STOPPING CLASSICAL COMPLEMENT AT THE START

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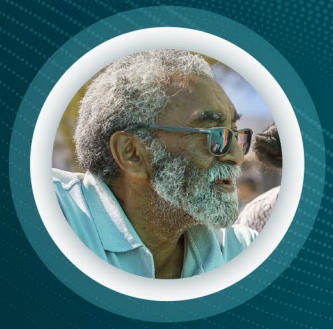



TREATING DISEASES OF THE BODY, BRAIN AND EYE

COMPANY PRESENTATION

JANUARY 11, 2021

Disclaimer

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 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,” “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 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.

Annexon: Pioneering Classical Complement Therapies to Treat Autoimmune, Neurodegenerative and Ophthalmic Diseases

- **Blocking upstream complement to stop disease processes at the start**
- **Broad platform potential** in **orphan and large patient populations** in autoimmune, neurodegenerative and ophthalmic diseases
- **Phase 2 pipeline** with **3 drug candidates** to deliver near-and mid-term catalysts
- **Precision medicine approach** leveraging complement and disease biomarkers
- **Well capitalized** with **worldwide rights** to development and commercialization

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Demonstrated Leadership Advancing Transformative Therapies

Doug Love, Esq.
President & CEO
Genentech, Amgen, Elan

Ted Yednock, Ph.D.
Chief Scientific Officer
Elan, Prothena, Athena

Jennifer Lew
Chief Financial Officer
Aduro, Dynavax, Ernst & Young

Sanjay Keswani, M.D.
Chief Medical Officer
Roche, Eli Lilly, Amgen,
Bristol-Meyers Squibb

Michael Overdorf
Chief Business Officer
Eli Lilly

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Building a Leading Multi-Faceted Complement Company

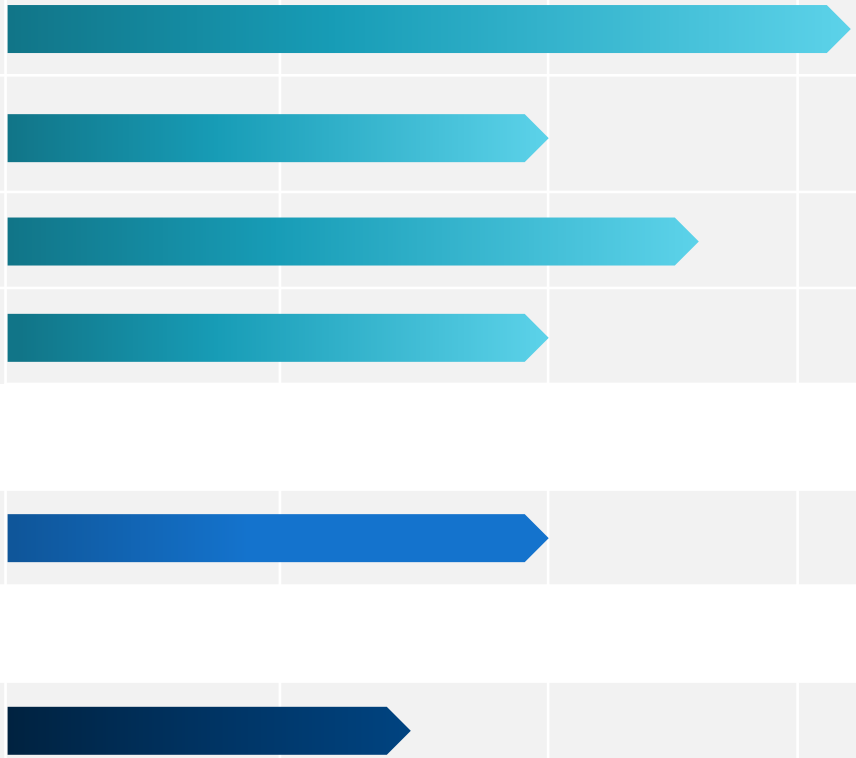
2020: A Foundational Year

- **$100M Series D** in June and **$263M Nasdaq IPO** in July
- **Robust ANX005 and ANX007 patient data** demonstrating tolerability, full target engagement, biomarker/clinical data
- **Rapidly advancing into multiple Ph2** autoimmune, neurodegenerative and ophthalmic trials
- **Developing innovative next generation drug candidates**
  - ANX009 subcutaneous First-in-Human trial ongoing
  - Follow-on small molecule and monoclonal antibody candidates advancing to IND

Robust Clinical Pipeline of C1q Inhibitors for Body, Brain & Eye

Multiple clinical stage drug candidates with diverse routes of administration

INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 2/3	CURRENT STATUS
ANX005 (IV)					
Guillain-Barré Syndrome (GBS)					Ph 2/3 Ongoing
Warm Autoimmune Hemolytic Anemia (wAIHA)					Ph 2 Initiating
Huntington's Disease (HD)					Ph 2 Ongoing
Amyotrophic Lateral Sclerosis (ALS)					Ph 2 Initiating
ANX007 (IVT)					
Geographic Atrophy (GA)					Ph 2 Initiating
ANX009 (SubQ)					
Autoimmune					Ph 1 Ongoing



