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STOP THE START of classical complement-driven diseases

# Topline Results from Phase 3 Study of ANX005 in Guillain-Barré Syndrome

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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, anticipated timing of submission of a Biologics Licensing Application, 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.

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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.

# ANX005 Achieved a Breakthrough Phase 3 Win for GBS Patients Worldwide

## A single infusion blocked complement for 1 week with robust, consistent benefit across multiple endpoints

### Met Primary Endpoint
### P=0.0058

**2.4-fold higher likelihood of being in a better state of health on GBS-DS at Week 8**

- ✓ FDA-agreed primary endpoint
- ✓ Multiple sensitivity analyses of the primary endpoint show consistent improvements
- ✓ Larger effect in sub-group with western baseline characteristics

### Expedited Recovery
### Patients Got Better Sooner

**Early, robust & clinically meaningful benefit on multiple outcome measures @ Week 8**

- ✓ Able to walk earlier vs placebo
- ✓ Able to run earlier vs placebo
- ✓ Less nerve damage vs placebo

### Durable Treatment Effect

**Maintained improvement over placebo at all timepoints across multiple measures**

- ✓ Less time on ventilation
- ✓ Less overall disability

### Generally Well Tolerated

**Safety data was similar to placebo**

- ✓ No new safety signals
- ✓ No increased infection rate
- ✓ No difference in all-cause mortality



Topline Results Subject to Change

# GBS: Neurological Emergency with Long-Term Disability; Requires an Immediately Targeted and Effective Intervention

**POST-INFECTIOUS COMPLEMENT-MEDIATED DISEASE**

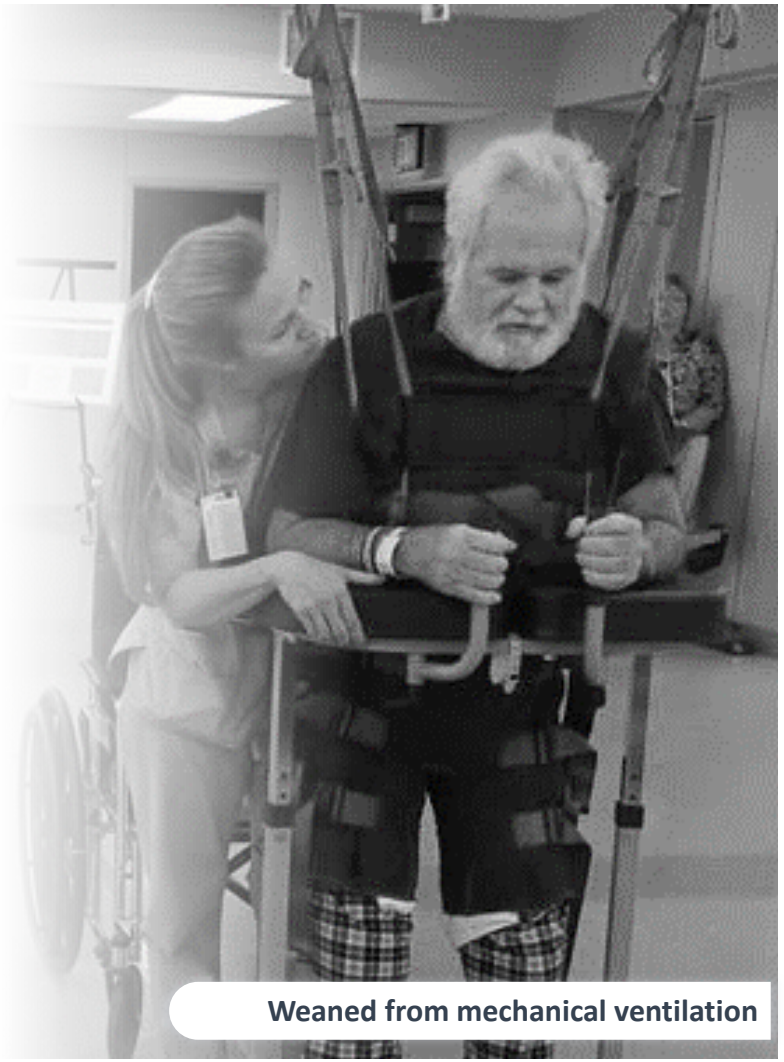
- Following infection, complement-activating autoantibodies attack nerves leading to nerve damage & acute paralysis
- Can happen to anyone, anytime, anywhere

**HIGH UNMET MEDICAL NEED**

- 22,000 patients hospitalized in US & Europe every year
- Global annual incidence ~150,000
- IVIg not FDA approved, unknown MOA, requires 5-day treatment

**SIGNIFICANT MORBIDITY**

- Notwithstanding IVIg treatment, GBS results in:
  - Severe weakness and paralysis
  - Mechanical ventilation in 25% of patients
  - Extensive nerve damage causing uncertain and incomplete recovery




MOA: mechanism of action

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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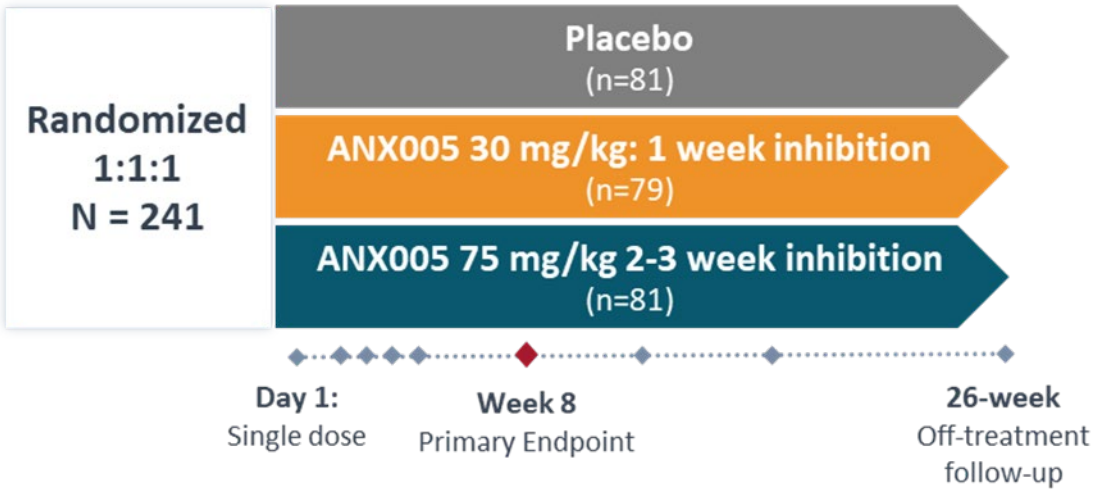
# Well Designed & Executed Pivotal Trial Showed Clear Results

## Randomized, Double-Blind, Placebo-Controlled Study

### 2 DOSES SELECTED TO DETERMINE MOST EFFECTIVE DURATION OF INHIBITION




*ANX005 for GBS Granted FDA **Fast Track and FDA / EMA Orphan Drug Designation***

### STUDY DESIGN

- Placebo-controlled (best standard of care, no IVIg or PE)
- Baseline GBS-DS score 3-5
- GBS diagnosed <10 days from onset of weakness
- Patients stratified for baseline prognostic factors: muscle strength and time from onset of weakness
- Conducted in Bangladesh and Philippines given high prevalence of GBS of all types, scientific leadership in GBS, and limited access to IVIg

### KEY ENDPOINTS

- **Primary Outcome Measure:** GBS-DS[1] at week 8: well-accepted regulatory endpoint assessing functional status
- **Secondary Endpoints:** Muscle strength (MRC sumscore), Motor Disability (ONLS), Duration of Ventilation, and others

[1]Analyzed using a proportional odds model, a common statistical analysis method (van Leeuwen, et al., 2019, doi.org/10.1371/journal.pone.0211404)



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# Baseline Characteristics Generally Well Balanced Across Treatment Groups

