BofA SECURITIES

Annexon Biosciences

GBS Deep Dive and Takeaways from R&D Day

Reiterate Rating: BUY | PO: 7.00 USD | Price: 5.97 USD

Pivotal ANX005 data in GBS to read out in 2Q

Ahead of ANNX's pivotal data readout for ANX005 in GBS anticipated in 2Q, we review '005's clinical data, ph 3 trial trial design and the current landscape for GBS treatment. GBS is a rare autoimmune condition with no approved therapies that causes acute neuromuscular paralysis and even death in otherwise healthy individuals following an infection. '005 is a C1q-targeting mAb that inhibits the classical complement pathway, which has been implicated in the pathology of GBS. '005 is being evaluated in a ph 3 trial as 1L treatment in GBS. We are encouraged by '005's early clinical data with potential differentiated profile and await the pivotal readout in 2Q to inform the commercial opportunity for '005. We maintain our Buy on ANNX with $7 PO (prev. $6).

KOLs view '005 as potentially shifting treatment paradigm

Currently, ~90% of the 12k+ GBS patients in the US and EU are being treated off-label with 5-7 courses of IVIg. Our KOLs typically observe a 2-point improvement in baseline GBS-DS score (avg. of ~3) with IVIg. KOLs highlight that ~20% are poor/non-responders, ~40% see continued symptom progression and ~25% of severe patients experience IVIg intolerability. Given this high unmet medical need and the positive early clinical efficacy and safety signals of '005, our KOLs view '005 as a potentially paradigm-shifting treatment and think they could use it in up to 50% of pts, if approved. However, KOLs noted they would like to see head-to-head data versus IVIg given this has been the long-standing SoC for GBS. We estimate '005 risk-adj. peak sales of $252mn under our 40% LoS and 45% US peak penetration assumptions contributing $4/sh (prev. $3) to our PO.

Takeaways from GBS R&D day; BLA filing in 2025

At the R&D Day, mgmt highlighted the high unmet need in GBS and 3 key points of differentiation for '005 including a targeted mechanism of action, rapid onset of response and early evidence of safety and efficacy. The company noted key features of the ph 3 trial design including enrollment within 10 days of diagnosis, which they think could help drive better responses, and using a modified GBS-DS scale using a proportional odds method. Mgmt also commented that FDA would also require a comparability study between the ph 3 pts and Western pts, which they plan to conduct using the IGOS registry. They plan to match pts based on key prognostic factors and expect most pts will have been treated with IVIg. The study is expected to complete in 1H25 to support BLA submission. We think adding the comparability study will help the regulatory process and provide some indirect comparison to IVIg, which could help drive uptake, but adds more questions on the bar for approval. In our DCF-based model, we increase our peak penetration assumptions to 45% (prev 40%) in GBS resulting in our new $7 PO.

Estimates (Dec) (US$)	2021A	2022A	2023E	2024E	2025E
EPS	(3.40)	(2.60)	(1.95)	(1.93)	(1.76)
EPS Change (YoY)	18.1%	23.5%	25.0%	1.0%	8.8%
Consensus EPS (Bloomberg)			(1.88)	(1.71)	(2.08)
DPS	0	0	0	0	0
Valuation (Dec)					
Free Cash Flow Yield*	-24.2%	-27.6%	-28.1%	-37.3%	-43.2%

* For full definitions of *iQmethod*℠ measures, see page 11.

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Refer to important disclosures on page 12 to 14. Analyst Certification on page 10. Price Objective Basis/Risk on page 10. **12666873**

Timestamp: 04 March 2024 06:42AM EST

04 March 2024

Equity

Key Changes

(US$)	Previous	Current
Price Obj.	6.00	7.00
2023E EPS	-2.03	-1.95
2024E EPS	-1.71	-1.93
2025E EPS	-1.64	-1.76

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Stock Data

Price	5.97 USD
Price Objective	7.00 USD
Date Established	4-Mar-2024
Investment Opinion	C-1-9
52-Week Range	1.57 USD - 6.67 USD
Mrkt Val (mn) / Shares Out (mn)	445 USD / 74.6
Free Float	79.0%
Average Daily Value (mn)	5.62 USD
BofA Ticker / Exchange	ANNX / NAS
Bloomberg / Reuters	ANNX US / ANNX.OQ
ROE (2023E)	-85.5%
Net Dbt to Eqty (Dec-2022A)	-60.6%
ESGMeter™	Low

ESGMeter is not indicative of a company's future stock price performance and is not an investment recommendation or rating. ESGMeter is independent of BofA Global Research's equity investment rating, volatility risk rating, income rating, and price objective for that company. For full details, refer to "BofA ESGMeter Methodology".

