Final Clinical Results from ANX005 Phase 2 HD Trial

June 7, 2022

Nasdaq: ANNX

Forward-looking Statements

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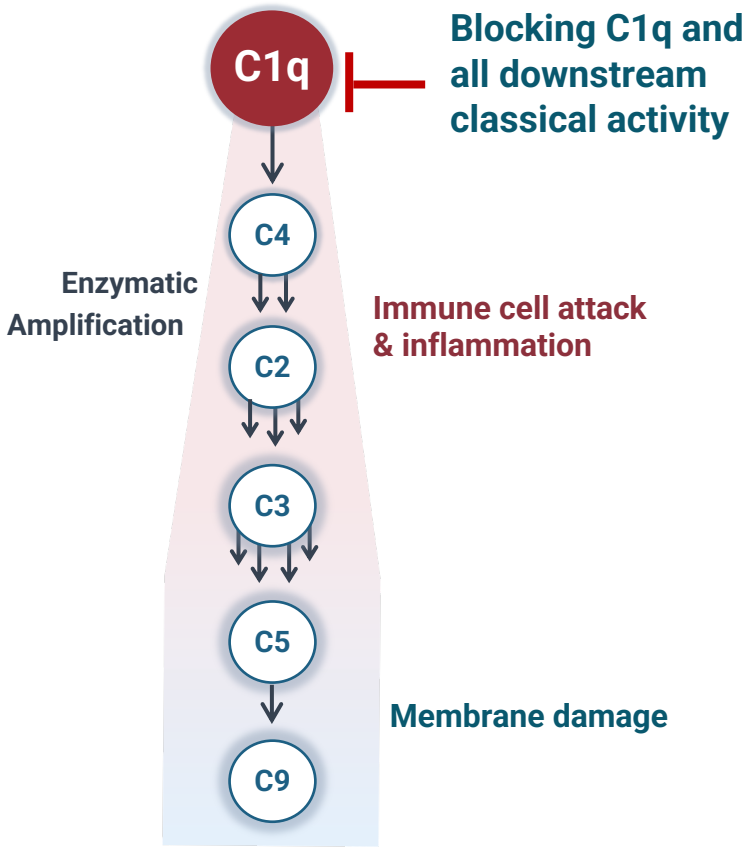
This presentation concerns drug candidates that are under clinical investigation, and which have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). These are currently limited by federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

Pioneering a Powerful Approach to Classical Complement Inhibition

Classical Complement Pathway



- Complement inhibition is a **validated clinical and commercial** approach
- Annexon's next-generation approach blocks **both upstream & downstream complement** for enhanced outcomes
- Advancing **5 fit-for-purpose drug candidates** for complement-mediated diseases of the body, brain & eye
- **Clinical benefit with ANX005 shown** in multiple indications
- Well-positioned to drive significant value with **7 clinical trial readouts anticipated in 2022-2023**

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Promising Phase 2 Results from Clinical Trial of ANX005 as a Complement Treatment for Patients with Huntington's Disease

- **Full C1q inhibition maintained** in the body & brain through treatment and well into follow-up periods
- **Stabilized disease progression** in full cohort through both treatment and follow-up period
- **Clinical improvements maintained** in patients with higher baseline complement through entire 9-month study
- **Generally well-tolerated** with no change in safety results from interim analysis

ROBUST, CONSISTENT DATA SUPPORT CONTINUED ADVANCEMENT FOR HD

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Huntington's Disease: Fatal Neurodegenerative Disorder Impacting Thousands of Patients

No approved therapies that slow or stop disease progression

- **Inherited, fatal disease** that causes progressive synapse damage and loss associated with neuroinflammation and loss of neurons
- **Affects ~80K people globally**, with ~300K at risk of inheriting the disease-causing HD gene[1]
- Life expectancy after diagnosis estimated to be **15-20 years**
- **Progressive decline** in motor, cognitive and psychiatric function

[1]GlobalData and Delvinsight market research

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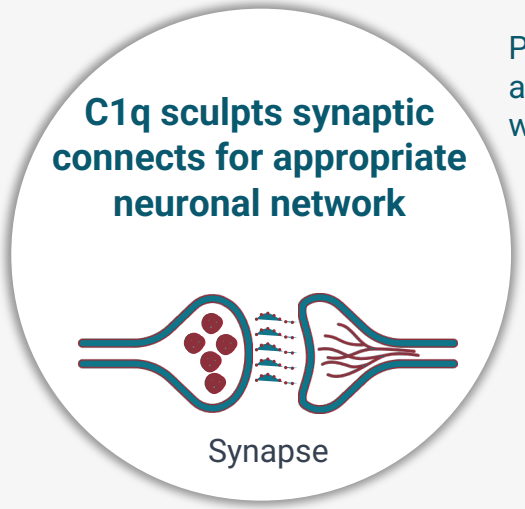
Loss of Functioning Synapses Results in Neurodegeneration

