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): June 4, 2024

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.

As reported under Item 8.01 of this Current Report on Form 8-K, on June 4, 2024, Annexon, Inc. ("Annexon" or the "Company") issued a press release (the "GBS Phase 3 Press Release") to report topline results from its randomized placebo-controlled pivotal Phase 3 trial in patients with Guillain-Barre syndrome ("GBS"). A copy of the GBS Phase 3 Press Release is furnished hereto as Exhibit 99.1 and is incorporated herein by reference.

A copy of the related presentation is posted on the Company's website and is furnished herewith as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated by reference herein.

This information in this Item 7.01 of this Current Report on Form 8-K shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that Section, or incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in any such filing.

Item 8.01. Other Events.

On June 4, 2024, Annexon announced positive topline results from a randomized placebo-controlled pivotal Phase 3 clinical trial in patients with GBS. The Phase 3 trial met its primary endpoint, with a single infusion of ANX005 30 mg/kg achieving a statistically significant 2.4-fold improvement on the GBS-disability scale ("GBS-DS") (proportional odds analysis, week 8, $p = 0.0058$). ANX005 30 mg/kg treatment also demonstrated improvements versus placebo on key secondary endpoints, including early gains in muscle strength (day 8, $p < 0.0001$* and week 8, $p = 0.0351$*) and a median of 28 fewer days on artificial ventilation (through week 26, $p = 0.0356$*). Additionally, ANX005 30 mg/kg demonstrated an early reduction in the prespecified analysis of serum levels of neurofilament light chain, a biomarker of nerve damage (11.2% reduction relative to placebo between weeks 2–4, $p = 0.03$*) and a 31-day reduction in the median time to walk independently (week 26, $p = 0.0211$*), each of which are important clinical care outcomes. (* nominal)

The randomized, placebo-controlled Phase 3 trial, which enrolled 241 subjects in Bangladesh and the Philippines, evaluated two doses of ANX005, 30 mg/kg and 75 mg/kg, which both delivered rapid and complete suppression of complement activity but differed in duration of C1q inhibition. The 30 mg/kg dose lasted one week and the 75 mg/kg dose lasted two to three weeks. ANX005 75 mg/kg outperformed placebo on multiple endpoints, however, it was not statistically significant on the primary endpoint of GBS-DS at week 8 ($p = 0.5548$). The two dose levels were evaluated based on findings in the earlier Phase 1b proof-of-concept study, which showed efficacy in pooled analysis of both shorter and longer duration of ANX005 C1q inhibition. Because classical complement drives tissue damage in the early phase of disease, while facilitating nerve repair after acute nerve injury, the strong positive Phase 3 results with the 30 mg/kg dose resulting in one week of C1q inhibition appeared to define the optimal treatment window.

The clinical safety and tolerability findings of ANX005 at both doses in the Phase 3 study support a generally well-tolerated profile with no new safety signals. The majority of adverse events were mild Grade 1 to moderate Grade 2 events. The most common treatment-related adverse events were infusion related reactions (30.4%) that were mostly mild transient rashes. There were no autoimmune related adverse events and no drug-related deaths or serious infections observed.

The GBS Phase 3 study was conducted in Bangladesh and Philippines due to the high prevalence of GBS and limited access to standard of care intravenous immunoglobulin. Based on feedback from the U.S. Food and Drug Administration ("FDA"), Annexon has initiated a real-world evidence ("RWE") protocol with International Guillain-Barré Syndrome Outcomes Study to establish comparability between Phase 3 participants and Western patients. RWE data and a potential biologics license application submission with the FDA are expected in the first half of 2025. Annexon plans to present the Phase 3 data at the 2024 Peripheral Nerve Society Annual Meeting on June 25, 2024.

GBS is a rapid and acute neurological disease with a narrow therapeutic window that results in the hospitalization of over 22,000 people annually in the U.S. and Europe. The significant and long-term disease burden associated with GBS on patients, caregivers, hospitals and payers has led to a multi-billion-dollar annual economic cost to the U.S. healthcare system. Currently, there are no approved treatments for GBS by the FDA.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release, dated June 4, 2024, titled "Annexon Announces Positive Topline Results from Pivotal Phase 3 Trial for First-in-Class C1q Blocking Antibody ANX005 in Guillain-Barré Syndrome."
99.2	Annexon, Inc. Presentation dated June 2024
104.1	Cover Page Interactive Data File, formatted in inline XBRL.

SIGNATURES

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

Dated: June 4, 2024

Annexon, Inc.

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

Exhibit 99.1

Annexon Announces Positive Topline Results from Pivotal Phase 3 Trial for First-in-Class C1q Blocking Antibody ANX005 in Guillain-Barré Syndrome

Single Infusion of ANX005 30 mg/kg Met Primary Endpoint, Delivering a Highly Statistically Significant and Clinically Meaningful 2.4-fold Improvement in GBS-DS vs. Placebo at Week 8, p=0.0058

ANX005 Demonstrated Early and Sustained Improvements in Key Secondary Endpoints Including Muscle Strength, Nerve Damage and Ventilation

ANX005 Displayed Rapid Target Engagement and was Generally Well-Tolerated Across Doses

Real-World Evidence (RWE) Comparability Data Expected in First Half 2025

Conference call and webcast today at 8:30 a.m. ET

BRISBANE, Calif., June 4, 2024 - Annexon, Inc. (Nasdaq: ANNX), a biopharmaceutical company advancing a late-stage platform of novel therapies for people living with devastating classical complement-mediated neuroinflammatory diseases of the body, brain, and eye, today announced positive topline results from its randomized placebo-controlled pivotal Phase 3 trial in patients with Guillain-Barré syndrome (GBS). The Phase 3 trial met its primary endpoint, with ANX005 30 mg/kg achieving a highly statistically significant 2.4-fold improvement on the GBS-disability scale (GBS-DS) at week 8 (proportional odds analysis, $p = 0.0058$).