See inside for abbreviations

iQprofile℠ Annexon Biosciences

iQmethod℠ **– Bus Performance***

(US$ Millions)	2021A	2022A	2023E	2024E	2025E
Return on Capital Employed	-38.5%	-49.6%	-69.2%	-170.7%	-257.9%
Return on Equity	-45.2%	-61.3%	-85.5%	-254.0%	-440.2%
Operating Margin	NA	NA	NA	NA	NA
Free Cash Flow	(108)	(123)	(125)	(166)	(193)

iQmethod℠ **– Quality of Earnings***

(US$ Millions)	2021A	2022A	2023E	2024E	2025E
Cash Realization Ratio	NM	NM	NM	NM	NM
Asset Replacement Ratio	0.8x	3.1x	3.1x	3.1x	3.1x
Tax Rate	NM	NM	NM	NM	NM
Net Debt-to-Equity Ratio	-32.3%	-60.6%	-97.7%	-86.9%	-82.6%
Interest Cover	NA	NA	NA	NA	NA

Income Statement Data (Dec)

(US$ Millions)	2021A	2022A	2023E	2024E	2025E
Sales	0	0	0	0	0
% Change	NA	NA	NA	NA	NA
Gross Profit	0	0	0	0	0
% Change	NA	NA	NA	NA	NA
EBITDA	(129)	(143)	(153)	(206)	(239)
% Change	-104.7%	-11.6%	-6.5%	-34.5%	-16.0%
Net Interest & Other Income	0	4	9	9	9
Net Income (Adjusted)	**(130)**	**(142)**	**(146)**	**(199)**	**(232)**
% Change	**-85.1%**	**-8.9%**	**-2.6%**	**-36.4%**	**-16.7%**

Free Cash Flow Data (Dec)

(US$ Millions)	2021A	2022A	2023E	2024E	2025E
Net Income from Cont Operations (GAAP)	(130)	(142)	(146)	(199)	(232)
Depreciation & Amortization	2	2	2	3	3
Change in Working Capital	2	5	2	2	2
Deferred Taxation Charge	NA	NA	NA	NA	NA
Other Adjustments, Net	20	18	24	36	43
Capital Expenditure	(2)	(7)	(7)	(8)	(9)
Free Cash Flow	**-108**	**-123**	**-125**	**-166**	**-193**
% Change	**-101.2%**	**-14.0%**	**-1.7%**	**-33.1%**	**-15.8%**
Share / Issue Repurchase	2	123	0	100	200
Cost of Dividends Paid	0	0	0	0	0
Change in Debt	0	0	0	0	0

Balance Sheet Data (Dec)

(US$ Millions)	2021A	2022A	2023E	2024E	2025E
Cash & Equivalents	75	140	107	41	48
Trade Receivables	NA	NA	NA	NA	NA
Other Current Assets	173	108	17	17	18
Property, Plant & Equipment	18	17	22	27	33
Other Non-Current Assets	21	20	20	20	20
Total Assets	**287**	**285**	**166**	**105**	**119**
Short-Term Debt	0	0	0	0	0
Other Current Liabilities	22	22	24	27	29
Long-Term Debt	0	0	0	0	0
Other Non-Current Liabilities	33	32	32	32	32
Total Liabilities	**55**	**54**	**56**	**58**	**61**
Total Equity	**232**	**231**	**110**	**47**	**58**
Total Equity & Liabilities	**287**	**285**	**166**	**105**	**119**

* For full definitions of *iQmethod*℠ measures, see page 11.

Company Sector

Biotechnology

Company Description

Annexon Biosciences (ANNX) is a clinical-stage biotechnology company developing therapeutics targeting a part of the immune system known as the complement system. Based in San Francisco, CA, the company's lead asset ANX005 is in clinical trials for a rare, acute nerve disease called Guillain-Barré syndrome. ANNX is also pursuing autoimmune, neurodegenerative and ocular indications for warm autoimmune hemolytic anemia, amyotrophic lateral sclerosis, Huntington's disease, and geographic atrophy.

Investment Rationale

We rate ANNX shares Buy. Lead asset ANX005 has the potential to be the first FDA-approved treatment for Guillain-Barré syndrome, which has high unmet need for effective treatments. Second asset ANX007 in geographic atrophy has the opportunity to address a large untapped market. Company reached alignment with FDA to use BCVA15 as primary. We view ANNX's complement inhibition platform favorably, as C1q inhibition is a differentiated mechanism of action with promising preclinical and clinical data.