Blocking C1q protects functioning synapses and decreases disability[2]

C1q's Normal Role In Development

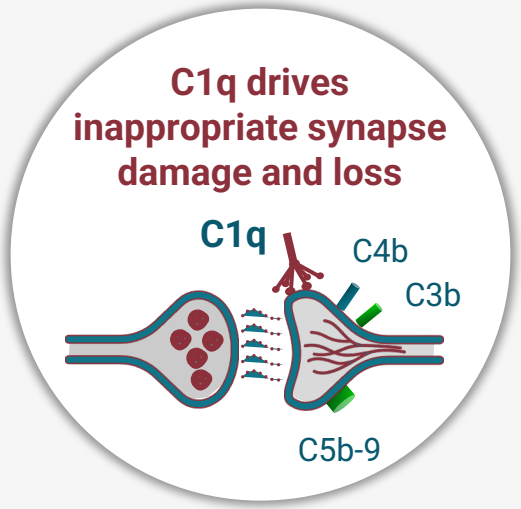
- C1q selectively recognizes, tags & drives removal of excess synapses
- Strong synapses remain to form appropriate circuits and normal brain health



Pathway turns off after developmental window

C1q's Role In Neurodegenerative Disease

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



Chronic pathway activation and functional decline

[1]Selkoe, 2002 *Science* **298**:789 | [2]Wilton 2021 doi.org/10.1101/2021.12.03.471180; Hong 2016 *Science* 10.1126/science.aad8373; Stevens 2007 *Cell* DOI 10.1016/j.cell.2007.10.036; Fonseca, 2004, *J Neurosci*; Dejanovic, 2018, *Neuron*; Vukojicic, 2019, *Cell Reports*; Howell, 2011, *J Clin Inves*; Williams, 2016, *Mol Neurodegen*; Jiao, 2018, *Mol Neurodeg*; Lui, 2016, Cell **165**:921; Krukowski, 2018, Int.*J Mol Sci*; Holden, 2021, *Science*; Annexon NfL reduction in SOD1 model, unpublished; Absinta, *Nature*, 2021

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Phase 2 Open-label Clinical Trial of ANX005 in Patients With, or at Risk for, Manifest Huntington's Disease

6-month treatment period (n=28) → **3-month follow-up**

Induction dosing of ANX005 administered by IV infusion on Days 1 and 5 or 6, followed by maintenance dosing every 2 weeks through Week 22

Follow up visits on Weeks 24, 28, and 36

Study Population

- Adults with, or at risk for, manifest HD ("Early HD")
- Total CAP score >400
- UHDRS independence score ≥ 80%

Primary Endpoints

- Safety and tolerability of ANX005
- PK of ANX005 in serum & cerebrospinal fluid (CSF)
- PD as measured by C1q, NfL, and C4a serum and CSF concentrations

Exploratory Endpoints

- Composite UHDRS and its components

Final Clinical Study Findings Include:

- Target engagement, clinical measures and NfL in patients who completed both treatment and follow-up periods (n=23)
- Clinical measures in patients with high vs. low C4a complement (n=23)
- Safety and tolerability (n=28)

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ANX005 Phase 2 Trial Patient Baseline Demographics

Study Participant Characteristics	All Patients % (N=28)	Treatment Completers % (N=23)	TRACK-HD* % (N=123)
Age, mean SD, years	49.7 (12.5)	48.5 (13.3)	48.8 (9.8)
Female, %	42.9	34.8	45
CAG repeat length mean (SD)	44.6 (3.5)	45.1 (3.7)	43.7 (3.0)
CAP score mean, (SD)	505.7 (57.9)	512.2 (60.4)	NR
Manifest HD, n (%)	25 (89.3)	21 (91.3)	123 (100)
CSF C4a, mean (SD) ng/mL	13.9 (8.2)	15.0 (7.0)	NR
Baseline plasma NfL, mean (SD) pg/mL	40.1 (13.7)	41.3 (13.3)	NR
Baseline CSF NfL, mean (SD) pg/mL	3104.1 (810.8)	3236.0 (816.8)	NR
cUHDRS, mean (SD)	10.4 (3.2)	10.1 (2.9)	11.7 (2.9)
Total Functional Capacity , mean (SD)	10.6 (2.2)	10.4 (2.3)	10.9 (2.0)
Total Motor Score, mean (SD)	21.6 (12.6)	22.3 (11.4)	23.7 (10.8)
Symbol Digit Modalities Test, mean (SD)	29.7 (11.3)	28.8 (11.0)	33.6 (10.2)
Stroop Word Reading Test, mean (SD)	59.0 (18.7)	56.7 (16.7)	78.3 (19.5)