ANX005 30 mg/kg treatment also demonstrated improvements versus placebo on key secondary endpoints, including early gains in muscle strength by Medical Research Council (MRC) sum score at day 8 ($p < 0.0001$*) and at week 8 ($p = 0.0351$*), and a median of 28 fewer days on artificial ventilation through week 26 ($p = 0.0356$*). Additionally, ANX005 30 mg/kg demonstrated a 31-day reduction in the median time to walk independently versus placebo ($p = 0.0211$*) in a prespecified analysis. ANX005 30 mg/kg treated patients got better sooner on each of these assessments, presenting important clinical care outcomes for patients and the healthcare community. ANX005 also provided an early reduction in the prespecified analysis of serum levels of neurofilament light chain (NfL), a biomarker of nerve damage (11.2% reduction relative to placebo between weeks 2–4, $p = 0.03$*). (* nominal)

GBS is a rapid and acute neurological disease with a narrow therapeutic window that results in the hospitalization of over 22,000 people annually in the U.S. and Europe. The significant and long-term disease burden associated with GBS on patients, caregivers, hospitals and payers has led to a multi-billion-dollar annual economic cost to the U.S. healthcare system. Currently, there are no approved treatments for GBS by the U.S. Food and Drug Administration (FDA).

“These data represent an important moment for the GBS community and Annexon,” said Douglas Love, president and chief executive officer of Annexon. “With the potential to be the first targeted treatment for GBS in the U.S., ANX005 demonstrated consistent improvement and functional benefits on key primary and secondary endpoints. Additionally, we observed in our Phase 3 trial that early treatment with ANX005 resulted in rapid neuroprotection that stopped the advancement of disease and helped GBS patients get better sooner. These results reinforce

Annexon's founding thesis that C1q inhibition is a powerful mechanism of action to stop the progression of neuroinflammation and underscore the potential of ANX005 and our classical complement platform to treat GBS and a host of other diseases of the body, brain and eye."

The randomized, placebo-controlled Phase 3 trial which enrolled 241 subjects in Bangladesh and the Philippines evaluated two doses of ANX005, 30 mg/kg and 75 mg/kg, which both delivered rapid and complete suppression of complement activity but differed in duration of C1q inhibition. The 30 mg/kg dose suppression lasted one week and the 75 mg/kg dose suppression lasted two to three weeks. ANX005 75 mg/kg outperformed placebo on multiple endpoints, however, it was not statistically significant on the primary endpoint of GBS-DS at week 8 ($p = 0.5548$). The two dose levels were evaluated based on findings in the earlier Phase 1b proof-of-concept study, which showed efficacy in pooled analysis of both shorter and longer duration of ANX005 C1q inhibition. Because classical complement drives tissue damage in the early phase of disease, while facilitating nerve repair after acute nerve injury, the strong positive Phase 3 results with the 30 mg/kg dose resulting in one week of C1q inhibition appeared to define the optimal treatment window.

Hugh Willison, MBBS, PhD, Professor Emeritus of Neurology, University of Glasgow said, "In the first placebo-controlled pivotal study in GBS in approximately 40 years, ANX005 demonstrated robust and immediate neuroprotection by inhibiting C1q and suppressing downstream complement components with a single dose during the critical progressive phase of the disease. By directly targeting complement-mediated inflammation, ANX005 has the potential to act early to prevent nerve damage in this acute neurological emergency. The outcomes of this study represent an important breakthrough in effectively tackling GBS and support the potential of ANX005 to address the significant unmet need in this vulnerable patient population."

David Cornblath, MD, Professor Emeritus of Neurology, Johns Hopkins University School of Medicine said, "This well designed, rigorous Phase 3 study demonstrated that acute and early intervention with ANX005 can deliver clinical benefits across the entire GBS disease spectrum. These data are consistent with the earlier Phase 1b findings, which showed improvements across multiple supportive functional and prognostic measures important to aid patient recovery. Among other outcomes in the Phase 3 trial, patients dosed with 30 mg/kg were able to walk independently one month earlier and removed off a ventilator one month sooner, which are paramount to getting patients back to normal activities of daily living and represent a potentially transformative advancement for the treatment landscape. I am excited by the potential of ANX005 to be the first FDA approved therapy to treat GBS."

The clinical safety and tolerability findings of ANX005 at both doses in the Phase 3 study support a generally well-tolerated profile with no new safety signals. The majority of adverse events were mild Grade 1 to moderate Grade 2 events. The most common treatment-related adverse events were infusion related reactions (30.4%) that were mostly mild transient rashes. There were no autoimmune related adverse events, and no drug-related deaths or serious infections were observed.