## Stratified by Key Prognostic Factors: MRC Sumscore and Time Since Onset of Weakness

| Baseline Characteristic | Placebo (N=81) | ANX005 30mg/kg (N=79) | ANX005 75mg/kg (N=81) |
|---|---|---|---|
| **Age at Screening (years); mean (SD)** | 34.2 (12.59) | 36.9 (14.88) | 37.9 (15.29) |
| **Sex, n (%) Male** | 57 (70.4) | 51 (64.6) | 51 (63.0) |
| **Baseline GBS-DS Score, n (%)** | | | |
| 3 Able to walk 10 meters across open space with help | 7 (8.6) | 12 (15.2) | 10 (12.3) |
| 4 Bedridden or chair bound | 64 (79.0) | 56 (70.9) | 60 (74.1) |
| 5 Requiring assisted ventilation for at least part of the day | 10 (12.3) | 11 (13.9) | 11 (13.6) |
| **Baseline MRC Sumscore (range 0-60), n (%)** | | | |
| 21-60 Mild/moderate loss of muscle strength | 42 (51.9) | 41 (51.9) | 44 (54.3) |
| 0 - 20 Severe loss of muscle strength | 38 (46.9) | 38 (48.1) | 37 (45.7) |
| **Time since of onset of weakness to randomization** Days, mean (SD) | 6.4 (1.7) | 6.3 (1.9) | 6.5 (2.0) |
| **Time since of onset of weakness to treatment** Days, mean (SD) | 6.5 (1.7) | 6.3 (1.9) | 6.6 (2.0) |
| **Electrophysiology by Hadden criteria, n (%)** | | | |
| Acute Inflammatory Demyelinating Polyneuropathy (AIDP) | 18 (22.2) | 16 (20.3) | 16 (19.8) |
| Acute Motor Axonal Neuropathy (AMAN) | 49 (60.5) | 50 (63.3) | 50 (61.7) |
| Other | 14 (17.3) | 13 (16.5) | 15 (18.5) |



Topline Results Subject to Change

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# Summary of Primary and Key Secondary Results

## Statistical testing hierarchy of clinically relevant endpoints

| Primary | Endpoint | Assesses | Timepoint | 30 mg/kg Efficacy | P-value | 75 mg/kg Efficacy | P-value |
|---|---|---|---|---|---|---|---|
| 1 | GBS-DS | GBS disability | Week 8 | OR[1] = 2.41 | 0.0058 | *OR[1] = 1.2* | *0.5548[3]* |

| Secondary Hierarchy | Endpoint | Assesses | Timepoint | 30 mg/kg Efficacy | P-value | 75 mg/kg Efficacy | P-value |
|---|---|---|---|---|---|---|---|
| 2 | Overall Neuropathy Limitations Scale (ONLS) | Functional disability | Week 8 | -0.8[2] | 0.0965[3] | *-0.3[2]* | *0.5033[3]* |
| 3 | MRC Sumscore | Muscle strength | Week 8 | 4.0[2] | 0.0351[3] Nominal | *2.0[2]* | *0.2952[3]* |
| 4 | | | Day 8 | 10.0[2] | <0.0001[3] Nominal | *8.3[2]* | *<0.0001[3]* |
| 5 | Ventilation | Duration of ventilation[3] | Week 26 | Median 28 fewer days | 0.0356[4] Nominal | *Median 34 fewer days* | *0.0011[3]* |

[1]Odds Ratio: Likelihood that a patient on ANX005 is in a better state of health relative to placebo

[2]LS mean point improvement relative to placebo

[3]P-values for nominal testing using 2-sided α=0.05

[4]For those requiring ventilation

# Early and Durable Treatment Effects of ANX005 30 mg/kg vs. Placebo

## Immediate impact to disease trajectory translated to improvements through week 26

| | | Early Impact on Disease Trajectory | | | | Durable Benefits | |
|---|---|---|---|---|---|---|---|
| **Pre-specified Analyses** | **Unit** | **At Week 1** | | **At Week 8** | | **Through Week 26** | |
| **GBS-DS** | Odds Ratio | OR[1]: 7.22 | p=<0.001[3] | OR[1]: 2.41 | p=0.0058 | OR[1]: 1.49 | p=0.0120[3] |
| **MRC** | Point Improvement | 10 points[2] | p=<0.0001[3] | 4 points[2] | p=0.0351[3] | 5.4[2] | p=0.0010[3] |
| **ONLS** | Point Improvement | -2.1 points[2] | p=<0.0001[3] | -0.8 points[2] | p=0.0965[3] | -1.1[2] | p=0.0063[3] |
| **Ventilation** | Median Days | N/A | | | | 28 days reduction[4] | p=0.0356[3] |
| **NfL** | % Reduction | **Week 2-4** 31.3% vs. 20.1% | p=0.03[3,5] | N/A | | | |

[1]Odds Ratio: Likelihood that a patient on ANX005 is in a better state of health relative to placebo
[2]LS mean difference relative to placebo
[3]P-values for nominal testing using 2-sided $\alpha$=0.05
[4]For those requiring ventilation
[5]LS Mean percent reduction

# Overview of Primary Endpoint: GBS-DS at Week 8

## FDA accepted endpoint with alignment on statistical methodology

### GBS-DS SCALE COLLAPSED INTO 3 CATEGORIES

**Enhances Clinical Interpretability**

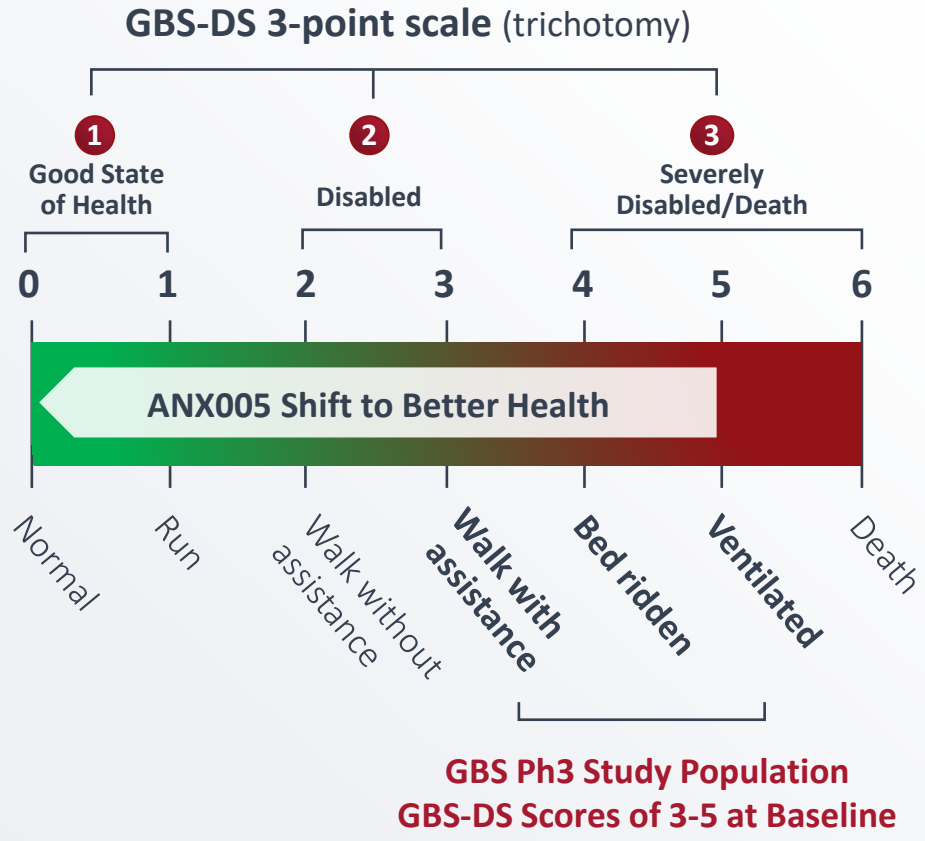
**Approach:** Collapse 7-grade scale to a 3-grade scale (trichotomy)

- **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
- ✓ Evaluates patients across all health states
- ✓ Most efficient statistical analysis approach