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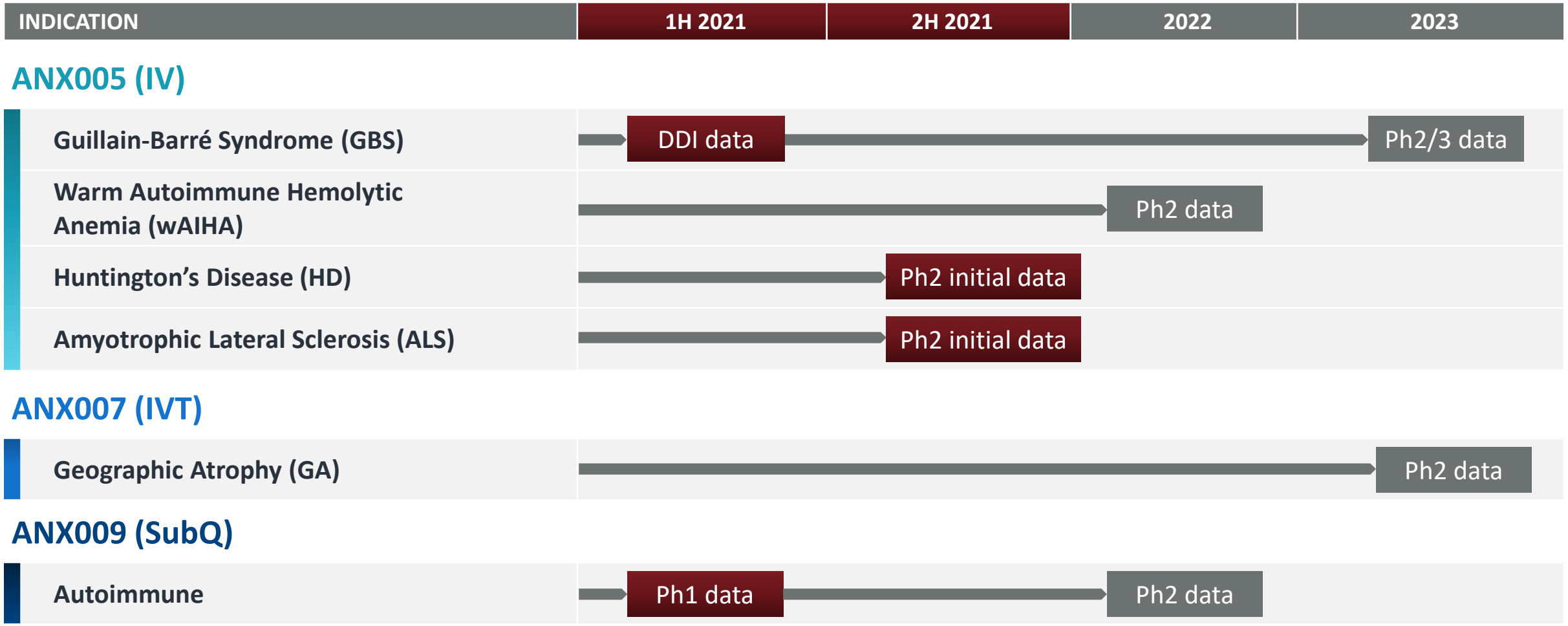
Significant Catalysts in 2021 and Beyond

Sufficient cash-runway to achieve these milestones



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Why C1q and the Classical Complement Pathway?

C1q is key driver of disease processes for indications Annexon has targeted

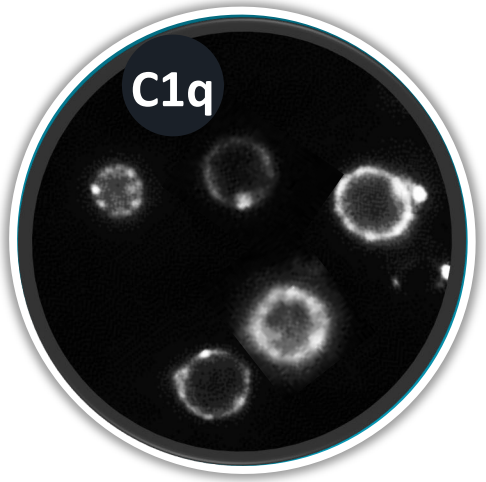
C1q directly binds to tissue, initiating and anchoring complement in diseases of the body, brain and eye

