ANNEXON biosciences

STOPPING Complement-Driven Diseases

AT THE START

COMPANY PRESENTATION I September 2021

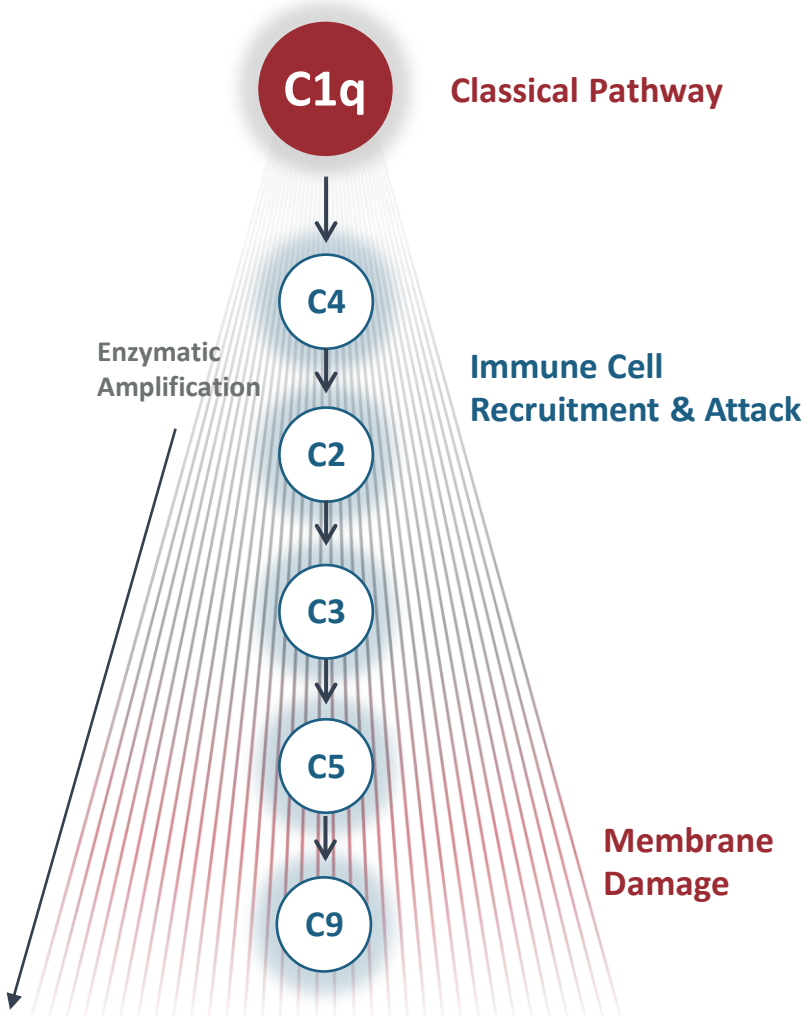
Forward-looking Statements

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 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 drugs 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.

Pioneering a Class of New Complement Medicines by Stopping C1q and Classical Complement at the Start



- **Targeting Enhanced Efficacy & Safety** by blocking downstream inflammation & tissue damage at the start
- **Pluri-Potential Across 3 Therapeutic Areas** - autoimmune, neurodegeneration & ophthalmology
- **Multiple Delivery Solutions** to fully inhibit the cascade with diverse routes of administration

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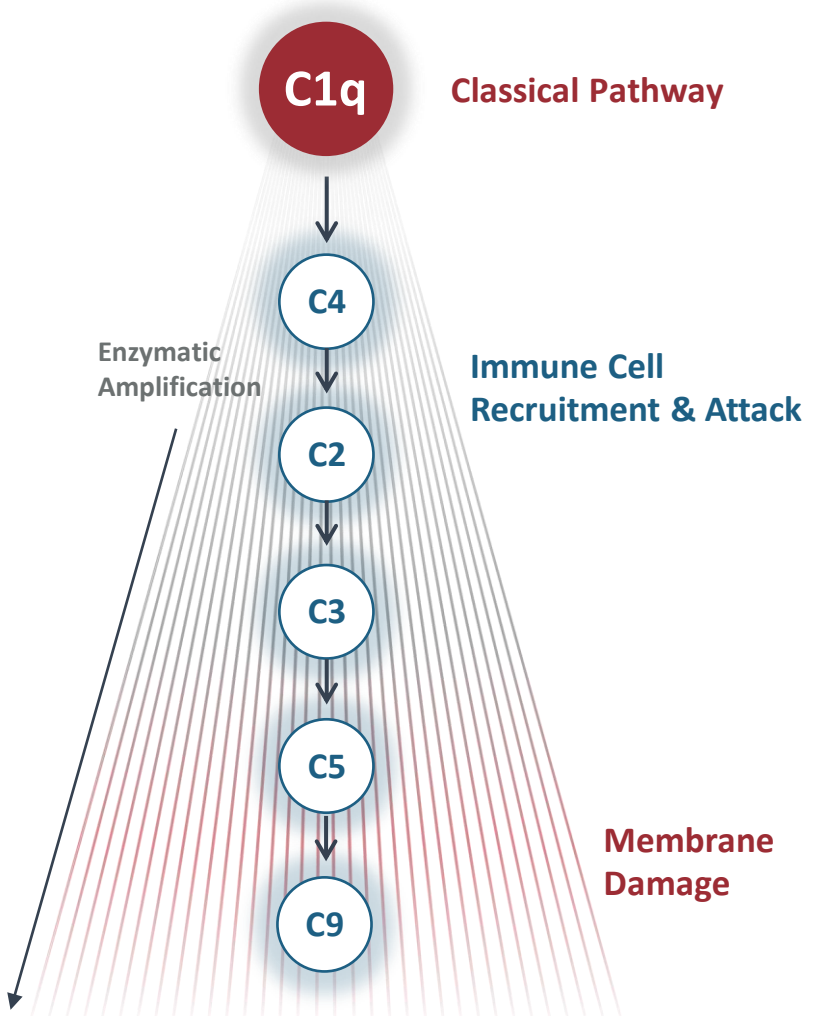
Foundation Established for Classical Complement Platform – Poised to Drive Significant Value



Treated >200 subjects with 3 distinct drug candidates in autoimmune, neurodegeneration and ophthalmology indications

- ✓ **Consistent translation of preclinical data** to the clinic
- ✓ Drug candidates have been **well-tolerated**
- ✓ **Full C1q inhibition** in periphery, across BBB & in the eye
- ✓ **Full inhibition of downstream classical complement activity** through C3, C5 and C9
- ✓ **Demonstrated impact** on autoimmune & neurodegenerative disease processes, including **POC in GBS placebo-controlled trial**

7 MID-TO-LATE STAGE CLINICAL READOUTS ANTICIPATED OVER NEXT 2 YEARS

Annexon data on file

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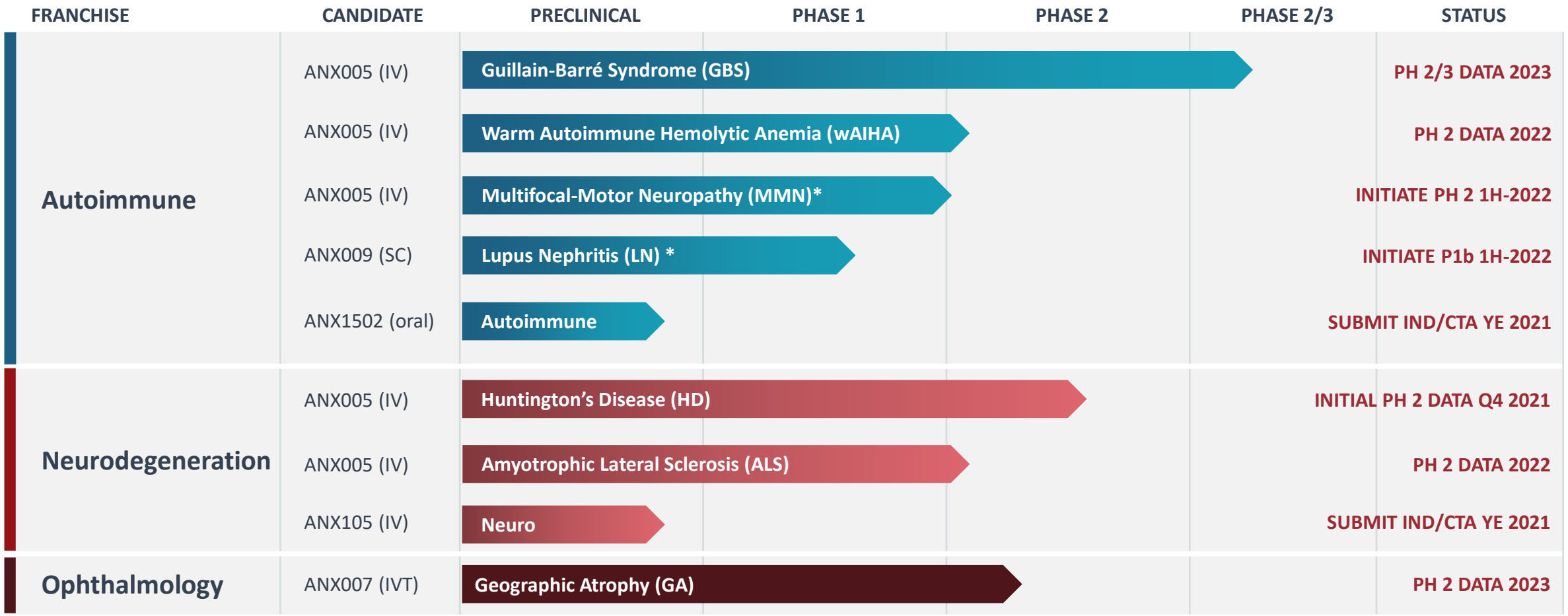
Diverse Wholly-Owned Classical Complement Pipeline

