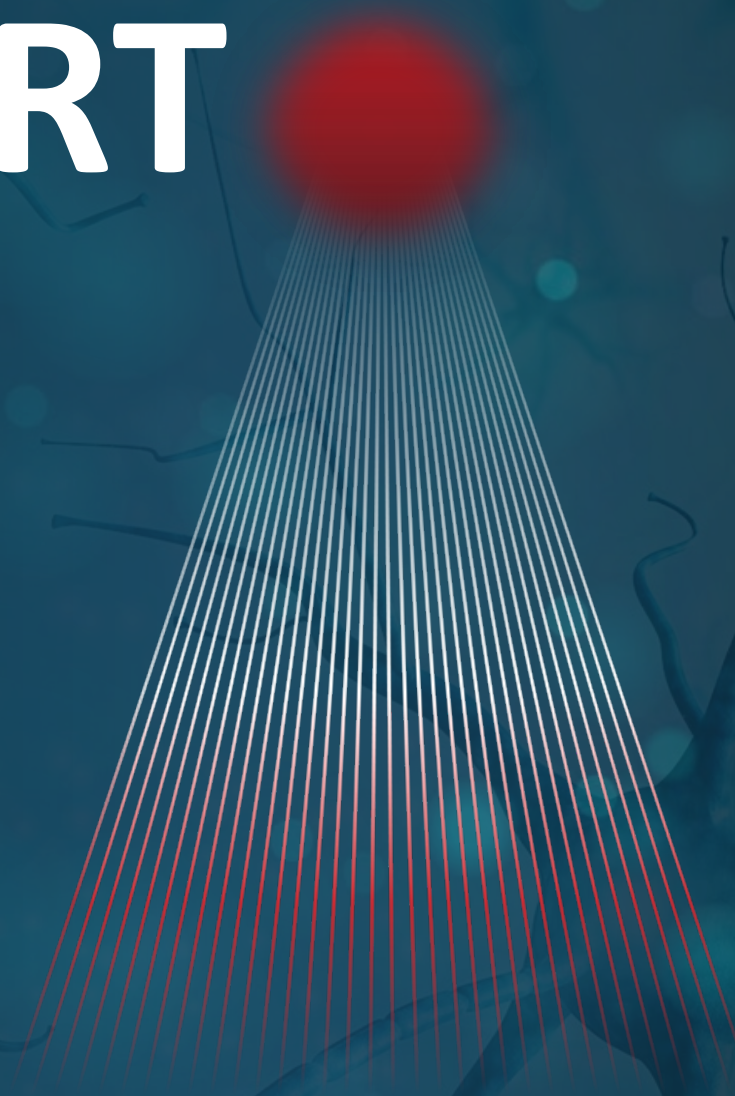
Stopping Complement-Mediated Diseases

AT THE START

COMPANY PRESENTATION I MAY 2021



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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 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.

Unlocking the Next Generation of Complement Therapies

Our Mission

To Deliver Transformative Therapies for Patients Suffering From Complement-Driven Autoimmune and Neurodegenerative Diseases

STOP the complement disease process at the start

TARGET devastating diseases with no approved therapies

EXECUTE beachhead strategy and rapidly expand platform

Building a Leading Complement Company

POSITIONED FOR SIGNIFICANT GROWTH

- 5 Phase 2 trials underway with expected read-outs over next 2 years

WHOLLY-OWNED PORTFOLIO of complement therapeutic assets

- 3 diverse candidates across multiple high value indications
- 2 next generation drug candidates advancing to IND

PROOF-OF-CONCEPT with ANX005 in lead GBS indication

- Beachhead indication de-risks portfolio expansion in related AI and neuro diseases

PROVEN, PASSIONATE TEAM to translate the opportunity

- Strong track record of innovation and success

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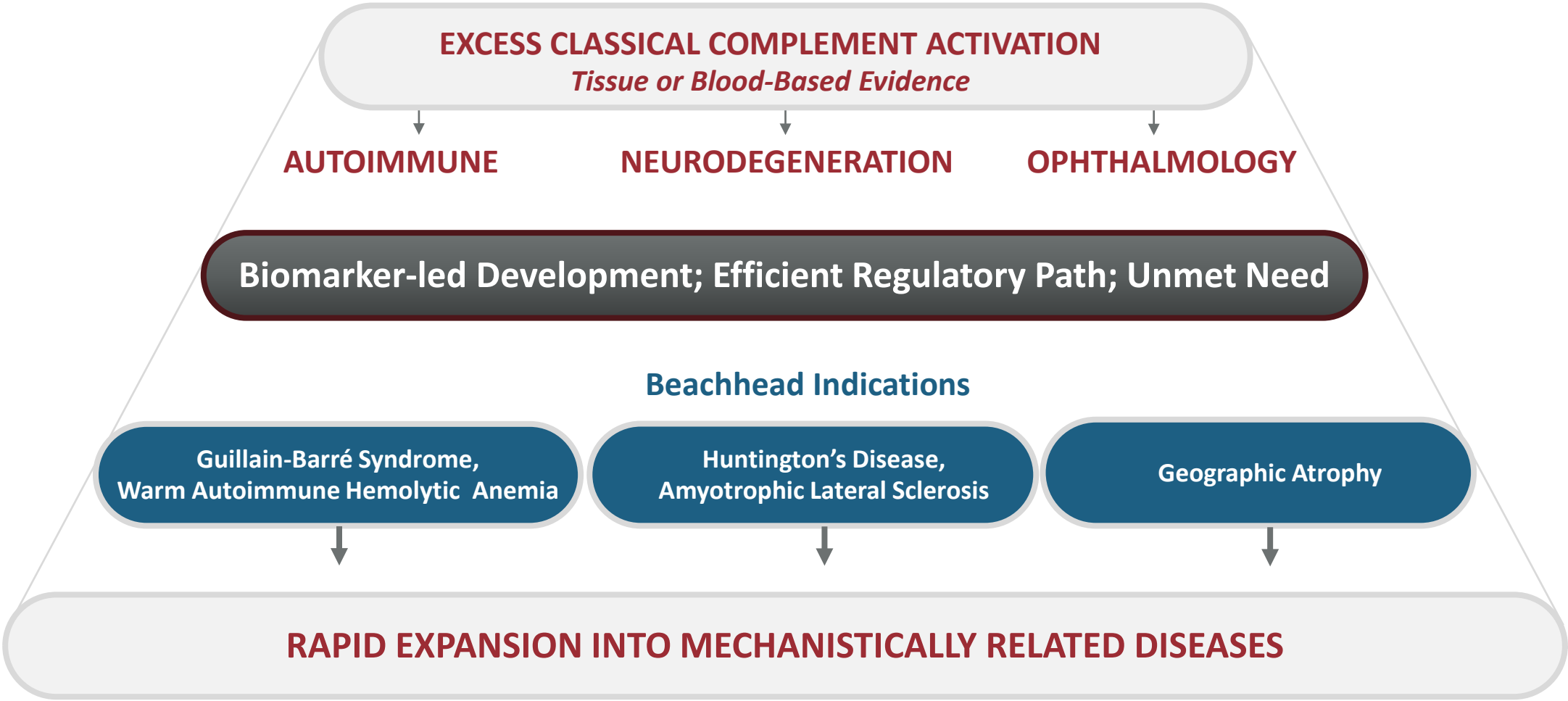
Rigorous Approach to Maximizing Our Broad Opportunity