GBS

C1q Targeting the Neuromuscular Junction

Halstead, et al. 2004 Brain 127: 2109–2123

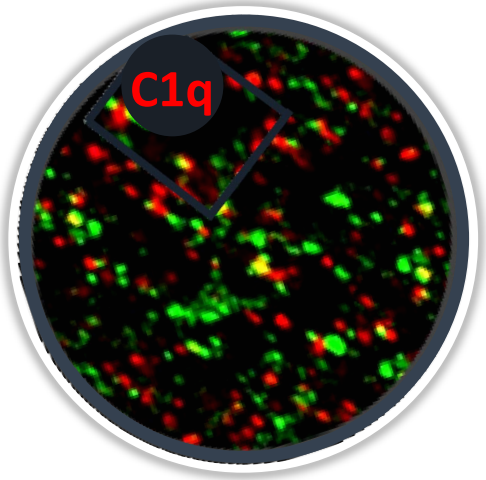
HEMOLYTIC ANEMIA



C1q Targeting Red Blood Cells

C1q bound to antibody coated RBC
Annexon data on file

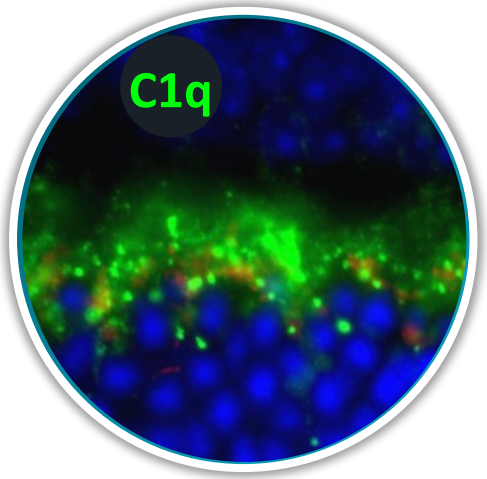
HUNTINGTON'S



C1q Targeting Striatal Synapses

Jiao, et al., 2018 Mol Neurodegen 14:45

GEOGRAPHIC ATROPHY



C1q Targeting Photoreceptor Synapses

C1q bound to photoreceptor cells synapses in aged mice: Annexon data on file

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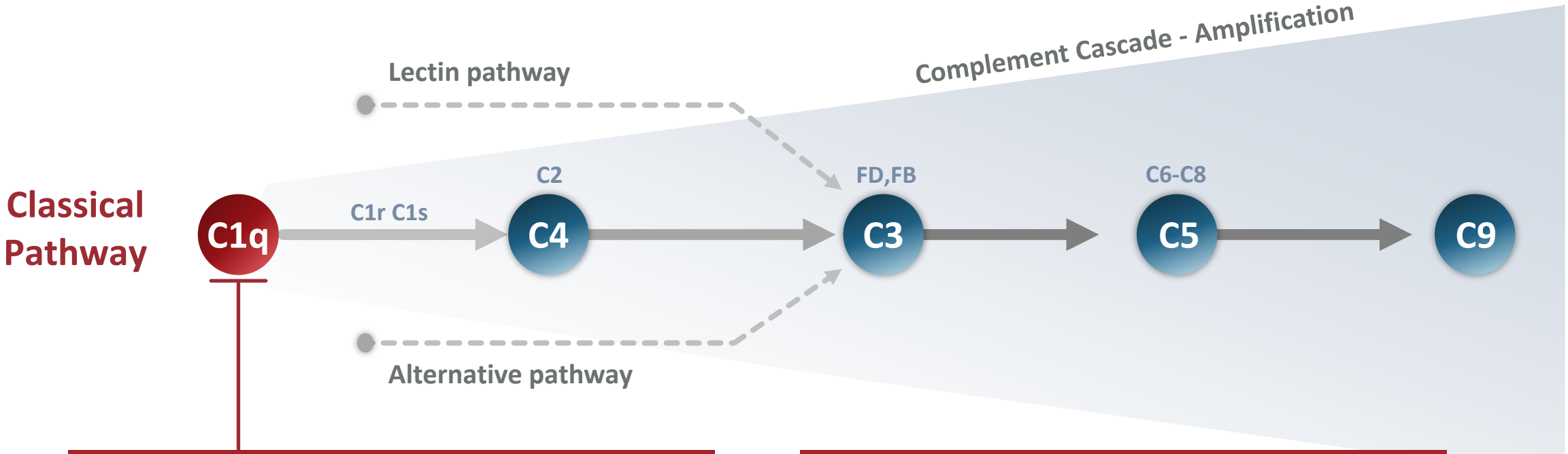
Inhibiting C1q Shuts Down Entire Classical Complement Pathway

Blocks C1q binding to tissues and downstream activation of C4, C3, C5 and C9



Potential Efficacy Advantages

- ✓ **Anti-C1q stops the cascade before it starts**[1]
- ✓ **Shuts down all tissue-damaging components** of classical pathway (C1q, C4, C3, C5, C9)[1]
- ✓ **C1q levels similar to C5, and 10-fold lower than C3**[2]

Potential Safety Advantages

- ✓ **Selectively targets C1q in indications where the classical cascade is a key driver**
- ✓ **Allows normal immune functions** of lectin and alternative complement pathways[1]

[1]Data on file; [2]Glovsky, *Ann Allery Asthma Immunol* 2004, 93:513

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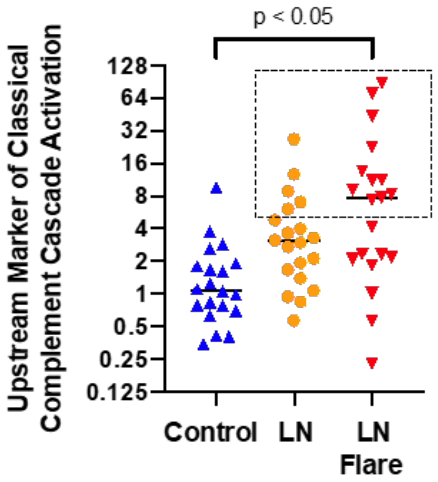
Leveraging Biomarkers to Increase Probability of Clinical Success

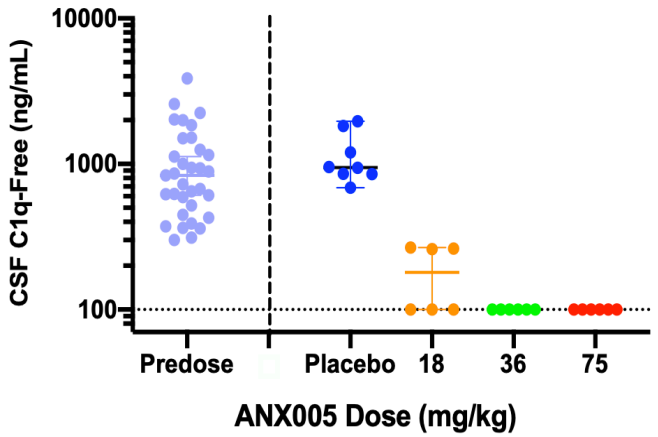
Measuring objective classical complement and disease markers in patients

Right Indication and Patient Selection

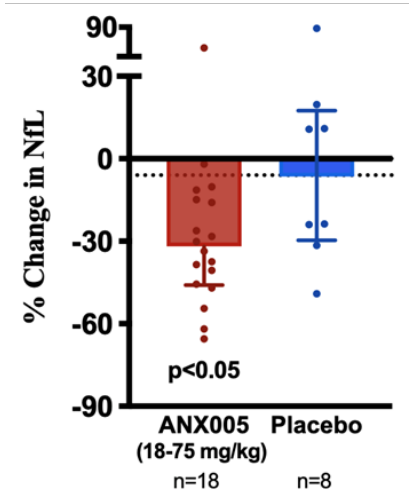


Target population for initial study
- 25% of lupus nephritis patients
- 55% of lupus nephritis patients in flare

Optimal Dose and Dosing Regimen



Objective Measures of Treatment Effect



Higher Classical Complement Activation in Patients with Lupus Nephritis, Particularly Those in Flare