The GBS Phase 3 study was conducted in Bangladesh and Philippines due to the high prevalence of GBS and limited access to standard of care intravenous immunoglobulin (IVIg). Based on feedback from the FDA, Annexon has initiated a real-world evidence (RWE) protocol with

International Guillain-Barré Syndrome Outcomes Study (IGOS) to establish comparability between Phase 3 participants and Western patients. IGOS is a global, prospective, observational, multicenter cohort study that has enrolled 2,000 patients who were followed for one to three years. Approximately 50% of all Western IGOS patients met the entry criteria for the Annexon GBS Phase 3 trial and, importantly, ANX005 30 mg/kg achieved a robust treatment effect on GBS-DS at week 8 in patients with Western characteristics and milder GBS. In a prespecified subgroup analysis of patients with baseline MRC sum score ≥20, ANX005 30 mg/kg treated patients were three times more likely to be in a better state of health compared to placebo on GBS-DS at week 8 ($p = 0.0102$*). (* nominal)

RWE data and BLA submission are expected in the first half of 2025. Annexon plans to present Phase 3 data at the 2024 Peripheral Nerve Society Annual Meeting on June 25, 2024.

ANX005 has been granted Fast Track and Orphan Drug Designations from the FDA. ANX005 has also been granted Orphan Drug Designation by the European Medicines Agency (EMA) based on a meta-analysis of past studies with ANX005 and IVIg demonstrating notable, early improvement in muscle strength with ANX005 that translated into observable gains in health status, including a reduction in the need of mechanical ventilation.

Conference Call and Webcast Information

Annexon management will hold a conference call and webcast today at 8:30 a.m. ET to discuss topline results from its Phase 3 trial evaluating ANX005 for patients with GBS. The dial-in number for the conference call is 1-877-407-0784 (U.S./Canada) or 1-201-689-8560 (international). The conference ID for all callers is 13747058. The live webcast and replay may be accessed by visiting Annexon's website at https://ir.annexonbio.com/events-and-presentations/events.

Call me™: Click here. Participants can use guest dial-in numbers above and be answered by an operator or they can click the Call me™ link for instant telephone access to the event (dial-out). The Call me™ link will be made active 15 minutes prior to scheduled start time.

About Guillain-Barré Syndrome (GBS)

GBS is a severe disease resulting from an acute autoantibody attack on peripheral nerves that generally occurs post-infection in otherwise healthy persons following activation of C1q and the classical complement cascade. It is a rapid and acute neurological disease with a narrow therapeutic window that results in hospitalization of over 22,000 people annually in the U.S. and Europe. The peripheral nerve damage progresses rapidly, causing acute neuromuscular paralysis, and may lead to significant morbidity, disability and mortality. Currently, there are no approved treatments for GBS in the U.S. The long-term disease burden associated with GBS has led to a multi-billion-dollar annual economic cost to the U.S. healthcare system alone.

About Annexon

Annexon Biosciences (Nasdaq: ANNX) is a biopharmaceutical company advancing a late-stage clinical platform of novel therapies for people living with devastating classical complement-mediated neuroinflammatory diseases of the body, brain, and eye. Annexon's novel scientific approach targets upstream C1q to block the classical complement inflammatory cascade before it starts, and its therapeutic candidates are designed to provide meaningful benefits across multiple

autoimmune, neurodegenerative and ophthalmic diseases. With proof-of concept data in Guillain-Barré syndrome, Huntington's disease and geographic atrophy, Annexon is rigorously advancing its mid-to late-stage clinical trials to bring their potential treatments to patients as quickly as possible. To learn more visit annexonbio.com.

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: ability of ANX005 to stop C1q activity; the clinical and regulatory status of ANX005; the potential of ANX005 to be the first approved treatment for GBS; the potential of the 75mg dose of ANX005 to be used in patients with severe disease; the timing of completion of RWE study and potential submission of a BLA with the FDA; the potential therapeutic benefit of ANX005 or any other product candidates on GBS, Huntington's disease or geographic atrophy; potential benefit of ANX005, if approved, compared to existing therapies; market size; the potential benefits from treatment with anti-C1q therapy; and Annexon's ability to rigorously advance mid-to late-stage clinical trials and continue development of the company's 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 potential for any final clinical trial results to differ from preliminary or topline results; 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 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.

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Exhibit 99.2

ANNEXON biosciences

STOP THE START

of classical complement-driven diseases

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

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, 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.

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 May 13, 2024 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.

Pursuing an Intentional and Rigorous Approach to Tackling an Array of Classical Complement-Mediated Diseases

Poised for a transformational 2024 and beyond

Stopping the Start of Classical Pathway Neuroinflammation

Broad Therapeutic Potential of Late-Stage Clinical Platform

Significant Near Term Value Creating Catalysts

ON A PATH TO HELPING PATIENTS GET THEIR LIVES BACK

Well-supported MOA demonstrated differentiated functional outcomes across GBS, GA, HD and ALS

Suite of fit-for-purpose drug candidates for diseases of the body, brain and eye

✓ ***GBS pivotal Ph3 data readout (Q2)***
GA pivotal Ph3 initiation (mid-yr)
Oral program POC data readout (2H)

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

ANNEXON biosciences

ANX005 Achieved a Breakthrough Phase 3 Win for GBS Patients Worldwide

A single infusion demonstrated consistent benefit across multiple endpoints meaningful to patients

