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## GAME-CHANGING MEDICINES FOR COMPLEMENT-MEDIATED DISEASES

TOPLINE ARCHER PHASE 2 RESULTS OF ANX007 FOR GEOGRAPHIC ATROPHY

May 24, 2023

Nasdaq: ANNX

# Forward-looking Statements

This presentation and accompanying oral presentation contain "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.

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 and Quarterly Reports on Form 10-Q and our other filings with the Securities Exchange Commission (SEC). 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.

Comparisons to third-party studies are provided for illustrative purposes only. Differences exist between trial designs, study sites, subject populations and applicable products or candidates, and caution should be exercised when comparing outcomes across studies.

# A bold mission to free the body, brain and eye from complement-mediated disease

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# ARCHER: First Successful Neuroprotective Trial in GA; Statistically Significant Preservation of Visual Function in 1 Year

## ARCHER data support therapeutic potential and market opportunity for ANX007 in GA

- ✓ Validation of Annexon's founding discovery by Dr. Ben Barres that blocking C1q preserves neuronal connections (synapses) and nerve function
- ✓ ANX007 demonstrated statistically significant, dose-dependent protection against vision loss on two prespecified measures: BCVA & LLVD
- ✓ Functional preservation by ANX007 supported by multiple analyses, including in both foveal and non-foveal populations
- ✓ Primary end-point, rate of lesion growth did not reach statistical significance
- ✓ Results reflect ANX007's unique neuroprotective approach and distinction from biomarker measurement of lesion growth
- ✓ ANX007 generally well-tolerated as monthly and every-other-month treatment through 12 months
- ✓ Data support company's plans to engage with regulatory authorities to determine optimal path forward



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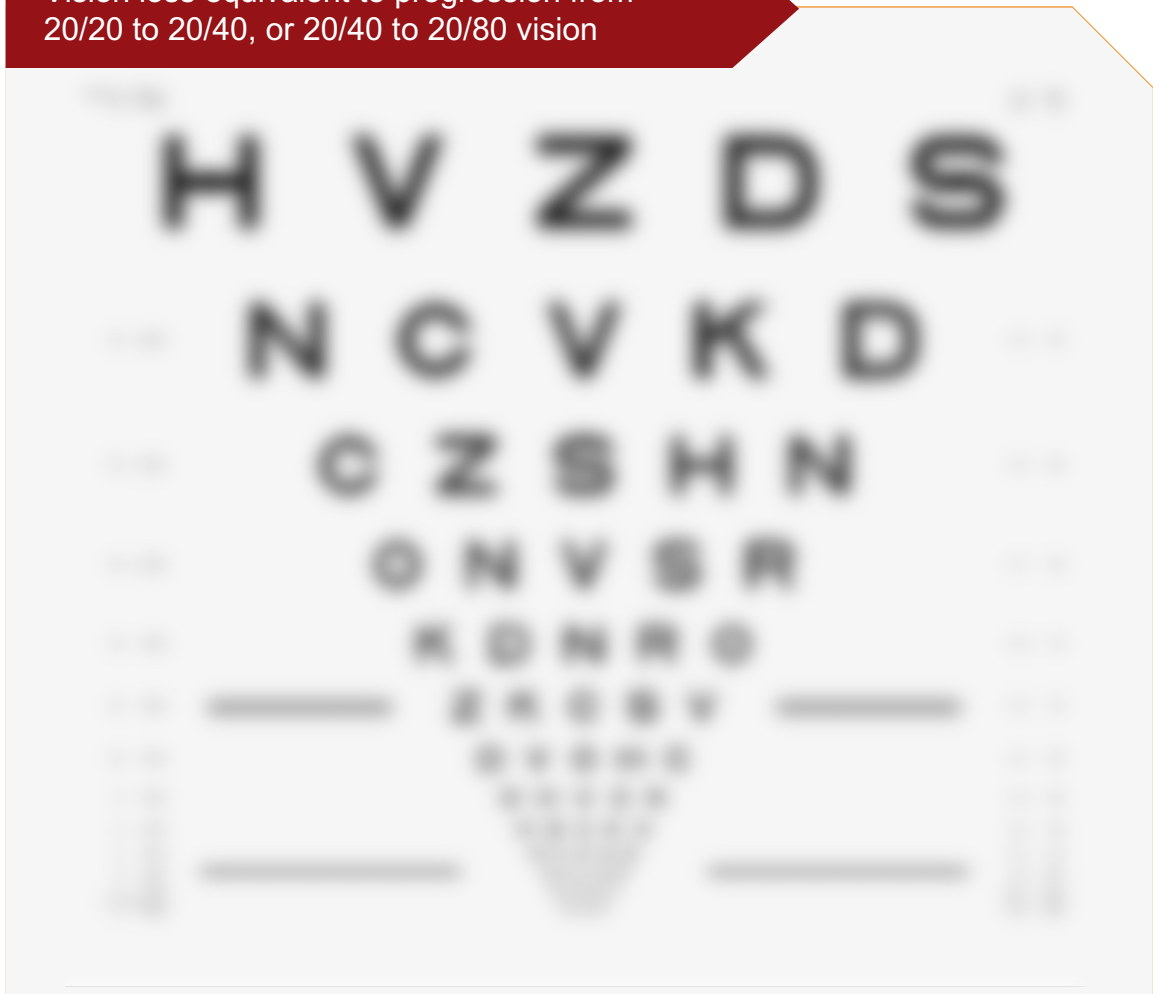
# Geographic Atrophy (GA): Progressive and Life-altering Disease that Remains the Leading Cause of Blindness in Elderly People