Stock Data

Average Daily Volume	941,126

Quarterly Earnings Estimates

	2022	2023
Q1	-0.92A	-0.52A
Q2	-0.96A	-0.47A
Q3	-0.51A	-0.43A
Q4	-0.48A	-0.52E

Guillain-Barré Syndrome Overview

Guillain-Barré syndrome (GBS) is a rare but serious autoimmune condition of the nervous system that can lead to acute neuromuscular paralysis and even death in otherwise healthy individuals. Typically triggered by a preceding infection, when an individual develops GBS, the body's immune system mistakenly attacks part of its own peripheral nervous system. The rapidly progressing nerve damage leads to a rapid onset of debilitating symptoms, usually developing over several days. Most patients begin feeling weakness and tingling in the legs before experiencing more widespread muscle weakness, loss of sensation in limbs, and problems swallowing or breathing. There are over 12k patients diagnosed with GBS per year in the US and EU. An estimated 25% of patients require mechanical ventilation, 70% develop autonomic dysfunction (arrythmias, hypo/hypertension, etc.), 65% have severe chronic fatigue and 5% die from GBS. Overall, GBS poses a significant burden to the health care system with US hospitals spending over $2 billion annually on related expenses, including ventilators, skilled nursing facilities, physical therapy, and ICU expenses.

GBS is typically triggered by a prior infection

Anyone regardless of gender or age can develop GBS, but it is most prevalent among adults and those over 50. While the exact cause of GBS remains unknown, symptom onset usually begins several days or weeks following a respiratory or gastrointestinal bacterial or viral infection. Notably, infection with the bacteria *Campylobacter jejuni* (causes gastroenteritis), and viral infections like Epstein-Barr, Zika and the flu are recognized as risk factors for developing GBS. Surgery has also been identified as a potential trigger for GBS.

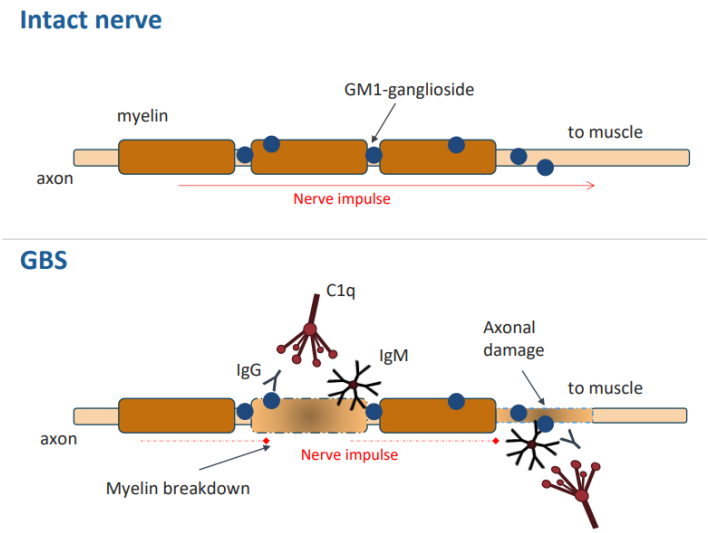
GBS causes the immune system to attack the body's nerve cells

In GBS patients, the body's immune cells mistake healthy nerve cells for the dangerous bacteria or viruses (antigens) associated with a recent infection (e.g. flu virus). Studies have shown that some bacterial cells (like *C. jejuni*) have structures on their cell walls (glycolipids) that closely resemble ganglioside epitopes on nerve cells. In the case of *C. jejuni,* this generates a cross-reactive immune response and results in nerve cell axons being attacked. The axon is a nerve cell's central conducting core, and it carries electrical signals (impulses) throughout the body (e.g. to control muscles or regulate breathing). Axons are coated with myelin – an insulating layer made of protein and fatty substances – which facilitates the rapid and efficient travel of the brain's impulses to distant tissues. In many instances of GBS, autoimmune attacks damage the myelin sheath – and sometimes the axons as well – which prevents muscles from exhibiting normal, timely responses to critical neural impulses (Exhibit 1). We note, however, that the exact pathogenesis of GBS following certain infections (e.g. Zika virus) is not yet fully understood.

The classical complement cascade is involved in the mechanism of GBS

Antibodies can also trigger activation of the complement system, an integral aspect of the human immune response. It is comprised of a group of approximately 35 proteins that interact to recognize invading antigens, unwanted cells, and foreign materials. The complement system employs a signaling cascade to tag these pathogens for destruction (via opsonization), ultimately recruiting various other immune cells to eliminate them. These distinct complement proteins exist in an inactive form and can proceed through three pathways once activated, with the classical complement pathway being implicated in the mechanism of GBS. The classical pathway cascade is activated through the interaction of its first molecule – complement component 1 (C1q) – with immune complexes containing immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies. In GBS patients, once antibodies are triggered by nerve cells, they activate the complement system and C1q initiates the cascade. Thereafter, the complement system begins to damage nerve cells and can also recruit other immune cells to do the same, quickly weakening a patient's muscles oftentimes to the point of paralysis (Exhibit 1).

