# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**Washington, D.C. 20549**

# FORM 8-K

**CURRENT REPORT**
**Pursuant to Section 13 or 15(d)**
**of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): January 11, 2021**

# ANNEXON, INC.
**(Exact name of registrant as specified in its charter)**

| **Delaware** | **001-39402** | **27-5414423** |
|---|---|---|
| **(State or other jurisdiction of incorporation)** | **(Commission File Number)** | **(IRS Employer Identification Number)** |

**180 Kimball Way, Suite 200**
**South San Francisco, California 94080**
**(Address of principal executive offices, including Zip Code)**

**Registrant's telephone number, including area code: (650) 822-5500**

**Not Applicable**
**(Former name or former address, if changed since last report)**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| **Common Stock, $0.001 par value per share** | **ANNX** | **The Nasdaq Stock Market** |

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

**Item 7.01 Regulation FD Disclosure.**

Attached hereto as Exhibit 99.1 is an investor presentation that Annexon, Inc. plans to present during the 39th Annual J.P. Morgan Healthcare Conference commencing on January 11, 2021.

**Item 9.01 Financial Statements and Exhibits.**

| Exhibit No. | Description |
|---|---|
| 99.1 | Annexon, Inc. Investor Presentation. |

The information in this report, including the exhibit hereto, shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that Section 11 and 12(a)(2) of the Securities Act of 1933, as amended. The information contained herein and in the accompanying exhibit shall not be incorporated by reference into any filing with the U.S. Securities and Exchange Commission made by Annexon, Inc., whether made before or after the date hereof, regardless of any general incorporation language in such filing.

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**ANNEXON, INC.**

Date: January 11, 2021

By: /s/ Jennifer Lew
Jennifer Lew
Executive Vice President and Chief Financial Officer

Exhibit 99.1

# 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.

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 Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2020 filed with the Securities and Exchange Commission (SEC) on November 16, 2020 as well as discussions of potential risks, uncertainties and other important factors in our other filings with the 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.

# 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

# 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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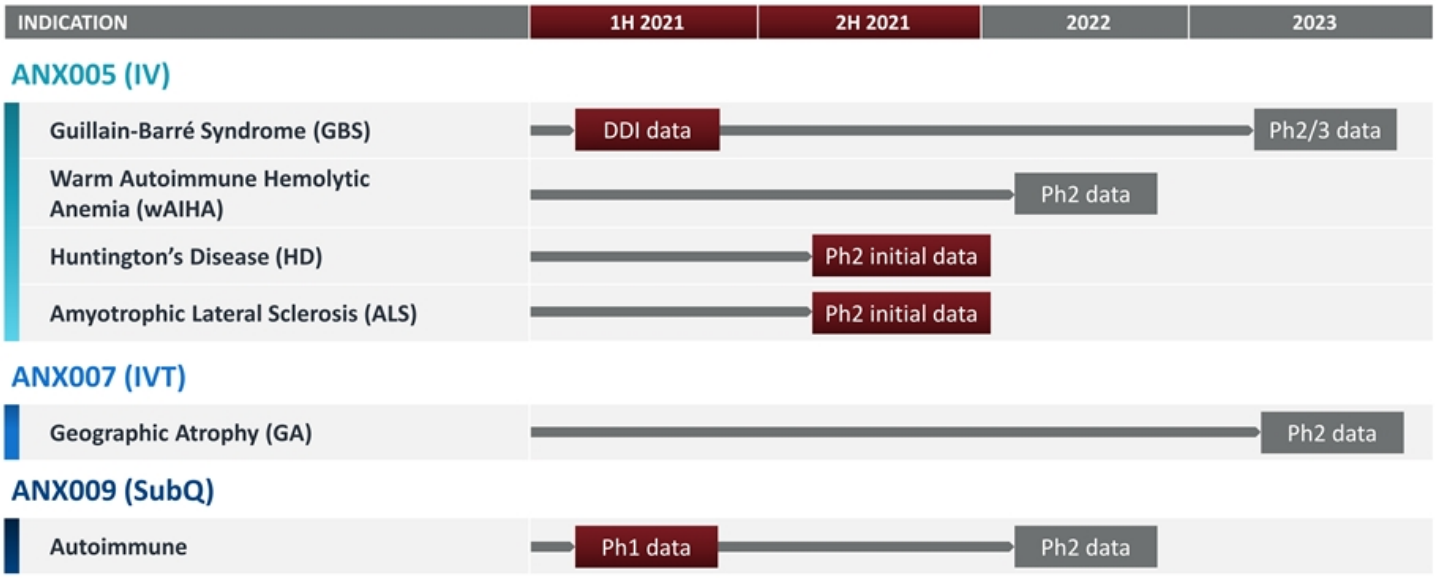
# Significant Catalysts in 2021 and Beyond

