Stopping Complement-Mediated Diseases

AT THE START

COMPANY PRESENTATION I MAY 2021



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

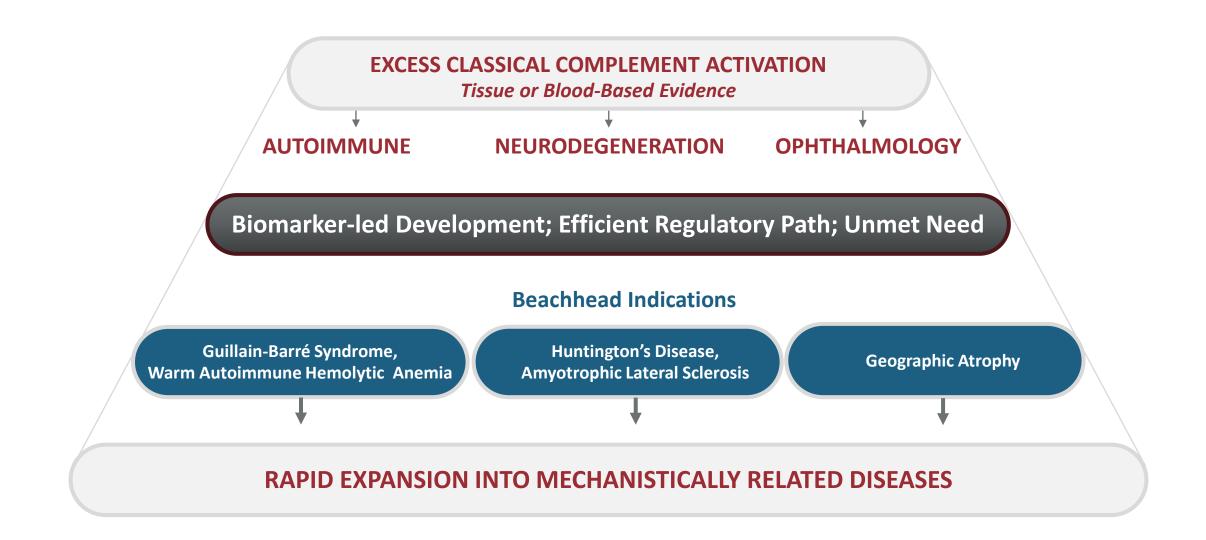
• Beachhead indication de-risks portfolio expansion in related AI and neuro diseases

PROVEN, PASSIONATE TEAM to translate the opportunity

• Strong track record of innovation and success



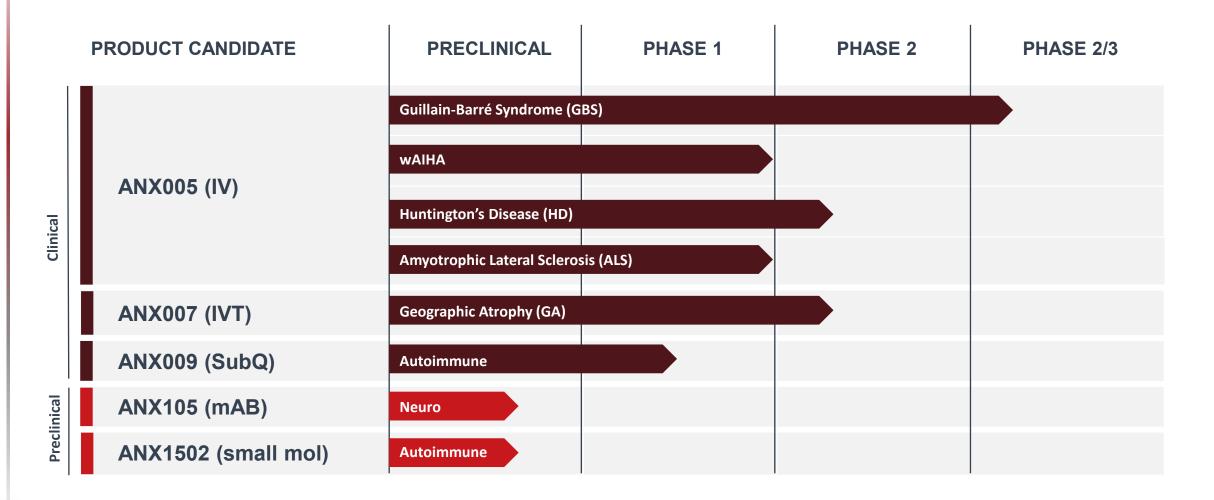
Rigorous Approach to Maximizing Our Broad Opportunity





