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STOP THE START

of classical complement-driven diseases

Virtual R&D Day | March 1, 2024

Nasdaq: ANNX

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Guillain-Barré Syndrome: A Focus on its Serious Unmet Need and Annexon's Novel Therapeutic Approach

Douglas Love, President & CEO
Annexon Biosciences

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 13, 2023 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.

Agenda

TIME (ET)	TOPIC	PRESENTER
10:00-10:05am	**Annexon: Overview and Commitment to GBS**	**Douglas Love** President & CEO
10:05-10:15am	**GBS Patient Voice**	**Lisa Butler** Executive Director, GBS | CIDP Foundation Intl.
10:15-10:35am	**GBS Disease Overview and Treatment Landscape**	**Hugh J. Willison, MBBS, PhD** Professor Emeritus of Neurology, University of Glasgow, Scotland
10:35-10:50am	**Annexon GBS Clinical Program Overview**	**David Cornblath, MD** Professor Emeritus of Neurology, Johns Hopkins University School of Medicine
10:50-11:00am	**GBS Market Opportunity and Annexon's Commercial Approach**	**Michael Overdorf** CBO
11:00-11:05am	**Closing Remarks**	**Douglas Love** President & CEO
11:05-11:30am	**Q&A Session**	

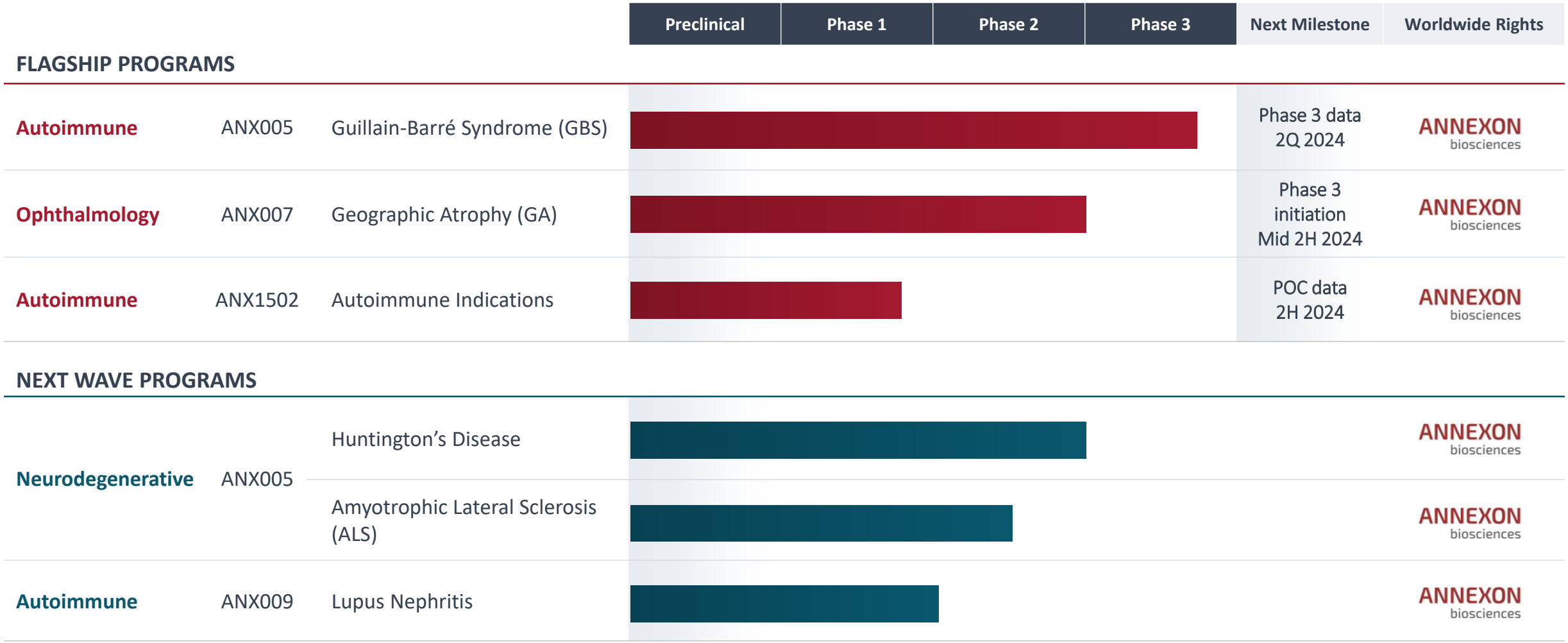
ANNEXON: Late-stage Clinical Platform for Classical Complement-mediated Neuroinflammatory Diseases of the Body, Brain and Eye

First-in-kind approach, wholly owned pipeline	**Large market opportunities supported by clinical proof-of-concept data in multiple indications**
Near-term registrational data in GBS	**2Q 2024 – Pivotal data in disease of high unmet medical need and no FDA-approved therapy**
Diverse GA registrational program & oral POC program	**Mid to 2H 2024 – Initiation of two pivotal Phase 3 trials in GA (Global ARCHER II sham trial | ARROW head-to-head trial vs. SYFOVRE®) and 2H 2024 – ANX1502 oral candidate proof of concept in autoimmune disease**
Well-capitalized into mid 2026	**Runway through multiple mid- and late-stage clinical catalysts**

GBS: Guillain-Barré Syndrome; GA: Geographic Atrophy

Only Complement-Pipeline for Diseases of the Body, Brain & Eye

Potential to treat >8 MILLION patients worldwide



POC: Proof-of-Concept

Annexon GBS Phase 1b data presented at American Academy of Neurology 2020 and Peripheral Nerve Society Annual Meetings 2021-2022.

Annexon Has a Deep-Rooted History and Commitment to GBS

Aligned With Our Mission
to treat diseases driven by classical complement activation

Strong Scientific Rationale
ANX005 is designed for rapid inhibition with a single dose

High Unmet Need
Well-characterized, underserved disease afflicting thousands globally

ANNEXON HAS KEY CLINICAL EXPERTISE AND RELATIONSHIPS IN GBS

Supported 2,000 patient registry at IGOS to inform clinical program

Conducted 3 clinical trials including:

- 1st placebo-controlled trial in ~40 yrs
- Monotherapy and combination trials

Large ongoing Phase 3 placebo-controlled trial

ANX005: Potential to be First FDA-approved Therapy for GBS

Pursuing a monotherapy label in GBS

Demonstrated POC across several clinically-meaningful measures

Granted US FDA Fast Track & Orphan Drug Designations

Granted EMA Orphan Drug Designation based on potential for benefit over available therapies

Phase 3 data on track for 2Q 2024; Real World Evidence comparability data 1H 2025 in support of BLA submission

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GBS Patient Voice

Lisa Butler
Executive Director of the GBS|CIDP Foundation

2001, age 5

2024, age 27

In The Voice of GBS Patients

"Went to ER, turned away for fatigue, dehydration and stress. The next day could not stand, legs buckled, back to ER, unable to move my entire body, put on respirator that same day."

"They told me they would give me something called IVIG to help stop this, but I had no idea what they were talking about."

"I did PT, OT and speech. I eventually stood up with assistance after 8 weeks, I took my first independent steps at 16 weeks."

"I was terrified, there was so much chaos around me as I was put in the ICU and told my body was paralyzed by this disease I had never heard of and that I would likely require a respirator to help me breathe."

"I have learned that I was put in a medically induced coma."

"They said I would recover to a "new normal", what was that?"

"At one point, I could only communicate by blinking my eyes. I had so many questions that I couldn't ask."

GBS|CIDP Foundation International

SUPPORT • EDUCATION • RESEARCH • ADVOCACY

The Foundation

1980

- 1980: First Meeting
- 8 people
- 1 Doctor, 2 residents
- 0 employees, 2 volunteers in Pennsylvania

2024

- 30,000 patients in database
- 20 members of Global Medical Advisory Board
- 57 Global Centers of Excellence
- 200 volunteers in 47 countries
- 18 FTE, 13 Members of Board of Directors

From day one we have never lost our focus on the patient! We exist so that no one takes this journey alone!

SUPPORT AND EDUCATION

Support:

- Approximately 100 patient inquiries monthly
- Chapter support group meetings
  - **357** registered community members
- Coffee Chats
  - **681** registered community members
- Speaker Series
  - **2,218** registered community members

Education:

- 17 symposiums and 7,000+ attendees
- Website
  - 108,000+ visitors on GBS page in 2023
  - 676K+ views on overall website in 2023
- Global Medical Advisors One-on-One Consultation

Global Medical Advisory Board

GMAB Members:

- United States: 12
- Barcelona: 1
- Denmark: 1
- United Kingdom: 1
- Brussels: 1
- Netherlands: 1
- Australia: 1
- Japan: 1
- Netherlands: 2
- Germany: 1

Doctor-to-Doctor Consultations:

2023

- 2 CIDP consultations
- 1 IVIG Dosage consultation

Centers of Excellence:

United States: 38 COEs
International: 22 COEs

GBS|CIDP Foundation International
Center of Excellence
2024

Research

- $8M total, $50k-$300k
  - *Elevation Grant, Discover Grant, 3-year Benson Fellowship*
- Consortium based
- Funding support for IGOS coordinating center's research
- NIH State of Science meeting: 2020 virtual meeting between NINDS and NIAID on state of GBS research

Advocacy

- **Dept of Defense Peer-Reviewed Medical Research Program (PRMRP):** $6 million between 6 researchers since 2017
- **Congressional Champion**: John Garamendi
- **2019: GBS patient listening session** with FDA to increase awareness of the unmet need in GBS despite the current SoC
- **2024:** Hosting FDA **Patient-Focused Drug Development Meeting** (PFDD) on GBS to address the continuing unmet need of patients with GBS for novel therapies to Get Better Sooner

GBS
GETTING BETTER SLOWLY

~~Getting better slowly~~ → **Getting better sooner**

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GBS Disease Overview and Treatment Landscape