- Advanced form of age-related macular degeneration (AMD)
- Chronic and progressive neurodegenerative disease of the eye that leads to progressive and irreversible vision loss
- 1M people diagnosed in US; 5M people globally
- Diagnosis can be traumatic and impact the social and financial aspects of patients lives, including reading, daily activities and recognizing faces
- **No currently approved therapies have demonstrated preservation of visual function**
- **Urgent unmet need to protect against vision loss**

Vision loss equivalent to progression from 20/20 to 20/40, or 20/40 to 20/80 vision




Illustrative image



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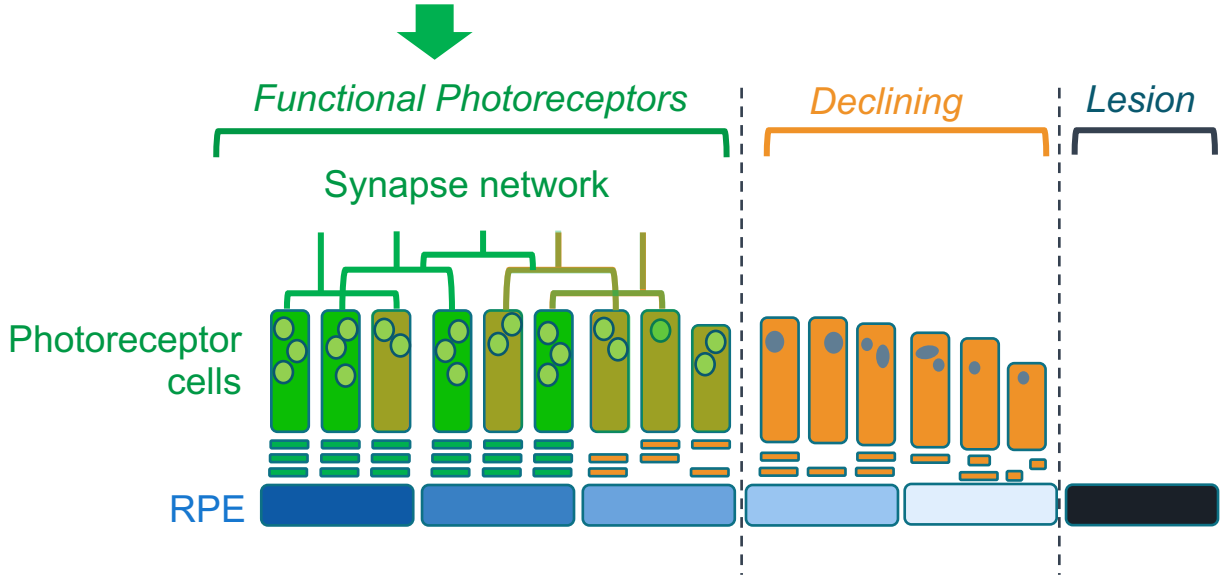
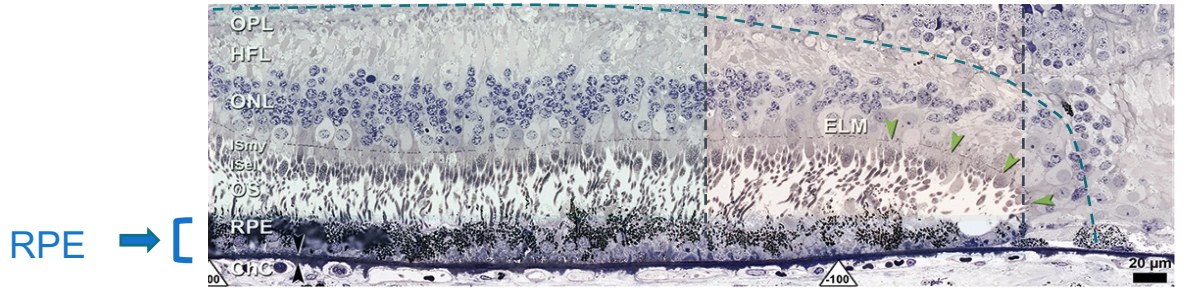
# Pioneering Approach Targeting Classical Complement to Protect Photoreceptor Cells, Synapses and Function