Wholly-Owned Pipeline of Classical Pathway Drug Candidates

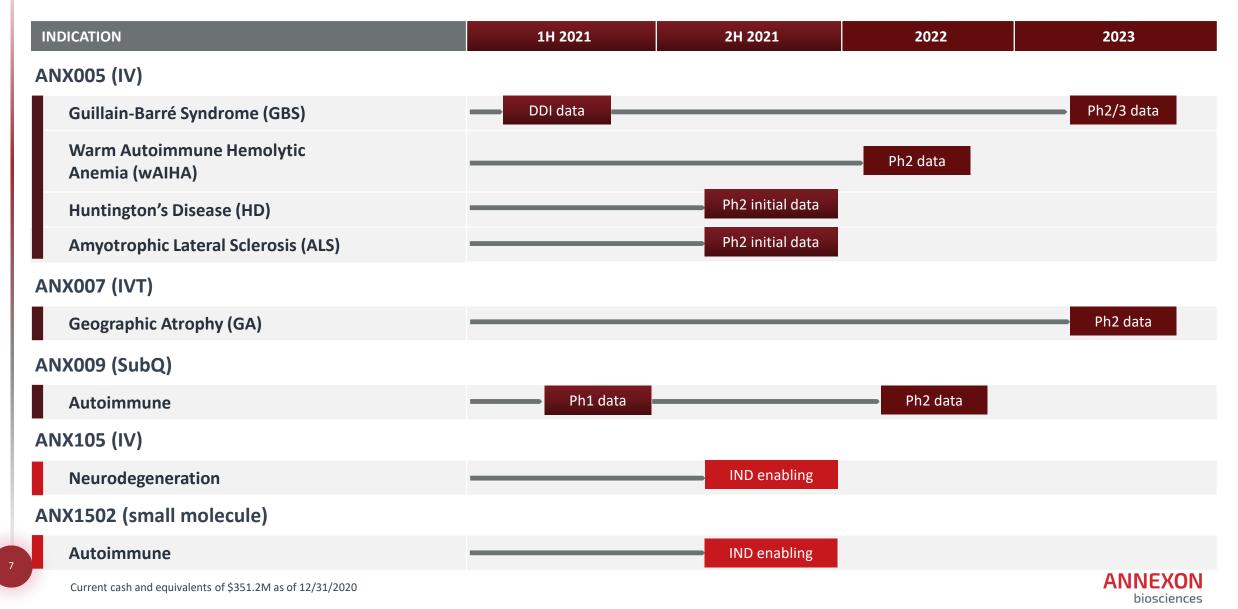
Three (3) clinical drug candidates with diverse routes of administration





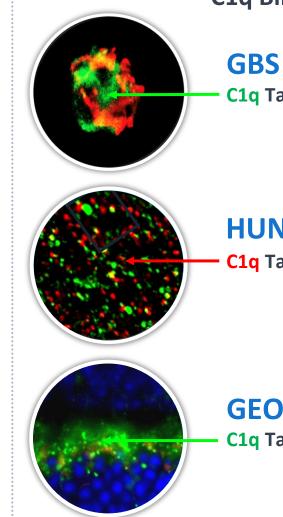
Multiple Value Creating Catalysts Through 2023

