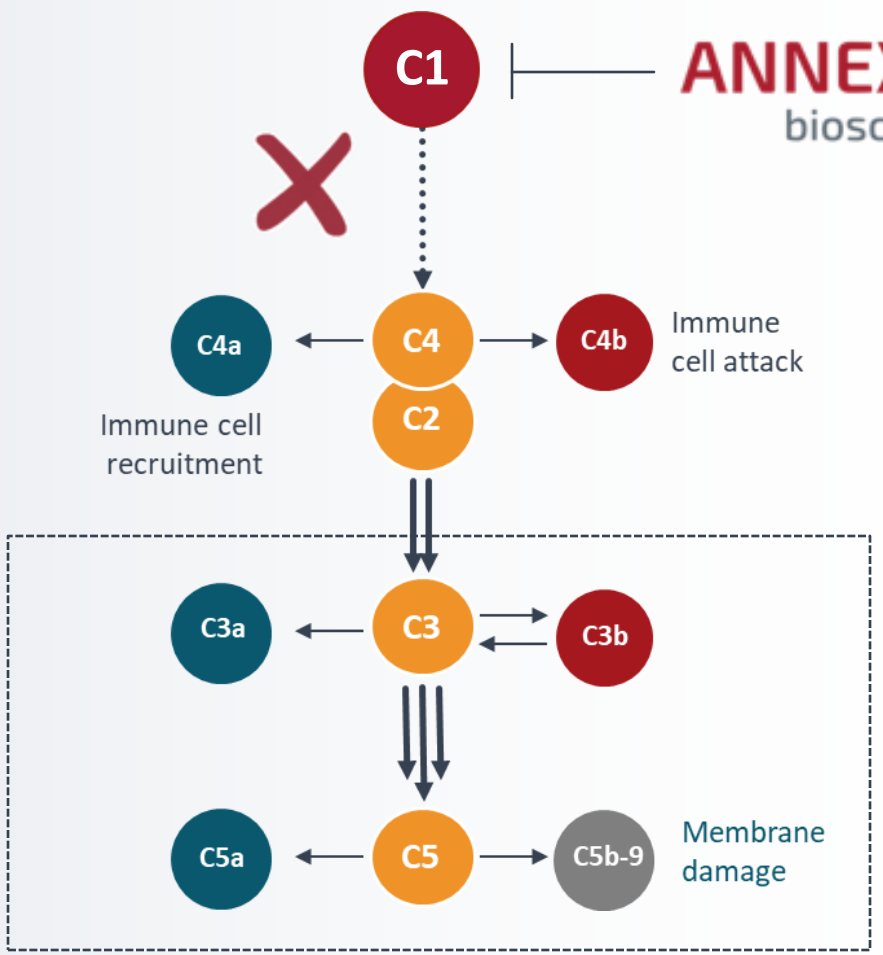
**Pipeline expansion opportunities including 1st oral inhibitor of classical complement in the clinic (ANX1502), and 1st demonstration of inhibition of C1q inflammation in CNS for an array of diseases (e.g., HD, TBI)**

# Validated Approach to Stop Neuroinflammation Where it Starts

Blocking C1 is clinically validated to halt neuroinflammation 'fire' at its source on disease tissue

~20 years of research / expertise in targeting C1q to stop neuroinflammation in several diseases

Differentiated clinical data from 1st gen approaches in multiple diseases (e.g., GBS, GA, HD, ALS)




**FIRST GENERATION APPROACHES**



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# Late-Stage Pipeline with Multiple Blockbuster Opportunities

| CANDIDATE | DESIGN | FRANCHISE/ INDICATION | PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 | ANTICIPATED MILESTONES |
|---|---|---|---|---|---|---|---|
| **FLAGSHIP PROGRAMS** | | | | | | | |
| **Tanruprubart (ANX005)** | IV mAb | Guillain-Barré Syndrome (GBS) | | | | | EU MAA filed Jan 2026; US BLA submission Q4 2026 |
| **Vonaprument (ANX007)** | IVT Fab | Geographic Atrophy (GA) | | | | | ARCHER II Month 15 results Q4 2026; Month 24 results Q3 2027 |
| **ANX1502** | Oral small molecule | Autoimmune Indications | | | | | Formulation optimization underway |
| **NEXT WAVE PROGRAMS** | | | | | | | |
| **ANX005** | IV mAb | Huntington's Disease (HD) | | | | | Poised for late-stage Phase 2b/3 development |
| | | Amyotrophic Lateral Sclerosis (ALS) | | | | | Poised for late-stage Phase 2b/3 development |
| **ANX009** | Subcutaneous Fab | Lupus Nephritis (LN) | | | | | Evaluating options for future development |

Autoimmune Neuro Ophthalmology



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# Anticipated Catalysts Supported by Cash Runway into 2028

## Tanruprubart
in GBS

- ✓ **EU MAA filed in Jan 2026** for first targeted therapy for GBS
- ✓ **US/EU FORWARD initial data** released Aug 2026

**FDA BLA filing anticipated Q4 2026**

## Vonaprument
in GA

**Phase 3 ARCHER II 15-Month results anticipated Q4 2026**
for first vision-protection program in dry AMD with GA

## ANX1502
in Autoimmune

- ✓ **POC study update** Nov 2026 for first oral C1 inhibitor





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# Experienced Leadership with Know-How to Win



**Doug Love**
**President & CEO**

- élan
- Genentech — A Member of the Roche Group
- AMGEN



**Ted Yednock, PhD**
**Chief Innovation Officer**

- élan
- TYSABRI (natalizumab)
- prothena



**Jamie Dananberg, MD**
**Chief Medical Officer**

- UNITY BIOTECHNOLOGY
- Takeda
- Lilly



**Rick Artis, PhD**
**Chief Scientific Officer**

- OCTANT
- élan
- Plexxikon



**Jennifer Lew**
**Chief Financial Officer**

- ADURO BIOTECH
- DYNAVAX
- EY



**Michael Overdorf, MBA**
**Chief Business Officer**

- Lilly



**Linda Fitzpatrick**
**Chief Human Resources Officer**

- SUTRO BIOPHARMA
- GILEAD
- Genentech — A Member of the Roche Group

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# Tanruprubart: Blockbuster Best-in-Class Treatment for GBS

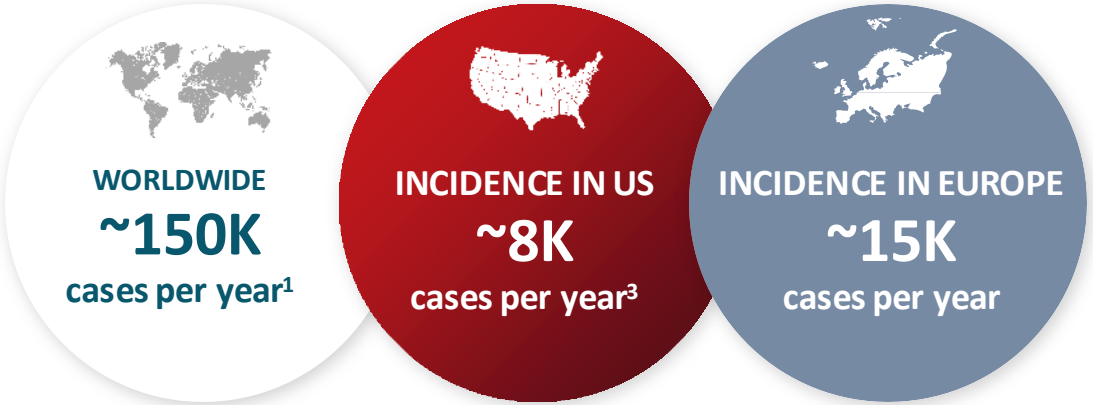
**Poised to Replace Standard of Care**



Shane S.
53-year-old patient with GBS

# GBS: Sudden Neurological Emergency

No FDA-approved therapies IVIg used off-label




**SIGNIFICANT DISEASE BURDEN DESPITE IVIG TREATMENT** 1,2,3,4,5,6,7,8

| ~30% | ~75% | ~20% | ~25% |
|---|---|---|---|
| admitted to ICU | in ICU require ventilation | can't walk a year after treatment | mortality rate for aged >65 |



- Most common cause of acute neuromuscular paralysis
- Typically caused by infection, vaccine side effects, other therapies
- **>$20B annual societal burden associated with the disease[8]**

1. ClearView Health Market Research (2024); 2. Hughes et al. (2003). Neurology, 61, 736-40; 3. Hund et al. (1993). Crit Care Med, 21, 433-46; 4. Doets, et al. (2018). Brain, 141, 2866-77; 5. Van den Berg et al. (2014). Nat Rev Neurol, 10, 469-82; 6. Leonhard et al. (2019). Nat Rev Neurol, 15, 671-83; 7. Inflation- and population-adjusted cost estimates from Frenzen (2008). Neurology, 71(1), 21-7; 8. Ongoing Annexon study submitted for AAN presentation.



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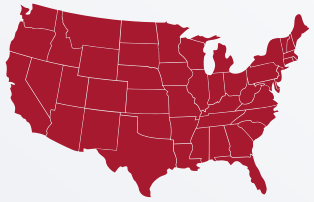
# GBS is Associated with Significant Morbidity and Mortality in US

**~2.5x longer GBS-related hospital length of stay** (13 days), compared to US average length of stay

**~30% of patients** hospitalized with GBS require **ICU care** and **20-25% mechanical ventilation,** substantially increasing the mortality risk

**~55%** received **other inpatient care** (e.g., SNF, inpatient rehab, LTC) during the 12 months following the hospitalization

## 1-YEAR MORTALITY



**~1 in 4 Medicare (24%) and ~1 in 20 (5.1%) commercially insured patients died** during the 12 months following hospitalization

ICU, intensive care unit; IVIg, intravenous immunoglobulin; LTC, long-term care; PLEX, plasma-exchange; SNF, skilled nursing facility