## 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

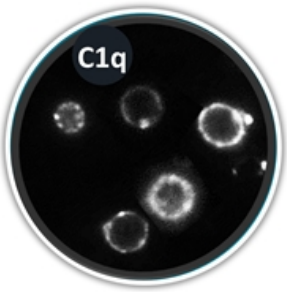
**C1q directly binds to tissue, initiating and anchoring complement in diseases of the body, brain and eye**

### GBS


*C1q Targeting the Neuromuscular Junction*

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

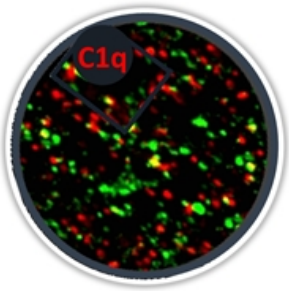
### HEMOLYTIC ANEMIA




*C1q Targeting Red Blood Cells*

C1q bound to antibody coated RBC
Annexon data on file

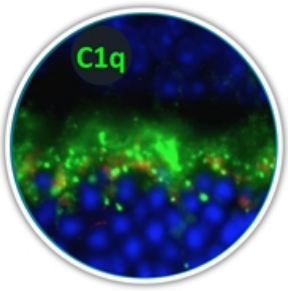
### HUNTINGTON'S




*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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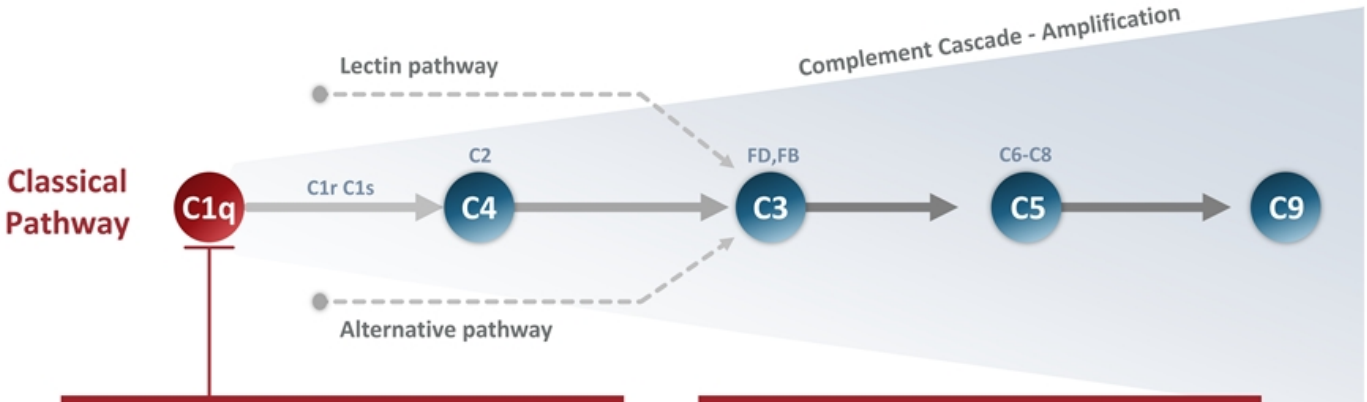
# Inhibiting C1q Shuts Down Entire Classical Complement Pathway

**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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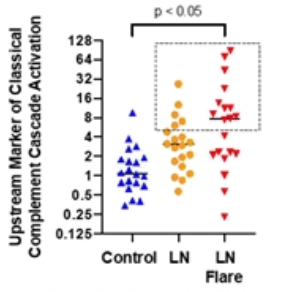
# Leveraging Biomarkers to Increase Probability of Clinical Success

## Measuring objective classical complement and disease markers in patients

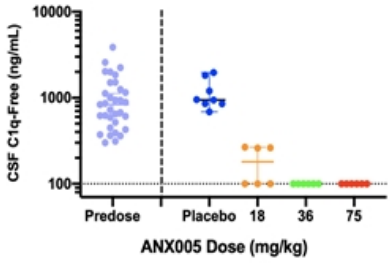
### Right Indication and Patient Selection