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



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

C1q Targeting the Neuromuscular Junction¹

HUNTINGTON'S DISEASE

C1q Targeting Striatal Synapses²

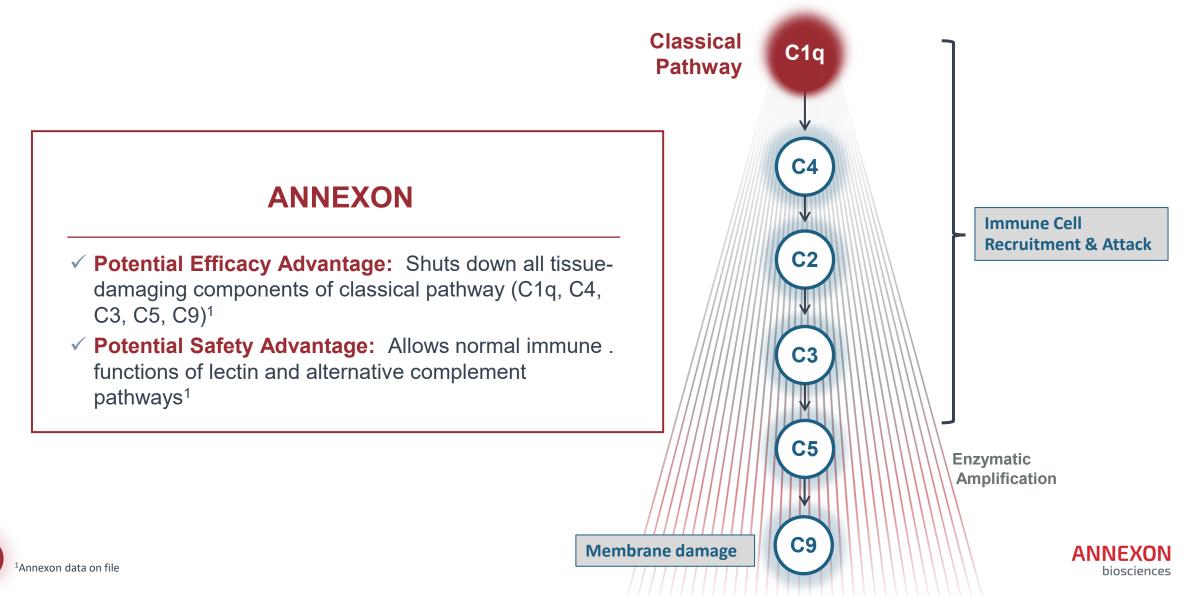


C1q Targeting Photoreceptor Synapses³



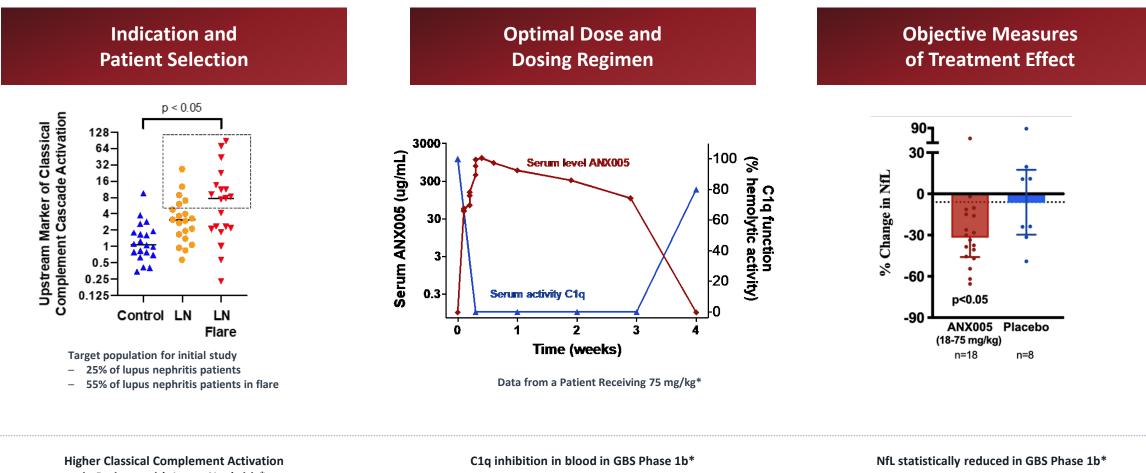
C1q Inhibition Stops Classical Complement Activity at the Start