AAN Annual Meeting 2026; Poster 003. EAN Annual Meeting 2026



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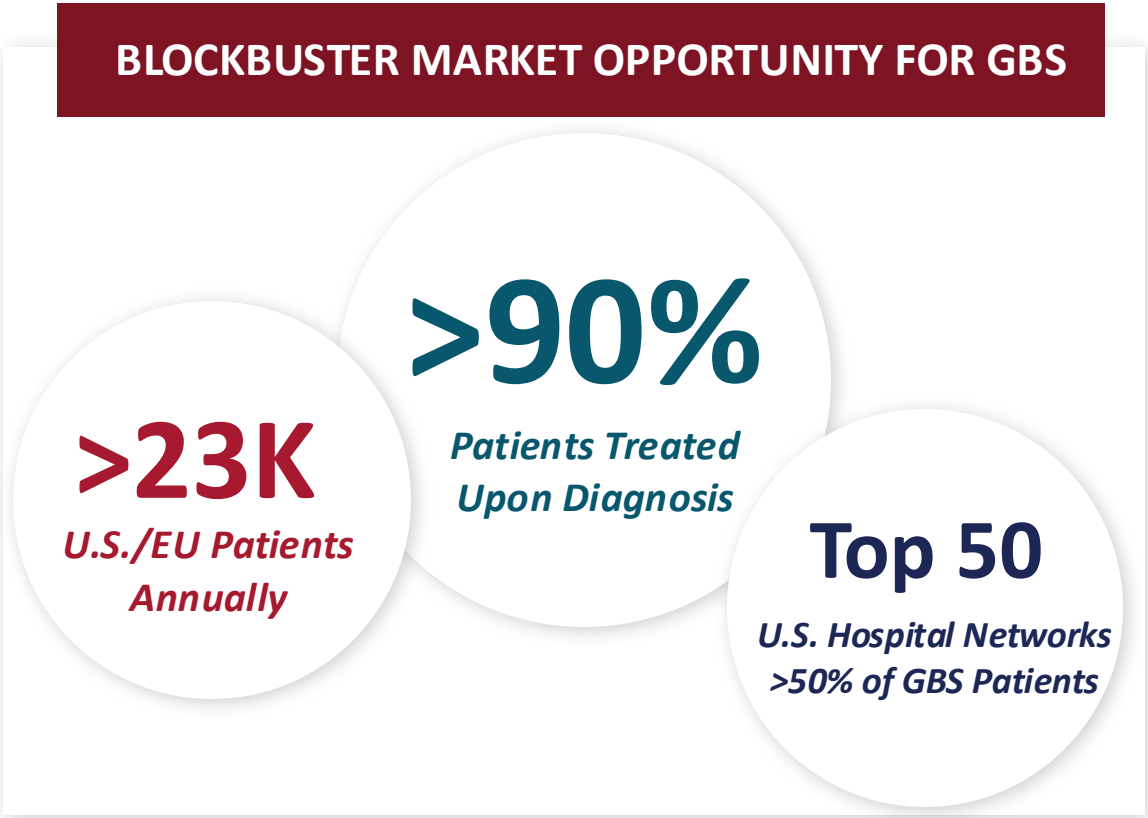
# GBS Provides a Compelling Market Opportunity

**Tanruprubart is first targeted therapy designed to create a new standard of care in GBS**




## Tanruprubart

- **Single infusion** halts neuroinflammation
- **~90% of treated patients improved** by week 1
- **Safety** data comparable to placebo
- **Significant potential savings to U.S. healthcare** system over IVIg/PE

Current treatments are slow and suboptimal
Most patients suffer from incomplete benefit

Targeted treatment offers faster, more complete recovery for patients to regain their independence



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# Phase 3 Demonstrated Tanruprubart 30 mg/kg Single Dose Led to Rapid, Robust, and Consistent Benefit Across Multiple Endpoints

## Met Primary Endpoint

**2.4x more likely of being better on GBS-DS at Week 8 relative to placebo ($p$ = 0.0058)**

- Primary outcome supported by multiple sensitivity analyses
- Fast onset with significant clinical improvement from week 1 onward; nearly all patients improved or stabilized
- Larger treatment effect in patients with Western World baseline characteristics (e.g., AIDP)

## Durable Treatment Effect

**Sustained improvement over placebo at all timepoints across multiple measures**

- Less time on ventilation
- Less overall disability
- >2x more patients return to normal (GBS-DS = 0) at week 26 vs. placebo

## Generally Well Tolerated

**Generally safe; common AEs generally consistent between placebo & treatment arms**

- No new drug related safety signals
- No increased infection rate while not requiring vaccination or prophylactic antibiotics
- No difference in all-cause mortality

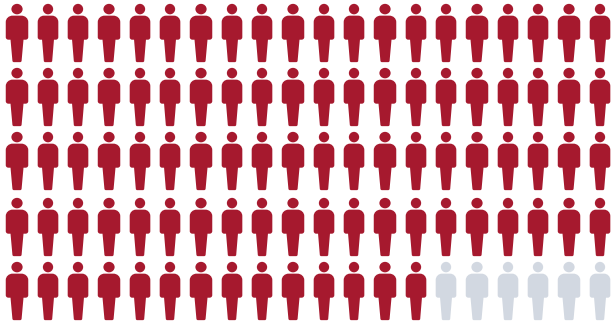


Topline Results Subject to Change

# Phase 3: Nearly All Tanruprubart Treated Patients Improve or Stabilize in Muscle Strength at Week 1

**Week 1 Response Rate From Baseline with Tanruprubart 30mg/kg**

Tanruprubart 30mg/kg



**94%** Respond or Stabilize

Placebo



**50%** Respond or Stabilize



1LS mean point improvement relative to placebo

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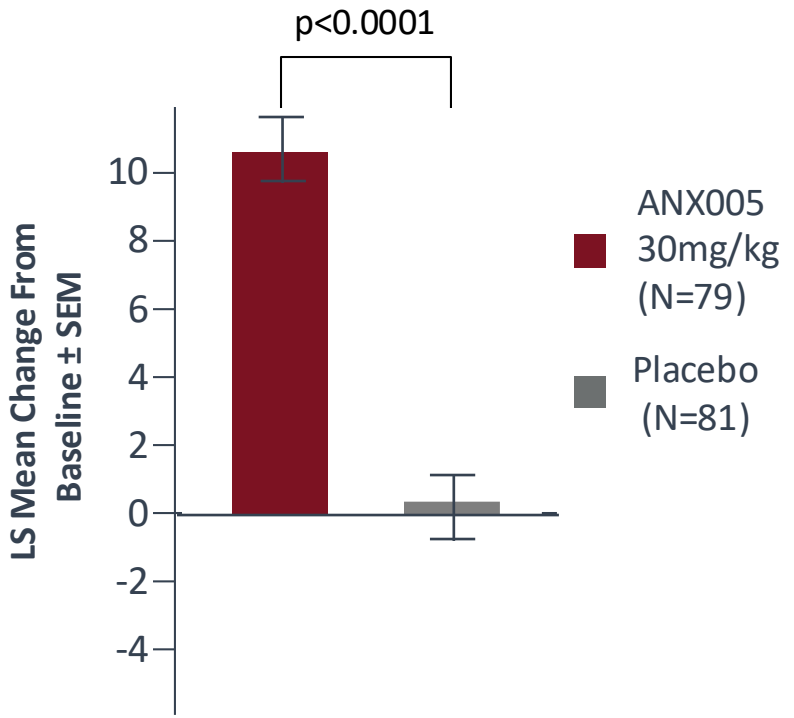
# Phase 3: Tanruprubart Treatment Outcomes Were Rapid and Durable, with >2x More Treated Patients Fully Recovered at Month 6

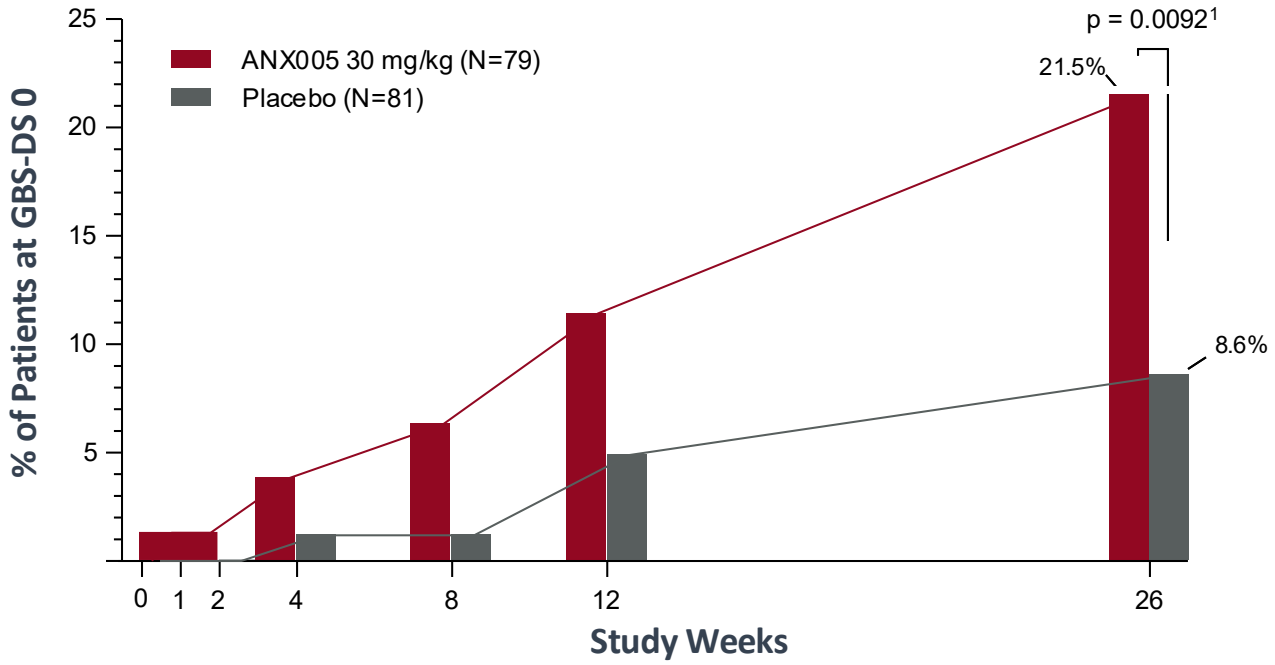
## 86% of Patients Treated with ANX005 Improved in Week 1 (10 pts on avg.)