3 Therapeutic Franchises. 7 Clinical Trials. 5 Drug Candidates. 3 Clinical Candidates.



IV, intravenous; IVT, intravitreal; SC, subcutaneous.

* Newly announced indications

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Line of Sight to Significant Additional Opportunities

Platform opportunity across breadth of mechanistically-related diseases

AUTOIMMUNE

wAIHA & LN

- **CAD** (Cold Agglutinin Disease)
- **Bullous Skin Diseases**
- **HIT** (Heparin-Induced Thrombocytopenia)
- **Rheumatoid Arthritis**
- **Crohn's Disease**

GBS & MMN

- **CIDP** (Chronic Idiopathic Demyelinating Polyneuropathy)
- **PMS** (Progressive Multiple Sclerosis)
- **ON** (Optic Neuritis)
- **MG** (Myasthenia Gravis)

NEURODEGENERATION

HD & ALS

- **FTD** (Frontal Temporal Dementia)
- **SMA** (Spinal Muscular Atrophy)
- **AD** (Alzheimer's Disease)
- **TBI** (Traumatic Brain injury)

OPHTHALMOLOGY

GA

- **GLA** (Glaucoma)

● Current Indications ● Sample Follow-on Indications

Targeting C1q and the Classical Complement Pathway

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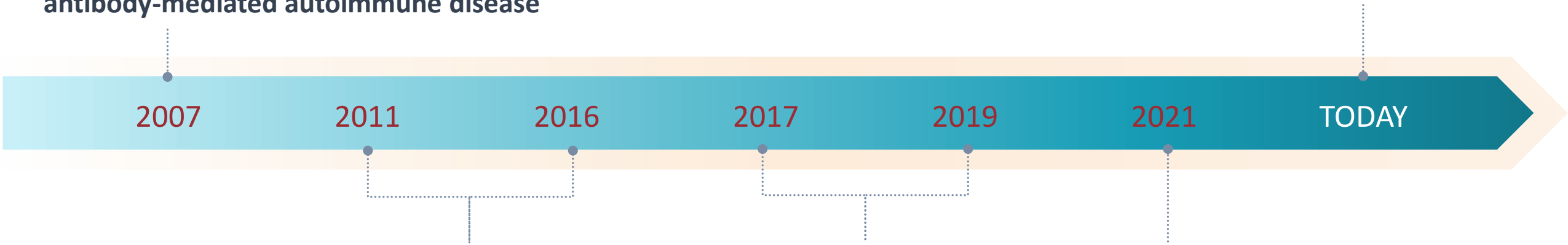
Annexon: Unique Domain Expertise in the Classical Pathway

Annexon co-founder **Ben Barres discovered that C1q drives synapse loss and disease progression** in neurodegenerative disorders

C1q also known to drive tissue damage in **antibody-mediated autoimmune disease**

Advancing Diverse Portfolio with biomarker-led development & multiple fit-for-purpose therapeutics



Annexon developed ANX005 (IV) and other classical pathway inhibitors (C1q, C1s, C2, C4)

Demonstrated **importance of inhibiting C1q at the top of the pathway**, blocking activity before it starts in the PNS, CNS & eye

ANX005: clinical **POC in GBS**, including full target engagement in periphery & centrally, and NfL reduction

ANX007: Full target engagement in the eye with intravitreal administration in glaucoma patients

ANX009: Full target engagement in the blood space with subcutaneous administration in healthy volunteers

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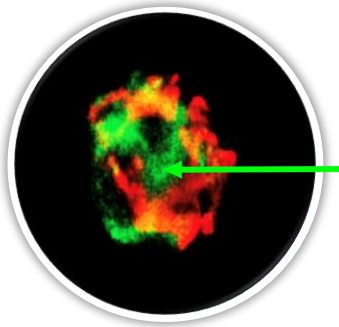
C1q Is a Key Driver of Complement-Mediated Disease

Initiator of aberrant complement activity in autoimmune and neurodegenerative diseases

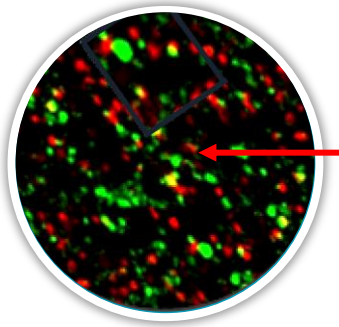
- **C1q directly binds to and accumulates on tissues** in complement-mediated diseases
- **C1q anchors complement activation** on tissue surface **and drives disease processes**
- **Inhibiting C1q at the top** of the classical pathway **blocks downstream inflammation & tissue damage**

C1Q BINDING TO TISSUES IN DISEASE



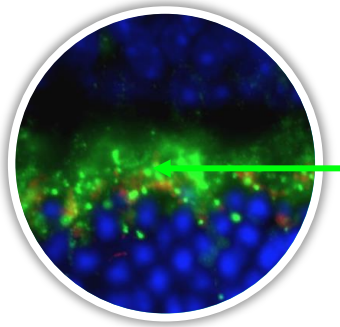
GBS

C1q Targeting the Neuromuscular Junction[1]



HUNTINGTON'S DISEASE

C1q Targeting Striatal Synapses[2]



GEOGRAPHIC ATROPHY

C1q Targeting Photoreceptor Synapses[3]

[1]Halstead, et al. 2004 *Brain* 127: 2109–2123 [2]Jia, et al, 2018 *Mol Neurodegen* 14:45 [3]C1q bound to photoreceptor synapses in aged mice: Annexon data on file

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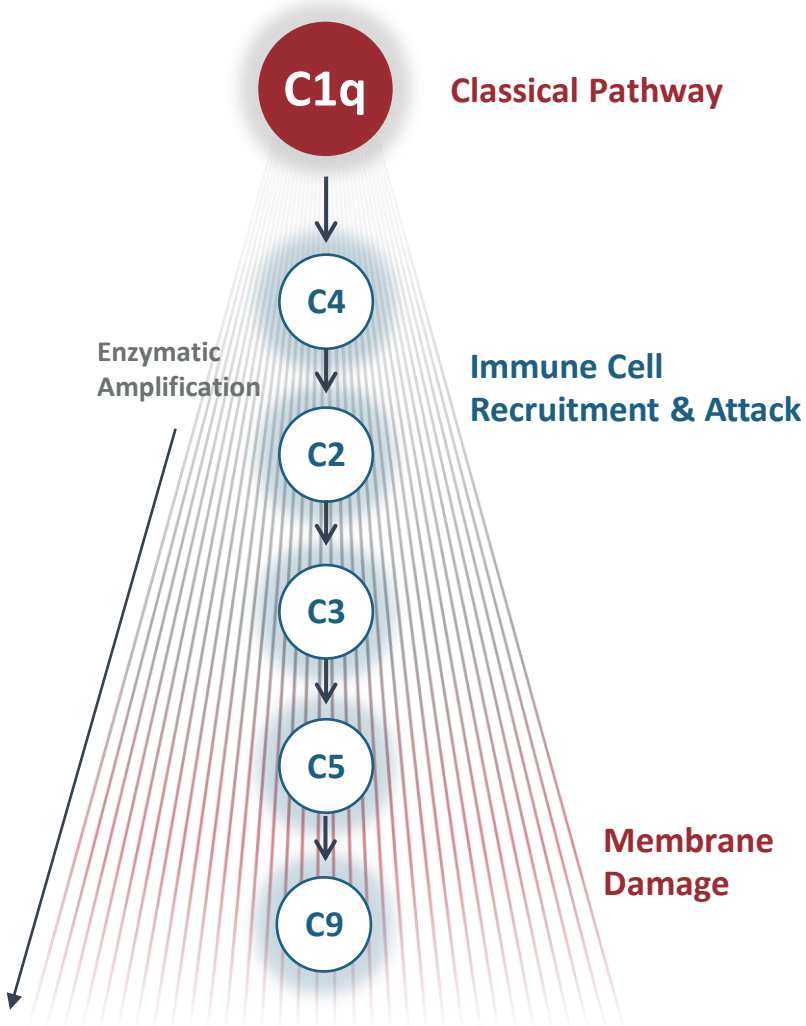
C1q Inhibition Stops Classical Complement Activity at the Start