- GA is a disease of vision loss due to damage and loss of functional photoreceptor cells (neurons)
- Neuronal synapses (photoreceptor connections) are targeted by C1q for elimination, which occurs prior to neuronal loss[1]
- Blocking C1q with ANX007 protects photoreceptor cell synapses and their function[2, 3]
- Blocking C1q leaves normal clearance function of the lectin and alternative pathways in place[4]
- Loss in fundus autofluorescence (FAF) measures clearance of pigmented retinal epithelial cells (RPEs), a surrogate biomarker of lesion growth[5]
- FAF does not measure photoreceptor cells and does not strongly correlate with visual function[6]
- By targeting C1q, ANX007 is protecting the functional retina

Annexon mechanism targets and preserves photoreceptor cell synapses and their function




*Drawing and Image[7] of GA retinal tissue*




[1]Yednock, et al., 2022 doi: 10.1186/s40942-022-00431-y; Stevens, et al., 2007 doi 10.1016/j.cell.2007.10.036; [2]Tassoni, Society for Neuroscience, 2022 and Annexon data on file; [3]Jiao, et al., 2018 doi.org/10.1186/s13024-018-0278-0; [4]Annexon data on file; [5]Schmitz-Valckenberg, et al. 2008 doi: 10.1097/IAE.0b013e318164a907; [6]Heier, et al., 2020 doi.org/10.1016/j.oret.2020.01.019; Miaoling, et al., 2018 *Retina* 38:1937



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# ARCHER: Pivotal in Design and Well-executed Phase 2 Trial of ANX007 in Foveal & Non-foveal GA Patients

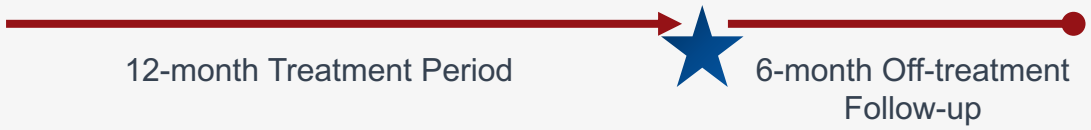
## Trial Design

- Randomized, double-masked, placebo-controlled trial (N=270)
- Patients stratified for lesion location and lesion size

ANX007 5.0 mg/eye once monthly (EM) (n=89)

ANX007 5.0 mg/eye every 2 months (EOM) (n=92)

Sham once monthly or every 2 months (n=89)




## Efficacy

- **Primary endpoint:** rate of GA lesion area change (slope) from baseline to month 12 in the study eye, as measured by FAF
- **Prespecified visual function endpoints:**
  15 letter loss a widely established functional endpoint

- ***Best Corrected Visual Acuity (BCVA):***
  Best corrected visual acuity assessed under normal light conditions
  - Higher BCVA = better vision

- ***Low Luminance Visual Acuity (LLVA):***
  Best corrected visual acuity assessed in low light conditions
  Higher LLVA = better vision

- ***Low Luminance Visual Deficit (LLVD):***
  Assesses health of outer retina from photoreceptors outer segments to synapses; LLVD = BCVA – LLVA
  Most relevant in patients with BCVA ≥ 55
  Lower LLVD = better vision