### MRC Sumscore at Week 1




## >2 Times More Treated Patients Fully Recover at Week 26 (GBS-DS = 0)

### GBS-DS=0 Through Week 26






1. MRC Sumscore; 2. nominal

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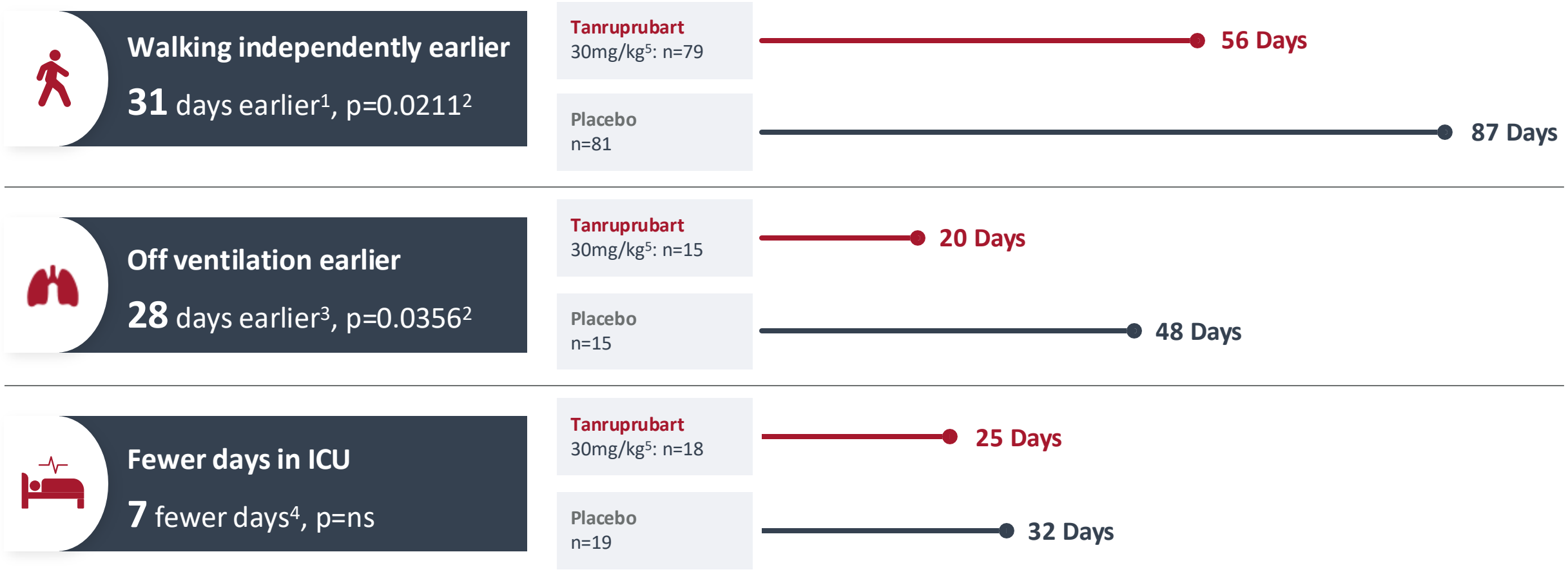
# Phase 3: Tanruprubart Demonstrated Profound Impact on Measures Most Important To Patients, HCPs and Payers

## Helped Patients Achieve Their Independence Sooner Versus Placebo




ICU, intensive care unit; ns, not significant.
1. Based on first scheduled visit of recording; 2. Nominal; 3. Among patients ventilated; 4. Among patients requiring ICU
*Phase 3 data reported on the 30 mg/kg dose



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# Fewer Tanruprubart Patients Required Ventilation and Trended to Less Ventilation Time and ICU: Measures of Decreased Burden of Care



## Fewer Patients Ventilated

**Half as many patients, *p* = 0.022**

**Tanruprubart 30mg/kg**
N = 15 of 79
**19%**

**IGOS IVIG/PE**
N = 32 of 79
**40.5%**



## Fewer Days on Ventilation

**Median 12 fewer days, *p* = n.s.**

**Tanruprubart 30mg/kg**
N =15
**20 Days**

**IGOS IVIG/PE**
N = 32
**32 Days**



## Fewer Days in ICU

**Median 12 fewer days, *p* = n.s.**

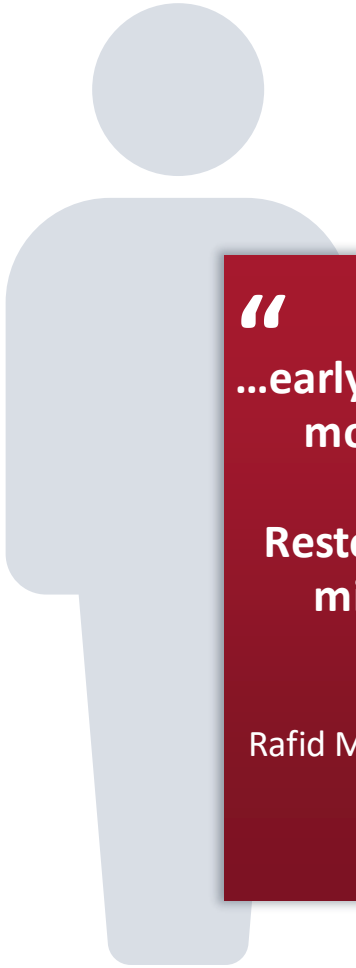
**Tanruprubart 30mg/kg**
N =18
**25 Days**

**IGOS IVIG/PE**
N = 36
**37 Days**



Preliminary Topline Results Subject to Change

# U.S./EU FORWARD Demonstrates Consistent Reproducible Tanruprubart Treatment Effect in GBS



Forward™ STUDY

> **"…early results from the FORWARD study are some of the most encouraging we have seen in GBS research…**
>
> **Restoring strength and mobility is not simply a clinical milestone; it is a pathway back to independence, dignity, and everyday life."**
>
> Rafid Mustafa, M.D., Associate Professor of Neurology and Vice Chair for Quality, Department of Neurology, Mayo Clinic

- **More than 18 patients treated** to date with moderate to severe GBS, ages 12 to 78 years old
- **Rapid benefit on function and disability, complete target engagement and generally well-tolerated safety profile consistent** with Phase 3 and RWE studies
- **Evidence of treatment effect across broad range of GBS patients** with different disease neurotypes, severities, ages and geographies



Topline Results Subject to Change

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# On the Path to Bringing Tanruprubart to GBS Patients Worldwide

- **Faster, More Complete Recovery** in Phase 3 Placebo-Controlled Trial and Favorable Safety Profile
- **Earlier and Greater Benefit Over IVIg** in Real World Evidence Study of Matched Western World Population
- **Rapid Response and Benefit in US/EU** FORWARD Study Consistent with Phase 3 and RWE Outcomes

## NEXT STEPS

- ✓ **MAA Filed in Europe Jan '26**
- **BLA Submission Planned Q4'26**
- **Ramping disease education and engaging payers on disease burden to optimize coverage and reimbursement**

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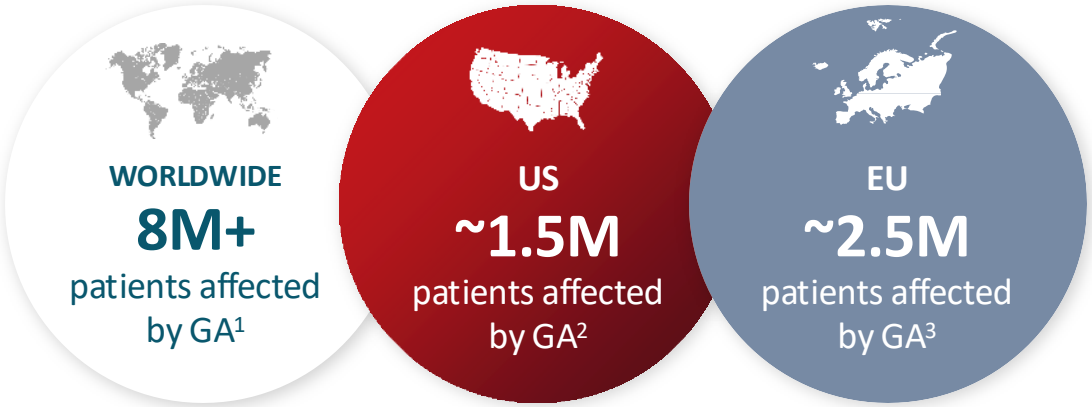
# Vonaprument: Only Geographic Atrophy Program to Show Significant Vision Protection



**Global Pivotal Program with Potential Blockbuster Market Opportunity**

# Geographic Atrophy Remains a Significant Unmet Need

No approved treatments demonstrating vision protection




**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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# 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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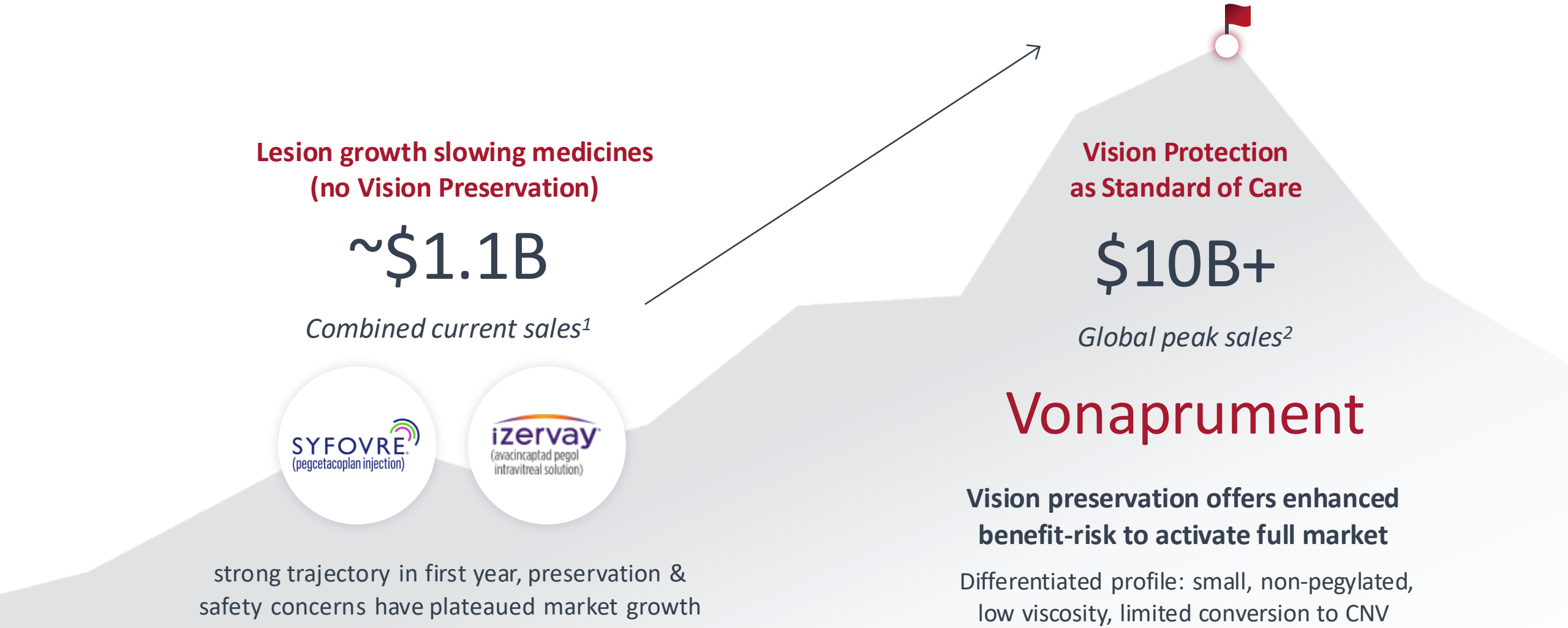
# Vonaprument Poised to Build GA Market Similar to wet AMD