- ~ 90% of patients had “early manifest HD”
- Demographics consistent with prior HD natural history study cohorts (e.g., TRACK-HD*)

* TRACK-HD, HD natural history study. For illustrative purposes only - differences exist between patient demographics, study designs, and other factors and caution should be exercised when comparing data across studies.
NR=not reported

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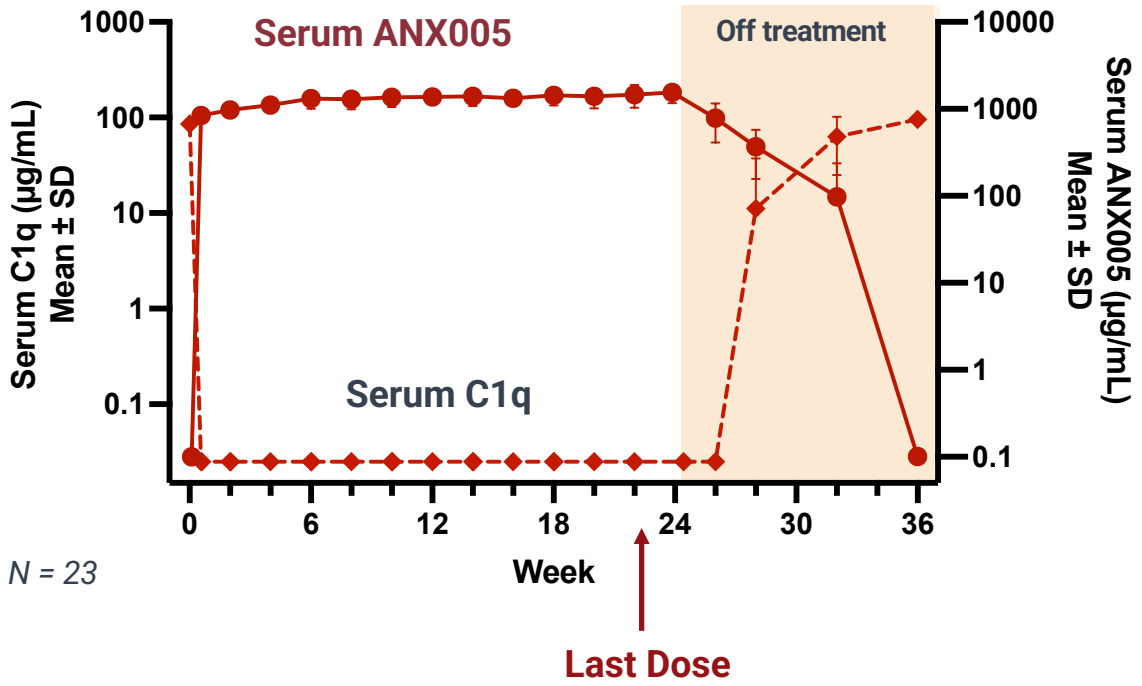
ANX005 Demonstrated Complete & Durable C1q Inhibition in Blood and CSF

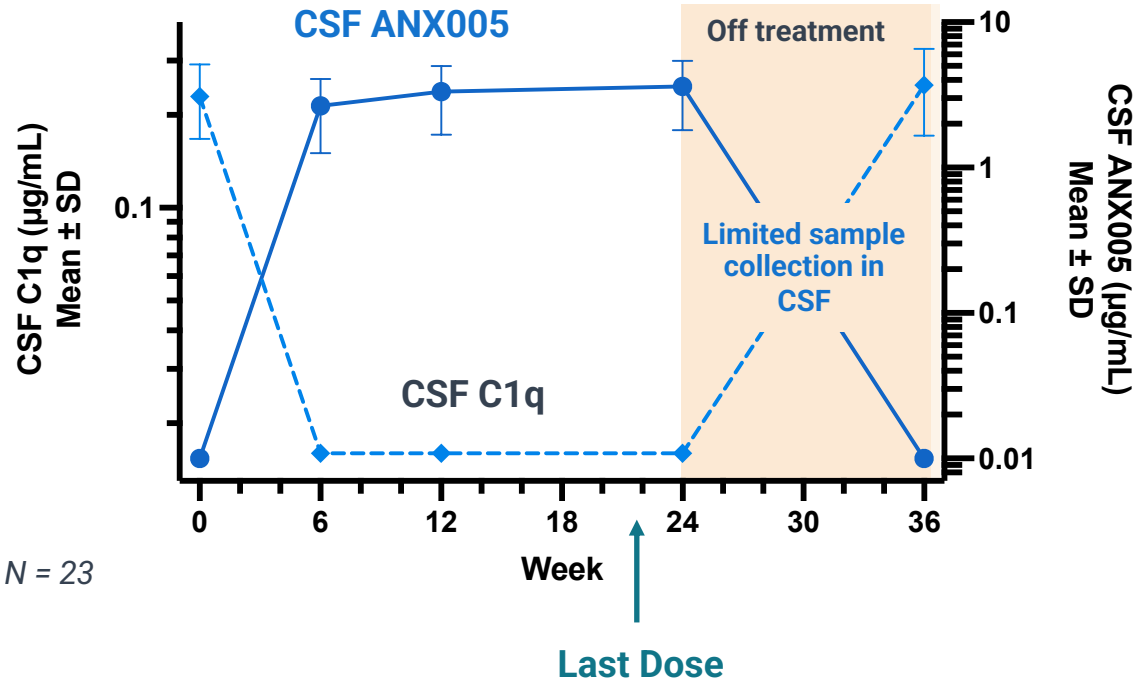
Target engagement 4-10 weeks in serum post last dose; may support less frequent dosing

