

ANNEXON
biosciences

STOP THE START

of classical
complement-driven
diseases

CORPORATE PRESENTATION | MARCH 2024

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, 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.

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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.



*A bold mission to help MILLIONS
of patients impacted by
complement-mediated diseases
of the body, brain and eye*



ANNEXON: Late-stage Clinical Platform for Classical Complement-Mediated Neuroinflammatory Diseases of the Body, Brain and Eye

Novel, Well-Supported MOA; Wholly Owned Pipeline

Upstream complement portfolio of both large and orphan diseases supported by multiple clinical proof-of-concept (POC) datasets

Near-Term Registrational Data in GBS

Pivotal GBS trial readout anticipated in Q2'2024 – supported by ~10 years of research and two prior GBS trials

Differentiated GA Pivotal & Oral POC Programs

- Initiation of two GA pivotal Phase 3 trials: global ARCHER II sham trial (mid'2024) & ARROW head-to-head trial vs. SYFOVRE® (2H'2024)
- 1st in class ANX1502 oral candidate POC in autoimmune disease (2H'2024)

Well-Capitalized into Mid-2026

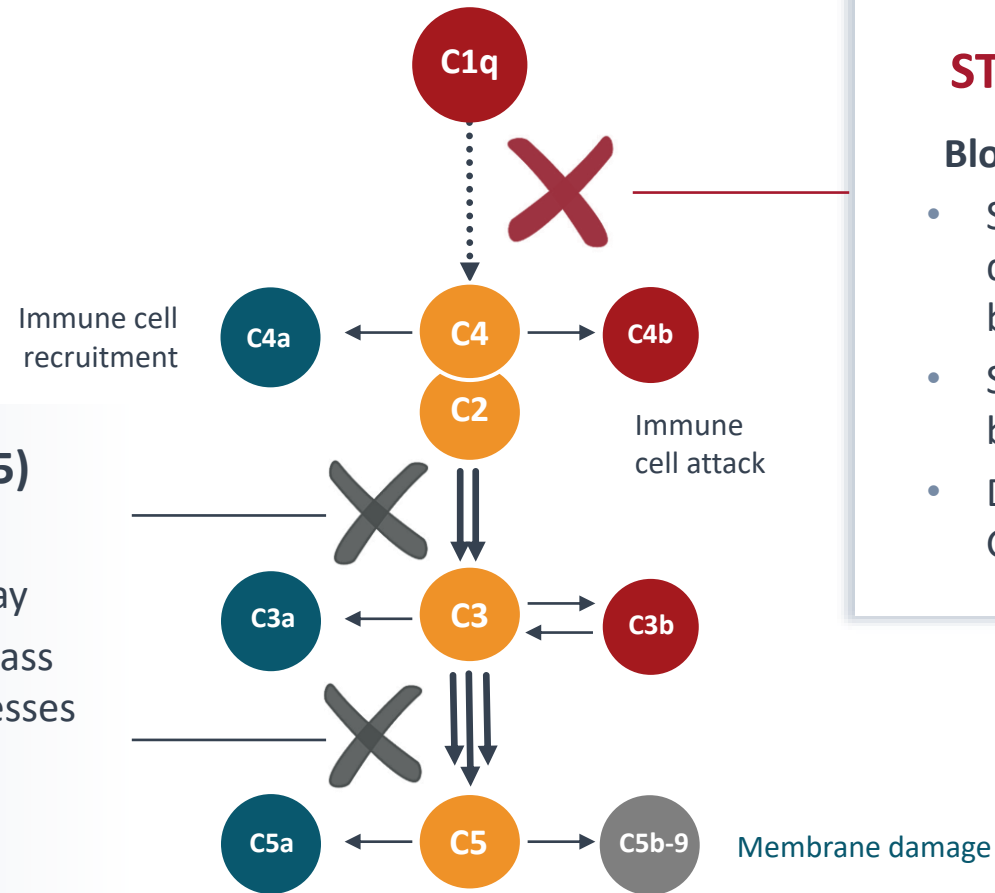
Runway through multiple mid- and late-stage clinical catalysts

Distinct Upstream Complement Approach to **STOP C1q** and its Neuro-Inflammatory Cascade Where it **STARTS** On Diseased Tissue

Classical complement: common inflammatory pathway driving diseases of the body, brain & eye

DOWNSTREAM APPROACHES (C3/C5)

- Do not block ongoing inflammatory pressure of upstream classical pathway
- More susceptible to complement bypass mechanisms (i.e., inflammatory processes continue to advance)



STOPPING C1q AT THE START

Blocks All Classical Pathway Activity¹

- Selectively stops upstream & downstream inflammation driven by classical pathway
- Stops pathway before downstream bypass mechanisms (breakthrough)
- Differentiated functional data in GBS, HD and GA

Only Complement-Pipeline for Diseases of the Body, Brain & Eye

Potential to treat >8 MILLION patients worldwide

			Preclinical	Phase 1	Phase 2	Phase 3	Next Milestone	Worldwide Rights
FLAGSHIP PROGRAMS								
Autoimmune	ANX005	Guillain-Barré Syndrome (GBS)					Phase 3 data 2Q 2024	ANNEXON biosciences
Ophthalmology	ANX007	Geographic Atrophy (GA)					Phase 3 initiation Mid 2H 2024	ANNEXON biosciences
Autoimmune	ANX1502	Autoimmune Indications					POC data 2H 2024	ANNEXON biosciences
NEXT WAVE PROGRAMS								
Neurodegenerative	ANX005	Huntington’s Disease					Phase 2a topline data reported	ANNEXON biosciences
		Amyotrophic Lateral Sclerosis (ALS)						ANNEXON biosciences
Autoimmune	ANX009	Lupus Nephritis						ANNEXON biosciences

Maximizing Pipeline Potential with THREE Clinical Priorities

1

Deliver
**1st placebo-controlled
pivotal dataset for
GBS** in 40 years

2

Initiate
**1st global pivotal
program for GA using
vision preservation**
as primary outcome
measure

3

Advance
**1st-in-kind oral
classical complement
inhibitor to clinical
proof-of-concept**

Poised for Potentially Transformational 2024 and Beyond

2024 ANTICIPATED MILESTONES

Operating runway
into **mid 2026**
funding **multiple**
clinical catalysts

2Q 2024

ANX005 GBS pivotal trial readout

ANX1502 CAD proof-of-concept trial initiation

Mid 2024

ANX007 GA P3 ARCHER II trial initiation

ANX007 GA P3 ARROW trial initiation

2H 2024

ANX1502 CAD proof-of-concept trial readout

ANX005 ALS P2a data at medical meeting

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

Pivotal Phase 3 Data Readout in 2Q 2024



Shane S.
53-year-old patient with GBS

Annexon Has a Deep-Rooted History and Commitment to GBS

Aligned With Our Mission

to treat diseases driven by classical complement activation

Strong Scientific Rationale

ANX005 is designed for rapid inhibition with a single dose

High Unmet Need

Well-characterized, underserved disease afflicting thousands globally

ANNEXON HAS KEY CLINICAL EXPERTISE AND RELATIONSHIPS IN GBS

Supported 2,000 patient registry at IGOS to inform clinical program

Conducted 3 clinical trials including:

- 1st placebo-controlled trial in ~40 yrs
- Monotherapy and combination trials

Large ongoing Phase 3 placebo-controlled trial

ANX005: Potential to be First FDA-approved Therapy for GBS

✓ Pursuing a monotherapy label in GBS

✓ Demonstrated POC across several clinically-meaningful measures

✓ Granted US FDA Fast Track & Orphan Drug Designations

✓ Granted EMA Orphan Drug Designation based on potential for benefit over available therapies

✓ Phase 3 data on track for 2Q 2024; Real World Evidence comparability data 1H 2025 in support of BLA submission

GBS Impacts Thousands of People Annually

- Completed first-ever analysis of 7 years of medical claims data to determine incidence of GBS
- Updated GBS incidence: 7,000 in US and 15,000 for all European countries¹
 - Previous US estimate = 6,000
 - Previous M5 Europe estimate = 6,000 (no total Europe estimate)
- Updated incidence numbers are conservative since represent hospitalized and treated patients, doesn't include patients (additional 5-10%) who are not hospitalized²



Significant Need and Opportunity for a New GBS Therapy

“I was put on my hands and knees, and **I had to learn how to crawl just like a baby...**

I crawled for 8 or 9 months, and **it took about 2.5 years to learn how to walk...** Then I had 5 years in physical therapy.”



Shane S.
53-year-old
financial advisor
and patient with
GBS

SIGNIFICANT DISEASE BURDEN DESPITE CURRENT TREATMENTS ^{1,2,3,4,5,6,7}

~25%	~40%	~20%	~10%	~5%
require mechanical ventilation	admitted to ICU	can't walk at 1 year	permanently disabled and can no longer work	mortality

>\$2B ANNUAL ECONOMIC COST OF GBS IN US⁷

~25% increase in daily cost of ICU care with mechanical ventilation⁸

GBS impacts patients' ability to work and places significant burden on caregivers⁷

ANX005 HAS POTENTIAL TO PROVIDE VALUE-BASED BENEFITS TO REDUCE COST TO CARE FOR GBS PATIENTS AND IMPACT OF DISEASE

Key Characteristics of an Effective Therapy to Combat GBS

Move expectations from *Getting Better Slowly* to *Getting Better Sooner*

1 Directly targets mechanism driving extensive nerve damage and paralysis

Treatment goal is to target complement-mediated acute nerve damage and inflammation to prevent paralysis, severe morbidity, disability and mortality

2 Rapid onset of action

Block acute and ongoing destruction of nerves immediately

3 Provides clinical benefit across entire disease spectrum

Effective in all GBS patients, and impacting all aspects of the disease that are important to patients

4 Minimal side-effects

Single infusion with manageable infusion related reactions

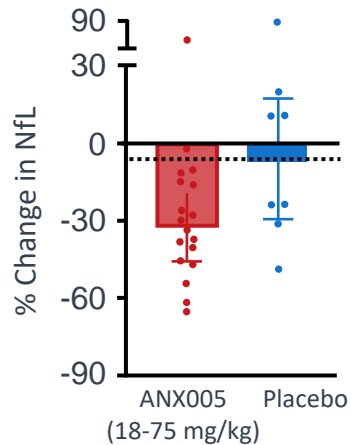
ANX005 Phase 1b: Consistent Demonstration of Getting Better Sooner

Rapid target engagement, early nerve damage reduction and recovery of muscle strength precedes gain of function



NEURAL DAMAGE

Rapid reduction in nerve fiber biomarker NfL

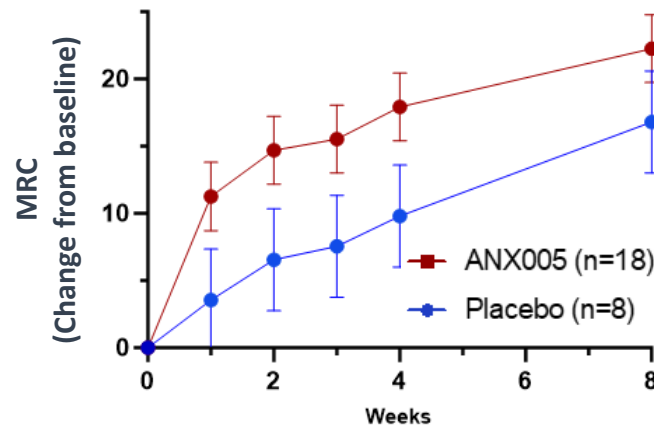


Statistically significant reduction (weeks 2-4)



MUSCLE WEAKNESS

Early gain in muscle strength

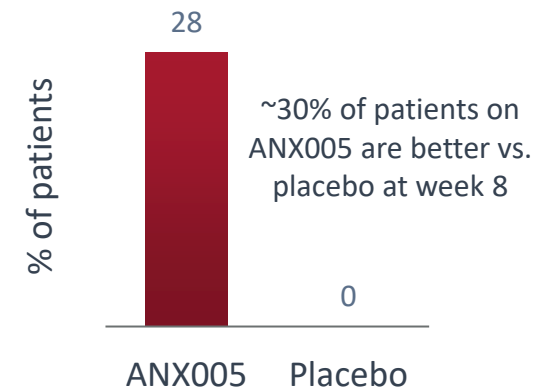


Change in MRC sumscore from Baseline



NEUROLOGICAL DISABILITY

Improvement in clinical function



≥3 point improvement in GBS-DS at week 8

ANX005 Phase 3 Pivotal Trial On Track for Data Readout Q2 2024

Randomized, double-blind trial, placebo-controlled Phase 3 trial; enrollment completed in 2H 2023

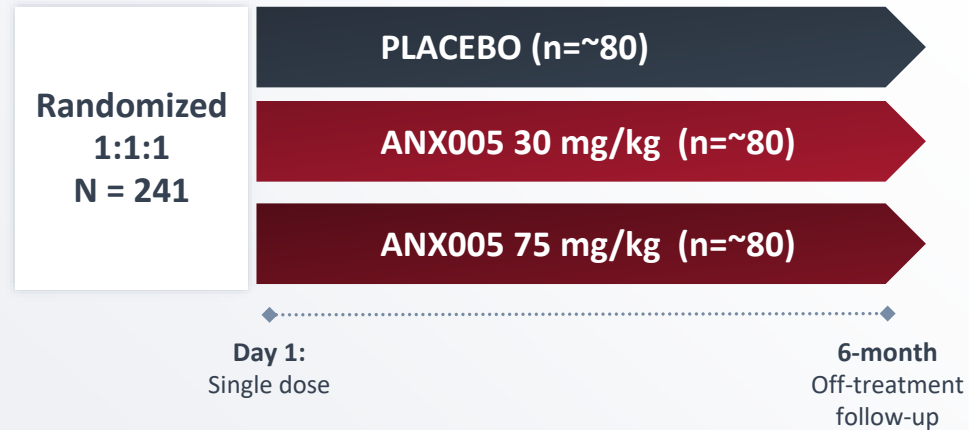
STUDY DESIGN

- Patients diagnosed <10 days from onset of weakness
- Baseline GBS-DS score 3-5
- Stratified for prognostic factors: muscle strength and time from symptom onset