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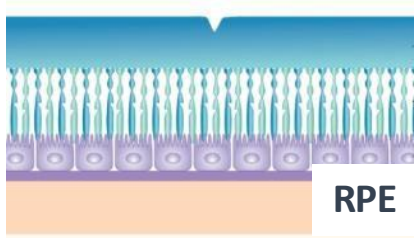
# GA is a Neurodegenerative Disease that Starts at Photoreceptor Synapses and Cells Necessary for Vision

## Normal Retina

Photoreceptors convert to electrical signals



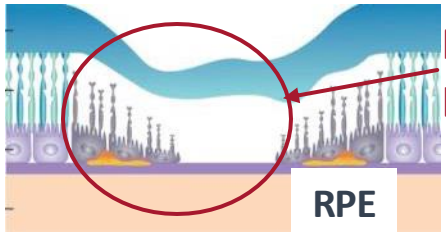

Intact Photoreceptors



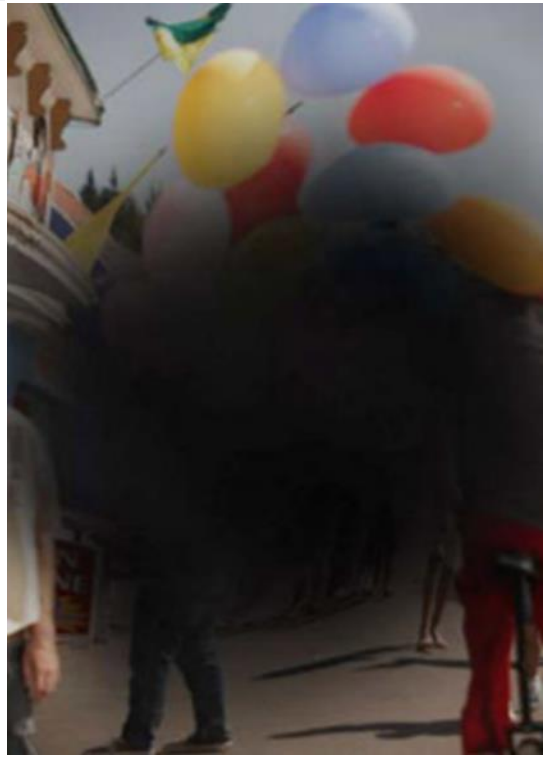
**Normal Vision**

## Retina with GA

Loss of signals due to damaged or missing photoreceptors




Photoreceptor Loss



**Reduced Vision**



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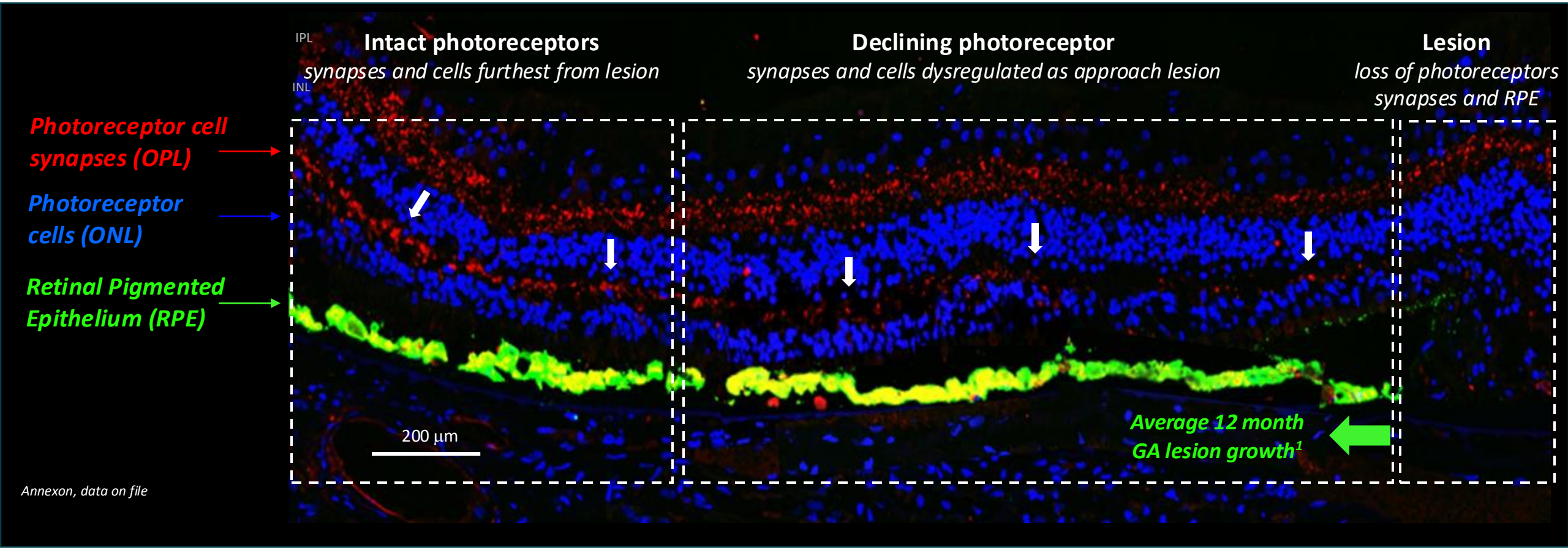
# In GA Photoreceptors and Synapses are Lost Before RPE Loss

## 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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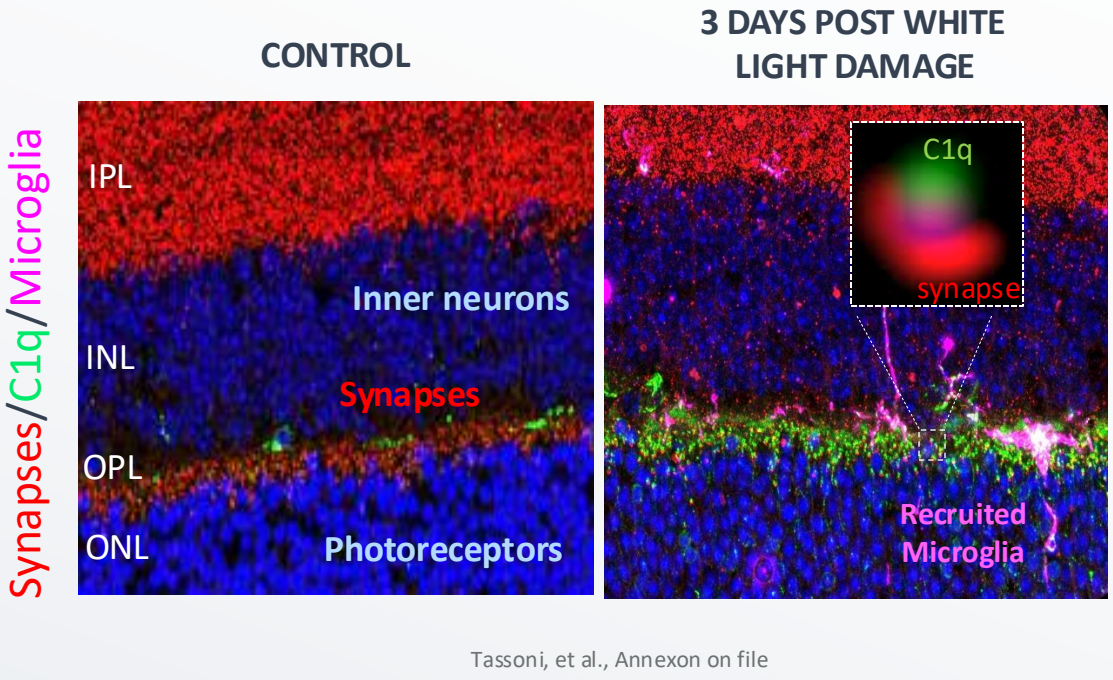
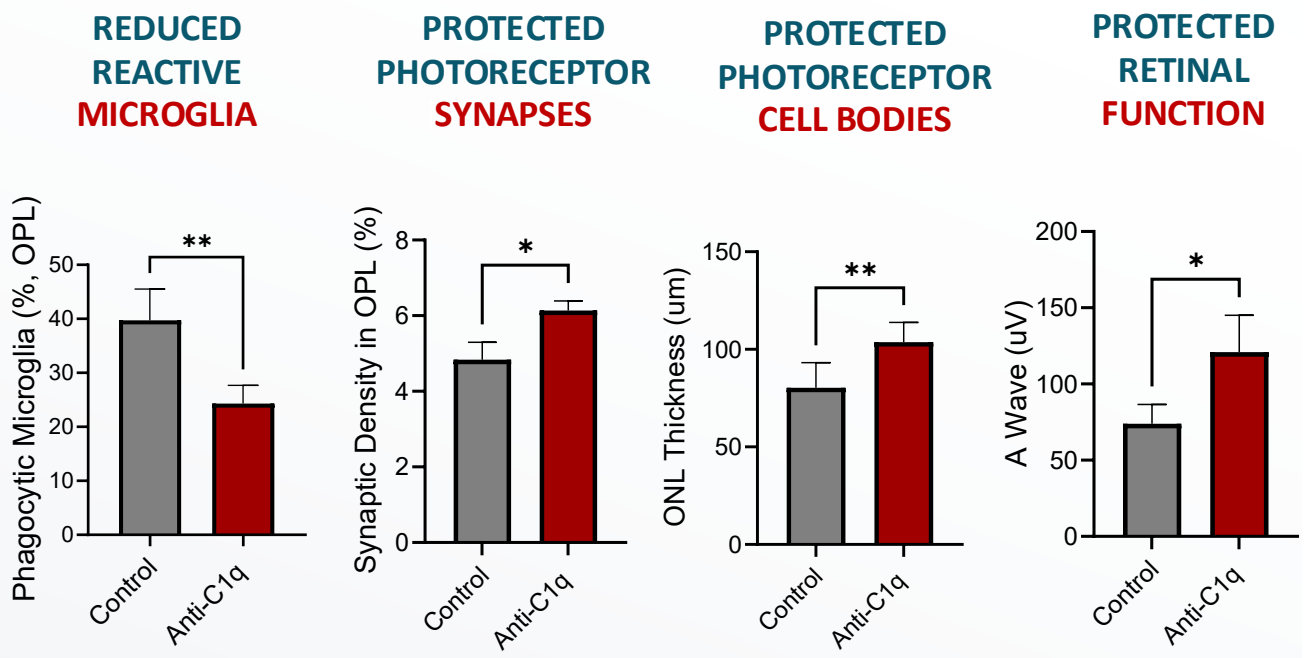
# Anti-C1q Protected Photoreceptor Cells and Their Function in Models of Photoreceptor Damage