Full Target Engagement in Serum



N = 23

Full Target Engagement in CSF



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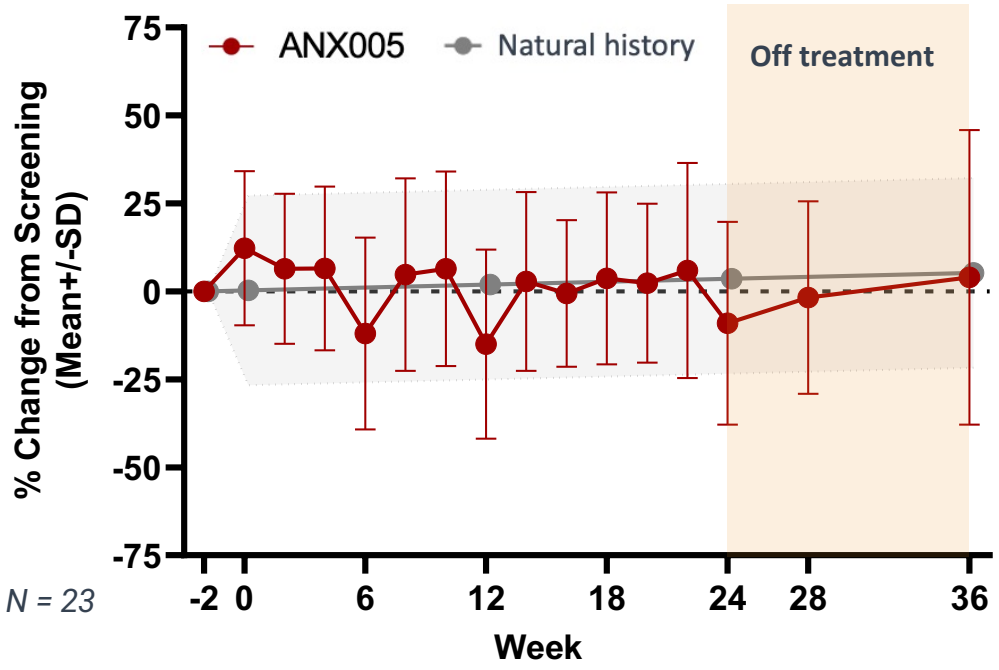
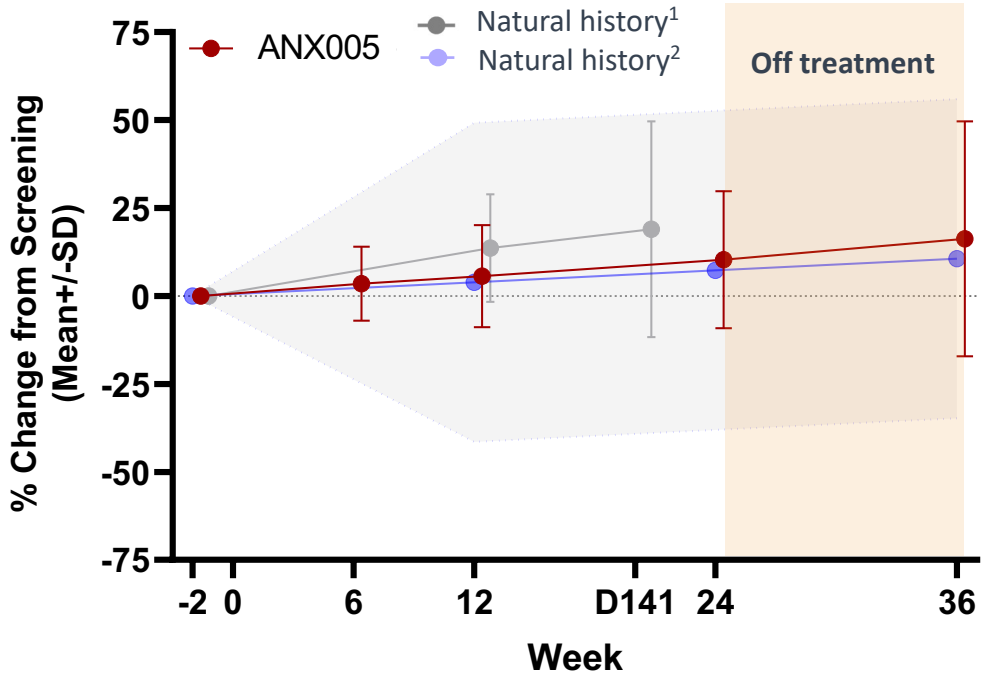
NfL Changes Stable and Consistent with Natural History Through Treatment and Follow-up Periods