Met Primary Endpoint P=0.0058	Expedited Recovery Patients Got Better Sooner	Durable Treatment Effect	Generally Well Tolerated
2.4-fold higher likelihood of being in a better state of health on GBS-DS at Week 8	**Early, robust & clinically meaningful benefit on multiple outcome measures @ Week 8**	**Maintained improvement over placebo at all timepoints across multiple measures**	**Safety data was similar to placebo**
✓ FDA-agreed primary endpoint ✓ Consistent, significant results from multiple pre-specified analyses ✓ Larger effect in sub-group with western baseline characteristics	✓ Able to walk earlier vs placebo ✓ Able to run earlier vs placebo ✓ Less nerve damage vs placebo	✓ Less time on ventilation ✓ Less overall disability	✓ 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

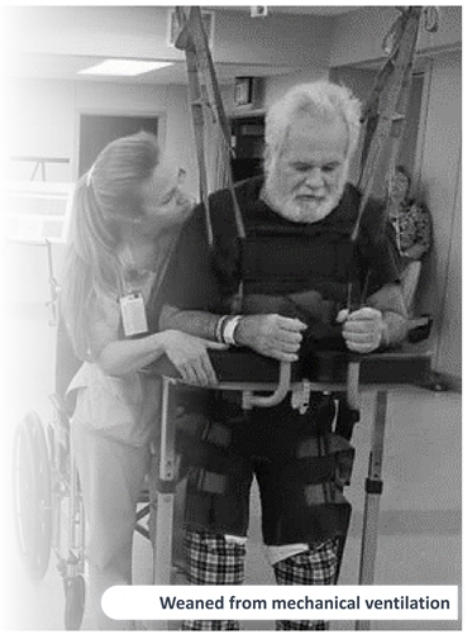
- Following infection, complement-activating autoantibodies attack nerves leading to nerve damage & acute paralysis
- Can happen to anyone, anytime, anywhere

HIGH UNMET MEDICAL NEED

- 22,000 patients hospitalized in US & Europe every year
- 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



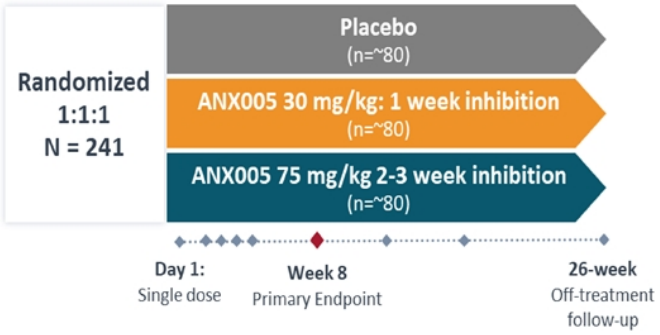
MOA: mechanism of action

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

ANNEXON biosciences

Well Designed & Executed Pivotal Trial Showed Clear Results

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



TWO DOSES SELECTED TO DETERMINE MOST EFFECTIVE DURATION OF INHIBITION

STUDY DESIGN

- 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)

Topline Results Subject to Change

ANNEXON biosciences

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)

ANX005 30 mg/kg Treated Patients Had Significant, Rapid and Sustained Improvement Across Multiple GBS Measures

Achieved Goal of Helping Patients GET BETTER SOONER

✓ Rapid & Complete Inhibition of classical complement cascade	✓ Statistically Significant[1] Early Reduction in NfL	✓ Statistically Significant Higher Odds of Being Better at Week 8 (Primary Endpoint)	✓ Statistically Significant[1] Early & Sustained Improvement in Muscle Strength	✓ Statistically Significant[1] Less Time on Ventilator over entire study period
				
C1q	NfL	GBS-DS	MRC Sumscore	Ventilation

[1]nominal p-value

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

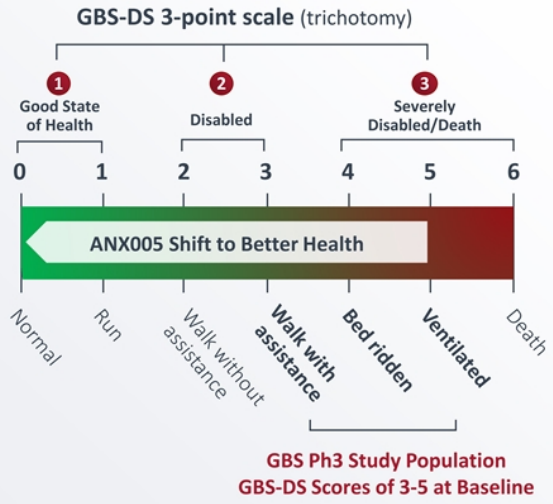
Approach: Collapse 7-grade scale to a 3-grade scale (trichotomy)