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# ARCHER Patient Demographics Generally Well-Balanced Across Sham and ANX007 Treatment Groups

| Characteristic | Sham Pooled (N=89) | ANX007 EM (N=89) | ANX007 EOM (N=92) |
|---|---|---|---|
| Age, mean (SD) | 79.8 (7.49) | 79.7 (8.64) | 80.5 (8.53) |
| Female, n (%) | 59 (66.3%) | 47 (52.8%) | 60 (65.2%) |
| Caucasian, n (%) | 87 (97.8%) | 87 (97.8%) | 89 (96.7%) |
| Foveal Lesion | 49.4% | 57.3% | 53.3% |
| GA Lesion Size ($mm^2$), mean (SD) | 7.28 (3.99) | 7.28 (3.96) | 7.53 (4.10) |
| GA Lesion < 7.5 $mm^2$ | 61.8% | 58.4% | 57.6% |
| Fellow Eye CNV | 22.5% | 24.7% | 17.4% |
| Mean BCVA, mean (SD) | 58.5 (16.2) | 58.8 (17.2) | 58.3 (15.0) |
| Multifocality, n (%) | 65 (73.0%) | 61 (68.5%) | 67 (72.8%) |

- Patient age, sex and ethnicity consistent with other GA studies
- Generally balanced between foveal and non-foveal patients
- CNV in fellow eye: 17.4% - 24.7%
- Drop-out rate consistent with other GA studies
  - Sham: 13.5%
  - Monthly: 18.0%
  - EOM: 16.3%



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# ANX007: ARCHER Trial Visual Function Data in Geographic Atrophy

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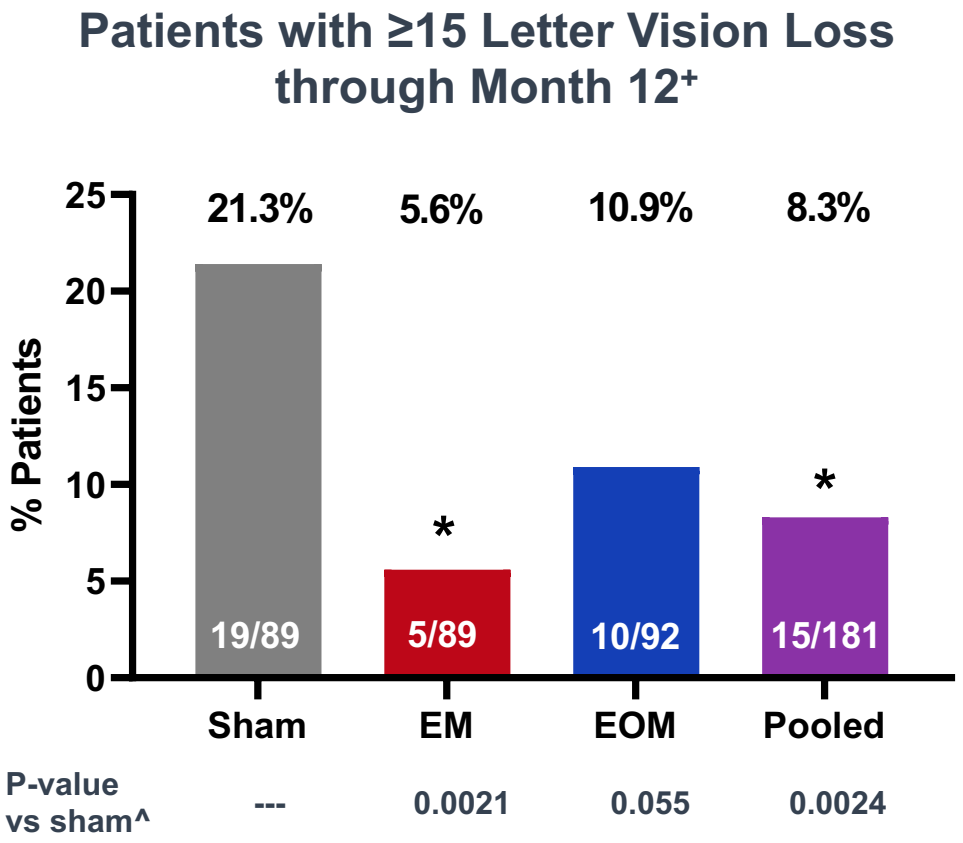
# BCVA through Month 12: ANX007 Significantly Protected GA Patients Against Vision Loss