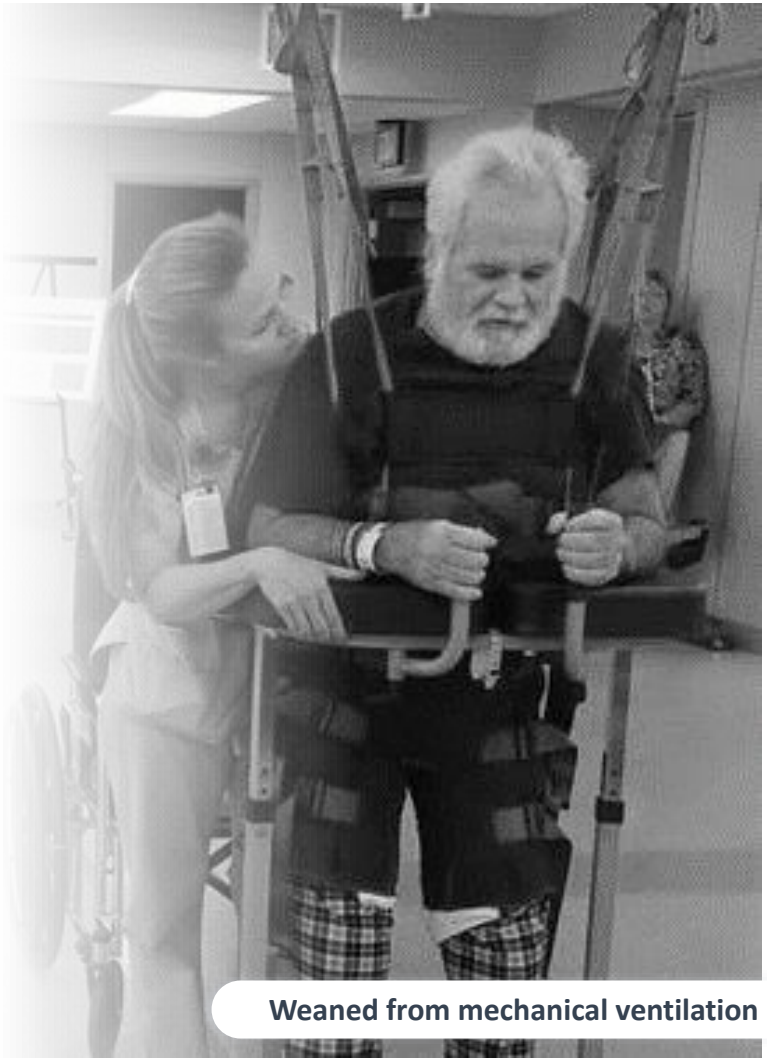
Hugh J. Willison, MBBS, PhD
Professor Emeritus of Neurology, University of Glasgow, Scotland

GBS: Neuro-Emergency Needing Urgent and Effective Intervention

Most common cause of acute paralytic inflammatory disease of the peripheral nervous system, known for its severity and rapid progression

Frequently follows an infection that generates complement activating auto-antibodies that attack peripheral nerve tissue leading to nerve conduction failure and nerve fiber death

Global annual incidence ~150,000, lifetime likelihood of 1 in 1,000



PERIPHERAL NERVE DAMAGE LEADS TO:

- Severe weakness
- Respiratory failure requiring mechanical ventilation in 25%
- Mortality rates of 3-17%
- Irreversible nerve damage preventing patients from resuming a normal life

Currently no treatment specifically and immediately targets complement mediated nerve damage

- IVIg has an ill-defined mechanism of action and requires 5-day course to complete therapy

1) van Doorn, 2013; Willison et al., 2016 2(van den Berg et al., 2014) 3 Walgaard et al (2021) Lancet Neurology 20(4):275, 4AAN Guidelines "Immunotherapy for GBS", 4Hund EF et al (1993) Crit Care Med 21:433, 454Fletcher D, et al. (2000) Neurology 27;54(12), 46, 5Van den Berg B, et al (2014) *Nat Rev Neurol* Aug;10(8), 6Stephan et al (2012) Neuroscience 35:369, 7Lansita et al (2017) Int. J. Toxicol. 36:449

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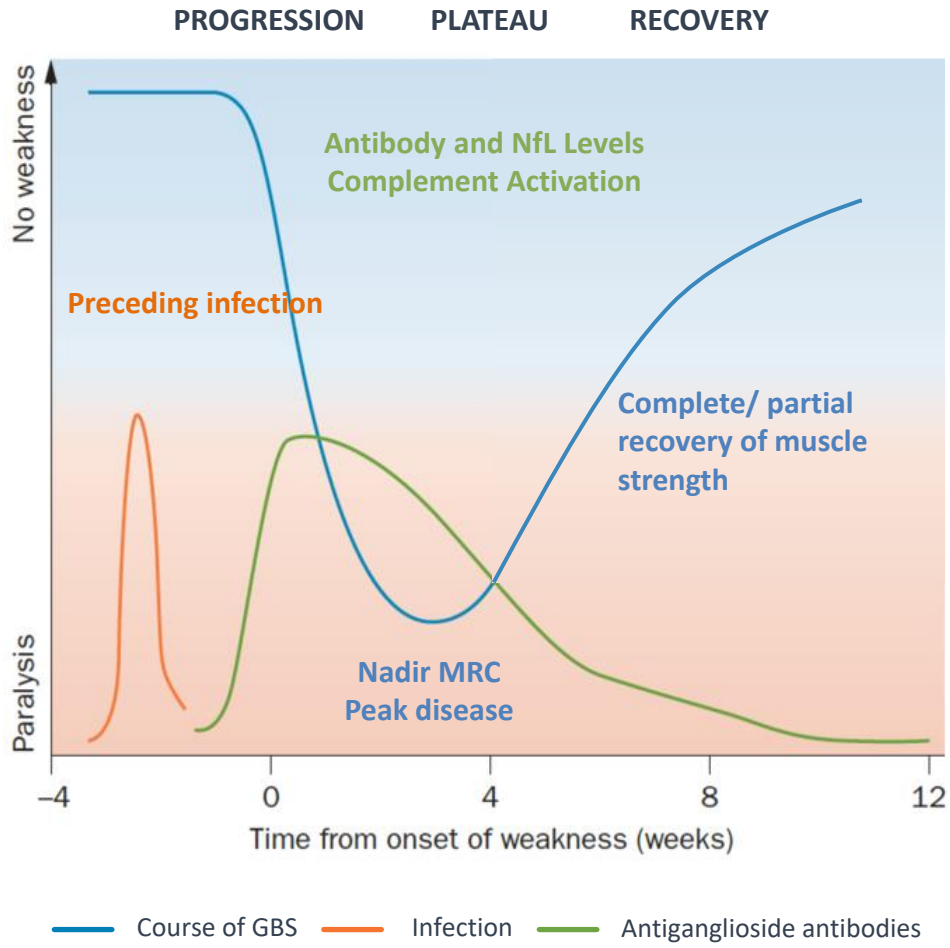
GBS is a Neurological Emergency Requiring Urgent Intervention

There is a limited time window in the acute illness phase to achieve a therapeutic effect



PROGRESSIVE PARALYTIC PHASE: rapidly progressive bilateral muscle weakness peaking by 1 week in most cases (ideal treatment window) and lasting up to 4 weeks maximum

- Nadir determines risk for mechanical ventilation or death and prognosis

PLATEAU PHASE: lasts weeks to months post-treatment window, with duration linked to severity at presentation

- Includes extended periods of ventilation in ICU, and intensive supportive care in the ward

RECOVERY PHASE: gradual muscle strength and functional improvement occurring over weeks to years as nerve regeneration takes place

- ~20% unable to walk or dead at 1 year
- Additional ~20% continue to experience symptoms

*Adapted from van den Berg, et al. (2014) Nat Rev Neurol **10**, 469–482*

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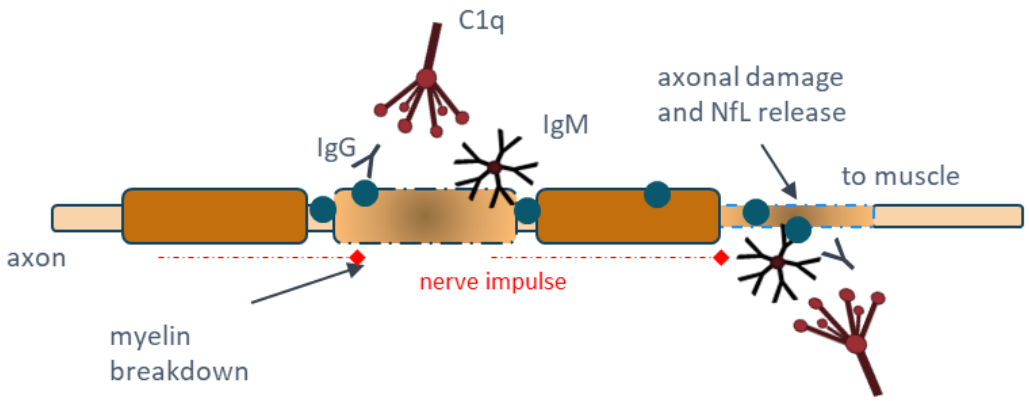
Auto-Antibodies Fix Complement to Peripheral Nerve Myelin & Axons

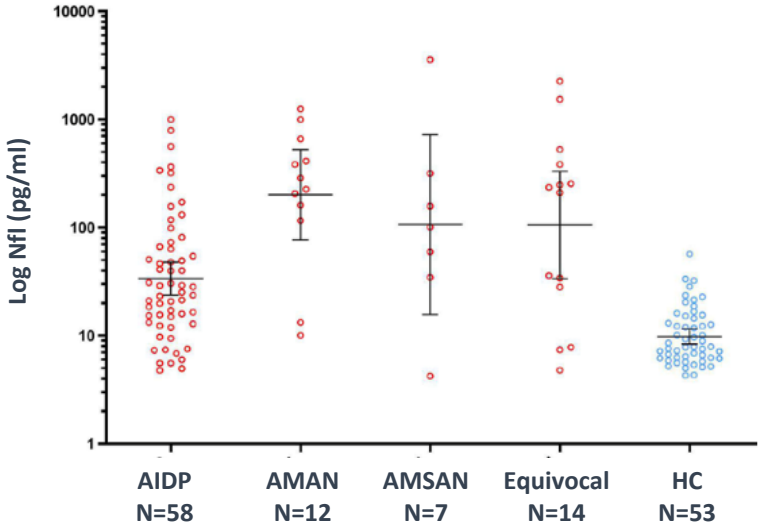
COMPLEMENT – MEDIATED NERVE DAMAGE



- Auto-antibody-mediated nerve damage affects both myelin and axon, as known antigens are present on both
- Autoantibodies fix complement to both myelin and axon
- All GBS neurotypes are present worldwide, but the proportion is variable: e.g. AIDP is more common in EU (54%) than in Bangladesh (40%)

Doets, et al (2018). Brain, 141(10), 2866–2877

ACUTE NERVE DAMAGE BIOMARKER ELEVATED IN ALL GBS NEUROTYPES



- The gold standard biomarker of axonal damage, neurofilament light (NfL) is elevated in all types of GBS
- NfL levels correlate with disease course, severity and prognosis, irrespective of GBS neurotype