Prevents downstream activation of all tissue damaging components



Established Biomarkers to Enhance Probability of Clinical Success

Leveraging classical complement and disease markers in patients



10





Improving Patient Outcomes In Autoimmune Diseases

ANX005

Guillain-Barré Syndrome

Warm Autoimmune Hemolytic Anemia

ANX005 Proof of Concept in GBS

Phase 1b Summary

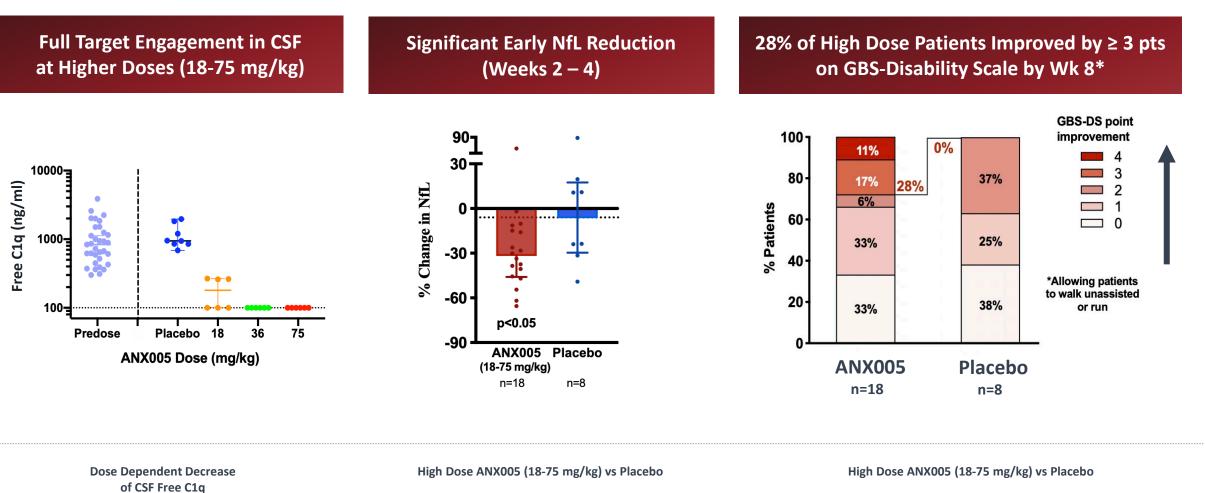
GBS is a severe disease resulting from autoantibody attack on peripheral nerves, triggering complement (C1q) and neurodegeneration

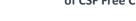
- Rapid and Complete Target Engagement in periphery and CSF enabling further study of GBS and additional C1q-mediated diseases
- Early and Statistical Decline of Serum NfL, a well-accepted marker of neurodegeneration in GBS and other neurological diseases (e.g., HD, ALS)
- Consistent positive trends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





ANX005 Reduced NfL and Improved Outcomes in GBS Patients







Ongoing Placebo-Controlled Phase 2/3 GBS Trial

Fast Track and Orphan Drug designations granted

ANX005 30 mg/kg (n =~60)

ANX005 75 mg/kg (n =~60)

Single Dose Treatment

- 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



Targeting Life Threatening RBC Autoantibody Attack in wAIHA

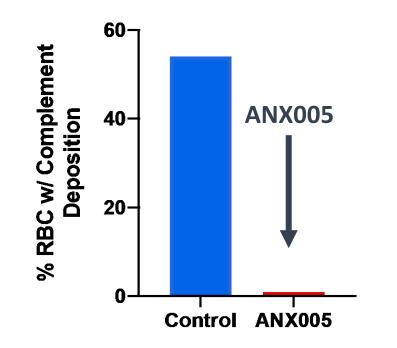
- Autoantibodies attack and destroy RBCs, resulting in anemia, can develop rapidly or gradually
- Complement activation amplifies RBC destruction in certain patients
- Targeted strategy to select patients who meet specific biomarker criteria of complement activation