- 15-letter loss: clinically meaningful endpoint
- Widely established functional endpoint
- Dose-dependent response
- Prespecified in ARCHER analysis

+Persistent for two consecutive visits at any time through month 12 or at last visit
^Nominal, from a Chi-square test in ITT population



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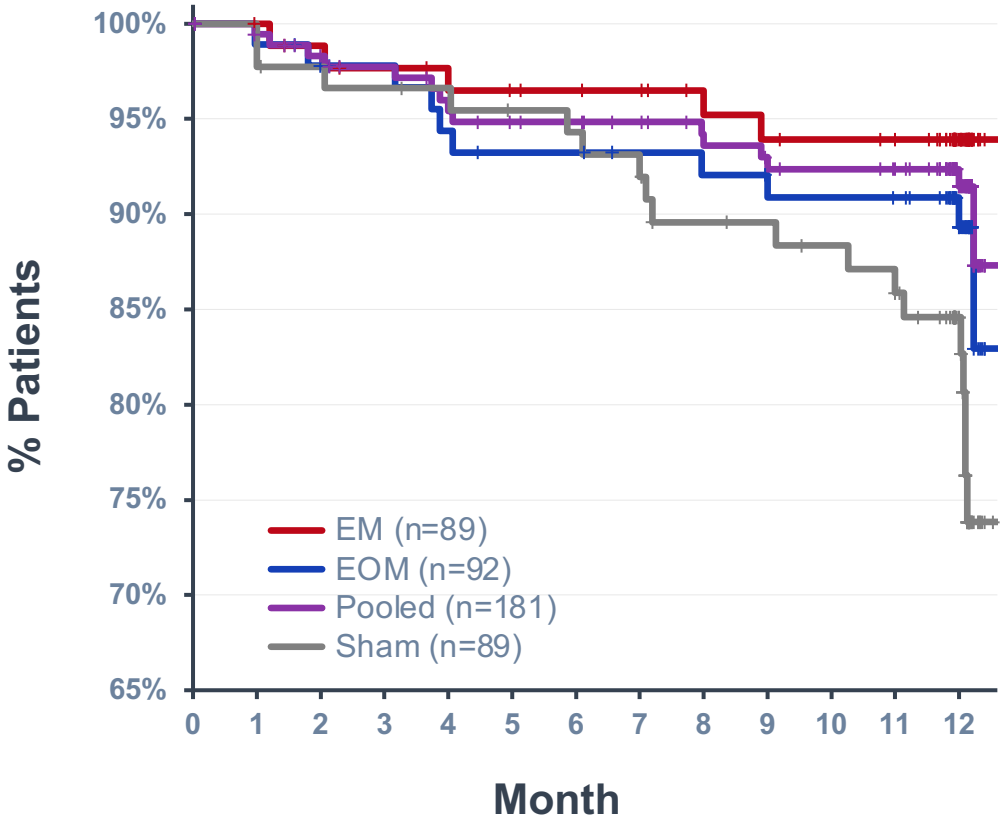
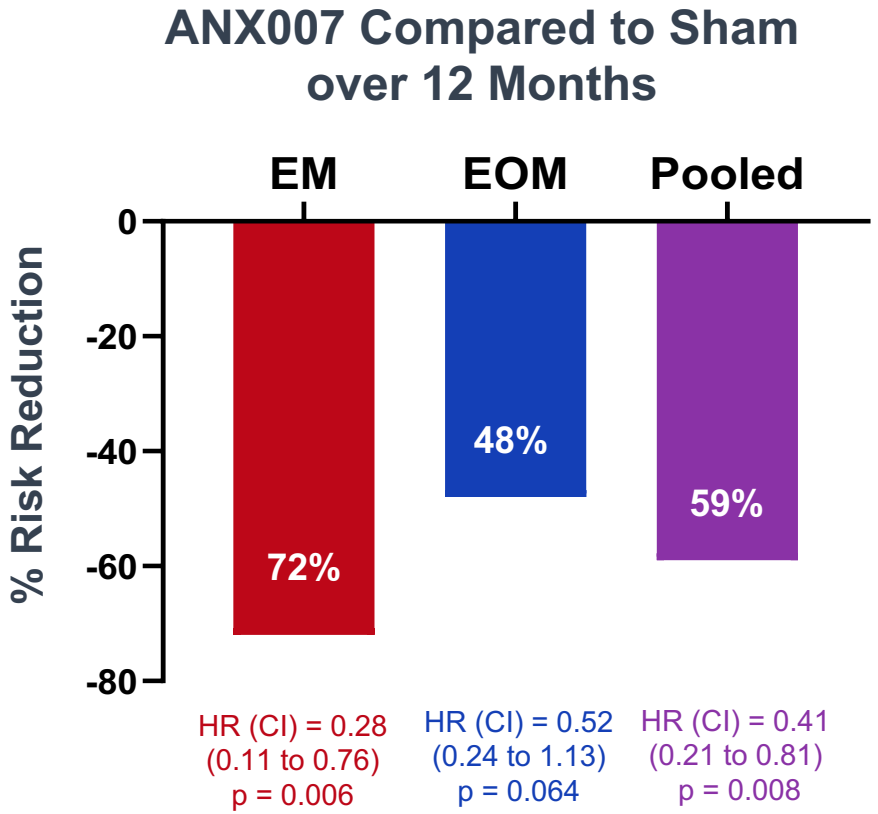
# BCVA: 72% Statistically Significant Reduction in Risk of ≥15 Letter Vision Loss* with ANX007 Monthly Treatment