Prevents downstream activation of all tissue-damaging components



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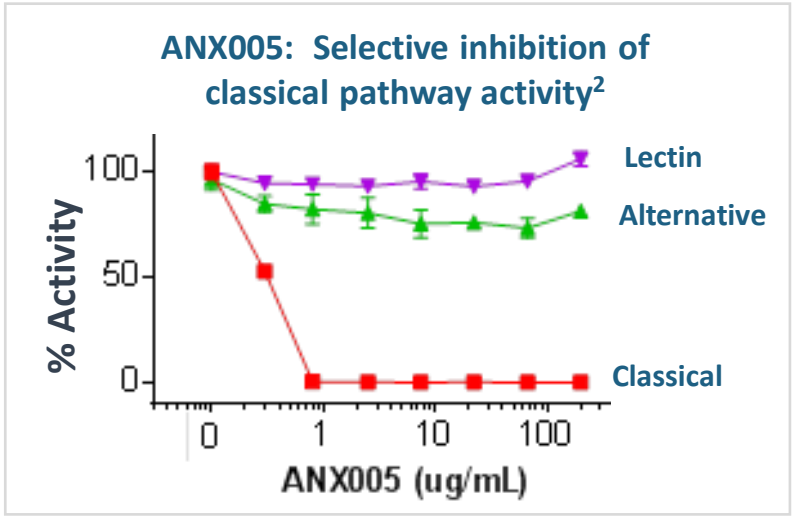
- **Targeting Enhanced Efficacy:** Shuts down all tissue-damaging components of classical pathway (C1q, C4, C3, C5, C9)[1]
- **Targeting Enhanced Safety:** Allows normal immune functions of lectin and alternative complement pathways[1]



[1]Annexon data on file
[2]Wieslab assay; Annexon data on file

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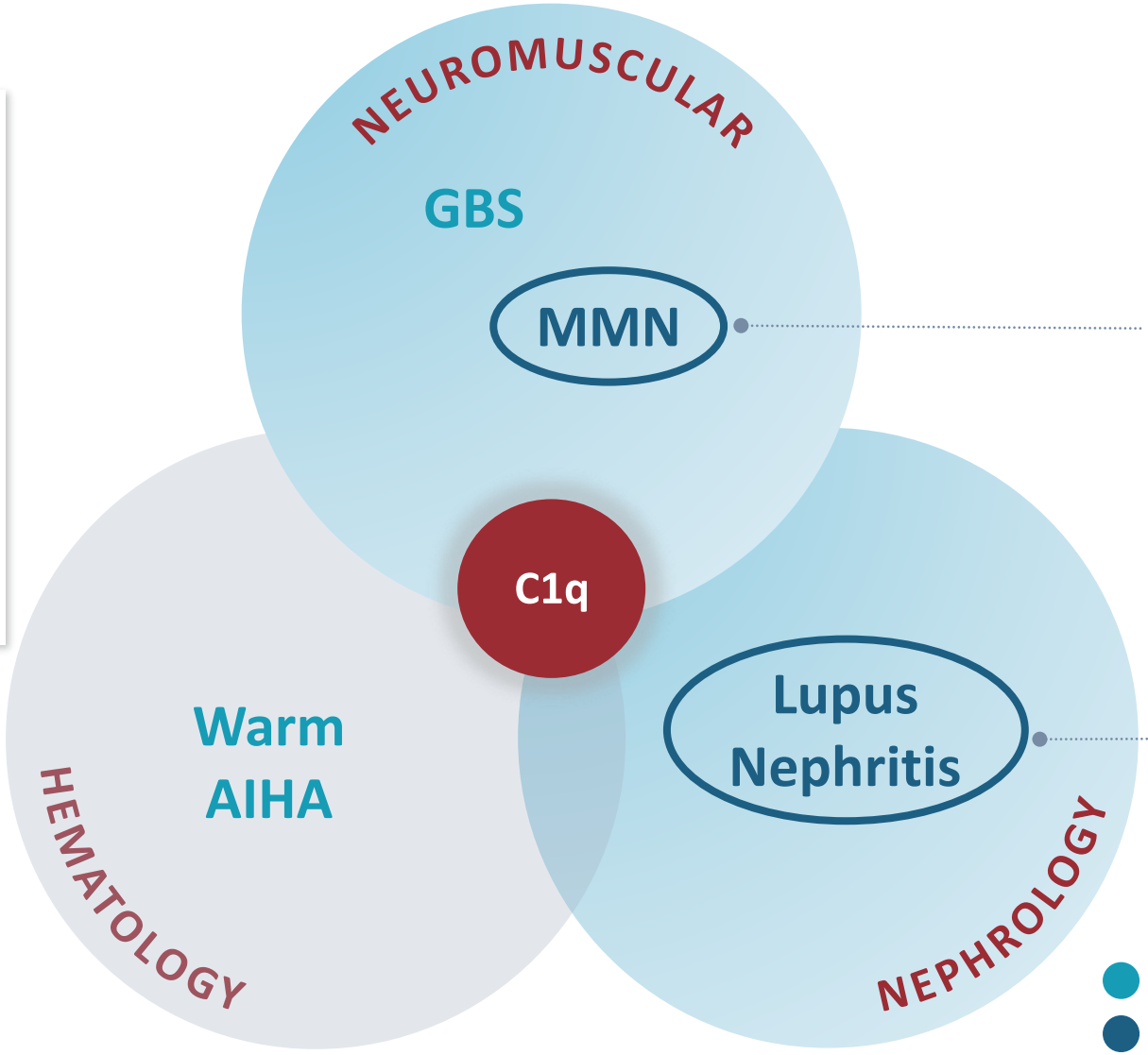
Improving Patient Outcomes in Devastating Autoimmune Diseases

- Guillain-Barré Syndrome
- Warm Autoimmune Hemolytic Anemia
- Multifocal Motor Neuropathy
- Lupus Nephritis

Broad Therapeutic Potential of Anti-C1q in Autoimmune Diseases

Demonstrated aberrant classical complement pathway activation in multiple autoimmune diseases with high unmet need



Leveraging GBS POC Data in mechanistically-related MMN

Precision-Medicine Approach in Lupus Nephritis

Current Beachhead Indications

New Indications

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ANX005 Proof of Concept in GBS

GBS is a severe disease resulting from autoantibody attack on peripheral nerves, triggering complement (C1q) and neurodegeneration

TRIAL SUMMARY

- ✓ **Rapid and Complete Target Engagement** in periphery and CSF enabling further study of GBS and additional C1q-mediated diseases
- ✓ **Early and Statistical Decline of Serum NfL,** a well-accepted marker of neurodegeneration in GBS and other neurological diseases (e.g., HD, ALS)
- ✓ **Consistent positive trends across key GBS clinical measures**

Fast Track & Orphan Drug Designations

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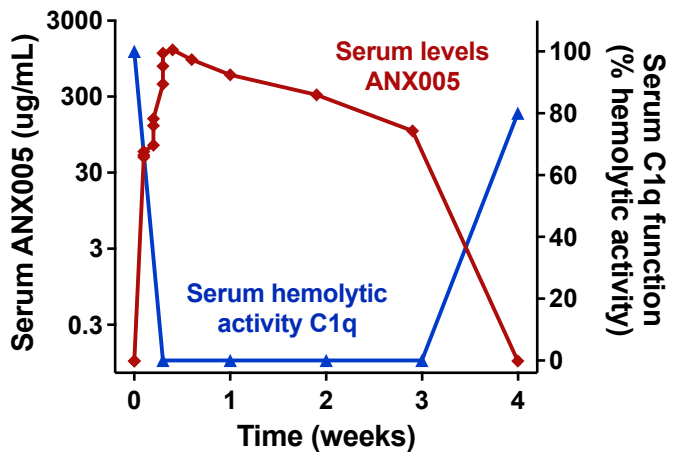
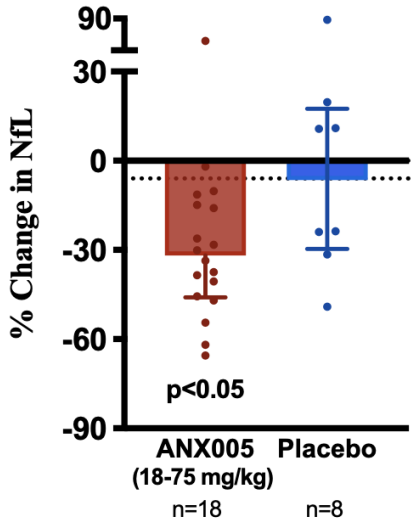
ANX005 Reduced NfL and Improved Outcomes in Patients with GBS

