ANNEXON biosciences

STOP THE START

of classical complement-driven diseases

CORPORATE PRESENTATION | JANUARY 2025

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 Quarterly Report on Form 10-Q filed with the Securities Exchange Commission (SEC) on November 14, 2024 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.

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A bold mission to enable MILLIONS of PATIENTS impacted by complement-mediated diseases of the body, brain and eye LIVE THEIR BEST LIVES

BREAKTHROUGH 2025: Annexon Well-Positioned to Transform the Complement Landscape and Drive Immense Value

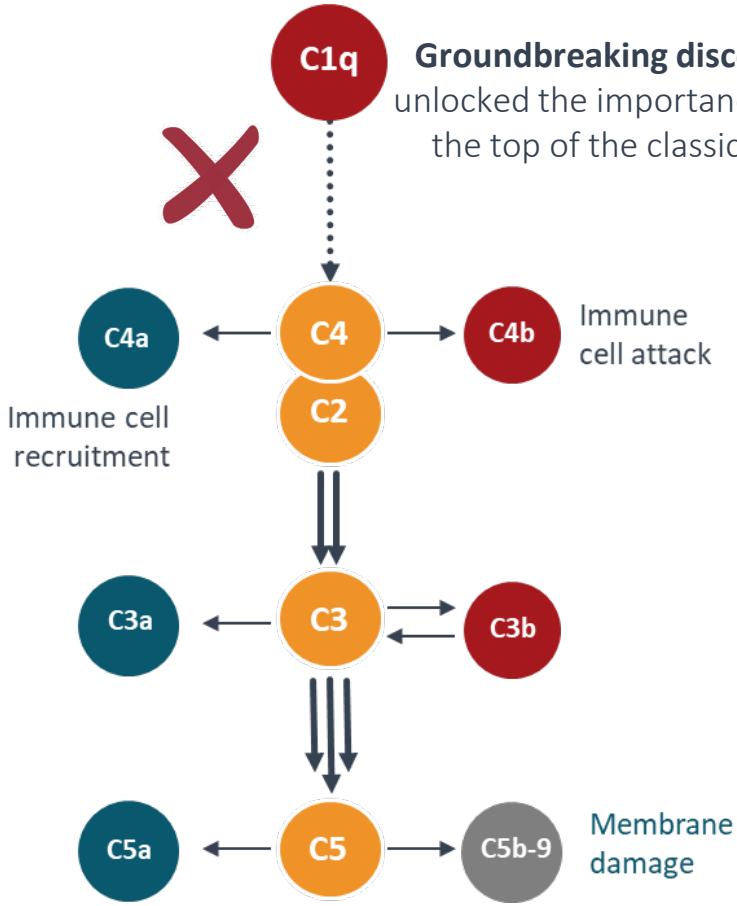
- **Clinically Validated Scientific Platform** with broad potential across multiple therapeutic areas
- **Near-term Blockbuster Opportunity in Guillain-Barré Syndrome (GBS)** poised to replace standard of care
- **Only Geographic Atrophy (GA) Program to Demonstrate Vision Preservation** in additional blockbuster opportunity
- **Disruptive Oral Classical Complement Inhibitor** with potential to transform biologics-treated indications

ANNEXON biosciences 10 years

Pioneering Scientific Approach to Stop Complement-Driven Neuroinflammation Where it Starts

Broad applicability to millions of patients with autoimmune, neurodegenerative and ophthalmic diseases

- **Blocking C1q to halt neuroinflammation in the body, brain and eye**
- **Deep understanding of C1q in neuroinflammatory diseases** – 20 yrs of research & >30 *de novo* classical complement assays
- **Strategic drug development and strong execution producing game-changing data across flagship programs**



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Strategic Drug Development and Strong Execution Has Resulted in Game-Changing Data Across Flagship Programs

ANX005 in GBS

Landmark pivotal program showed early & robust benefits on strength, disability, ventilation days, etc. vs placebo & standard of care

Patients got better sooner and more completely

ANX007 in GA

Only program to show significant vision preservation & protection of retinal structures associated with vision

Patients retained vision in normal & low light conditions

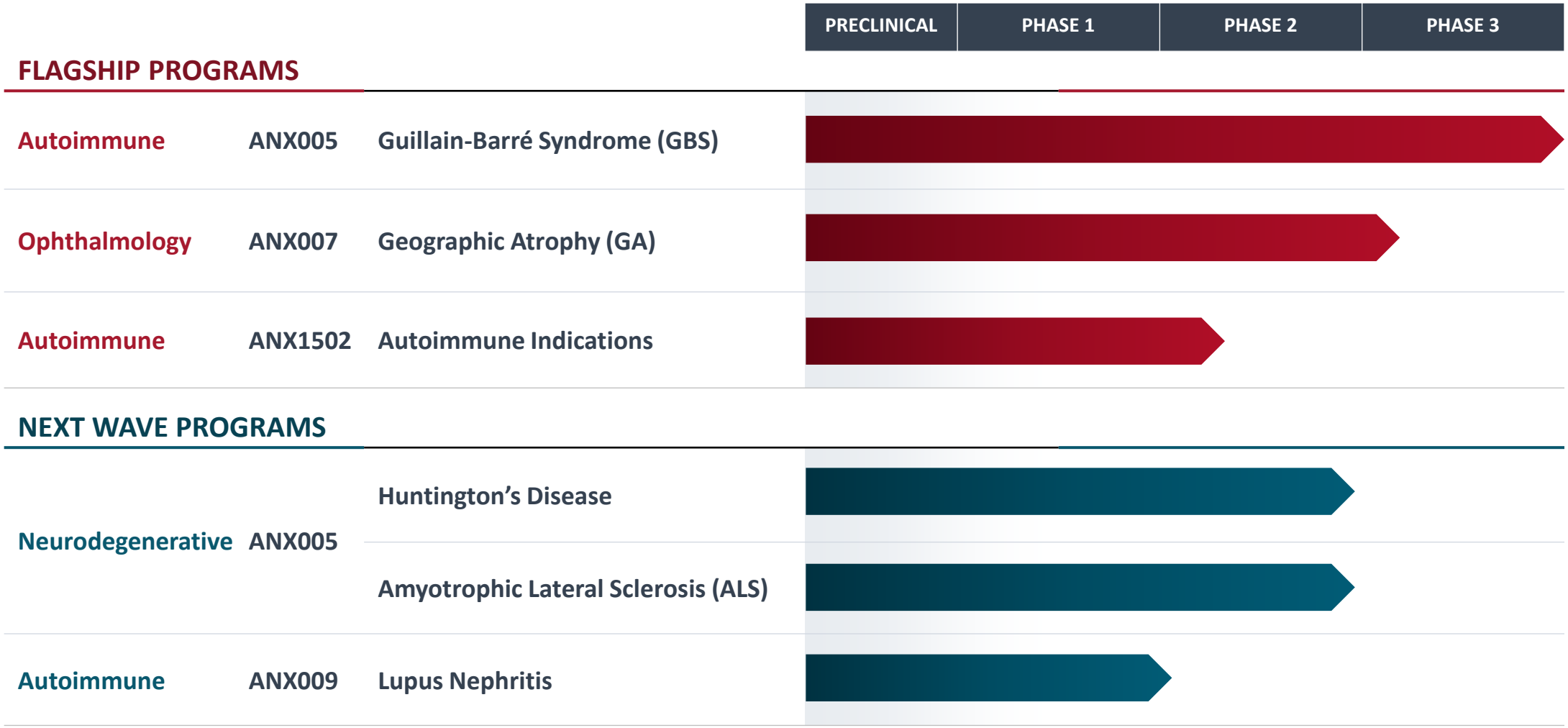
ORAL ANX1502

Oral C1s inhibitor tablet showed tolerability, target drug levels & supportive PD in healthy volunteers

Potential for patient dosing convenience and flexibility

Leading Complement-Focused Pipeline with MULTIPLE WAYS TO WIN

Diverse late-stage clinical platform for classical complement-mediated neuroinflammatory diseases of the body, brain and eye



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BREAKTHROUGH 2025: Significant Catalysts Anticipated Across Flagship Programs Pave the Way for Transformative Year

1 ANX005 in GBS
BLA Submission

Submit US BLA 1H’25 & EMA advancement to MAA over the year

2 ANX007 in GA
Global Pivotal Enrollment

Complete Ph 3 ARCHER II enrollment 2H'25

3 ORAL ANX1502
Clinical POC

Clinical PoC data in CAD & update on future target indications in Q1’25

Cash Runway into 2H 2026 to Achieve Key Milestones

CAD = Cold agglutinin disease

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ANX005: First-in-Kind C1q Inhibitor for Guillain-Barré Syndrome

Positive Topline Results from Pivotal Phase 3 Trial

Shane S.
53-year-old patient with GBS

ANX005: Blockbuster Opportunity as First Targeted Therapy for GBS Poised to Replace Standard of Care

ANX005 TARGETED IMMUNOTHERAPY

- Anti-C1q therapy rapidly blocks classical complement mediated neuroinflammation in a single dose to halt ongoing nerve damage
- Annexon portfolio opens a new era of complement medicines to treat neuroinflammatory disease

GBS IS A SEVERE UNMET NEED

- Rapid and acute neurological disease with no FDA-approved treatment
- 22,000 patients hospitalized in US and Europe annually
- Involves common underlying pathophysiology worldwide

ADVANCING ANX005 FOR GBS WORLDWIDE

- Phase 3 trial demonstrated significant benefit with ANX005 over placebo
- Real-world evidence showed ANX005 benefit over IVIg/PE, strengthening body of evidence for ANX005 in GBS
- Blockbuster commercial opportunity – single infusion first-line monotherapy

Urgent Need for Targeted Treatment to Address Significant Burden of GBS on Patients, Caregivers, Hospitals & Payers

> ***GBS is a medical emergency that doesn't allow time to try one treatment and then another. ANX005 provides an immediate, aggressive and complete mechanism of action.***
>
> **—Hugh Willison, MBBS, PhD**
> **Prof Emeritus of Neurology**
> **University of Glasgow**

RECOVERY IS SLOW AND SUBOPTIMAL WITH CURRENT STANDARD OF CARE[1,2,3,4,5,6,7]

- **~40%** admitted to ICU; **~25%** require mechanical ventilation
- **~20%** can't walk at 1 year
- **>$2B** annual cost US economy
- **No FDA-approved treatments**