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



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



ANNEXON biosciences

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 Neurod

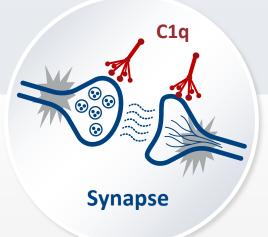
Original discoveries of Annexon co-founder, the late Dr. Ben Barres, on the role of C1q in neurodegenerative diseases

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

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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 Disease¹

Alzheimer's Disease²

Spinal Muscular Atrophy³

Glaucoma⁴

Geographic Atrophy (AMD)⁵

Frontotemporal Dementia⁶

Traumatic Brain Injury & Stroke⁷

SYNAPSE LOSS IS A MAJOR DRIVER OF NEUROLOGICAL DISABILITY AND BLINDNESS

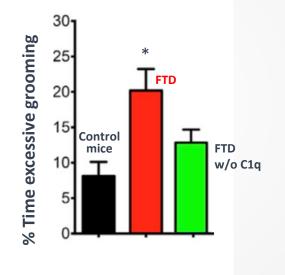
*¹Wilton and Stevens, Harvard, unpublished. ²Fonseca, 2004, J Neurosci; Hong, 2016, Science; Dejanovic, 2018, Neuron; ³Vukojicic, 2019, Cell Reports; ⁴Howell, 2011, J Clin Inves; Williams, 2016, Mol Neurodegen; ⁵Jiao, 2018, Mol Neurodeg; ⁶Lui, 2016, Cell; ⁷Krukowski, 2018, Int.J Mol Sci; Jeanne Paz,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



Blocking C1q Provides Functional Benefit in Models of Disease

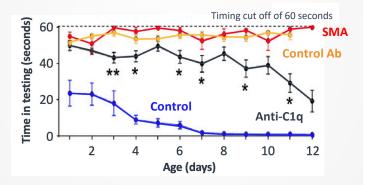
Prevents Obsessive Behavior in Frontotemporal Dementia

Mouse model of FTD with progranulin genetic deletion



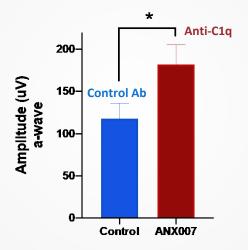
Allows gain of motor function in Spinal Muscular Atrophy

> Transgenic SMN-Δ7 mouse model of SMA



Increases Retinal Function in Geographic Atrophy

Mouse model of photoreceptor cell loss induced by bright light



Liu, et al., 2016 Cell 165:921

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

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



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

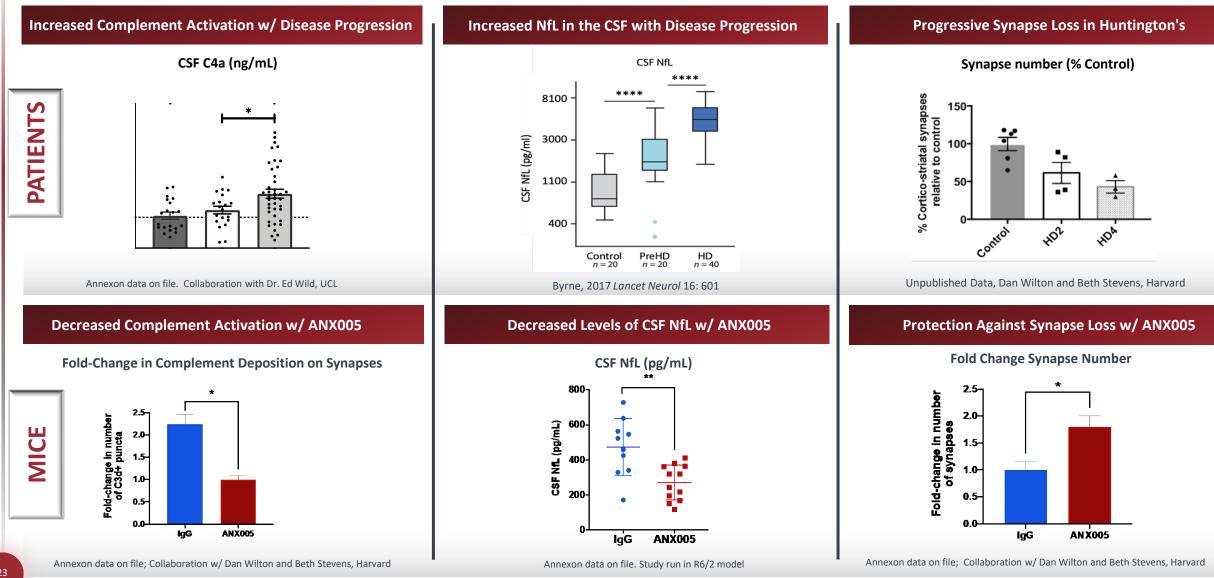
- Progressive movement disorder, dementia, psychosis driven by classical complement pathway activation
- C1q localized on synapses
- High and sustained NfL levels
- Targeting synaptic loss and neuronal death to tackle neurodegeneration