Martín-Aguilar et al, J Neurol Neurosurg Psych (2020)

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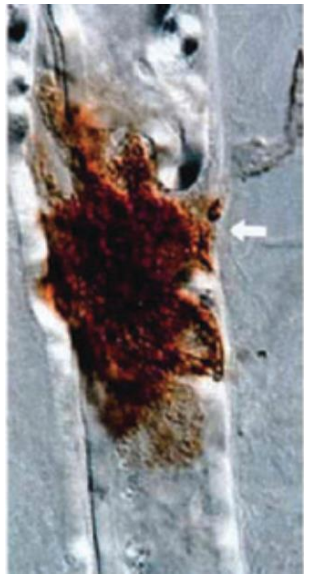
Complement is Pivotal Force in Driving Nerve Damage in GBS

C1q binds to IgG and IgM antibodies on nerve and activates the classical complement pathway
leading to neuroinflammation, directs clearance of debris by macrophages (C3b) and inflicts direct membrane damage (C5b-9) causing sudden and prolonged loss of muscle strength

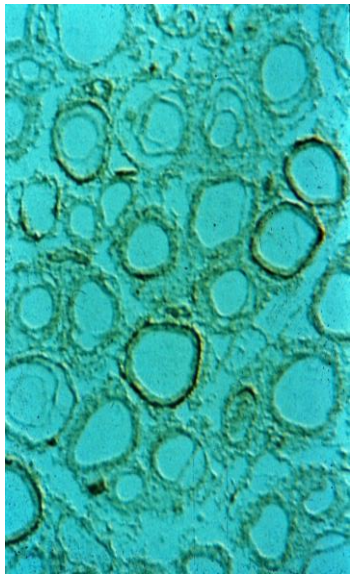
NERVE FROM HUMAN AUTOPSIES

Activated complement
Node of Ranvier

Macrophage
Node of Ranvier

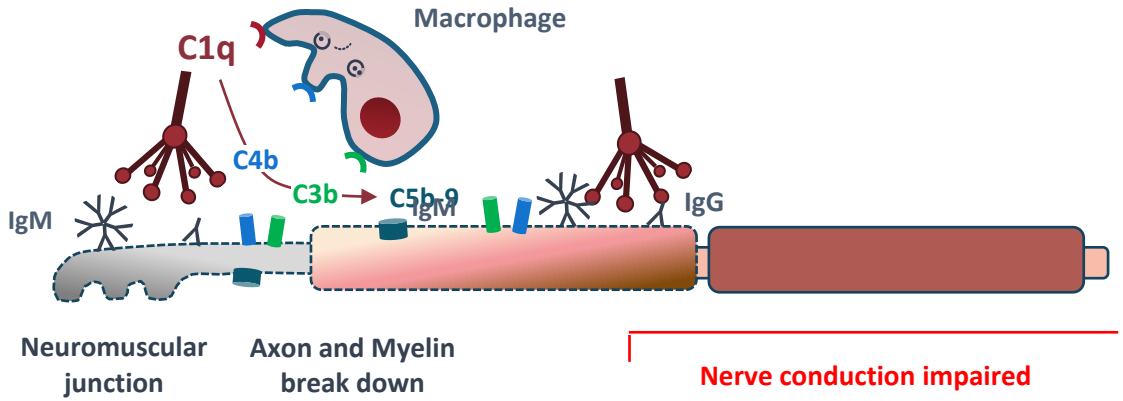


Activated complement
myelin sheath



Hafer-Macko C et al., (1996) Ann Neurol 39 & 40

CLASSICAL COMPLEMENT PATHWAY DIRECTS IMMUNE CELLS TO SITE OF INFLAMMATION



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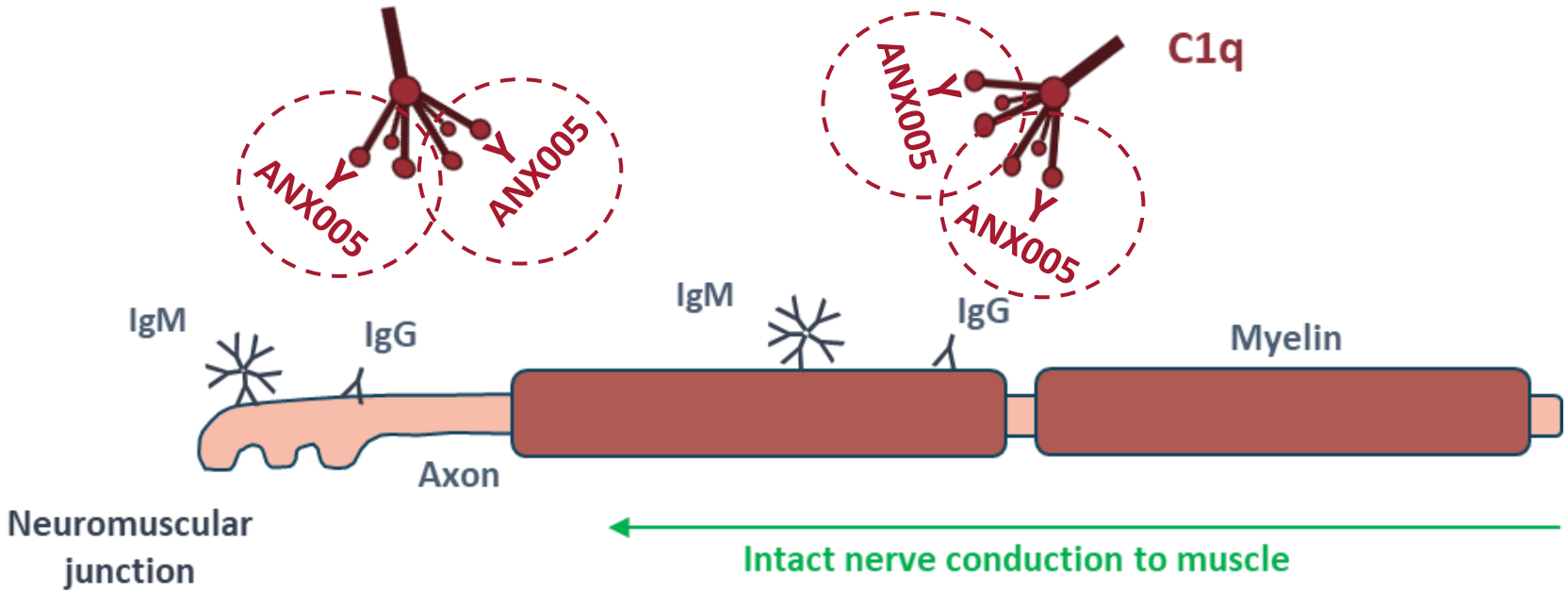
ANX005 is a Targeted Immunotherapy Against Complement-Mediated Nerve Fiber Damage

Immediate C1q inhibition with a single dose of ANX005 is designed to block all downstream complement components involved in acute or ongoing inflammation and nerve damage and allow nerve fiber recovery to start



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Prognostic Factors of Functional Recovery

Used in clinical prognostic tools, critical in clinical trial design, essential to show comparability between populations

Baseline factors have been identified from multiple, large, prospective and retrospective studies including IGOS that are highly prognostic for functional outcome and need for mechanical ventilation

1. MRC sum score (muscle strength ranging from 0-60)
2. GBS-DS (function: ranging from 0-6)
3. Age
4. Time of onset of weakness
5. Preceding diarrhea
6. Serum neurofilament light (NfL)
7. Electrophysiology: ulnar distal compound muscle action potential (CMAP)

Walgaard 2011; Papri 2022, Islam 2019; Hughes et al., 1978; van Koningsveld et al., 2007; Papri 2021; Walgaard 2010; Doets 2022; Martín-Aguilar et al., 2021; van Tilburg et al., 2022; Cornblath et al., 1988

Characteristics of an Effective Therapy to Combat GBS – Get Better Sooner

1 **Directly targets mechanism driving extensive nerve damage and paralysis**

Treatment goal is to target complement-mediated acute nerve damage and inflammation to prevent paralysis, severe morbidity, disability and mortality

2 **Rapid onset of action**

Block acute and ongoing destruction of nerves immediately

3 **Provides clinical benefit across entire disease spectrum**

Effective in all GBS patients, and impacting all aspects of the disease that are important to patients

4 **Minimal side-effects**

Single infusion with manageable infusion related reactions

ANX005 GBS Phase 1b POC Study

Randomized, double-blind trial, placebo-controlled Phase 1 trial; completed 2020

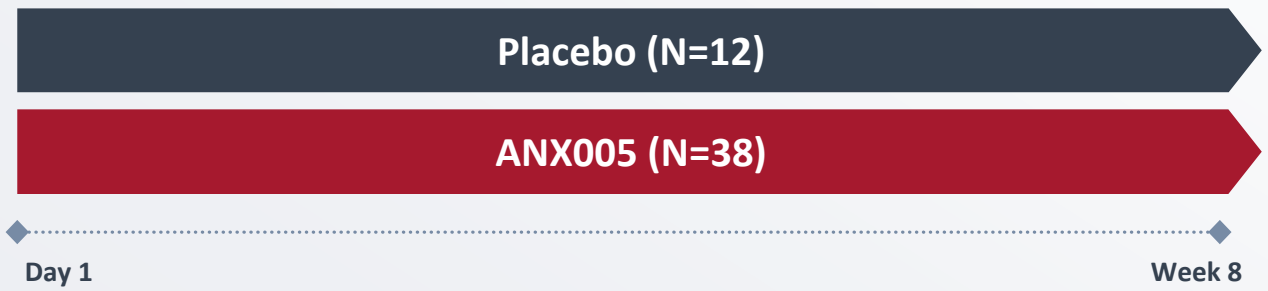
STUDY DESIGN

- N=50 Adults with GBS in Bangladesh
- SAD: ANX005 3 mg/kg to 100mg/kg
- MAD: 2 x 75mg/kg
- Mean time from onset of weakness to treatment: 8.1 days
- Mean GBS-DS at baseline: 4[1]

KEY OBJECTIVES

- Safety / Tolerability / PK
- C1q target engagement

STUDY SCHEMATIC



KEY RESULTS

- ✓ No deaths
- ✓ No treatment-related SAEs
- ✓ Full C1q inhibition >1 week 18mg/kg and above
- ✓ Target engagement in blood & CSF
- ✓ MTD not established
- ✓ Early Reduction in Nerve Damage[1]
- ✓ Early Improvement in MRC[1]
- ✓ Consistent shift to better on GBS-DS[1]