Exhibit 1: GBS is caused by a harmful autoimmune response
Breakdown of myelin and damage to neuronal axons disrupts critical nerve impulses



Source: Company filing

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Muscle weakness has serious implications for GBS patients

Most patients reach maximal weakness within 2-3 weeks of symptom onset before entering a (days to weeks long) plateau period. Thereafter, patients begin a slow and variable recovery phase. An estimated 25% of severe (non-ambulatory) patients require artificial ventilation due to weakness of respiratory muscles and – even after receiving treatment – 20% of severe patients are unable to walk after 6 months. Overall, many patients continue experiencing a diminished quality of life (chronic fatigue and/ or disability) due to GBS for several years after receiving a diagnosis.

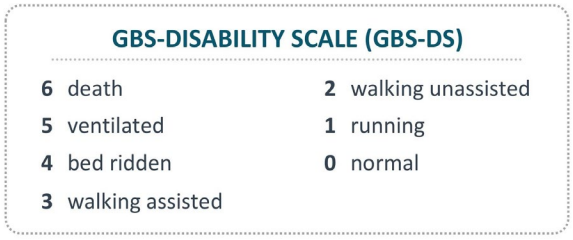
Clinical diagnosis and treatment of GBS

Presentation of GBS can appear similar to that of other diseases and onset may vary between patients, rendering early diagnosis potentially challenging. Diagnosis of GBS begins with a physical exam by a physician to determine whether a patient's muscle and nerve function has been impaired. The physician will look for a loss of reflexes, rapid symptom onset and symptoms appearing on both sides of the body. Patients may also undergo a nerve conduction velocity (NCV) test, which can detect slowed neuronal impulses due to damaged axons. Doctors may also conduct a cerebrospinal fluid (CSF) analysis to look for a depletion of immune cells around the spinal cord or they may even perform magnetic resonance imaging (MRI) of the brain and spinal cord to further assess a patient's condition.

The GBS disability score assesses the functional status of GBS patients

The GBS disability scale (GBS-DS) is a widely accepted scoring system to assess the functional status of GBS patients (Exhibit 2). We note that our key opinion leaders (KOLs) identified their average GBS patient as scoring between 2-4 at baseline and viewed a decrease of one point as being a clinically meaningful score change.

Exhibit 2: GBS Disability Scale
GBS-DS quantifies the functional status and disease progression of patients with GBS



Source: Company filing

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Current standard of care includes IVIg and plasmapheresis

There are currently no FDA approved therapies indicated for the treatment of GBS. Limited non-specific treatment options are available and are effective in shortening recovery time and improving clinical outcomes, but these have unclear mechanisms of action in GBS. Current standard of care consists of providing most (~90%) patients with intravenous immunoglobulin (IVIg) or performing a therapeutic exchange of blood plasma (plasmapheresis). Despite an unknown mechanism of action, IVIg has been found to prevent inflammatory autoimmune responses against the body's own tissues. IVIg is given intravenously over several hours over the course of 1-5 days depending on patient severity. An estimated 10% of patients experience minor side effects from IVIg and repeat IVIg treatments are usually not performed for GBS patients. We note that our KOLs typically observe a ~2 point decrease in GBS-DS at 8 weeks post-IVIg treatment.

ANX005: ANNX's C1q inhibitor for GBS

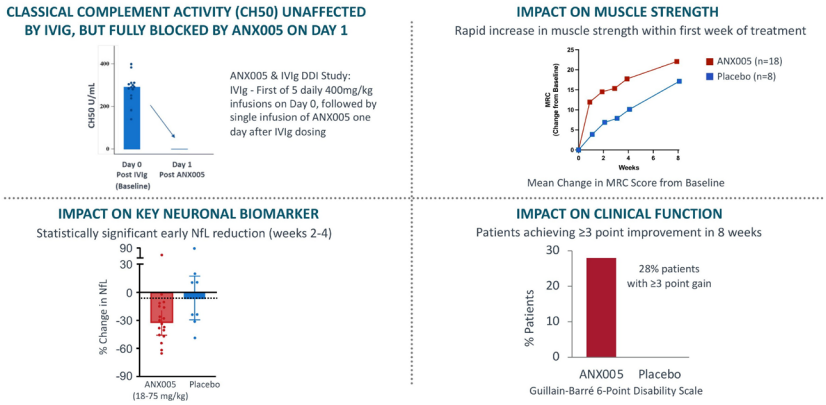
ANNX's ANX005 ('005) is an investigational humanized monoclonal antibody (mAb) designed to inhibiting C1q, the initiator molecule of the classical complement pathway. Activation of the classical complement pathway has been linked to the pathogenesis of GBS. Initial phase 1b data suggests the potential efficacy of '005 in GBS with a faster onset of response than current standard of care. The US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have both granted Orphan Drug Designation to '005 for the treatment of GBS. '005 is being evaluated in a phase 3 trial as first line treatment in GBS with topline data expected in 2Q24.