- **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

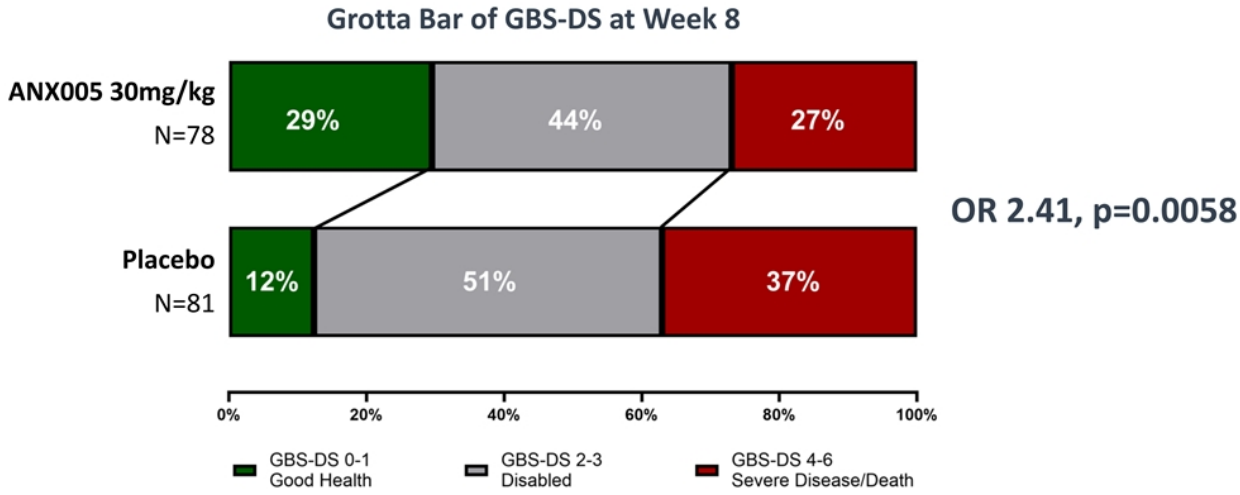


Topline Results Subject to Change

ANNEXON biosciences

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

Topline Results Subject to Change

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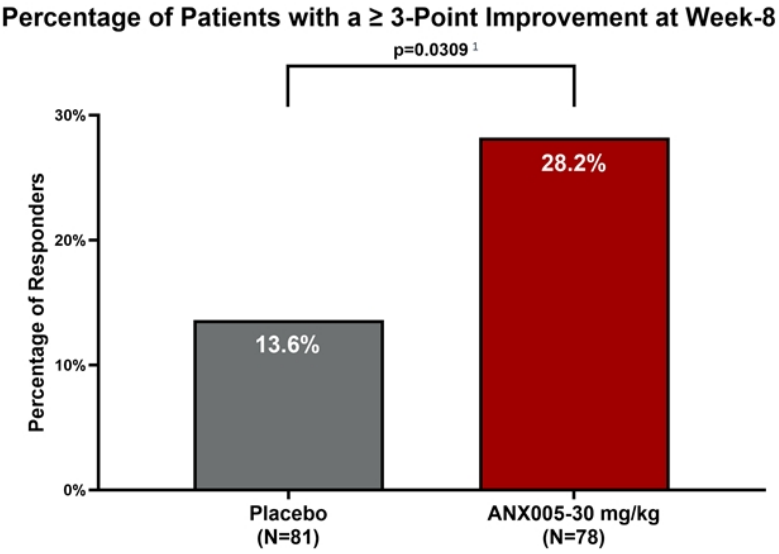
Pre-Specified GBS-DS Responder Analysis at Week 8: ANX005 30 mg/kg Demonstrated a Significant ≥3-Point Improvement vs. Placebo

Substantial treatment effect at week 8, further supporting primary analysis



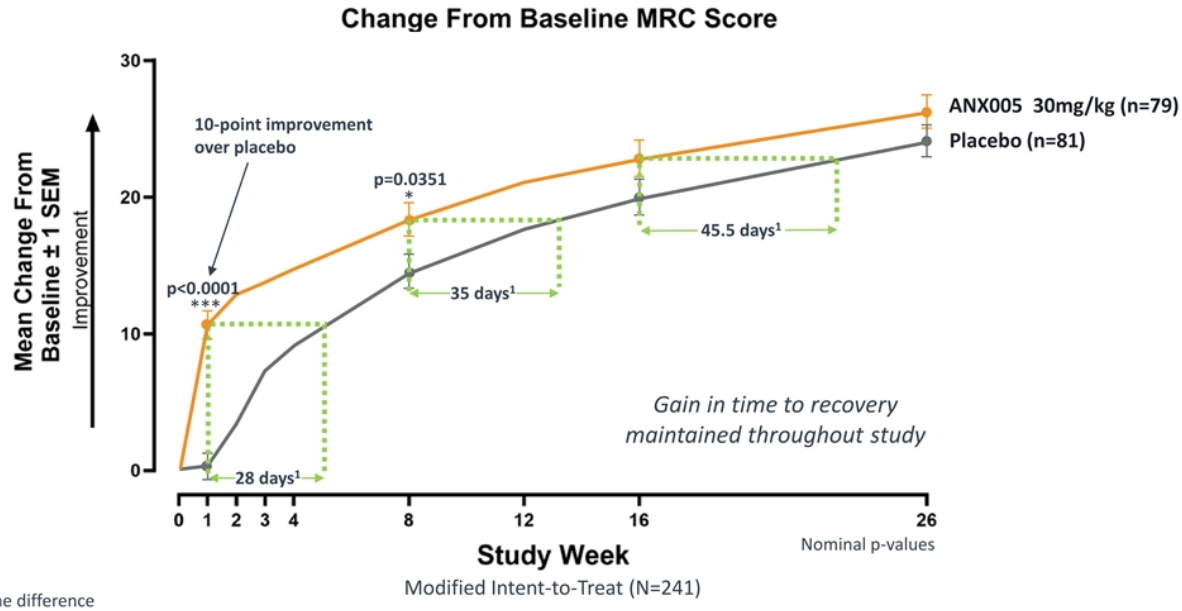
[1]nominal p-value

Topline Results Subject to Change

ANNEXON biosciences

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)