### GBS-DS SCALE FOR PIVOTAL PHASE 3



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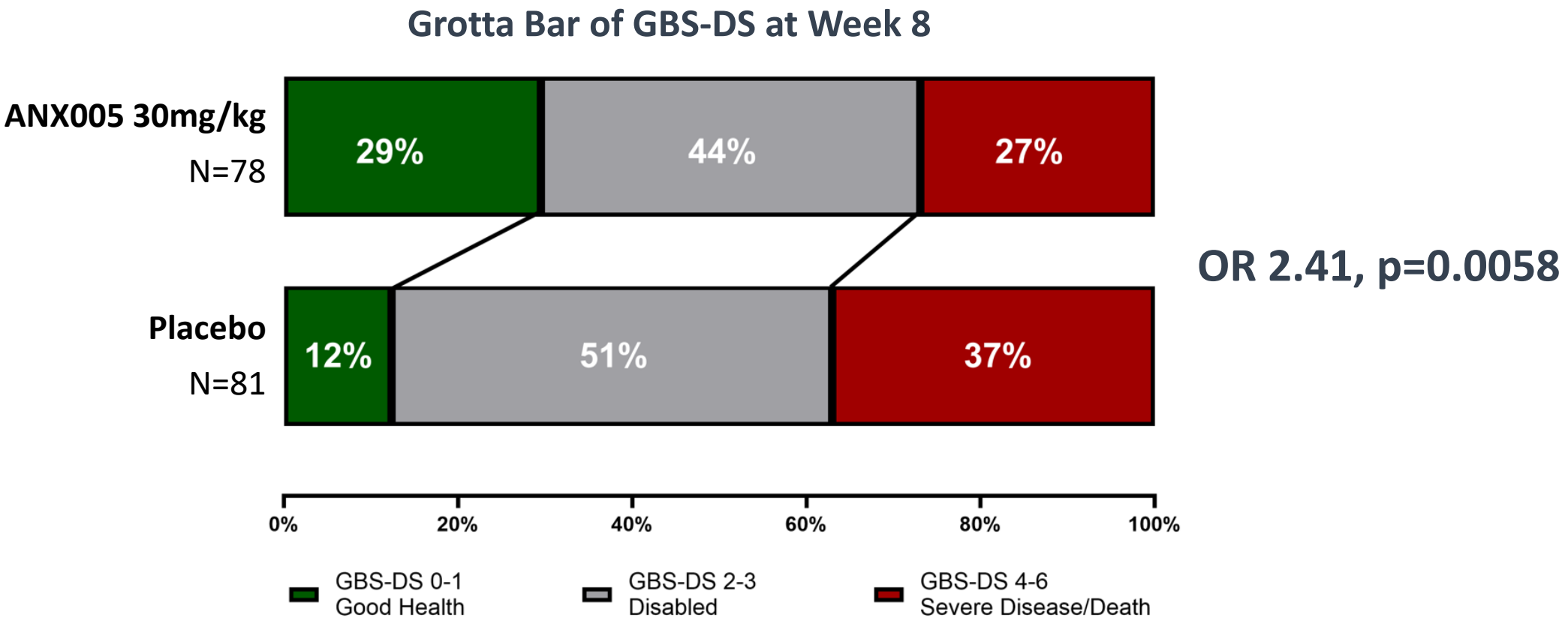
# ANX005 30 mg/kg Showed Highly Significant and Clinically Meaningful Treatment Effect on GBS-DS at Week 8 (Primary Endpoint)

## 2.41-fold higher likelihood of being in a better state of health relative to placebo




**OR 2.41, p=0.0058**



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# Multiple Sensitivity Analyses of the Primary Endpoint, GBS-DS, Show Consistent and Statistically Significant[1] Improvements with ANX005 30 mg/kg

| Pre-Specified Sensitivity Analyses | GBS-DS Results for ANX005 30 mg/kg arm | Interpretation & Key Takeaways |
|---|---|---|
| **Traditional Dichotomy** (0-1, 2-6) | OR: **3.34**, p=0.0065 | **3.34x more likely to be able to run** vs. pbo at week 8 |
| **Responder Analysis** ≥3-point at week 8 | **28.2%** vs. 13.6% on placebo p=0.0309 | **2x more patients improved** 3 points or more at week 8 vs. pbo |
| **Longitudinal Proportional Odds** | OR: **1.49x**, p=0.012 | **Durable effect: 1.5x more likely to be better** vs. pbo through the end of the full 26-week study |

[1]P-values for nominal testing using 2-sided $\alpha$=0.05



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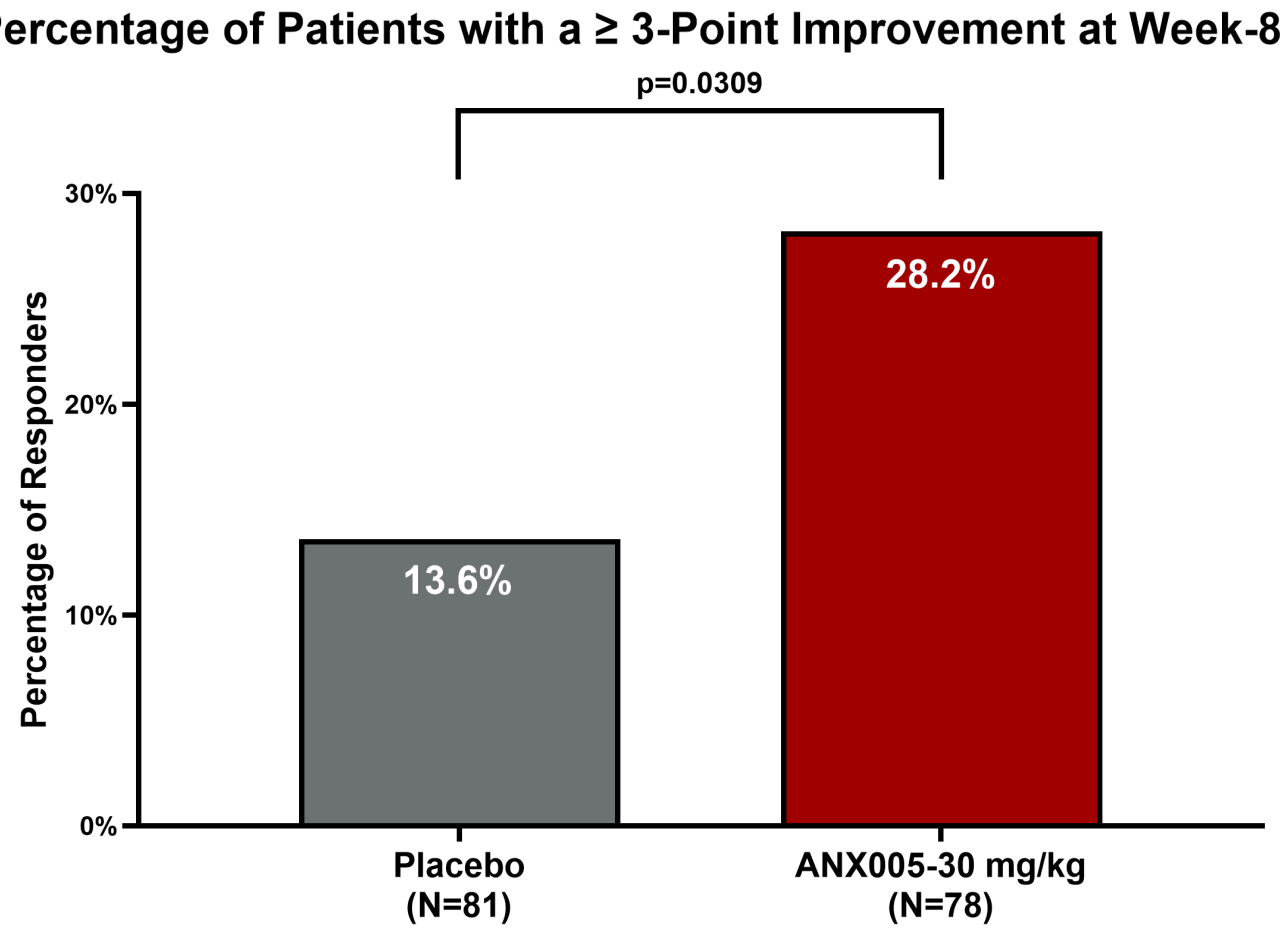
# Pre-Specified GBS-DS Responder Analysis at Week 8: ANX005 30 mg/kg Demonstrated a Significant ≥3-Point Improvement vs. Placebo