[1]ClearView Health market research analysis, [2]AAN Guidelines "Immunotherapy for GBS", [3]Hund EF et al (1993) Crit Care Med 21:433, [4]Doets, et al., Brain 2018, 141, 2866-2877 (2018), [5]Van den Berg, B. et al. Nat. Rev. Neurol. 10, 469–482 (2014), [6]Leonhard, et al, Nature Reviews, Neurology (2019), [7]Inflation-adjusted from Frenzen, PD (2008) Neurology 71:21-27 7, [8]Kaier K, et al (2019).Epidemiology and Infection 147

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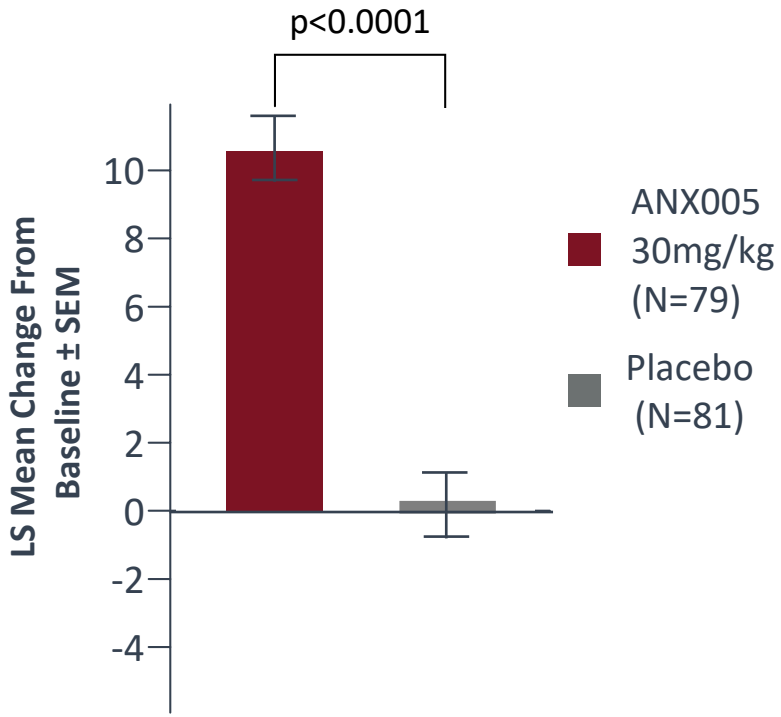
ANX005 Phase 3: Rapid Increase in Muscle Strength (Week 1) Translated to Long Term Benefit (Week 26) vs. Placebo

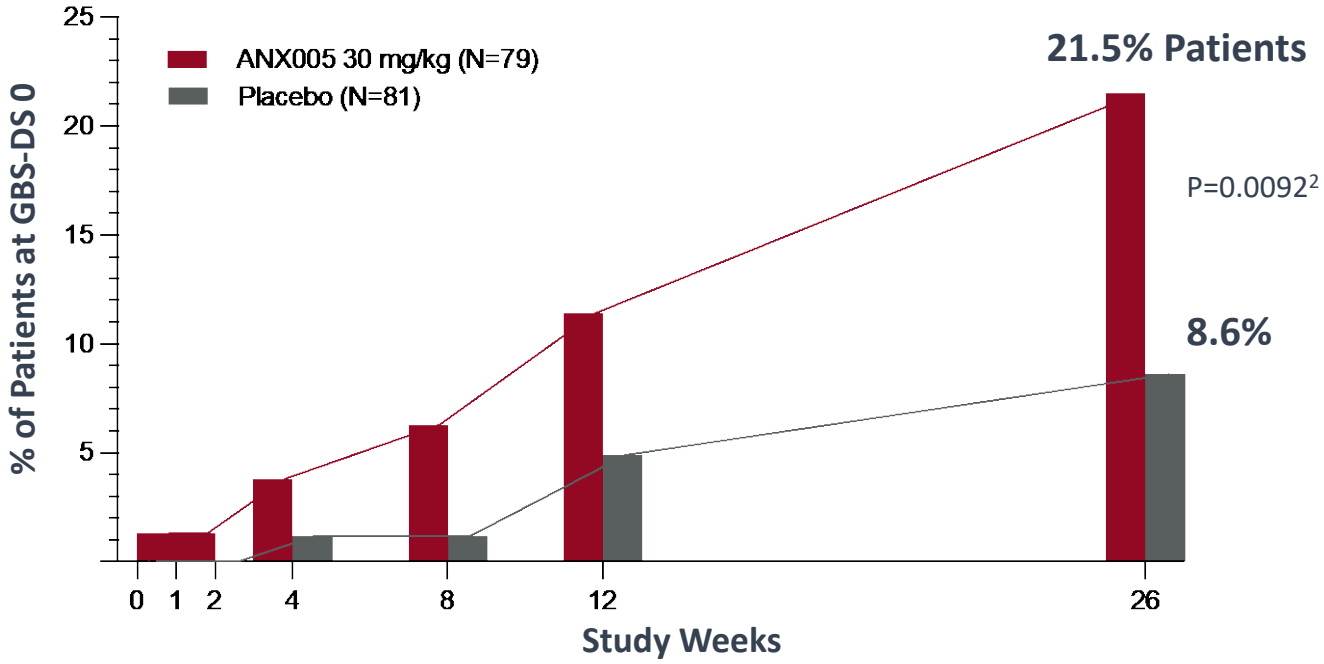
MORE THAN A 10-POINT IMPROVEMENT IN MUSCLE STRENGTH[1] OVER PLACEBO AT WEEK 1

MRC Sumscore at Week 1



2½ TIMES MORE TREATED PATIENTS FULLY RECOVER AT WEEK 26 (GBS-DS = 0)

GBS-DS Through Week 26



[1]MRC Sumscore
[2]nominal

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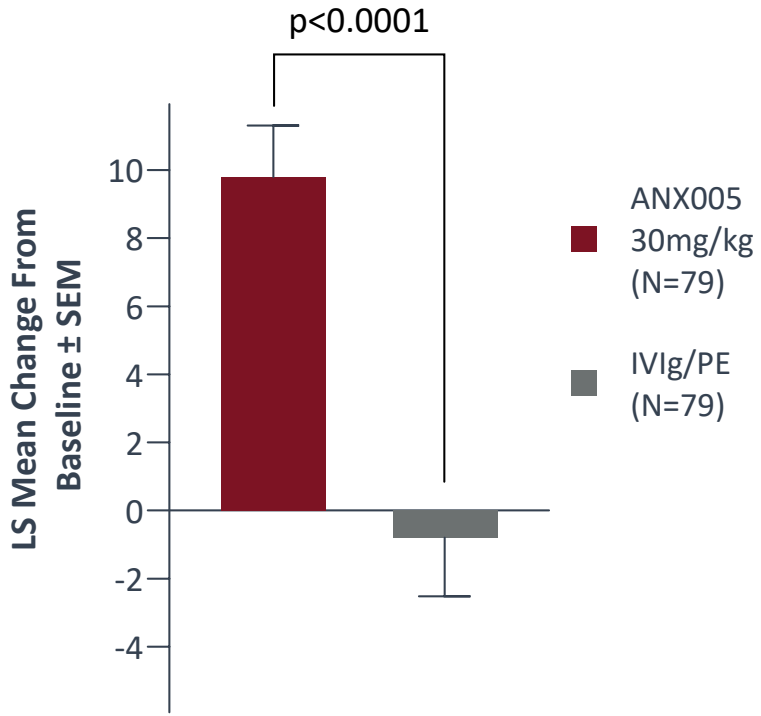
ANX005 RWE*: Consistent with Phase 3, Rapid Increase in Muscle Strength with More Complete Recovery vs. Standard of Care

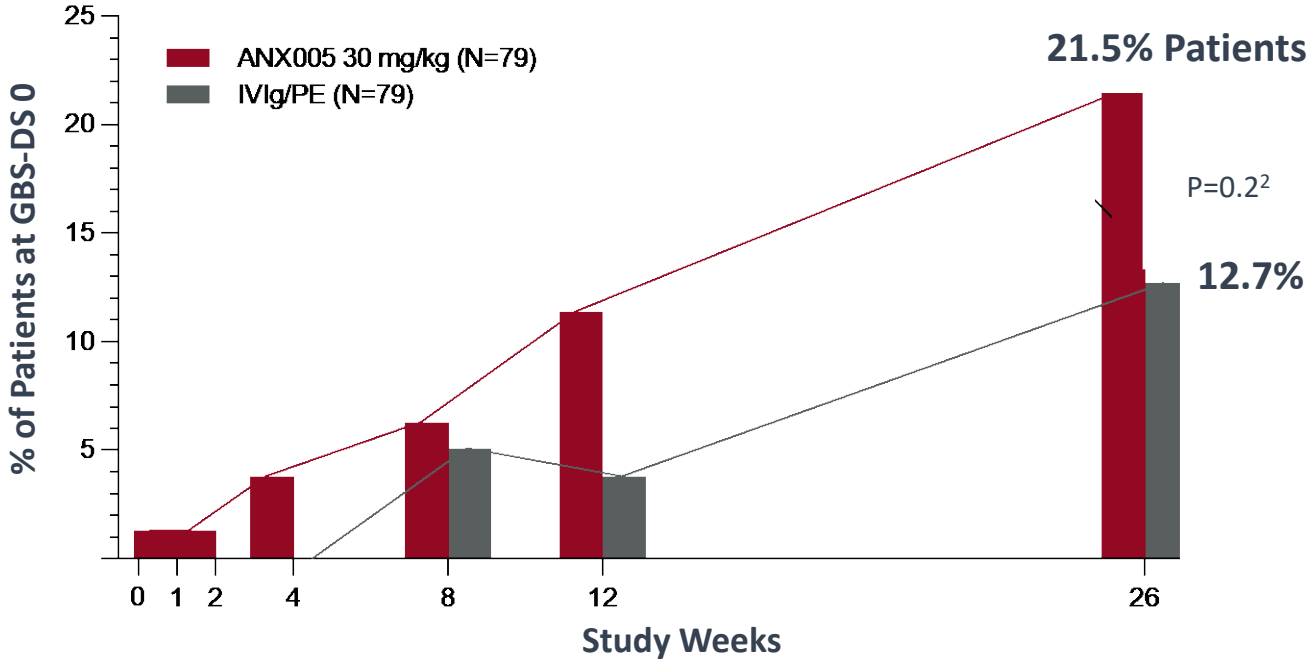
MORE THAN A 10-POINT IMPROVEMENT IN MUSCLE STRENGTH[1] OVER IVIG/PE AT WEEK 1

MRC Sumscore at Week 1



PATIENTS MORE LIKELY TO FULLY RECOVER AT WEEK 26 (GBS-DS = 0) WITH ANX005 VS. IVIG/PE

GBS-DS Through Week 26



Preliminary Topline Results Subject to Change

*RWE = Real World Evidence comparing ANX005 Ph 3 patients matched 1:1 for baseline characteristics with patients in IGOS database

[1]MRC sumscore results are adjusted for Age, Onset, and Baseline MRC

[2]nominal

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ANX005 RWE: Fewer ANX005 Patients Required Ventilation and ICU Time vs. Standard of Care

Measures of Decreased Burden of Care

FEWER SUBJECTS VENTILATED

Half as many patients, *p* = 0.022

ANX005 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.

