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 8, 2023

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 No.)

1400 Sierra Point Parkway, Bldg C, Suite 200
Brisbane, California 94005
(Address of principal executive offices) (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, par value $0.001 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 as Exhibit 99.1 is an investor presentation that Annexon, Inc. (the "Company") plans to present during the 41st Annual J.P. Morgan Healthcare Conference commencing on January 9, 2023.

The information in this Item 7.01 of this Current Report on Form 8-K and Exhibit 99.1 attached 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 Securities and Exchange Commission made by the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Item 8.01 Other Events.

On January 8, 2023, the Company provided a corporate update. A copy of the press release, titled "Annexon Highlights Strategic Focus to Advance Four Flagship Complement Programs through Late-Stage Development and Progress Across Three Therapeutic Franchises," is filed as Exhibit 99.2 hereto and is incorporated by reference herein.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Company Presentation, dated January 2023.
99.2	Press Release, dated January 8, 2023, titled "Annexon Highlights Strategic Focus to Advance Four Flagship Complement Programs through Late-Stage Development and Progress Across Three Therapeutic Franchises."
104.1	Cover Page Interactive Data File, formatted in inline XBRL.

SIGNATURES

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

Dated: January 9, 2023

Annexon, Inc.

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

Exhibit 99.1

ANNEXON biosciences

GAME-CHANGING MEDICINES FOR COMPLEMENT-MEDIATED DISEASES

JANUARY 2023

Nasdaq: ANNX

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, runway 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 Quarterly Report on Form 10-Q filed with the Securities Exchange Commission (SEC) on November 3, 2022 and our other filings with the SEC from time to time. 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 drug candidates 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.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates or statistical data. Neither we nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this presentation.


A bold mission to free the body, brain and eye from complement-mediated disease

Annexon Overview: Pursuing Our Mission & Significant Value

Pioneering Classical Complement Platform in Autoimmunity, Neurodegeneration & Ophthalmology

- Complement clinically / commercially validated with downstream approaches (C1s, C3, C5)
- ANNX building on prior learnings to block both up & downstream complement where it starts
  - Pursuing indications where (i) C1q localizes on disease tissue to anchor complement activation & (ii) complement activity drives disease progression
- Multi-faceted 'beach-head' portfolio with 'informed signal finding' and 'confirming' trials
- Clinical POC with lead drug candidate (ANX005) in multiple indications: GBS, HD, CAD, ALS

Significant 'Enterprise Value' Potential with multiple drivers over the next 3 years

- Targeting both Orphan and large patient population diseases with 4 Flagship Programs -- ~$10B market opportunity
- Multiple value driving clinical readouts over 2023 & 2024, including GA & GBS confirming trials
- Potential 1st-in-class GBS commercialization & initiation of 1st-in-class anti-complement HD pivotal trial
- Potential 1st-in-class oral compound for Autoimmune diseases

Well-Capitalized with Additional Opportunities

- Runway into 2025
- Robust IP estate
- Wholly-owned with specific therapeutic-area partnering opportunities

ANNEXON biosciences

Meaningful Progress Across Our Portfolio of Complement-targeted Therapies in 2022

ANNEXON biosciences

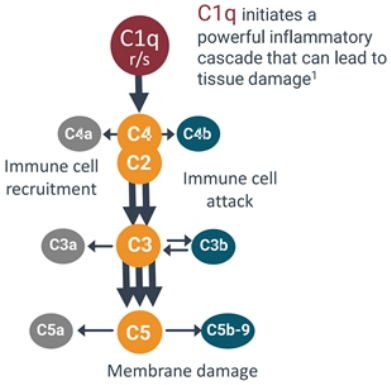
- Positive clinical outcomes with ANX005 in patients with HD, CAD & ALS
- Favorable safety profile with ANX005 across >200 people treated
- Enrollment completed early for Phase 2 trial of ANX007 for GA
- First-in-kind oral small molecule shows target drug levels achieved
- $130M capital raise to expand and extend runway into 2025

Revolutionizing Complement Biology in Pursuit of Our Mission

Targeting C1q & classical complement cascade to treat autoimmune and neurodegenerative disease

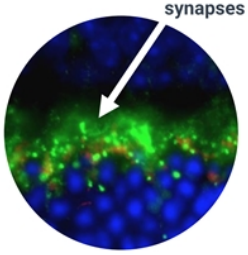
1960-70s — **2007** — **2014 - 2022** →

Understanding **C1q's role** in autoimmune disease



Discovery of C1q's role in **brain & eye neurodegeneration** by ANNX founder, Dr. Ben Barres

C1q anchors damaging complement activation on photoreceptor synapses in GA[2]



C1q Drives Removal of Functioning Synapses[3]

Annexon launched & advanced into mid- and late-stage trials targeting C1q-mediated diseases of the body, brain & eye

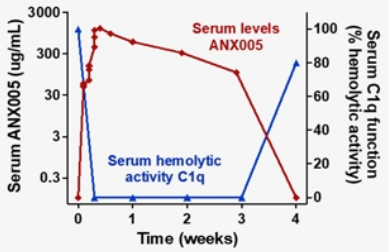
- ✓ **Validated role of C1q** in autoimmune & neurodegenerative disease
- ✓ **Full target engagement** with multiple drug candidates
- ✓ **Clinical POC in multiple diseases**
- ✓ **Well-capitalized** with runway into 2025
- ✓ **Talented 'Warrior Spirit' team**

[1]McGonigal et al. Acta Neuropathologica Communications (2016) 4:23 ; [2]C1q bound to photoreceptor synapses in aged mice: Annexon data on file; [3]Stevens, et al., 2007, Cell

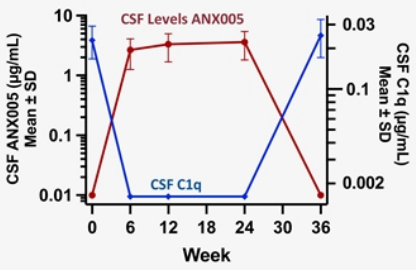
ANNEXON biosciences

Robust Clinical Target Engagement of C1q Demonstrated in the Body, Brain & Eye

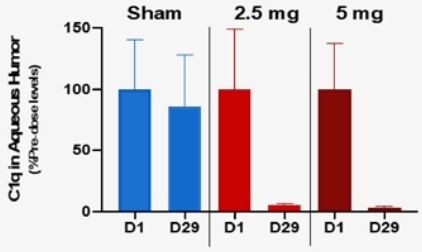
Full C1q Inhibition in Serum with ANX005



Full C1q Inhibition in CSF with ANX005



Full C1q Inhibition in Aqueous Humor with ANX007



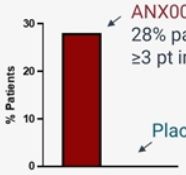
ANNEXON biosciences

Clinical Proof-of-Concept Demonstrated in Both Autoimmune and Neurodegenerative Indications

Guillain-Barré Syndrome (GBS)

GBS 6-point disability scale:

1. Slight symptoms
2. Walk / no running
3. Walk with support
4. Bedridden / chair bound
5. Ventilator-assisted breathing
6. Death

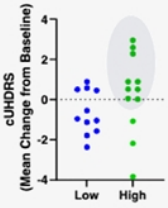


ANX005
28% patients
≥3 pt improvement

Placebo 0%

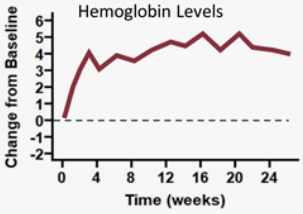
Huntington's Disease (HD)

Composite Unified Huntington's Disease Rating Scale



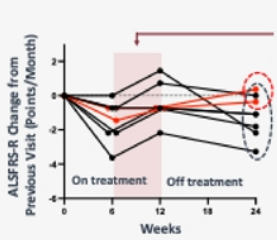
ANX005
75% patients improved

Cold Agglutinin Disease (CAD)



ANX005
Patients showed
> 2-point improvement

Amyotrophic Lateral Sclerosis (ALS)



ANX005
All patients improved or maintained progression rate during treatment

Both patients that stayed on drug continued to improve

All patients who went off treatment declined

ANNEXON biosciences

Achieving Our Mission With **FOUR FLAGSHIP PROGRAMS**

Stopping Harmful Inflammation and Tissue Damage in the Body, Brain & Eye

Guillain-Barré Syndrome (GBS)

AUTOIMMUNE

Well-validated MOA
Fast path to market in rare disease

1st placebo-controlled trial in ~40 years

Huntington's Disease (HD)

NEURODEGENERATION

Pioneering MOA
No disease-modifying treatments available

1st complement inhibition in a brain disorder

Geographic Atrophy (GA)

OPHTHALMOLOGY

Well-validated MOA
Localized inhibition in eye

1st up & downstream complement approach

Orally Administered Small Molecule

AUTOIMMUNE

Well-validated MOA
Ease and convenience of oral dosing

1st oral compound targeting classical complement

Flagship Programs Advancing in Mid-stage and Pivotal Trials

INDICATION	CANDIDATE	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	2023 ANTICIPATED MILESTONE
Guillain-Barré Syndrome	**ANX005**					Complete Phase 3 enrollment in 2H 2023
Huntington's Disease	**ANX005**					Initiate Phase 2/3 trial 2023
Geographic Atrophy	**ANX007**					Report Phase 2 data mid-2023
Autoimmune Indications	**ANX1502**					Complete MAD trial and initiate POC trial in patients

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ANX005 Summary

ANX005 Powerfully Inhibits C1q and Entire Classical Complement Pathway in the Body and Brain

Key Attributes

- ✓ **Diverse**: Utilized in autoimmune & neurodegenerative trials
- ✓ **Potency:** High binding affinity to C1q (<10 pM)
- ✓ **Target Engagement:** Full C1q inhibition in blood and CSF
- ✓ **Safety:** Generally well-tolerated in acute and chronic trials
  - ✓ No drug-related deaths & no serious infections observed
  - ✓ No autoimmune events observed post enhanced ANA screening / monitoring
- ✓ **Clinical:** Rapid clinical benefit demonstrated in GBS, HD, CAD & ALS

Administered to >200 patients to date

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ANX005 Generally Well-Tolerated in Several Patient Populations

KEY TAKEAWAYS

Leveraged learnings to optimize safety profile

- Low grade, transient IRRs during first infusion: managed by infusion rate and pre-medication
- Single serious event of autoimmunity (SLE/ lupus-like syndrome): no further events of autoimmunity observed post enhanced ANA screening / safety monitoring to date

No drug related deaths & no serious infections observed throughout all studies

6 completed and 2 ongoing acute and chronic autoimmune & neurodegenerative trials

- >100 patients from completed trials
- >110 patients in ongoing trials
- Exposure up to 1 year

ANNEXON biosciences

ANX005 Generally Well-Tolerated Across Clinical Trials

Treatment Emergent Adverse Events (TEAE)	Safety Population (N=116*)	
	All CTCAE Grades N (%)	CTCAE Grade ≥3 N (%)
Any reported TEAEs, N (%)	116 (100.0)	38 (32.8)
Most Common TEAE, N (%)		
Infusion Related Reaction (IRR)	38 (32.8)	3 (2.6)
Most Common TEAEs (non-IRR), N (%)		
Headache	37 (31.9)	0 (0)
Pain in extremity	24 (20.7)	0 (0)
Rash**	26 (22.4)	7 (6.0)
Pyrexia	18 (15.6)	0 (0)
Lab abnormality - CPK	15 (12.9)	7 (6.0)
Constipation	13 (11.2)	0 (0)
Pruritus	13 (11.2)	0 (0)
Serious TEAEs, N (%)	14 (12.1)	14 (12.1)
Related to ANX005	3 (2.6)	3 (2.6)
Infections	0 (0)	0 (0)