Plasma NfL



[1]Interpolated data for manifest cohort; Rodriguez, et al., Sci Transl Med. 2020 12 16;12(574)

CSF NfL



[1]Tabrizi, NEJM 2019, 38:2307
[2]Interpolated from Rodrigues, et al., Sci Transl Med. 2020 12 16;12(574)

Results independent of baseline complement activity

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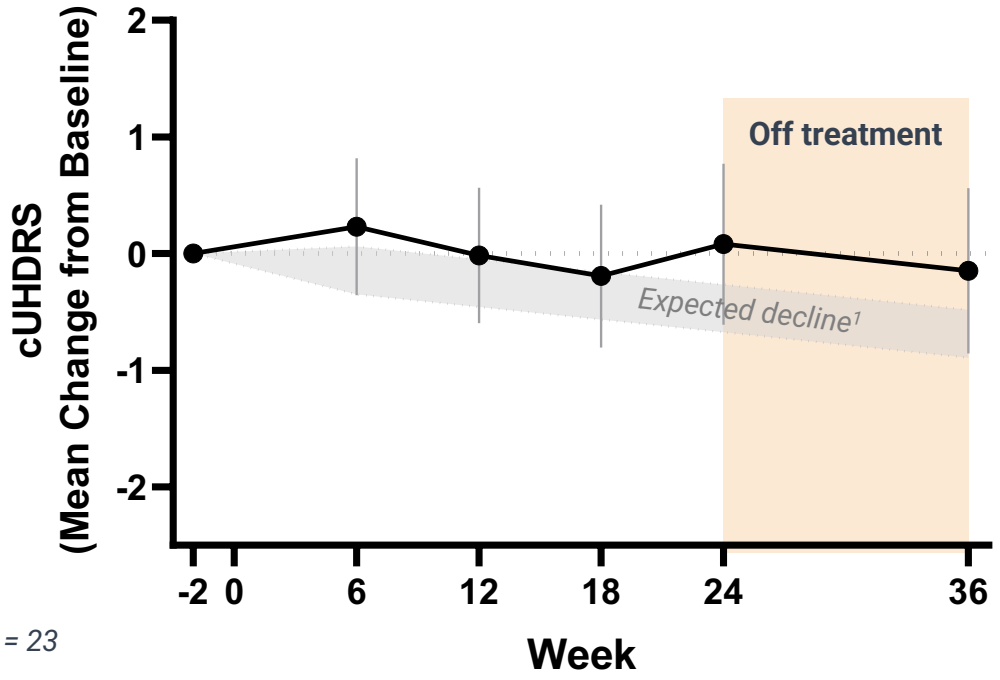
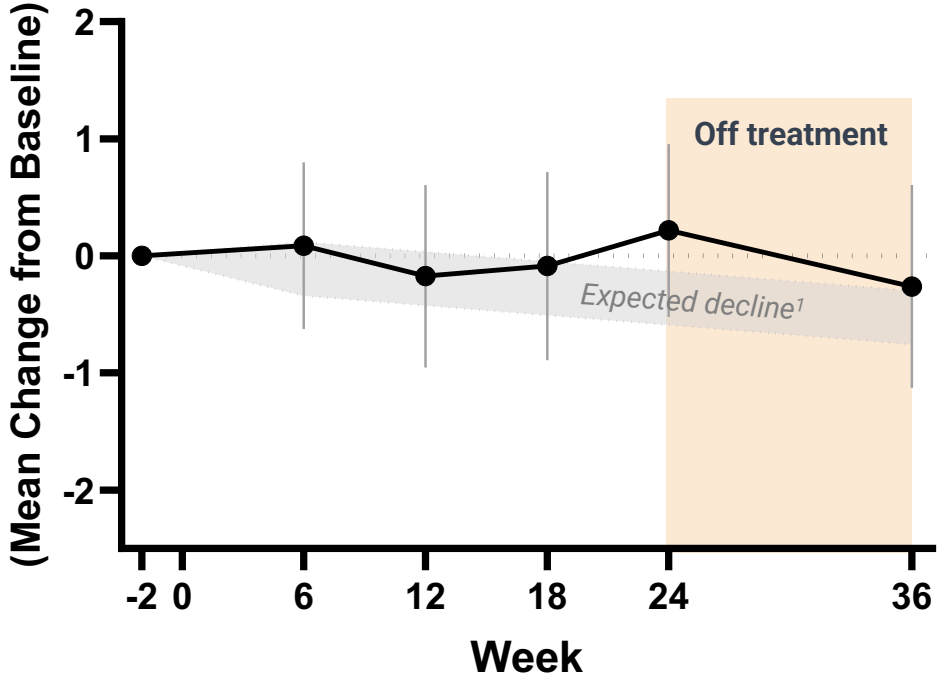
Clinical Disease Progression Stable in Overall Patient Population Through Entire 9-month Study