## C1q Deposition on Photoreceptor Cells and Synapses with Light-Induced Damage




Tassoni, et al., Annexon on file

## Anti-C1q Protected Photoreceptors and Function



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# ARCHER Phase 2: Vonaprument Protected Vision Across Multiple Functional Measures and Key Retinal Structures Important for Vision

## Vonaprument Protected Functional Photoreceptors Responsible for Visual Acuity

- OCT-based Ellipsoid Zone measurements provide objective measure of photoreceptor health
- Central retinal structures are critical for visual acuity and are key therapeutic target
- Significant protection of photoreceptors across entire macula, greatest preservation in central retina necessary for visual acuity

## 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 Protection 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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# ARCHER: Phase 2 Trial of C1q Inhibitor ANX007 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) | ANX007 5mg monthly (EM) (n=89) | ANX007 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 SECONDARY FUNCTIONAL ANALYSES

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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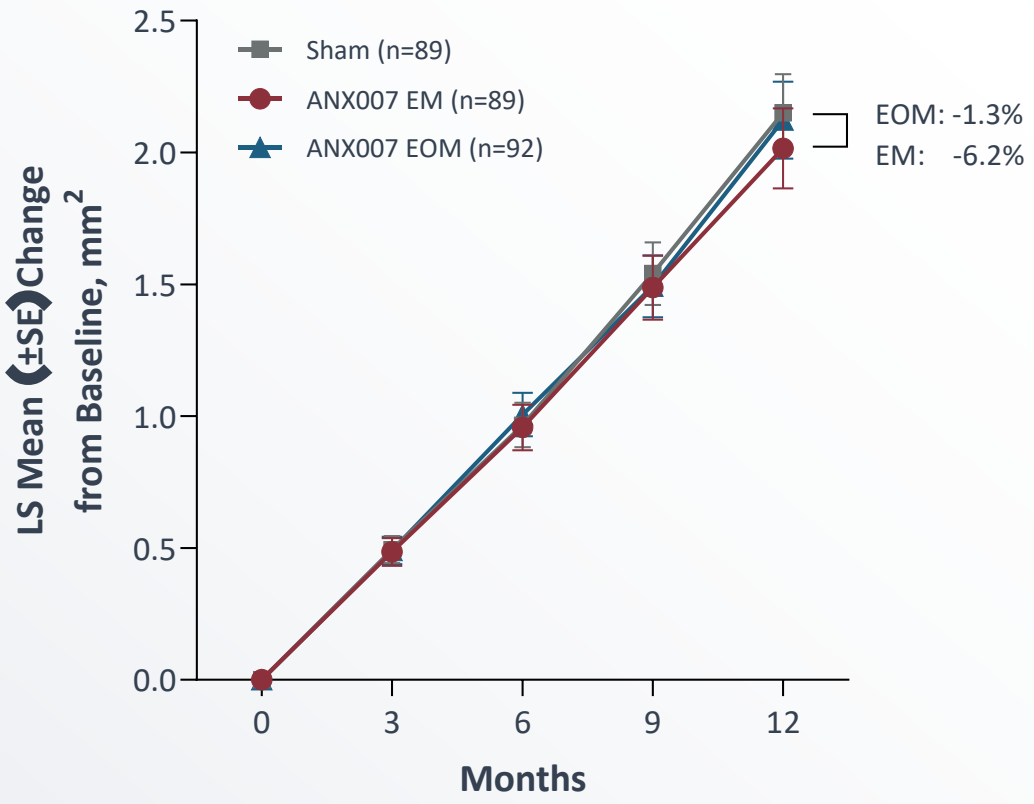
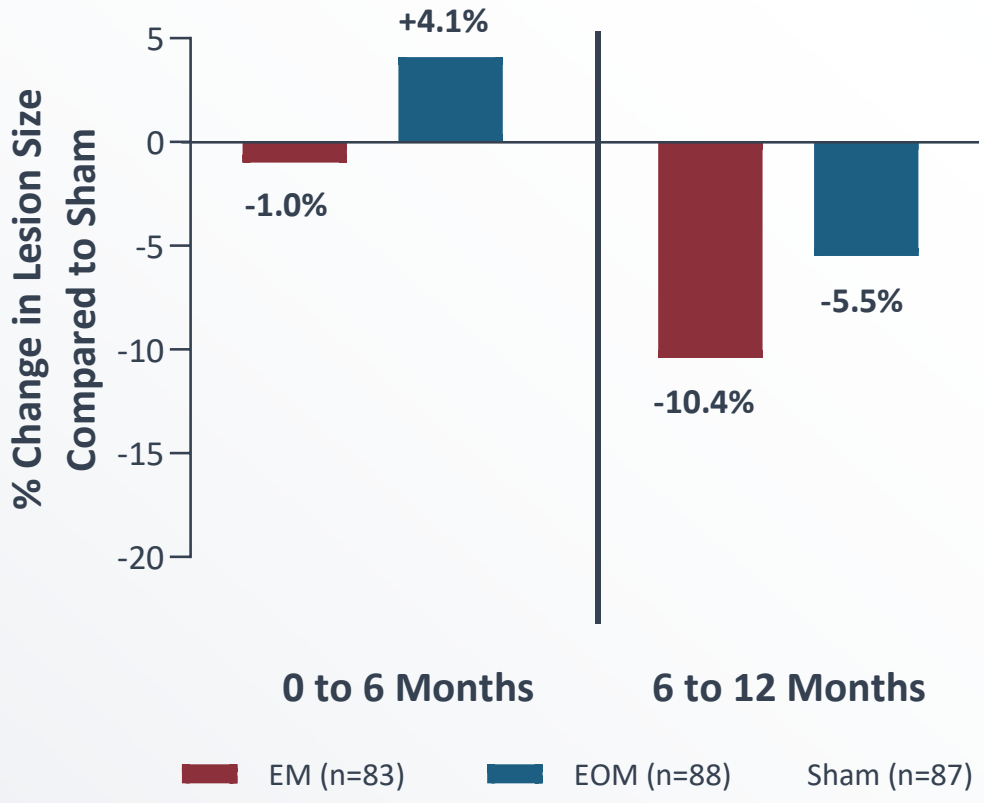
# ARCHER Phase 2: Vonaprument Treatment Effect on RPE Loss through 12 Months

## 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#






#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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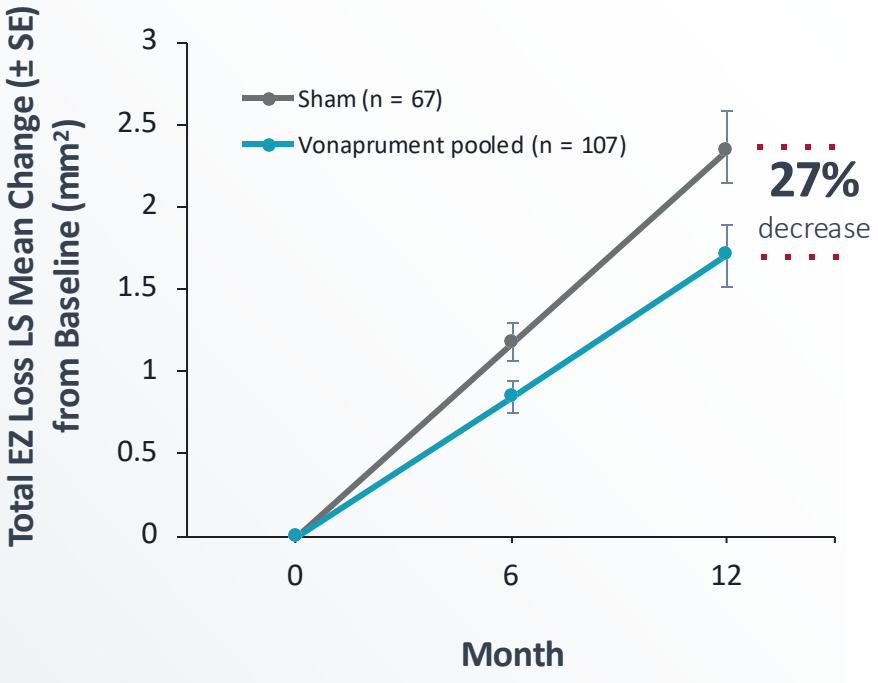
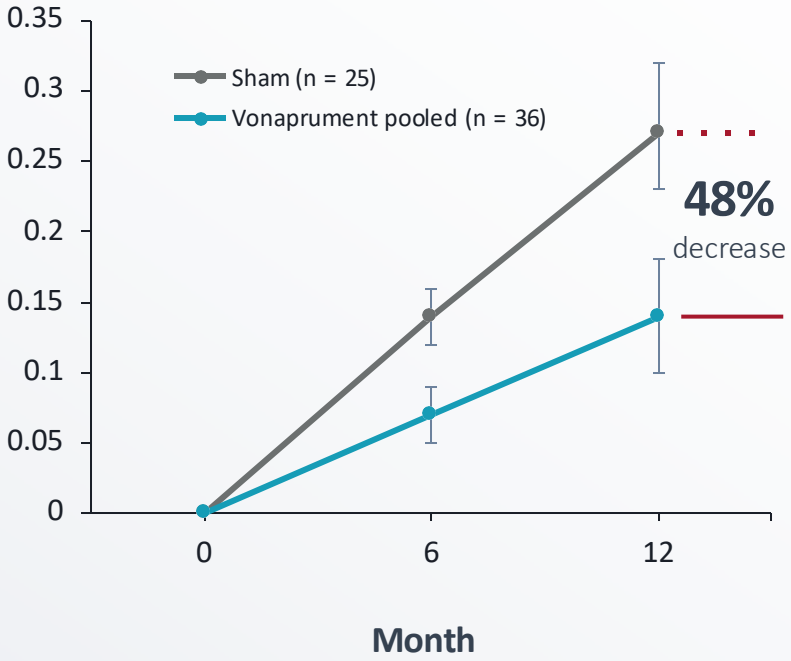
# ARCHER Phase 2: Vonaprument Protects Photoreceptors in GA; Greater Effect in Central Retina Necessary for Visual Acuity