Study Deaths and Serious Adverse Events

- No deaths and no serious infections observed
- 3 observed serious adverse events related to ANX005
  - 1 IRR in NHV prior to dosing optimization
  - 2 in HD P2a trial (lupus like syndrome and idiopathic pneumonitis) prior to implementation of ANA screening and safety monitoring plan

Adverse Events of Note

- Infusion Related Reactions (IRR) primarily first dose effect across indications (~95%) and almost always associated with transient rash
  - Adverse events coded as rash were primarily IRR
  - No IRR observed after 2nd dose of ANX005
- Elevated creatine phosphokinase (CPK) seen in placebo and ANX005 treated GBS patients – consistent with GBS

* All completed and open label studies with ANX005 as per 01/05/2023; Includes: FIH, GBS P1b, GBS DDI, HD P2a, ALS P2a, CAD P2, wAIHA P2 trials
** Primarily initial dose IRRs, but coded as rash

ANNEXON biosciences


Flagship Programs
• Guillain-Barré Syndrome (GBS)
• Huntington’s Disease (HD)
• Geographic Atrophy (GA)
• Oral small molecule

First-In-Class Treatment for GBS

Acute, antibody-mediated autoimmune disease driven by aberrant C1q activation

GBS Overview

Rapid onset of **neuromuscular weakness** and paralysis

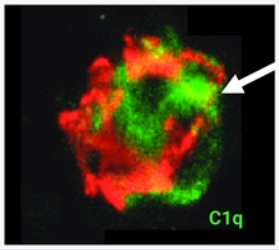
12,000 patients diagnosed/year in North America & Europe

No FDA-approved therapies

Role of C1q

C1q binds autoantibodies on nerve components, anchoring complement activation, inflammation & tissue damage

ANX005 blocks all inflammatory / damaging components of classical pathway for rapid recovery



C1q targeting the neuromuscular junction

ANX005

- ✓ Fast Track & Orphan Drug Designations
- ✓ Pursuing monotherapy label
- ✓ **Phase 3 pivotal trial ongoing**
- ✓ **Productive engagement with FDA on the statistical analysis plan for the ongoing pivotal trial**

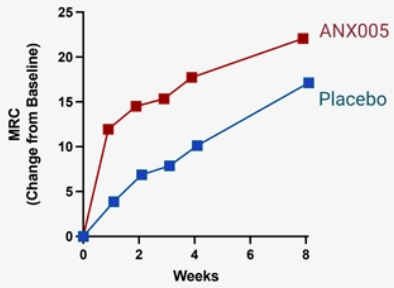
ANNEXON biosciences

ANX005 Demonstrated Clinical POC in GBS Placebo-Controlled Trial

Early improvement in muscle strength and reduction in neuronal damage preceding gain of function

Impact on Muscle Strength

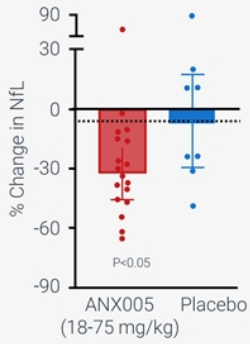
Rapid increase in muscle strength within first week of treatment



Mean Change in MRC Score from Baseline

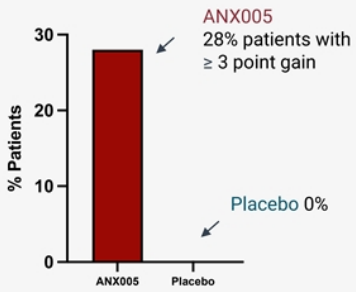
Impact on Key Neuronal Biomarker

Statistically significant early NfL reduction (weeks 2-4)



Impact on Clinical Function

Patients achieving ≥3 point improvement in 8 weeks



Guillain-Barré
6-Point Disability Scale

All graphs: ANX005 n=18, Placebo, n=8

ANNEXON biosciences

ANX005 GBS Phase 3 Pivotal Trial Underway

On track to complete expanded enrollment in 2H23 with Phase 3 data in 1H24

Trial Design

Specifications

- **Randomized, double-blind trial (N~220)**
- Recently diagnosed severe patients (3 or higher on GBS-DS)
- **Primary endpoint: GBS Disability Scale at week 8**
- Patients stratified for baseline muscle strength and time from symptom onset
- **Productive engagement with FDA on the statistical analysis plan for the ongoing pivotal trial**
  - **Increased study population by ~40 patients**

ANNEXON biosciences

First-In-Class Treatment for HD

Progressive neurodegenerative disease involving excessive synapse loss and neuronal damage

HD Overview

Progressive, inherited neurodegenerative disorder

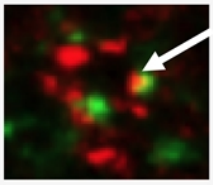
80K people affected globally; ~300K at-risk[1]

No approved treatments that reverse or slow disease progression

Role of C1q

C1q triggers synapse damage, synapse removal and neuroinflammation [2,3]

ANX005 blocks classical complement activation to protect synapses, reduce neuroinflammation and improve clinical outcomes



C1q targeting synapses on striatal neurons of HD patient[3]

ANX005

- ✓ Phase 2 results demonstrated benefit in clinical outcomes
- ✓ Orphan Drug Designation
- ✓ **Productive engagement with FDA**
- ✓ **Pivotal trial design aimed at slowing rate of disease progression**
- ✓ **Phase 2/3 trial expected to initiate in 2023**

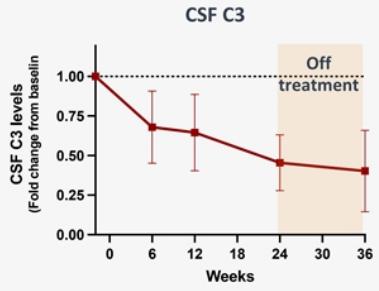
[1]1GlobalData and market research reports, [2]Wilton 2021 doi.org/10.1101/2021.12.03.471180; [3]Hong 2016 *Science* doi 10.1126/science.aad8373; Stevens 2007 *Cell* doi 10.1016/j.cell.2007.10.036; Fonseca, 2004, *J Neurosci*; Dejanovic, 2018, *Neuron*; Vukojicic, 2019, *Cell Reports*; Howell, 2011, *J Clin Inves*; Williams, 2016, *Mol Neurodegen*; Jiao, 2018, *Mol Neurodeg*; Lui, 2016, Cell **165**:921; Krukowski, 2018, Int.*JMol Sci*; Holden, 2021, *Science*; Annexon NfL reduction in SOD1 model, unpublished; Absinta, *Nature*, 2021

ANNEXON biosciences

ANX005 Improved Clinical Outcomes in HD Phase 2 Trial

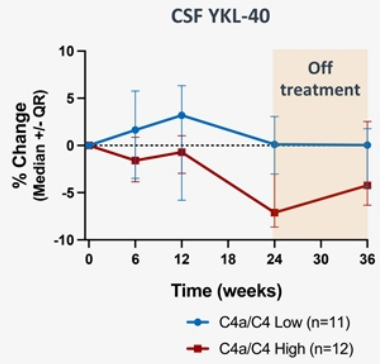
Reduced Downstream Complement

CSF C3 levels decreased in all patients during on and off treatment period



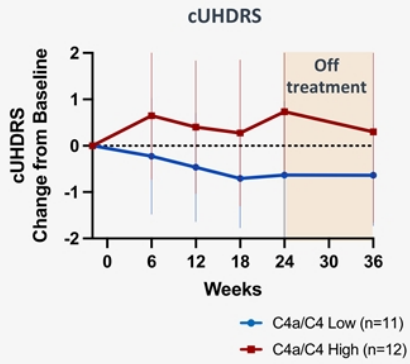
Reduced Neuroinflammation

HD inflammation marker (YKL-40*) reduced in patients with high baseline complement activity (C4a/C4)



Improved Clinical Function

Benefit at all time points in high complement group (cUHDRS)



*Produced by activated glia - Elevated in HD and other neurological diseases

ANNEXON biosciences

Initiating Pivotal Phase 2/3 Trial of ANX005 in HD

Trial Design

- Randomized, double-blind, placebo-controlled
- **Leveraging precision medicine approach** for patients with elevated baseline complement levels

Patient Population

- **Patients with manifest and pre-manifest HD**
- CAP score > 400
- UHDRS independence score ≥ 80

Key Objectives

- **Disease progression** measured by cUHDRS and TFC
- **Confirm observations with rapid drug impact on high complement baseline patients**
- Patient motor, cognition, behavior, functional capacity and quality of life assessments
- Safety and tolerability of ANX005

EXPECT TO INITIATE IN 2023

ANNEXON biosciences

First-In-Class for Early Complement Inhibition in GA

Progressive neurodegenerative retinal disease involving C1q-driven synapse and photoreceptor loss

GA Overview

Leading cause of blindness in the elderly

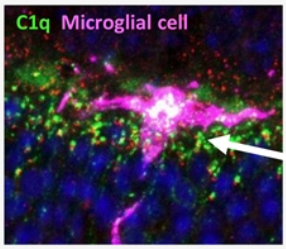
1M people diagnosed in US; 5M people globally

Current approaches target downstream complement

Role of C1q

C1q drives tissue damage in the retina by anchoring complement activation on drusen, photoreceptor cells and synapses

ANX007 has potential to provide more complete protection by shutting down all classical pathway components



C1q directing synapse engulfment by microglial cells[1]

ANX007

- ✓ Targeting up and downstream complement activation
- ✓ Aim to slow rate of lesion growth
- ✓ Fast Track Designation
- ✓ **Administered to 200 patients to date**
- ✓ **Phase 2 data anticipated mid-2023**

ANNEXON biosciences

[1]Annexon data on file

ANX007 Provides Powerful Inhibition of C1q & Classical Pathway in All Layers of the Retina

Key Attributes

- ✓ **Potency: <10 pM** Fab antibody formulated for intravitreal administration
- ✓ **Target Engagement:** Complete C1q inhibition in the eye for at least 4 weeks
- ✓ **Safety:** Generally well-tolerated in Phase 1b trial
- ✓ **Efficacy:** Preclinical data demonstrating protection of photoreceptor cells and retinal function
- ✓ **Dosing:** Pharmacokinetics in patient aqueous humor supports monthly/every other month dosing; optimizing formulation for less frequent dosing

Administered to 200 patients to date

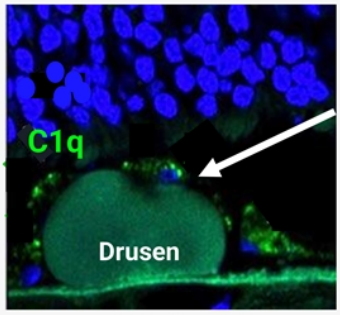
ANNEXON biosciences

Targeting C1q's Dual Role in Vision Loss in GA

C1q drives inflammation in retina and specific mechanism of synapse loss on photoreceptor neurons

C1q Well Positioned to Drive Retinal Damage

C1q localized on drusen (hallmark pathology of GA)

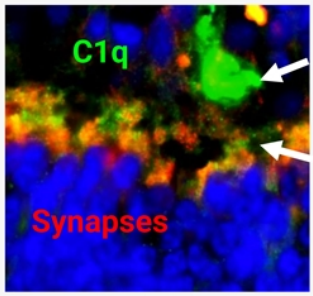


Modified Image from Jiao, 2018

C1q anchors classical complement activation on drusen

C1q's Unique Role in Neurodegeneration

C1q tags photoreceptor synapses to drive inflammation and neuronal damage



Activated microglial cells engulf synapses

C1q guides microglial cells to target synapses in GA

C1q initiates & propagates neuroinflammation in the retina

Retina specimens from GA patients were procured from the San Diego Eye Bank; Annexon data on file; Tassoni et al, IOVS 2022 (ARVO Abstract)