ANX005 30mg/kg
N =15
20 Days

IGOS IVIG/PE
N = 32
32 Days

FEWER DAYS IN ICU

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

ANX005 30mg/kg
N =18
25 Days

IGOS IVIG/PE
N = 36
37 Days

Preliminary Topline Results Subject to Change

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ANX005 Well-Positioned for Potential GBS Blockbuster Opportunity

SIGNIFICANT GBS MARKET OPPORTUNITY

150,000 patients worldwide

15k in Europe and 7k in US

and growing

CURRENT STANDARD OF CARE SUBOPTIMAL

- No placebo-controlled IVIg data
- **90% of US patients** treated with off- label IVIg due to severity
- **Up to 50% of IVIg patients** receive 2nd-line IVIg/PE counter to treatment guidelines
- IVIg Black Box warnings

CONCENTRATED GBS TREATMENT LANDSCAPE IN US

440 hospitals account for **80%** of GBS admissions

~3k US physicians make most GBS initial diagnoses and Tx decisions

ANX005 DIFFERENTIATED GBS OUTCOMES

INCREASE
in functional ability & generally well-tolerated

AVOIDANCE
of ICU stay

REDUCED
days on ventilation support

*Data on file.

On the Path to Bringing ANX005 to GBS Patients Worldwide

PHASE 3 PLACEBO-CONTROLLED TRIAL POSITIVE OUTCOMES AND FAVORABLE SAFETY PROFILE

Faster and more complete recovery with ANX005 30mg/kg vs. placebo

REAL WORLD EVIDENCE DEMONSTRATED BENEFIT OVER IVIg

Ph 3 patients matched with majority Western World population

Earlier and greater benefits of ANX005 30 mg/kg single dose over IVIg/PE

NEXT STEPS

US and EU regulatory engagement underway

BLA submission targeted for 1H'25

Ramping disease education and engaging payers on disease burden to optimize coverage and reimbursement

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ANX007: Phase 3-ready Complement Therapy for Geographic Atrophy

First Global Pivotal Program for GA Using Vision Preservation as Primary Outcome Measure

Nancy S.
wife and caregiver

Paul S.
85-year-old patient with GA

Global Opportunity for New GA Treatments that Preserve Vision

> ***Unfortunately, current treatments have not translated to protection of clinically meaningful vision for patients.***
>
> **—Eleanora Lad, MD, PhD**
> **Vice Chair of Clinical Research**
> **Duke Eye Center**

GA SEVERELY LIMITS INDEPENDENCE,

CAUSING FRUSTRATION, ANXIETY AND EMOTIONAL HARDSHIP

- **A leading cause of blindness** in the elderly
- **8 Million patients** worldwide
- **No FDA-approved treatments** demonstrating vision preservation
- **No Treatments approved in EU or Asia**

[1]ClearView Health market research analysis, [2]AAN Guidelines "Immunotherapy for GBS", [3]Hund EF et al (1993) Crit Care Med 21:433, [4]Doets, et al., Brain 2018, 141, 2866-2877 (2018), [5]Van den Berg, B. et al. Nat. Rev. Neurol. 10, 469–482 (2014), [6]Leonhard, et al, Nature Reviews, Neurology (2019), 7Inflation-adjusted from Frenzen, PD (2008) Neurology 71:21-27 7, 8 Kaier K, et al (2019).Epidemiology and Infection 147

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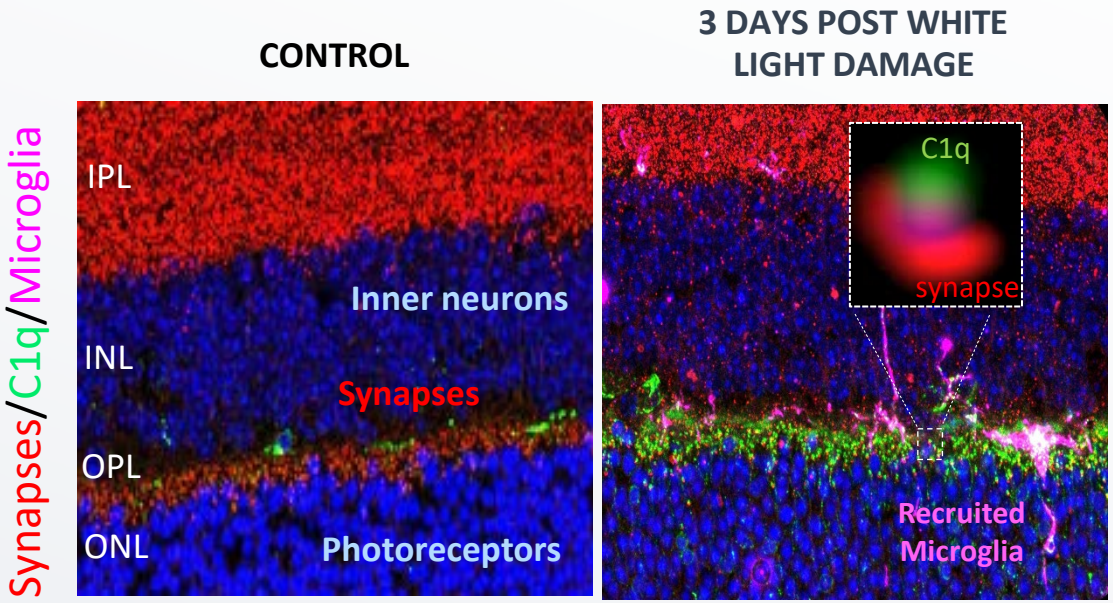
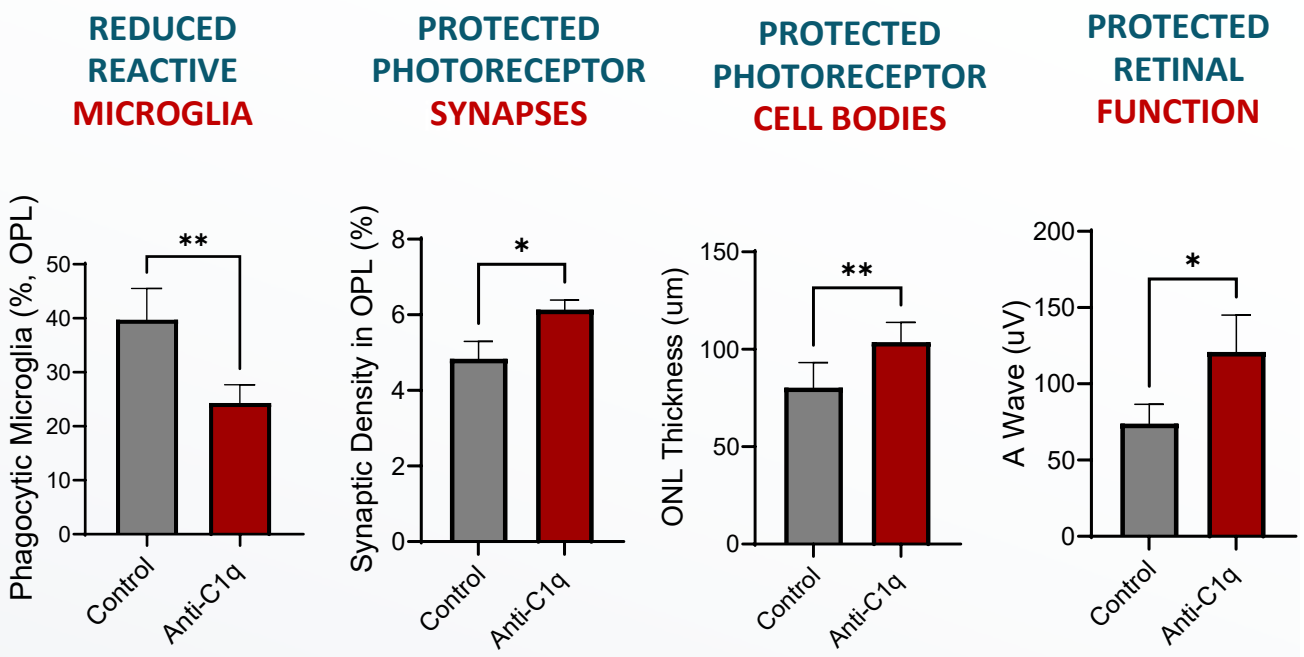
Anti-C1q Protected Photoreceptor Cells and Their Function in Models of Photoreceptor Damage