Full C1q Inhibition in Blood



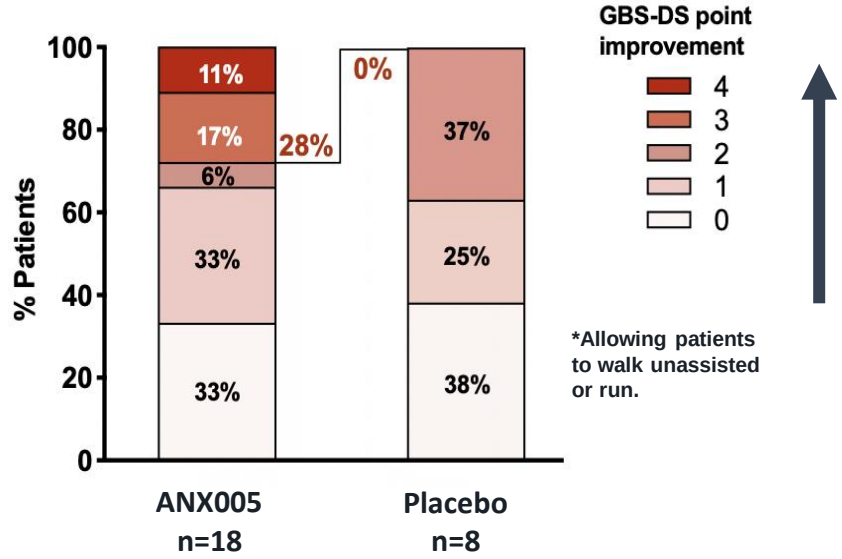
Data From a Patient Receiving 75 mg/kg (Target Ph 2/3 dose)

Significant Early NfL Reduction (Weeks 2-4)



High-Dose ANX005 (18-75 mg/kg) vs Placebo

28% of High-Dose Patients Improved by ≥3 pts on GBS-Disability Scale by Week 8*



High-Dose ANX005 (18-75 mg/kg) vs Placebo

Annexon data on file

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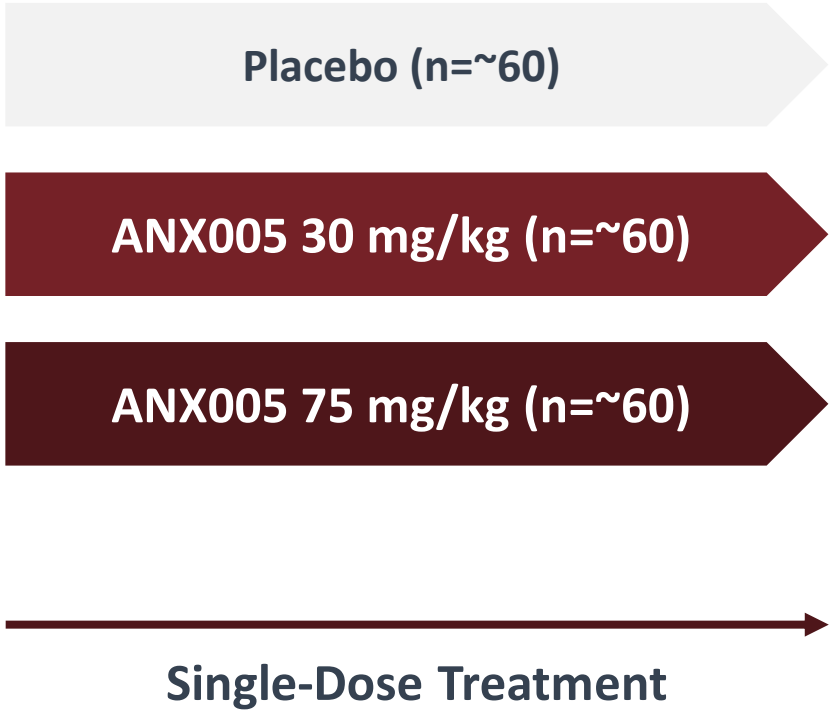
Ongoing Placebo-Controlled Phase 2/3 GBS Trial

Fast Track and Orphan Drug designations granted



- **Randomized, double-blind trial** (N=~180)
- **Primary endpoint:** GBS Disability Scale
- **Patients stratified for baseline muscle strength and time from symptom onset**

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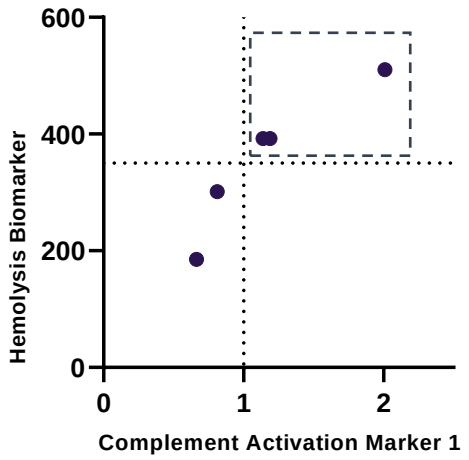
Targeting Life Threatening RBC Autoantibody Attack in wAIHA

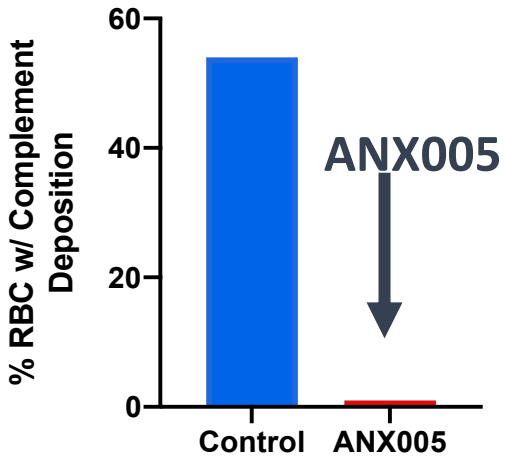
- Autoantibodies attack and destroy RBCs, resulting in anemia, can develop rapidly or gradually
- Complement activation amplifies RBC destruction in certain patients
- Targeted strategy to select patients who meet specific biomarker criteria of complement activation

Enriching for wAIHA Patients with Excess Classical Complement Activity In Vivo and In Vitro

Ongoing Phase 0:
Patient selection based on classical complement signature



ANX005 inhibits complement deposition on RBC with wAIHA patient serum *in vitro*



ACTIVITY FULLY INHIBITED BY ANX005

- **Detected complement-activating antibodies in 4 of 12 wAIHA patients** (consistent with literature ~30 %)
- **Activity fully inhibited by ANX005 *in vitro***

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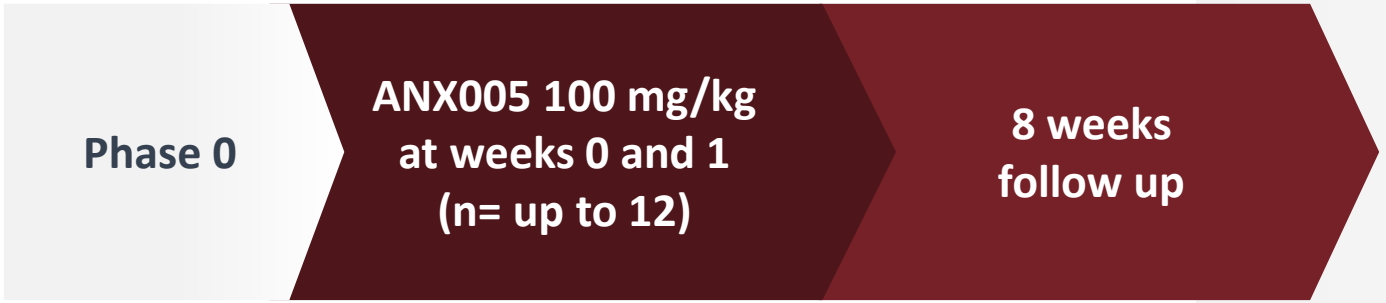
Precision Medicine Approach Underway in wAIHA Phase 0/2 Trial