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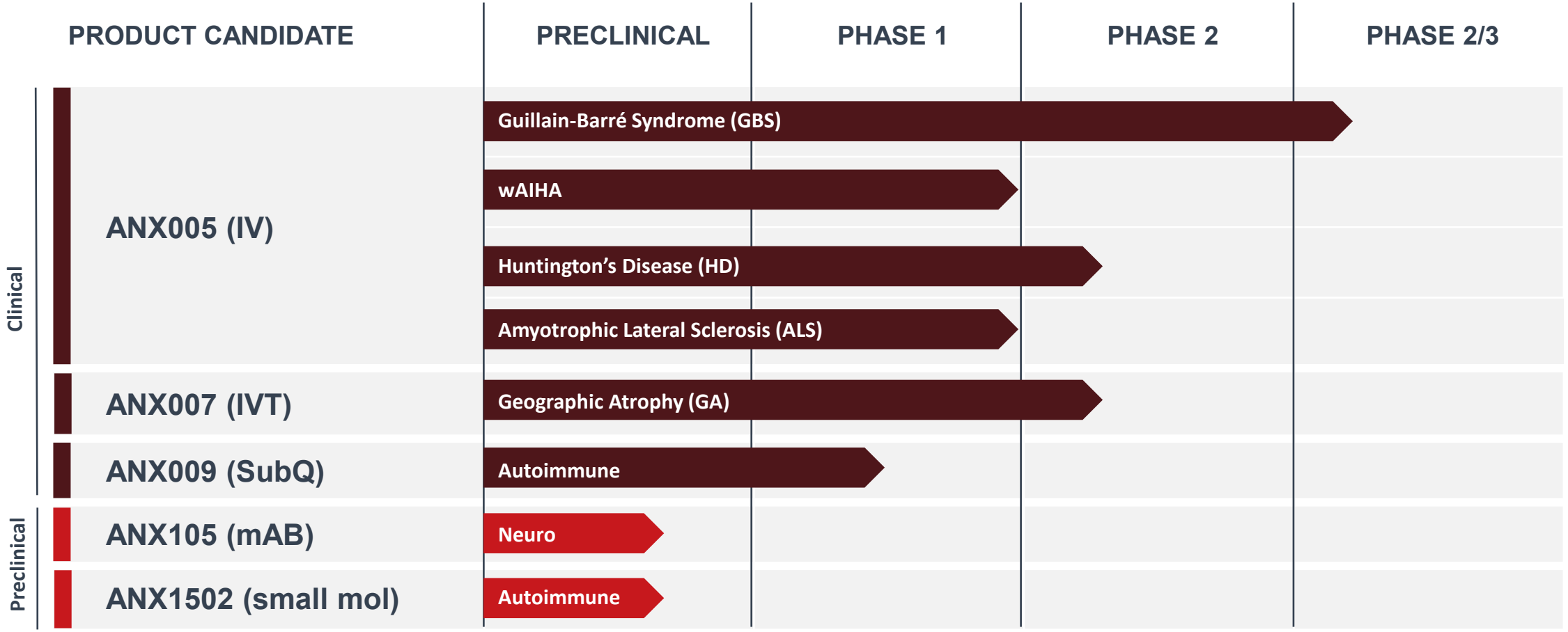
Wholly-Owned Pipeline of Classical Pathway Drug Candidates

Three (3) clinical drug candidates with diverse routes of administration



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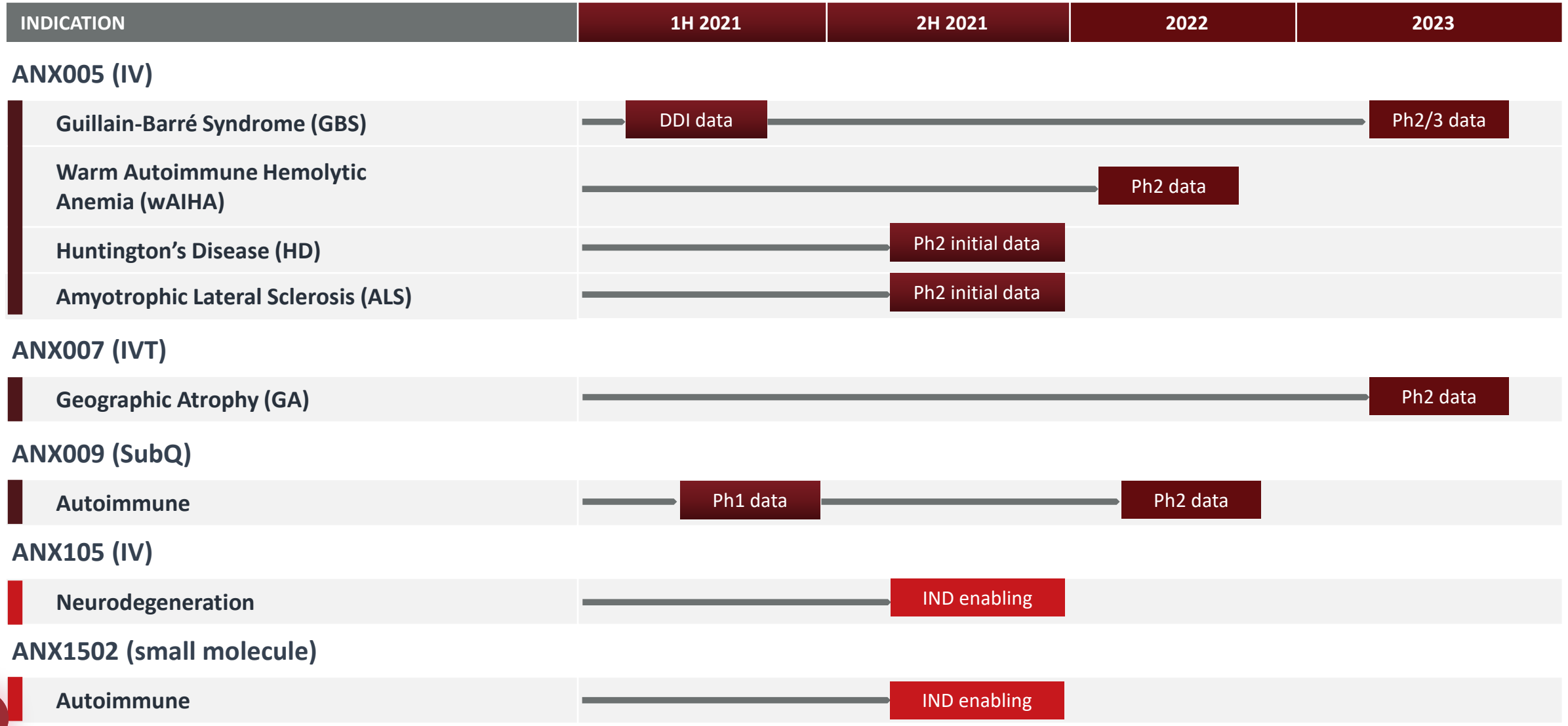
Multiple Value Creating Catalysts Through 2023

~$351M in cash; runway to achieve these milestones



Current cash and equivalents of $351.2M as of 12/31/2020

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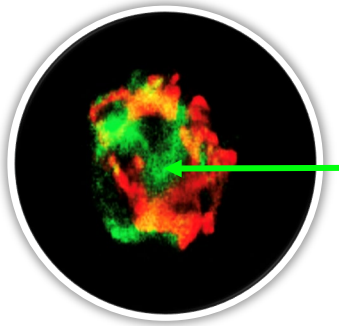
C1q is a Key Driver of Complement-Mediated Disease