¹Approximate Time difference

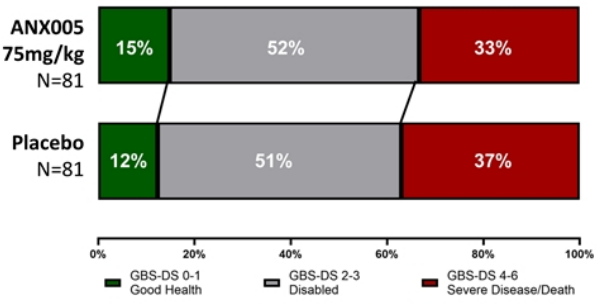
Topline Results Subject to Change

ANNEXON biosciences

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

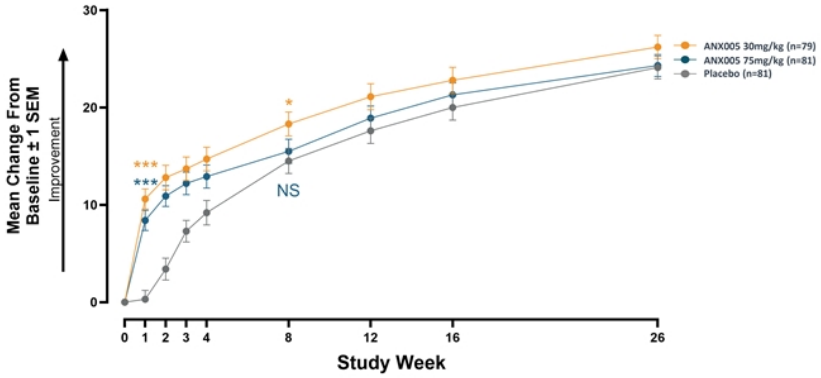
75mg/kg did improve muscle strength similar to 30 mg/kg at early timepoints to week 4

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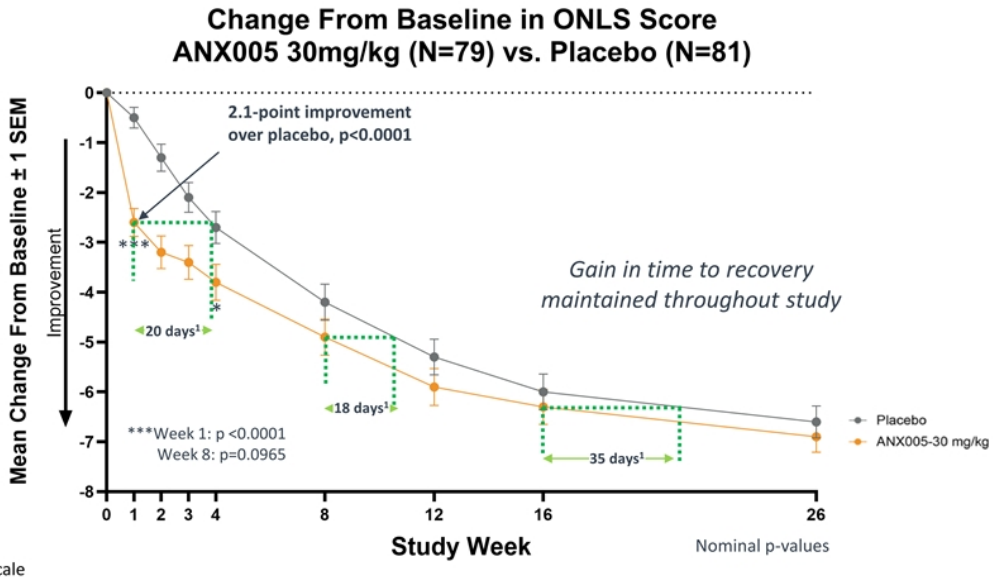
Getting Better Sooner: ANX005 30 mg/kg Showed Significant Early Improvement in Motor Disability vs. Placebo on the ONLS* Scale

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



*Overall Neuropathy Limitation Scale
[1]Approximate Time difference

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

Topline Results Subject to Change

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Through Week 26, ANX005 30mg/kg-Treated Patients had Better Outcomes Relative to Placebo

ANX005 treatment demonstrated better outcomes than placebo at all time points in the study

Through Week 26, Patients Treated with ANX005 30mg/kg Were More Likely to:

Be in a better state of health	**GBS-DS: 1.49x** more likely of being better p=0.012
Have more muscle strength	**MRC: 5.4** mean point improvement p=0.0010
Perform daily tasks better	**ONLS: 1.1** mean point improvement p=0.0063

Nominal p-values

GBS Phase 3 Results are Highly Relevant to Western Populations

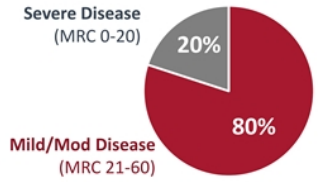
ANX005 30 mg/kg treatment effect more pronounced in Western World-type patients

Western patients tend to have less severe disease and an AIDP neurotype

ANX005 30 mg/kg impact on patients with these characteristics

Disease Severity

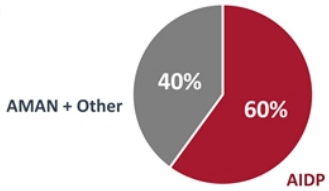
US/Europe



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

3.03x more likely to be in a better state of health at **Week 8**
p=0.0102
(47% of patients had milder disease)

Neurotype



60% of US/European patients have AIDP

5.31x more likely to be in a better state of health at **Week 8**
p=0.0130
(21% of patients had AIDP)

Nominal p-values

Topline Results Subject to Change

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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)