## Substantial treatment effect at week 8, further supporting primary analysis




Nominal p-values

Source: Table 14.2.5.1.1



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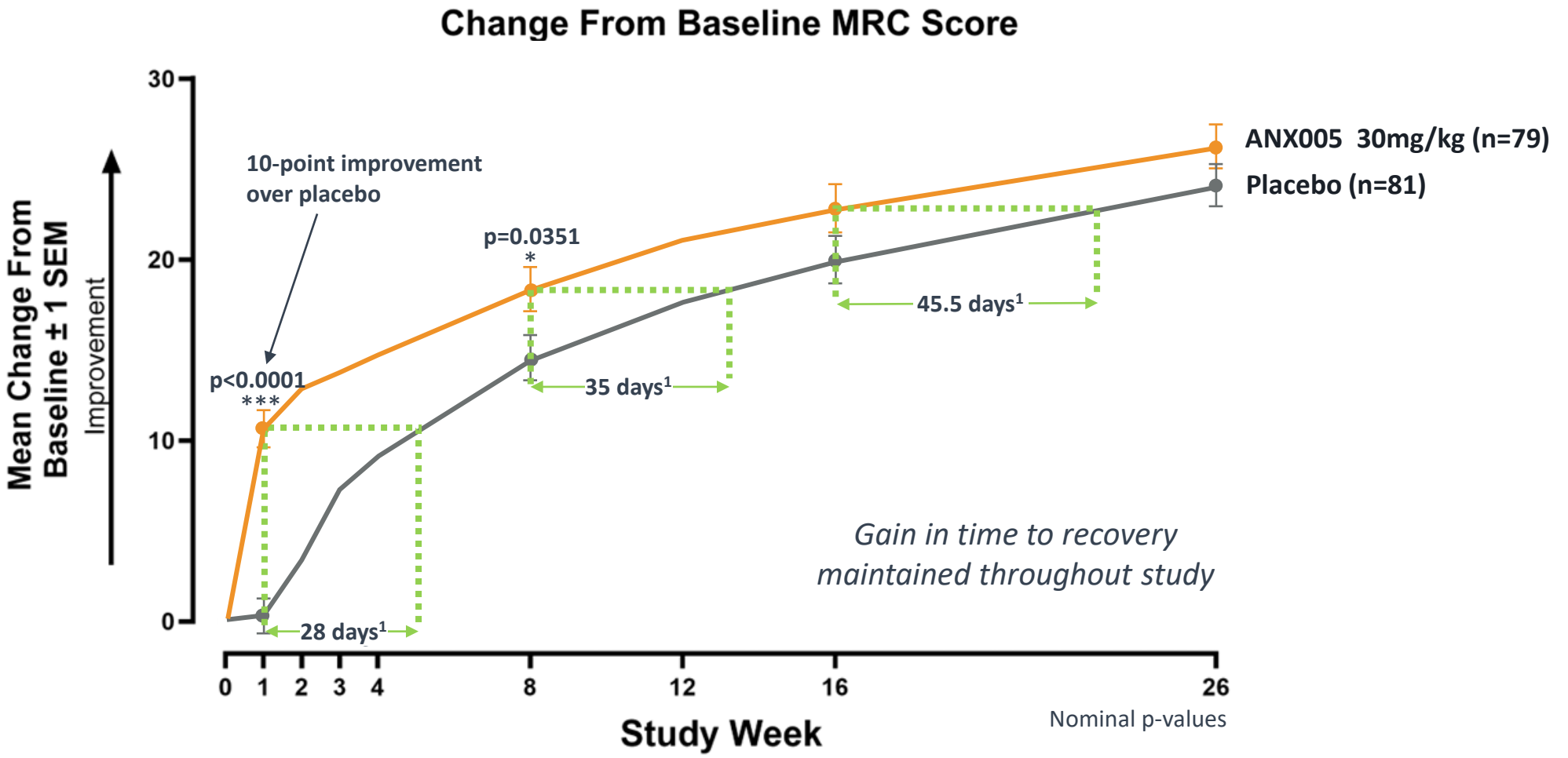
# Getting Better Sooner: ANX005 30 mg/kg Increased Muscle Strength Earlier Relative to Placebo, and the Advantage Grew Over Time

## Early muscle strength improvement maintained & increased through full 26-week study (p=0.001)




Modified Intent-to-Treat (N=241)

[1]Approximate Time difference





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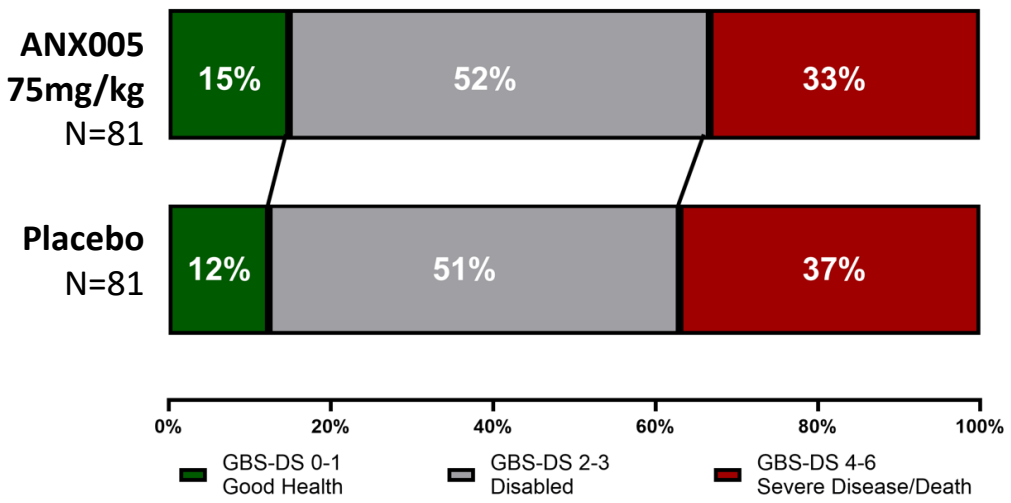
# ANX005 75 mg/kg Did Not Meet the Primary Endpoint with Inhibition Beyond Active Disease Process

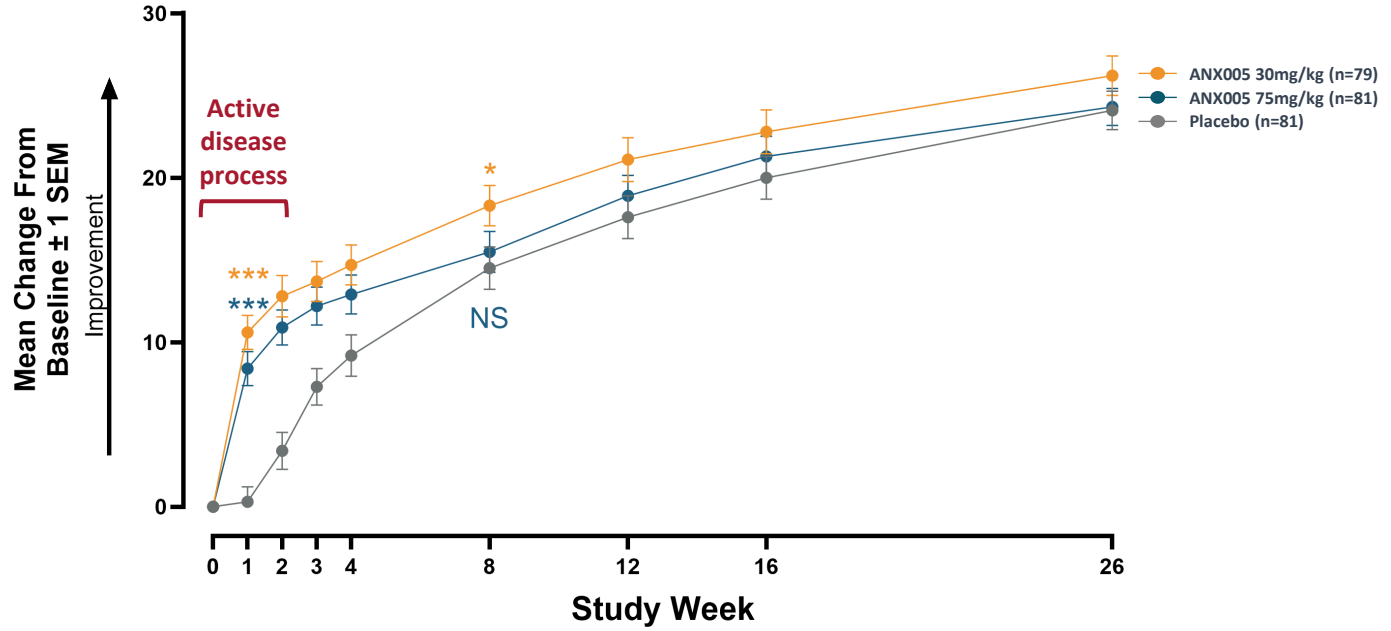
## 75 mg/kg improved muscle strength similar to 30 mg/kg during active disease process