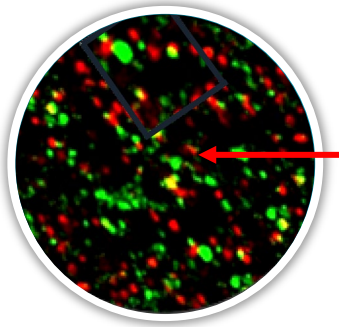
- **C1q directly binds and accumulates on tissues** in complement-mediated diseases
- **C1q anchors complement activation** on tissue surface **and drives disease processes**
- **Inhibiting C1q at the top** of the classical pathway **blocks downstream inflammation & tissue damage**

C1q Binding to Tissues in Disease



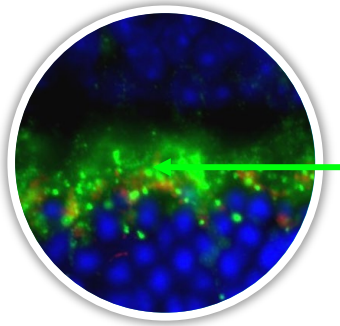
GBS

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]Jiao, et al., 2018 Mol Neurodegen 14:45 [3]C1q bound to photoreceptor cells 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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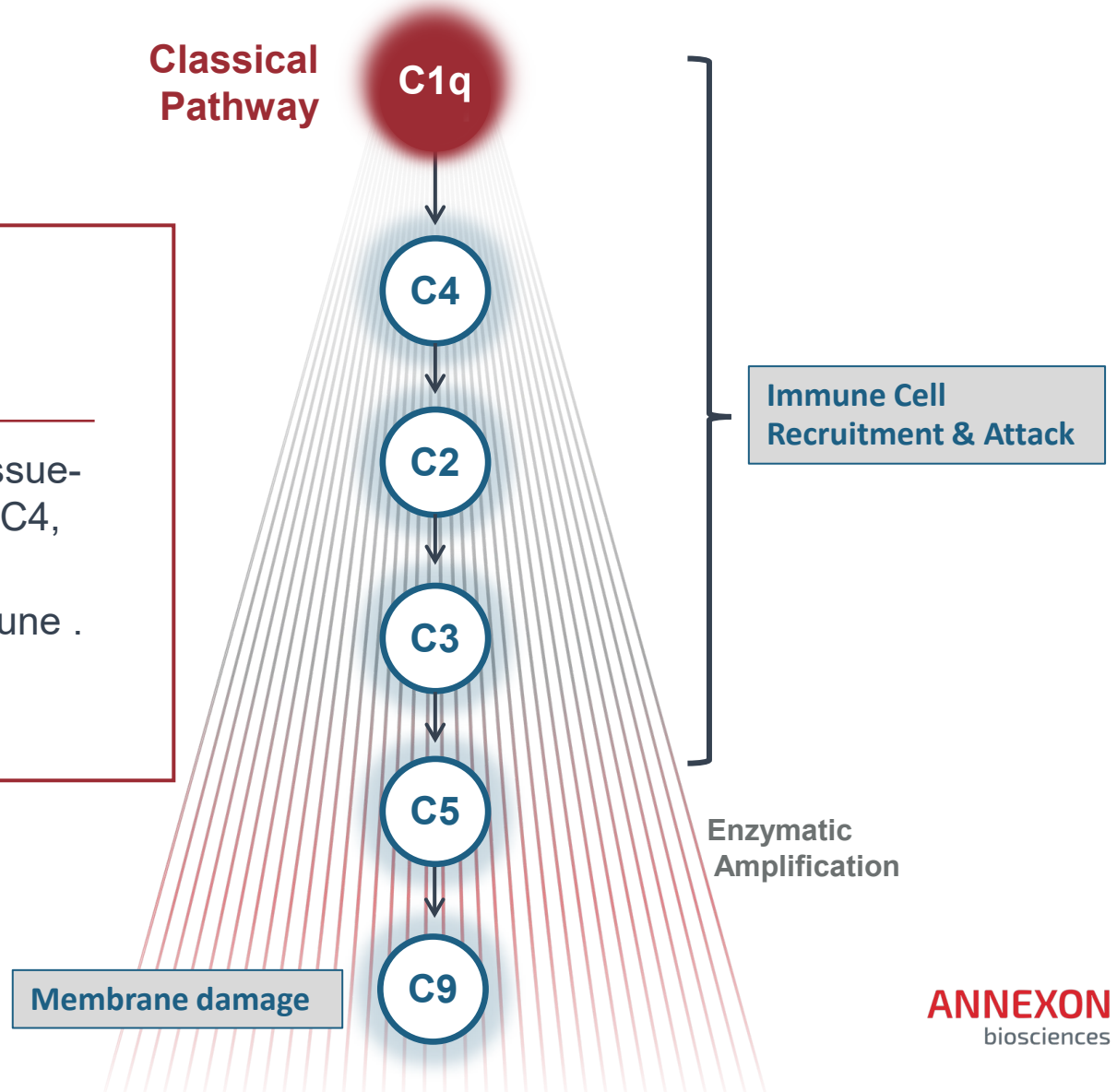
- ✓ **Potential Efficacy Advantage:** Shuts down all tissue-damaging components of classical pathway (C1q, C4, C3, C5, C9)[1]
- ✓ **Potential Safety Advantage:** Allows normal immune . functions of lectin and alternative complement pathways[1]



[1]Annexon data on file

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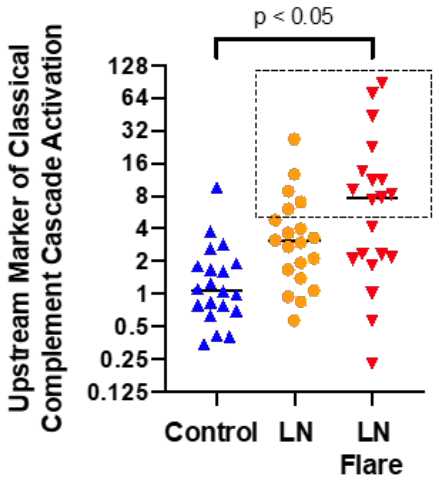
Established Biomarkers to Enhance Probability of Clinical Success

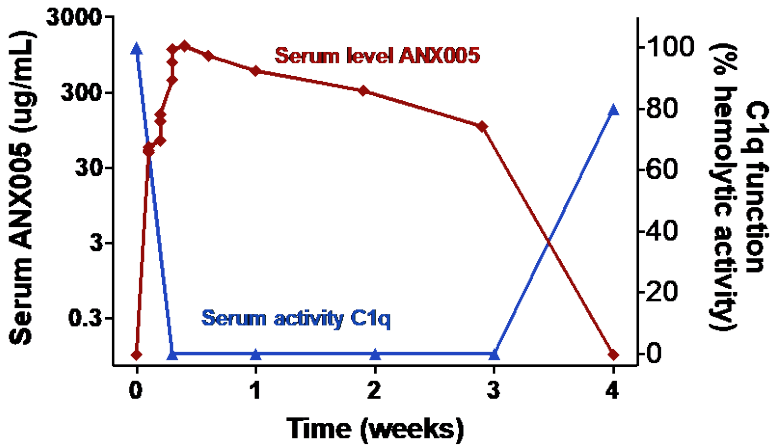
Leveraging classical complement and disease markers in patients