GBS-disability Scale (GBS-DS)

0	Normal
1	Running
2	Walking unassisted
3	Walking assisted
4	Bed ridden
5	Ventilated
6	Death

MONOTHERAPY SINGLE DOSE TREATMENT



US FDA Fast Track & Orphan Drug Designation
EMA Orphan Drug Designation

ENDPOINTS

Primary Outcome Measure¹
GBS-DS at week 8: well-accepted regulatory endpoint assessing functional status

Secondary Endpoints include muscle strength, mortality, and time on ventilator

What is considered a win?
2-fold shift to better on GBS-DS vs. placebo at week 8

¹Analyzed using a proportional odds model, a common statistical analysis method (van Leeuwen, et al., 2019, doi.org/10.1371/journal.pone.0211404) with an expected outcome of approximately 2x more patients in a good state of health and 2x fewer patients remaining severely disabled

Phase 3 GBS-DS Analysis Approach

GBS-DS SCALE COLLAPSED INTO 3 CATEGORIES Enhances Clinical Interpretability

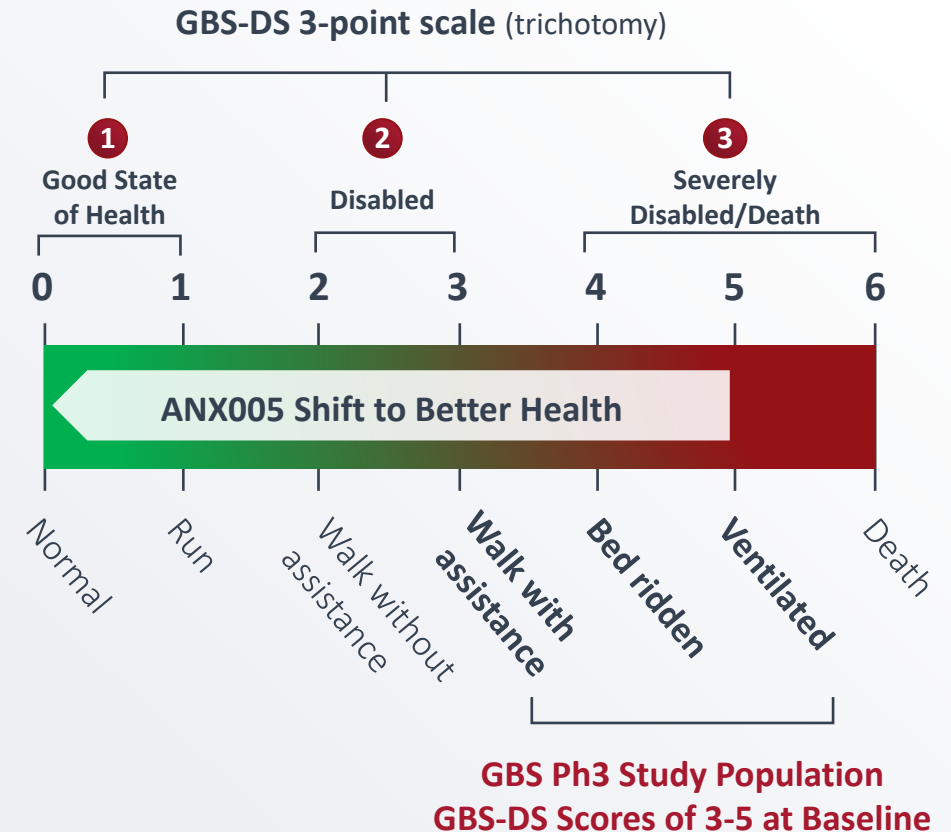
Approach: Collapse 7-point scale to a 3-point scale (trichotomy)

- **0-1:** Good State of Health
- **2-3:** Disabled
- **4-6:** Severely Disabled/Death

Rationale:

- ✓ Enhances clinical interpretability by focusing on a subject's actual health status at week 8 after receiving ANX005 or placebo
- ✓ Includes all patients across all health states vs. dichotomy which would only include subset
- ✓ Most efficient statistical analysis approach

GBS-DS SCALE FOR PIVOTAL PHASE 3



Key Phase 3 Secondary Endpoints

Designed to assess total clinical benefit and demonstrate durability of response with measures that are interpretable and relevant to patients and clinicians



MUSCLE STRENGTH

MRC Sum Score

Clinically meaningful prognostic indicator of outcome

- MRC sum score at Day 8
- MRC sum score at Week 8



CHRONIC DISABILITY

GBS Disability Score

Durability of response over full study length

- Multiple sensitivity analyses
- Longitudinal analysis
 - Responder analyses



MORBIDITY AND MORTALITY

Ventilation, Time in ICU, Death

Overall reduction in morbidity and mortality

- Number of patients requiring ventilation
- Number of days on ventilator
- All-cause mortality
- Days in ICU

Real-World Evidence in Support of Regulatory Path

- **FDA agreement that a single pivotal study would be sufficient for BLA assuming it demonstrates:**
 - Substantial evidence of ANX005's treatment effect vs. placebo
 - Comparability between Ph3 population & Western patients
- **FDA agreement with Annexon's plan to establish comparability - Real World Evidence (RWE)**
 - Ph3 patients will be compared with patients from IGOS
 - IGOS is a global, prospective, observational, multicenter cohort study
 - IGOS is led by global experts in GBS and has enrolled 2000 patients who were followed for 1-3 years
 - Annexon has initiated a real-world evidence (RWE) comparability protocol with IGOS (ANX005-GBS-04)
 - Initial comparability data 1H25 in support of BLA submission

Annexon + IGOS RWE Comparability Study



Global GBS Real-World Evidence Cohort



Annexon Phase 3 Study

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

Chronic, progressive neurodegenerative disease of the eye resulting in vision loss

Paul S., 85-year-old patient with GA

“I look normal. My eyes look normal. **But what I see through my eyes is not what you see through your eyes.** It’s cloudy, it’s hazy, it’s fuzzy. It’s not clear, it’s not crisp...I don't drive anymore. It really impacts my photography hobby. **Nothing is like it used to be.**”



Nancy S., wife and caregiver

“**He isn’t able to function in the way he once did. Eye problems can take a toll not just on your sight, but emotionally too.** ...When we are walking somewhere I get very tense. I try to tell him if the ground changes, but then it can start to get demeaning if I’m telling him things all the time. **I walk on eggshells.**”