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

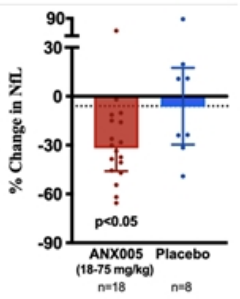
Higher Classical Complement Activation in Patients with Lupus Nephritis, Particularly Those in Flare

### Optimal Dose and Dosing Regimen




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

### Objective Measures of Treatment Effect




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

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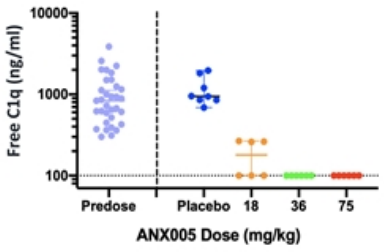
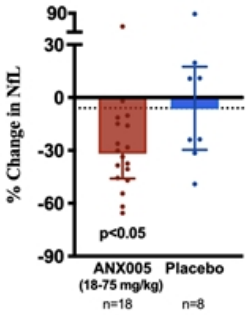
# ANX005 Well-Tolerated, Achieved Full Target Engagement, Reduced NfL and Prevented Disability in GBS Phase 1b Dose-Ranging Trial

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



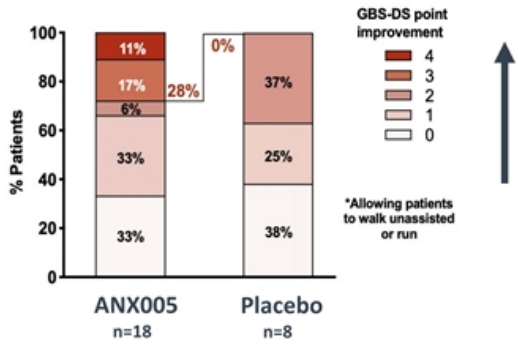

Dose Dependent Decrease of CSF Free C1q

**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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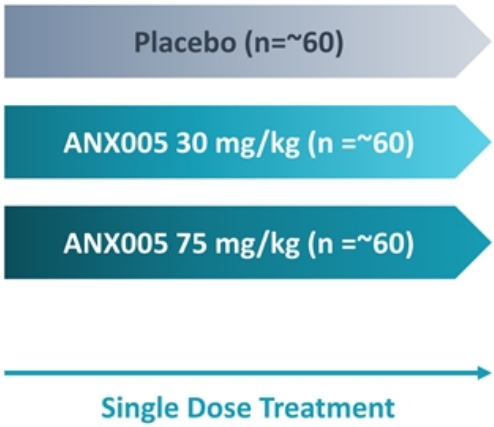
# Ongoing GBS Phase 2/3 Trial with ANX005

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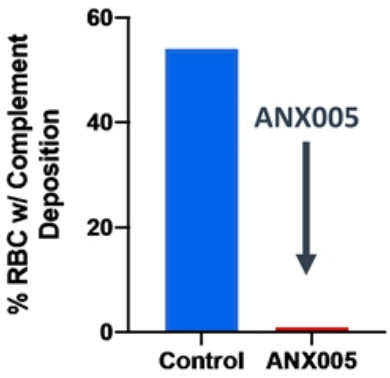
# Antibody-Mediated Complement Activation in wAIHA Patient Sera – Identifying an Enriched Patient Population

**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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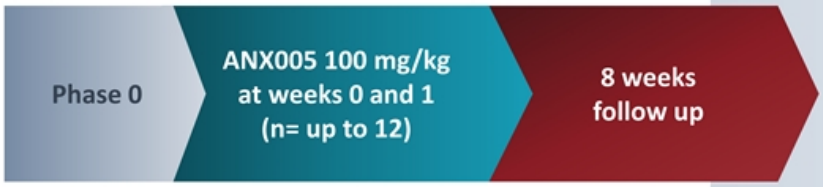
# Planned Phase 2 wAIHA Trial with ANX005




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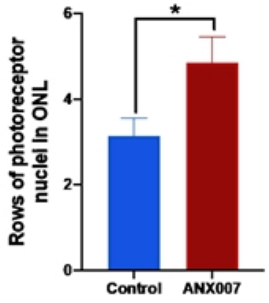
# Intravitreal Administration of Anti-C1q Provides Neuroprotection in a Mouse Model of Photoreceptor Cell Loss / Geographic Atrophy