ANX005 phase 1b proof-of-concept data

ANNX completed a phase 1b proof-of-concept trial in 2020 investigating the anti-C1q activity of '005 in 38 treated patients, compared to 12 patients given placebo. The single-site (Bangladesh), double-blind, placebo-controlled, ascending-dose study evaluated treatment with '005 versus placebo on axonal damage, serum neurofilament light (NfL) chain biomarker levels (elevated levels correlate with poor outcomes), and functional measures in patients with GBS. Treated patients were randomized to 5 different cohorts, receiving a single intravenous (IV) infusion of between 3-75 mg/kg of drug. 19 patients received one of the two exploratory higher doses (75mg/kg x 2; 100mg/kg) and were evaluated for safety and pharmacokinetics (PK). The mean baseline GBS-DS score at randomization was 4.0.

The study found '005 successfully inhibited complement pathway activity, with 28% of patients treated with high-dose '005 improving by 3+ points on GBS-DS by week 8 compared to 0% with placebo. Treatment with '005 also showed early dose-dependent improvements in muscle strength (within 1 week) and a statistically significant early reduction in serum NfL levels compared to placebo (Exhibit 3). Patients treated with '005 also required fewer mean days on a ventilator (10 versus 17 for placebo) and fewer mean days in the ICU (4.78 versus 6.25 for placebo). '005 was well tolerated in GBS patients at all dose levels.

Exhibit 3: Phase 1b clinical data for '005
Treated patients saw improved clinical function, muscle strength and reduced classical complement activity



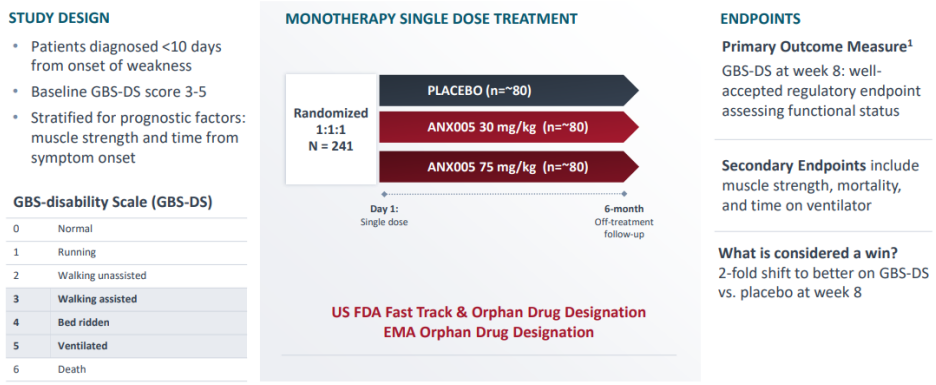
Source: Company filing

BofA GLOBAL RESEARCH

ANX005 Phase 3 pivotal trial design

ANNX's phase 3 study of '005 in patients recently diagnosed with GBS has enrolled 241 participants in Southeast Asia and aims to evaluate the asset's efficacy, safety, pharmacokinetics and pharmacodynamics at 2 doses (Exhibit 4). The study is randomized, double-blind and placebo-controlled and will take place across multiple centers. Patients with baseline GBS-DS of 3-5 will be randomized to receive either placebo (n=~80) or a single IV infusion of either 30mg/kg (n=~80) or 75mg/kg (n=~80) of '005. Importantly, the company has highlighted they enrolled patients who received within 10 days of the onset on weakness, which they think will help maximize the potential efficacy of '005. Topline data is expected in 2Q.

Exhibit 4: Phase 3 trial design for ANX005 in GBS
Summary of the phase 3 trial design



Source: Company filing

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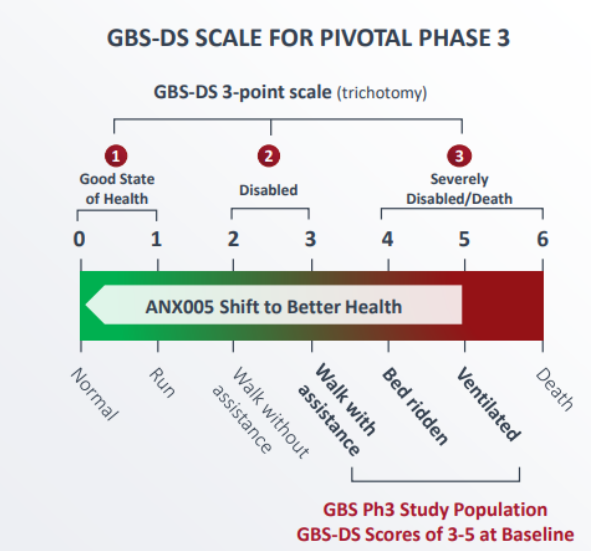
Primary endpoint is based on collapsed GBS-DS using proportional odds model