[1]18-75mg/kg dose cohorts

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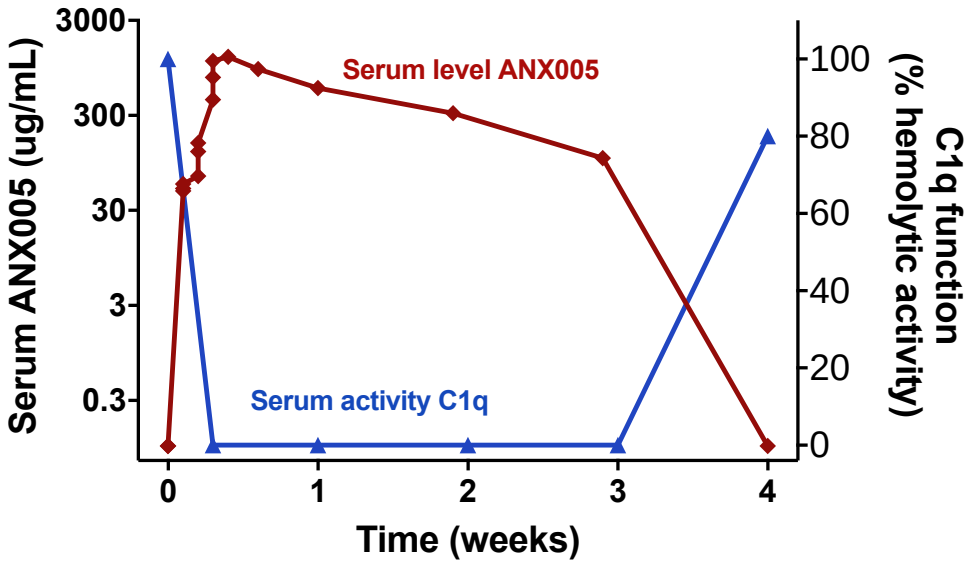
ANX005 Phase 1b: Rapid and Complete Complement Inhibition

ANX005 DEMONSTRATED RAPID COMPLEMENT INHIBITION AT DAY 1

- Single dose of ANX005 rapidly inhibits C1q in both serum and CSF
- ANX005 doses of 18-75 mg/kg inhibit complement during progressive stage of the disease (1-3 weeks from admission)
- Aim to block immediate and ongoing neural damage and show early improvement in muscle strength and function

Serum PK/PD after Single 75 mg/kg Dose



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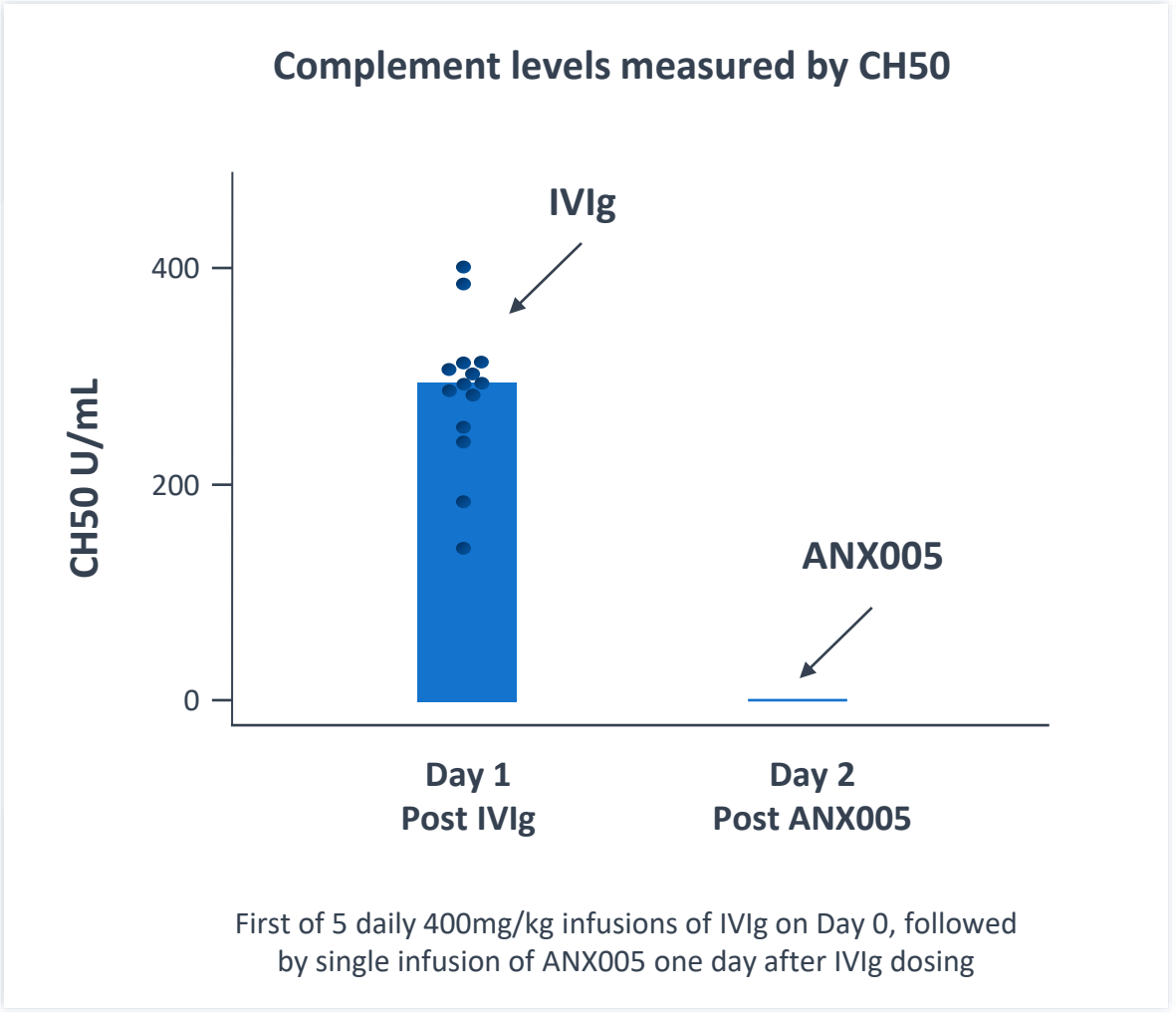
ANX005 Rapidly Inhibits Complement Alone or Following IVIg

- IVIg alone does not inhibit complement on Day 1
- ANX005 alone or following IVIg results in complete inhibition



First of 5 daily 400mg/kg infusions of IVIg on Day 0, followed by single infusion of ANX005 one day after IVIg dosing

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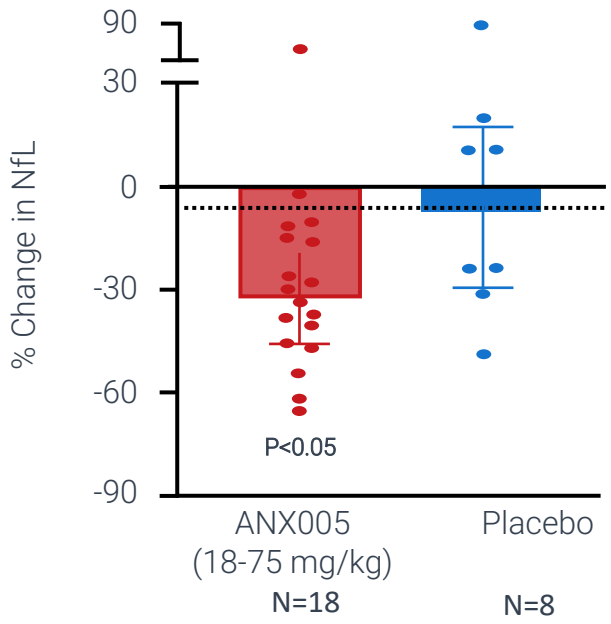
ANX005 Phase 1b: Early Reduction in Nerve Damage

RELEVANCE OF NfL

- Neurofilament light chain increases proportionally to the degree of axonal injury or degeneration
- Elevated NfL levels in serum are associated with more severe disease and predicts poor outcome
- In Phase 1b, ANX005 showed significant early NfL reduction which correlated with improved GBS-DS outcome at week 8 (Spearman's r=0.431 p=0.028)

ANX005 PHASE 1b NfL RESULTS

Statistically significant early NfL reduction (weeks 2-4)



Altmann et al., 2020; Axelsson et al., 2018; Martín-Aguilar et al., 2021; van Tilburg et al., 2022

Annexon data on file

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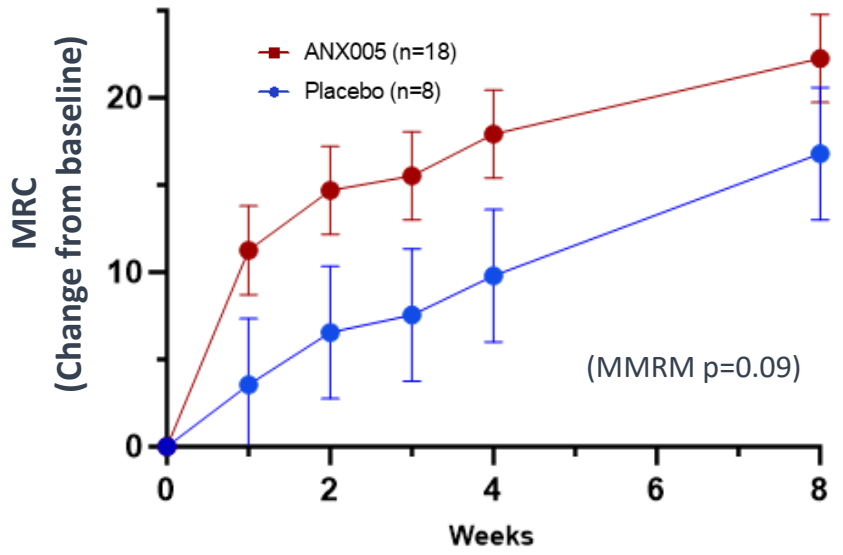
ANX005 Phase 1b: Early Improvement in Muscle Strength

RELEVANCE OF MUSCLE STRENGTH

- Loss of muscle strength is considered the primary clinical manifestation of GBS
- Muscle strength is most important prognostic marker for outcomes
- Improvement in MRC sumscore at week 1 is most important parameter for future function
- In Phase 1b, ANX005 improved muscle strength at week 1 and thereafter
- Change in MRC correlated with change in GBS-DS at Week 8 (Spearman r = -0.6155; p < 0.001)