cUHDRS Stable Over 9 Months



N = 23

TFC Stable Over 9 Months



MMRM; LS means +/- 95% CI
[1] Expected decline = interpolated natural history from Schobel 2017 (TRACK-HD)

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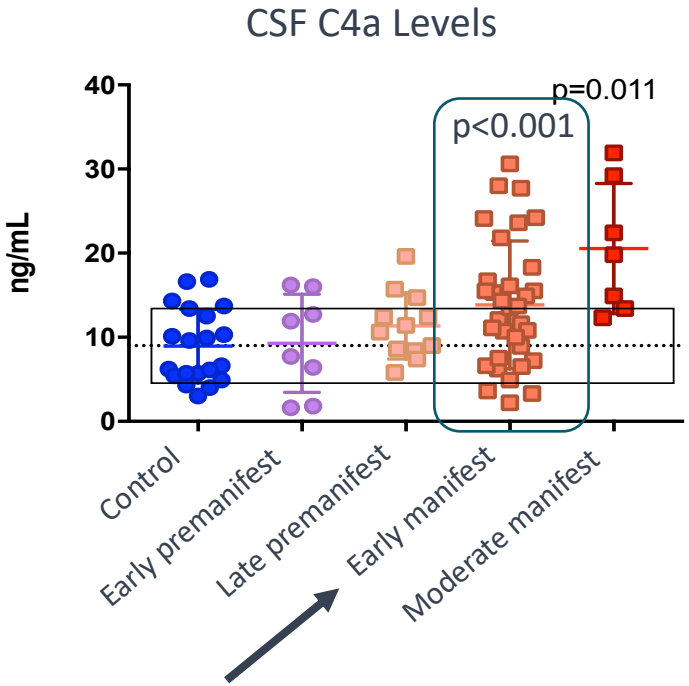
Complement Activation Correlates with Disease and Functional Decline in HD

Patients with higher baseline complement activity may uniquely respond to anti-C1q therapy