The primary endpoint of the pivotal study is the GBS-DS score at week 8 and secondary endpoints include safety, duration of ventilation support, duration of ICU stays, muscle strength, mortality, neuronal damage, and patient global impression of change scores. The GBS-DS was modified to a collapsed version including 3 different levels: good state of health (0-1), disabled (2-3) and severely disabled/death (4-6) for purposes of the statistical analysis using a proportional odds model (Exhibit 5). The study will mee the primary endpoint if '005 achieves a 2-fold shift to better on GBS-DS compared to

placebo. They highlighted this change allows for enhanced clinical interpretability of the results and increases efficiency for statistical analysis.

Exhibit 5: Collapsed GBS-DS scale for analysis of phase 3 study
The phase 3 study will use a simplified 3-point GBS-DS for the proportional odds model



Source: Company filing

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Comparability study using real-world evidence to support 2025 BLA submission
The company also plans to conduct a comparability study between the phase 3 patient population to Western patients based on FDA feedback. The study will be conducted comparing results from the phase 3 study to natural history data from the IGOS (International GBS Outcomes Study) registry, which contains data from ~2000 patients with 1-3 year follow-up. The company commented they will match patients based on key prognostic factors including muscle strength and time to symptom onset. They noted most patients in IGOS will have received IVIg, which is the standard of care in most countries around the world. The comparability study has initiated, and the company expects initial comparability data ion 1H25 which will support a biologics license application (BLA) submission in 2025. We think these changes will help strengthen a regulatory submission and could provide some initial data indirectly comparing '005 to IVIG, which our KOLs highlighted could help drive uptake. However, we think this study introduces some uncertainty regarding the bar for approval and we will look for more color on the specifics of what the study needs to demonstrate for approval.

Key takeaways from our conversations with KOLs

Our KOLs view a positive readout of '005 data in 2Q as having the potential to possibly shift the GBS treatment paradigm in the future. The current standard of care consists of 5-7 courses of IVIG treatment, which typically provides a ~2 point improvement in baseline GBS-DS score (average of ~3) when patients are treated early. KOLs highlighted that, while IVIg is generally efficacious, some patients (~10-20%) respond poorly or not at all to treatment and many (~40%) continue to see symptom progression. Additionally, KOLs estimated that up to ~25% of more severe patients experience IVIG intolerability. These factors highlight the significant unmet need for another treatment option in GBS, which could potentially be met by ANX005. KOLs also explained that '005

having a label indicated for the treatment of GBS could give it a slight edge over IVIG (used off-label for GBS) when choosing a therapy, especially if pricing is similar.

KOLs also noted that complement inhibition has been researched in several other neuromuscular disorders and early clinical models of '005 support its mechanism of action in GBS. On '005's proof-of-concept data, KOLs found it to be promising and viewed the rapid increase in muscle strength, reduction of the NfL biomarker and blocking of classical complement activity as positive signals of clinical efficacy.

KOLs were not concerned about '005's pivotal trial being ran completely ex-US (in Southeast Asia). They noted that a 1-2 point change in GBS-DS versus placebo would be clinically meaningful and highlighted muscle strength and grip strength as a key, clinically validated secondary endpoint of interest. However, KOLs expressed a desire to see a head-to-head comparison of '005 to IVIG sometime in the future, to determine whether a significant clinical benefit over the current standard of care exists. They also mentioned that – while a positive readout in 2Q would be promising – they look forward to reviewing long-term data on the effects '005 in GBS. Ultimately, KOLs expressed excitement about the potential to add another option to their treatment arsenal and noted that a positive readout could result in widespread usage of '005 in the long term, with over 50% of their GBS patients being good candidates.