*Persistent for two consecutive visits at any time through month 12 or at last visit. HR, hazard ratio. Log-rank test (versus Sham) p-values are presented.



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# BCVA by Lesion Location: ANX007 Protected Against Vision Loss Across Patient Subgroups – Both Foveal or Non-Foveal

## Data Support Treatment Opportunity in All-comer Population

**Patients with ≥15 Letter Vision Loss through Month 12⁺**

| Location | Sham | EM | EOM | ANX007 Pooled |
|---|---|---|---|---|
| Foveal | 25.0% (11/44) | 5.9% (3/51) | 18.4% (9/49) | 12.0% (12/100) |
| Non-Foveal | 17.8% (8/45) | 5.3% (2/38) | 2.3% (1/43) | 3.7% (3/81) |
| p-value vs sham^ | -- | 0.0019 | 0.0439 | 0.0015 |

⁺Persistent for two consecutive visits at any time through month 12 or at last visit
^Nominal, from a Cochran-Mantel-Haenszel test (General Association) in ITT population



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# LLVA: ANX007 Protected Against Vision Loss Further Supported by Additional Measures of Visual Function

## BVCA Assessed in Low Light Conditions

### Patients with ≥15 Letter Loss in LLVA through Month 12[+]

| | Sham | EM | EOM | ANX007 Pooled |
|---|---|---|---|---|
| | 20.3% (16/79) | 10.1% (8/79) | 11.8% (10/85) | 11.0% (18/164) |
| p-value vs Sham^ | -- | 0.076 | 0.14 | 0.051 |

[+]Patients with at least one post baseline LLVA measurement
^Nominal, from a Chi-square test in ITT population



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# BCVA by Retinal Health Status: ANX007 Protected Against Vision Loss Across Patient Subgroups – Healthier or Less Healthy Eyes

## Data Support Treatment Opportunity Early in Disease

**Patients with ≥15 Letter Vision Loss through Month 12⁺**

| | Sham | EM | EOM | ANX007 Pooled |
|---|---|---|---|---|
| LLVD <30 (healthier) | 16.9% (10/59) | 0.0% (0/56) | 6.3% (3/48) | 2.9% (3/104) |
| LLVD ≥30 (less healthy) | 30.8% (8/26) | 16.1% (5/31) | 16.3% (7/43) | 16.2% (12/74) |
| p-value vs sham^ | -- | 0.0016 | 0.029 | 0.0009 |

⁺Persistent for two consecutive visits at least 20 days apart or at last visit
^Nominal, from a Cochran-Mantel-Haenszel test (General Association) in ITT population



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# LLVD: ANX007 Protected Against Vision Loss, Further Supported by Additional Measures of Visual Acuity