CSF C4a Elevated and Increase with HD Progression*



Early manifest consistent with patients enrolled in current study

CSF C4a Activation Correlate with HD Functional Decline

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

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

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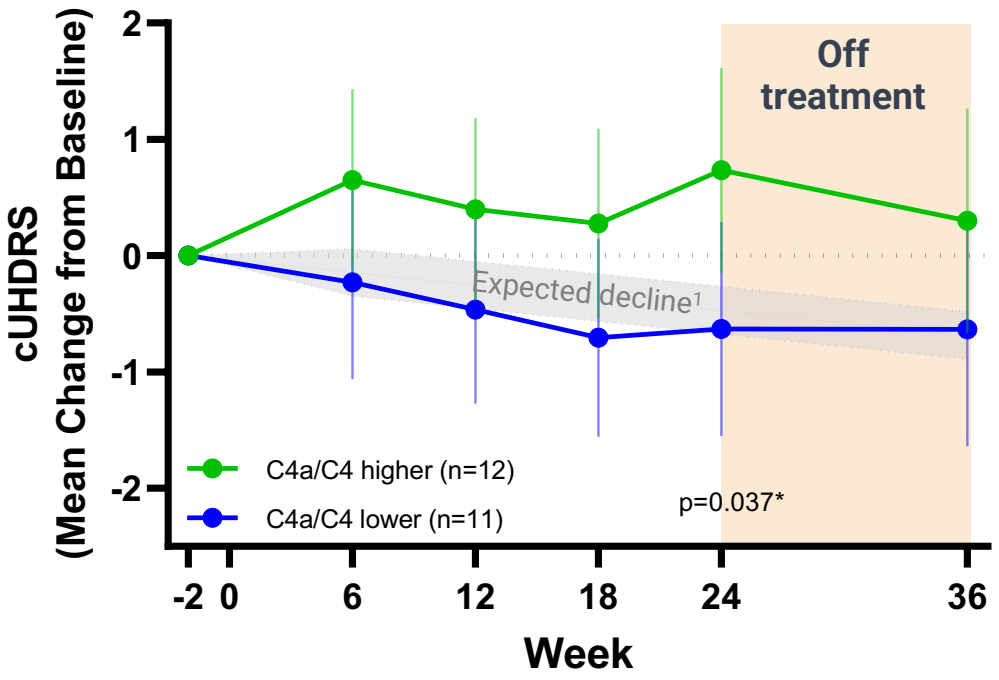
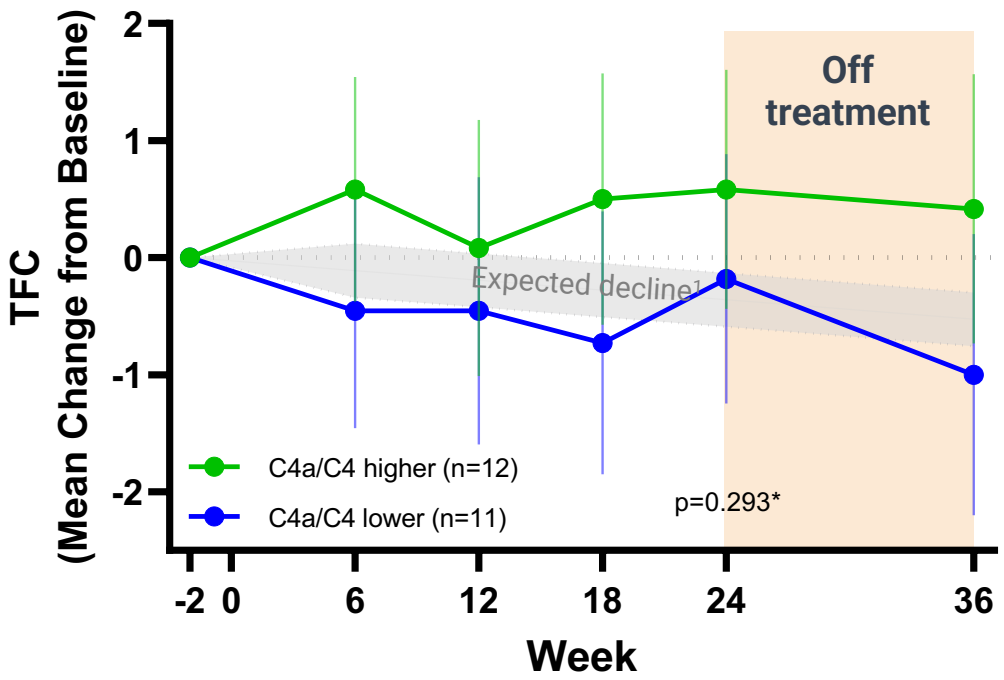
Rapid Benefit Maintained in Patients with High Baseline Complement Activity Through Treatment and Follow-up Periods

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



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



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

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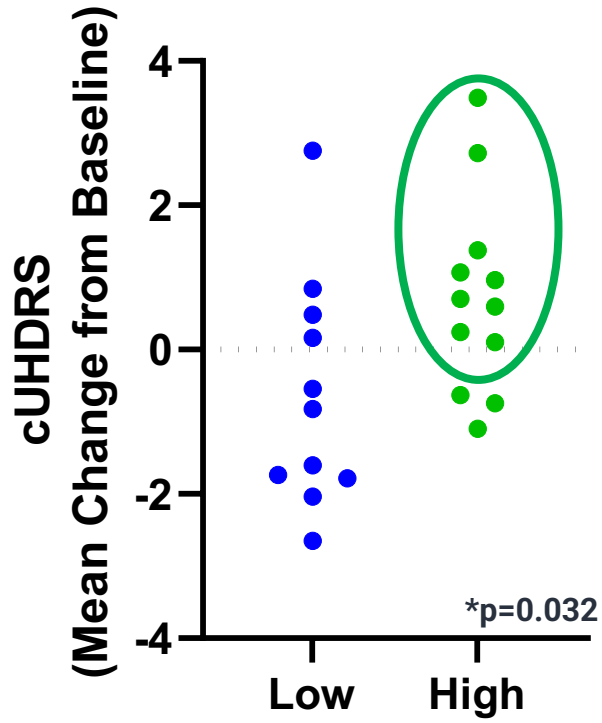
75% of Patients with High Baseline Complement Levels Showed Improvement at Week 24, Maintained at Week 36