### Grotta Bar of GBS-DS at Week 8




**OR 1.20, p=0.5548**

### Change from Baseline MRC Score




Modified Intent-to-Treat (N=241)  Nominal p-values



Topline Results Subject to Change

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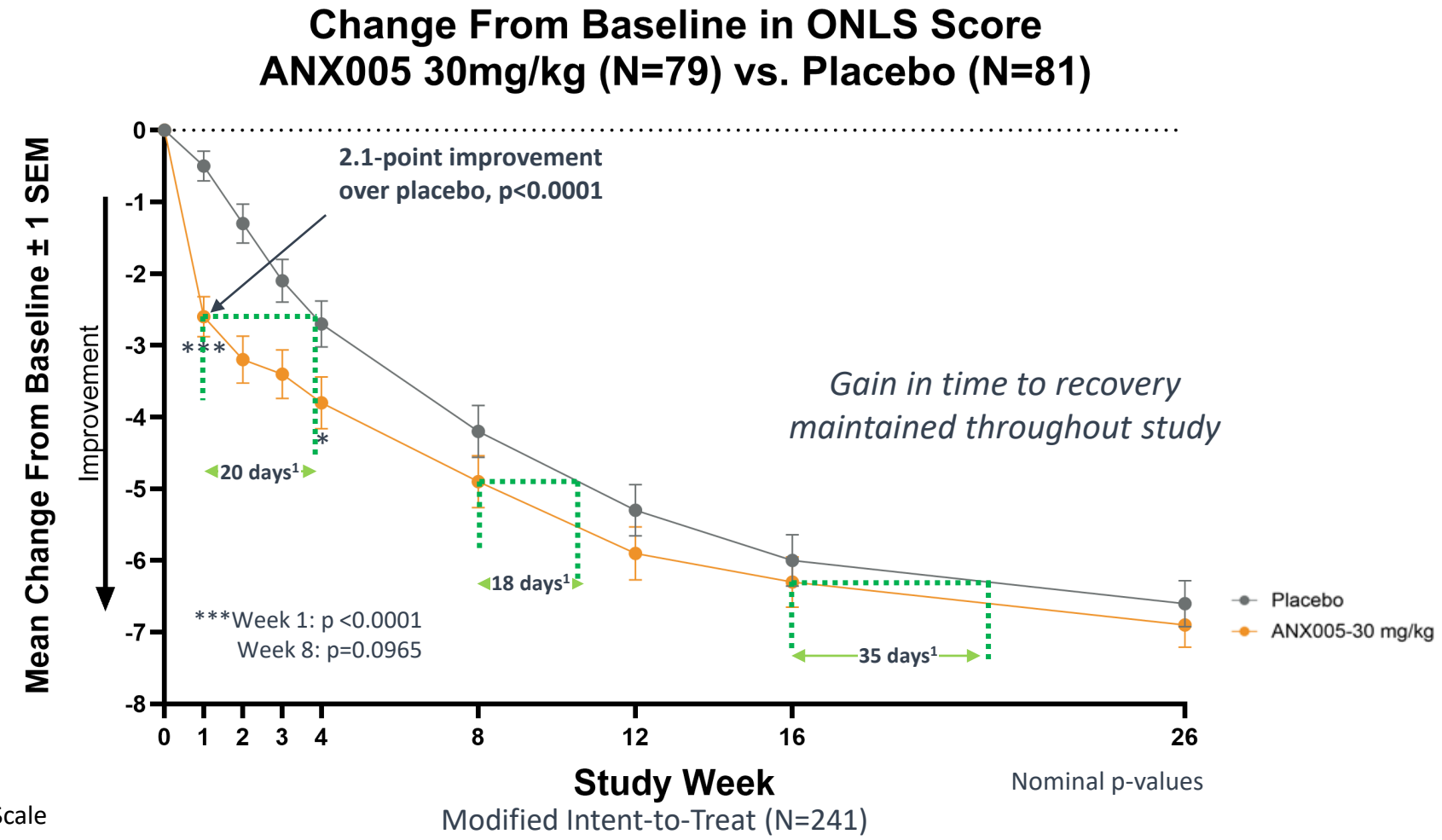
# Getting Better Sooner: ANX005 30 mg/kg Showed Significant Early Improvement in Motor Disability vs. Placebo on the ONLS* Scale

## Maintains ability to perform daily tasks through 26 weeks p=0.0063




Modified Intent-to-Treat (N=241)

*Overall Neuropathy Limitation Scale

[1]Approximate Time difference





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# Getting Better Sooner: ANX005 30 mg/kg Consistently Showed Faster Recovery Across Clinically Important Measures Relative to Placebo

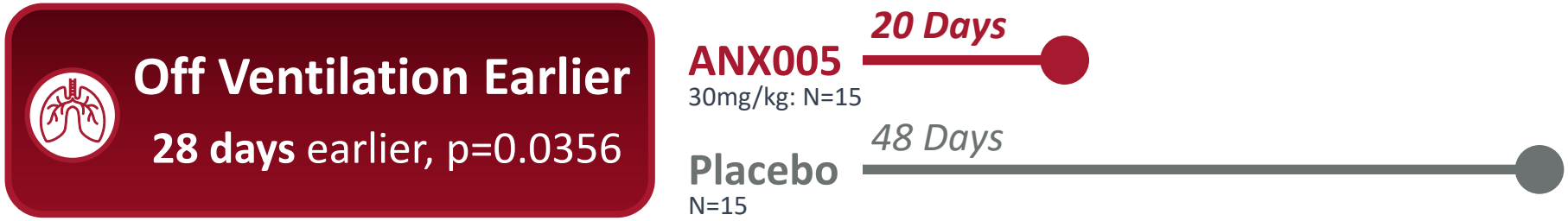
## Helping patients achieve their independence sooner

**Walking Earlier**

**31 days** earlier, p=0.0211


**Off Ventilation Earlier**

**28 days** earlier, p=0.0356




Nominal p-values

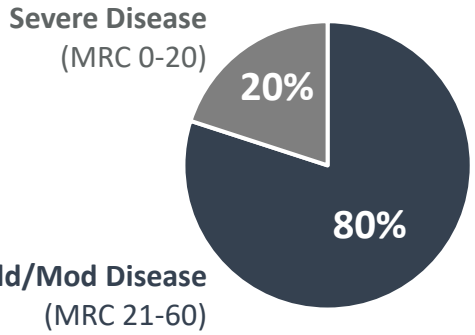
# GBS Phase 3 Results are Highly Relevant to Western Populations

## ANX005 30 mg/kg treatment effect more pronounced in Western World-type patients

### US and Europe tend to have less severe GBS

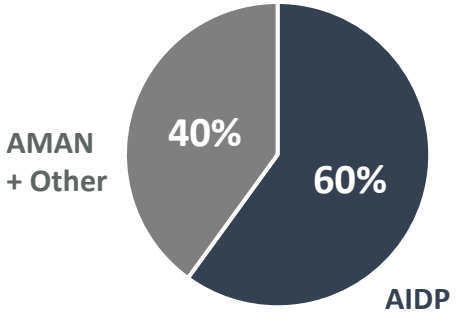
**Disease Severity**

US/Europe




**80% of US/European** patients have baseline **MRC of >20 points**

**Neurotype**




**60% of US/European patients have AIDP**

### ANX005 30 mg/kg impact on patients with less severe GBS

**47% with MRC 21-60** → **3.03x** more likely to be better state at Week 8 **p=0.0102**[1]

**21% with AIDP** → **5.31x** more likely to be better at Week 8 **p=0.0130**[1]

[1]Nominal

# Summary of Primary, Key Secondary Results & Pre-Specified Sensitivity

## Consistent & meaningful outcomes following 1 week of complement inhibition (30 mg/kg)

| | | | |
|---|---|---|---|
| **Primary Endpoint** | GBS-DS at Week 8 | **2.4x more** likely better state of health | p=0.0058 |
| **Secondary Endpoints** | ONLS at Week 8 | 0.8-point improvement in daily activities | p=0.0965 |
| | MRC Sumscore at Week 8 | **4-point improvement** in muscle strength | p=0.0351[1] |
| | MRC Sumscore at Day 8 | **10-point improvement** in muscle strength | p<0.0001[1] |
| | Duration of Ventilation | **28 fewer days** on ventilation | p=0.0356[1] |
| **Pre-specified Sensitivity Analyses** | GBS-DS Dichotomy at Week 8 | **3.3x more** likely to run | p=0.0065[1] |
| | GBS-DS Responder at Week 8 | **2x more** patients with ≥3-point improvement | p=0.0309[1] |
| | GBS-DS Through Week 26 | **1.49x more** likely better state of health | p=0.0120[1] |
| **Getting Better Sooner** | Muscle Strength | **1-month sooner** to 10-point improvement | |
| | Activities of Daily Living | **20 days sooner** to 2-point improvement | |
| | Time to Walk | **1-month sooner** to walking independently | p=0.0211[1] |
| | Off Ventilation | **1-month sooner** to come of ventilator | p=0.0356[1] |

[1]Nominal p-values

Topline Results Subject to Change

# ANX005 Generally Safe and Well-Tolerated

**Majority of AEs were mild (Grade 1) to moderate (Grade 2)**

- Most common related events were infusion related reactions
  - Majority were mild transient rashes
- No autoimmune related adverse events reported
- Infection rates were comparable across dose groups and consistent with typical hospital acquired infections
- 3 patients had treatment discontinuations
  - 1 in each dose group