Indication and Patient Selection



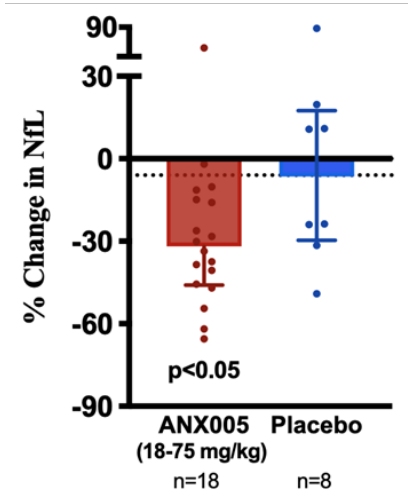
Target population for initial study
- 25% of lupus nephritis patients
- 55% of lupus nephritis patients in flare

Optimal Dose and Dosing Regimen



Data from a Patient Receiving 75 mg/kg*

Objective Measures of Treatment Effect



Higher Classical Complement Activation in Patients with Lupus Nephritis*

C1q inhibition in blood in GBS Phase 1b*

NfL statistically reduced in GBS Phase 1b*

*Annexon data on file

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Improving Patient Outcomes In Autoimmune Diseases

ANX005

Guillain-Barré Syndrome

Warm Autoimmune Hemolytic Anemia

ANX005 Proof of Concept in GBS

Phase 1b Summary

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

- ✓ **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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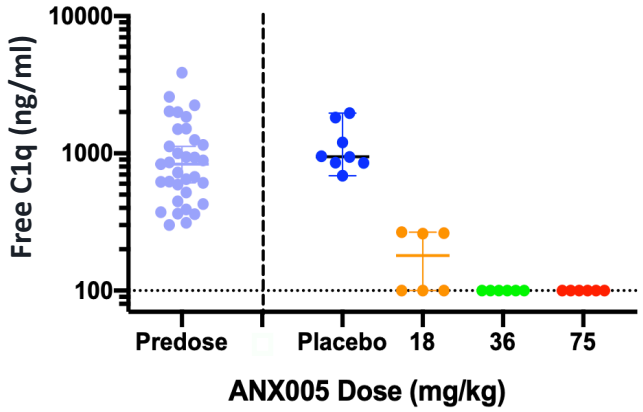
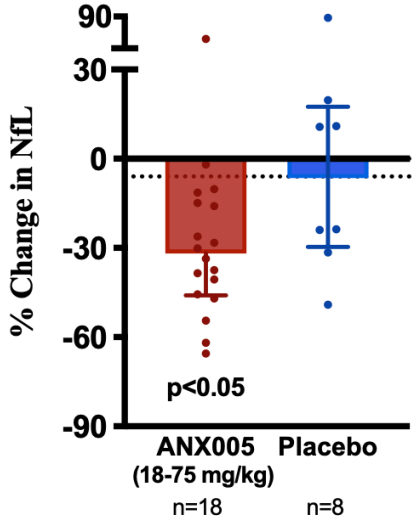
ANX005 Reduced NfL and Improved Outcomes in GBS Patients

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



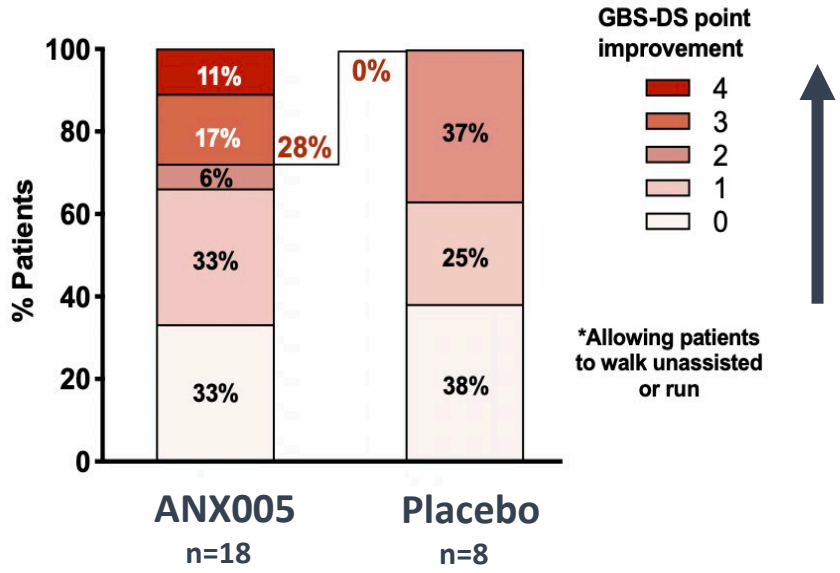
Dose Dependent Decrease of CSF Free C1q

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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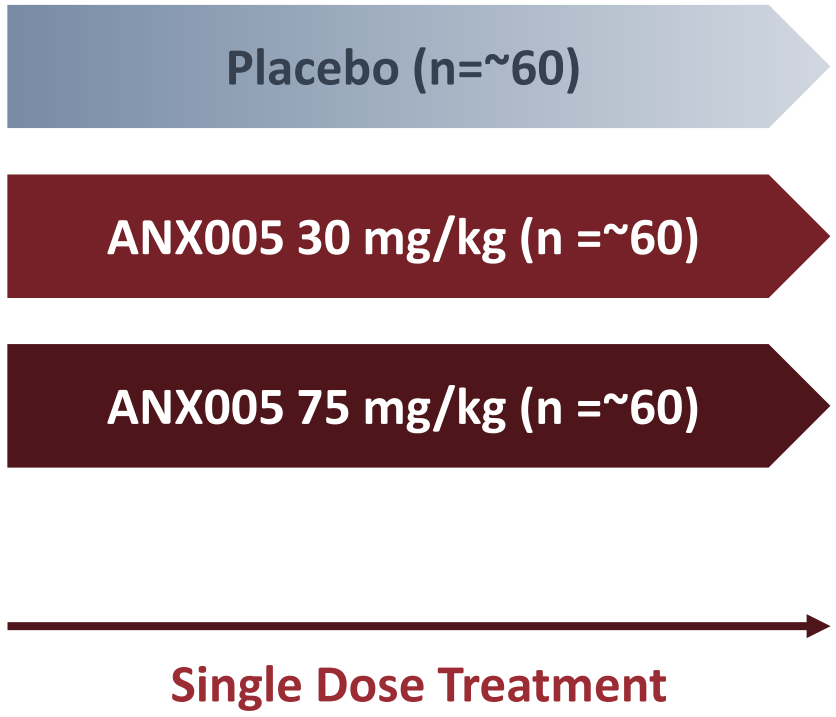
Ongoing Placebo-Controlled Phase 2/3 GBS Trial

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**
- **Data expected 2023**

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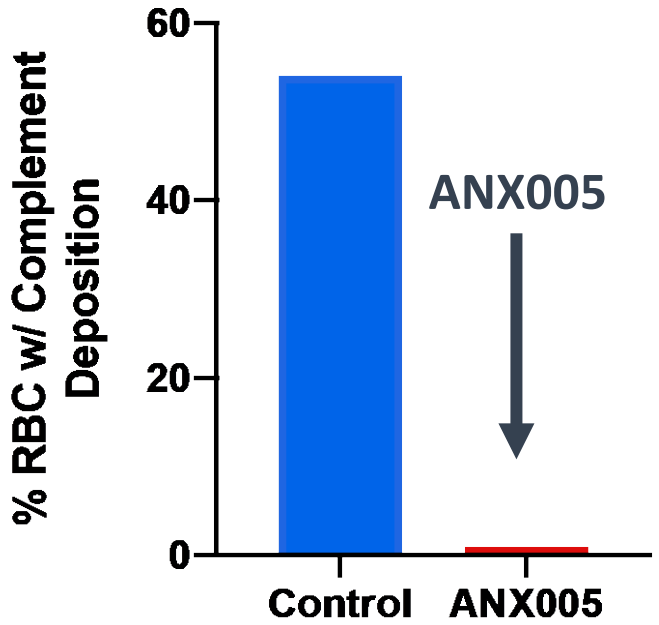
Targeting Life Threatening RBC Autoantibody Attack in wAIHA