- **Open label trial** (n= up to 12)
- Using **Phase 0 'feeder' study to identify/select patients for Phase 2**
- **Objective endpoints:** safety, PK/PD, hemolysis markers, improvement in hemoglobin

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Tackling Patient Disability in Devastating Neurodegenerative Diseases

ANX005

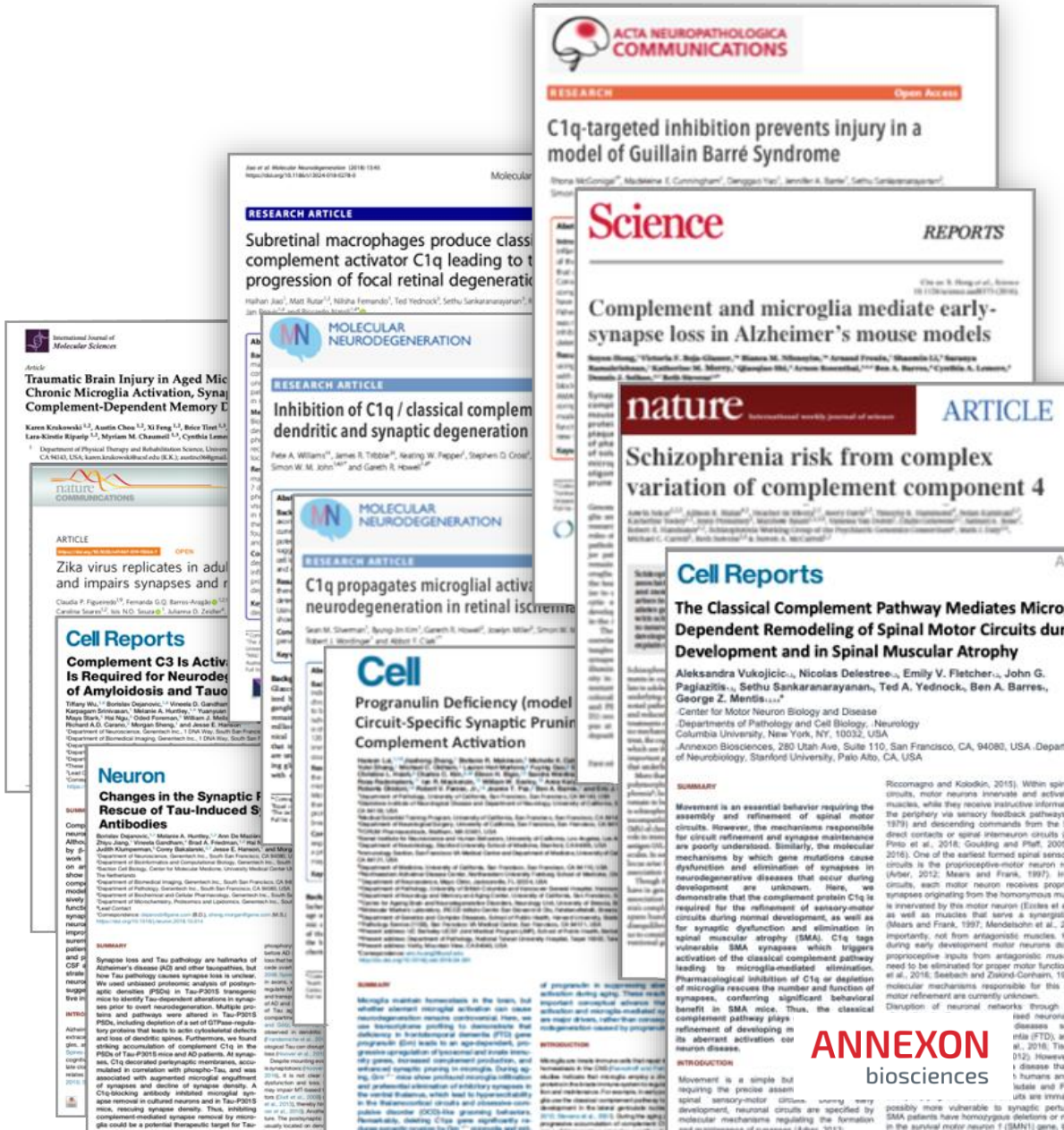
Huntington’s Disease

Amyotrophic Lateral Sclerosis

Strong Support for Role of C1q as a Major Driver of Synaptic Loss and Neurodegeneration

Original discoveries of Annexon co-founder, the late Dr Ben Barres, on the **role of C1q in neurodegenerative diseases**

- **Synapse loss is a major driver of neurological disability and blindness**
- **Precedes loss of neurons**
- **Correlates with functional loss/cognitive decline**

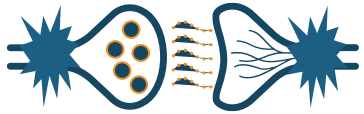


Targeting Aberrant C1q Activity in Complement-mediated Neurodegeneration

Normal
C1q Function

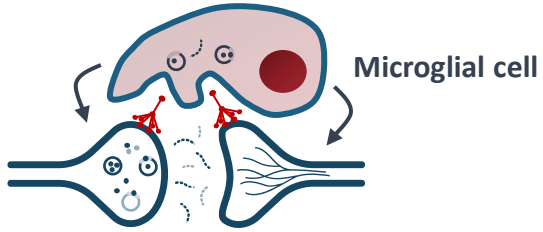
Sculpts the brain and retina in development

Aberrant
Triggers



Neuronal Stress

Disease
C1q Dysfunction



Removes functioning synapses
Anti-C1q potentially protects against synaptic loss

C1q blockade results in functional benefits in multiple disease models, including:*

- Huntington's Disease[1]
- Alzheimer's Disease[2]
- Spinal Muscular Atrophy[3]
- Glaucoma[4]
- Geographic Atrophy (AMD)[5]
- Frontotemporal Dementia[6]
- Traumatic Brain Injury & Stroke[7]

*[1]Wilton and Stevens, Harvard, *unpublished*. [2]Fonseca, 2004, *J Neurosci*; Hong, 2016, *Science*; Dejanovic, 2018, *Neuron*; [3]Vukojicic, 2019, *Cell Reports*; [4]Howell, 2011, *J Clin Inves*; Williams, 2016, *Mol Neurodegen*; [5]Jiao, 2018, *Mol Neurodeg*; [6]Lui, 2016, *Cell*; [7]Krukowski, 2018, *Int.J Mol Sci*; Jeanne Paz, UCSF, *unpublished*

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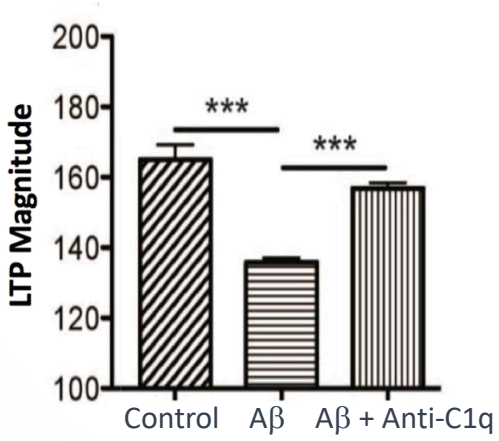
Blocking C1q Provides Synaptic and Functional Benefit in Several Models of Neurodegeneration

Protects Synaptic Function in Alzheimer's Disease (Aβ models)

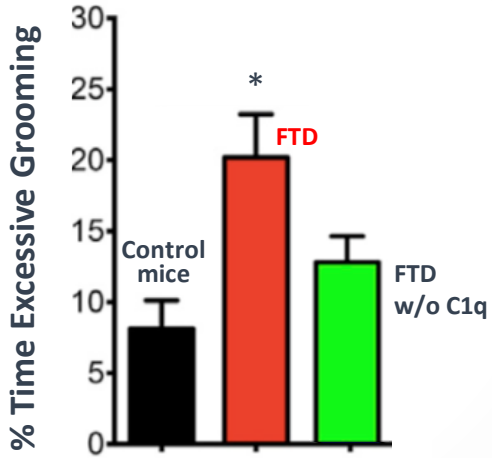
Mouse model with Aβ overexpression



Hong, et al., Stevens Science 2016

Prevents Obsessive Behavior in Frontotemporal Dementia

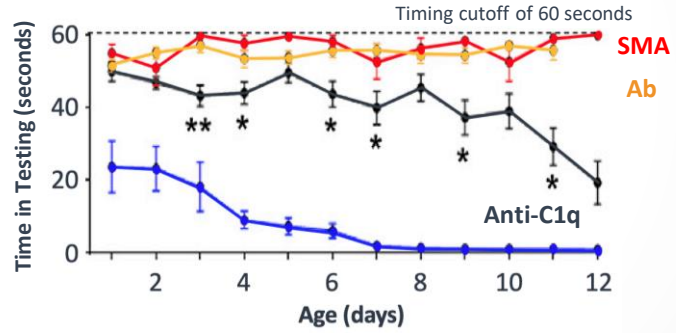
Mouse model of FTD with progranulin genetic deletion