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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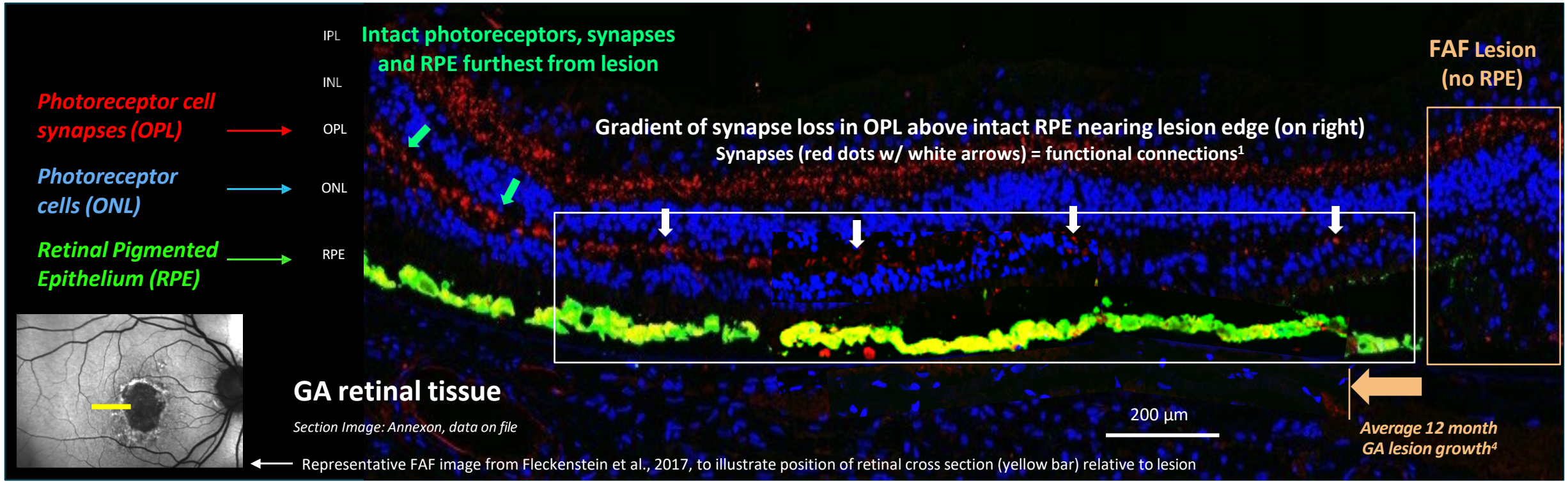
Photoreceptor Cells, Synapses & Function Lost Prior to RPE in GA

- Photoreceptor cells and their synapses are lost over intact RPE (white box)
  - Decreasing gradient of red-labeled synapses (w/ white arrows) moving toward the lesion on right - loss of synapses is loss of function[1]
  - Also, decreasing gradient of blue-labeled photoreceptor cells toward lesion – photoreceptors are lost prior to RPE[2]
- FAF measures RPE loss/lesion growth, but not photoreceptor or synapse loss and correlates poorly w/ visual function[3]



[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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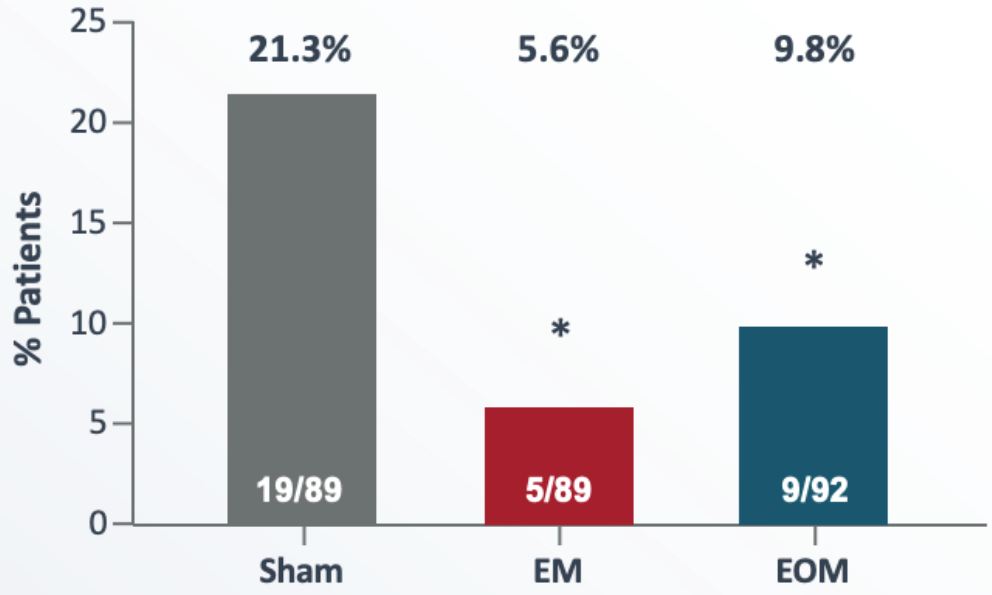
Consistent, Significant Protection from Vision Loss: BCVA and LLVA

First demonstration of consistent, dose dependent preservation across multiple measures of visual acuity

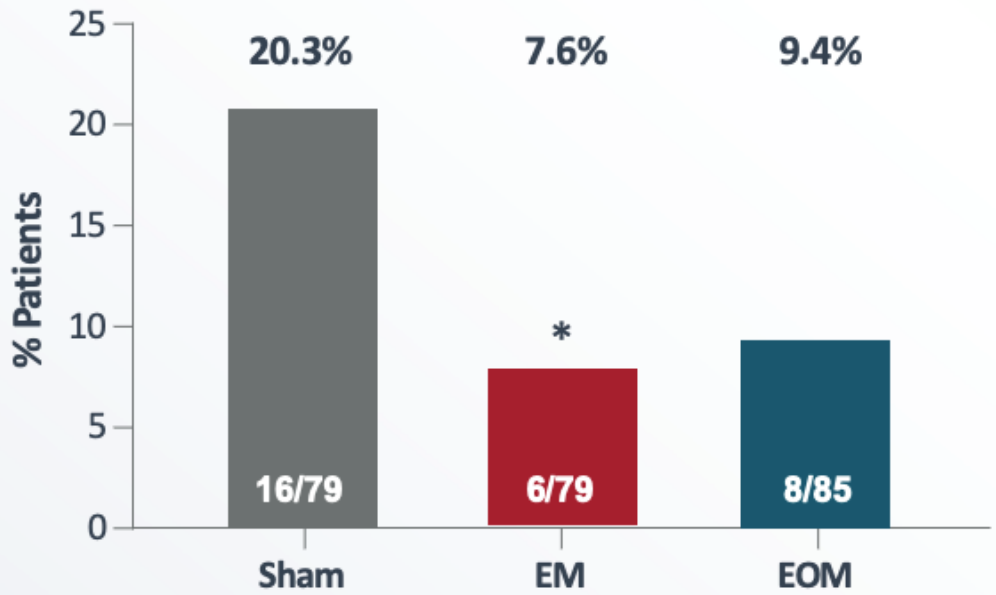
PATIENTS WITH PERSISTENT BCVA ≥15-LETTER LOSS THROUGH MONTH 12#



Nominal p-value vs Sham^	--	0.021	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 $p < 0.05$
Final data

LLVA ≥15-LETTER LOSS THROUGH MONTH 12#

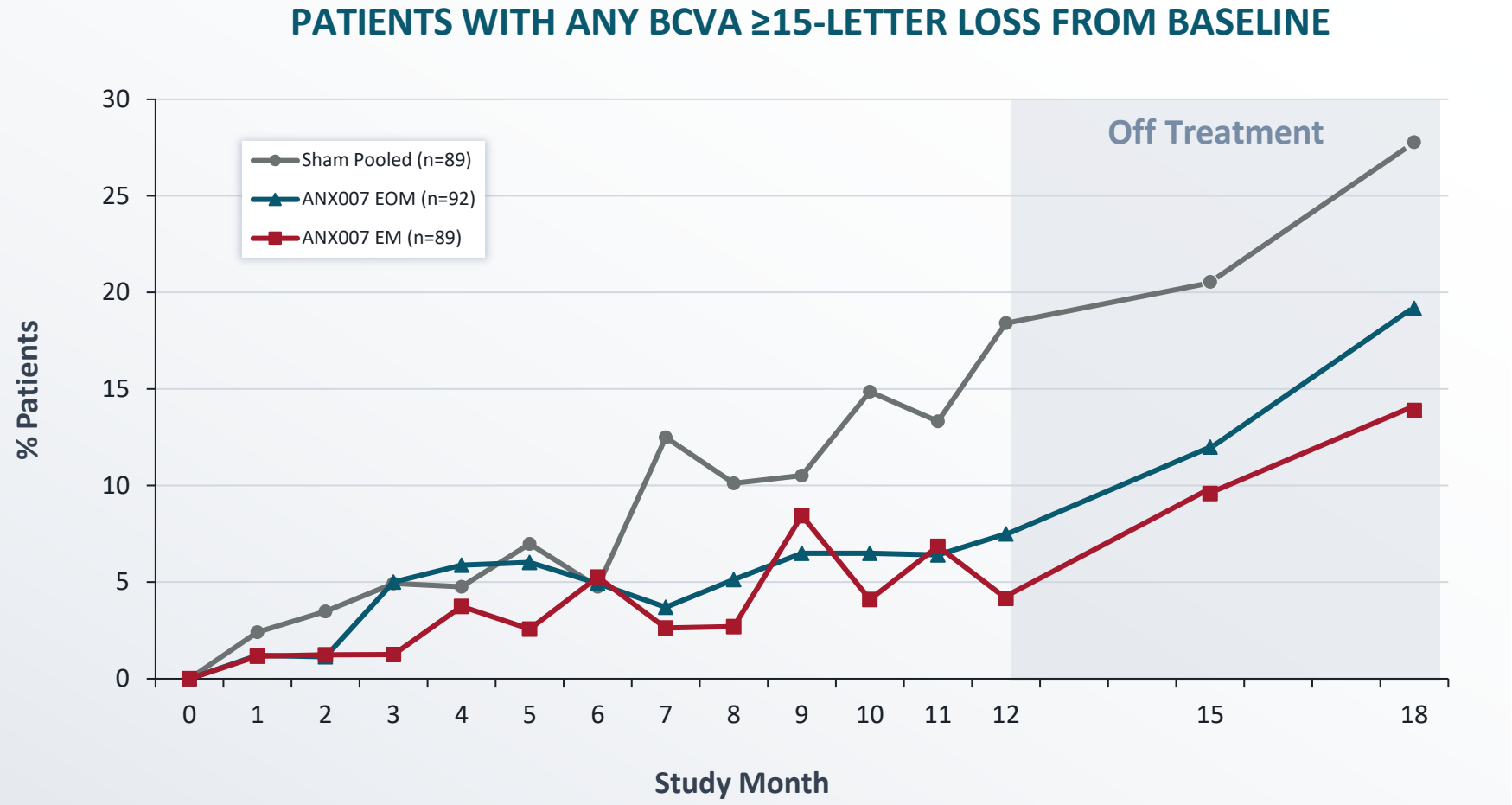


Nominal p-value vs Sham^	--	0.022	0.050

#Patients with single LLVA ≥15-letter loss event and at least one post-baseline LLVA measurement; ^Nominal p-value from a Chi-square test
Final data

BCVA ≥15-Letter Loss Accelerated After Cessation of Treatment

Consistent with true on-treatment drug effect and disease-modifying mechanism of action