Topline Results Subject to Change

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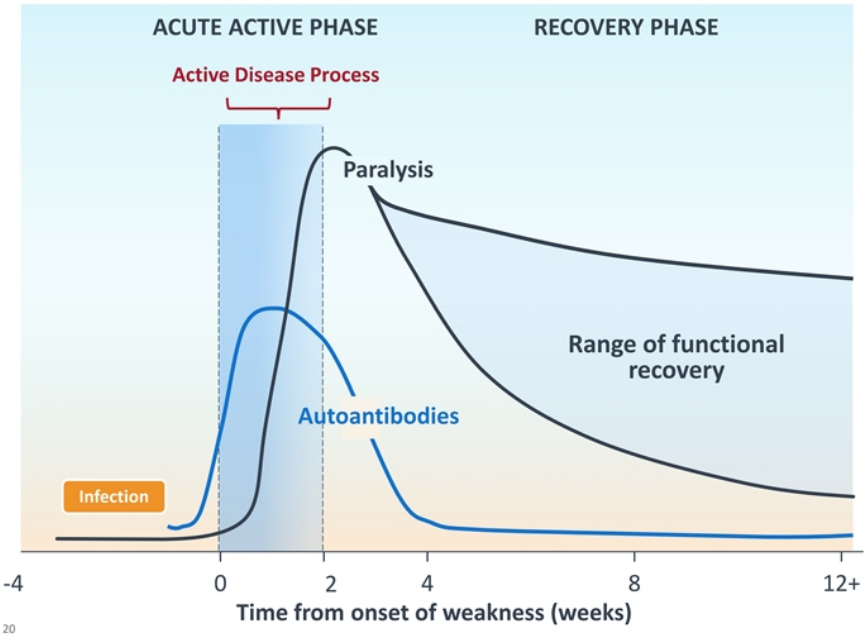
GBS Pathophysiology and the Targeted MOA of ANX005

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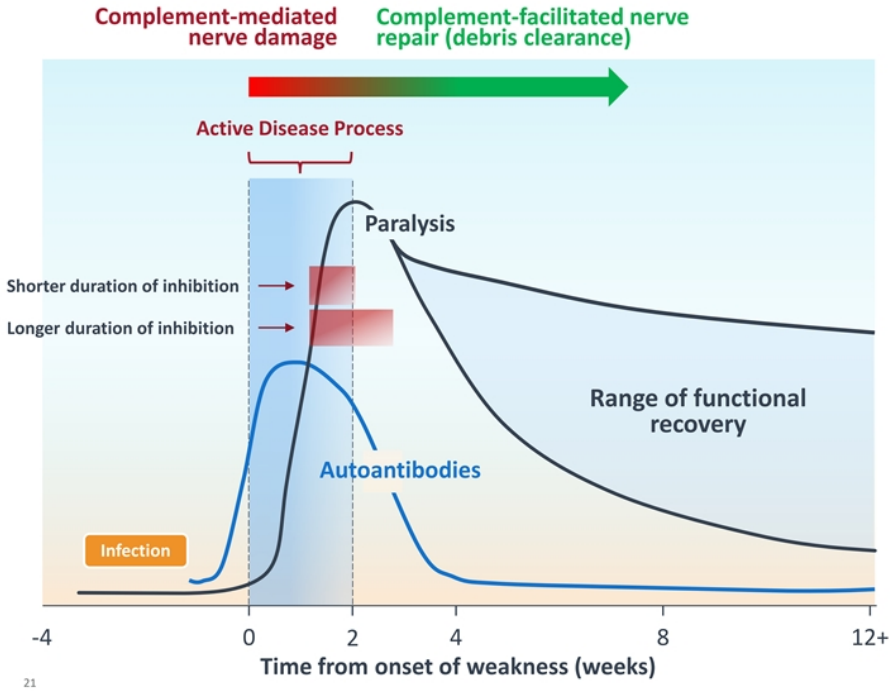
GBS Time Course: Autoimmune Complement-Mediated Nerve Damage Followed by Normal Complement-Facilitated Repair



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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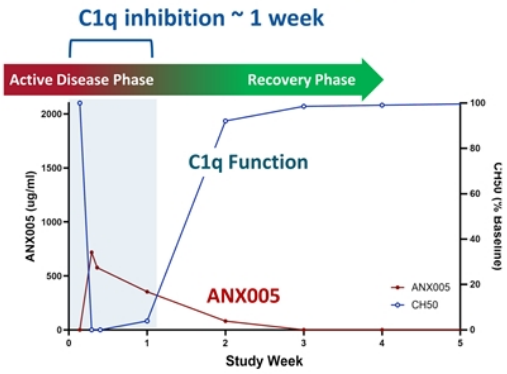
ANX005: Expected Pharmacokinetic and Dynamic Response for Both Doses

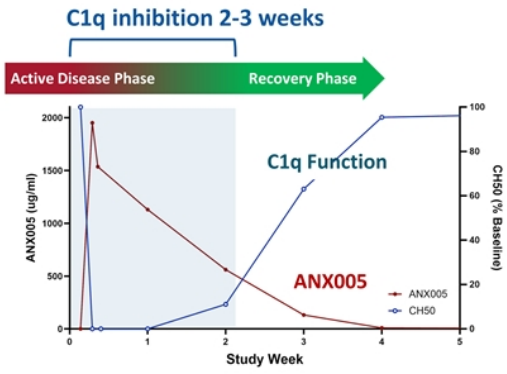
Duration of complement inhibition defines active treatment window