MRC RESULTS PHASE 1b STUDY

Early Change in mean MRC Sumscore from Baseline



**Walgaard, et al., 2011; Papri et al. 2022; Luijten, 2023*

Annexon data on file

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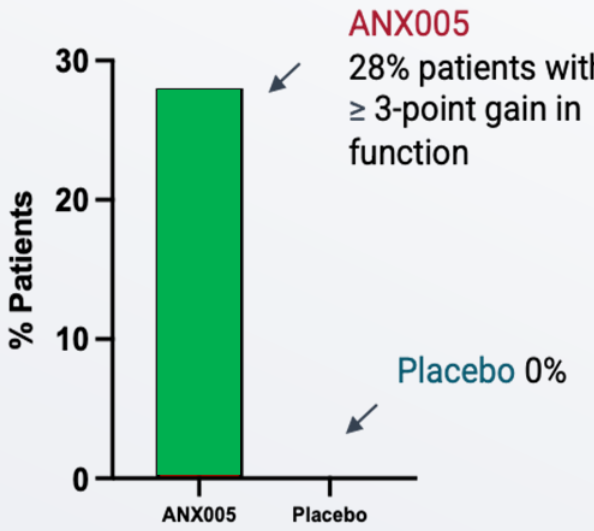
ANX005 Phase 1b: Consistent Shift to Better on Disability (GBS-DS)

Large shifts to better from baseline demonstrated on GBS-DS @ week 8



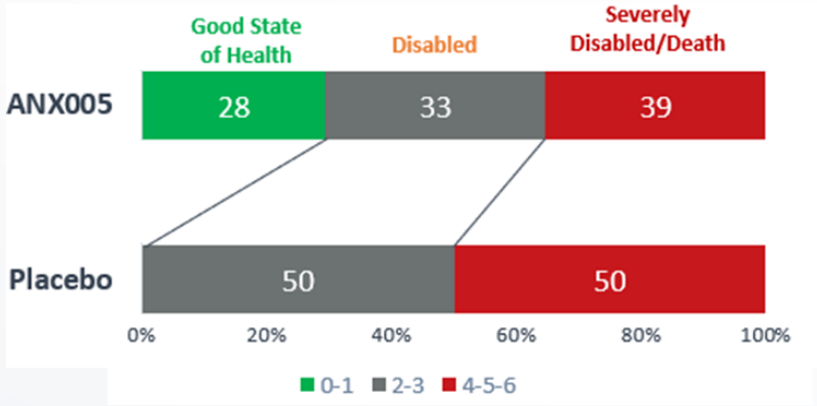
GBS Disability Scale
ANX005 n=18 & Pooled Placebo, n=8
(treatment data from 18, 36, and 75mg/kg dosing cohorts)

Represents shifting from ventilated or bed ridden, to walking unassisted or running

Translated to Grotta Bar

28% of patients treated with ANX005 **shifted to being in a good state of health** from being severely disabled or disabled

GBS-DS Grotta Bar: Consistent shifts to better in ANX005 groups vs. pbo @ week 8



GBS Disability Scale Grotta Bar
ANX005 n=18 & Pooled Placebo, n=8
(treatment data from 18, 36, and 75mg/kg dosing cohorts)

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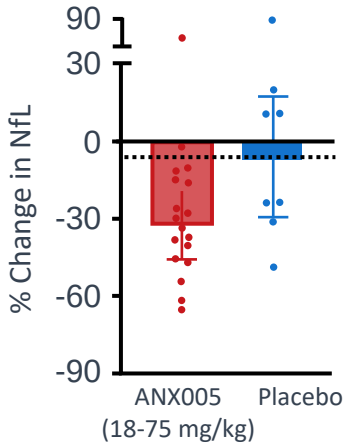
ANX005 Phase 1b: Consistent Demonstration of Getting Better Sooner

Rapid target engagement, early nerve damage reduction and recovery of muscle strength precedes gain of function

NEURAL DAMAGE

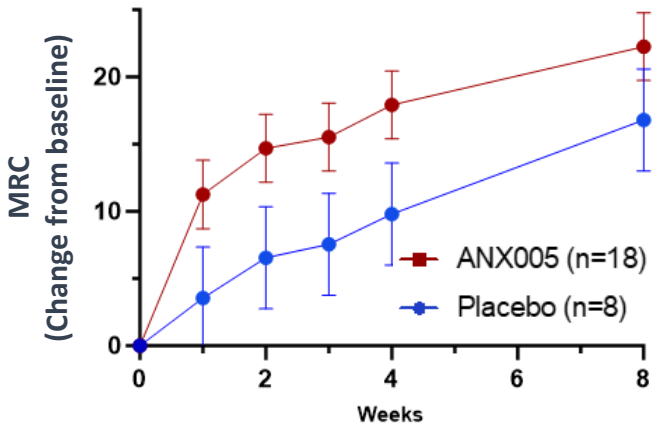
Rapid reduction in nerve fiber biomarker NfL



Statistically significant reduction (weeks 2-4)

MUSCLE WEAKNESS

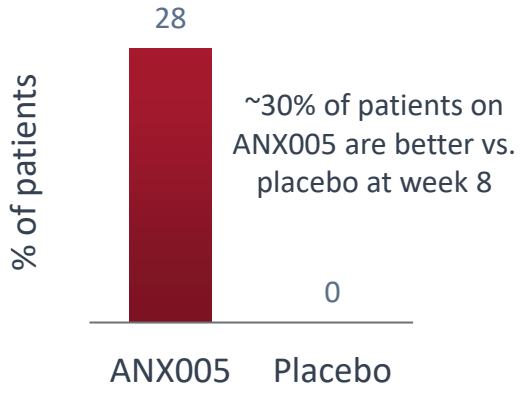
Early gain in muscle strength



Change in MRC sumscore from Baseline

NEUROLOGICAL DISABILITY

Improvement in clinical function



≥3 point improvement in GBS-DS at week 8

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EMA Review of Ph1b Data Highlights Potential of ANX005

- **ODD granted late 2023 based on potential of providing 'significant benefit' over approved SoC (IVIg)**
- **EMA recognizes relevance of data from Bangladesh**

DATA PACKAGE IN ODD APPLICATION

- ANX005 Ph1b data compared to
  - Real-world data
  - Published data from a randomized clinical trial

"…[the data] showed **an increased response of ANX005** regarding muscle weakness recovery and need for ventilation **as compared to IVIg**. **Given the modest response to SOC and the unmet medical need**, the data was considered **sufficient for establishing significant benefit** in the context of an orphan designation."

"Regarding the applicability of the AMAN subtype to the EU, the COMP acknowledged that although the axonal subtype (AMAN) is seen more often in Bangladesh, **it was agreed that the data from Bangladeshi patients was still relevant for the EU target population with severe disease**."

– European Medicines Agency

ANX005 Has Demonstrated Characteristics Required to Combat GBS

✓ Directly targets mechanism driving extensive nerve damage and paralysis

- Complement is an established target in GBS
- C1q binds to autoantibodies on nerve components initiating local activation of complement leading to inflammation, recruitment of immune cells, and damage to nerves

✓ Rapid onset of action

- ANX005 has demonstrated rapid target engagement in blood & CSF across multiple central and peripheral neurological disorders
- A single dose of ANX005 inhibits classical complement pathway on day 1
- Prevents acute and ongoing nerve damage to promote nerve repair

✓ Provides clinical benefit across entire disease spectrum

- Complement-mediated nerve destruction present in all neurotypes of GBS
- ANX005 mechanism of action is agnostic to neurotype or disease severity
- Early improvement in MRC seen across disease spectrum

✓ Minimal side-effects

- ANX005 has been safely administered in > 250 patients with GBS
- Generally well-tolerated
- No drug-related deaths & no serious infections observed

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Annexon GBS Clinical Program Overview

David Cornblath, MD
Professor Emeritus, Johns Hopkins University

The Phase 3 Study Embodies Key Characteristics of a Smart, Data-Driven, & Patient-Centric Design

HOW I WOULD DESIGN A PH3 GBS STUDY	HOW ANNEXON DESIGNED THE PHASE 3 PIVOTAL STUDY
Use all available global data and routinely seek expert input	✓ Data-driven by Ph1b, IGOS, and multiple external IVIg/PE datasets ✓ Routinely engaged with leading experts in GBS
Measures all meaningful outcomes through all phases of disease	✓ Proportional odds uses full GBS-DS scale, includes all patients, increases power ✓ Efficacy assessments cover all GBS symptoms & signs at all important timepoints
Control for disease heterogeneity	✓ Patients stratified by baseline MRC and days since onset of GBS symptoms ✓ Using MRC, time of onset of weakness, baseline NfL and age as covariates
Rigorous execution	✓ Streamlined time from onset to treatment increasing likelihood of better outcomes ✓ Conducted at sites with internationally recognized GBS clinical experience

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ANX005 Phase 3 Pivotal Trial On Track for Data Readout Q2 2024

Randomized, double-blind trial, placebo-controlled Phase 3 trial; enrollment completed in 2H 2023

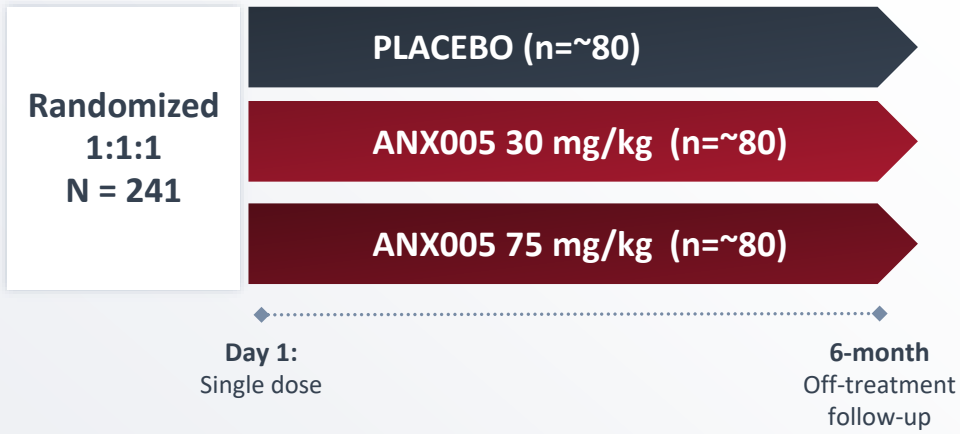
STUDY DESIGN

- Patients diagnosed <10 days from onset of weakness
- Baseline GBS-DS score 3-5
- Stratified for prognostic factors: muscle strength and time from symptom onset

GBS-disability Scale (GBS-DS)