Abbreviations

2Q: second quarter

C1q: complement component 1

CSF: cerebrospinal fluid

EMA: European Medicines Agency

FDA: Food and Drug Administration

GBS: Guillain-Barre Syndrome

GBS-DS: GBS disability scale

ICU: intensive care unit

IgG: immunoglobulin G

IgM: immunoglobulin M

IGOS: International GBS Outcome Study

IV: intravenous

IVIG: intravenous immunoglobulin

KOL: key opinion leader

mAb: monoclonal antibody

mgmt: management

MRI: magnetic resonance imaging

NCV: nerve conduction velocity test

NfL: neurofilament light chain

PK: pharmacokinetics

Pts: patients

Price objective basis & risk

Annexon Biosciences (ANNX)

Our price objective (PO) of $7 is based on a probability-adjusted NPV analysis. Our DCF-based valuation for ANNX includes $4/sh for ANX005 in Guillain-Barré syndrome (GBS) and $4/sh for ANX007 in geographic atrophy (GA). The remainder of our valuation comes from pipeline (-$3/sh) and cash ($2/sh). Our model goes out to 2039, with 12% WACC for GBS, 11% WACC for GA, and 14% WACC for the early pipeline.

Upside to our price objective are: 1) accelerated path to regulatory approval, 2) faster-than-expected enrollment in clinical trials, 3) positive results in clinical trials, 4) wider market penetration than expected.

Downside risks are: 1) negative results in clinical trials, 2) entry or progress of competitors in target indications, 3) failure to replicate GBS Bangladesh clinical trial results in US and EU trials, and 4) lower-than-expected market penetration.

Analyst Certification

I, Tazeen Ahmad, hereby certify that the views expressed in this research report accurately reflect my personal views about the subject securities and issuers. I also certify that no part of my compensation was, is, or will be, directly or indirectly, related to the specific recommendations or view expressed in this research report.

US - Biotechnology Coverage Cluster

Investment rating	Company	BofA Ticker	Bloomberg symbol	Analyst
BUY				
	4D Molecular Therapeutics, Inc.	FDMT	FDMT US	Tazeen Ahmad
	Alnylam Pharmaceuticals	ALNY	ALNY US	Tazeen Ahmad
	Amicus Therapeutics	FOLD	FOLD US	Tazeen Ahmad
	Annexon Biosciences	ANNX	ANNX US	Tazeen Ahmad
	Apellis Pharmaceuticals	APLS	APLS US	Tazeen Ahmad
	Argenx SE	ARGX	ARGX US	Tazeen Ahmad
	Arvinas	ARVN	ARVN US	Tazeen Ahmad
	Ascendis Pharma	ASND	ASND US	Tazeen Ahmad
	Biocryst Pharmaceuticals Inc	BCRX	BCRX US	Tazeen Ahmad
	BioNTech	BNTX	BNTX US	Tazeen Ahmad
	Denali Therapeutics	DNLI	DNLI US	Tazeen Ahmad
	Inozyme Pharma, Inc.	INZY	INZY US	Tazeen Ahmad
	Merus	MRUS	MRUS US	Tazeen Ahmad
	Neurocrine Biosciences	NBIX	NBIX US	Tazeen Ahmad
	Ocular Therapeutix	OCUL	OCUL US	Tazeen Ahmad
	PepGen Inc	PEPG	PEPG US	Tazeen Ahmad
	Rhythm Pharmaceuticals	RYTM	RYTM US	Tazeen Ahmad
	Sarepta Therapeutics	SRPT	SRPT US	Tazeen Ahmad
	Ultragenyx Pharmaceuticals	RARE	RARE US	Tazeen Ahmad
NEUTRAL				
	Acadia Pharmaceuticals	ACAD	ACAD US	Tazeen Ahmad
	Incyte Corporation	INCY	INCY US	Tazeen Ahmad
	Prothena Corporation	PRTA	PRTA US	Tazeen Ahmad
	SAGE Therapeutics	SAGE	SAGE US	Tazeen Ahmad
UNDERPERFORM				
	Achilles Therapeutics	ACHL	ACHL US	Tazeen Ahmad
	Fate Therapeutics	FATE	FATE US	Tazeen Ahmad
	Fulcrum Therapeutics	FULC	FULC US	Tazeen Ahmad
	Pharvaris	PHVS	PHVS US	Tazeen Ahmad
	PTC Therapeutics	PTCT	PTCT US	Tazeen Ahmad

iQmethod℠ Measures Definitions

Business Performance	Numerator	Denominator
Return On Capital Employed	NOPAT = (EBIT + Interest Income) × (1 – Tax Rate) + Goodwill Amortization	Total Assets – Current Liabilities + ST Debt + Accumulated Goodwill Amortization
Return On Equity	Net Income	Shareholders' Equity
Operating Margin	Operating Profit	Sales
Earnings Growth	Expected 5 Year CAGR From Latest Actual	N/A
Free Cash Flow	Cash Flow From Operations – Total Capex	N/A