- 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

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

ANX005 inhibits complement activation in wAIHA *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*
- **Precision medicine approach will facilitate appropriate patient selection for Phase 2 study**

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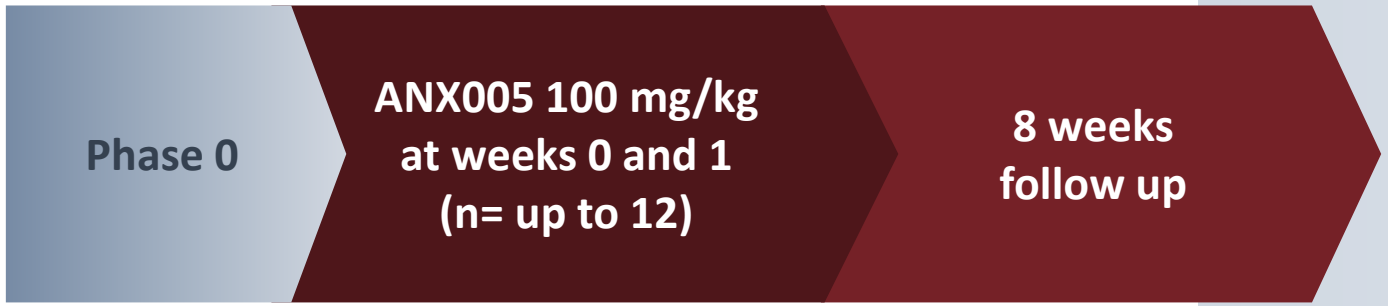
Patient Selection Ongoing for Phase 2 wAIHA Trial



- **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
- **Data expected 2022**

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Tackling Patient Disability in Devastating Neurodegenerative Diseases

ANX005

Huntington's Disease

Amyotrophic Lateral Sclerosis

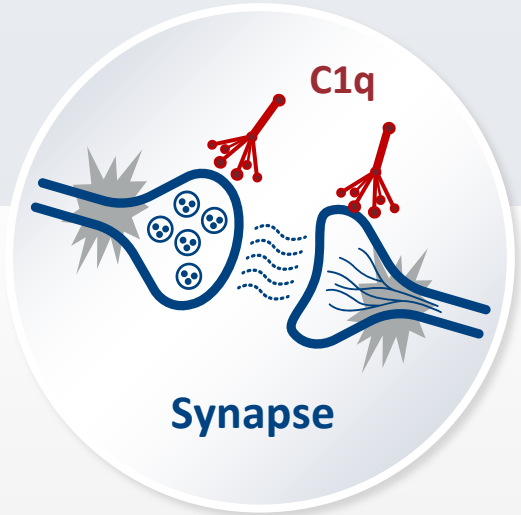
Strong Support for Role of C1q as a Major Driver of Synaptic Loss and Neurodegeneration

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**

Synaptic Protection via C1q Blockade Results In Functional Benefits in Many Disease Models

Neuronal stress triggers C1q accumulation and activation on synapses



Inhibition of C1q protects against synapse loss and neurodegeneration in many diseases* (animal models)

- 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]

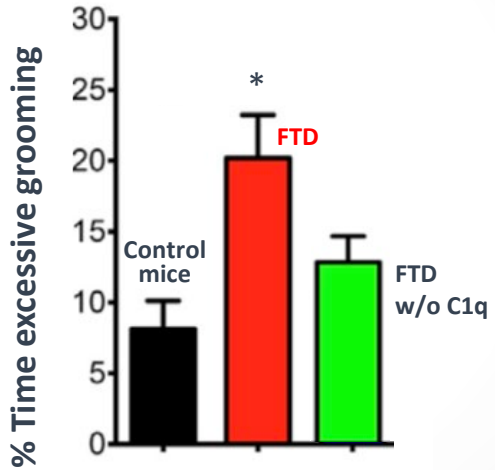
SYNAPSE LOSS IS A MAJOR DRIVER OF NEUROLOGICAL DISABILITY AND BLINDNESS

*[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*

Blocking C1q Provides Functional Benefit in Models of Disease

Prevents Obsessive Behavior in Frontotemporal Dementia

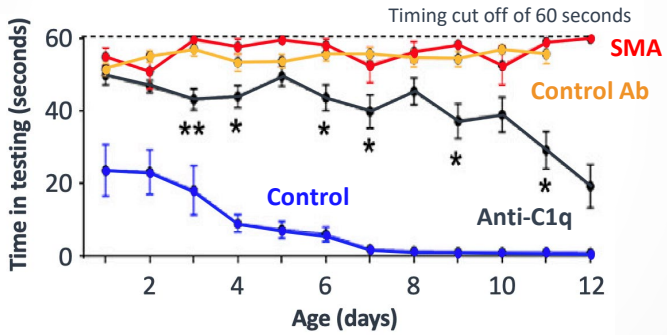
Mouse model of FTD with progranulin genetic deletion



Liu, et al., 2016 Cell 165:921

Allows gain of motor function in Spinal Muscular Atrophy

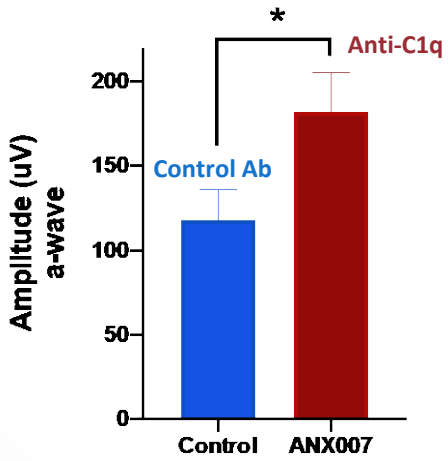
Transgenic SMN-Δ7 mouse model of SMA



Vukojicic, et al., 2019 Cell Reports 29, 3087-3100

Increases Retinal Function in Geographic Atrophy

Mouse model of photoreceptor cell loss induced by bright light



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

* $p < 0.05$

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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

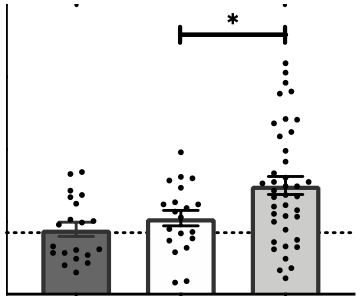
Markers of Disease Activity in HD Patients Reduced by ANX005 in HD Mice

Classical Complement Activation, Elevated NfL and Synapse Loss

PATIENTS

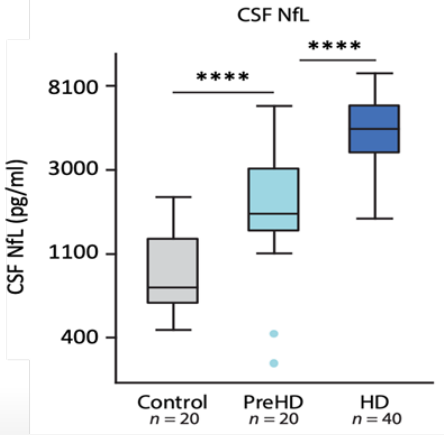
Increased Complement Activation w/ Disease Progression