0	Normal
1	Running
2	Walking unassisted
3	**Walking assisted**
4	**Bed ridden**
5	**Ventilated**
6	Death

MONOTHERAPY SINGLE DOSE TREATMENT



US FDA Fast Track & Orphan Drug Designation
EMA Orphan Drug Designation

ENDPOINTS

Primary Outcome Measure[1]

GBS-DS at week 8: well-accepted regulatory endpoint assessing functional status

Secondary Endpoints include muscle strength, mortality, and time on ventilator

What is considered a win?
2-fold shift to better on GBS-DS vs. placebo at week 8

[1]Analyzed using a proportional odds model, a common statistical analysis method (van Leeuwen, et al., 2019, doi.org/10.1371/journal.pone.0211404) with an expected outcome of approximately 2x more patients in a good state of health and 2x fewer patients remaining severely disabled

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Phase 3 GBS-DS Analysis Approach

GBS-DS SCALE COLLAPSED INTO 3 CATEGORIES
Enhances Clinical Interpretability

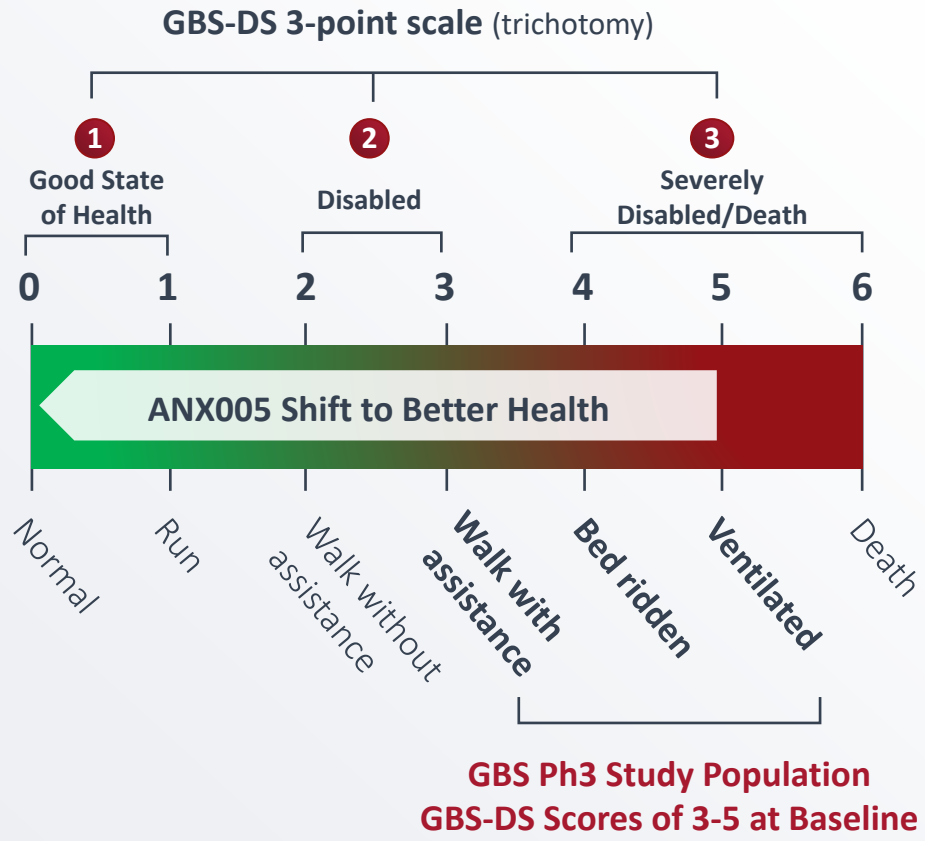
Approach: Collapse 7-point scale to a 3-point scale (trichotomy)

- **0-1:** Good State of Health
- **2-3:** Disabled
- **4-6:** Severely Disabled/Death

Rationale:

- ✓ Enhances clinical interpretability by focusing on a subject's actual health status at week 8 after receiving ANX005 or placebo
- ✓ Includes all patients across all health states vs. dichotomy which would only include subset
- ✓ Most efficient statistical analysis approach

GBS-DS SCALE FOR PIVOTAL PHASE 3



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Phase 3 Key Secondary Endpoints

Designed to assess total clinical benefit and demonstrate durability of response with measures that are interpretable and relevant to patients and clinicians

MUSCLE STRENGTH

MRC Sum Score

Clinically meaningful prognostic indicator of outcome

- MRC sum score at Day 8
- MRC sum score at Week 8

CHRONIC DISABILITY

GBS Disability Score

Durability of response over full study length

Multiple sensitivity analyses
- Longitudinal analysis
- Responder analyses

MORBIDITY AND MORTALITY

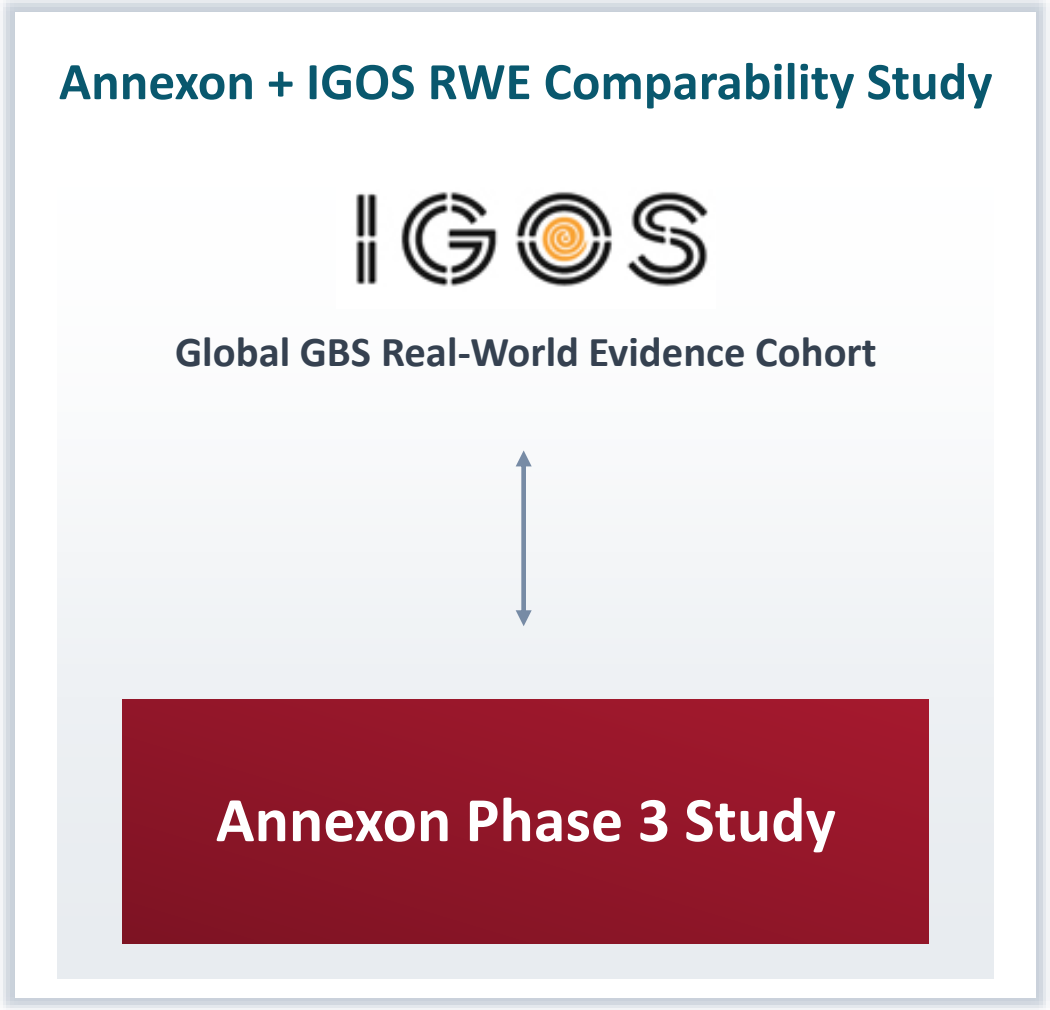
Ventilation, Time in ICU, Death

Overall reduction in morbidity and mortality

- Number of patients requiring ventilation
- Number of days on ventilator
- All-cause mortality
- Days in ICU

Real-World Evidence in Support of Regulatory Submission

- **FDA agreed that a single pivotal study would be sufficient for BLA assuming it demonstrates:**
  - Substantial evidence of ANX005's treatment effect vs. placebo
  - Comparability between Ph3 population & Western patients
- **FDA agreed with Annexon's plan to establish comparability**
  - Ph3 patients will be compared with patients from IGOS
  - IGOS is a global, prospective, observational, multicenter cohort study
  - IGOS is led by global experts in GBS and has enrolled 2000 patients who were followed for 1-3 years
  - Annexon has initiated a real-world evidence comparability protocol with IGOS (ANX005-GBS-04)
  - Initial comparability data 1H25 in support of BLA submission



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GBS Market Opportunity and Annexon's Commercial Approach

Michael Overdorf, Chief Business Officer
Annexon Biosciences

GBS Market Opportunity and Annexon's Commercial Approach

Significant commercial opportunity for ANX005 achieved through focused commercial footprint

Significant Commercial Opportunity

Increased GBS incidence numbers show full magnitude of disease and market opportunity for ANX005

No approved drugs in US and significant disease burden on patients despite available treatments

Targeting ANX005 as first-line monotherapy single infusion treatment for GBS patients

Unique Commercial Dynamics

Indiscriminate and urgent disease combined with confidence in diagnosis drive lower referrals compared to other rare diseases

GBS patients are geographically concentrated based on population

Focused Commercial Launch

Planning to target major metropolitan centers at launch, expand to large community hospitals and then to mid-sized community hospitals

Will have focused commercial team of Key Account Managers, Medical Liaisons, and Sales Reps

Value-based Benefits

GBS results in significant cost burden on patients, caregivers, hospitals, and payers

ANX005 has opportunity to provide value-based benefits that reduce cost to care for GBS patients

Increased GBS Incidence Numbers Reveal Full Magnitude of Disease and Commercial Opportunity

- **Completed first-ever analysis of 7 years of medical claims data to determine incidence of GBS**
- **Updated GBS incidence: 7,000 in US and 15,000 for all European countries**[1]
  - Previous US estimate = 6,000
  - Previous M5 Europe estimate = 6,000 (no total Europe estimate)
- **Updated incidence numbers are conservative since represent hospitalized and treated patients**, doesn't include mild patients (additional 5-10%) who are not hospitalized[2]