Inhibition of C1q observed in CSF at 18-75 mg/kg

High Dose ANX005 (18-75 mg/kg) Led to Significant Early NfL Reduction (Weeks 2 – 4)

*Annexon data on file

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IMPROVING PATIENT OUTCOMES IN AUTOIMMUNE DISEASES

- Guillain-Barré Syndrome
- Warm Autoimmune Hemolytic Anemia

GBS, a Destructive Neuromuscular Autoimmune Disease

Severe disease that causes acute paralysis

GUILLAIN-BARRÉ SYNDROME (GBS)

Rare orphan disease:

- **12K patients diagnosed annually in North America/Europe**
- **No approved therapy in the U.S.**

Autoantibody attack on peripheral nerves, triggering complement (C1q) and neurodegeneration

Anti-C1q blocks autoantibody activation of complement and potentially prevents disability

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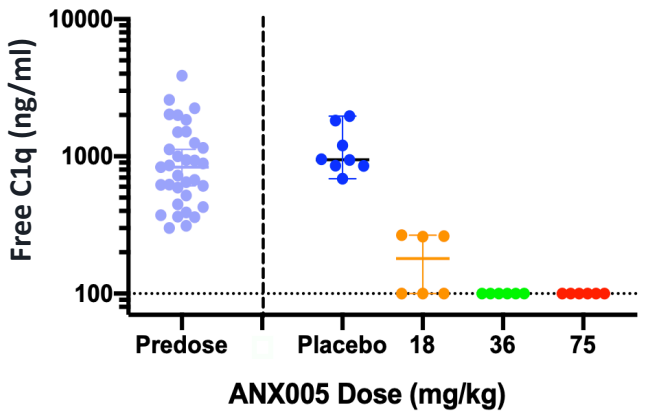
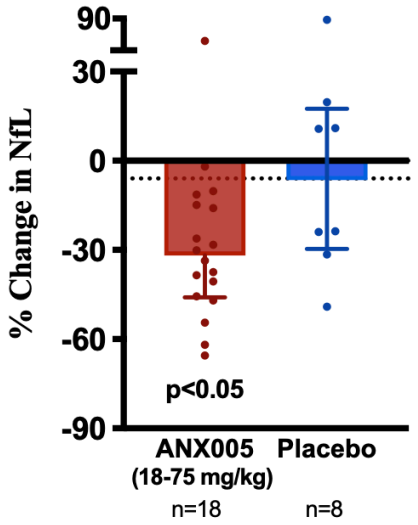
ANX005 Well-Tolerated, Achieved Full Target Engagement, Reduced NfL and Prevented Disability in GBS Phase 1b Dose-Ranging Trial

Full Target Engagement in CSF at Higher Doses (18-75 mg/kg)



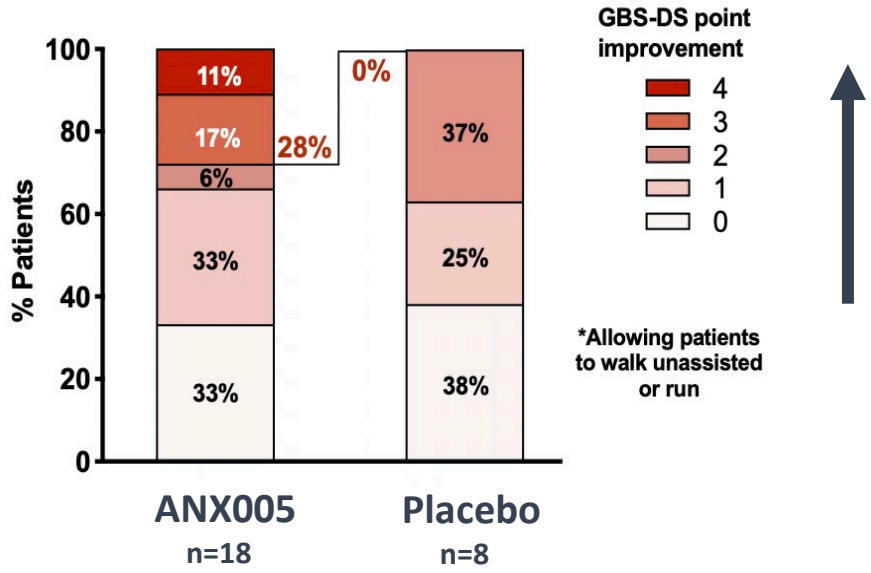
Dose Dependent Decrease of CSF Free C1q

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 Wk 8



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

Annexon data on file

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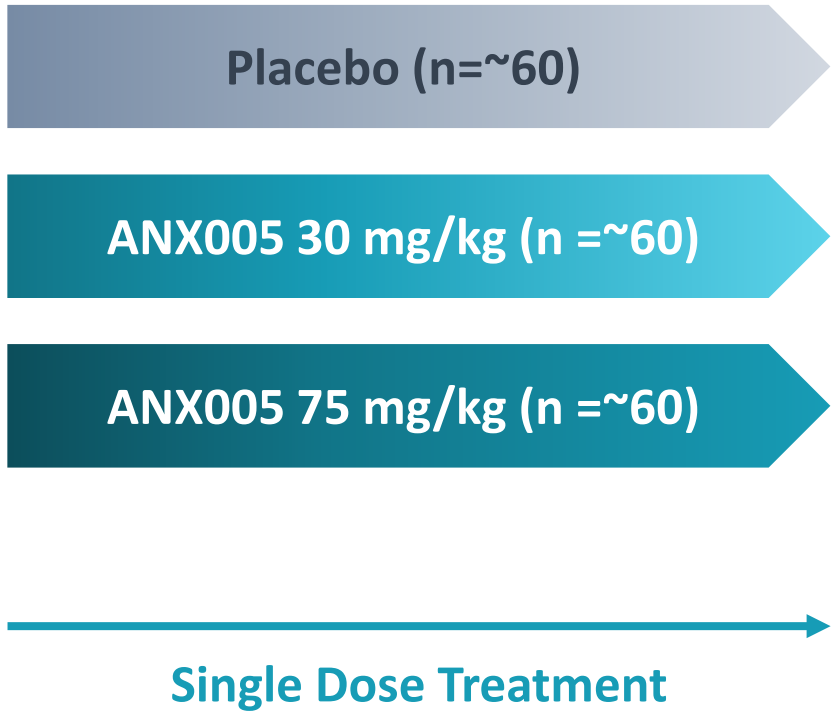
Ongoing GBS Phase 2/3 Trial with ANX005