1 MILLION people diagnosed in US; **8 MILLION** people globally¹

ZERO

FDA-approved treatments demonstrating
preservation of visual function

Treatments approved in the EU or Asia

SIGNIFICANT DISEASE BURDEN

PROGRESSIVE DISEASE

leading to vision loss

2.5 YEARS

median time to developing
central GA from diagnosis²

TRAUMATIC IMPACT ON PERSONAL LIVES AND DAILY LIVING,

including limited or no ability to read, drive, or recognizing faces

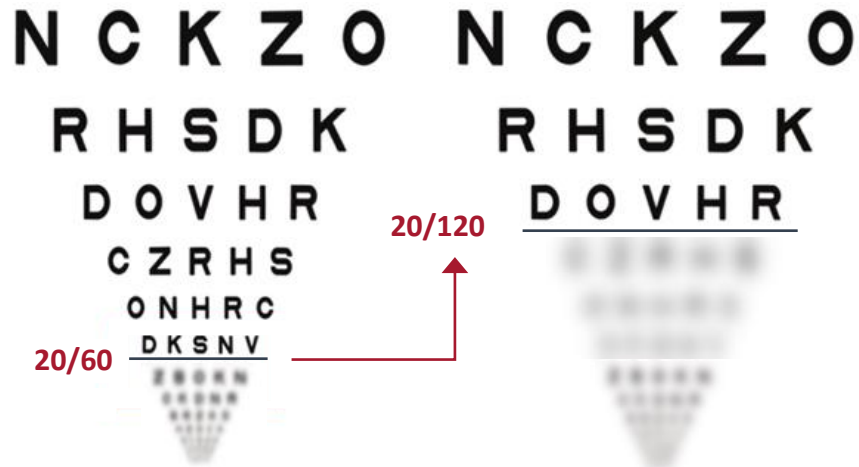
Vision Preservation is the Most Important Outcome for GA Patients

BCVA ≥ 15 -letter loss is rigorous and meaningful as it represents 50% loss of a patient's central visual acuity

BEST CORRECTED VISUAL ACUITY (BCVA)

15 Letter Loss

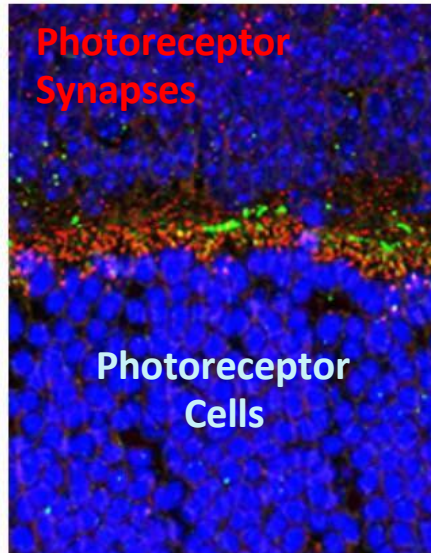
20/60 to 20/120 vision



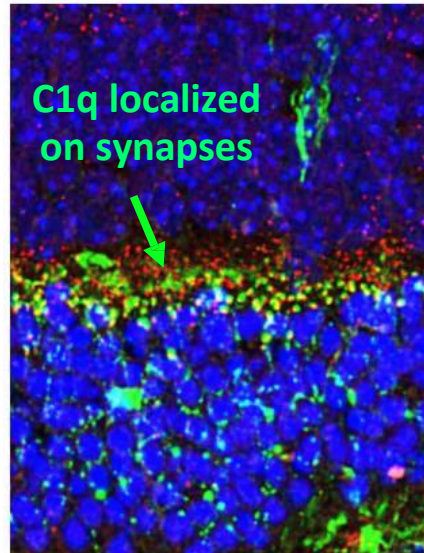
Anti-C1q Protected Photoreceptor Cells and Their Function in Models of Photoreceptor Damage