[1]81qd claims data analysis, [2]ClearView Health market research analysis

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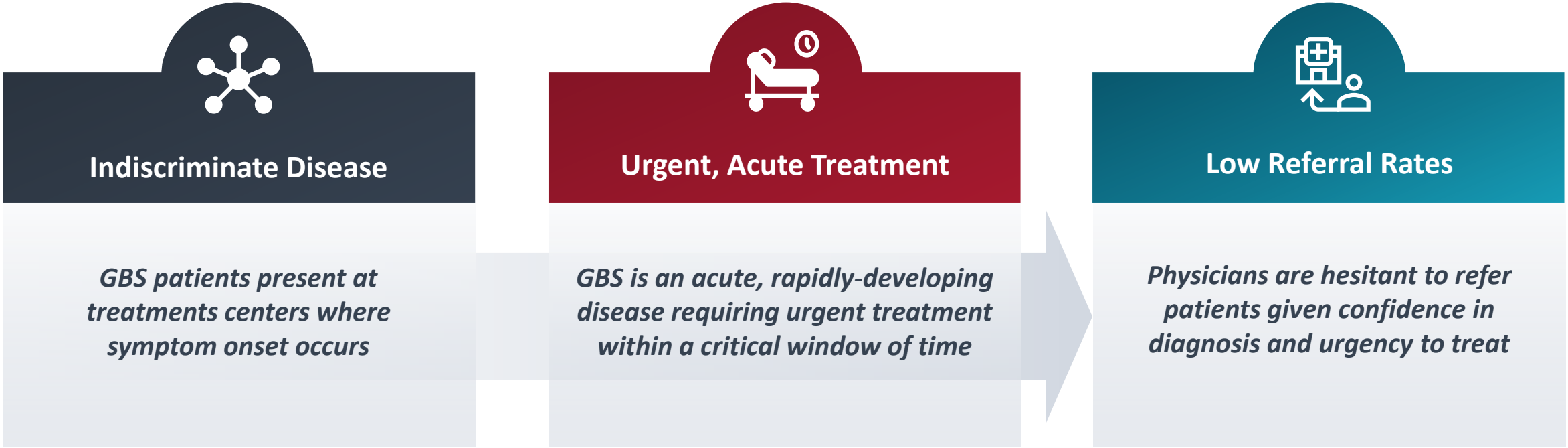
Unique Commercial Dynamics

Unlike other rare diseases, indiscriminate and urgent nature of GBS drives low referrals



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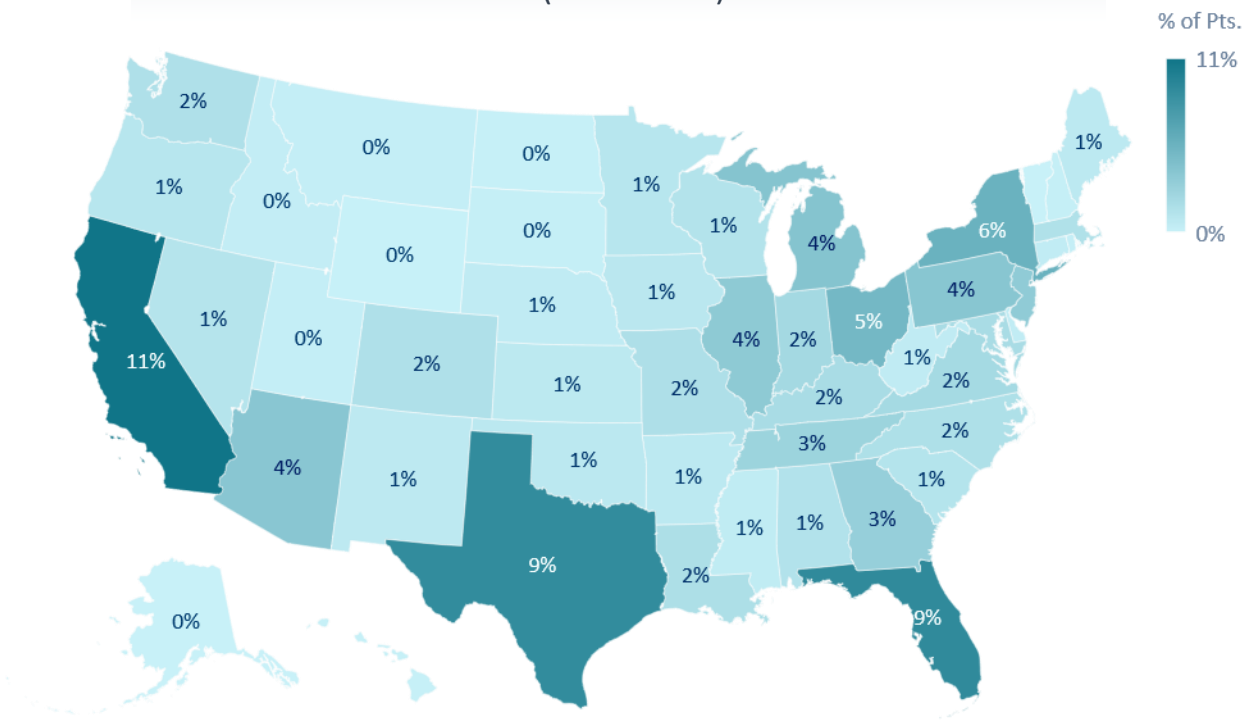
GBS Patients Geographically Concentrated Based on Population

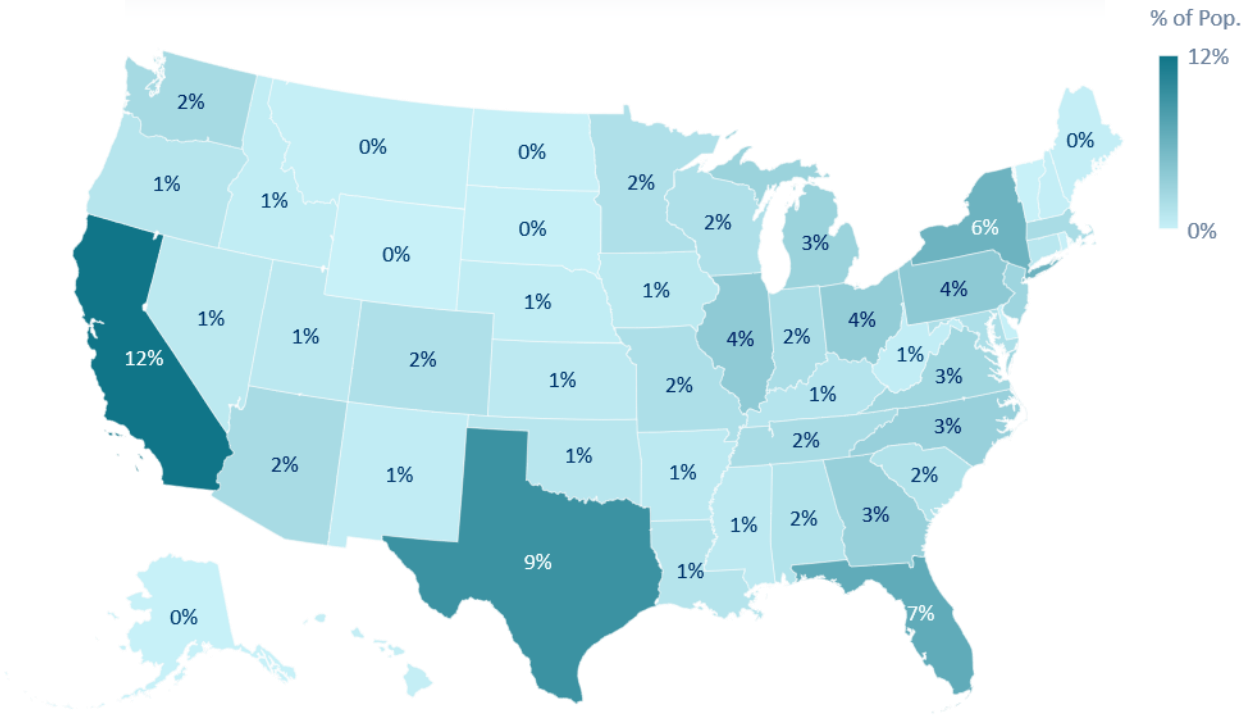
Initial targeting of large metropolitan areas where GBS patients and treaters are concentrated

GBS PATIENTS
Geographic Distribution

(2016-2022)



NATIONAL POPULATION
Geographic Distribution



Source: 81qd claims data analysis and Census data

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Planning Focused Launch Targeting Top Treatment Centers

Intend to target hospitals in three waves leveraging physician experience and endorsement

WAVE 1

Large Metropolitan and Academic hospitals (n~60) are initial launch targets since they treat the majority of GBS patients
Top 15 hospitals treat ~15% of all GBS patients

WAVE 2

Second wave targets Large Community Hospitals leveraging experience and endorsement of physicians from Wave 1

WAVE 3

Third wave targets Mid-sized Community Hospitals leveraging digital and per-to-peer platforms

Sources: 81qd and ClearView analysis

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Planning Focused Commercial Footprint

Commercial team will provide education, support, and access to hospitals, neurologists, and care teams

Key Account Managers

- ✓ Higher-level hospital engagement
- ✓ Helps facilitate P&T discussions

Targeted interactions with systems-level roles to facilitate ANX005 access and use through education on clinical and value-based benefits

Medical Science Liaisons

- ✓ GBS education
- ✓ ANX005 education
- ✓ Scientific interactions
- ✓ KOL engagement