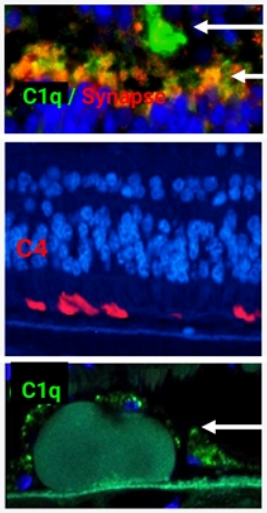
ANNEXON biosciences

Broader Overview of C1q's Role in GA Progression

C1q accumulates in all layers of the outer retina and positioned as key driver of complement activation

- Drusen contain activating C1q substrates
- **C1q activation / inflammation contributes to retinal damage**
- Microglia/macrophages infiltrate the retina, expressing more C1q
- **C1q directly recognizes components of photoreceptor neurons → cell damage**
- **C1q tags photoreceptor synapses on stressed neurons → synapse pruning / degeneration**

GA Retinal Tissue



C1q-expressing microglial cell[1]

C1q on photoreceptor synapses[1]

C4, downstream of C1q, on photoreceptor cells at leading edge of pathology[2]

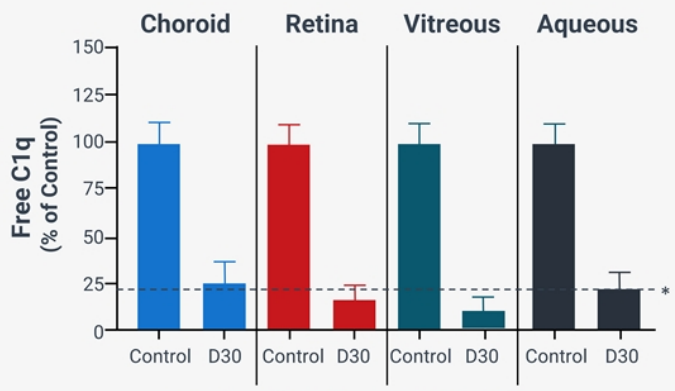
C1q on and around drusen[3]

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

ANNEXON biosciences

ANX007 Inhibits C1q Throughout the Retina

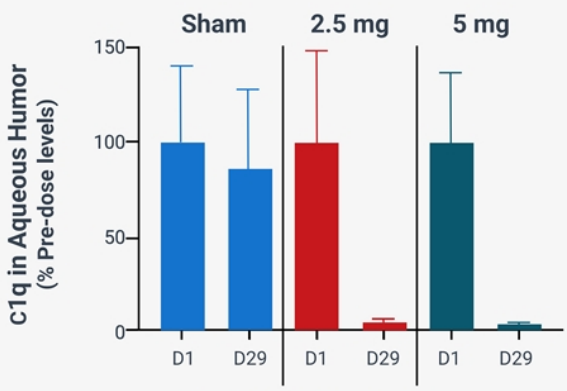
C1q Occupancy by ANX007 Following Intravitreal Administration in Primates



D30 = Day 30 (30 days post-2nd ANX007 dose)

Two doses of 5 mg ANX007 administered by IVT 28 days apart in cynomolgus monkeys

C1q Occupancy by ANX007 In Patient Aqueous Supports Monthly/Every Other Month Dosing



D1 = Day 1 (before ANX007 dosing)

D29 = Day 29 (post-1st dose)

*Within resolution limits of assay

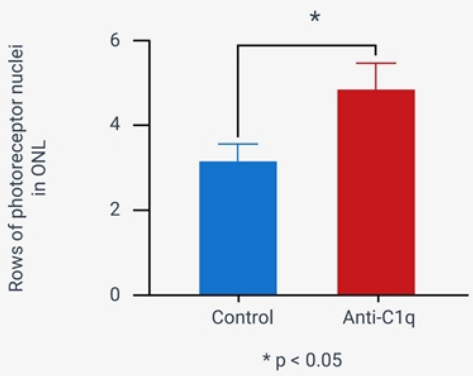
Grover et al, IOVS (in press); Sun et al, AAO Annual Meeting 2020; Annexon Data on File

ANNEXON biosciences

Blocking C1q Protects Photoreceptor Structure and Function in Mouse Light Damage Model

Protection of Retinal Layer Thickness / Cell Number

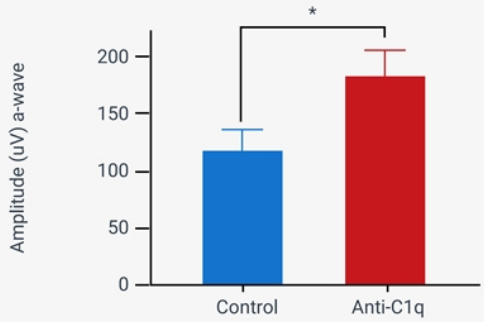
Anti-C1q Protects Photoreceptor Cells / Retinal Thickness



* p < 0.05

Protection of Photoreceptor Cell Function

Protects Retinal Function



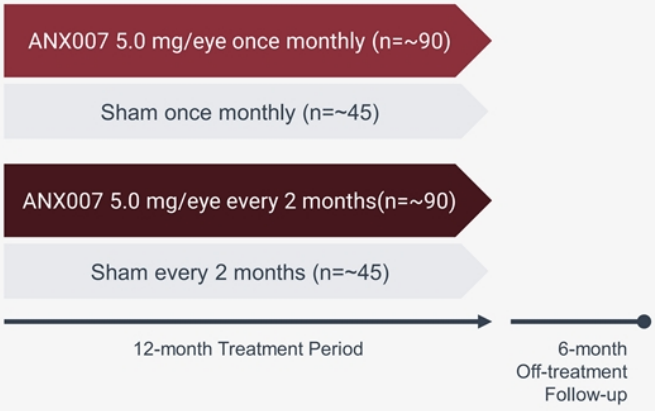
* p < 0.05

Jiao, 2018

ANNEXON biosciences

Ongoing ANX007 Phase 2 GA Trial with Data in mid-2023

ARCHER Trial Design



Specifications

- Randomized, double-masked, sham-controlled trial
- **Patients stratified based on lesion size and location (>45% patients with non-foveal lesions)**
- Primary endpoint: Rate of change (slope) in GA lesion area assessed by fundus autofluorescence (FAF)
- **>50% of patients through 12-month treatment period with >90% adherence with office follow-ups**

PHASE 2 DATA EXPECTED MID-2023

ANNEXON biosciences

ANX1502: First Oral, Small Molecule for Classical Complement-Mediated Autoimmune Diseases

Opportunity

Autoimmune indications with strong scientific rationale, including:

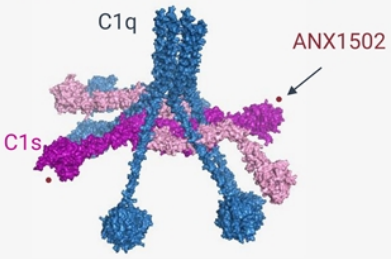
- Multifocal motor neuropathy (MMN)
- Lupus Nephritis
- Myasthenia gravis
- Cold agglutinin disease (CAD)

Role of C1s

Targeting active form of C1s responsible for classical pathway activation

Potent and selective inhibitor of C1s (serine protease): selective over related proteases (200 – 50,000-fold)

Highly specific for classical pathway



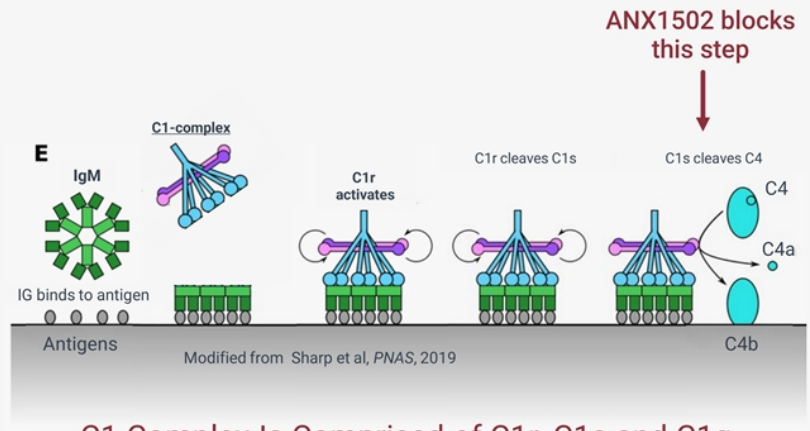
ANX1502

- ✓ **Orally administer** for chronic therapy in several diseases
- ✓ **Achieved target drug levels** in on-going Phase 1 SAD trial
- ✓ **Conducting MAD in healthy volunteers**
- ✓ **Initiating POC in 2023**

ANNEXON biosciences

Following C1q Binding to a Surface, ANX1502 Inhibits Activated C1s

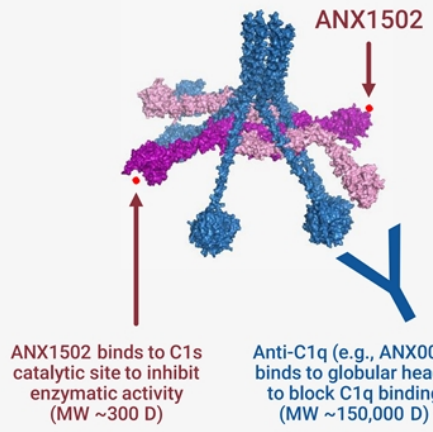
Structure of C1-complex bound to IgM-antigen on a surface



C1 Complex Is Comprised of C1r, C1s and C1q

Sharp et al, *PNAS*, 2019

Structure of unbound C1-complex



Mortensen et al, *PNAS*, 2017

ANNEXON biosciences

ANX1502: Structure-Based Screening and Design

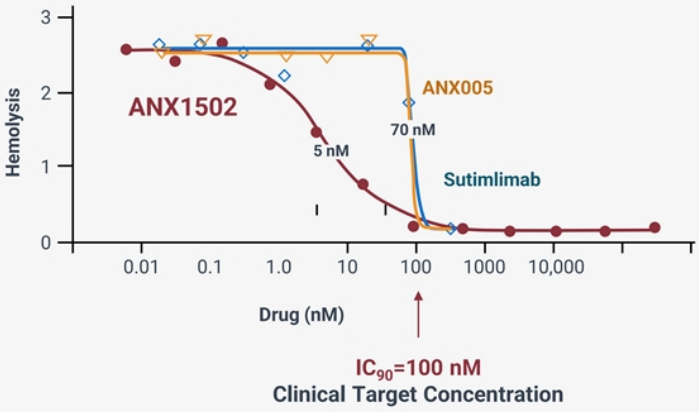
ANX1502 Discovery From HTS To CTA Submission

ANNEXON biosciences

ANX1502: Highly Potent and Selective Inhibitor of C1s

- **High affinity C1s:** 0.6 nM (Biacore)
- **Potent inhibitor:** 1 nM purified enzymatic assay
- **Selective** over related serine proteases (200 – 50,000-fold)
- **Robust functional inhibition** of classical pathway (comparable to sutimlimab)
  - *In vitro* hemolysis assay (IC_{50} = 5 nM)
  - Clinical target concentration =100 nM

Potent for *In Vitro* Hemolysis in Human Serum



IC_{90}=100 nM
Clinical Target Concentration

ANNEXON biosciences

ANX1502 Well-Tolerated in Ongoing Phase 1 SAD Trial; Supports Further Dose Escalation and Multiple Dosing