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

Classical Complement Activation, Elevated NfL and Synapse Loss



ANNEXON

biosciences

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



Anti-C1q Approach to Treat Neurodegeneration in ALS

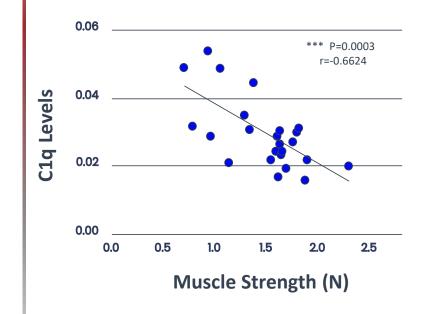
- Progressive weakness of limb and respiratory muscles
- Aberrant C1q activity potentially drives synaptic/ NMJ loss and disability
- Subjects have high baseline NfL levels
- Only upstream approach targeting both CNS and PNS aspects of the disease

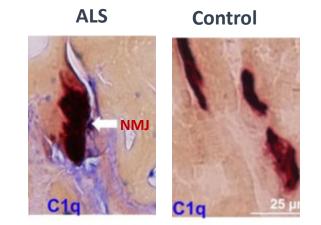


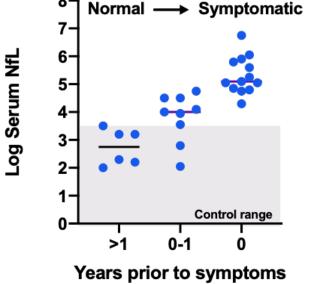


C1q Deposition Correlated w/ Muscle Weakness in Mouse Model and Preceded Denervation in ALS Patients; NfL Elevated w/Disease

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



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





Tackling Blindness in Retinal Diseases

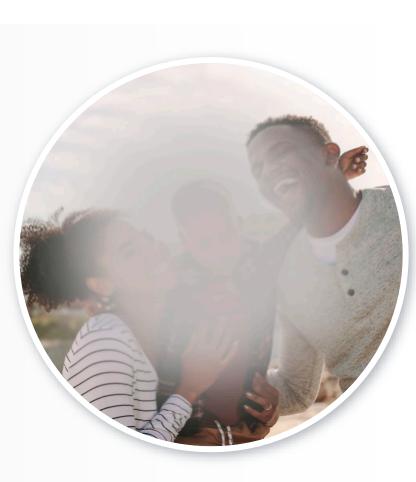
ANX007

Geographic Atrophy

Differentiated Neuroprotective Approach for Geographic Atrophy

ANX007 in GA

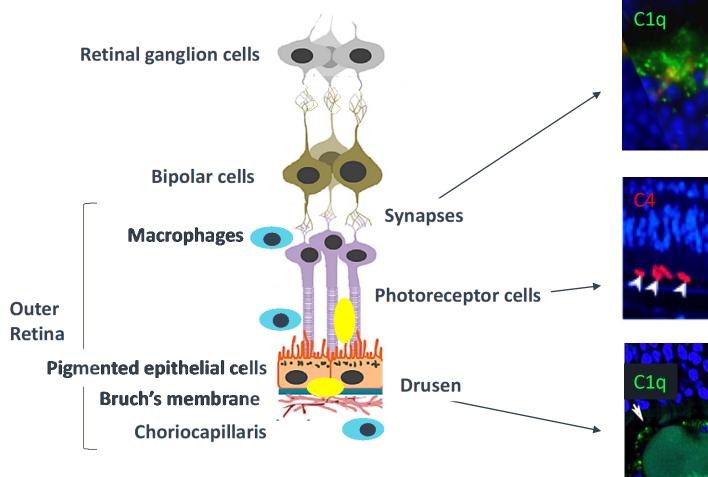
- Prevent vision decline due to loss of photoreceptor neurons caused by excess classical complement activity
- C1q and its activating substrates are present in all layers of the outer retina
- Blocking C1q at top of cascade stops downstream C1q, C3, and C5 activities that drive local immune response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