**Deaths**

- No difference observed in incidence of all-cause mortality - 3 deaths in each dose group
- Mortality rate of 3.7% was consistent with rates seen in US and EU
- Deaths occurred in older and more severe subjects

| | Placebo N=81 | | ANX005 30mg/kg N=79 | | ANX005 75mg/kg N=81 | |
|---|---|---|---|---|---|---|
| | All Grades | Grade ≥ 3 | All Grades | Grade ≥ 3 | All Grades | Grade ≥ 3 |
| **Number of Subjects Reporting TEAEs, n (%)** | 79 (97.5) | 35 (43.2) | 79 (100.0) | 33 (41.8) | 80 (98.8) | 36 (44.4) |
| **Number of Subjects with Infusion Related Reaction** | 4 (4.9) | 1 (1.2) | 24 (30.4) | 4 (5.1) | 32 (39.5) | 7 (8.6) |
| Rash (most common with IRR) | 2 (2.5) | 0 | 20 (25.3) | 1 (1.3) | 25 (30.9) | 2 (2.5) |
| **Most Common TEAEs (non-IRR), n (%)** | | | | | | |
| Blood CPK Increased | 46 (56.8) | 16 (19.8) | 44 (55.7) | 14 (17.7) | 35 (43.2) | 12 (14.8) |
| Musculoskeletal Pain | 35 (43.2) | 0 | 36 (45.6) | 0 | 26 (32.1) | 1 (1.2) |
| ALT Increased | 23 (28.4) | 6 (7.4) | 21 (26.6) | 2 (2.5) | 23 (28.4) | 6 (7.4) |
| Urinary Tract Infection | 18 (22.2) | 6 (7.4) | 19 (24.1) | 5 (6.3) | 18 (22.2) | 1 (1.2) |
| Hypokalemia | 24 (29.6) | 8 (9.9) | 16 (20.3) | 4 (5.1) | 11 (13.6) | 3 (3.7) |
| Constipation | 10 (12.3) | 0 | 15 (19.0) | 0 | 17 (21.0) | 0 |
| AST Increased | 16 (19.8) | 3 (3.7) | 11(13.9) | 1 (1.3) | 17 (21.0) | 3 (3.7) |



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**2.4-fold higher likelihood of being in a better state of health on GBS-DS at Week 8**

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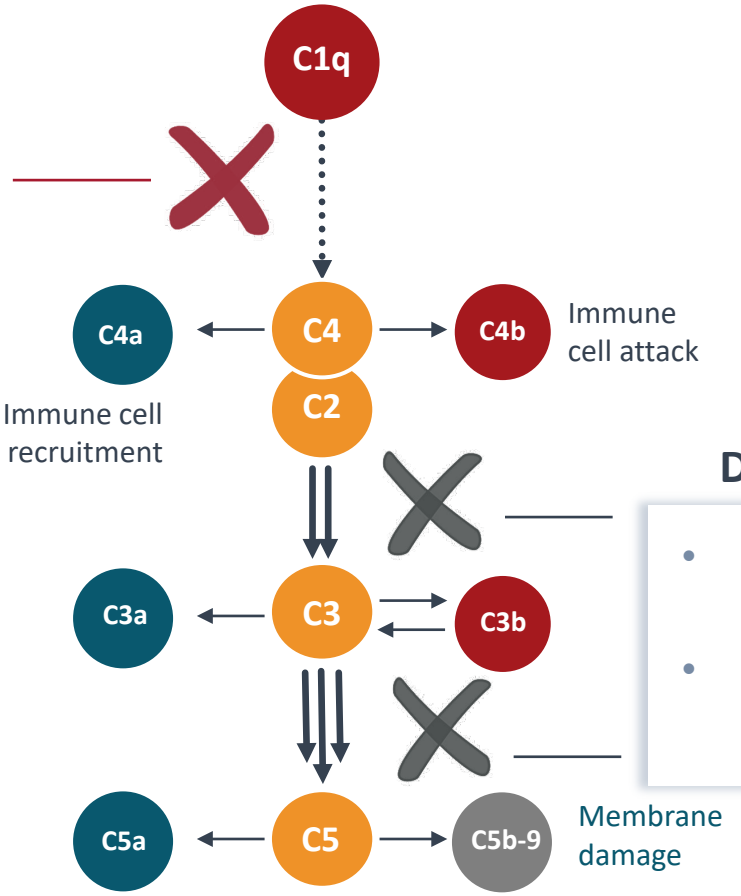
# Targeted MOA of ANX005, GBS Pathophysiology and ANX005 PK / PD

# ANX005 Rapidly Shuts Down Activation of the *ENTIRE* Classical Complement Cascade on the Nerve to Prevent Acute Injury

## Classical Complement Drives Harmful Inflammation and Tissue Destruction

### STOPPING AT THE START

- Blocks upstream and downstream inflammation & tissue damage
- Before downstream bypass mechanisms (breakthrough) and pathway amplification
- Differentiated functional outcomes shown in GBS, GA, HD and ALS




### DOWNSTREAM APPROACHES (C3/C5)

- Do not block ongoing inflammatory pressure of upstream classical pathway
- More susceptible to complement bypass mechanisms / inflammatory breakthrough



GBS: Guillain-Barré Syndrome; GA: geographic atrophy; HD: Huntington's Disease; ALS: amyotrophic lateral sclerosis

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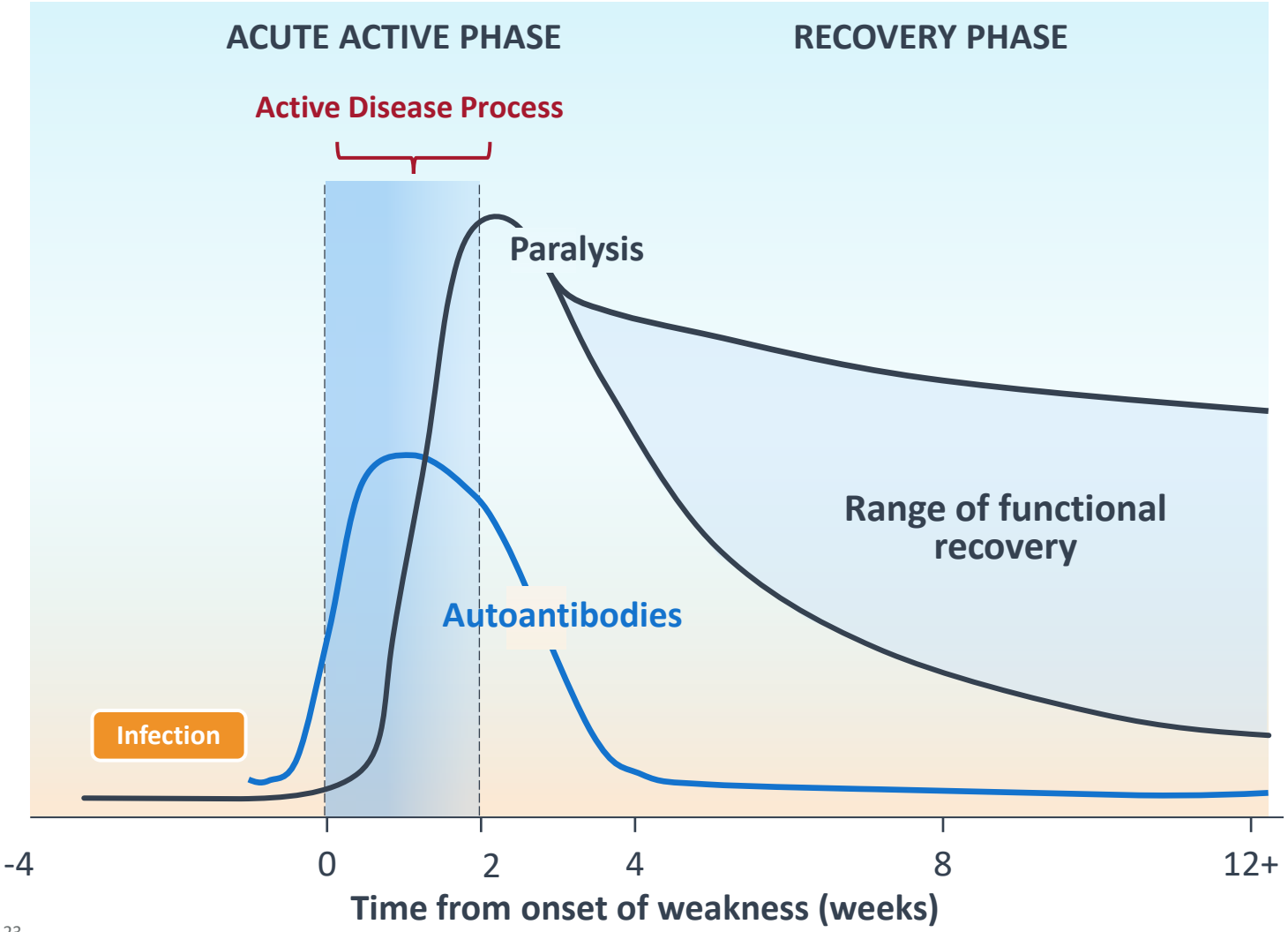
# GBS is a Neurological Emergency Requiring Urgent Intervention

## Limited time window to stop the active disease process and achieve a therapeutic effect




### ACUTE ACTIVE PHASE

- Rapidly progressive bilateral muscle weakness peaking by 1 – 2 weeks in most cases
- Paralysis in legs, arms and potentially breathing muscles
- Extended periods of ventilation in ICU, and intensive supportive care