Liu et al., 2016 *Cell* 165:921

Allows Gain of Motor Function in Spinal Muscular Atrophy

Transgenic SMN-Δ7 mouse model of SMA



Vukojicic et al., 2019 *Cell Rep* 29, 3087-3100

* p < 0.05; ** p < 0.01; *** p < 0.001

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Anti-C1q Approach to Treat Neurodegeneration in Huntington's Disease

- Progressive movement disorder, dementia, psychosis driven by classical complement pathway activation
- C1q localized on synapses
- High and sustained NfL levels
- Targeting synaptic loss and neuronal death to tackle neurodegeneration

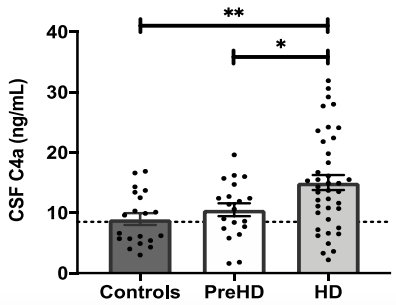
Markers of Disease Activity in Patients With HD Reduced by ANX005 in Mice With HD

Classical complement activation, elevated NfL, and synapse loss

PATIENTS

Increased Complement Activation With Disease Progression

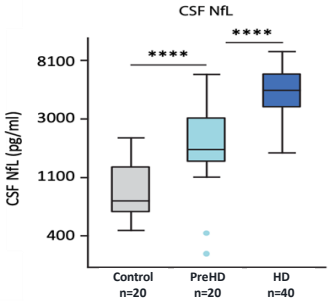
CSF C4a (ng/mL)



Annexon data on file; Collaboration with Dr. Ed Wild, UCL

Increased NfL in the CSF With Disease Progression

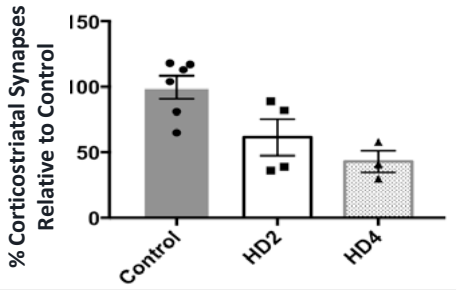
CSF NfL (pg/mL)



Byrne, 2017 *Lancet Neurol* 16: 601

Progressive Synapse Loss in HD

Synapse number (% Control)

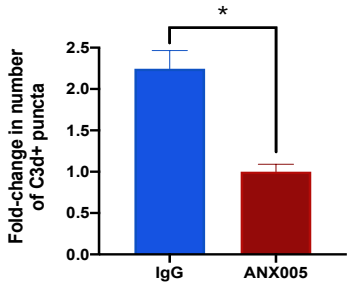


Unpublished Data, Dan Wilton and Beth Stevens, Harvard

MICE

Decreased Complement Activation With ANX005

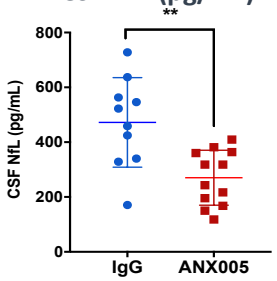
Fold-Change in Complement Deposition on Synapses



Annexon data on file; Collaboration w/ Dan Wilton and Beth Stevens, Harvard

Decreased Levels of CSF NfL With ANX005

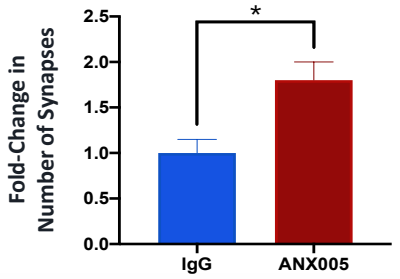
CSF NfL (pg/mL)



Annexon data on file.; Study run in R6/2 model

Protection Against Synapse Loss With ANX005

Fold-Change Synapse Number



Annexon data on file; Collaboration w/ Dan Wilton and Beth Stevens, Harvard

* p < 0.05; ** p < 0.01; **** p < 0.0001

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Ongoing Phase 2 HD Trial

Leveraging biomarkers to inform the next stage of development and future neuro indications

- **Open-label trial** (N=~24)
- **Objective endpoints:** Safety, PK, C1q target engagement, and NfL reduction from baseline
- Development informed by **large natural history cohorts**

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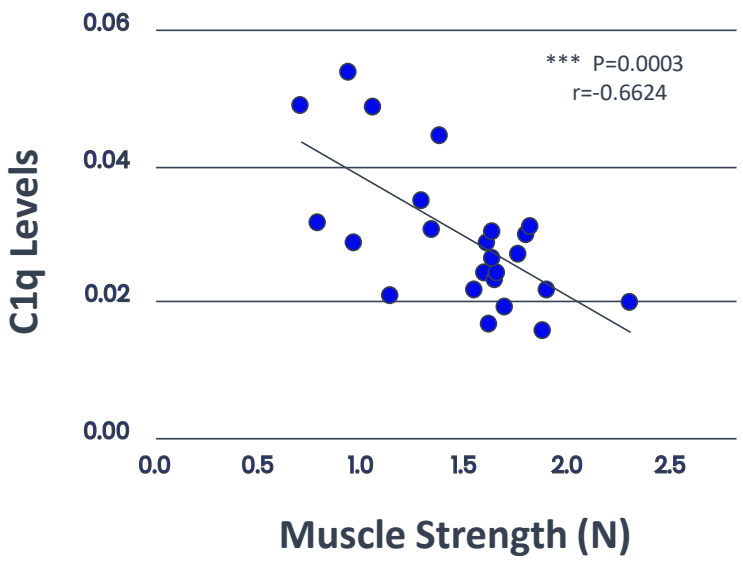
Anti-C1q Approach to Treat Neurodegeneration in ALS

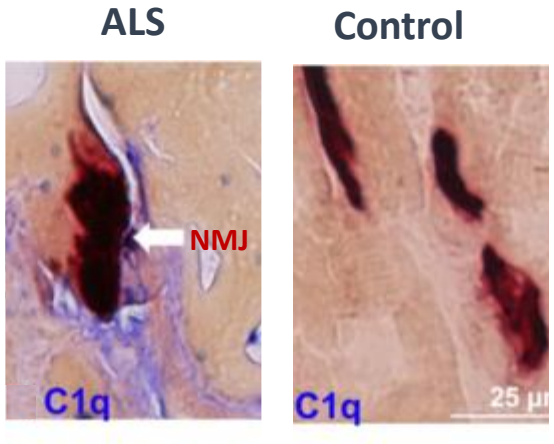
- Progressive weakness of limb and respiratory muscles
- Aberrant C1q activity potentially drives synaptic/ NMJ loss and disability
- Subjects have high baseline NfL levels
- Only upstream approach targeting both CNS and PNS aspects of the disease

C1q Deposition Correlated w/ Muscle Weakness in Mouse Model and Preceded Denervation in ALS Patients; NfL Elevated w/Disease

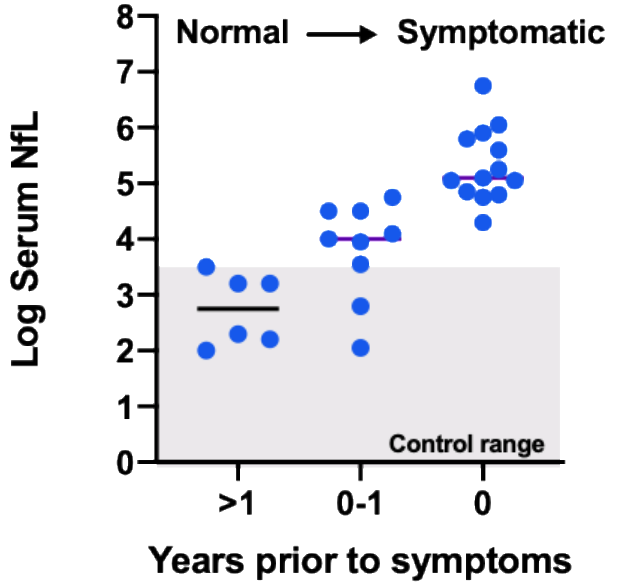
C1q Levels in NMJ of ALS Mouse Model Correlate with Weakness