- **ANX1502 generally well-tolerated**
- **Maximum tolerated dose not yet reached**
- All treatment-emergent adverse events (TEAEs) mild or moderate
  - TEAEs included nausea, emesis and headache
- **No serious adverse events (SAEs)**
- No significant clinical/lab findings (e.g., liver enzymes, serum chemistry, hematology)

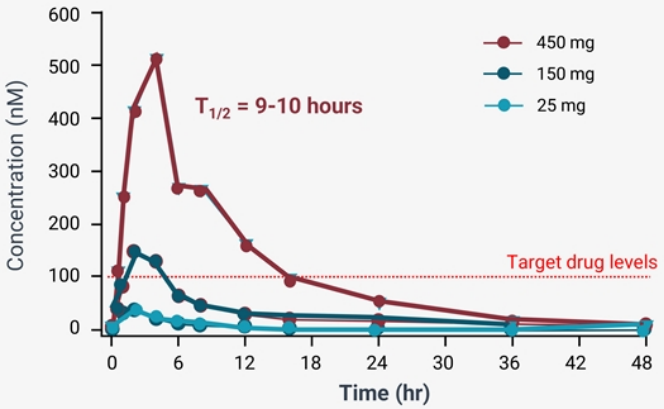
Subjects with TEAEs	25 mg dose (N=8)	150 mg dose (N=8)	450 mg dose (N=8)
Dose	25 mg	150 mg	450 mg
Subjects with any TEAE	4 (50.0)	3 (37.5)	5 (62.5)
Subjects with any Serious TEAE	0	0	0
Subjects with at least one Grade 1 Drug-related TEAE	3 (37.5)	3 (37.5)	4 (50.0)
Subjects with any ≥ Grade 2 TEAE	0	0	0

ANNEXON biosciences

ANX1502 Pharmacokinetic Profile Supports Twice Daily Dosing

- **Single dose of 450 mg achieves target drug levels** (100 nM) consistent with twice daily dosing
  - 450 mg dose achieved >100 nM for 12 hours
- SAD dosing to MTD on-going
- **MAD cohorts initiating 1H23**

Plasma levels after single dose*



*Cohorts where ANX1502 was administered with consistent dosing protocol

ANNEXON biosciences

ANX1502 Advancing Into Multiple Clinical Trials for Development in Autoimmune Indications

ANX1502 Development Plan

- **Complete Phase 1 SAD / MAD** study in healthy volunteers — **Phase 1 data 2023**
  - Establish dose for patient studies
- **Establish rapid POC in CAD** — **Initiate POC trial 2023**
  - Validate 1502 PK/PD in a short duration trial with objective readout
- **Expand autoimmune franchise into multifocal motor neuropathy (MMN)** — **Initiate P2 trial 2024**
  - Strong scientific rationale; supporting data from mechanistically-related GBS indication

Next Steps for Program Expansion

- Additional franchise expansion informed by emerging data 2H23 — **Expansion 2H23**
  - Ph 1b LN data expected in 1H23; informs late-stage trial related diseases
  - Ongoing assessment of Myasthenia gravis (MG) and other indications

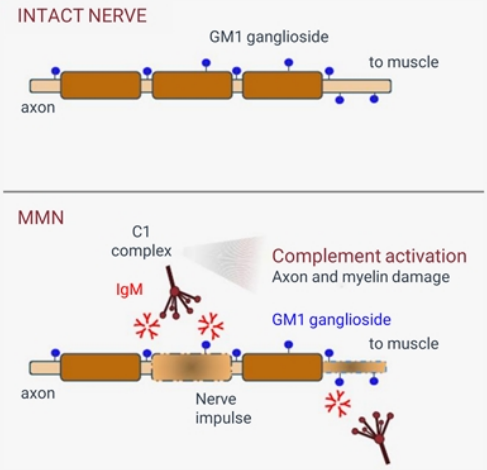
ANNEXON biosciences

MMN: Progressive Disability Despite Treatment With Standard Therapy

Disease Overview

- **Clinical features**
  - Slowly progressive asymmetrical distal limb weakness
  - Muscle wasting over time
- **Patients**
  - ~12K in US / EU
  - Commonly middle-aged men
- **Pathophysiology**
  - Anti-GM1 antibodies
  - Motor conduction block
- **Treatment**
  - Treated with IVIg, but progressive nerve damage continues
  - Life-long and time-consuming treatment

Nerve Damage Mediated by Classical Complement in MMN



National Organization for Rare Diseases
https://rarediseases.org/rare-diseases/multifocal-motor-neuropathy/
Vlam, Lotte et al., Neuroimmunology Neuroinflammation, 2015

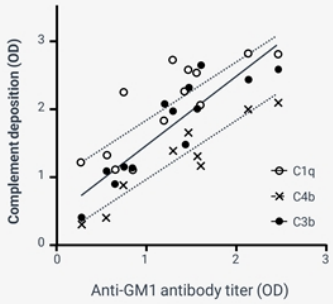
ANNEXON biosciences

Strong Rationale for C1 Inhibition as Therapy for MMN

IgM driven disease related to GBS

Classical Complement Activation in MMN

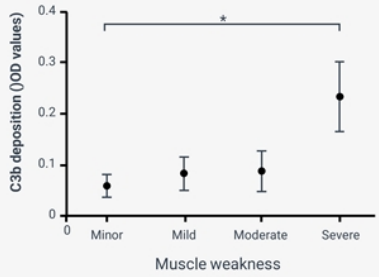
Patient sera: C1q, C4b and C3b deposition on GM1 ganglioside *in vitro* correlates with anti-GM1 IgM titers



Yuki, et al., J Neurol Neurosurg Psychiatry 2011

Complement Activation Correlates with Severity

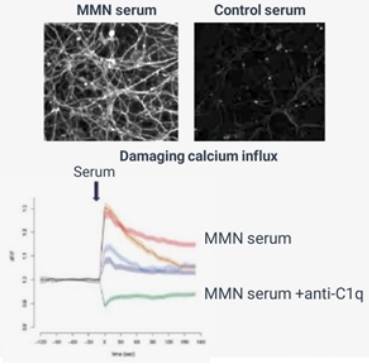
Patient sera: *In vitro* complement deposition on GM1 ganglioside correlates with MMN disease severity



Vlam, et al., Neurology 2015

C1 Inhibition Reduces Effect of MMN Antibodies

Neuronal culture: Anti-C1q blocks neurotoxic calcium influx caused by IgM GM1antibodies



Harschnitz, et al., Annals Neurol 2016

ANNEXON biosciences

Early Plans for MMN Study With ANX1502

Trial Design

- **Randomized, double-blind trial** assessing efficacy of ANX005 vs. IVIg
- IVIg rescue provided

Target Patient

- "Early" MMN and documented response to IVIg (run-in period)

Key Objectives

- Safety and tolerability
- **Confirm first use of oral drug candidate in MMN patient population**
- **Measures of peripheral muscle strength** using MRC sum score and hand-held dynamometry
- **Patient function**
- Need of IVIg retreatment

TIMELINE: INITIATE IN 1H 2024

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Additional Near-
Term Opportunities
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Numerous Opportunities with Next Wave Programs

INDICATION	CANDIDATE	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	2023 ANTICIPATED MILESTONE
Amyotrophic Lateral Sclerosis (ALS)	**ANX005**					Report Phase 2 data in 2023
Lupus Nephritis (LN)	**ANX009**					Report Phase 1 data in 1H 2023
Autoimmune/ Neuro	**ANX105**					Report Phase 1 data in 2023

*warm autoimmune hemolytic anemia (wAIHA) evaluated in Phase 2 trial; wAIHA development deprioritized as company intends to pursue autoimmune diseases with greater market potential.

ANNEXON biosciences

First-In-Class Treatment for ALS

Targeting up & downstream complement activity in both the brain and peripheral nerves

ALS Overview

Rapidly progressing neurodegenerative disorder (fatal within 3-5 years from diagnosis)

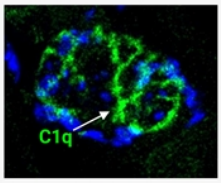
Affects **~19,000 people each year** in the US

Role of C1q

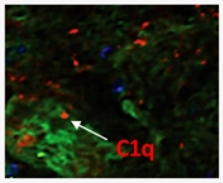
C1q targets both central and peripheral nerve components – motor neurons (MN) and peripheral neuromuscular junction (NMJ)[1, 2, 3]

C1q activation drives inflammation and neurodegeneration[1,2]

ANX005 blocks all downstream components of classical cascade **to prevent tissue damage**



C1q on NMJ[4]



C1q on central motor neurons[3]

ANX005

Differentiated, targeting both central and peripheral nervous system

Aim to slow rate of disease progression

Phase 2a trial actively enrolling, data expected 2023

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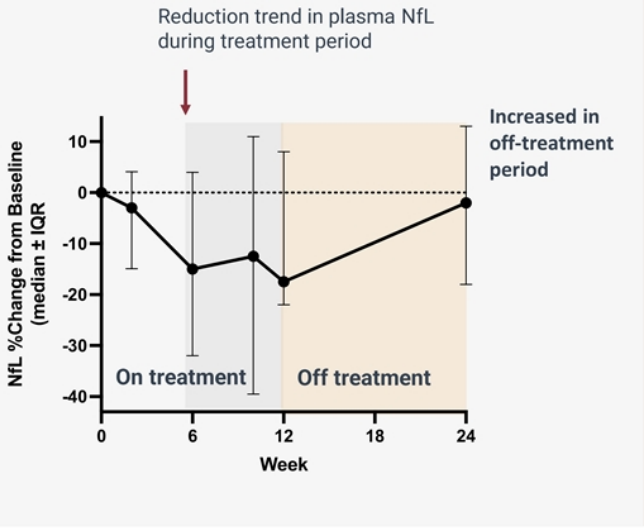
[1]Bahia El Idrissi 2016, [2]Henkel et al 2004, Kawamata et al 1992, Sta et al 2011, Kjaldgaard 2018; [3]Lee, et al. 2018; [4]Data on file

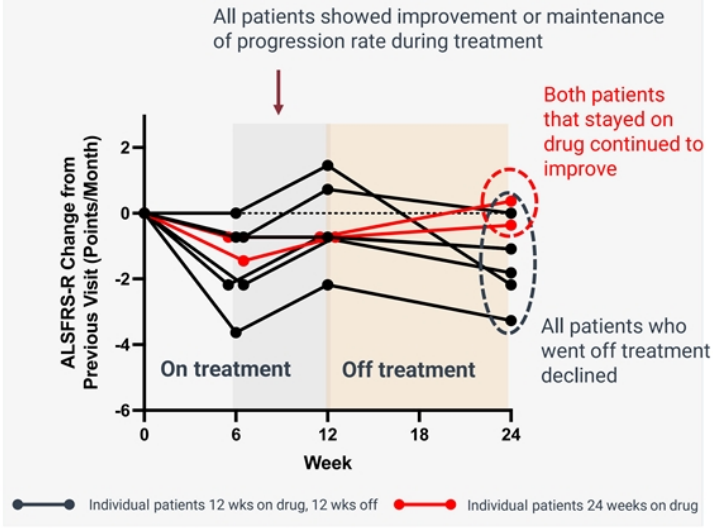
ANX005 Preliminary ALS Phase 2a 12-Week Data Show Disease Progression Slowed During Treatment, Increased Off-treatment

Reduction in Plasma NfL



On-treatment: N=8; Off-treatment: n=6 (all patients who completed 12-week treatment protocol): Data as of 12/6/2022