### RECOVERY PHASE

- Gradual muscle strength and functional improvement over months to years as nerve regeneration takes place
- ~20% unable to walk or dead at 1 year and additional 20% continue to experience symptoms

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



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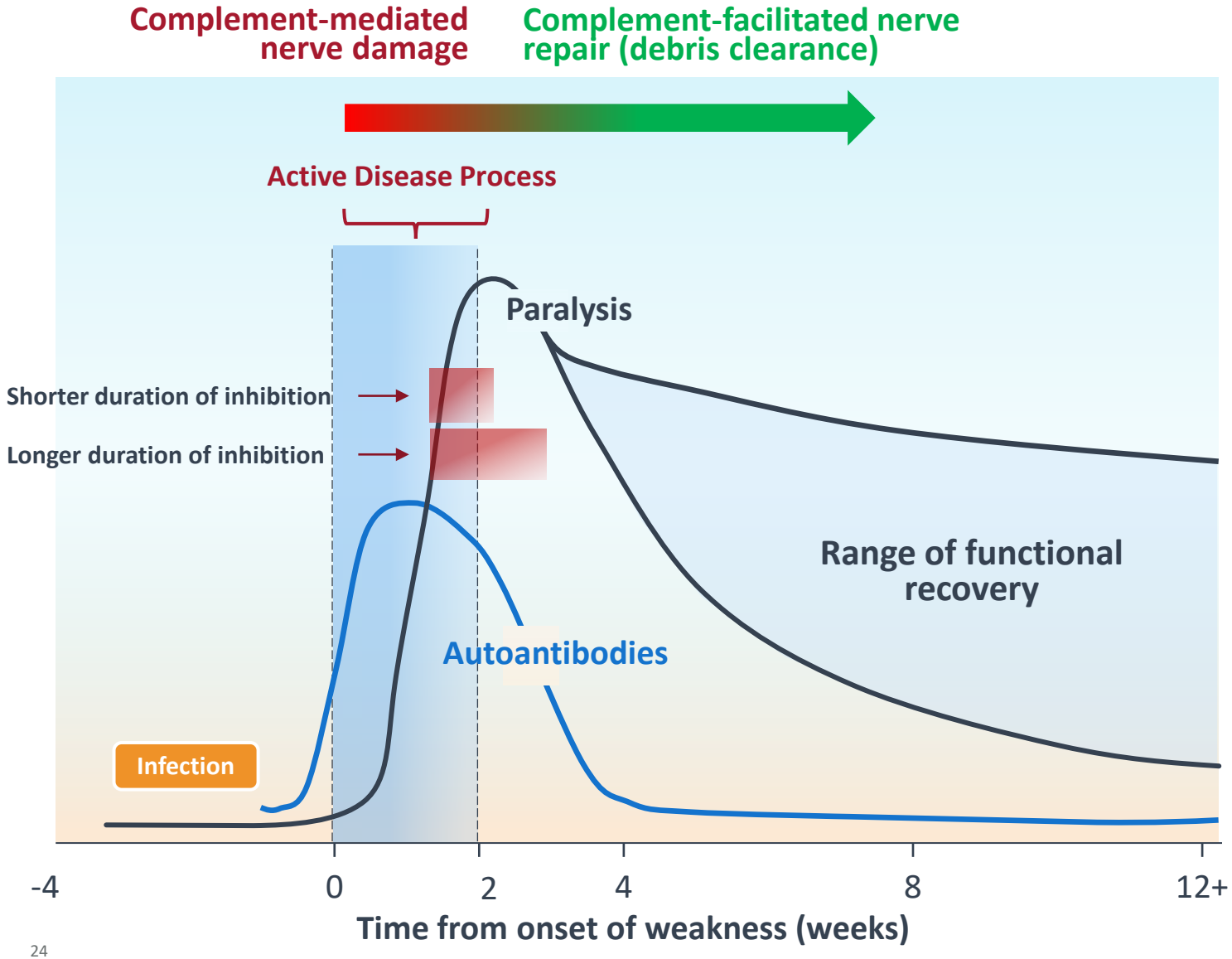
# GBS Time Course: Autoimmune Complement-Mediated Nerve Damage Followed by Normal Complement-Facilitated Repair




## IDENTIFY MOST EFFECTIVE TREATMENT WINDOW

**BLOCK AUTOIMMUNE COMPLEMENT-MEDIATED NERVE DAMAGE DURING ACTIVE DISEASE**

**ALLOW NORMAL COMPLEMENT FACILITATED NERVE REPAIR DURING RECOVERY PHASE**

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



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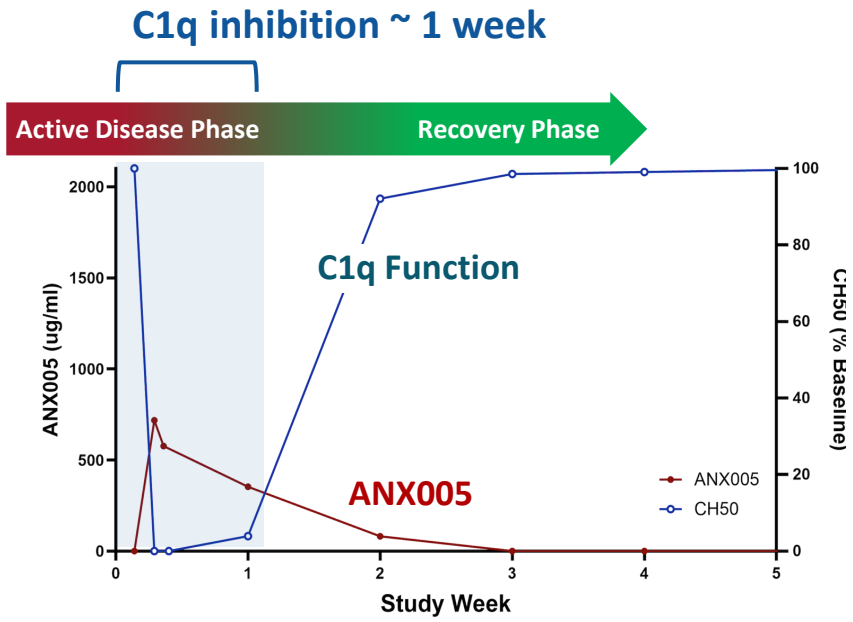
# ANX005: Expected Pharmacokinetic and Dynamic Response for Both Doses

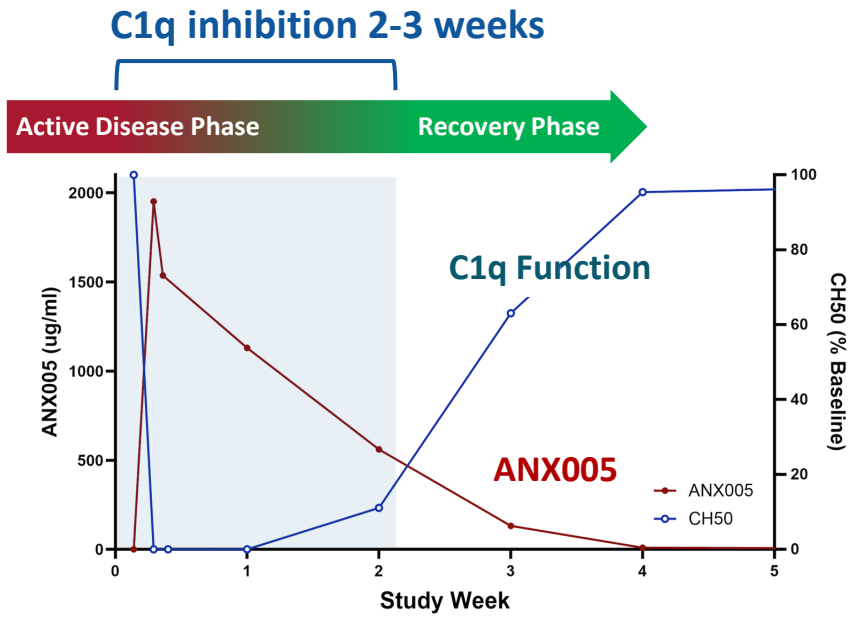
## Duration of complement inhibition defines active treatment window

- **Rapid C1q engagement and functional inhibition** (CH50 assay)
  - 30 mg/kg provided: ~1 week duration of inhibition
  - 75 mg/kg provided: 2-3 weeks duration of inhibition

### ANX005 30 mg/kg




### ANX005 75 mg/kg






Topline Results Subject to Change

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# ANX005 GBS Phase 3 Trial Summary and Path Forward