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

CONTROL



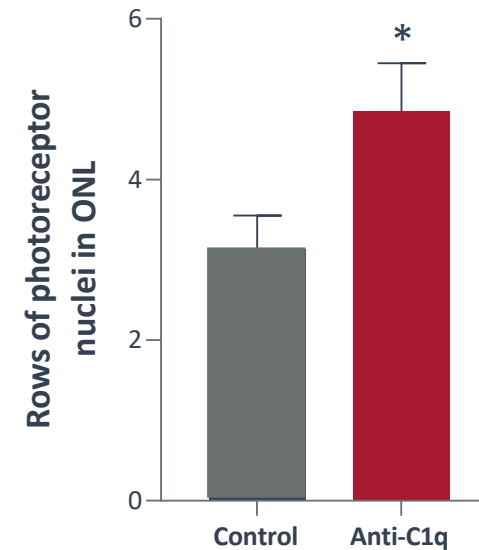
3 DAYS POST WHITE LIGHT DAMAGE



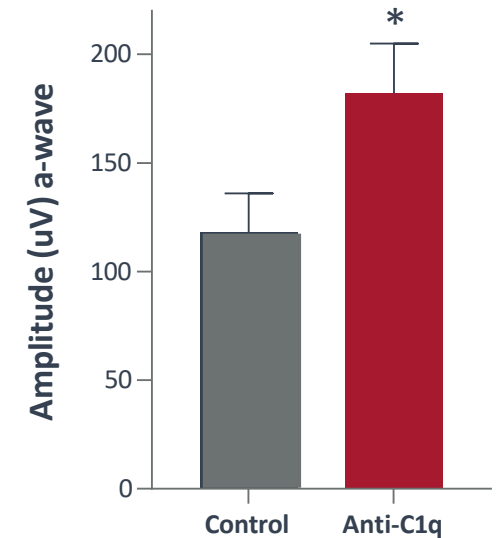
Annexon data on file

Anti-C1q Protected Photoreceptors and Function

ANTI-C1Q PROTECTED PHOTORECEPTOR CELLS/ RETINAL THICKNESS



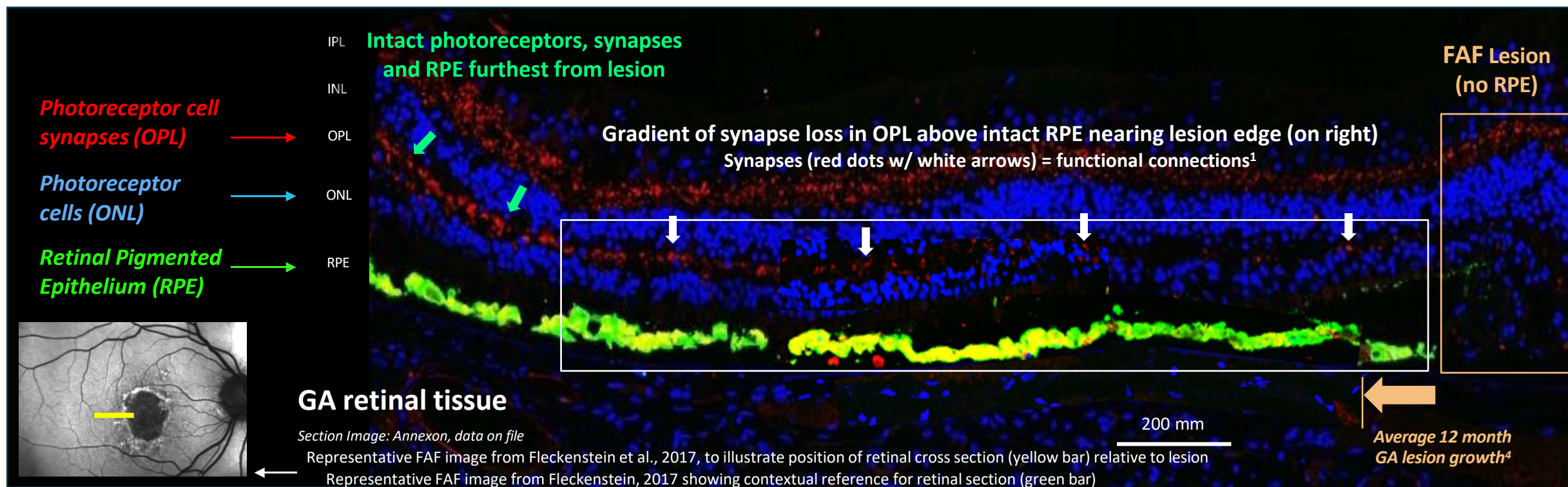
PROTECTED RETINAL FUNCTION



Jiao, et al., 2018 *Mol Neurodegener* 13(1):45

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

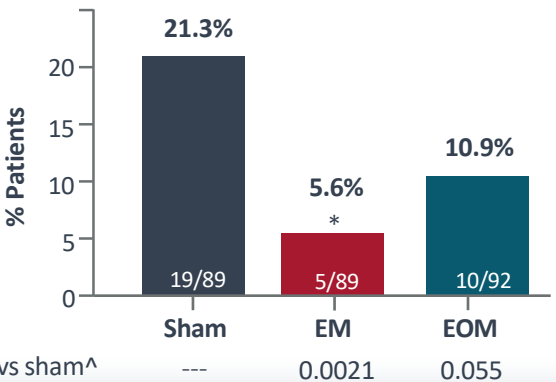
- Photoreceptor cells and their synapses are lost over intact RPE (white box)
 - Decreasing gradient of **red-labeled synapses** (w/ white arrows) moving toward the lesion on right - loss of synapses is loss of function¹
 - Also, decreasing gradient of **blue-labeled photoreceptor cells** toward lesion – photoreceptors are lost prior to RPE²
- FAF measures RPE loss/lesion growth, but not photoreceptor or synapse loss and correlates poorly w/ visual function³



ANX007 ARCHER Proof-of-Concept Trial – 1st Significant Demonstration of Vision Preservation in GA Patients

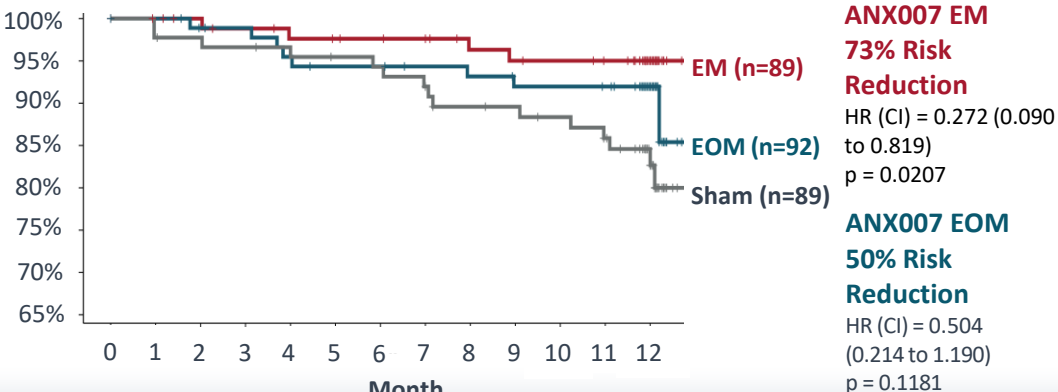
SIGNIFICANT VISION PROTECTION MEASURED BY BCVA ≥ 15 -LETTER LOSS

Patients with persistent BCVA ≥ 15 -letter loss through month 12+



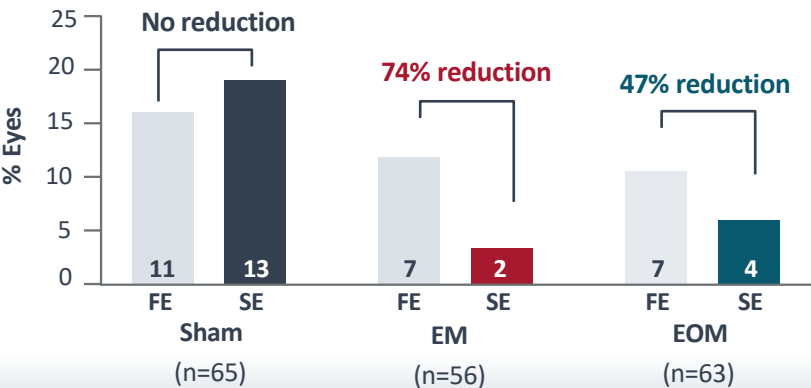
SIGNIFICANT TIME AND DOSE-DEPENDENT VISION PROTECTION

BCVA ≥ 15 -letter loss at 2 consecutive visits



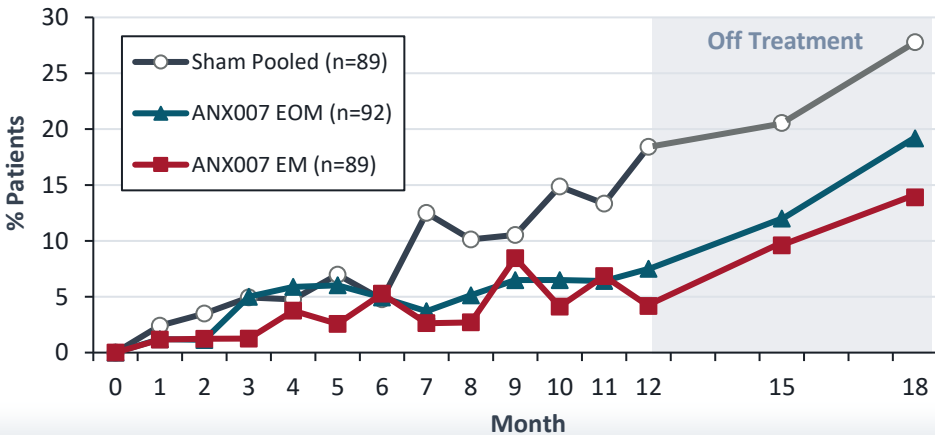
FELLOW-EYE ANALYSIS: VISION PROTECTION IN TREATED EYE BUT NOT IN NON-TREATED FELLOW EYE