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**
- **Data expected 2023**

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Targeting Life Threatening RBC Autoantibody Attack in wAIHA

WARM AUTOIMMUNE HEMOLYTIC ANEMIA (wAIHA)

Autoantibodies attack and destroy RBCs, resulting in anemia, can develop rapidly or gradually

- **~30,000 patients globally**
- **No approved therapy in U.S.**

Complement activation amplifies RBC destruction in certain patients

Targeted strategy to select patients who meet specific biomarker criteria of complement activation

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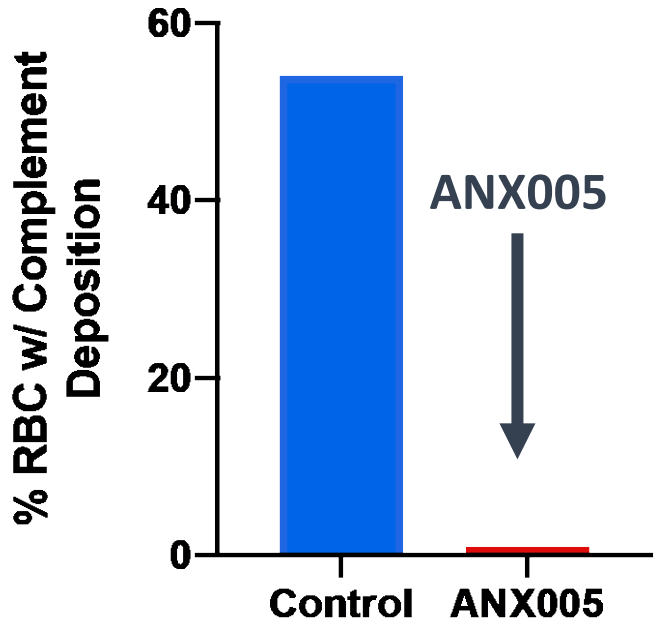
Antibody-Mediated Complement Activation in wAIHA Patient Sera – Identifying an Enriched Patient Population

ANX005 inhibits complement activation in wAIHA *in vitro* (n=1)



ACTIVITY FULLY INHIBITED BY ANX005

- Detected complement-activating antibodies in 4 of 12 wAIHA patients (literature suggests 20 – 30 %)
- Activity fully inhibited by ANX005 *in vitro*
- **Precision medicine approach will enable appropriate patient selection for Phase 2 study**

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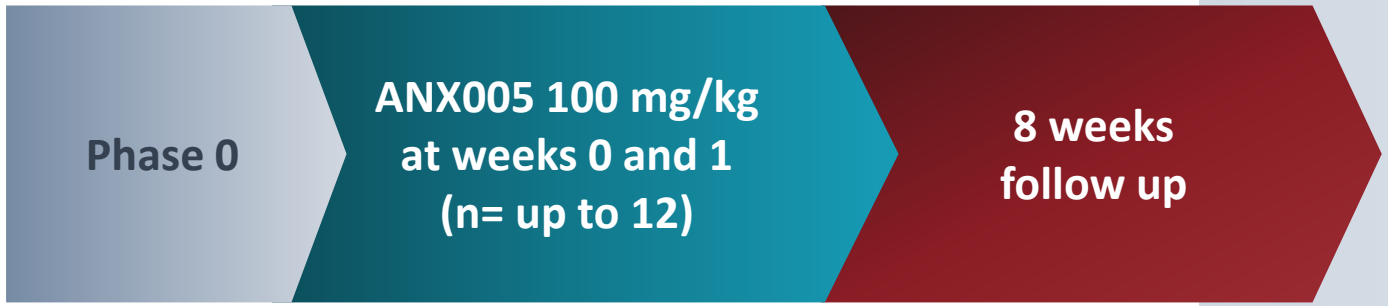
Planned Phase 2 wAIHA Trial with ANX005



- **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
- Plan to initiate 1H 2021

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TACKLING BLINDNESS IN RETINAL DISEASES

- Geographic Atrophy

Pioneering Treatment of Complement-Mediated Neurodegeneration

Well-researched role of C1q inhibition to protect against synapse loss and neurodegeneration

Ben Barres, M.D., Ph.D.
Discoverer of C1q Technology
Scientific Co-Founder, Annexon

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

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Differentiated Neuroprotective Approach for Geographic Atrophy

Targeting up and downstream complement activity associated with retinal nerve loss

GEOGRAPHIC ATROPHY (GA)

Loss of vision due to loss of neurons (photoreceptors)

- **~1 million U.S. patients;** ~5 million worldwide
- **No approved therapies to prevent onset or progression**

Aberrant C1q activity results in neuronal loss

Anti-C1q is **neuroprotective in GA models**

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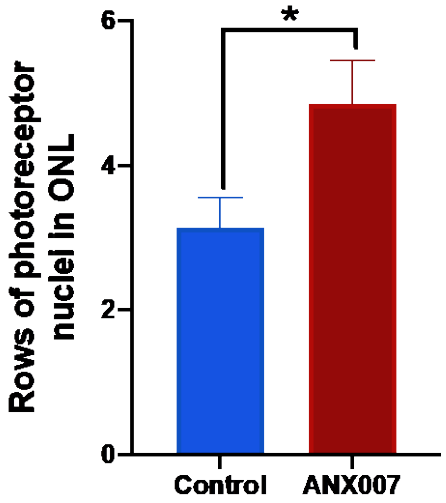
Intravitreal Administration of Anti-C1q Provides Neuroprotection in a Mouse Model of Photoreceptor Cell Loss / Geographic Atrophy