## PAN-MACULA



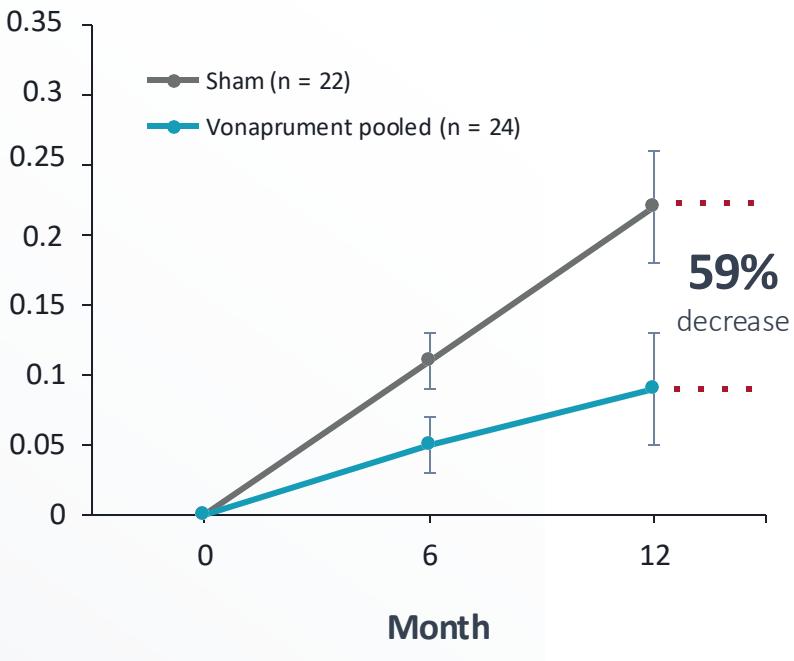

Nominal p-value^ Vonaprument Pooled vs Sham 0.0457

## CENTRAL 2.0 MM




Vonaprument Pooled vs Sham 0.0218

## CENTRAL 1.5 MM




Vonaprument Pooled vs Sham 0.0319

^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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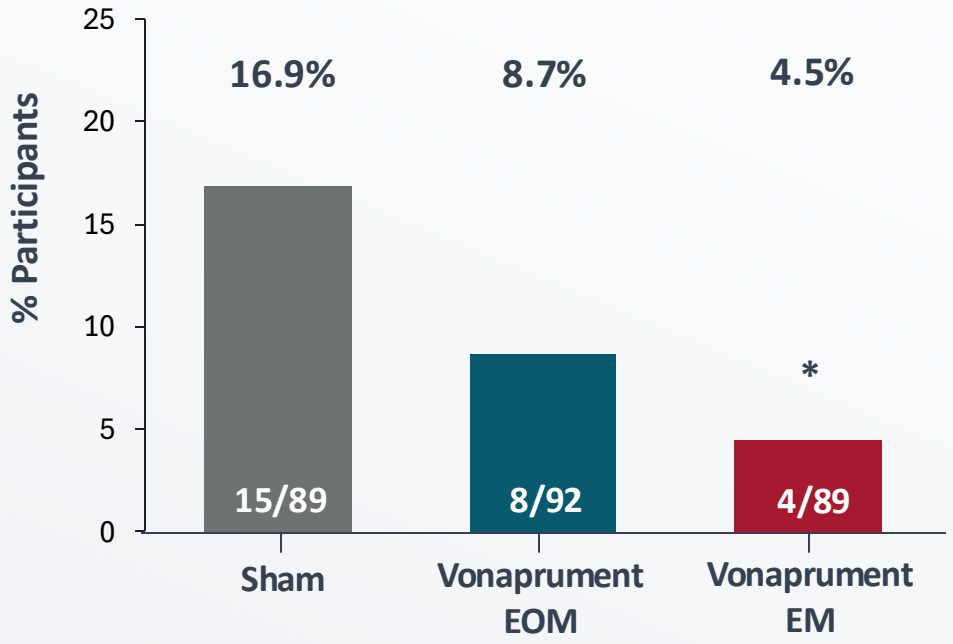
# ARCHER Phase 2: Dose-Dependent Vision Protection at Month 12 and Over Time

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

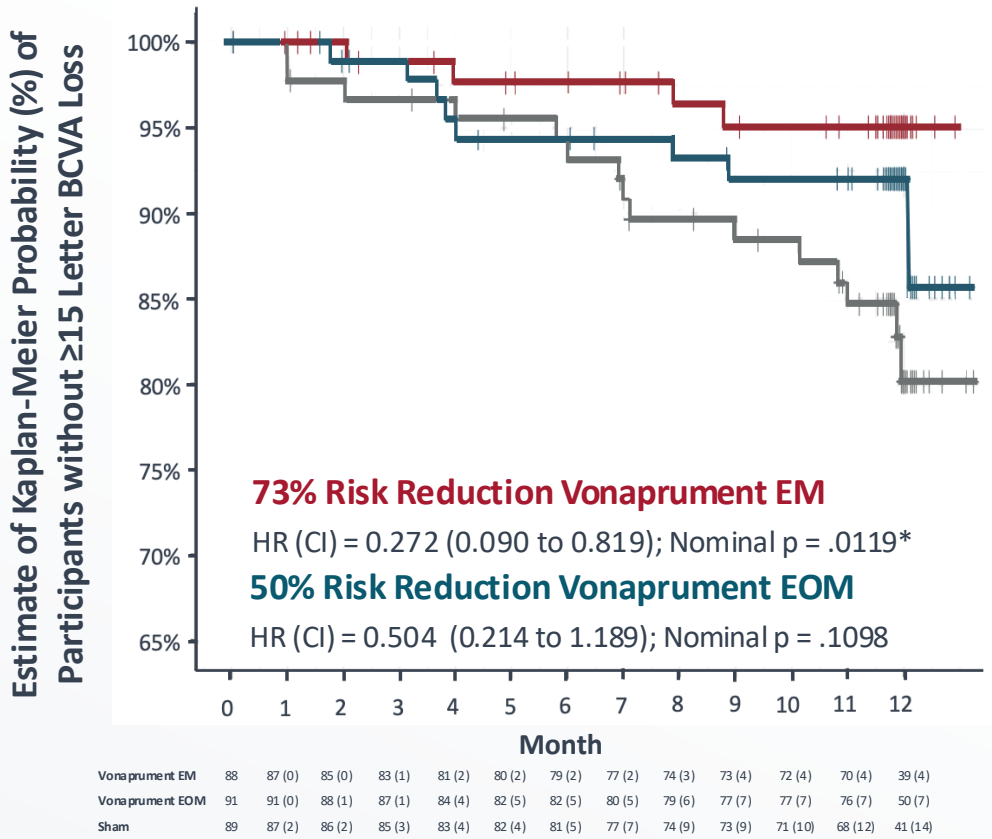
*Month 12 event confirmed at month 15*




| | Sham | Vonaprument EOM | Vonaprument EM |
|---|---|---|---|
| Nominal p-value vs sham^ | --- | .0994 | .0076 |

#Confirmed BCVA 15-LL at two consecutive visits including month 12 supported by ensuing (off-treatment) visit; visits were monthly through Month 12 and then at Months 15 and 18
^Nominal p-value from a Chi-square test in ITT population: *Nominal p < .05

## PROBABILITY OF CONFIRMED BCVA ≥15-LETTER LOSS 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) |

#Confirmed BCVA 15-LL at two consecutive visits including month 12 supported by ensuing (off-treatment) visit
HR, hazard ratio; Nominal log-rank test (versus sham) p-values are presented; *Nominal p < 0.05



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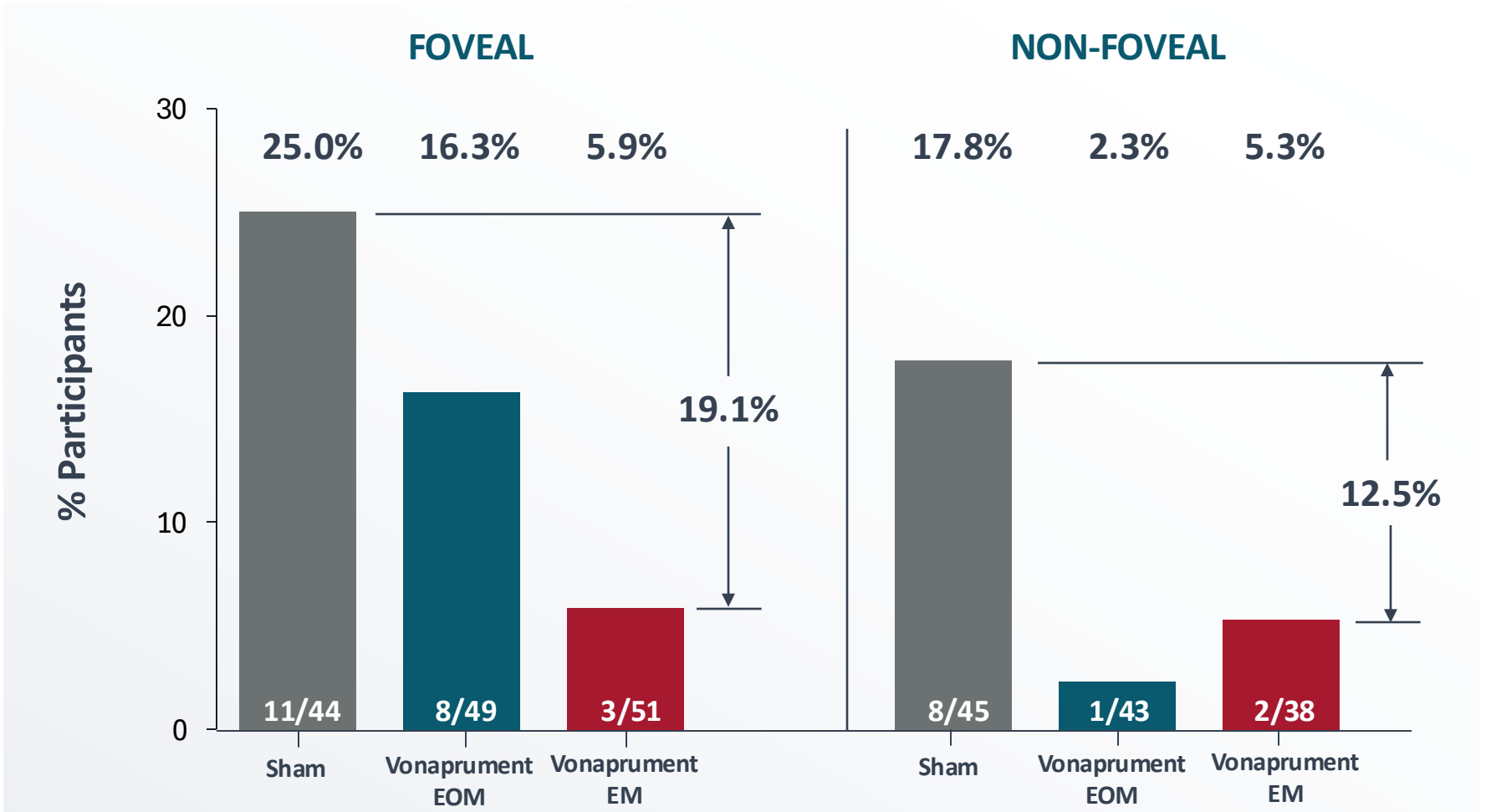
# ARCHER Phase 2: Demonstrated Dose-Dependent Vision Protection in Participants with Foveal and Non-Foveal Lesions