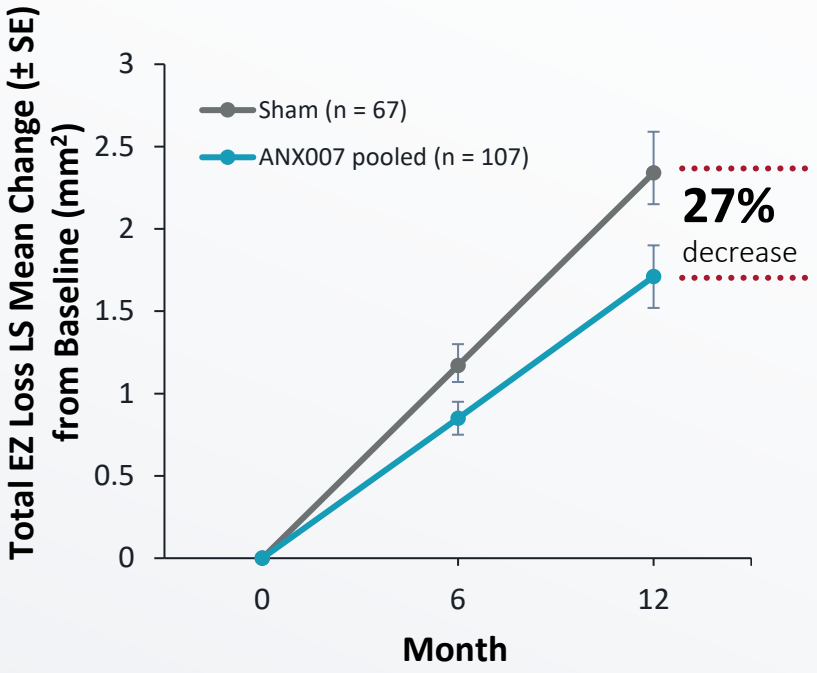


- Low frequency (<0.6% per month) of single BCVA ≥15-letter losses in EM- and EOM-treated groups during 12-month treatment period
- While benefit was maintained after treatment cessation the rate of BCVA≥15-letter loss increased to parallel that of sham (>1.6% per month)

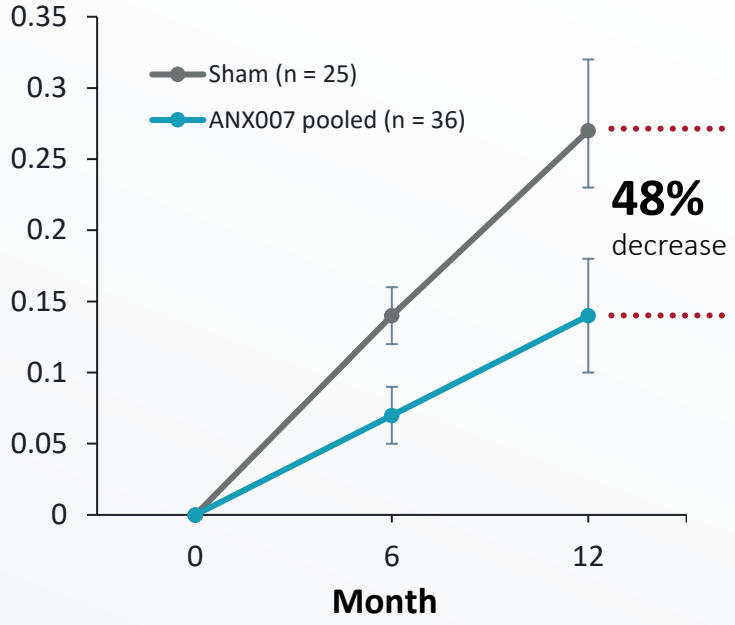
Significant Photoreceptor Protection Through 12 Months

More robust protection with ANX007 in center, area best associated with vision, compared to pan-macula

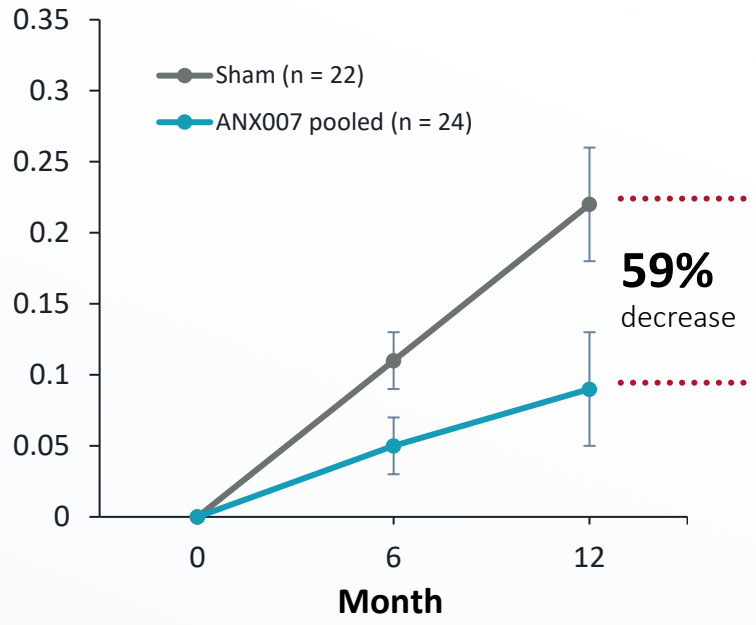
PAN-MACULA



CENTRAL 2.0 MM



CENTRAL 1.5 MM

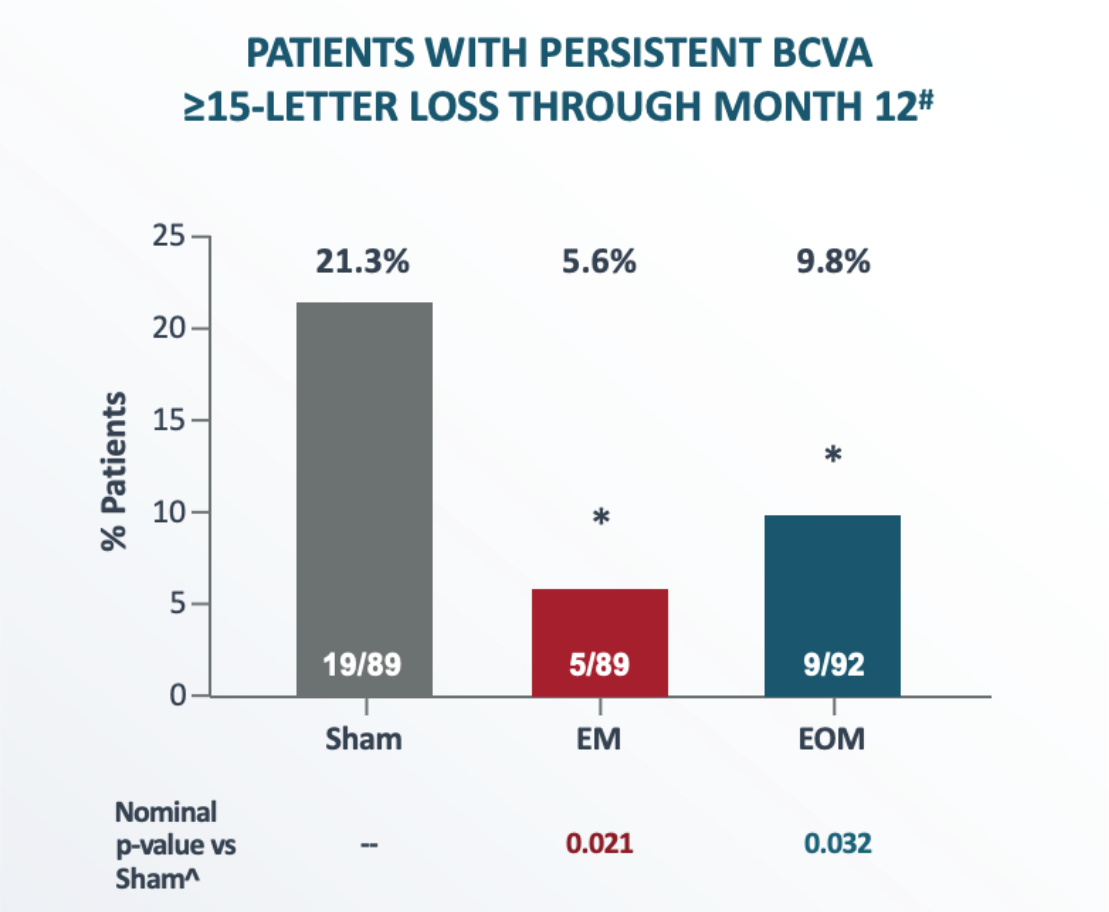


Nominal p-value^		
ANX007 Pooled vs Sham	0.0457	
ANX007 Pooled vs Sham	0.0218	
ANX007 Pooled vs Sham	0.0319	