C1q Deposition in NMJ of ALS Patients Prior to Denervation



Serum NfL Elevated in ALS Patients a Year Prior to Symptom Onset



Reference ALS animal model: Lee et al., (2018) J Neuroinflam 15:171

Bahia El Idrissi et al. Journal of Neuroinflammation (2016) 13:72

Reference ALS patient data: Benatar, et al., 2018, Ann Neurol 84:130

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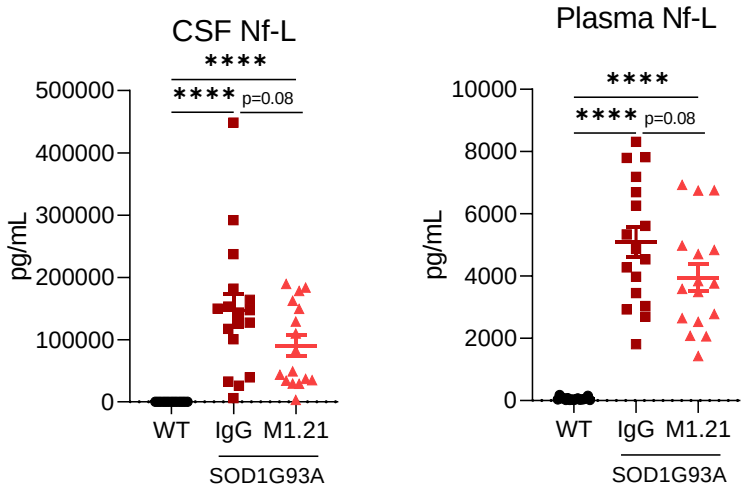
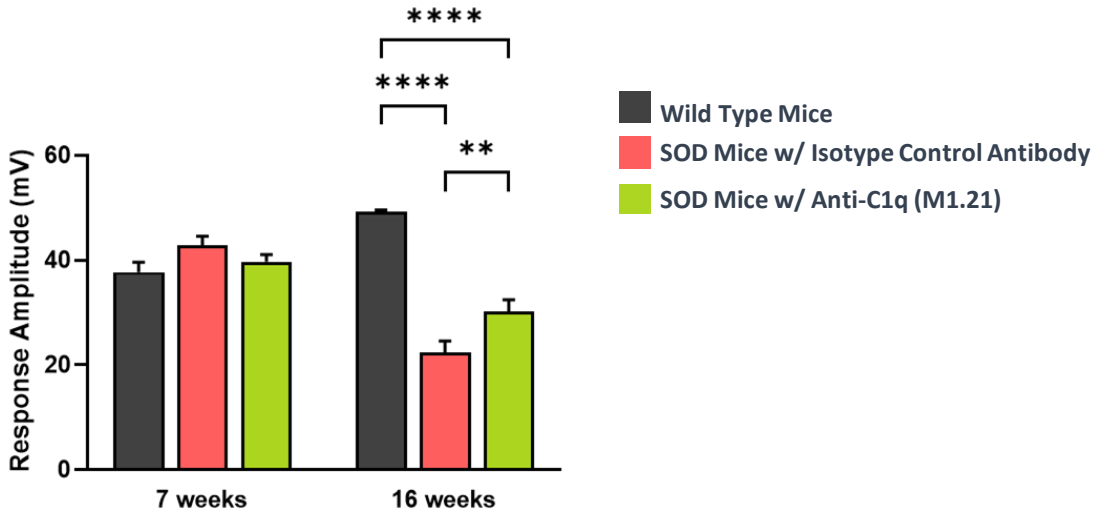
ANX005 Reduced NfL & Improved CMAP Response Amplitude in ALS SOD1 Mouse Model

ANX005 Reduction in CSF & Plasma NfL



ANX005 Improvement in CMAP Response Amplitude



Annexon data on file

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Ongoing Phase 2 ALS Trial

Leveraging biomarkers to inform next stage of development and future neuro indications

- Open label trial (N= ~24)
- **Objective endpoints:** Safety, PK, C1q target engagement, and NfL reduction from baseline
- Targeting all forms of ALS

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Tackling Blindness in Retinal Diseases

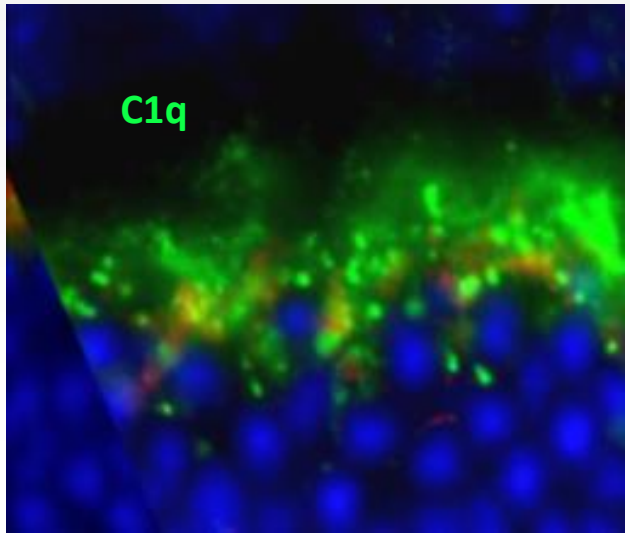
ANX007

Geographic Atrophy

Differentiated Neuroprotective Approach for Geographic Atrophy Caused by Excess Classical Complement Activity in the Retina

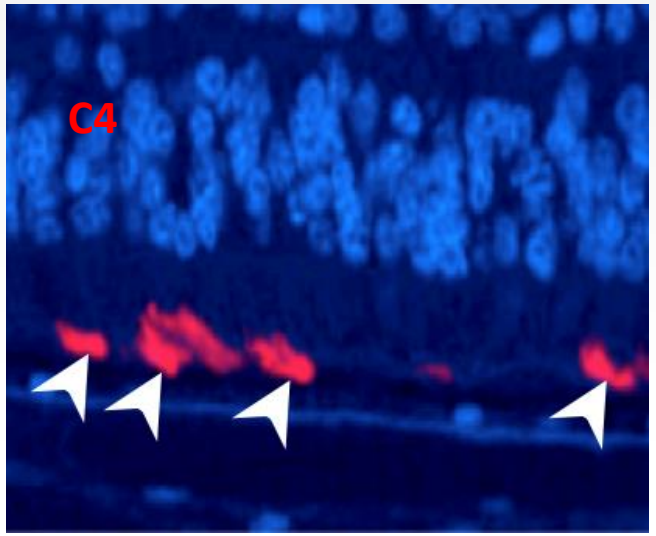
C1q and early complement components deposited in multiple layers of the retina

Photoreceptor synapses



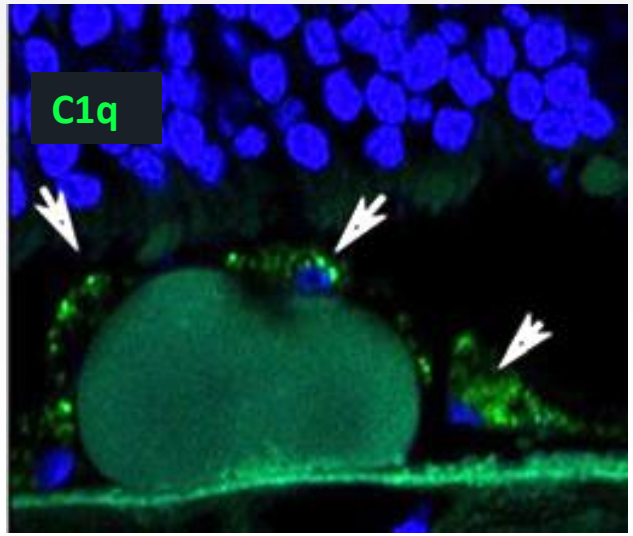
C1q on synapses of photoreceptor cells in aged mice[1]

Photoreceptor cells



Downstream C4 deposited on photoreceptor cell outer segments in GA patients[2]

Drusen
(below photoreceptor cells)



C1q on Drusen in GA patients[3]