CSF C4a (ng/mL)



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

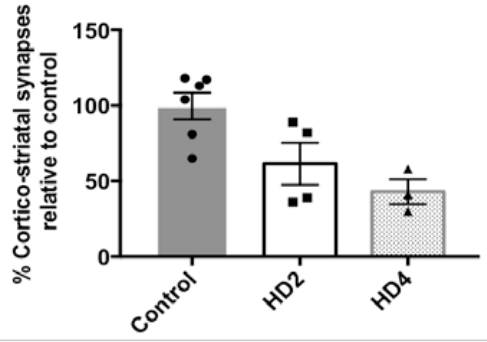
Increased NfL in the CSF with Disease Progression



Byrne, 2017 *Lancet Neurol* 16: 601

Progressive Synapse Loss in Huntington's

Synapse number (% Control)

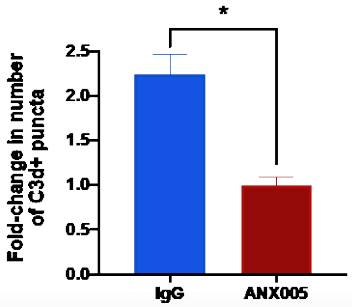


Unpublished Data, Dan Wilton and Beth Stevens, Harvard

MICE

Decreased Complement Activation w/ ANX005

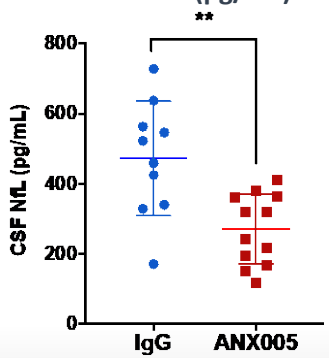
Fold-Change in Complement Deposition on Synapses



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

Decreased Levels of CSF NfL w/ ANX005

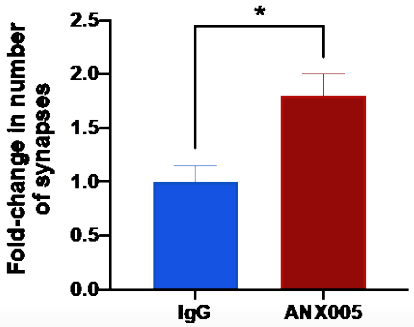
CSF NfL (pg/mL)



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

Protection Against Synapse Loss w/ 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 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**
- **Initial data expected 2H 2021**

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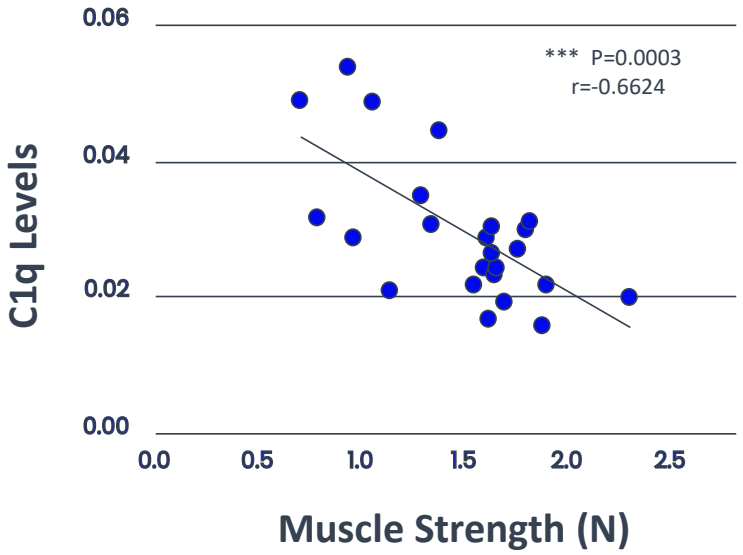
Anti-C1q Approach to Treat Neurodegeneration in ALS

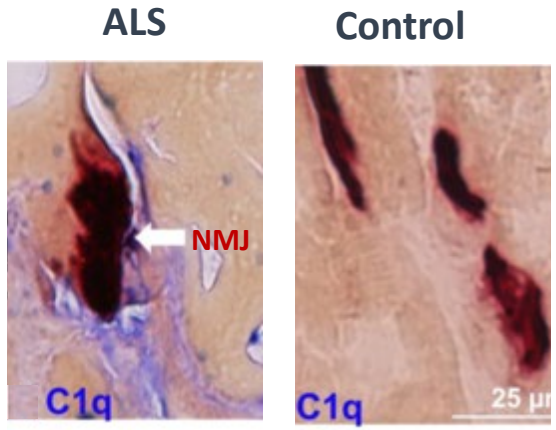
- Progressive weakness of limb and respiratory muscles
- Aberrant C1q activity potentially drives synaptic/ NMJ loss and disability
- Subjects have high baseline NfL levels
- Only upstream approach targeting both CNS and PNS aspects of the disease

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

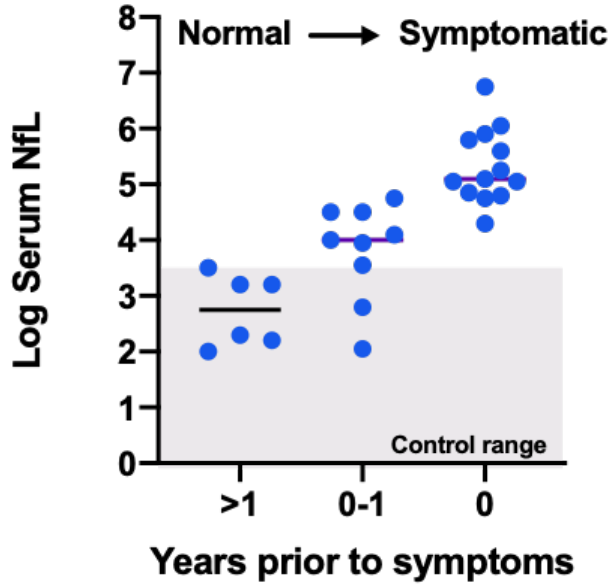
C1q Levels in NMJ of ALS Mouse Model Correlate with Weakness



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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Planned 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
- **Initial data expected 2H 2021**

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Tackling Blindness in Retinal Diseases