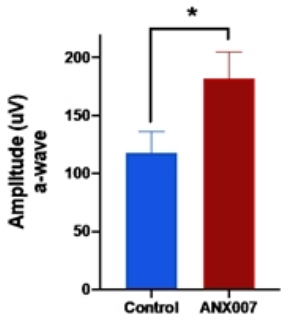
- **C1q is locally produced in the retina and a key driver of cell loss**
- **Upstream activator of C3**
- **Selective C1q inhibition allows normal function** of lectin and alternative pathway

**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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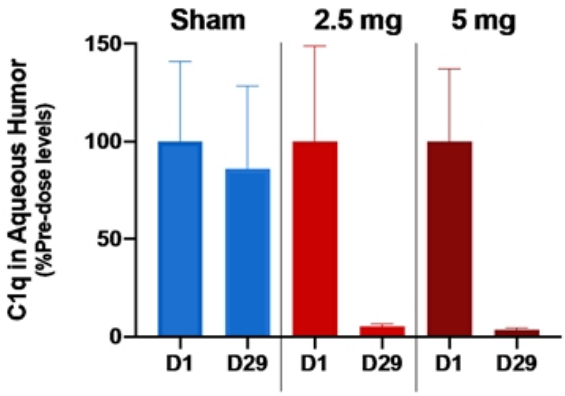
# Intravitreal ANX007 Effectively Inhibits C1q in Phase 1b Patients

**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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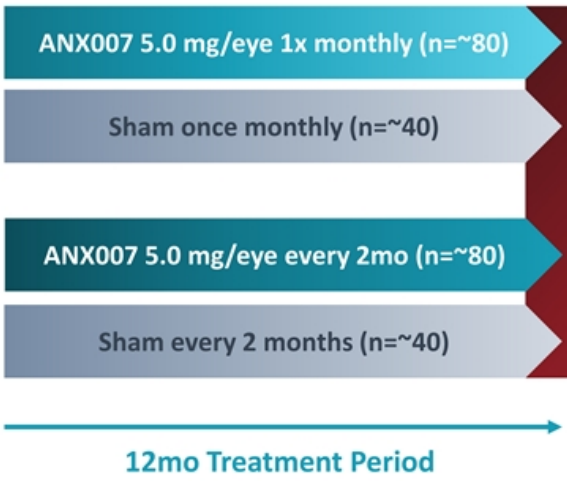
# Initiating GA Phase 2 Trial with ANX007 in Q1 2021




- **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

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# 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



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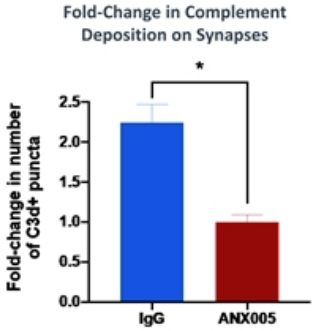
# ANX005 Reduced Key Markers of Disease Activity in HD Mice

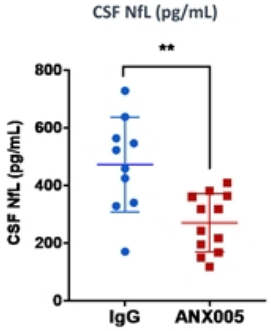
## Decreased Complement Activation on Synapses, CSF NfL and Synapse Loss