## Low Luminance Visual Deficit is a Marker of Deteriorating Retinal Health

### Patients with ≥15 Letter Worsening in LLVD through Month 12

| BCVA | Sham | EM | EOM | ANX007 Pooled |
|---|---|---|---|---|
| ≥55 (better vision) | 25.5% (13/51) | 9.4% (5/53) | 16.4% (9/55) | 13.0% (14/108) |
| <55 (impaired vision) | 17.9% (5/28) | 7.7% (2/26) | 3.3% (1/30) | 5.4% (3/56) |
| p-value vs sham^ | -- | 0.0161 | 0.0597 | 0.0091 |

^Nominal, from a Cochran-Mantel-Haenszel test (General Association) in ITT population who had at least one post-baseline LLVA assessment

# ANX007: ARCHER Trial
# GA Lesion Biomarker Data

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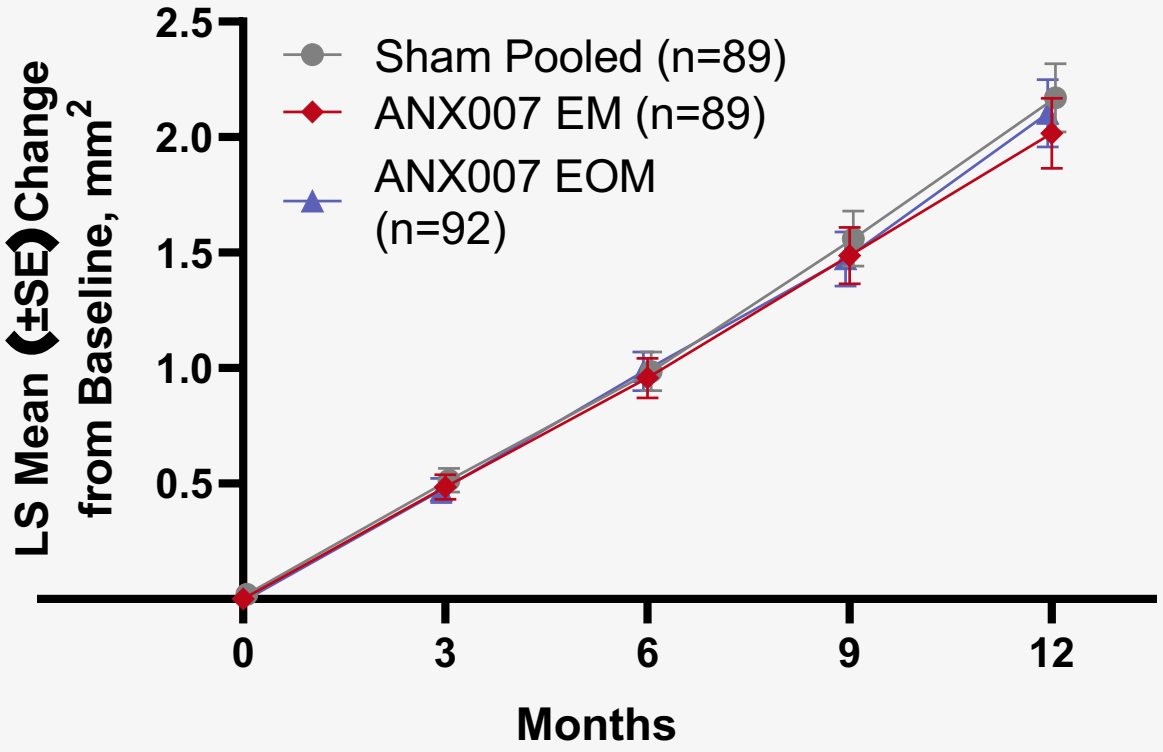
# ANX007 Did Not Significantly Reduce Lesion Area, a Surrogate Biomarker of Functional Change in GA

## GA Lesion Area Change from Baseline to Month 12+




## GA Area Change from Baseline at 12 Month

| Arm | mm² | % | p-value |
|---|---|---|---|
| Sham | 2.15 | --- | --- |
| EM^ | 2.02 | 6.2% | 0.526 |
| EOM^ | 2.12 | 1.3% | 0.896 |
| ANX007 Pooled* | 2.07 | 3.7% | 0.673 |

^3-arm MMRM model
*2-arm MMRM model

+The least-square (LS) mean, its standard error (SE), and p-value 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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# ANX007: ARCHER Trial Safety Results