Quality of Earnings	Numerator	Denominator
Cash Realization Ratio	Cash Flow From Operations	Net Income
Asset Replacement Ratio	Capex	Depreciation
Tax Rate	Tax Charge	Pre-Tax Income
Net Debt-To-Equity Ratio	Net Debt = Total Debt – Cash & Equivalents	Total Equity
Interest Cover	EBIT	Interest Expense

Valuation Toolkit	Numerator	Denominator
Price / Earnings Ratio	Current Share Price	Diluted Earnings Per Share (Basis As Specified)
Price / Book Value	Current Share Price	Shareholders' Equity / Current Basic Shares
Dividend Yield	Annualised Declared Cash Dividend	Current Share Price
Free Cash Flow Yield	Cash Flow From Operations – Total Capex	Market Cap = Current Share Price × Current Basic Shares
Enterprise Value / Sales	EV = Current Share Price × Current Shares + Minority Equity + Net Debt + Other LT Liabilities	Sales
EV / EBITDA	Enterprise Value	Basic EBIT + Depreciation + Amortization

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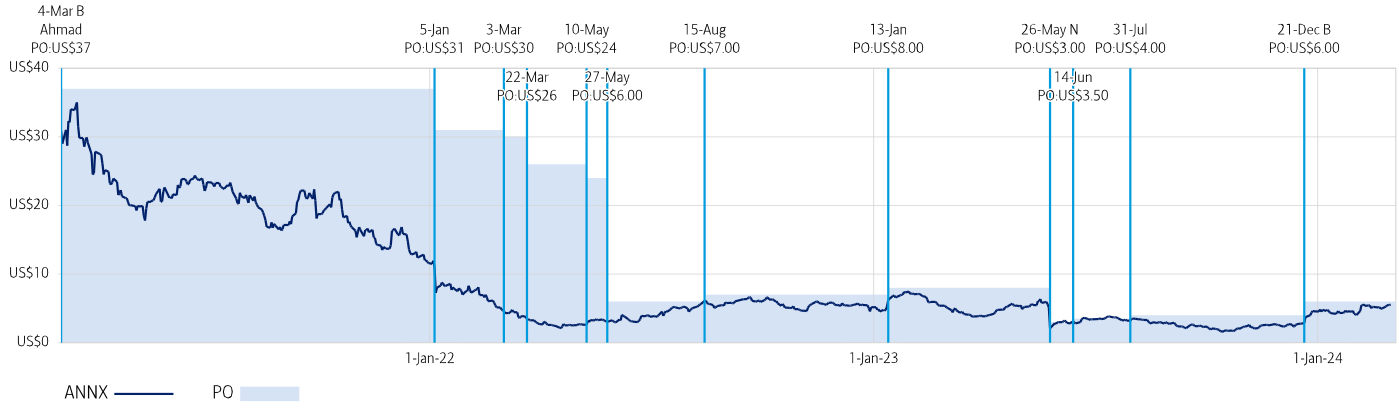
Annexon Bios (ANNX) Price Chart



B: Buy, N: Neutral, U: Underperform, PO: Price Objective, NA: No longer valid, NR: No Rating

The Investment Opinion System is contained at the end of the report under the heading "Fundamental Equity Opinion Key". Dark grey shading indicates the security is restricted with the opinion suspended. Medium grey shading indicates the security is under review with the opinion withdrawn. Light grey shading indicates the security is not covered. Chart is current as of a date no more than one trading day prior to the date of the report.

Equity Investment Rating Distribution: Health Care Group (as of 31 Dec 2023)

Coverage Universe	Count	Percent	Inv. Banking Relationships [R1]	Count	Percent
Buy	234	60.94%	Buy	115	49.15%
Hold	80	20.83%	Hold	36	45.00%
Sell	70	18.23%	Sell	29	41.43%

Equity Investment Rating Distribution: Global Group (as of 31 Dec 2023)

Coverage Universe	Count	Percent	Inv. Banking Relationships [R1]	Count	Percent
Buy	1895	53.62%	Buy	1083	57.15%
Hold	832	23.54%	Hold	454	54.57%
Sell	807	22.84%	Sell	383	47.46%

[R1] Issuers that were investment banking clients of BofA Securities or one of its affiliates within the past 12 months. For purposes of this Investment Rating Distribution, the coverage universe includes only stocks. A stock rated Neutral is included as a Hold, and a stock rated Underperform is included as a Sell.

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Investment rating	Total return expectation (within 12-month period of date of initial rating)	Ratings dispersion guidelines for coverage cluster[R2]
Buy	≥ 10%	≤ 70%
Neutral	≥ 0%	≤ 30%
Underperform	N/A	≥ 20%

[R2] Ratings dispersions may vary from time to time where BofA Global Research believes it better reflects the investment prospects of stocks in a Coverage Cluster.

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