### Decreased Complement Activation on Synapses



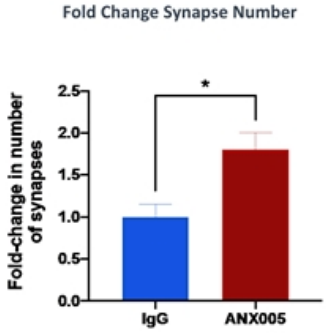

Annexon data on file; Collaboration w/ Dan Wilton and Beth Stevens, Harvard

### Decreased Levels of CSF NfL




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

### Protection Against Synapse Loss




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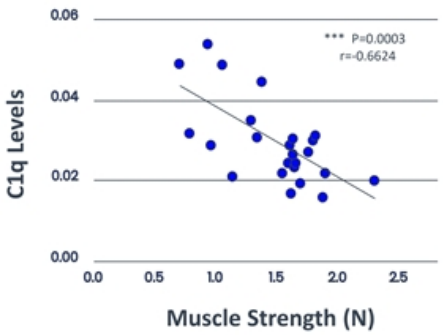
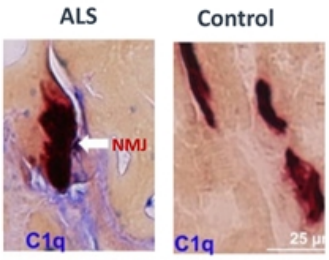
# C1q Deposition Correlated w/ Muscle Weakness in Mouse Model and Preceded Denervation in ALS Patients; NfL Elevated w/ Disease

**C1q Levels in NMJ of ALS Mouse Model Correlate with Weakness**



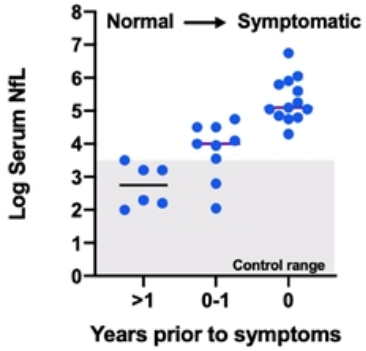

Reference ALS animal model: Lee et al., (2018) J Neuroinflam 15:171

**C1q Deposition in NMJ of ALS Patients Prior to Denervation**




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

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




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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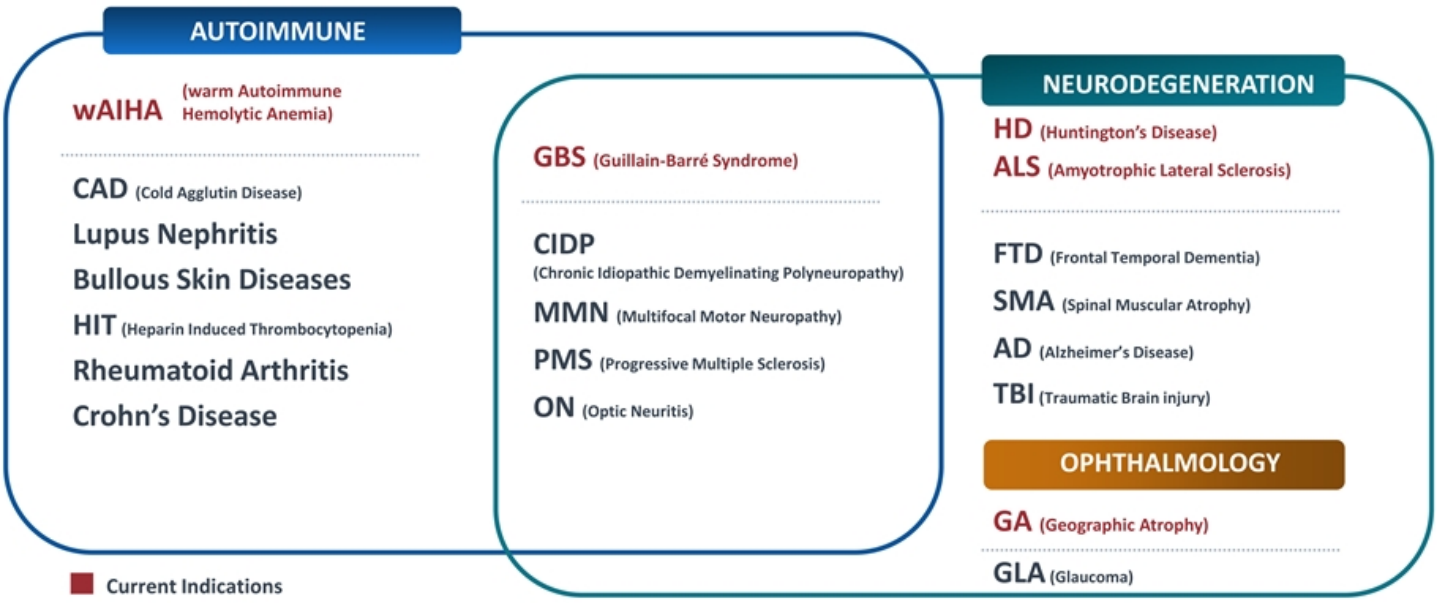
# Potential to Expand Platform Across A Breadth of Diseases

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



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# 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