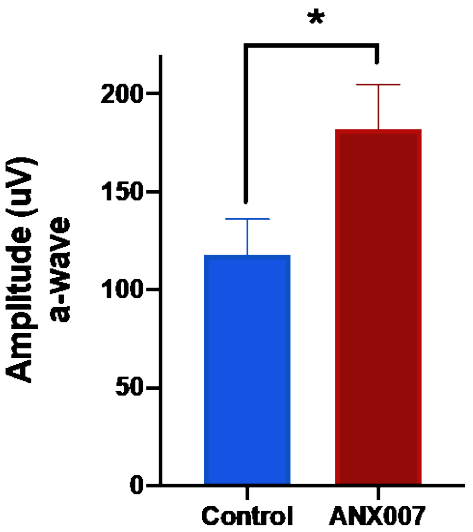
- **C1q is locally produced in the retina and a key driver of cell loss**
- **Upstream activator of C3**
- **Selective C1q inhibition allows normal function** of lectin and alternative pathway

Intravitreal Administration of ANX007 Protects Photoreceptor Cells and Retinal Function

Anti-C1q Protects Photoreceptor Cells / Retinal Thickness



Protects Retinal Function



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

* $p < 0.05$; **<0.001

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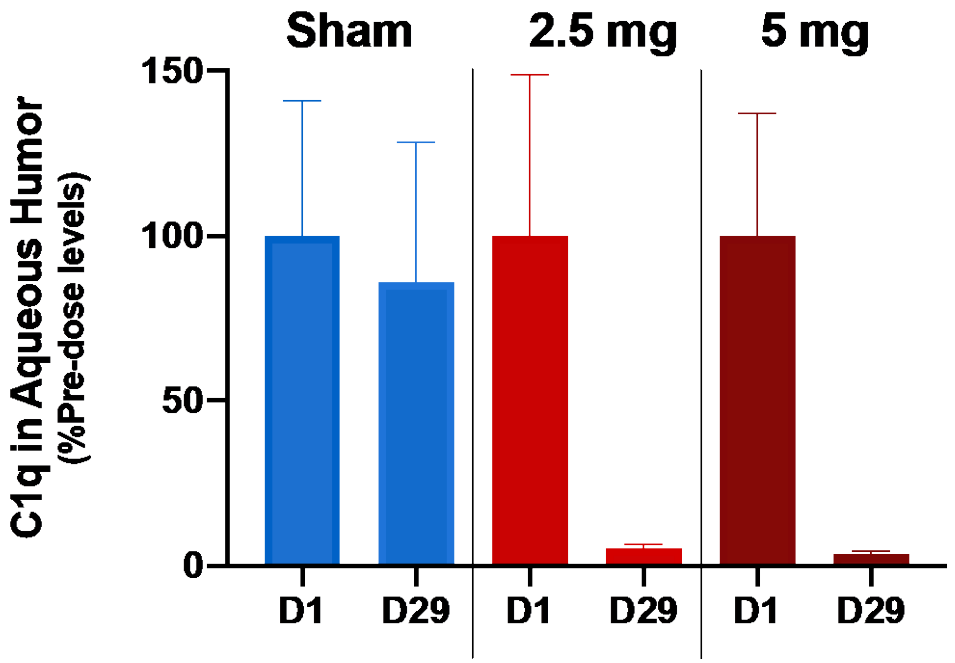
Intravitreal ANX007 Effectively Inhibits C1q in Phase 1b Patients