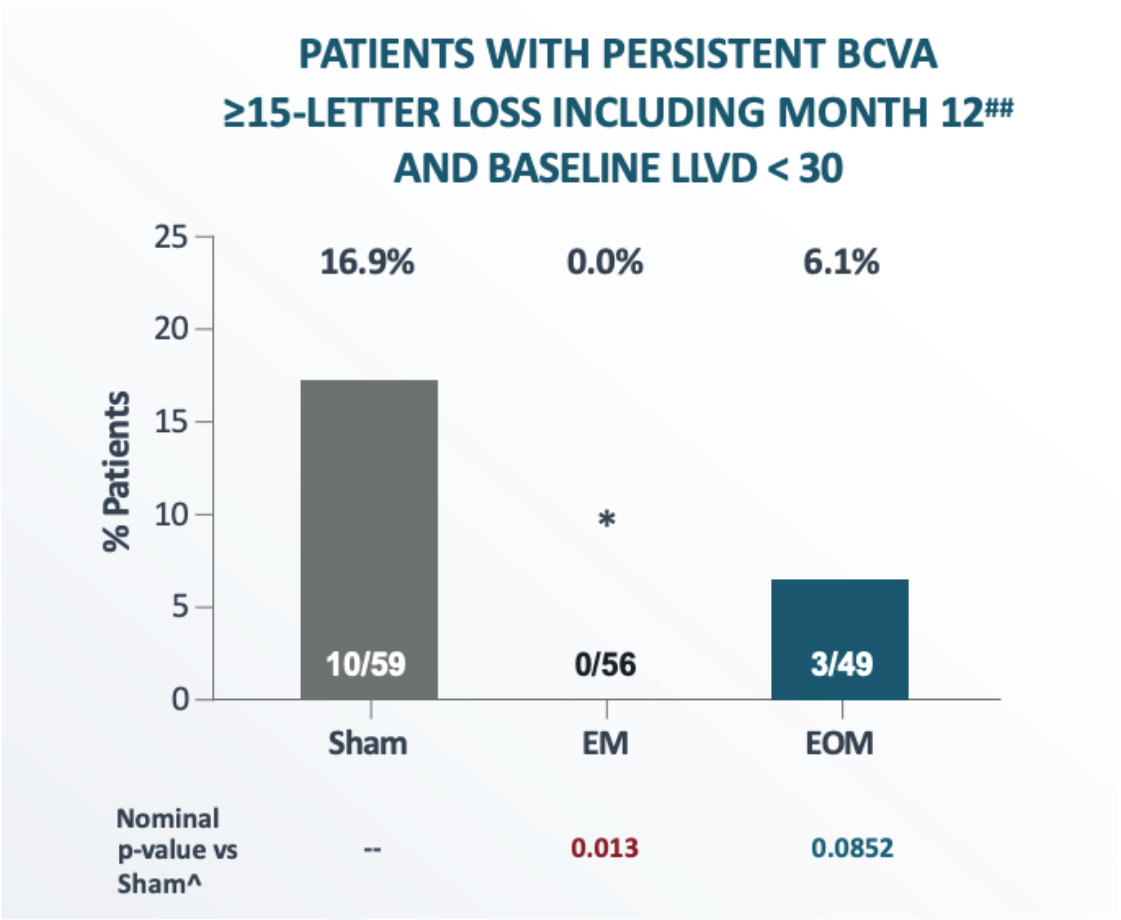
^Nominal p-values from a linear mixed model for repeated measures model (slope) analysis;
Heidelberg Spectralis OCT population with baseline OCT data, excludes patients with >98% atrophy/attenuation at baseline

Profound Effect of ANX007 in Eyes with Less Advanced Disease

Protection from vision loss (BCVA ≥15-letter) based on retina health at baseline (LLVD < 30)



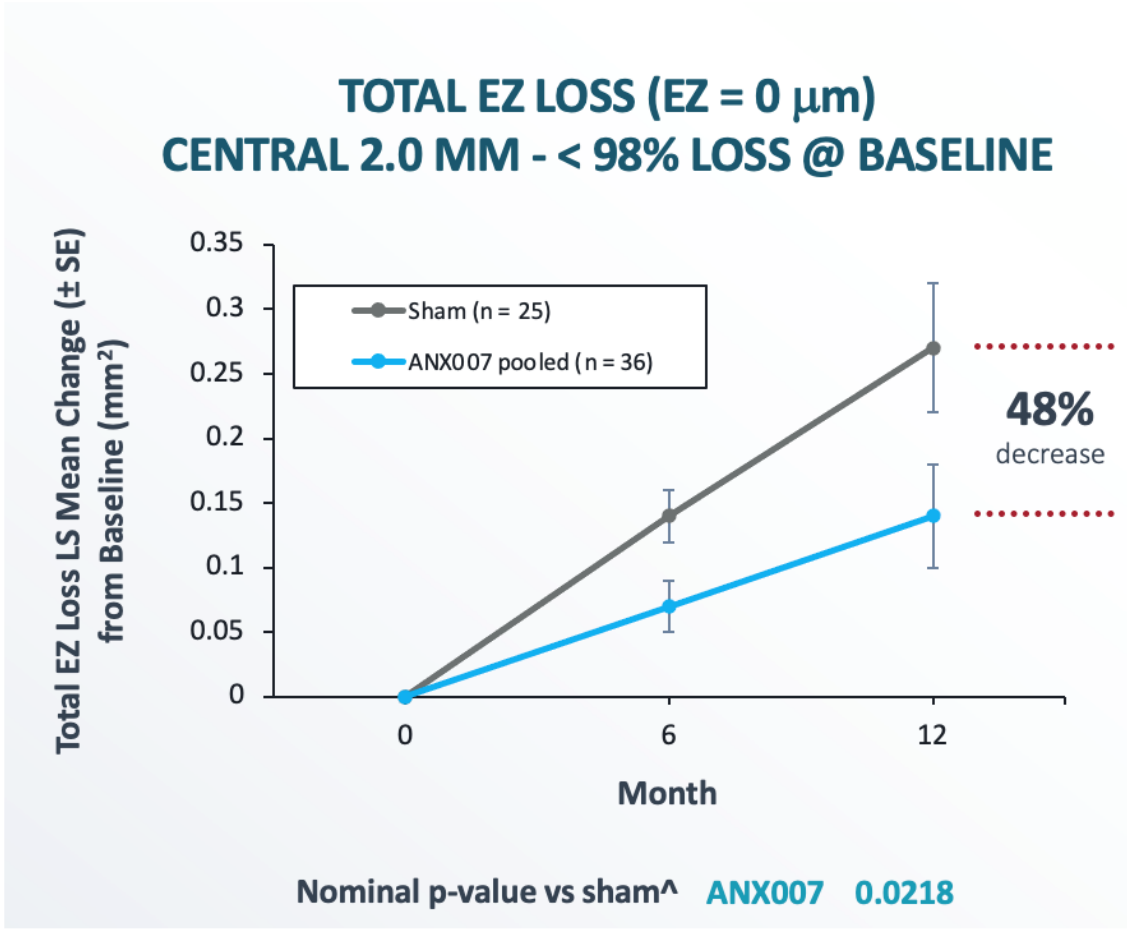
#Persistent for two consecutive visits through month 12 or at last study visit
^Nominal p-value from a Chi-square test in ITT population: * Nominal p < 0.05
Final data



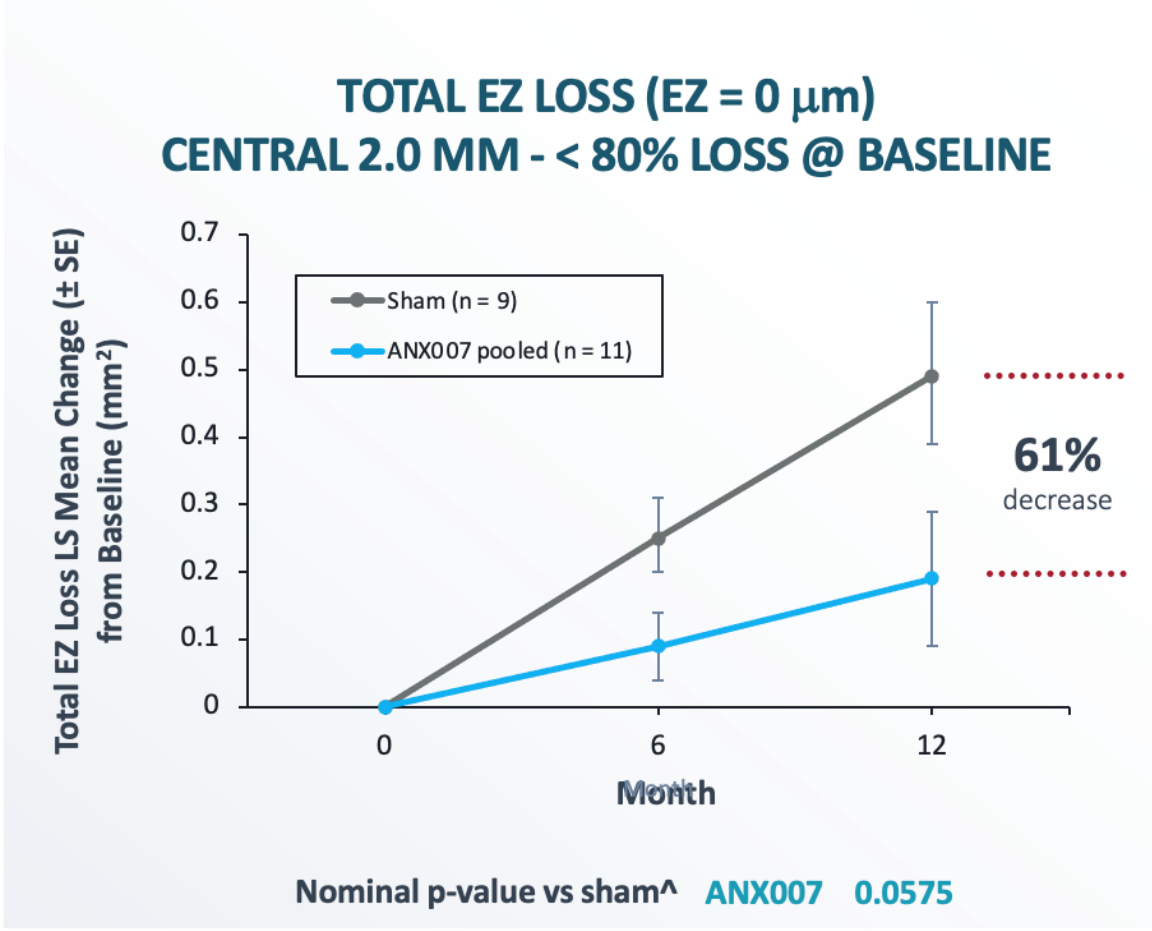
##Persistent for two consecutive visits including month 12 supported by month 15
^Nominal p-value from a Chi-square test in ITT population: * Nominal p < 0.05
Final data

Enhanced EZ Protection in Central Fovea in Less Advanced Disease

Protection from structural loss (EZ Loss) based on EZ health at baseline (< 80% loss)