ANX007

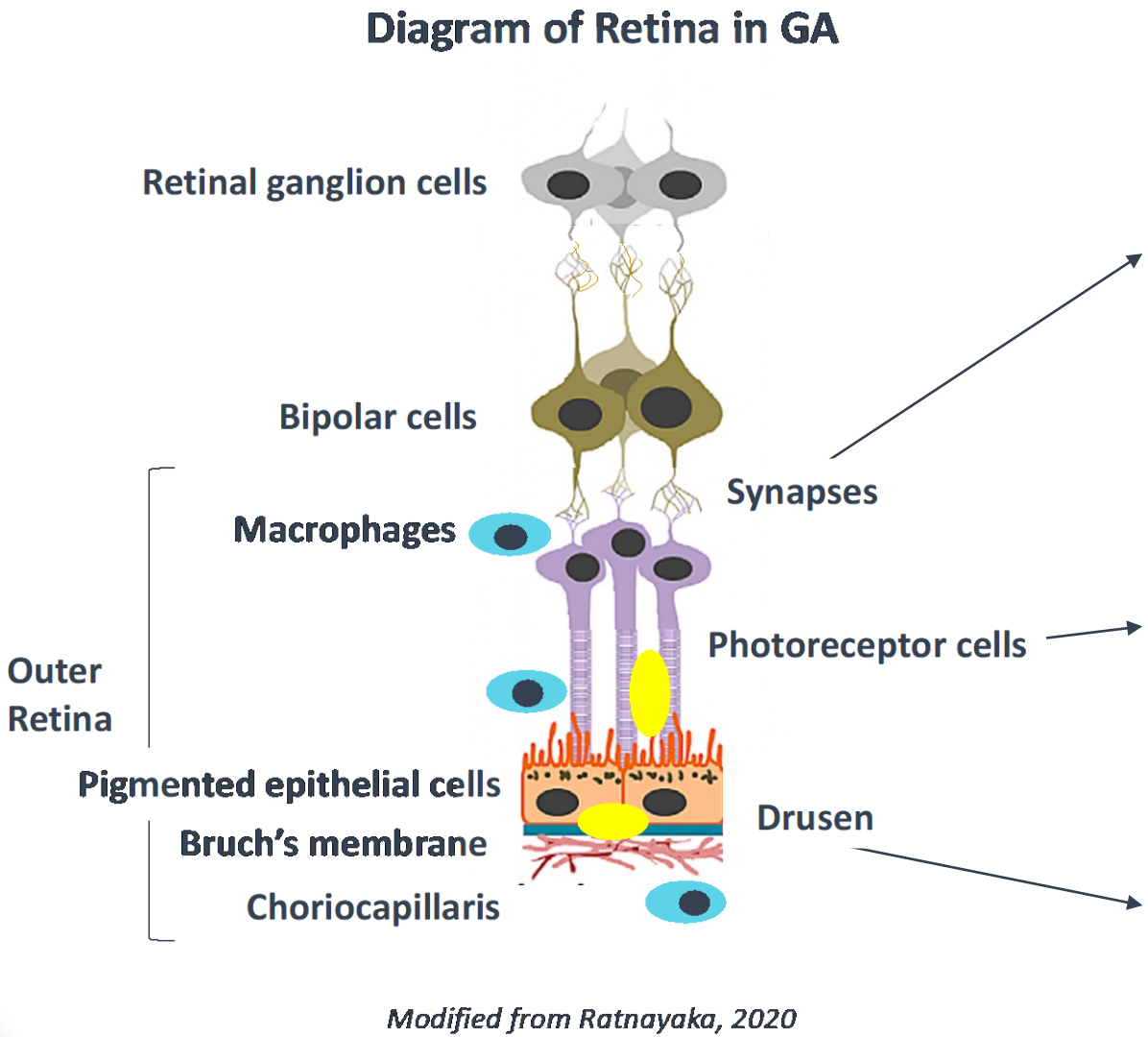
Geographic Atrophy

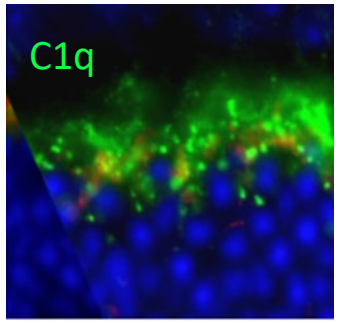
Differentiated Neuroprotective Approach for Geographic Atrophy

ANX007 in GA

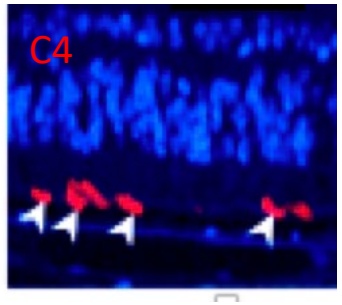
- **Prevent vision decline due to loss of photoreceptor neurons caused by excess classical complement activity**
- **C1q and its activating substrates are present in all layers of the outer retina**
- **Blocking C1q at top of cascade stops downstream C1q, C3, and C5 activities** that drive local immune response and destruction in the retina

C1q and Downstream Activated Complement Components are Deposited in Multiple Layers of Outer Retina in GA

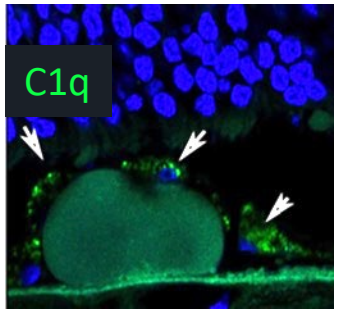




C1q on synapses of photoreceptor cells in aged mice[1]



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



C1q on Drusen in GA patients[3]

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

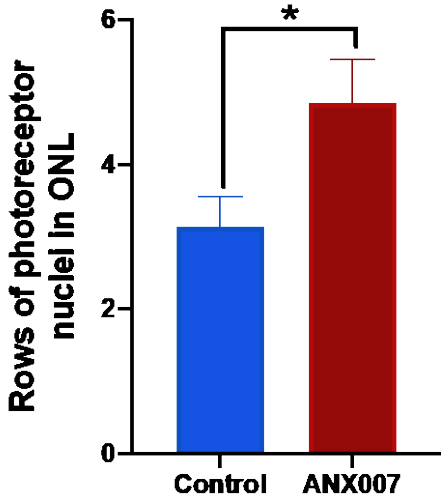
ANNEXON biosciences

ANX007 Provides Neuroprotection in Mouse Model of Photoreceptor Cell Loss/Geographic Atrophy

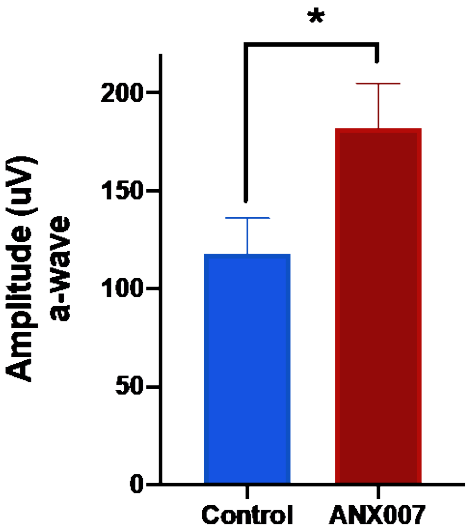
- **C1q is locally produced in the retina and a key driver of cell loss**
- **Upstream activator of C3**
- **Selective C1q inhibition allows normal function** of lectin and alternative pathway

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

* $p < 0.05$

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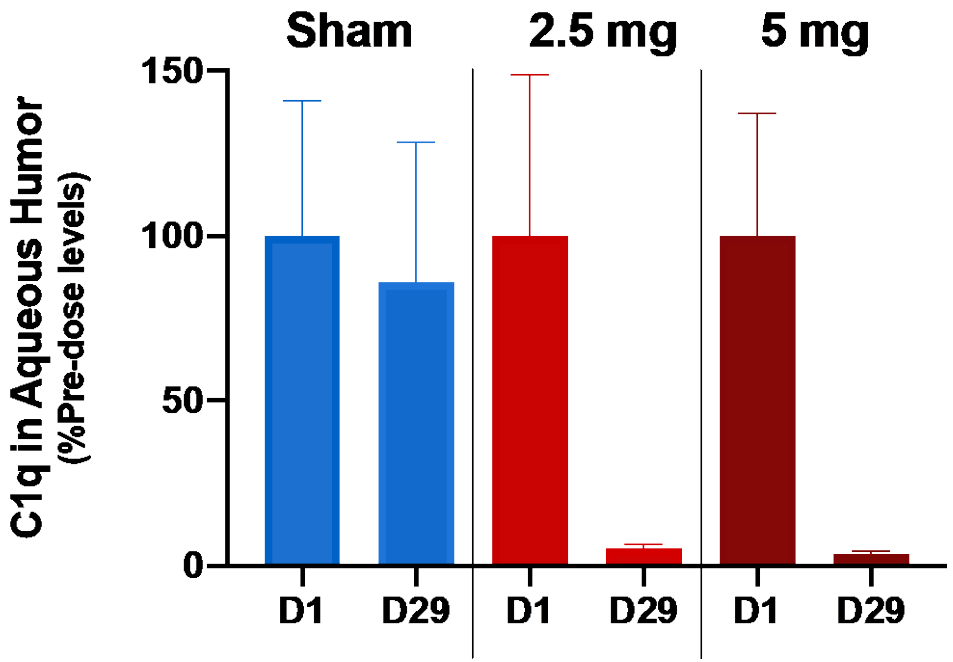
ANX007 Effectively Inhibits C1q in Phase 1b Patients