Eyes with BCVA ≥ 15 -letter loss at month 12 in all patients with bilateral GA

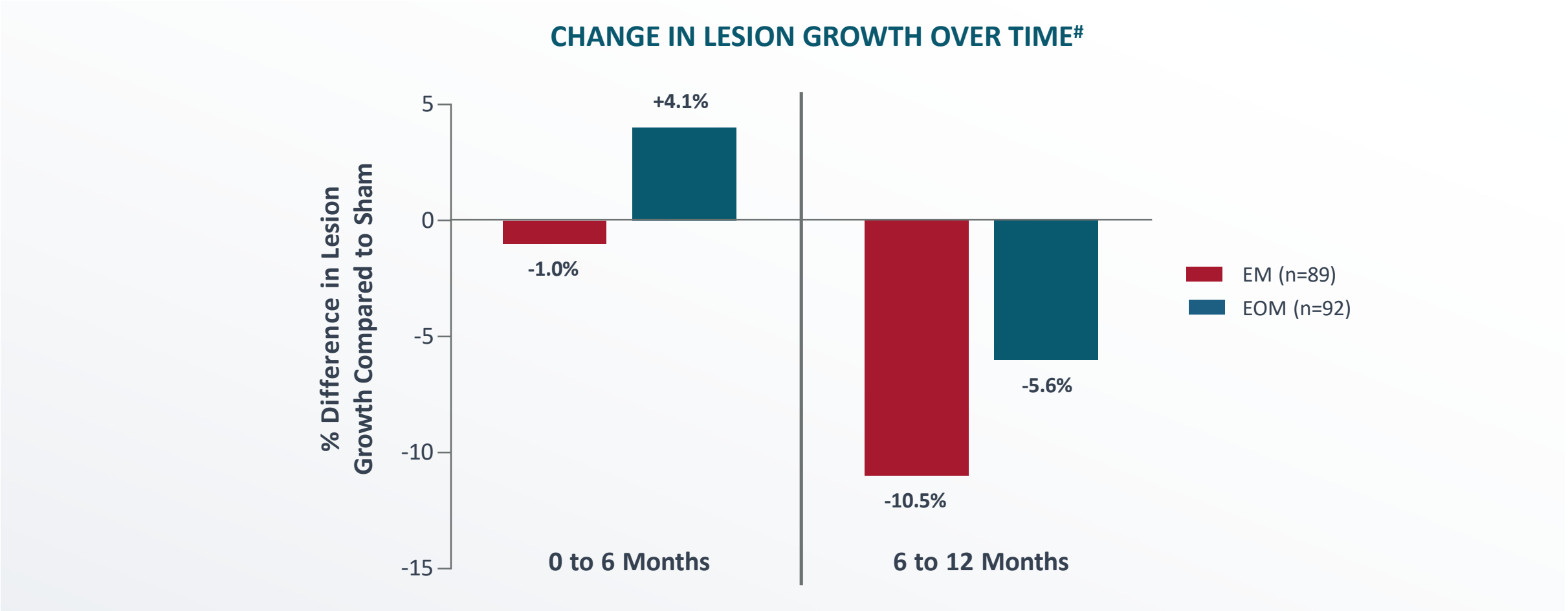


OFF TREATMENT ANALYSIS: ON-TREATMENT VISION PROTECTION WANES POST-TREATMENT

% of patients with any BCVA ≥ 15 -letter loss from baseline



ANX007 Effect on Lesion Growth Improves with Longer Treatment



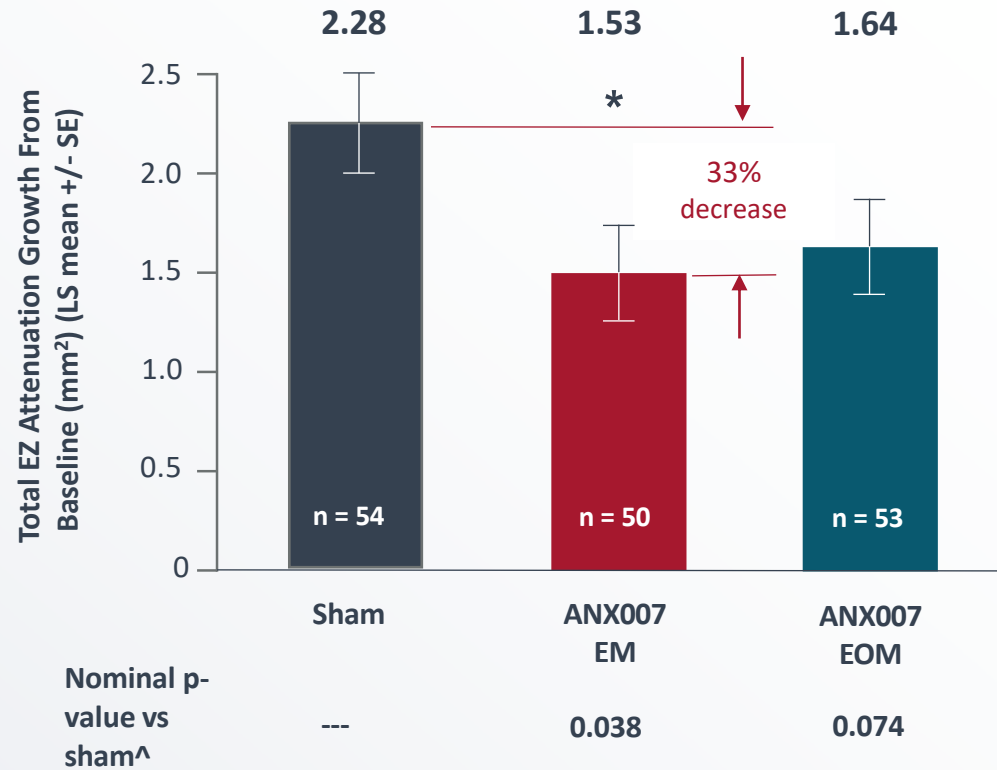
Increasing ANX007 Impact Over Time

#The 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

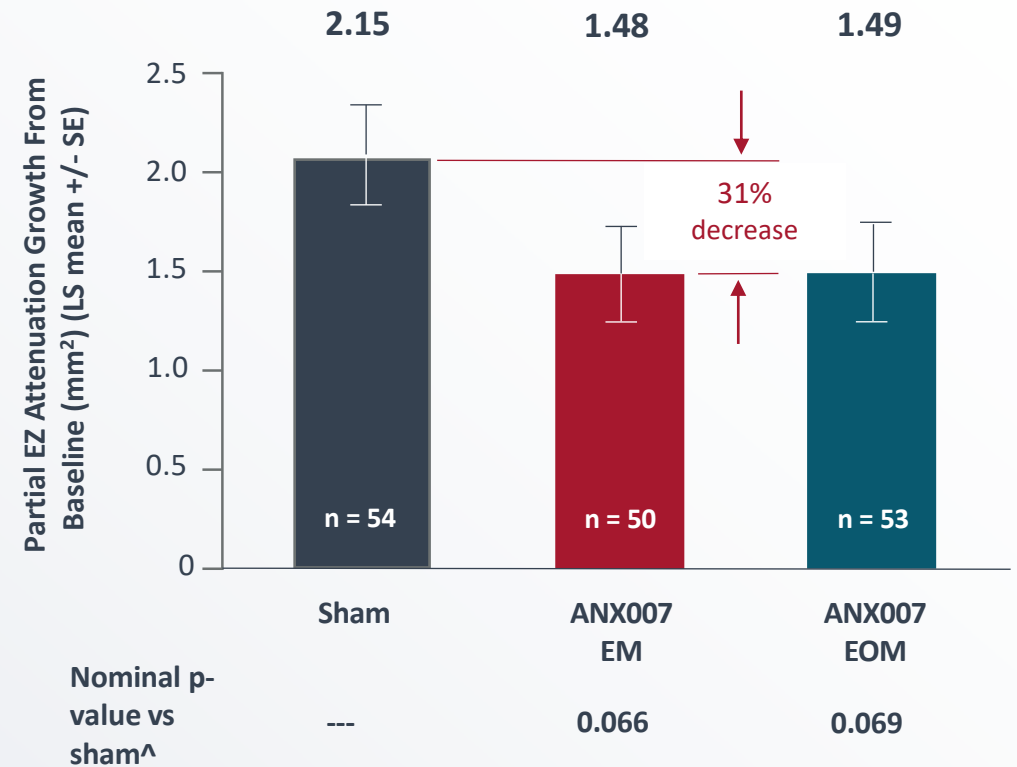
Initial Assessment of Ellipsoid Zone Change: ANX007 Demonstrated ~30% Change from Sham in EZ Attenuation

As observed 12-month completer data; MMRM analysis ongoing, pending full timepoint assessment

**TOTAL EZ ATTENUATION (EZ = 0 μ m)
CHANGE FROM BASELINE AT MONTH 12 #**



**PARTIAL EZ ATTENUATION (EZ < 20 μ m)
CHANGE FROM BASELINE AT MONTH 12 #**



#Data as observed

^Nominal p-value from a linear regression with Heidelberg Spectralis OCT population with baseline and month 12 EZ data (n = 157)

* Nominal P < 0.05

ANX007 1st & Only Recipient of PRIME Designation - Best-in-Class Potential By Disconnecting Lesion Growth Surrogate from Vision Preservation