## 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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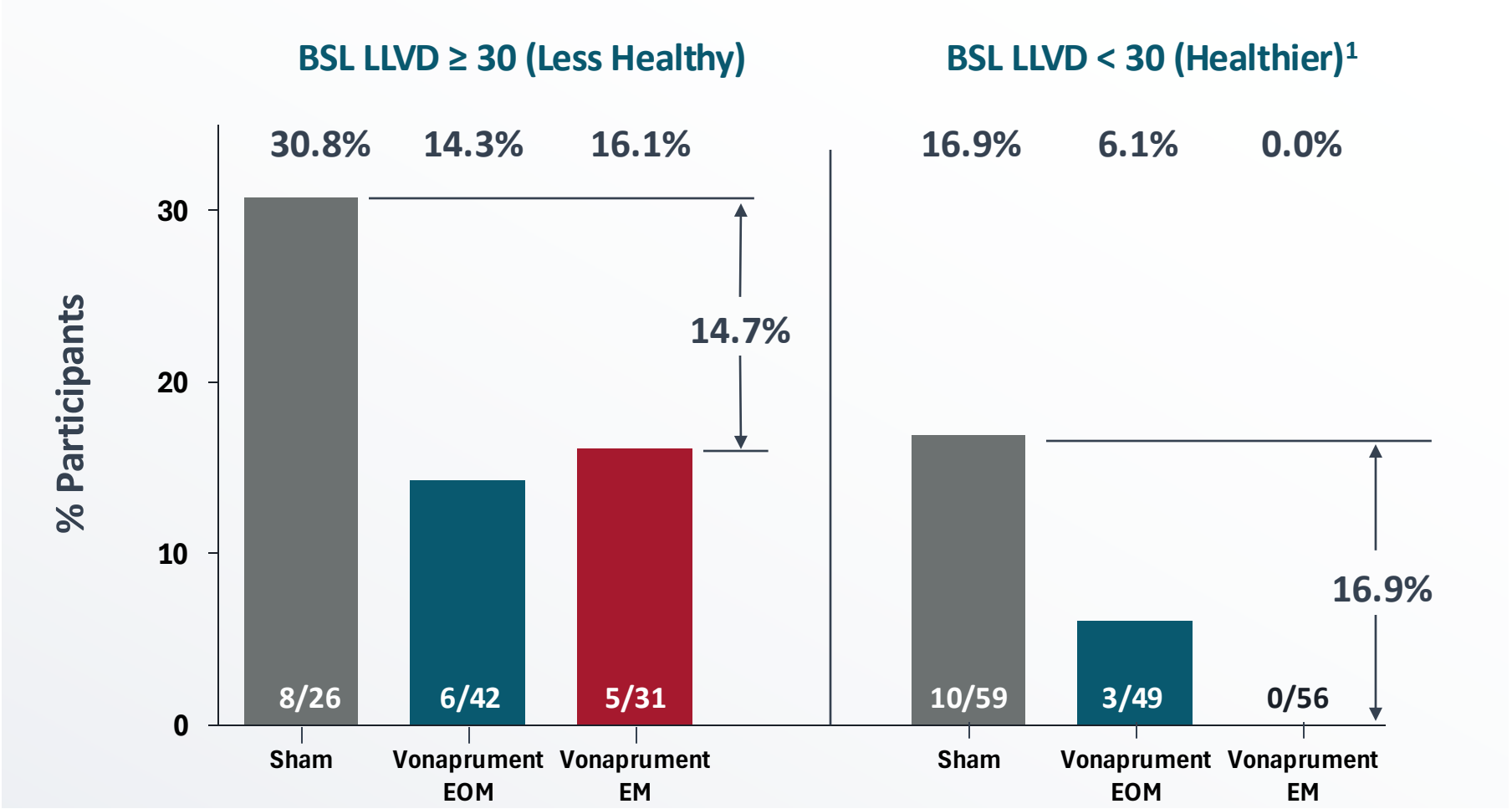
# ARCHER Phase 2: Demonstrated Dose-Dependent Vision Protection in Both Healthier and Less Healthy Eyes

## 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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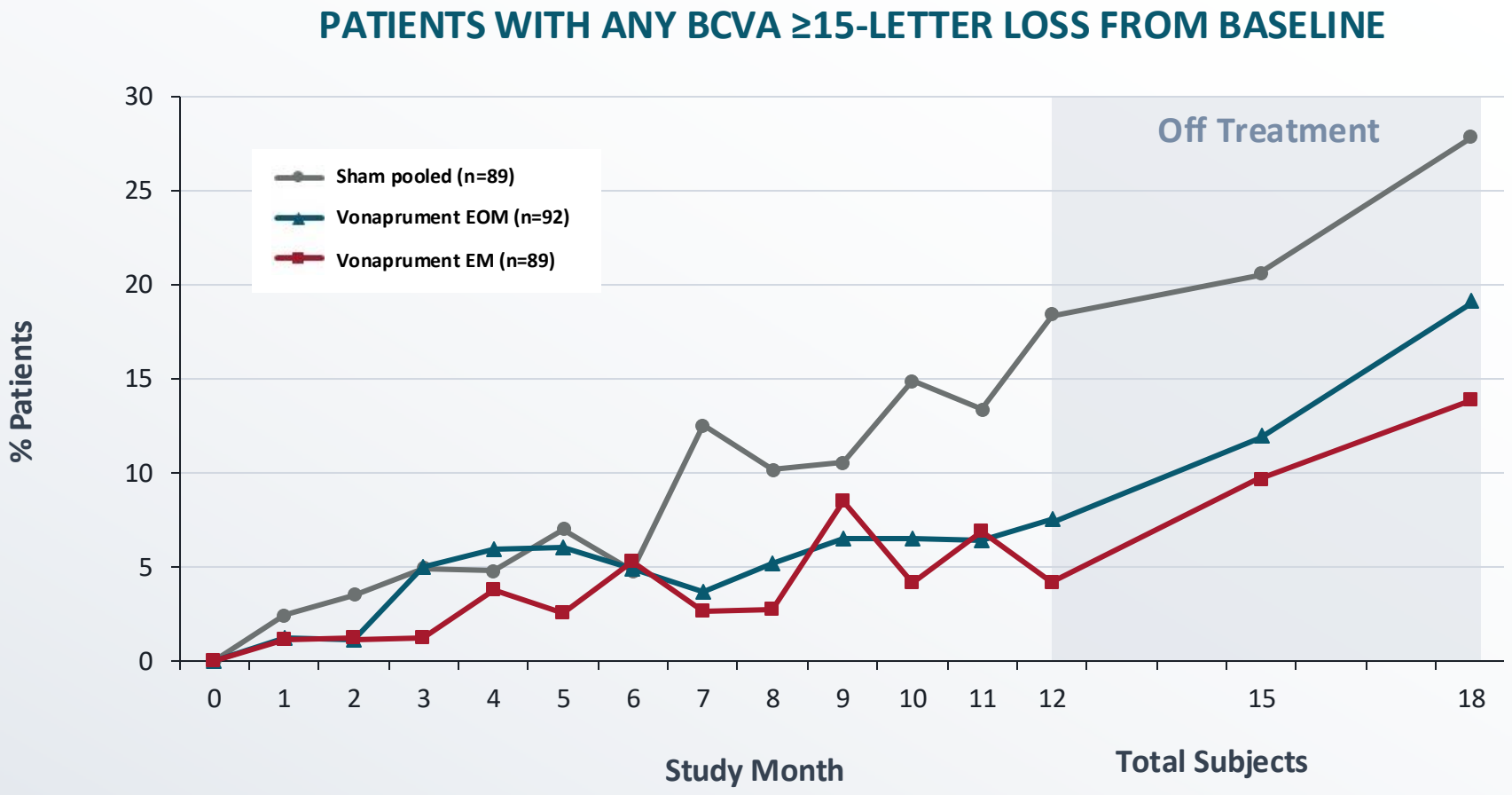
# ARCHER Phase 2: Demonstrated Dose-dependent, Disease-modifying Effect of Vonaprument




Demonstration of treatment effect and disease-modifying mechanism of action

**Total Subjects**

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



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# Safety Overview: Vonaprument was Well-Tolerated in Phase 2

| 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 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

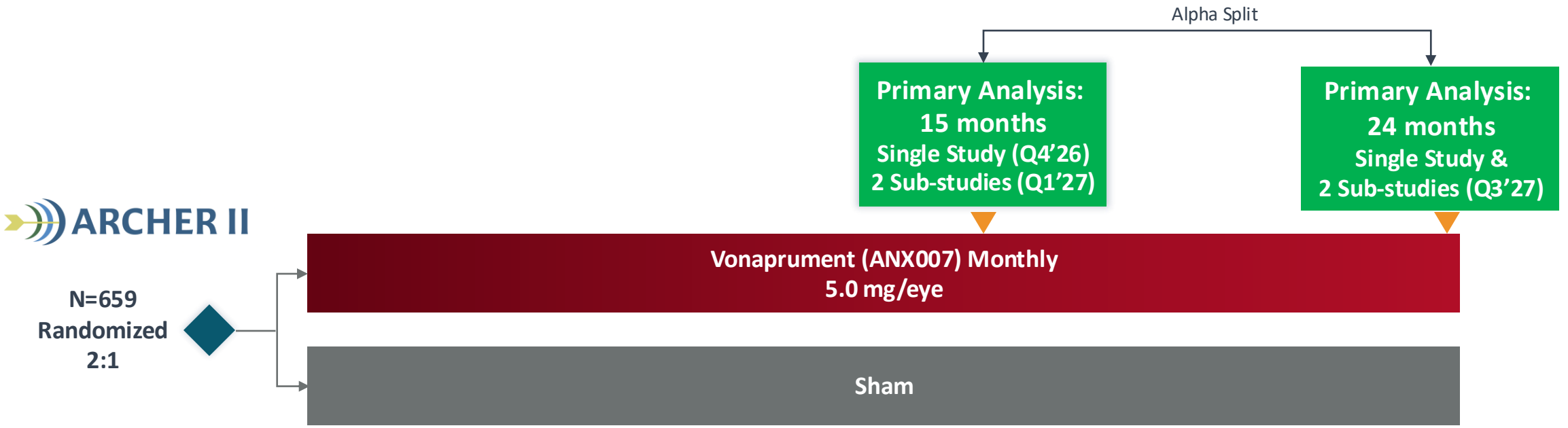
- Represents 3 lines of letter loss
  - Loss of independence (e.g., inability to read, drive)
  - Impact on independent living