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

Free C1q Levels in Aqueous Humor



D1 = Day 1 (before ANX007 dosing)

D29 = Day 29 (post-1st dose)

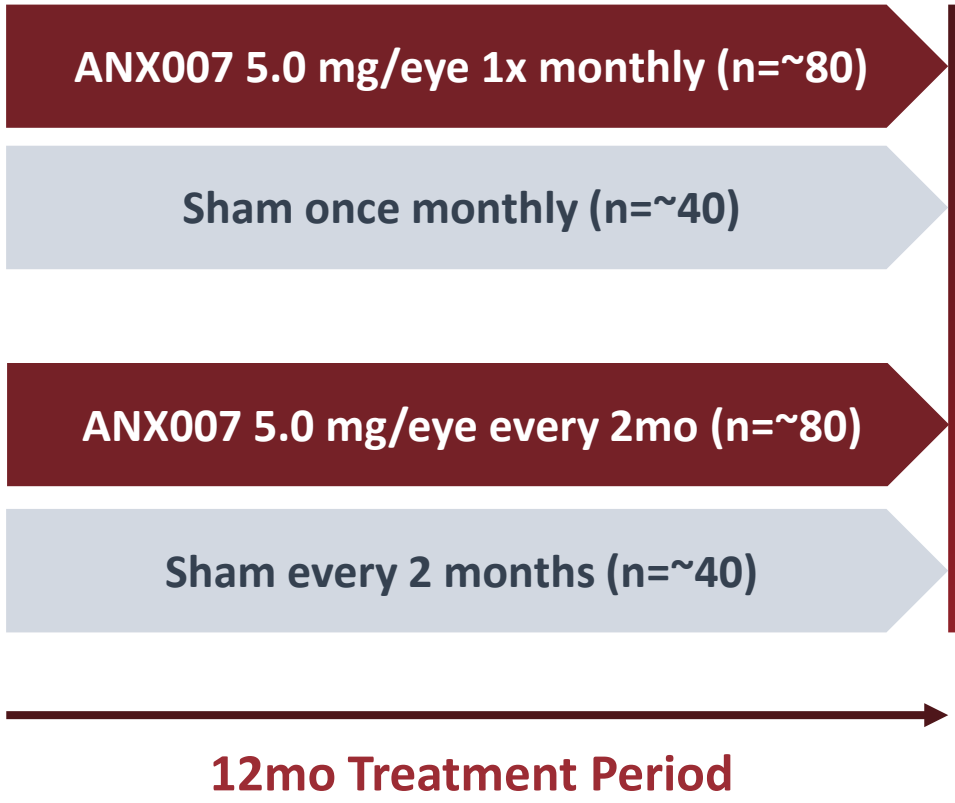
ANX007 DATA SUMMARY

- **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

ANNEXON biosciences

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
- **Data expected 2023**

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Potential to Rapidly Expand Platform Across a Breadth of Diseases

AUTOIMMUNE

wAIHA

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

GBS

- **CIDP** (Chronic Idiopathic Demyelinating Polyneuropathy)
- **MMN** (Multifocal Motor Neuropathy)
- **PMS** (Progressive Multiple Sclerosis)
- **ON** (Optic Neuritis)

NEURODEGENERATION

HD & ALS

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

OPHTHALMOLOGY

GA

- **GLA** (Glaucoma)

Current Beachhead Indications Sample Follow-on Indications

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Significant Opportunity Over the Next 24 Months

NEXT GENERATION COMPLEMENT COMPANY

Broad anti-C1q platform in orphan and large patient populations

VAST NEAR-TERM GROWTH POTENTIAL

Execute 5 Phase 2 clinical trials in autoimmune, neurodegenerative and ophthalmic diseases

PLAYING WITH OUR HEARTS & MINDS

Dedicated team with track record of success

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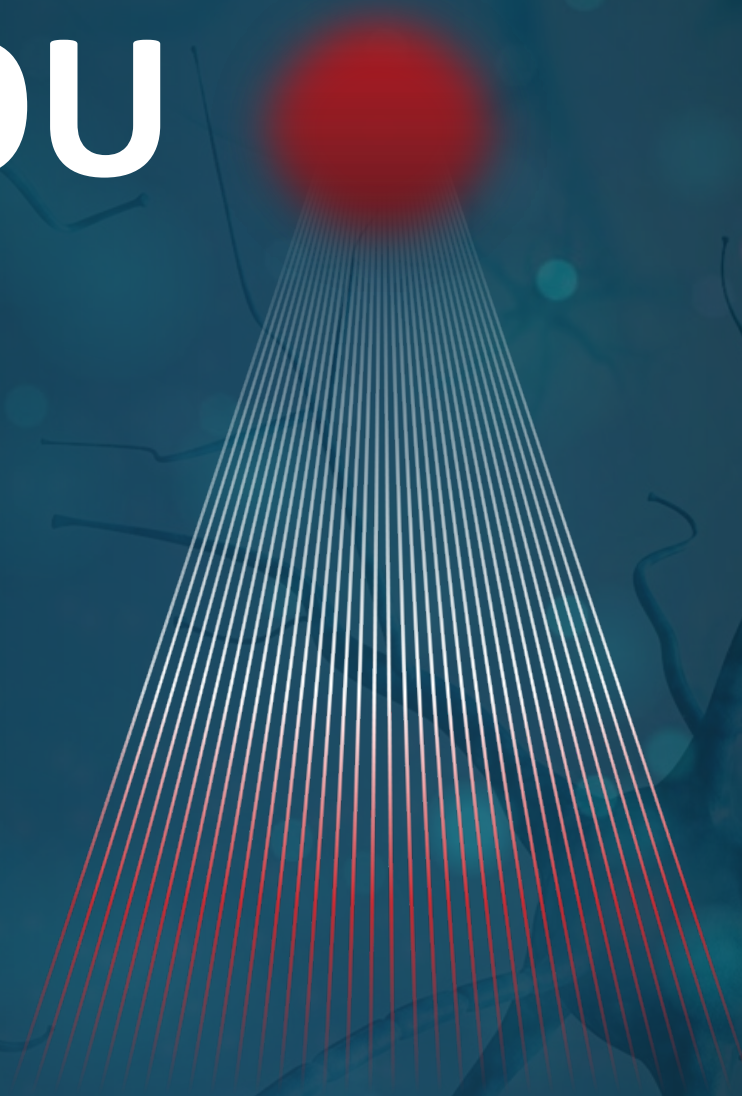
THANK YOU



ANNEXON
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