FDA Alignment on
BCVA \geq 15-Letter Loss as
Primary Outcome Measure

No FDA requirement to study slowing of
GA lesion growth by FAF

Program to include comparison to an
injection agent of choice, consistent with
trials across ophthalmic indications

PRIME Designation
Granted in EU

“The unmet need in Geographic atrophy (GA) secondary to age-related macular degeneration (AMD) is agreed. The potential to address the unmet need relies on the Phase 2 clinical data and effects on visual function at 12 months...**the consistent effects on visual function across measures, analyses and subgroups indicated a potential to address the unmet need.**”

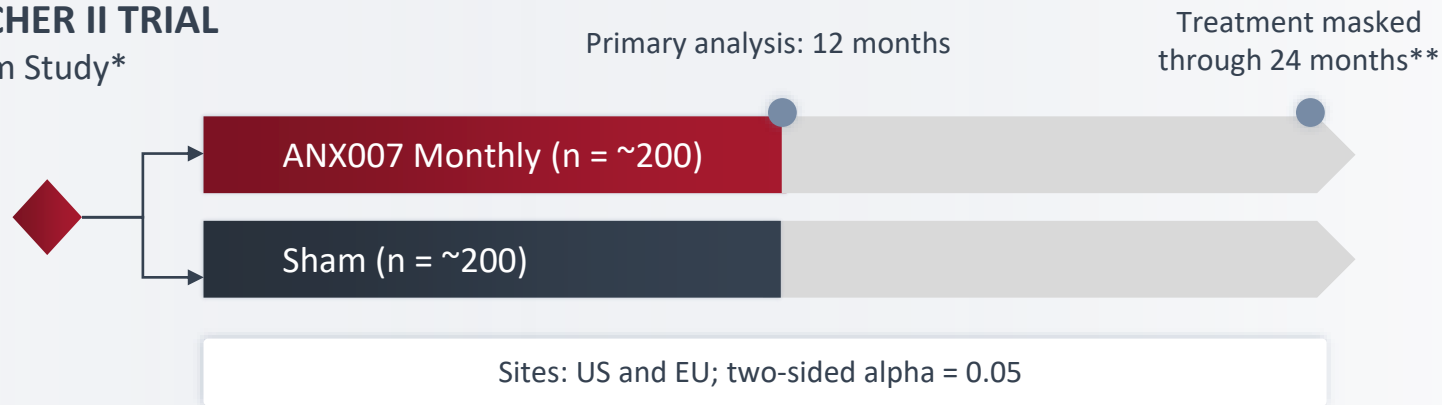
— *European Medicines Agency*

ANX007 Global GA Pivotal Program to begin Mid-2024

ARCHER II initiation in mid-2024; ARROW trial initiation in late-2024

ARCHER II TRIAL

Sham Study*



PRIMARY ENDPOINT

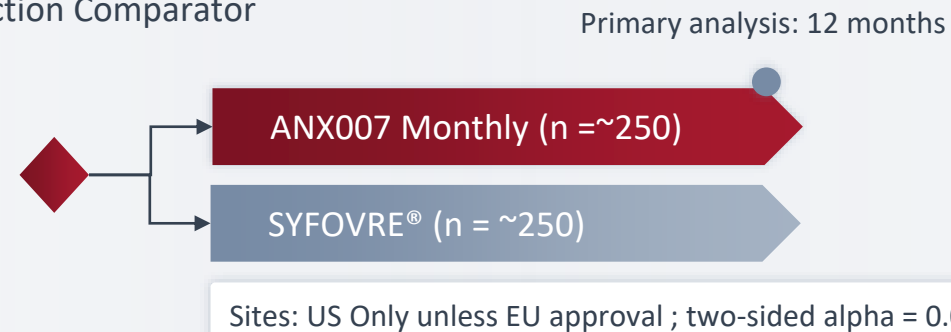
Persistent ≥ 15 -Letter BCVA Loss through 12 months, or accumulation of appropriate number of events

KEY SECONDARY ENDPOINTS

Safety, Low Luminance VA (LLVA), Low Luminance Visual Deficit (LLVD)