[1]Annexon data on file; [2]Katschke, 2018; [3]Jiao, 2018

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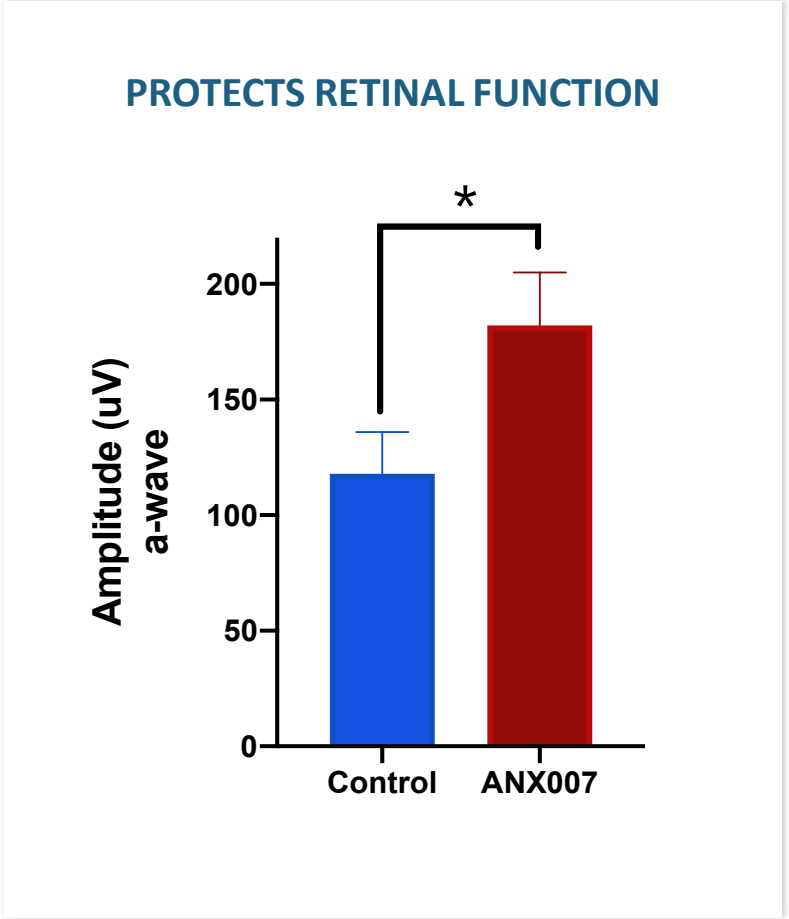
Blocking C1q Protects Photoreceptors in Model of Retinal Damage

ANX007 in GA

- Intravitreal administration of **ANX007 protects photoreceptor cells and retinal function**
- **Potential Efficacy Advantage:** Blocking C1q at top of cascade stops downstream C1q, C4, C3, and C5 activities that drive local immune response and destruction in the retina
- **Potential Safety Advantage:** Allows normal immune activity of lectin and alternative complement pathways, maintaining vascular function of C3a and C5a[1, 2]



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

* $p < 0.05$

[1] Annexon data on file; [2] Langer 2010

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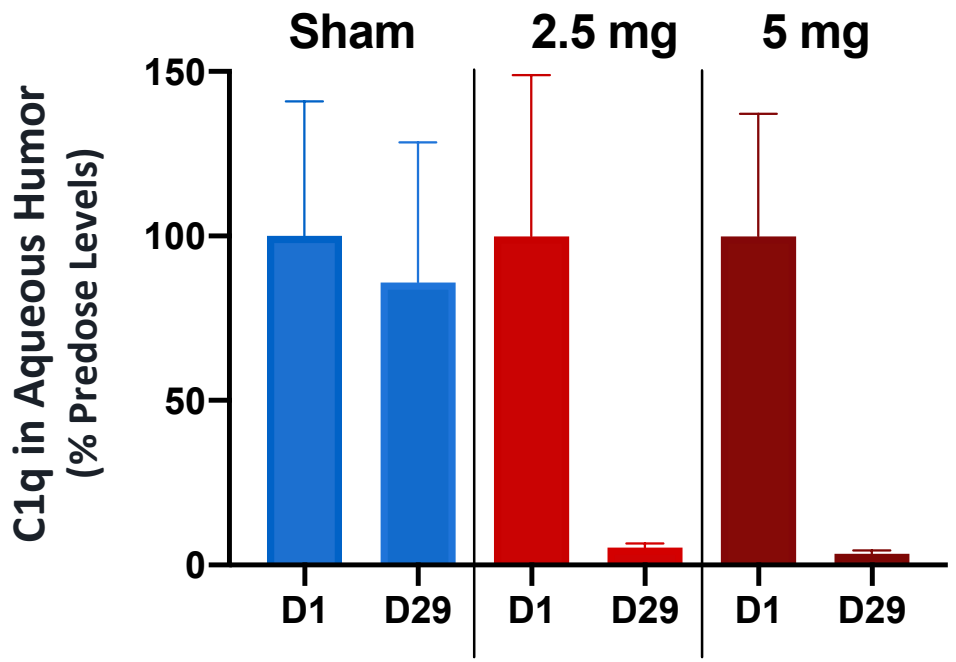
ANX007 Effectively Inhibits C1q in Phase 1b Patients

Full inhibition at low and high doses support monthly or less frequent dosing



Repeat doses, N=17

D1 = Day 1 (before ANX007 dosing)

D29 = Day 29 (post-1st dose)

ANX007 DATA SUMMARY

- **ANX007 well-tolerated** at all dose levels
- Single intravitreal injection **inhibited C1q in aqueous humor for at least 29 days** at both low and high doses

Annexon data on file

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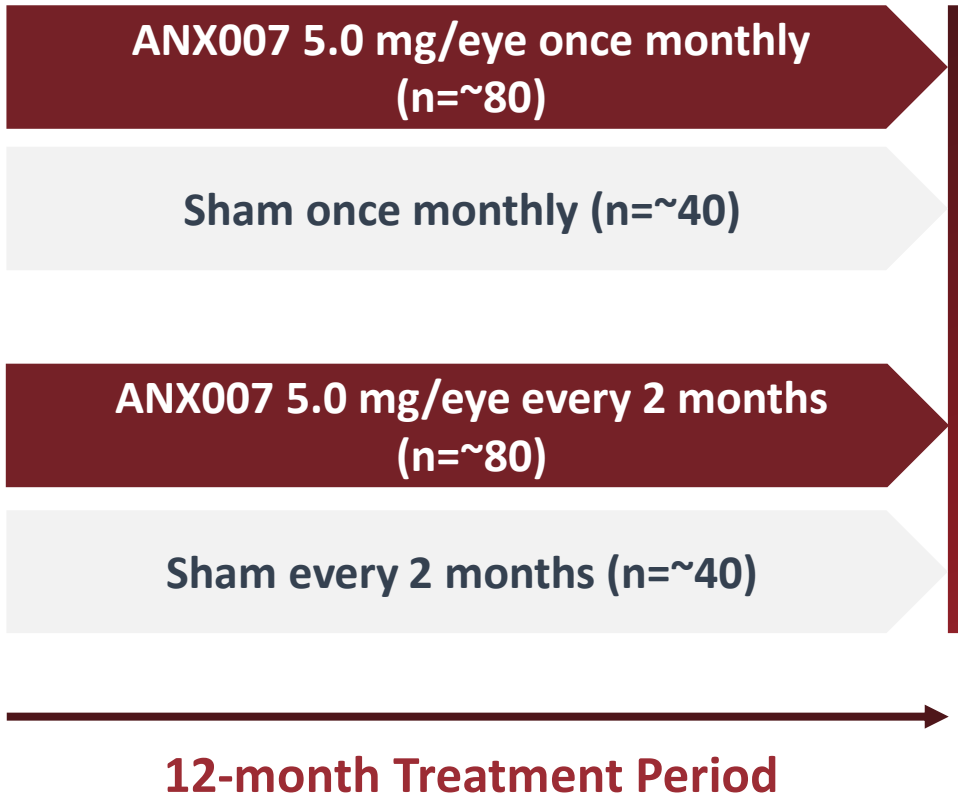
Ongoing Phase 2 Geographic Atrophy Trial



- **Randomized, double-masked trial** (N=~240)
- **Primary endpoint:** Change in area of geographic atrophy on FAF
- Leveraging experience from related complement trials

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Annexon is Well-Positioned to Drive Significant Value Over the Next 2 Years

- **Anti-C1q platform pioneering** a new class of complement medicines
- **Broad and deep applicability** across autoimmune and neurodegenerative diseases
- **Platform foundation established** with robust target engagement, POC data and 5 diverse drug candidates
- **Poised for significant value creation** with 7 mid to late-stage data sets anticipated over next 2 years
- **Winning team and well capitalized** to achieve milestones over next 2 years

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THANK YOU