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# ANX007 Monthly & EOM Treatment was Generally Well-Tolerated

| Adverse Events of Special Interest n (%) | Sham Pooled (N=89) | ANX007 Monthly (N=89) | ANX007 EOM (N=92) |
|---|---|---|---|
| Choroidal Neovascularization | 3 (3.4%) | 4 (4.5%) | 4 (4.3%) |
| Endophthalmitis | 0 | 1 (1.1%) | 2 (2.2%) |
| Intraocular Inflammation | 0 | 2* (2.2%) | 1^ (1.1%) |
| Retinal Vascular Occlusion | 0 | 0 | 1 (1.1%) |
| Ischemic Optic Neuropathy | 0 | 0 | 0 |

- Low incidence of CNV consistent across all 3 study arms
- Incidence of adverse events of special interest generally consistent with other IVT studies
  - 3 cases of endophthalmitis, related to IVT procedure
  - 3 cases of intraocular inflammation, not associated with retinal vasculitis
- 1 case of retinal artery occlusion, not associated with retinal vasculitis

*1 case iritis, 1 uveitis/vitreous debris
^1 case vitritis

# ANX007: ARCHER
# Phase 2 Trial Summary

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# ANX007: First-in-Kind Neuroprotective Approach to Slowing Clinical Progression in Patients with Geographic Atrophy

## First pre-specified demonstration of protection against vision loss in GA patients

- ✓ Neuroprotective effect of ANX007 translated into statistically significant, dose-dependent protection against vision loss in both foveal and non-foveal patients
- ✓ 72% reduction in risk of ≥15-letter loss with ANX007 monthly treatment (statistically significant), using BCVA, a widely-established functional endpoint
- ✓ Results supported by multiple pre-specified visual function measures
- ✓ ANX007 demonstrates favorable safety in a trial of 270 patients
- ✓ ARCHER results mark the 3rd trial to support Annexon's founding hypothesis on neuroprotection, and validates that classical complement inhibition works by a mechanism distinct from downstream complement inhibition
- ✓ Planning for regulatory interactions to determine optimal path forward for ANX007

**20%**

of sham patients in ARCHER lost ≥15 letters (~50% of their vision) in just 1 YEAR

Urgency remains to deliver a treatment that protects against vision loss, regardless of lesion growth



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*To the patients, families, caregivers, physicians and medical teams who participated in our trial, we are eternally grateful for your support and contributions!*

*To our employees, collaborators and advisors, thank you for your Warrior Spirit and All For One commitment!*



# Closing Remarks by Invited Speaker: Charles C. Wykoff, MD, PhD

- Deputy Chair for Ophthalmology and Clinical Associate Professor, Blanton Eye Institute, Houston Methodist Hospital, Weill Cornell Medical College
- Director of Research, Retina Consultants of Texas
- Chairman of the Research and Clinical Trials Committee, Retina Consultants of America
- Author and publisher of more than 250 peer-reviewed scientific manuscripts, book chapters, national meeting presentations and abstracts
- Awarded the American Academy of Ophthalmology Secretariat, Achievement & Senior Achievement Awards, and the American Society of Retina Specialists Honor, Senior Honor, and Presidential Honor Awards
- M.D. from Harvard Medical School, Ph.D. from Oxford University
- Investigator in ARCHER Phase 2 clinical trial of ANX007 for treatment of GA

# Multiple Annexon Programs Advancing in Mid- to Late-stage Trials

| THERAPEUTIC AREA | INDICATION | CANDIDATE | PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 | 2023 ANTICIPATED MILESTONES |
|---|---|---|---|---|---|---|---|
| **FLAGSHIP PROGRAMS** | | | | | | | |
| Autoimmune | Guillain-Barré Syndrome | **ANX005** | | | | | Complete Phase 3 enrollment in 2H 2023 |
| | Autoimmune Indications | **ANX1502** | | | | | Complete MAD trial and initiate POC trial in patients |
| Ophthalmic | Geographic Atrophy | **ANX007** | | | | | ✓ Reported positive Phase 2 results |
| Neuro | Huntington's Disease | **ANX005** | | | | | Initiate Phase 2/3 trial 2023 |
| **NEXT WAVE** | | | | | | | |
| | Amyotrophic Lateral Sclerosis (ALS) | **ANX005** | | | | | Report Phase 2 data in 2023 |
| | Lupus Nephritis (LN) | **ANX009** | | | | | Report Phase 1 data in 1H 2023 |
| | Autoimmune/ Neuro | **ANX105** | | | | | Report Phase 1 data in 2023 |



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