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

Week 24 cUHDRS
Change from Baseline

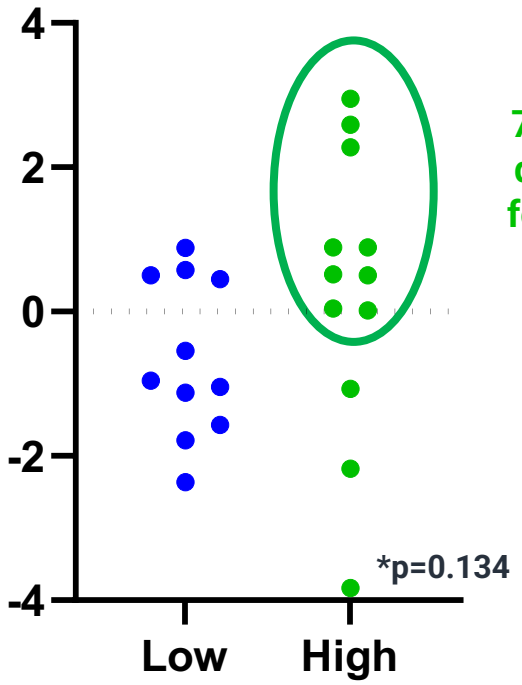


75% patients with elevated baseline complement improved (9/12)

vs.

36% with lower baseline complement (4/11)

Week 36 cUHDRS
Change from Baseline



75% maintained during 3-month follow-up period

Baseline Complement Activity (C4a/C4)

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

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Chronic Dosing of ANX005 Generally Well-Tolerated with Favorable Benefit-Risk Profile Demonstrated in HD

Treatment Emergent Adverse Events	Safety Population (N=28)	
	All Grades, N (%)	Grade 3, N (%)
Any reported TEAEs	28 (100.0)	12 (42.9)
Most Common TEAE		
Infusion Related Reactions (IRR)	28 (100.0)	8 (28.6)
Most Common TEAEs (non-IRR)	25 (89.3)	6 (21.4)
Dizziness	5 (17.9)	0 (0)
Nausea	5 (17.9)	0 (0)
Headache	4 (14.3)	0 (0)
Vomiting	4 (14.3)	0 (0)
COVID-19	4 (14.3)	0 (0)
Rash	4 (14.3)	1 (3.6)
Serious TEAEs	2 (7.1)	2 (7.1)
Related to ANX005	2 (7.1)	2 (7.1)
Infections	0 (0)	0 (0)
TEAE with Fatal Outcome	0 (0)	0 (0)

- No change in safety results from interim analysis
- IRR primarily first dose effect – none after 2nd dose
- No deaths and no serious infections observed
- Two treatment discontinuations unrelated to drug (Covid-19, consent withdrawn)
- Three treatment discontinuations potentially related to drug: all improved/resolved after drug cessation
  - One event each: idiopathic pneumonitis (SAE), systemic lupus erythematosus (SAE), asymptomatic hemolytic anemia (AE)
- All cases of treatment discontinuation had elevated ANA titers at baseline; no patients with normal ANA titers developed SAE
- Enhanced screening of ANA autoantibody levels at baseline and additional monitoring incorporated into ongoing/future trial to reduce risk in chronic ANX005 dosing protocols

No grade 4 TEAEs reported

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Promising ANX005 Phase 2 Results Support Continued Advancement in Huntington's Disease

Phase 2 HD Trial Learnings and Next Steps

- ✓ **Full C1q target engagement in blood and CSF into follow-up period**
- ✓ **Stabilized disease progression in full cohort over 9-month study**
- ✓ **Rapid clinical improvement maintained in patients with higher baseline complement activity over 9-month study**
- ✓ **Generally well-tolerated with favorable benefit-risk demonstrated in HD;** enhanced safety management approach implemented
- ✓ **First evaluation of widely-researched MOA in the clinic; increasing appreciation for preserving functioning synapses for brain health**
- ❑ Planning engagements with US and EU regulators
- ❑ Assessing opportunity to conduct well-controlled study in HD, leveraging precision medicine approach

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THANK YOU

Patients, their families and caregivers, who participate in our clinical trials

Physicians, nurses and medical staffs who share our passion for treating patients

Employees, collaborators and advisors for their constant dedication to achieving our vision

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