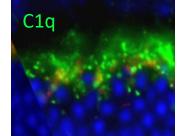


C1q and Downstream Activated Complement Components are **Deposited in Multiple Layers of Outer Retina in GA**

Diagram of Retina in GA



Modified from Ratnayaka, 2020



C1q on synapses of photoreceptor cells in aged mice¹



Downstream C4 deposited on photoreceptor cell outer segments in GA patients²

C1q on Drusen in GA patients³



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

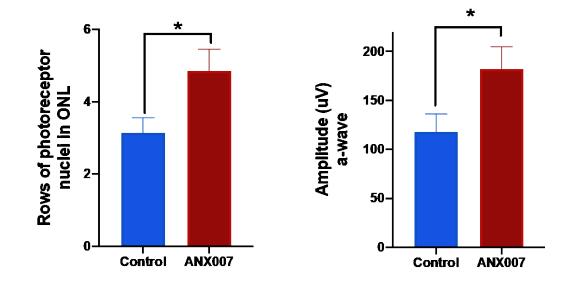
- C1q is locally produced in the retina and a key driver of cell loss
- Upstream activator of C3
- Selective C1q inhibition allows normal function of lectin and alternative pathway

Intravitreal Administration of ANX007 Protects Photoreceptor Cells and Retinal Function

Anti-C1q Protects Photoreceptor Cells / Retinal Thickness

Protects Retinal Function

biosciences

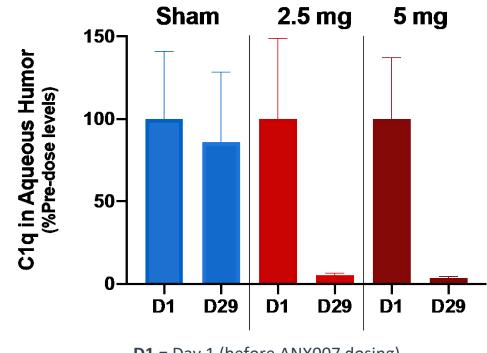


Jiao,, et al., 2018 Mol Neurodegener 13(1):45

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)

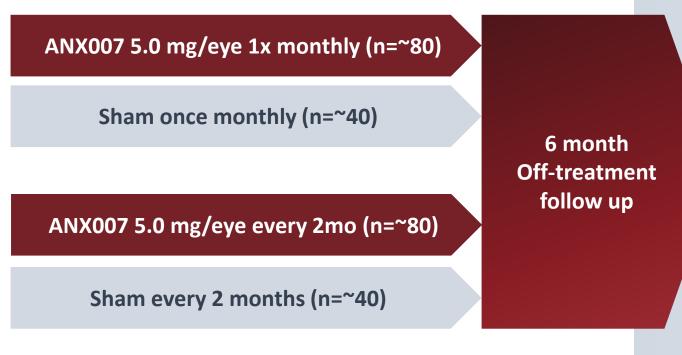
ANX007 DATA SUMMARY

- 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



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Ongoing Phase 2 Geographic Atrophy Trial



12mo Treatment Period

 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



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

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

GBS

NEURODEGENERATION

HD & ALS

FTD (Frontal Temporal Dementia)

SMA (Spinal Muscular Atrophy)

AD (Alzheimer's Disease)

TBI (Traumatic Brain injury)

OPHTHALMOLOGY

GA

GLA (Glaucoma)



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



THANK YOU