Impact on ALSFRS Rate of Progression

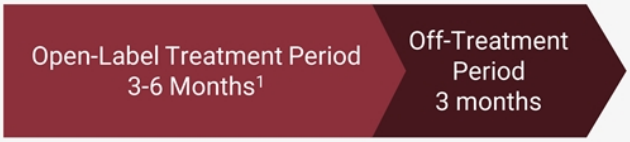


N=8 (All patients who completed 12 or 24-week treatment protocol): Data as of 12/6/2022

ANNEXON biosciences

Ongoing ANX005 Phase 2 Signal-Finding Study in ALS

Trial Design



[1]Protocol amendment extended treatment period from 3 months to 6 months

Specifications

Target patients:

- All forms of ALS, onset of weakness within 3 years prior to enrollment, ALSFRS-R ≥ 30

Endpoints:

- Primary: Safety, PK, C1q target engagement, and NfL concentrations in serum
- Secondary: Clinical outcomes (ALSFRS)

ENROLLMENT ONGOING WITH DATA EXPECTED IN 2023

ANNEXON biosciences

ANX005 in Two Types of Autoimmune Hemolytic Anemia

ANNX Approach

Confirm efficacy in CAD (n=3) with prior validation in anti-complement therapy

Inform patient enrichment strategy in primary wAIHA via natural history / feeder study (n=60)

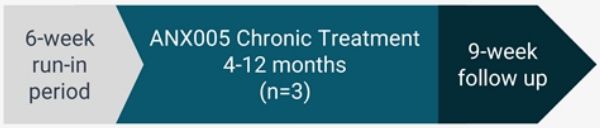
Test precision medicine approach in wAIHA in subset of patients with CAD-like complement activity (n=6)

Endpoints:

- Safety, target engagement and complement inhibition
- Anemia and hemolysis markers (e.g., hemoglobin and bilirubin)
- Quality of Life (FACIT fatigue score)

Cold Agglutinin Disease (CAD)

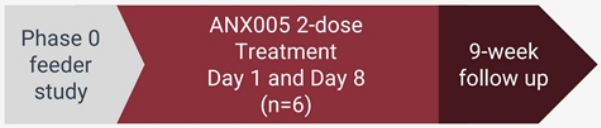
Ph2a Study Design (Confirmatory 1-Year Study)



Primary CAD patients with active hemolysis & anemia (Hgb <10 g/dL)

Warm Autoimmune Hemolytic Anemia (wAIHA)

AIHA Ph2a Study Design (Signal Finding 1-Month Study)



Primary wAIHA patients with high levels of complement activation and with active hemolysis & anemia (Hgb < 10 g/dL)

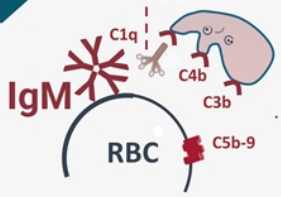
ANNEXON biosciences

Summary of AIHA Phase 2a Results

- **ANX005 generally well tolerated for up to 1 year in CAD**, longest treatment duration of ANX005 to date
- **ANX005 achieved full target engagement**, completely inhibiting C1q and downstream complement components – consistent with ANX005 in other indications
- **Positive outcomes in all CAD patients** (n=3), consistent with other complement-based inhibitors
- **Mixed outcomes in signal-finding study with wAIHA patients** (n=6)
  - Successfully identified patients with active complement deposition – blocked by anti-C1q
  - Indication that 2 doses of drug was insufficient (3-6 weeks complement inhibition)
- Due to disease heterogeneity / mixed response **will not pursue further development of ANX005 in wAIHA**

CAD and wAIHA: Autoantibody-Mediated Diseases
Different Overlapping Processes of Red Blood Cell Elimination

CAD – IgM autoantibodies
Driven by 1 process of elimination

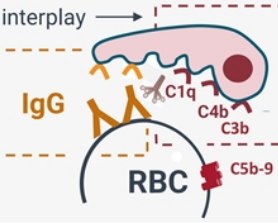


1 **Complement-receptor** dependent extravascular RBC removal by macrophages and intravascular lysis

wAIHA – IgG autoantibodies
Heterogeneous - driven by 2 processes of elimination

Complex interplay

2 **Fc Receptor-**dependent removal by macrophages



1 **Complement-receptor** dependent extravascular removal of RBC by macrophages and intravascular lysis

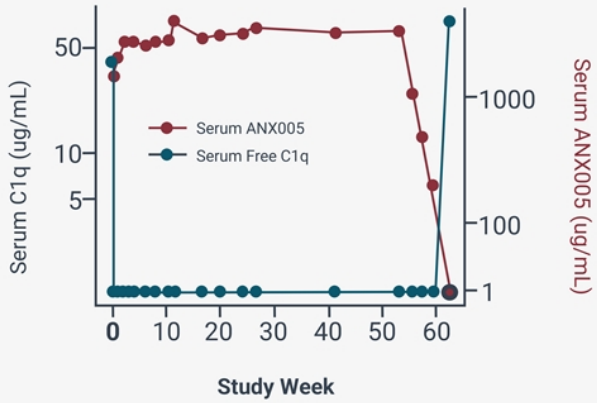
Michalak, et al., 2020 Immunity & Aging 17:3; Barcellini and Fattizzo, 2021 Blood 136:1283

ANNEXON biosciences

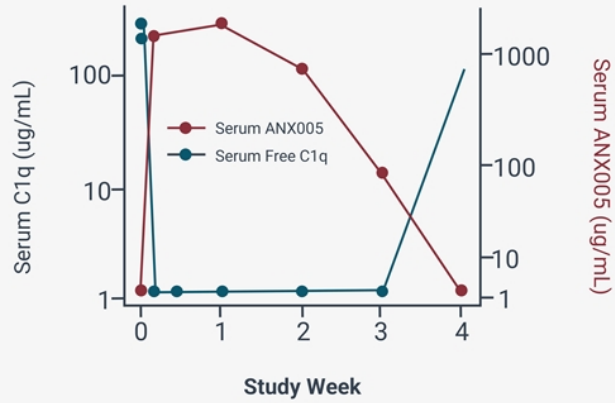
ANX005: Full Target Engagement in CAD and wAIHA Patients

Results consistent with findings in other ANX005 studies

CAD Patient 1



wAIHA Patient 1



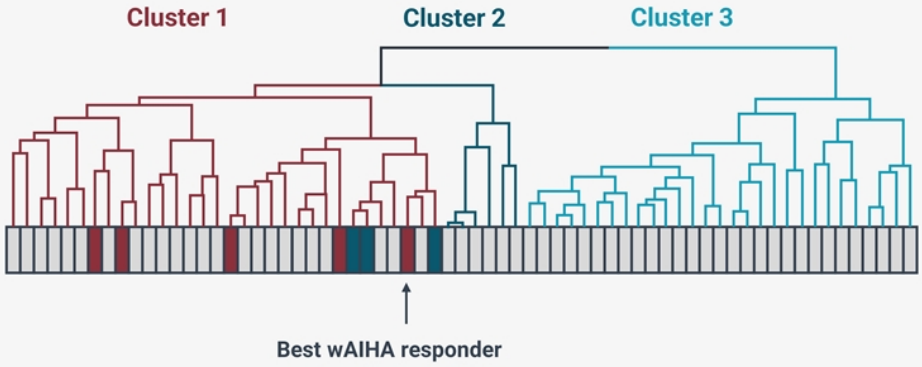
Annexon data on file

ANNEXON biosciences

Considerable Heterogeneity in wAIHA Patients
Muti-Parameter Analysis of Plasma Samples in wAIHA & CAD Patients

Cluster analysis of 17 parameters of disease pathology, including:

- Hemolysis markers (e.g., bilirubin)
- Anemia markers (e.g., hemoglobin)
- Complement levels (e.g., C3, C4)
- Complement deposition on RBC (e.g., C1q, C4d, C3d)



Key takeaways (63 samples from 60 primary wAIHA and 3 CAD patients)

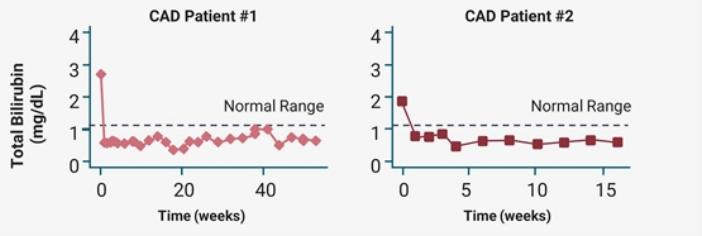
- Samples from 60 patients with primary wAIHA revealed significant heterogeneity within multiple subgroups
- Samples from three CAD patients clustered together (all with with low C4 levels, <1.5 lower limit of normal)
- Samples from five wAIHA patients with low, CAD-like levels of C4 selected for treatment (N=5) demonstrated significant heterogeneity in multiple baseline parameters; best responder most closely resembled CAD based on all parameters

Annexon data on file

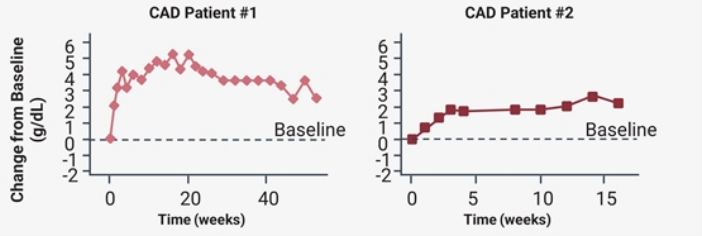
ANNEXON biosciences

ANX005 in CAD: Rapid Inhibition of Hemolysis and Sustained Increases in Hemoglobin

Total Bilirubin



Hemoglobin Change From Baseline



CAD: Key Data Takeaways

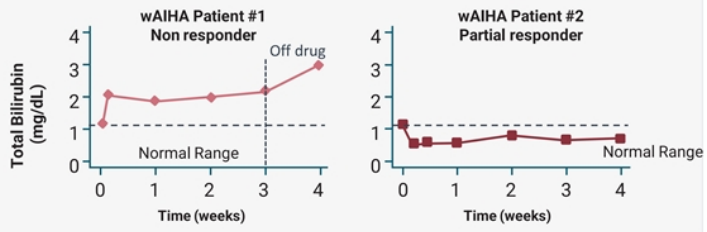
- **ANX005 fully blocked complement deposition on red blood cells in all patients**
- **Rapid and sustained normalization of hemolysis (bilirubin)**
- **Significant and durable improvement in anemia (increase in hemoglobin)**
  - Hgb ≥2 g/dL & achieved Hgb > 10 g/dL
- **ANX005 generally well tolerated for up to 1 year**
  - Longest treatment duration of ANX005 to date

Annexon data on file

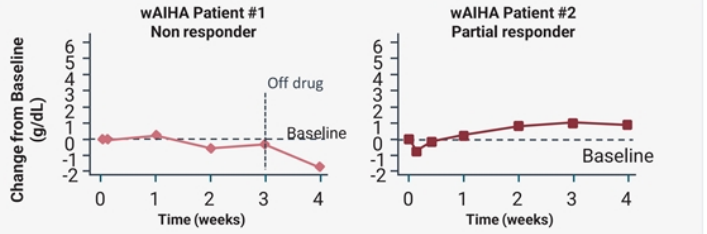
ANNEXON biosciences

ANX005 in wAIHA: Complement Deposition Blocked on RBC, But Mixed Effects on Hemolysis and Hemoglobin

Total Bilirubin



Hemoglobin Change From Baseline



wAIHA: Key Data Takeaways

- **ANX005 fully blocked complement deposition on red blood cells in all patients**
  - Measured by flow cytometry (data not shown)
- **Mixed responses on bilirubin and hemoglobin**
- ANX005 generally well tolerated