Physician interaction with greater scientific depth

Customer Support Reps

- ✓ ANX005 promotion to label
- ✓ Active, ongoing customer support

Customer support and sales interactions with physicians and care teams

Commercial team will also ensure availability of ANX005

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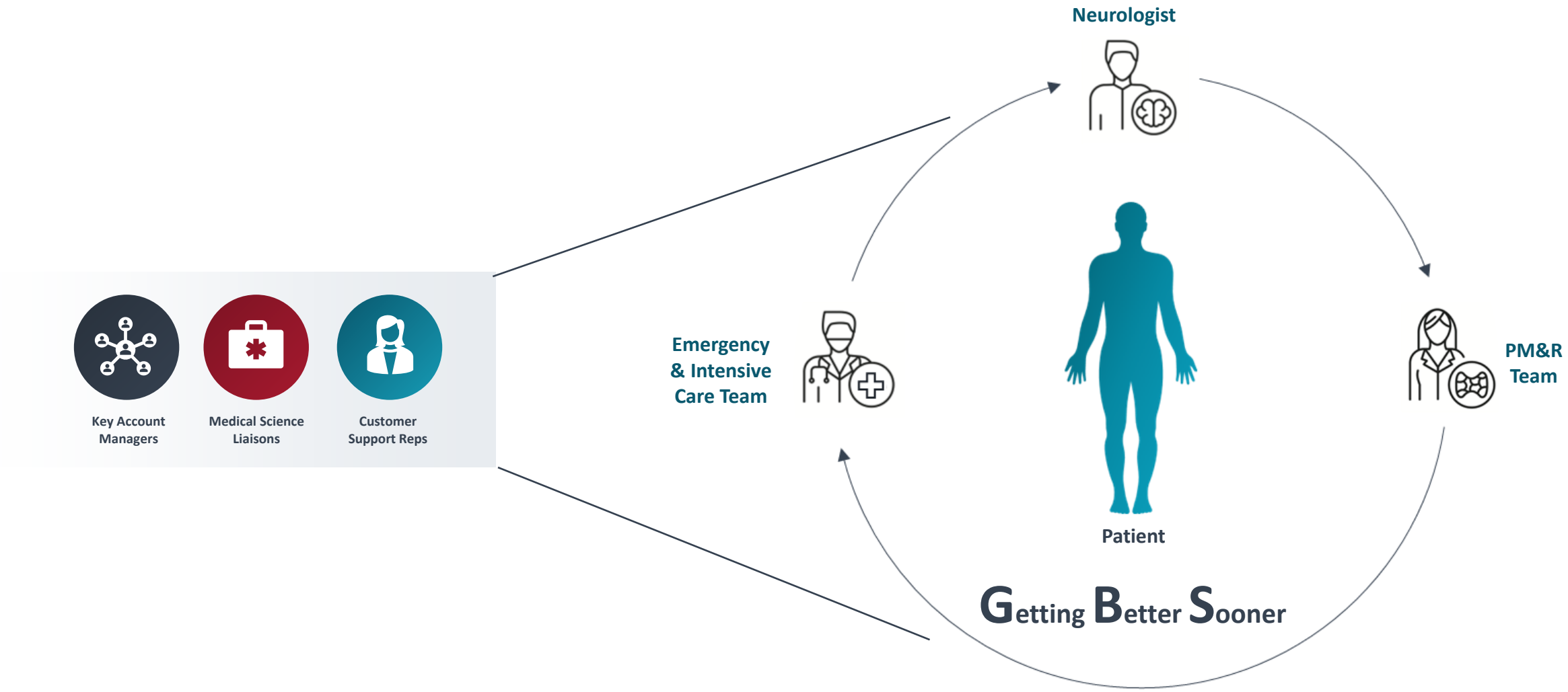
Commercial Teams Help Patients Achieve Goal of Getting Better Sooner

Reinforce patient outcome benefits of ANX005 across care teams



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Potential ANX005 Value-Based Benefits

"I was put on my hands and knees, and **I had to learn how to crawl just like a baby…**

I crawled for 8 or 9 months, and **it took about 2.5 years to learn how to walk…** Then I had 5 years in physical therapy."

Shane S.
53-year-old financial advisor and patient with GBS

SIGNIFICANT DISEASE BURDEN DESPITE CURRENT TREATMENTS [1,2,3,4,5,6,7]

~25%	~40%	~20%	~10%	~5%
require mechanical ventilation	admitted to ICU	can't walk at 1 year	permanently disabled and can no longer work	mortality

>$2B ANNUAL ECONOMIC COST OF GBS IN US[7]

~25% increase in daily cost of ICU care with mechanical ventilation[8]

GBS impacts patients' ability to work and places significant burden on caregivers[7]

ANX005 HAS POTENTIAL TO PROVIDE VALUE-BASED BENEFITS TO REDUCE COST TO CARE FOR GBS PATIENTS AND IMPACT OF DISEASE

[1]ClearView Health market research analysis, [2] AAN Guidelines "Immunotherapy for GBS", [3]Hund EF et al (1993) Crit Care Med 21:433, [4]Doets, *et al., Brain* 2018, 141, 2866-2877 (2018), [5]Van den Berg, B. *et al. Nat. Rev. Neurol.* 10, 469–482 (2014), [6]Leonhard, *et al, Nature Reviews, Neurology* (2019), [7]Inflation-adjusted from Frenzen, PD (2008) Neurology 71:21-27 7, [8] Kaier K, et al (2019).Epidemiology and Infection 147

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Closing Remarks & Q&A Session

Douglas Love, President & CEO
Annexon Biosciences

Annexon GBS Program Key Takeaways and Next Steps

ANX005 potential to be the first FDA-approved treatment for GBS

HIGH UNMET MEDICAL NEED WITH STANDARDS OF CARE

- Devastating and rapid nerve disease afflicting over 20K in the US and Europe
- No change in mortality rates in decades
- Annexon is leveraging anti-classical complement mechanism to fully block IgG and IgM

CLINICAL PROOF-OF-CONCEPT ON SEVERAL KEY MEASURES:

- Rapid and full C1q inhibition during critical progressive phase of disease
- Rapid improvement in neurodegeneration as measured by NfL, a key neuronal biomarker
- Rapid improvement in muscle strength (MRC) and GBS-DS

WELL-DESIGNED PIVOTAL PHASE 3 TRIAL

- FDA alignment on GBS-DS as primary endpoint, a well-accepted functional measure
- Other endpoints designed to demonstrate enhanced clinical benefit and durability

NEXT STEPS

Pivotal Phase 3 data expected in Q2 2024

Initial data from **real-world-evidence comparability protocol** with IGOS (ANX005-GBS-04) **expected in 1H 2025** to support a planned BLA submission

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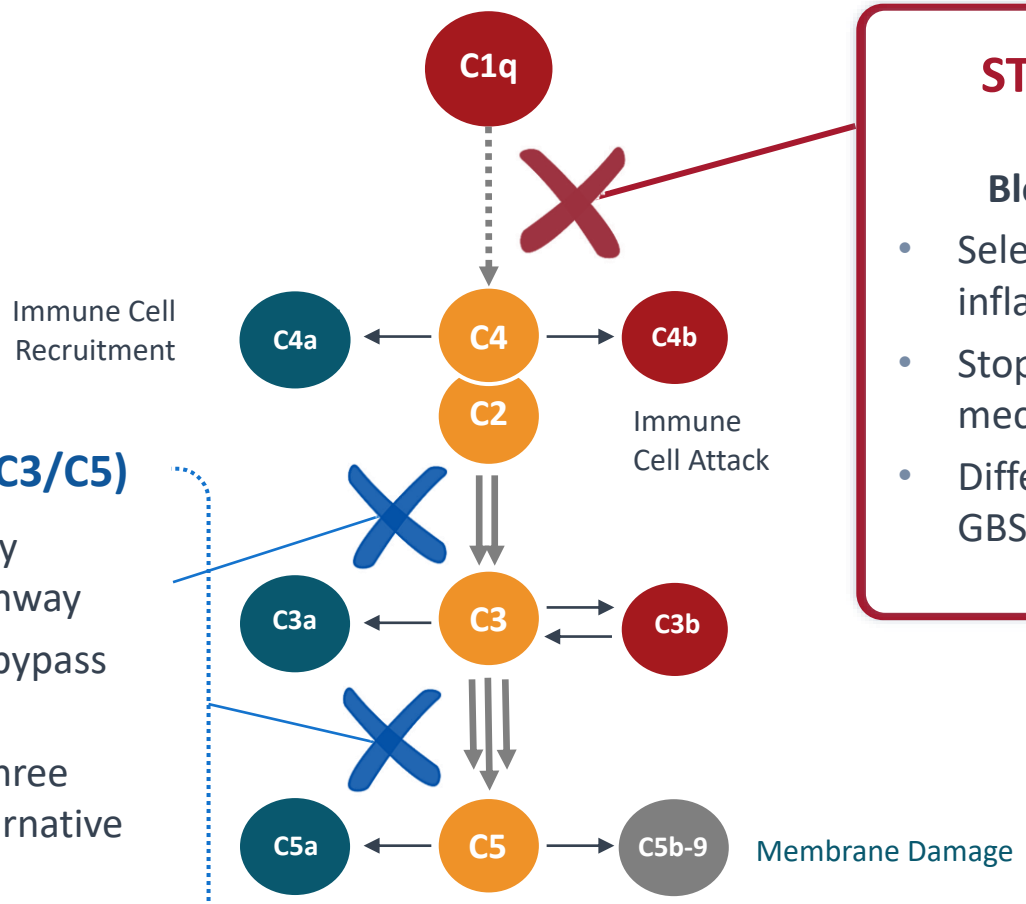
THANK YOU

Annexon Biosciences sincerely thanks all the patients, families, and study staff who are helping make the ANX005 Ph3 GBS study possible.

Powered By a Distinct Complement Approach Targeting C1q to STOP the Inflammatory Cascade Where it STARTS

Classical complement: common inflammatory pathway driving diseases of the body, brain & eye



STOPPING C1q AT THE START

Blocks All Classical Pathway Activity[1]

- Selectively stops upstream & downstream inflammation driven by classical pathway
- Stops pathway before downstream bypass mechanisms (breakthrough)
- Differentiated functional data in GBS, HD and GA

DOWNSTREAM APPROACHES (C3/C5)

- Do not block ongoing inflammatory pressure of upstream classical pathway
- More susceptible to complement bypass mechanisms
- Affect downstream activity of all three complement pathways (lectin, alternative and classical

[1]Lansita, et al., 2017; DOI: 10.1177/1091581817740873

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5 Key IVIg Topics That Are Advantageous to ANX005

1. IVIg's MOAs in GBS remain largely unknown
2. In the era of targeted immunotherapy, IVIg is a dated approach
3. Full course of IVIg treatment takes 5 days allowing disease mechanisms to continue
4. IVIg does not significantly affect plasma CH50 in the initial acute phase
5. IVIg has an incomplete therapeutic effect as patients often deteriorate on IVIg treatment and recovery is slow and suboptimal

Phase 3 Comparison of Eculizumab vs. ANX005

	Eculizumab Ph3 GBS Trial	ANX005 GBS Ph3 Trial
MOA	Targets downstream complement (C5) - misses important upstream complement drivers of nerve damage	**Blocks entire classical complement cascade**
Mean time from onset of weakness to treatment	>7 days	**< 7 days***
N	57	**241**
Stratification by prognostic factors	Not stratified leading to imbalance	**Stratified**

*Stratified for days since onset of weakness (<7 days, ≥7 days)