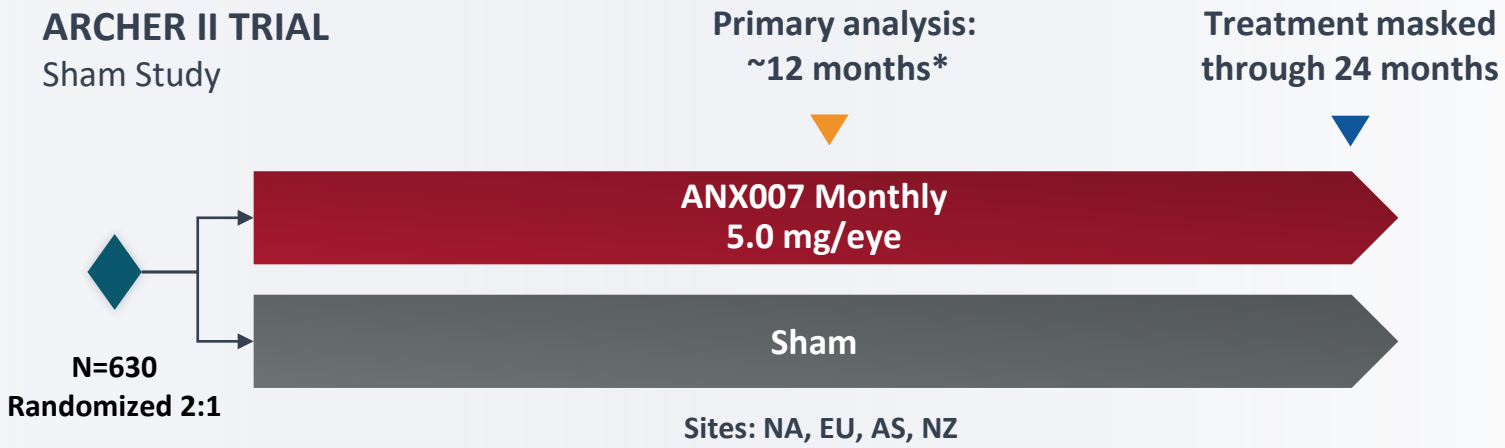
^Nominal p-values from a linear mixed model for repeated measures model (slope) analysis; Heidelberg Spectralis OCT population with baseline OCT data, excludes patients with >98% atrophy at baseline



^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 >80% atrophy at baseline

ANX007 Global Phase 3 Program Ongoing in Dry AMD / GA

PRIME designation from EMA; Fast Track from FDA



PRIMARY ENDPOINT

Persistent BCVA ≥15-Letter Loss through ~12 months*

*Primary analysis based on accumulation of BCVA ≥15-letter loss target events assessed between months 12-18 from initiation of dosing

SECONDARY ENDPOINTS

Safety, Low Luminance VA (LLVA), Ellipsoid zone (EZ)

On the Path to Bringing ANX007 to Millions of GA Patients Worldwide

PHASE 2 ARCHER TRIAL ESTABLISHED PROOF-OF-CONCEPT

Demonstrated preservation of vision and protection of structures associated with visual function

EMA PRIME DESIGNATION AWARDED

ANX007 awarded first and only PRIME designation in GA based on functional benefit shown in ARCHER trial

NEXT STEPS

Phase 3 ARCHER II trial ongoing expected to complete enrollment in 2H'25

US and EU regulatory engagement underway

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ANX1502: First-in-Kind Oral Small Molecule Complement Therapy

Advancing for Complement-Mediated Autoimmune Diseases

Potential to Transform Treatment of Complement-Mediated Diseases

ANX1502 designed to provide robust efficacy with increased oral convenience

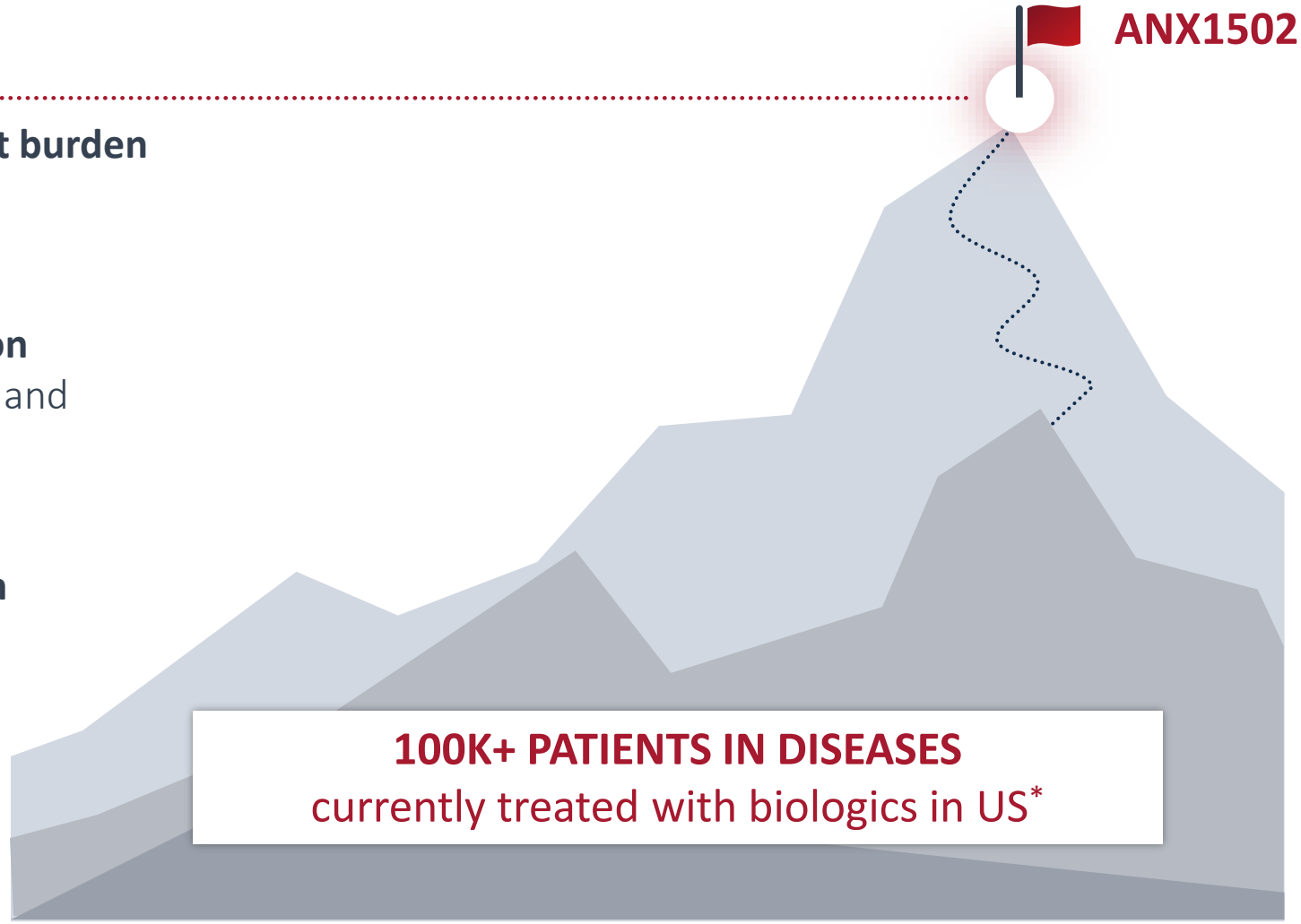
ORAL DOSING

Convenient with reduced patient burden

Subcutaneous self-administration
Self-administered needle-phobia and less flexibility

Daily self- or HCP-administration
Less convenience and flexibility

In clinic administration
Time consuming, expensive, and inconvenient



*Data on file.

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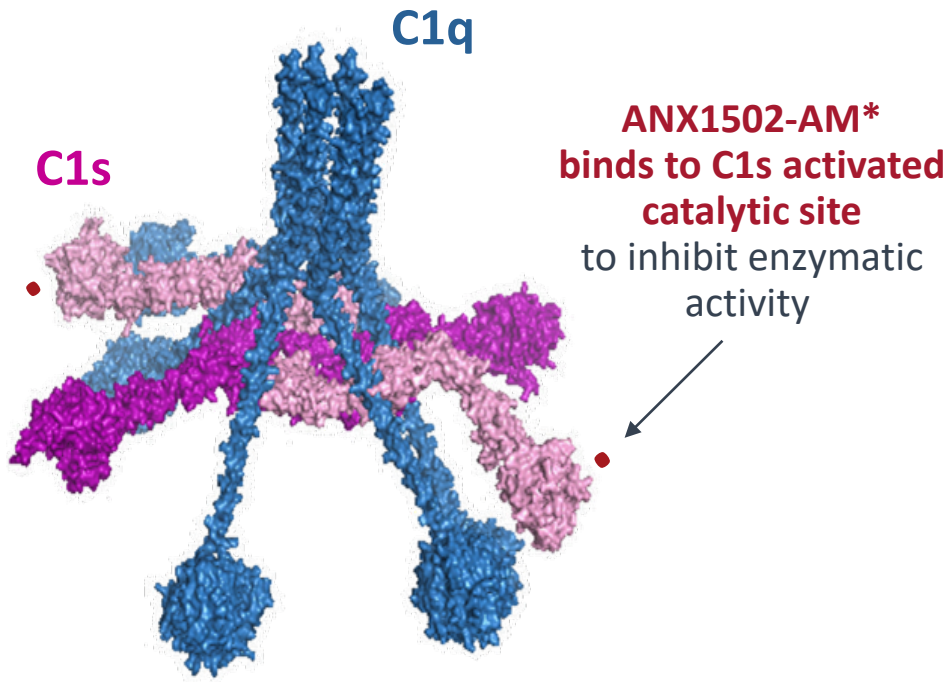
Advancing ANX1502 as the First Oral, Small Molecule Inhibitor of Classical Complement Pathway in Development

- **Orally administered***
- **Targeting active form of C1s** responsible for transmitting classical pathway activation from C1q
- **Potent and selective inhibitor of C1s** (serine protease): selective over related proteases (200 – 50,000-fold)