Annexon data on file

ANNEXON biosciences

ANX009 Selectively Inhibits Complement Activation in Vascular Space

Key Attributes

- ✓ **Subcutaneous formulation** of an antigen-binding fragment (Fab)
- ✓ **Target Engagement:** Selectively inhibits C1q *in the vascular space*
- ✓ **Safety:** Well-tolerated in Phase 1 trial, twice weekly dosing provided sustained C1q inhibition in the circulation
- ✓ **Dosing:** Designed to **enable chronic dosing** for use in future trials of autoimmune indications

ANNEXON biosciences

Ongoing First-In-Class Approach for Lupus Nephritis; Data 1H23

Endogenous, pathogenic autoantibodies against C1q enhance its activity and uniquely amplify kidney inflammation and damage

LN Overview

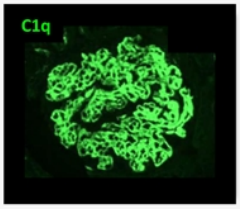
~60,000 US patients/year

Pathogenetic auto-antibodies against C1q (PACAs) enhance LN disease activity

Role of C1q

C1q and PACAs amplify kidney inflammation and damage

ANX009 blocks binding, activation & **tissue damaging inflammation in LN**



C1q targeting the renal glomerulus

ANX009

Targeting patients with high baseline complement activity by increased C4d/C4

Well-tolerated in Phase 1 trial, twice weekly dosing provided sustained C1q inhibition in the circulation

Phase 1b signal-finding trial underway, with initial data in 1H23

*Induced by injection of auto-reactive antibodies against kidney glomerular basement membrane antigens
Trouw et al. J Clinical Investigation (2004) 114:679

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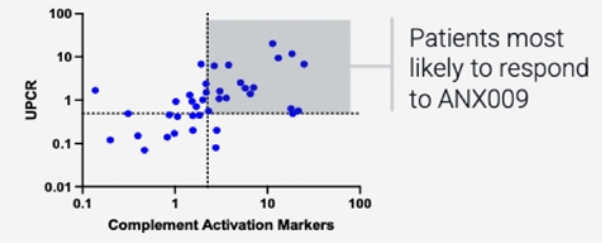
Preclinical and Phase 1 Support for ANX009 in Lupus Nephritis

Precision Medicine Approach

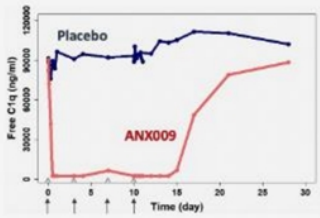
High baseline complement activity correlated with disease activity



Patients most likely to respond to ANX009

Selectively Inhibiting C1q to Stop Complement-Mediated Disease

Full inhibition of C1q in serum with ANX009 in Phase 1 study



Healthy volunteers; Dosing on days 0, 3, 7 and 10

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Progressing ANX009 in Signal-Finding Study for Lupus Nephritis

Trial Design

Specifications

Target patients:

- Classical complement activity, smoldering disease, proteinuria, stable background therapy

Objective endpoints:

- Safety and tolerability, complement PD markers, exploratory markers of renal tissue damage and function

ENROLLMENT ONGOING WITH DATA EXPECTED IN 1H 2023

ANNEXON biosciences

ANX105 Next Generation Inhibitor of C1q & Classical Pathway

Key Attributes

- ✓ **Full-length mAb for IV administration**
- ✓ **Target Engagement:** Designed to fully inhibit C1q in blood and CSF
- ✓ **Dosing:** Designed with potentially improved dosing properties for use in future trials of autoimmune and neurodegenerative indications
- ✓ **Phase 1 SAD study in normal healthy volunteers ongoing**

ANNEXON biosciences

Advancing Robust Portfolio of Anti-C1 Clinical Candidates

Protecting against tissue damage, neuroinflammation and cell death to improve patient outcomes

ANNX Programs

ANX005

- Full-length mAb for IV administration
- Inhibition of C1q and classical complement pathway in the body & brain

ANX007

- Subcutaneous formulation of a Fab for IVT administration
- Selective inhibition of C1q and classical pathway in the eye

ANX1502

- Oral, small molecule
- Inhibition of active form of C1s and classical pathway in the body

ANX009

- Subcutaneous formulation of a Fab
- Selective inhibition of C1q and classical pathway in the body (vascular space)

ANX105

- Full-length mAb for IV administration
- Fast follower to ANX005 designed to offer enhanced dosing administration

ANNEXON biosciences


A Mission to Enable People to Live Freely from Complement-mediated Diseases
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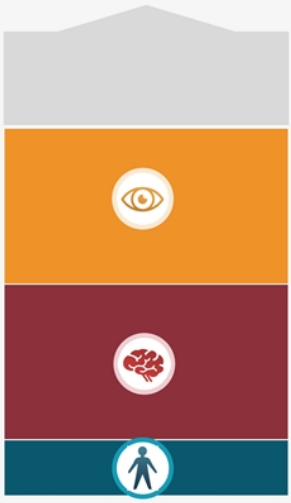
Game-Changing Opportunity for C1q-directed Complement Therapies in Current Indications and Beyond

Significant Unmet Need

- **0** **C1q-directed complement agents** on the market or in late-stage development
- **0** **Disease-modifying treatments** available for GBS or HD
- **0** Treatments that target **both up and downstream** complement pathway for GA
- **0** **Orally administered, small molecule** complement treatments available

Multi-Billion Market Opportunity



Expansion into additional complement-mediated diseases of the body, brain and eye

>$10 BILLION

Market opportunity in current pipeline indications

Annexon data on file

ANNEXON biosciences

2023 Clinical Milestones Primed to Unlock Significant Value

Well capitalized with runway into 2025

Complete enrollment in pivotal GBS trial	**ANX005** Phase 3 complete enrollment in 2H 2023
Initiate pivotal HD trial	**ANX005** Phase 2/3 initiates in 2023
Demonstrate clinical efficacy in GA	**ANX007** Phase 2 data in mid-2023
Initiate clinical POC trial with oral, small molecule	**ANX1502** Phase 1 MAD data in healthy subjects by end of 2023 Initiate POC trial in CAD patients by end of 2023
Demonstrate efficacy signal in "next wave" indications and target engagement with next generation mAb	**ANX005** Ph 2 ALS data in 2023 **ANX009** Ph 1 LN data in 1H 2023 **ANX105** Ph1 data in 2023

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WARRIOR SPIRIT
SOUND JUDGEMENT
PASSION
ALL-FOR-ONE
THRIVE!

Committed to Serving Patients, Families and Communities through Game-changing Medicines

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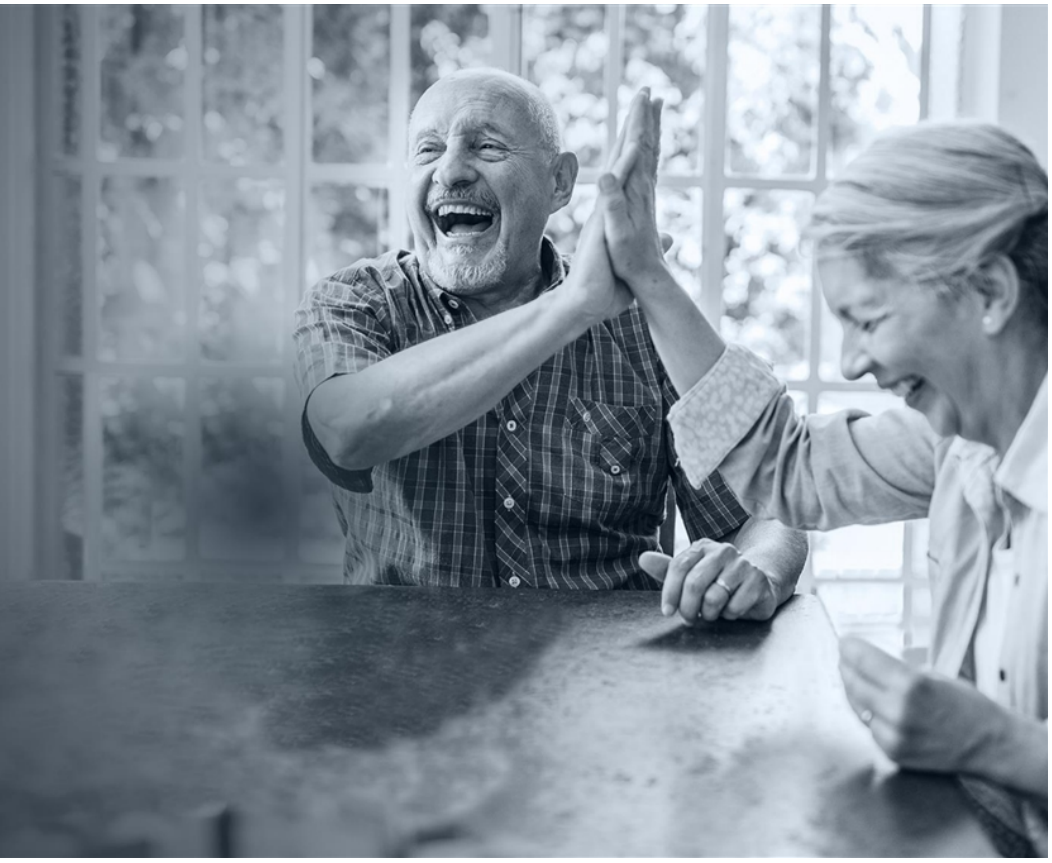


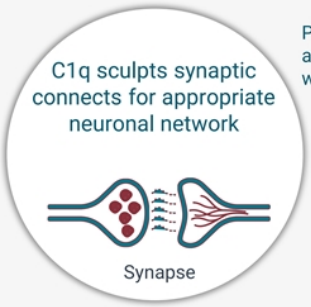
APPENDIX

Loss of Functioning Synapses Results in Neurodegeneration

Blocking C1q protects functioning synapses, prevents loss and decreases disability[2]

C1q's Normal Role In Development

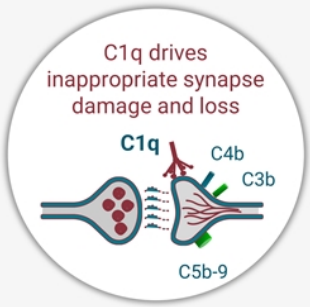
- C1q recognizes, tags & drives removal of excess synapses
- Strong synapses remain to form appropriate circuits and normal brain health



Pathway turns off after developmental window

C1q's Role In Neurodegenerative Disease

- C1q recognizes, tags & drives removal of functioning synapses
- Triggers inappropriate synapse damage and loss, neuroinflammation and degeneration



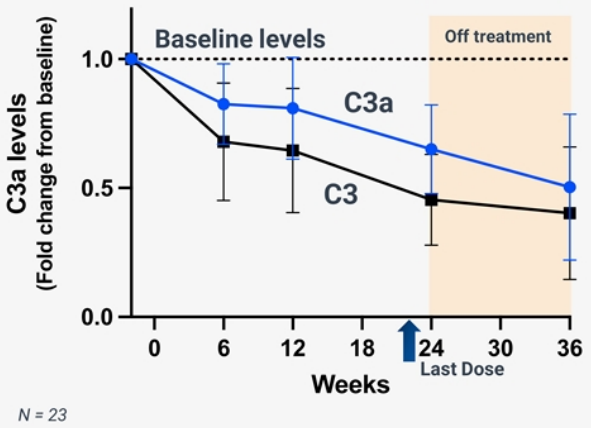
Chronic pathway activation and functional decline