Clinically relevant, stable endpoint when confirmed at two consecutive visits

# 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%<br>• 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<br>• 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<br>• 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<br>• Consistent treatment effect across broad spectrum of disease<br>• 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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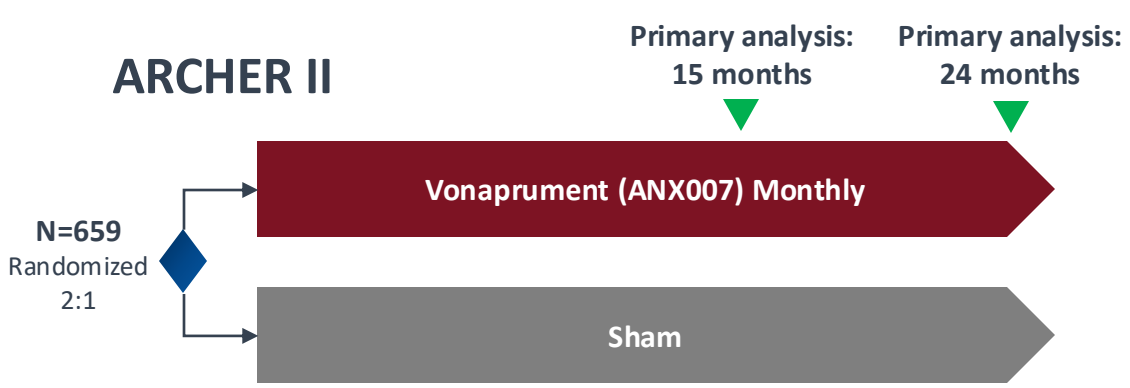
# ARCHER II: One Protocol Supporting Both EMA and FDA Filings

## Phase 3 powered at Sub-study level

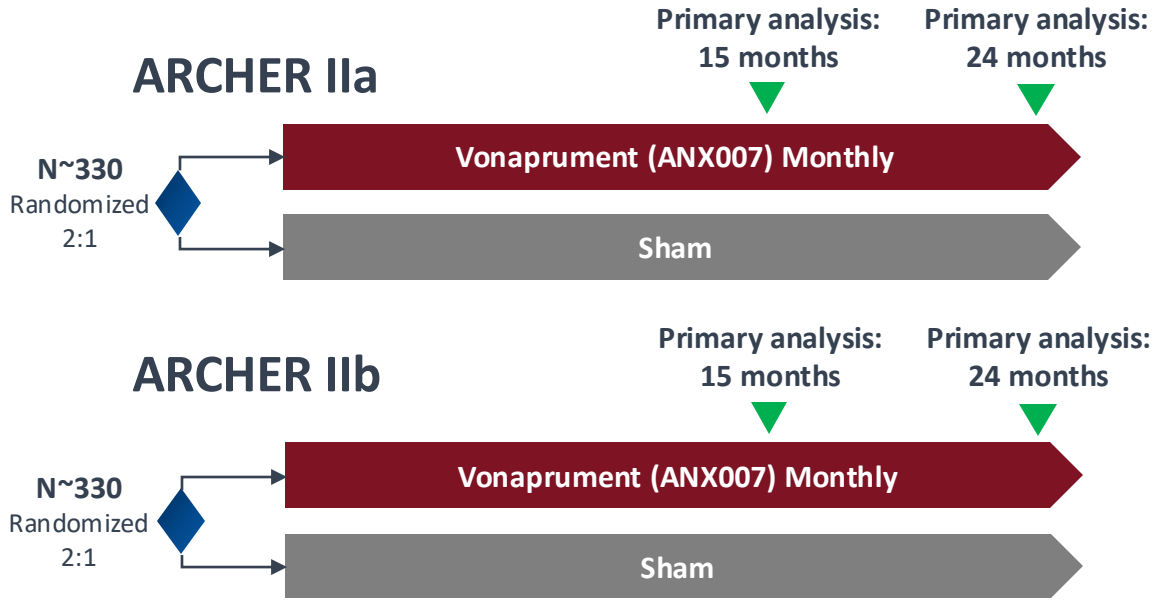
### EMA

### Single Study




### FDA

### 2 Sub-studies



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# ARCHER II 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



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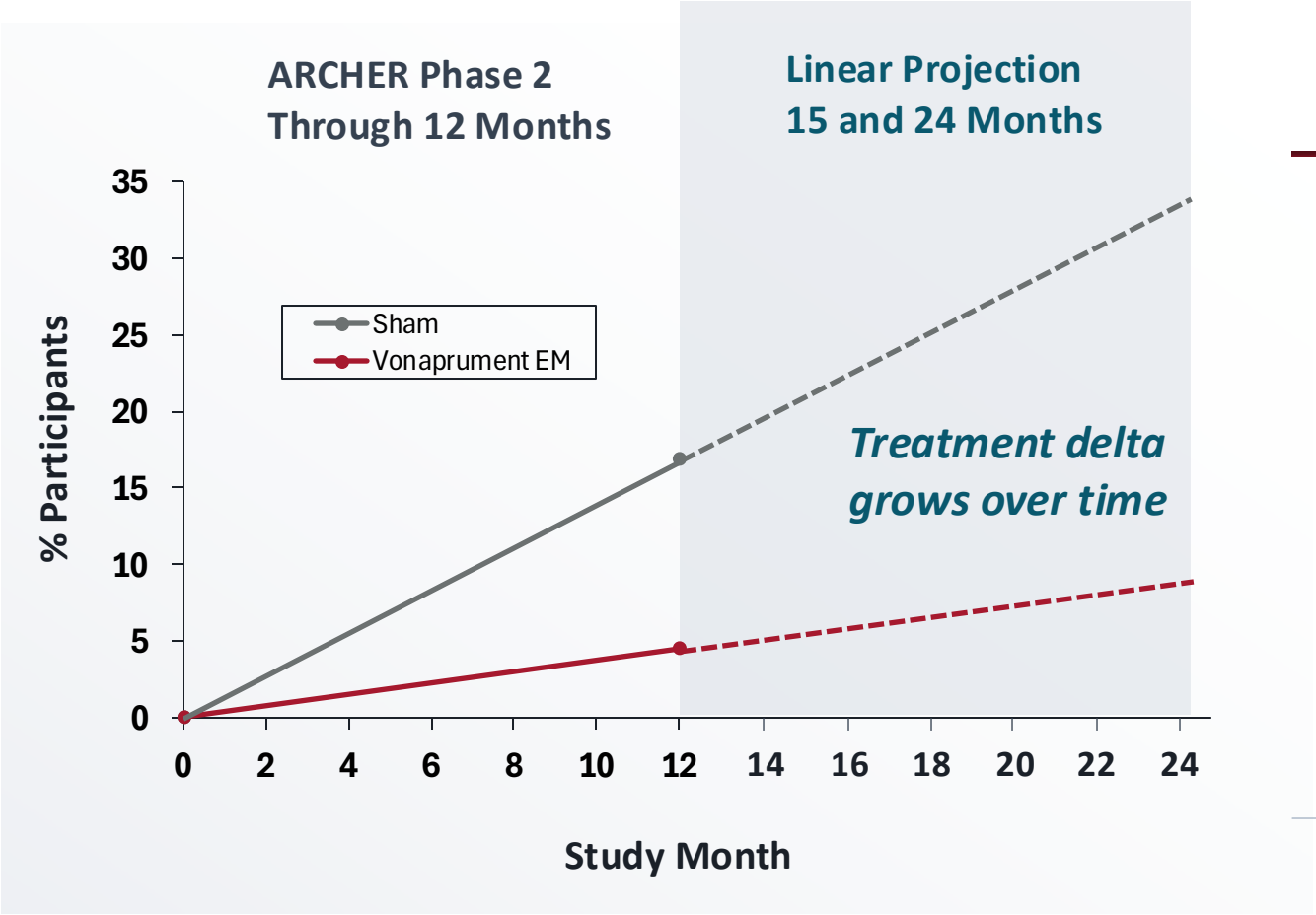
# Illustration of Event Based Analysis Which Gets Stronger Over Time

## 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 Phase 3: Potential Outcomes Scenarios & Expected Timing

| | Q4'26 | Q1'27 | Q3'27 |
|---|---|---|---|
| **SINGLE STUDY & SUBSTUDIES HIT**<br>15 Mos Primary Analysis | **PR: SINGLE STUDY HITS**<br>Primary Endpoint for EU at 15 mos (no p value) | **PR 1: TWO SUBSTUDIES HIT**<br>Primary Endpoint for US at 15 mos (no p value)<br>**PR 2: TOPLINE 15 MO DATA for Single Study & Substudies** | **PR: TOPLINE 24 MO DATA for Single Study & Substudies** |
| **SINGLE STUDY HITS**<br>15 Mos Primary Analysis<br>**SUBSTUDIES CONTINUE**<br>to 24 Mos | **PR: SINGLE STUDY HITS**<br>Primary Endpoint for EU at 15 mos (no p value) | **PR: TWO SUBSTUDIES CONTINUE** to 24 mos | **PR: TOPLINE 24 MO DATA for Single Study & Substudies** |
| **SINGLE STUDY CONTINUES**<br>to 24 Mos | **PR: SINGLE STUDY CONTINUES** to 24 mos | | **PR: TOPLINE 24 MO DATA for Single Study & Substudies** |

**Futility – assessed by Data Monitoring Committee*



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# *A BOLD MISSON:*

***To enable MILLIONS of PATIENTS impacted by complement-mediated diseases of the body, brain and eye LIVE THEIR BEST LIVES***