**Douglas Love, President & CEO**
Annexon Biosciences

# Real-World Evidence to Support Planned Regulatory Submission

## Interim RWE Data Support Comparability & Relevance of Phase 3 Findings to the West

- **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
- **Annexon has developed a real-world evidence (RWE) comparability protocol with IGOS (ANX005-GBS-04)**
- **IGOS data supports ongoing comparability study, including:**
  - >50% of all Western IGOS patients met the entry criteria for GBS Ph3
  - Robust ANX005 impact on 'Western World' type Phase 3 patients
  - Preparing matched cohort for comparison with IVIg

### Annexon + IGOS RWE Comparability Study

IGOS

**Global GBS Real-World Evidence Cohort**

↕

**Annexon Phase 3 Study**



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# GBS is an Untapped Commercial Opportunity and Annexon is Pursuing a Tailored Approach

## Significant commercial opportunity for ANX005 achieved through focused commercial footprint

**22,000** people in US & Europe **hospitalized** with GBS **every year**

**90%** of GBS patients **treated** with **off-label IVIg in US**

- **Daily infusions** over **5 days**
- **Non-specific mechanistic approach** to treating GBS

**>$2B annual cost burden** on patients, caregivers, hospitals, and payers[1]

Majority of patients treated in **major metro areas and large community hospitals**[2]

**ANX005**
***First-line, monotherapy treatment for GBS***

**ANX005** helped **GBS patients Get Better Sooner**

- ✓ **Single infusion, targeted mechanism**
- ✓ **Faster recovery / independence**
- ✓ **Potential for significant cost reductions for health care system**

**Robust HEOR plan** to demonstrate **reduced cost of care**

**Focused and targeted** commercial launch plan

**Commercial manufacturing** partnership with Lonza

**GBS a beachhead** for **mechanistically-related neuro and autoimmune** indications

[1]Frenzen, PD (2008) Neurology 71:21-27 7, [2]ClearView Health market research



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# ANX005 GBS Phase 3 Summary of Key Results

**A profound moment for the GBS community – first targeted therapy to demonstrate positive outcomes**

**1** **Phase 3 Met Primary Endpoint, confirming earlier study**

GBS-DS at Week 8: Patients treated with ANX005 were 2.4 times more likely to be in a better state of health compared to placebo, p=0.0058

**2** **ANX005 Helped Patients with GBS Get Better Sooner**

Early, robust, and clinically meaningful benefit on multiple outcome measures by week 8 including ability to walk earlier and less nerve damage vs. placebo

**3** **Durable Treatment Effects Across Full Course of 26-Week Study**

Maintained improvement over placebo at all timepoints across multiple measures including less time on ventilation and less overall disability

**4** **Generally Safe and Well Tolerated**

Safety profile similar to placebo – no increased rate of infections, convenient single dose

**5** **Clear Path to BLA Submission and Launch**

Preparing to engage FDA later this year to support BLA submission 1H25
On-track to complete RWE study by 1H25 to support BLA timelines
Preparing clear launch strategy with focused commercial team



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**To the patients, families, caregivers, physicians and medical teams who participated in our trial, we are eternally grateful for your support and contributions!**

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**To our employees, collaborators and advisors,**
**thank you for your WARRIOR SPIRIT AND ALL FOR ONE COMMITMENT!**

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# Thank You!
# Q&A

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


GBS|CIDP Foundation International

IGOS

icddr,b

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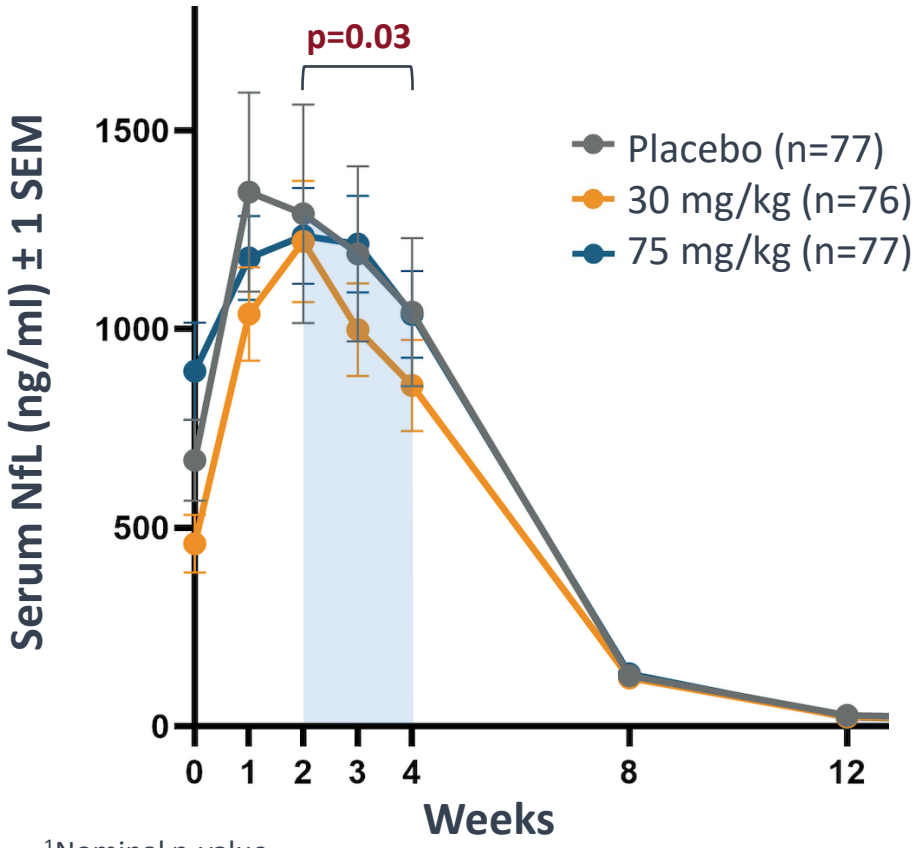
# Appendix

# ANX005 30 mg/kg Demonstrated Significant Early Reduction in Prespecified Analysis of Neurofilament Light Chain (NfL)

## Assessment of reduction of neuronal damage

### Change in Serum NfL Weeks 2 - 4




[1]Nominal p-value

### Key Takeaways

- Prespecified assessment of NfL reduction during weeks 2-4 consistent with Ph1b
- Captures transition from acute progressive to recovery phase of disease
- Both 30 and 75 mg/kg may have blunted peak NfL response compared to placebo
- **30 mg/kg ANX005 achieved significant early reduction (wks 2-4), as prespecified** based on Ph1b results (31.3% vs. 20.1%, p=0.03[1])

# Complement is Pivotal Force in Driving Nerve Damage in GBS

## ANX005 is a Targeted Immunotherapy which Rapidly Blocks Complement

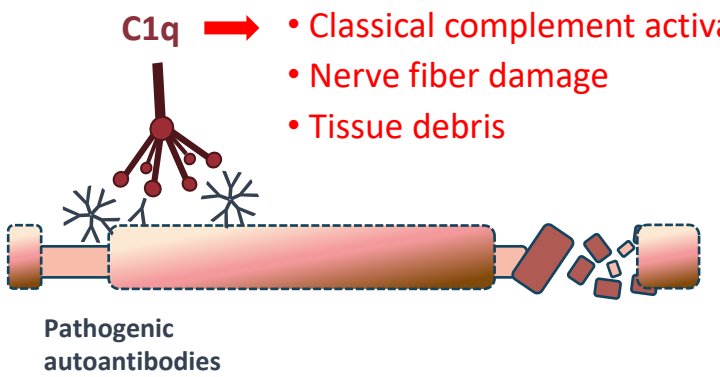
**GBS**

- C1q binds to autoantibodies on nerve surface
- Activates classical complement pathway
- Results in neuroinflammation, nerve damage, tissue debris and paralysis

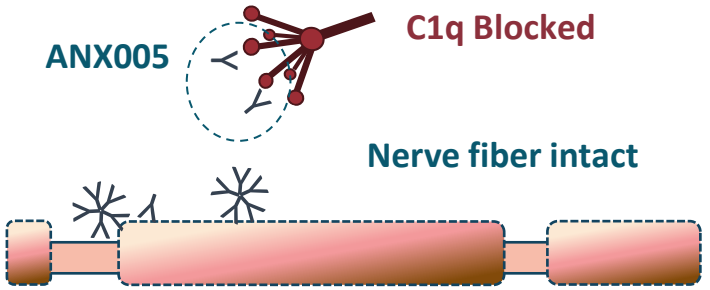
**ANX005**

- One dose of ANX005 rapidly blocks C1q
- Stops activation of entire classical pathway
- Blocks nerve fiber damage during the active disease phase

**Peripheral Nerve Fiber Under Attack in GBS**




**Peripheral Nerve Fiber in GBS with ANX005**






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

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# 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)

# 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

# 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<br>✓ 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<br>✓ 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<br>✓ 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<br>✓ Conducted at sites with internationally recognized GBS clinical experience |



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