[1]Wilton 2021 doi.org/10.1101/2021.12.03.471180; Hong 2016 *Science* 10.1126/science.aad8373; Stevens 2007 *Cell* DOI 10.1016/j.cell.2007.10.036; Fonseca, 2004, *J Neurosci*; Dejanovic, 2018, *Neuron*; Vukojicic, 2019, *Cell Reports*; Howell, 2011, *J Clin Inves*; Williams, 2016, *Mol Neurodegen*; Jiao, 2018, *Mol Neurodeg*; Lui, 2016, Cell **165**:921; Krukowski, 2018, Int.*J Mol Sci*; Holden, 2021, *Science*; Annexon NfL reduction in SOD1 model, unpublished; Absinta, *Nature*, 2021

ANNEXON biosciences

Evidence of Reduced Downstream Complement Activation & Neuroinflammation Through Entire 9 Month Study

Drug Effects Continue into Off-treatment Period



N = 23

ANX005 showed:

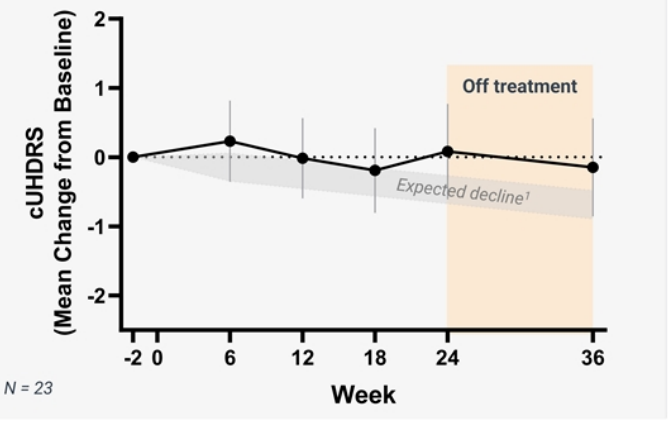
- Reduction of downstream complement activation (C3a)
- Reduction of neuroinflammation (C3)
  - C3 is produced by activated, neurotoxic astrocytes in the brain[1]

[1]Liddelow, Barres, 2017 *Nature* **541**: 481–487

ANNEXON biosciences

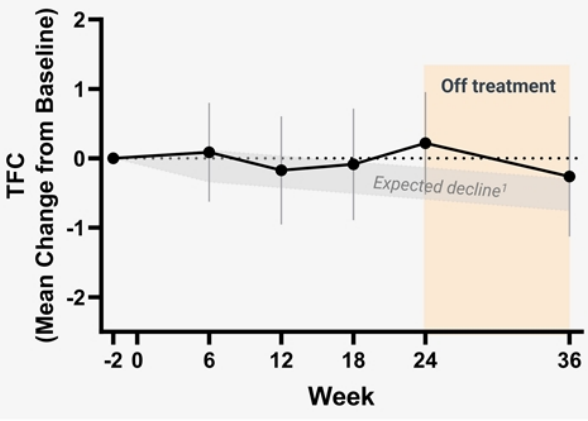
Clinical Disease Progression Stable in Overall Patient Population Through Entire 9-month Study

cUHDRS Stable Over 9 Months



N = 23

TFC Stable Over 9 Months



MMRM; LS means +/- 95% CI

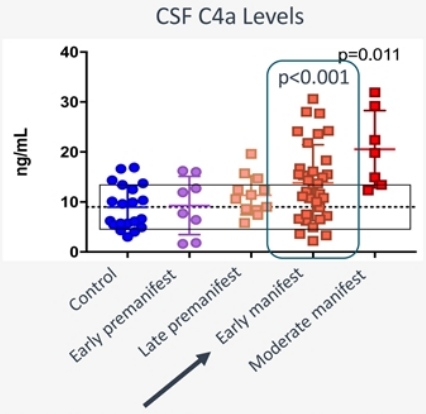
[1] Expected decline = interpolated natural history from Schobel 2017 (TRACK-HD)

ANNEXON biosciences

Complement Activation Correlates with Disease and Functional Decline in HD

Patients with higher baseline complement activity may be more likely to respond to anti-C1q therapy

CSF C4a Elevated and Increase with HD Progression*



Early manifest consistent with patients enrolled in current study

CSF C4a Activation Correlate with HD Functional Decline

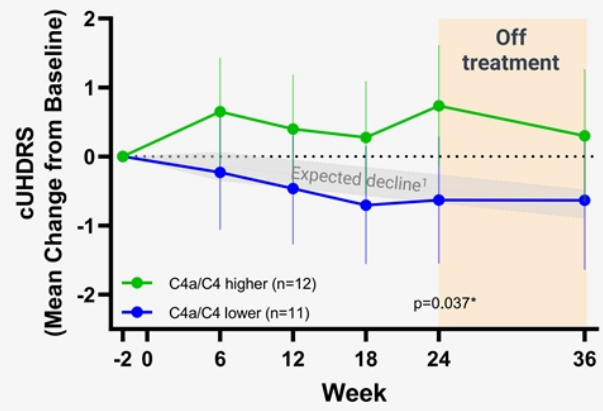
Clinical endpoints	p-value	
Total functional score (TFC)	0.0333	Motor & Function
Total motor score (TMS)	0.0181	
Disease burden score (DBS)	0.1310	
Symbol digit mod. Test (SDMT)	0.0324	Cognitive Scales
Verbal fluency	0.0255	
Stroop color naming (SCN)	0.0454	
Stroop word recall (SWR)	0.0710	

*Higher complement activity in CSF (C4a) of HD Patients associated with disease severity & functional decline
Presented at HSG, November 2021; Annexon Collaboration with Ed Wild UCL

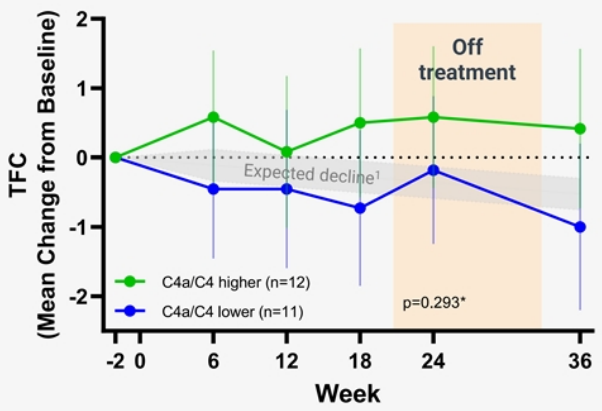
ANNEXON biosciences

Rapid Benefit Maintained in Patients with High Baseline Complement Activity Through Treatment and Follow-up Periods

Benefit at All Time Points in High Complement Group (cUHDRS)



Benefit at All Time Points in High Complement Group (TFC)

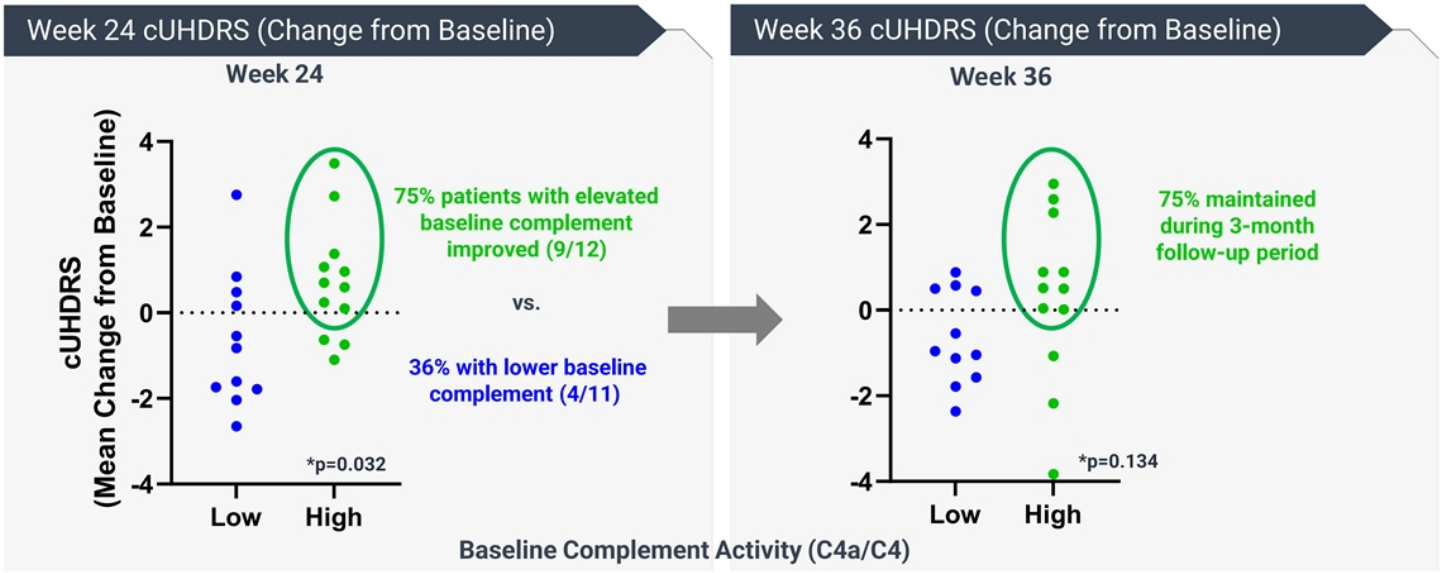


*Comparing higher vs lower C4a/C4 groups at week 2; MMRM; LS means +/- 95% CI; N=23
¹Expected decline = interpolated natural history from Schobel 2017 (TRACK-HD)

ANNEXON biosciences

75% of Patients with High Baseline Complement Levels Showed Improvement at Week 24, Maintained at Week 36r

Twice as many patients with high complement improved compared to patients with low complement

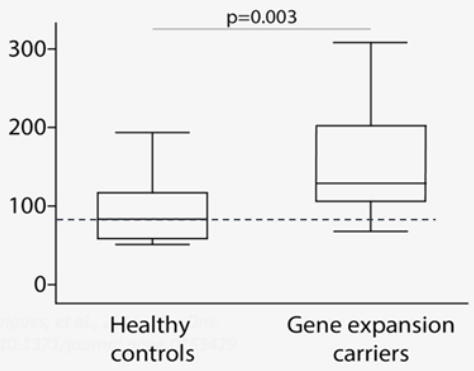


Baseline demographics evenly matched between patients with higher and lower CSF complement activation
*Wilcoxon-Mann-Whitney Test

ANNEXON biosciences

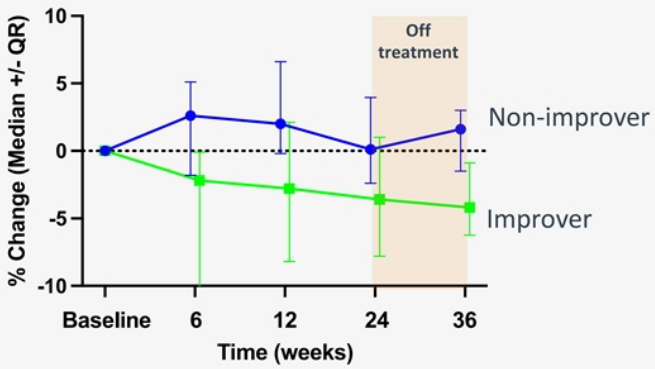
Independent Marker of Inflammation in HD (YKL-40*) Decreased in ANX005-treated Patients Exhibiting Clinical Improvement

YKL-40 Increased in CSF of HD Patients



Rodrigues 2016 *PLoS One* **11** e0163479

ANX005-treated Improvers Showed Rapid, Consistent Decrease of YKL-40



Annexon data on file

*Produced by activated glia - Elevated in HD and other neurological diseases

ANNEXON biosciences

Annexon Highlights Strategic Focus to Advance Four Flagship Complement Programs through Late-Stage Development and Progress Across Three Therapeutic Franchises

Mid-stage and Pivotal Trials of ANX005, ANX007 and ANX1502 Poised to Achieve Numerous Catalysts in Multiple Disease Indications

Well-Capitalized with Operating Runway into 2025

Company to Present Pipeline Updates at 41st Annual J.P. Morgan Healthcare Conference on January 11, 2023, at 7:30 a.m. PT

BRISBANE, Calif., Jan. 8, 2023 – Annexon, Inc. (Nasdaq: ANNX), a clinical-stage biopharmaceutical company developing a new class of complement medicines for patients with classical complement-mediated autoimmune, neurodegenerative and ophthalmic disorders, today reported progress across its broad portfolio of complement therapies and outlined its focus on four flagship programs to support its advancement to a late-stage biopharmaceutical company developing first-in-class treatments for complement-mediated diseases of the body, brain and eye.