* ANX1502 prodrug administered; ANX1502-AM = Active Moiety

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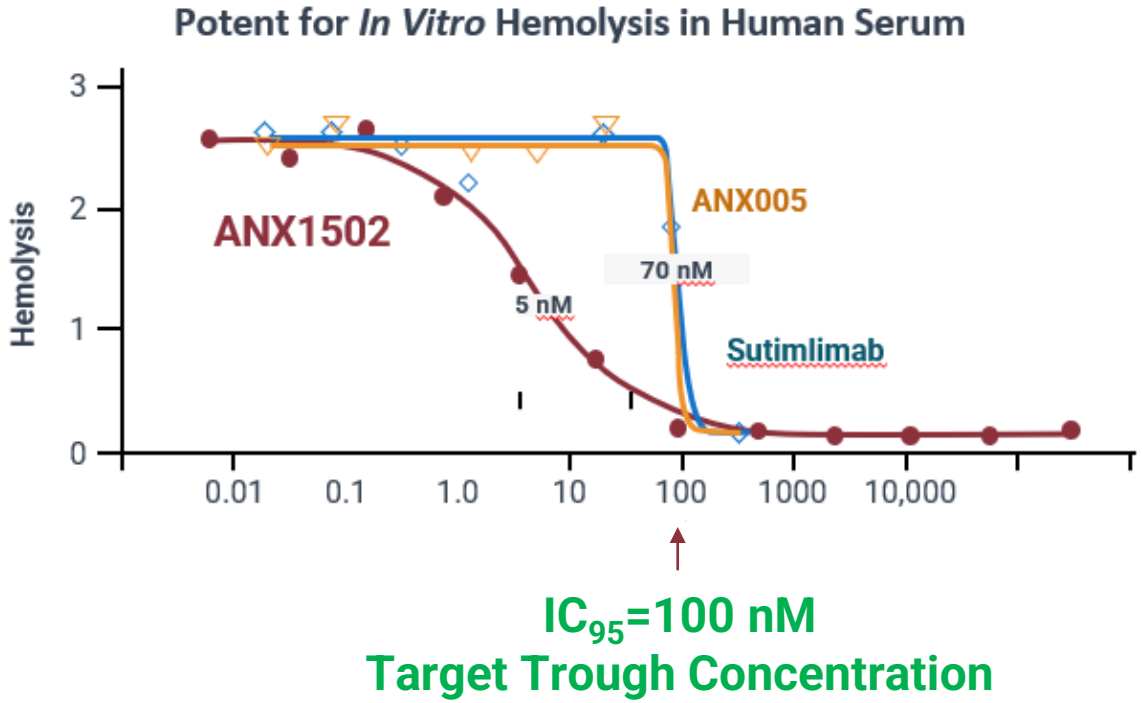
Minimum Target Drug Level (100 nM) ANX1502-AM* for Robust Functional Inhibition of Classical Complement Pathway

- ANX1502-AM* demonstrated **robust functional inhibition of classical pathway** (IC_{50} = 5 nM)
  - Comparable to ANX005 and sutimlimab
  - *In vitro* hemolysis assay w/ high serum (30%)
- Normal sigmoidal dose response vs. antibodies likely due to rate-limiting concentrations of activated C1s
- **Minimum target drug levels for IC_{95}, desired at trough, set conservatively at 100 nM**



* ANX1502-AM: ANX1502 Active Moiety

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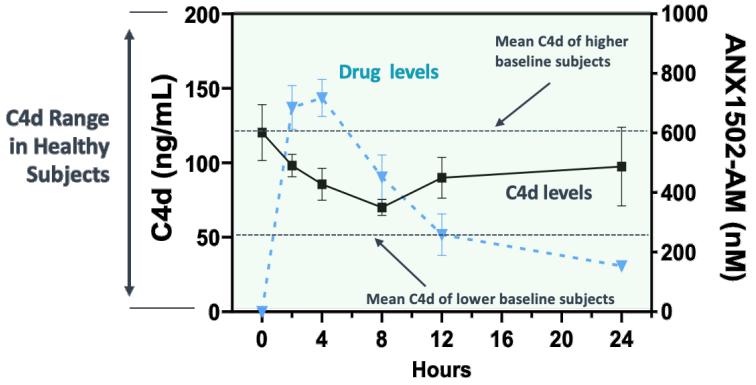
ANX1502 Ph 1 Program Well Tolerated and Achieved Dosing Objectives

Target drug levels reached in healthy volunteers with oral twice-daily dosing; supportive impact on PD biomarker

SAFETY AND TOLERABILITY SHOWN WITH LIQUID SUSPENSION FORMULATION

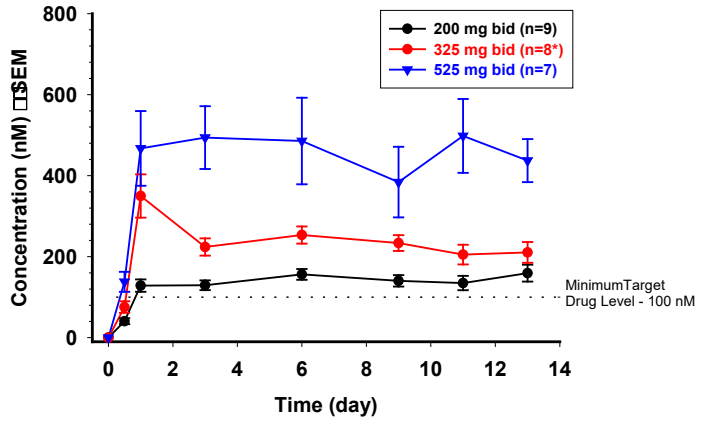
- All treatment-emergent adverse events (TEAEs) mild or moderate
- Most frequent TEAEs were GI related[1]
- **No serious adverse events (SAEs)**
- **No significant clinical/lab findings[2]**

INITIAL *IN VIVO* PD SIGNAL WITH COMPLEMENT ACTIVATION BIOMARKERS (SAD STUDY)



- C4d used as a biomarker reflects drug's *in vivo* impact on C1s activation
- ANX1502 suppressed C4d serum levels in healthy volunteers w/ higher than median baseline C4d

TARGET LEVELS OF ACTIVE DRUG CONSISTENT WITH BID DOSING (MAD STUDY)



- Dose-proportional PK (AUC) was observed in the MAD cohorts

[1]Gastro-intestinal (nausea, emesis, and diarrhea)
[2] Liver enzymes, serum chemistry, or hematology

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ANX1502 Suspension Formulation Generally Well-Tolerated Across SAD & MAD Cohorts in Healthy Volunteers

Manageable GI tolerability issues

Safety Results from Phase 1

- **ANX1502 generally safe and well tolerated through the highest dose level tested**
- All treatment-emergent adverse events (TEAEs) mild or moderate
- Most frequent TEAEs are gastro-intestinal and include nausea, emesis, and diarrhea
- **No serious adverse events (SAEs) observed**
- **No significant clinical/lab findings** (e.g., liver function enzymes, serum chemistry, hematology) observed

Subjects with TEAEs	SAD (Single Dose)						MAD (BID Dose)			
	25mg (N=6)	150mg (N=6)	450mg (N=6)	525mg (n=6)	1050mg (N=6)	**Placebo (N=10)**	200mg BID (N=9)	325mg BID (N=9)	525mg BID (N=9)	**Placebo BID (N=9)**
Subjects with any TEAE (%)	4 (66.6)	2 (33.3)	4 (66.6)	5 (83.3)	6 (100.0)	**6 (60.0)**	7 (77.7)	8 (88.9)	6 (66.6)	**7 (77.7.)**
Subjects with TEAE reported as related (%)	3 (50.0)	2 (33.3)	4 (66.6)	4 (66.6)	6 (100.0)	**4 (40.0)**	6 (66.6)	8 (88.9)	5 (55.5)	6 (66.6)
Subjects with any ≥ Grade 2 TEAE* (%)	1	0	0	0	0	**0**	0	2 (22.2)	1 (11.1)	**1 (12.5)**
Subjects with any Serious TEAE (%)	0	0	0	0	0	**0**	0	0	0	0

***No AEs higher than Grade 2**

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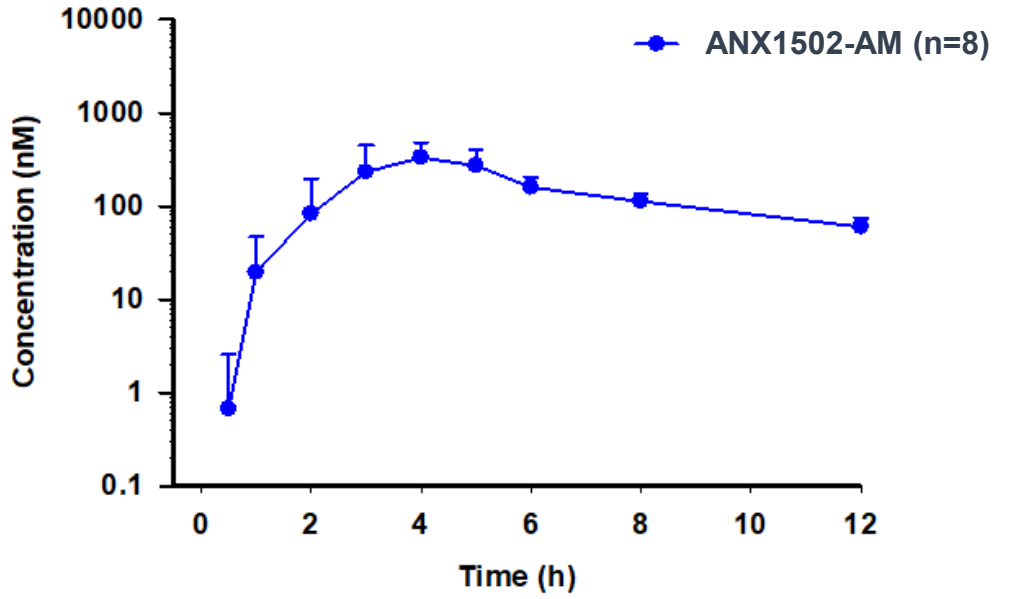
Leveraging Oral Delivery To Disrupt Biologics-treated Indications

ANX1502 IS THE FIRST ORAL INHIBITOR OF THE CLASSICAL PATHWAY, targeting active form of C1s

- **Generally well-tolerated tablet formulation**
- **Convenient dosing twice per day**
- **Robust inhibition of classical pathway** comparable to antibodies ANX005 and sutimlimab (100 nM target trough concentration)

ENTERIC-COATED TABLET FORMULATION SINGLE 400 MG DOSE OF ANX1502



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On the Path to Treating Several Complement-Mediated Diseases with ANX1502 Oral Tablet

PHASE 1 HEALTHY VOLUNTEER TRIAL ESTABLISHED TOLERABILITY & PHARMACOKINETICS

Target levels of active drug consistent with BID Dosing

INITIAL *IN VIVO* PD SIGNAL WITH COMPLEMENT ACTIVATION BIOMARKERS (SAD STUDY)

ANX1502 suppressed C4d serum levels in healthy volunteers w/ higher than median baseline C4d

NEXT STEPS

Clinical POC in CAD and update on future indications Q1'25

- Key endpoints include change from baseline in hemolysis as measured by bilirubin, and complement activation markers

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A bold mission to enable MILLIONS of PATIENTS impacted by complement-mediated diseases of the body, brain and eye LIVE THEIR BEST LIVES