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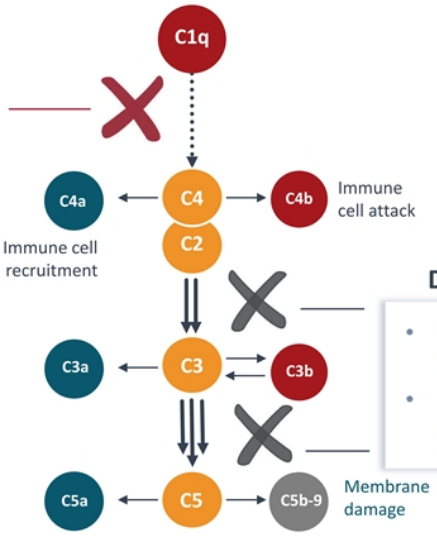
ANX005 Rapidly Shuts Down Activation of the *ENTIRE* Classical Complement Cascade on the Nerve to Prevent Acute Injury

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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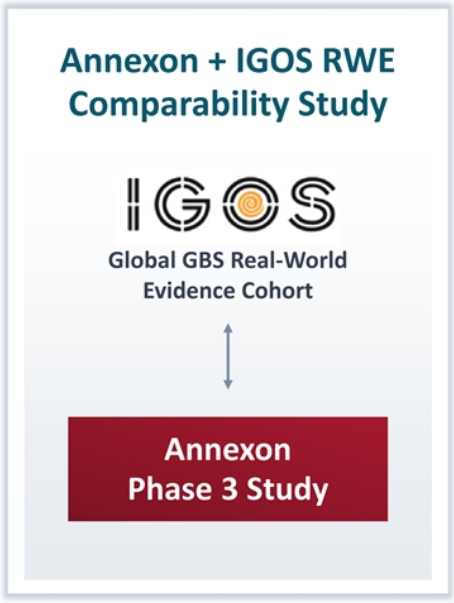
ANX005 GBS Phase 3 Trial Summary and Path Forward

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



Topline Results Subject to Change

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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 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**
- ✓ **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

Topline Results Subject to Change

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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

Topline Results Subject to Change

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

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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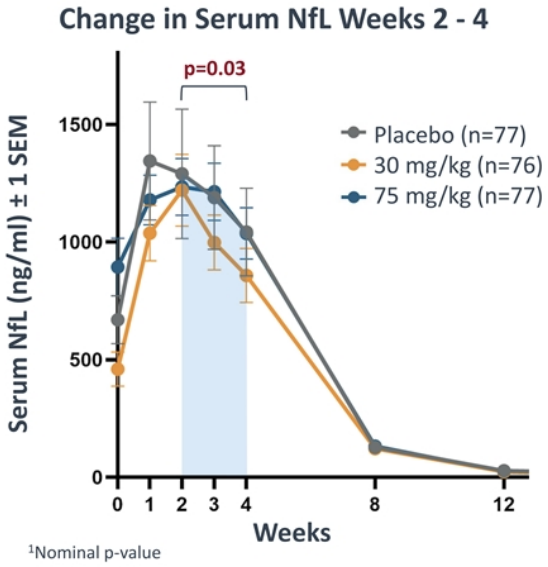
Appendix

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

Assessment of reduction of neuronal damage



[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
- **ANX005 30 mg/kg achieved significant early reduction in NfL between weeks 2 – 4 vs. pbo** (31.3% vs. 20.1%, p=0.03[1])

Complement is Pivotal Force in Driving Nerve Damage in GBS

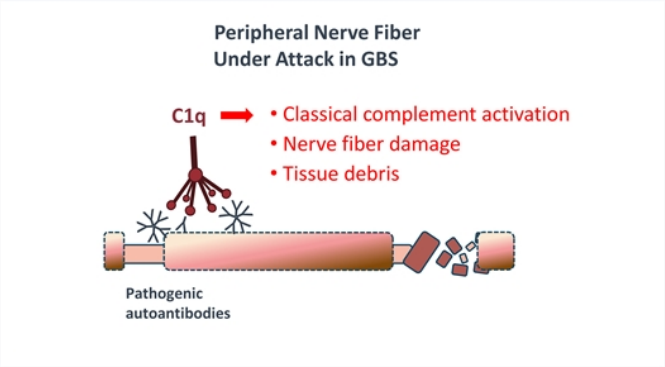
ANX005 is a Targeted Immunotherapy which Rapidly Blocks Complement

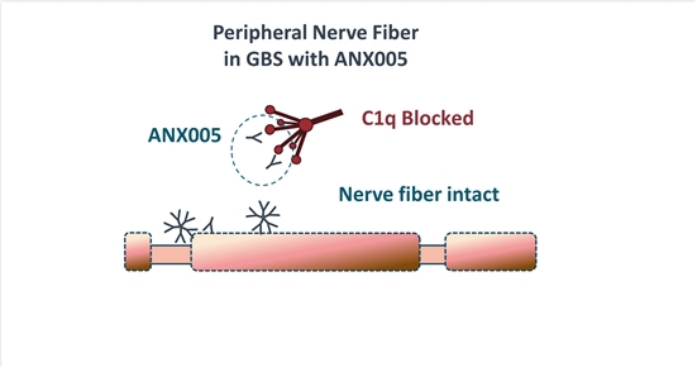
GBS

- 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





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 ✓ 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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