Annexon has prioritized resources and execution of late-stage development of its four flagship programs: Guillain-Barré syndrome (GBS), Huntington's disease (HD), geographic atrophy (GA) and its first-in-kind oral small molecule, ANX1502. In so doing, Annexon's goal is to create near-term value for patients, physicians and stakeholders with the achievement of the following objectives by the end of 2023:

- Complete expanded enrollment in its ongoing pivotal Phase 3 trial for ANX005 in patients with GBS – the first placebo-controlled trial in this indication in nearly 40 years
- Initiate a pivotal Phase 2/3 trial for ANX005 in patients with HD – the first complement inhibitor in development to treat a brain disorder
- Demonstrate clinical efficacy in an ongoing Phase 2 trial for ANX007 in patients with GA – the first up- and downstream complement approach for this indication
- Initiate a clinical proof-of-concept trial with ANX1502 and expand into additional autoimmune indications – the first oral small molecule therapy targeting classical complement

"At Annexon, we envision a world in which every person gets to live out their talents, without being robbed of their physical and cognitive health due to disease. Our mission is to free the body, brain and eye from diseases driven by the classical complement cascade," said Douglas Love, president and CEO of Annexon. "To achieve this, we've purposefully developed a broad pipeline across three therapeutic franchises – autoimmune, neurodegeneration and ophthalmology – allowing us to rigorously evaluate an array of diseases for which the classical pathway drives disease burden. Based on data and learnings generated to-date, we're advancing four flagship programs that each have game-changing potential for patients and their families."

Love continued, "Throughout 2022, we made significant progress across our pipeline and our business, setting up a strong foundation for growth and multiple catalysts on the horizon in 2023 and beyond. We're encouraged by the recent engagements with the FDA on the pivotal trial design for ANX005 in two indications – GBS and HD – and are well-underway with our flagship program for GA, with initial clinical data anticipated mid-year. Across each therapeutic franchise, we've shown that our approach to stopping the classical pathway at its start can have a measurable impact on devastating and difficult-to-treat diseases."

Flagship Program Progress

- **ANX005 Pivotal Phase 3 Trial for GBS Underway:** Annexon is evaluating ANX005, a monoclonal antibody (mAb) designed to *fully* inhibit C1q and the entire classical complement pathway, in a randomized, double-blind, placebo-controlled Phase 3 trial in patients with GBS. GBS is an autoimmune condition with no U.S. Food and Drug Administration (FDA)-approved therapies, and where maximum suppression of C1q and the classical cascade early in the disease process may act to rapidly prevent nerve damage and irreversible neurological disability. Following a productive engagement with the FDA regarding the statistical analysis plan for the ongoing pivotal trial, the company increased the study population by approximately 40 patients for a total of 220 patients. Expanded enrollment is expected to be completed in the second half of 2023 with pivotal data anticipated in the first half of 2024.
- **Initiation of a Pivotal Trial for ANX005 for HD Planned in 2023:** Annexon successfully completed a Phase 2 clinical trial in 2022 in patients with HD, a slowly progressing, inherited and fatal neurodegenerative disease that leads to excessive synapse loss and neuronal damage. Following Phase 2 trial results demonstrating benefit in clinical outcomes in HD patients and a productive engagement with the FDA, the company plans to advance ANX005 into a randomized, double-blind, placebo-controlled Phase 2/3 pivotal trial for patients with HD in 2023.
- **ANX007 Phase 2 Trial in GA On-track for Initial Data in Mid-2023:** ANX007 is being evaluated in a global Phase 2 clinical trial in patients with GA, the leading cause of blindness resulting from damaged and dying retinal cells. ANX007 is designed to block C1q locally in the eye, to provide more complete protection against excess classical complement activity, a key driver of disease. Enrollment in the trial is complete and the company anticipates reporting initial data in mid-2023, with additional data to be presented after the conclusion of the six-month off-treatment period by the end of 2023. Additionally, Annexon is continuing to collaborate with DelSiTech to further optimize ANX007 for an extended-release formulation designed to enable less frequent administration.
- **ANX1502 Achieved Target Drug Levels and was Well-Tolerated in Phase 1 Single-Ascending Dose (SAD) Trial Preliminary Data; Advancing into Multiple Clinical Trials in 2023:** Annexon is evaluating ANX1502 in an ongoing Phase 1 SAD trial in healthy volunteers. In the SAD trial, a single dose of ANX1502 has achieved target drug levels in plasma in patients dosed at 450 mg, consistent with twice daily dosing. Additionally, ANX1502 has been generally well-tolerated with no safety signals observed. The SAD trial is ongoing to identify the maximum tolerated dose, and Annexon is preparing to initiate a multiple-ascending dose (MAD) study of ANX1502 in the first half of 2023, as well as a proof of concept study in 2023 in patients with cold agglutinin disease (CAD), which is supported by positive data generated by ANX005 in CAD patients. The company also plans to expand development into additional autoimmune indications with strong scientific rationale, including multifocal motor neuropathy (MMN), in early 2024.

Continued Progress Across Broad Pipeline of Complement Programs

- **Preliminary Phase 2a Data with ANX005 in Amyotrophic Lateral Sclerosis (ALS) Show Slowing of Disease Progression During Treatment; Full Data Expected in 2023:** ANX005 is being evaluated in a Phase 2a signal-finding trial in patients with ALS, a fatal neurodegenerative disorder characterized by loss of central and peripheral motor neurons. Preliminary data (n=8) showed that treatment with ANX005 has resulted in a reduction in neurofilament light (NfL) and slowing of disease progression, as measured by reductions in revised ALS functional rating scores, during the initial 12-week on-treatment period, followed by an increase in disease progression while off treatment. Enrollment in the trial is ongoing with full data expected in 2023.

- **Deprioritizing wAIHA to Focus on Diseases with a Clearly Defined Role for C1q Inhibition:** Annexon completed its Phase 2 signal-finding trials in two types of autoimmune hemolytic anemia, CAD and warm autoimmune hemolytic anemia (wAIHA). ANX005 achieved full target engagement and blocked complement deposition on red blood cells in both CAD and wAIHA. ANX005 improved clinical outcomes for the CAD patients (n=3) but demonstrated a mixed effect on hemolysis and anemia in wAIHA patients (n=5). The company's enrichment strategy selected patients with signs of excess complement activation; however, patients enrolled exhibited heterogeneity in other factors contributing to disease. Following an assessment of the market opportunity in wAIHA and a range of additional autoimmune indications, Annexon has determined not to advance development in wAIHA. The company intends to evaluate its anti-C1q drug candidates, including ANX1502, in indications where classical complement is an understood driver of disease, such as CAD and MMN.
- **Data from Signal-finding Trial of ANX009 for Lupus Nephritis (LN) Expected in the First Half of 2023:** The company's Phase 1b signal-finding trial of ANX009 using a precision medicine approach for patients with LN who have high baseline complement activity is underway. LN is an autoimmune disease for which pathogenic autoantibodies against C1q enhance activity and uniquely amplify kidney inflammation and damage. ANX009 is a subcutaneously administered agent designed to selectively inhibit C1q in the vascular space for use as a chronic treatment. Enrollment in the trial is ongoing with multiple patients dosed and data are expected in the first half of 2023.
- **Continued Progress with ANX105 in Phase 1 SAD Study:** Annexon is evaluating ANX105, its next-generation full-length mAb, in a Phase 1 SAD study in healthy volunteers. Enrollment is ongoing and initial data are expected in 2023.

More information on Annexon's programs across its autoimmune, neurodegenerative and ophthalmologic franchises can be found in the corporate presentation accessible on the company's website at www.annexonbio.com.

"This is a remarkable time in the evolution of Annexon. Since the company was founded, the field of complement therapeutics has advanced dramatically. I am proud of the role Annexon has played in revolutionizing complement biology, carrying on our founders' legacy with ground-breaking discoveries in the brain-body-eye connection," stated Mr. Love. "Today, we have an extensive complement pipeline in development with several late-stage trials underway, and a strong balance sheet and disciplined investment approach that supports our near- and long-term plans for our company. Together with a passionate and talented team, we have an incredible opportunity to achieve something tremendous in the field of medicine, and I am excited and confident in the future ahead for us and most importantly, for patients."

Cash Position and Updated Operating Runway

As of September 30, 2022, Annexon had $269.5 million in cash, cash equivalents and short-term investments. Annexon is updating its runway guidance to into 2025 from into the second half of 2025. The update is based on the company's plan to initiate a pivotal trial of ANX005 in HD in 2023, which it has now incorporated into its financial forecast.

J.P. Morgan Healthcare Conference

Mr. Love will present Annexon's pipeline updates at the 41st Annual J.P. Morgan Healthcare Conference on Wednesday, January 11, 2023, at 7:30 a.m. PT in San Francisco. A live webcast of the event can be accessed under the 'Events & Presentations' section on the Investors page at www.annexonbio.com. A replay of the webcast will be archived on the Annexon website for 30 days following the presentation.

About Annexon

Annexon (Nasdaq: ANNX) is a clinical-stage biopharmaceutical company seeking to bring game-changing medicines to patients with classical complement-mediated diseases of the body, brain and eye. The classical complement cascade is a seminal pathway within the immune system that anchors and drives a host of autoimmune, neurodegenerative and ophthalmic diseases. Annexon is advancing a new class of complement medicines targeting the early classical cascade and all downstream pathway components that contribute to disease, while selectively preserving the beneficial immune functions of other complement pathways. Annexon is rigorously developing a pipeline of diversified product candidates across multiple mid- to late-stage clinical trials, with clinical data anticipated throughout 2023 and beyond.

Forward Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. 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," "suggest," "target," "on track," "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. All statements other than statements of historical facts contained in this press release are forward-looking statements. These forward-looking statements include, but are not limited to, statements about: anticipated milestones; cash operating runway; engagement with regulators; the potential benefits from treatment with anti-C1q therapy; timing of data reports; and continuing advancement of the company's innovative portfolio. 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: the company's history of net operating losses; the company's ability to obtain necessary capital to fund its clinical programs; the early stages of clinical development of the company's product candidates; the effects of COVID-19 or other public health crises on the company's clinical programs and business operations; the company's ability to obtain regulatory approval of and successfully commercialize its product candidates; any undesirable side effects or other properties of the company's product candidates; the company's reliance on third-party suppliers and manufacturers; the outcomes of any future collaboration agreements; and the company's ability to adequately maintain intellectual property rights for its product candidates. These and other risks are described in greater detail under the section titled "Risk Factors" contained in the company's Annual Report on Form 10-K and Quarterly Reports on Form 10-Q and the company's other filings with the SEC. Any forward-looking statements that the company makes in this press release are made pursuant to the Private Securities Litigation Reform Act of 1995, as amended, and speak only as of the date of this press release. Except as required by law, the company undertakes no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise.

The contents of the company's website at www.annexonbio.com and the presentation accessible through the company's website are not incorporated by reference into this press release.

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