ARROW TRIAL

Injection Comparator



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

Advancing for Complement-
Mediated Autoimmune Diseases



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



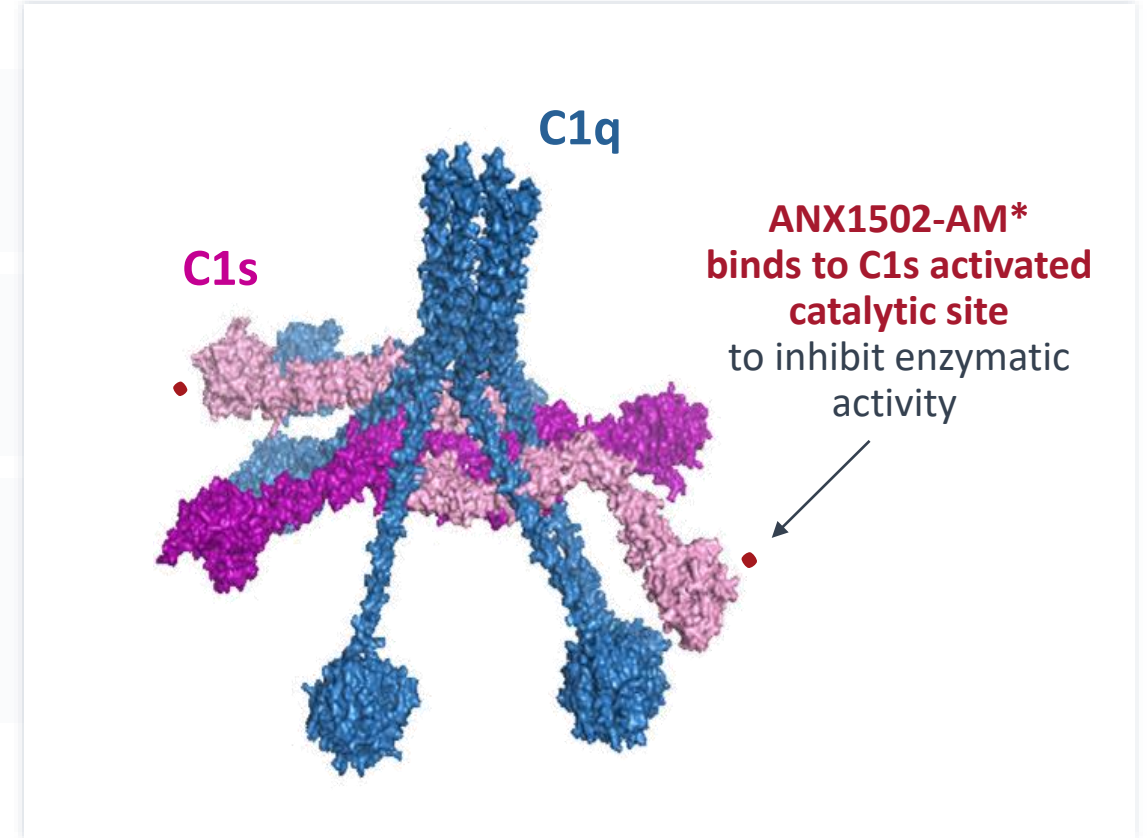
Orally administered*



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)



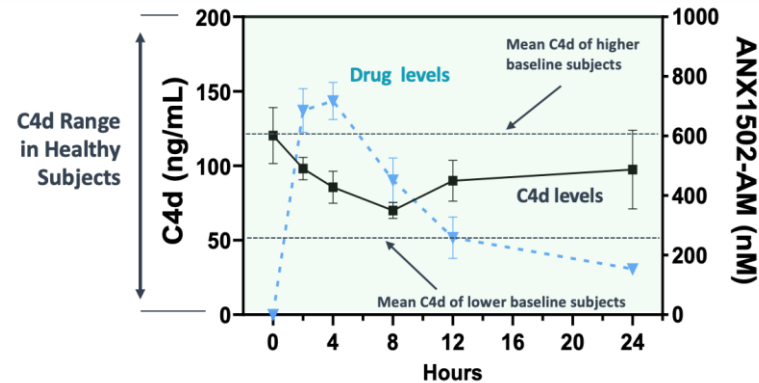
ANX1502 Ph 1 Program Well Tolerated and Achieved Dosing Objectives

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

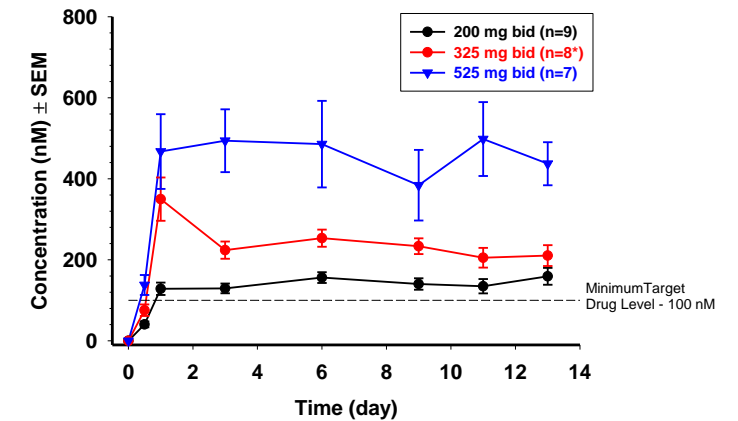
- All treatment-emergent adverse events (TEAEs) mild or moderate
- Most frequent TEAEs were GI related¹
- No serious adverse events (SAEs)
- No significant clinical/lab findings²

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

ANX1502 Clinical Development Plan Designed for Rapid Proof-of-Concept and Expansion

Oral tablet formulation provides significant market potential as a chronic treatment

FIRST-IN-HUMAN STUDY in Healthy Volunteers

- ✓ Generally safe & well tolerated
- ✓ Targeted serum drug levels reached with suspension formulation
- ✓ Supportive PD data in participants with higher C4d baseline measures
- ✓ Data support advancing tablet formulation of ANX1502

PROOF-OF-CONCEPT TRIAL in Patients

- Clinically validated indication
- Block complement activation triggered by cold agglutinins (CAD)
- **Rapid path to establish clinical POC on objective measures (e.g., hemoglobin) in small number of patients**
- Study to begin 1H 2024; readout in 2H 2024

PROGRAM EXPANSION upon Clinical POC

- **Autoimmune diseases with prior clinical validation and scientific rationale, including:**
- **CIDP:** Chronic inflammatory demyelinating polyradiculoneuropathy
- **MG:** Myasthenia gravis
- **MMN:** Multifocal motor neuropathy
- **Other** antibody-mediated autoimmune diseases

Next Wave Programs



Promising Next Wave Programs in Development Provide Optionality

HUNTINGTON'S DISEASE

80K patients globally

No approved treatments

ANX005 Ph2a Completed

- ✓ Rapid and sustained target engagement
- ✓ Reduction in markers of neuroinflammation
- ✓ Improved clinical function

**Poised for late-stage
Phase 2/3 development**

ALS

~200K patients globally

Current approved treatments
offer modest benefit or benefit in small patient
segment (SOD1 - ~2%)

ANX005 Phase 2a Completed

- ✓ Generally well tolerated
- ✓ Rapid, sustained target engagement
- ✓ Reduced downstream PD complement markers
- ✓ Achieved better outcomes in patients with higher baseline classical complement activity

**Poised for late-stage
Phase 2/3 development**

***A bold mission to help MILLIONS
of patients impacted by
complement-mediated diseases
of the body, brain and eye***



ANNEXON: Late-stage Clinical Platform for Classical Complement-Mediated Neuroinflammatory Diseases of the Body, Brain and Eye

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Runway through multiple mid- and late-stage clinical catalysts