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

Free C1q Levels in Aqueous Humor



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
- Repeat doses, N = 17

Annexon data on file

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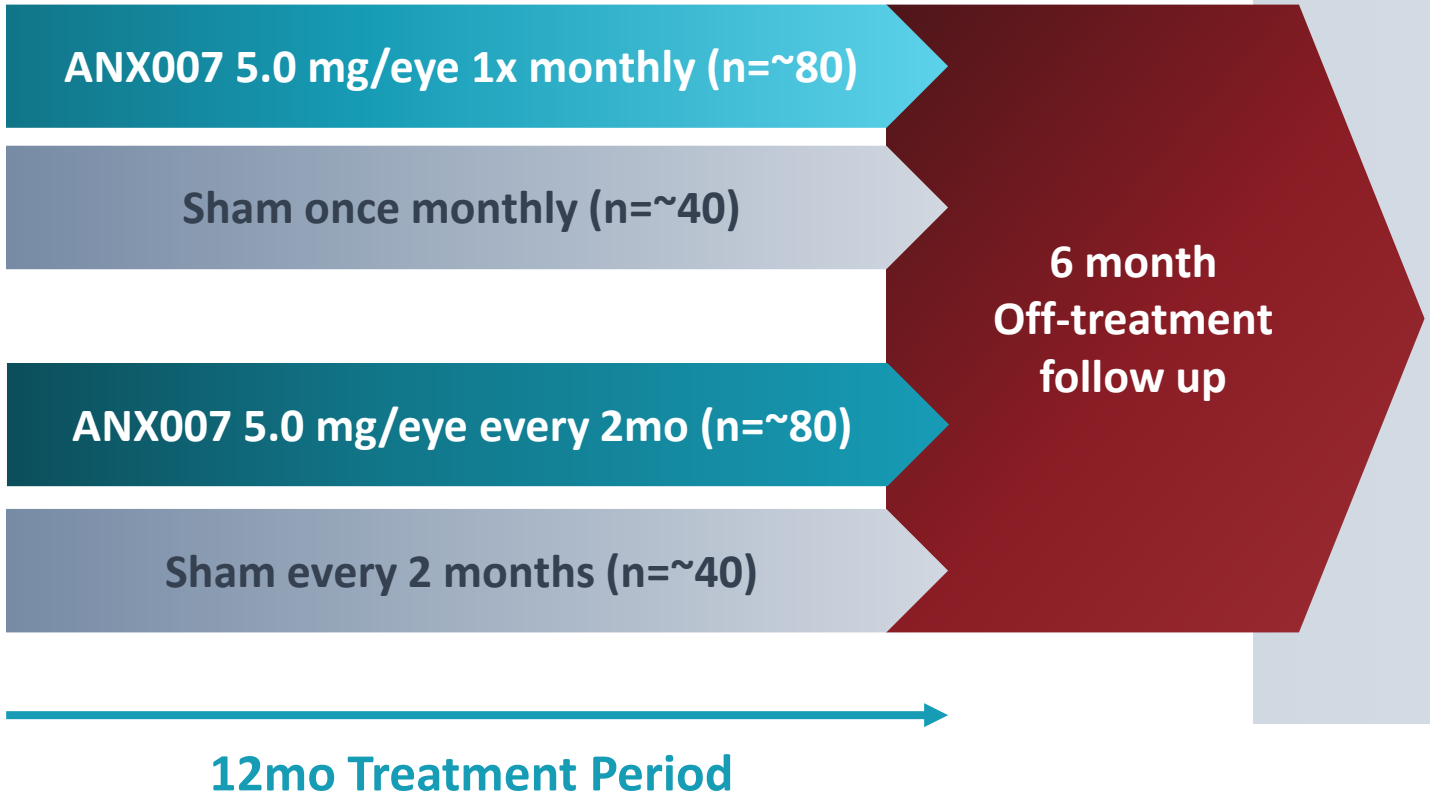
Initiating GA Phase 2 Trial with ANX007 in Q1 2021



- **Randomized, double-masked trial** (N= ~240)
- **Primary endpoint:** change in area of geographic atrophy on FAF
- Leveraging experience from related complement trials
- **Data expected 2023**

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TACKLING PATIENT DISABILITY IN DEVASTATING NEURODEGENERATIVE DISEASES

- Huntington's Disease
- ALS

Pioneering Classical Complement Approach in Huntington's Disease

Targeting synaptic loss and neuronal death to tackle neurodegeneration

HUNTINGTON'S DISEASE (HD)

Progressive movement disorder, dementia, psychosis

- **~35,000 U.S. patients (Orphan)**
- Subjects have **high** and **sustained NfL** levels

Aberrant C1q activity drives synaptic loss and disability

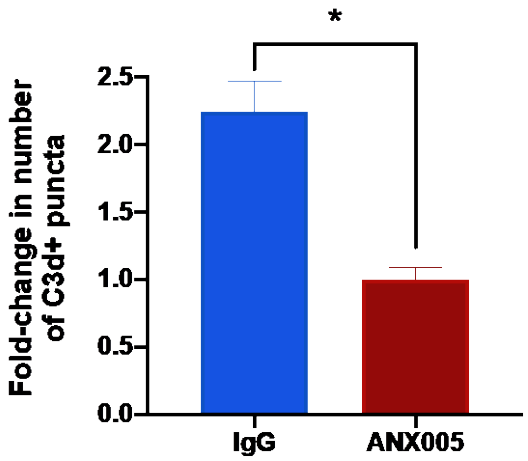
C1q inhibition protects against synapse loss and neurodegeneration in HD models

ANX005 Reduced Key Markers of Disease Activity in HD Mice

Decreased Complement Activation on Synapses, CSF NfL and Synapse Loss

Decreased Complement Activation on Synapses

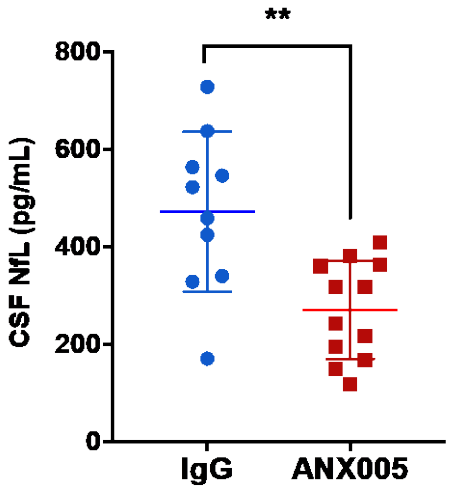
Fold-Change in Complement Deposition on Synapses



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

Decreased Levels of CSF NfL

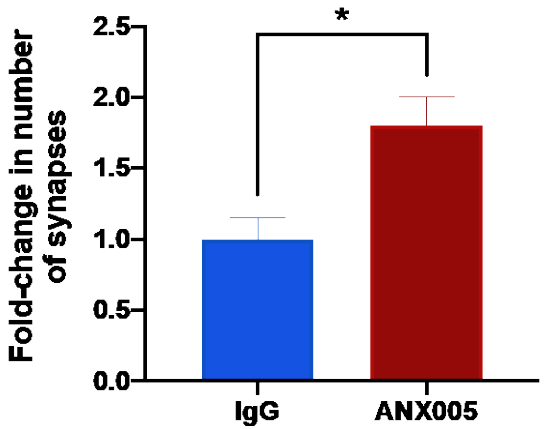
CSF NfL (pg/mL)



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

Protection Against Synapse Loss

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 HD Phase 2 Trial with ANX005

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

- **Open label trial** (N= ~24)
- **Objective endpoints:** Safety, C1q target engagement, and NfL reduction from baseline
- Development informed by large natural history cohorts
- **Initial data expected 2H 2021**

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Targeting Downstream Neuronal Loss in ALS

Only upstream approach targeting both CNS and PNS aspects of the disease

AMYTROPHIC LATERAL SCLEROSIS (ALS)

Progressive weakness of limb and respiratory muscles

- **~30,000 patients globally (Orphan)**
- **Subjects have high baseline NfL levels**

Aberrant C1q activity potentially drives synaptic/ NMJ loss and disability

Strong preclinical data supporting anti-C1q approach

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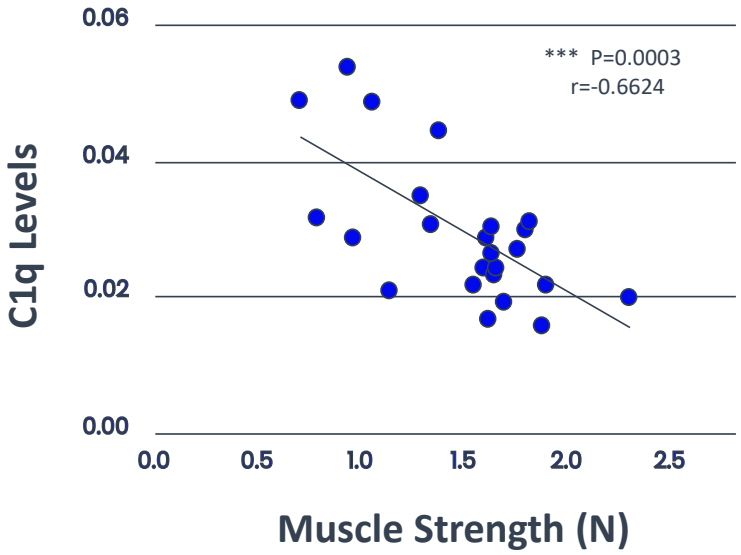
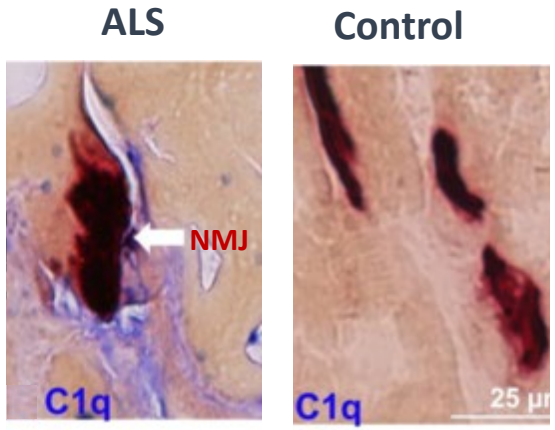
C1q Deposition Correlated w/ Muscle Weakness in Mouse Model and Preceded Denervation in ALS Patients; NfL Elevated w/ Disease

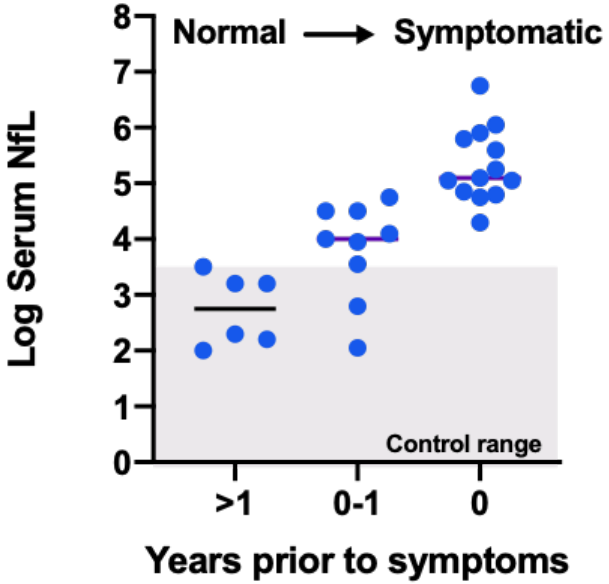
C1q Levels in NMJ of ALS Mouse Model Correlate with Weakness



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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Planned ALS Phase 2 Trial with ANX005

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

- Open label trial (N= ~24)
- **Objective endpoints:** Safety, PK/PD, C1q target engagement, and NfL reduction from baseline
- Targeting all forms of ALS
- **Plan** to initiate early 2021
- **Initial data expected 2H 2021**

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Potential to Expand Platform Across A Breadth of Diseases

Current indications and future opportunities in both orphan and large patient populations

AUTOIMMUNE

wAIHA (warm Autoimmune Hemolytic Anemia)

CAD (Cold Agglutin Disease)

Lupus Nephritis

Bullous Skin Diseases

HIT (Heparin Induced Thrombocytopenia)

Rheumatoid Arthritis

Crohn's Disease

GBS (Guillain-Barré Syndrome)

CIDP
(Chronic Idiopathic Demyelinating Polyneuropathy)

MMN (Multifocal Motor Neuropathy)

PMS (Progressive Multiple Sclerosis)

ON (Optic Neuritis)

NEURODEGENERATION

HD (Huntington's Disease)

ALS (Amyotrophic Lateral Sclerosis)

FTD (Frontal Temporal Dementia)

SMA (Spinal Muscular Atrophy)

AD (Alzheimer's Disease)

TBI (Traumatic Brain injury)

OPHTHALMOLOGY

GA (Geographic Atrophy)

GLA (Glaucoma)

■ Current Indications

Poised to Drive Value in 2021 and Beyond

- **Targeting aberrant C1q / classical pathway activation** to treat devastating tissue damage in the diseases we're pursuing
- **Broad platform potential** in **orphan and large patient populations** in autoimmune, neurodegenerative and ophthalmic diseases
- **Great momentum** and **well-resourced to deliver** on 2021 priorities
  - **Execute 5 clinical trials**
  - **Report initial clinical data from 4 diverse trials**
  - **Advance to IND** next generation small molecule and mAB drug candidates

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THANK YOU