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High-dose AMT-130 met primary and key secondary endpoints at 36-months

Statistically-significant 75% slowing of disease based on **cUHDRS** (p=0.003)

Statistically-significant slowing of disease based on **TFC** (p=0.033)

CSF **NfL** levels **below baseline** at 36 months

Continues to be **generally welltolerated**

All data presented here in is as of the data cut off date of June 30, 2025, unless otherwise indicated
Abbreviations: cUHDRS, composite Unified Huntington's Disease Rating Scale; TFC total functional capacity, CSF, Cerebrospinal fluid; NfL Neurofilament light chain
References: Data on file. September 2025

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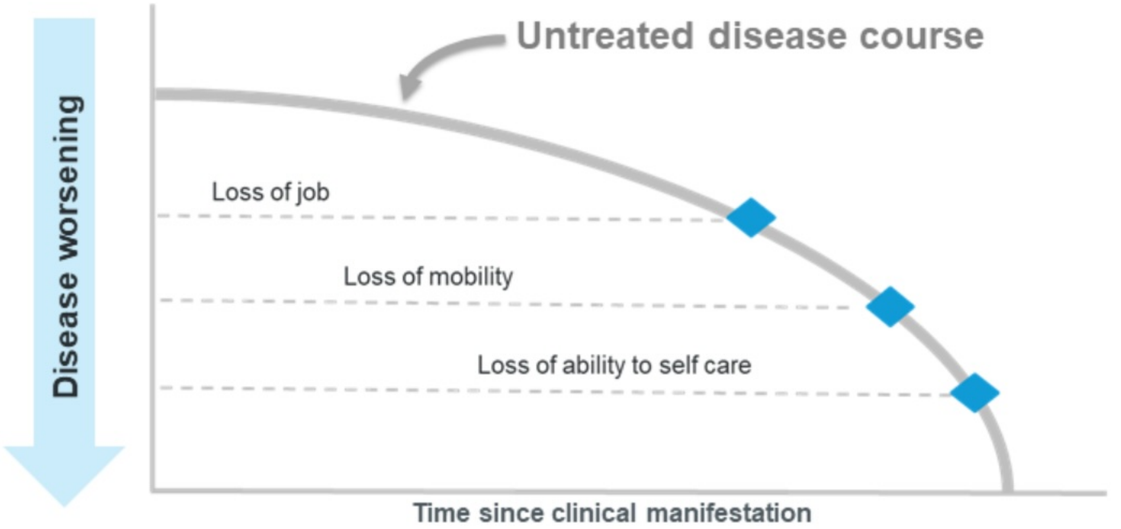
Slowing progression of Huntington's disease could extend patients' quality of life

HD is a progressive neurodegenerative disease with **no disease-modifying treatments available.**

AMT-130 aims…

1. To **slow the rate of disease progression**
2. To provide HD patients with an **improved quality of life**



Abbreviations: HD, Huntington's Disease.

References: Ross CA, *et al. Nat Rev Neurol.* 2014; 10(4): 204-16.

AMT-130: A potential first disease modifying treatment for HD

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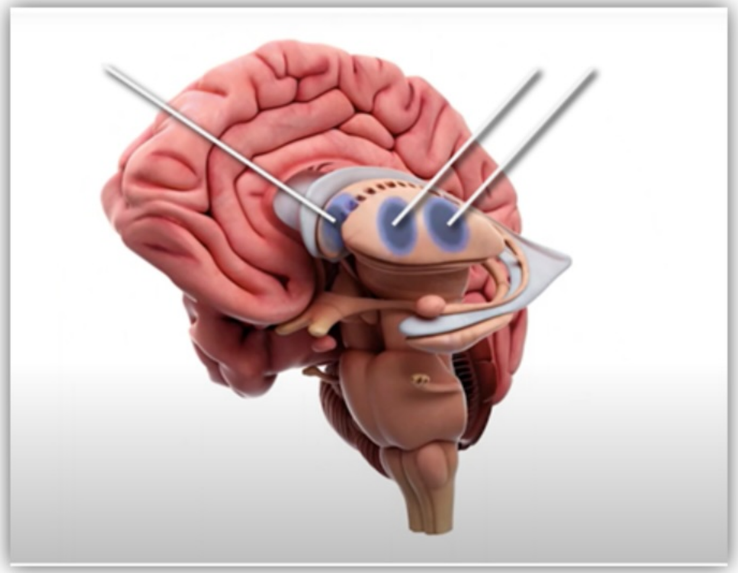
The construct design and targeted administration of AMT-130 provide key advantages

Key AMT-130 Attributes:

- **One-time administration** with potentially **long-term effects**
- **Precision-delivery** directly to diseased areas of the brain
- **Minimizes systemic exposure** of drug
- Suppresses both **HTT** and the **highly toxic exon-1 isoform**
- Standard stereotactic **procedure can be broadly performed**



Abbreviations: HD, Huntington's Disease; HTT, Huntingtin protein.
References. Data on file. September 2025

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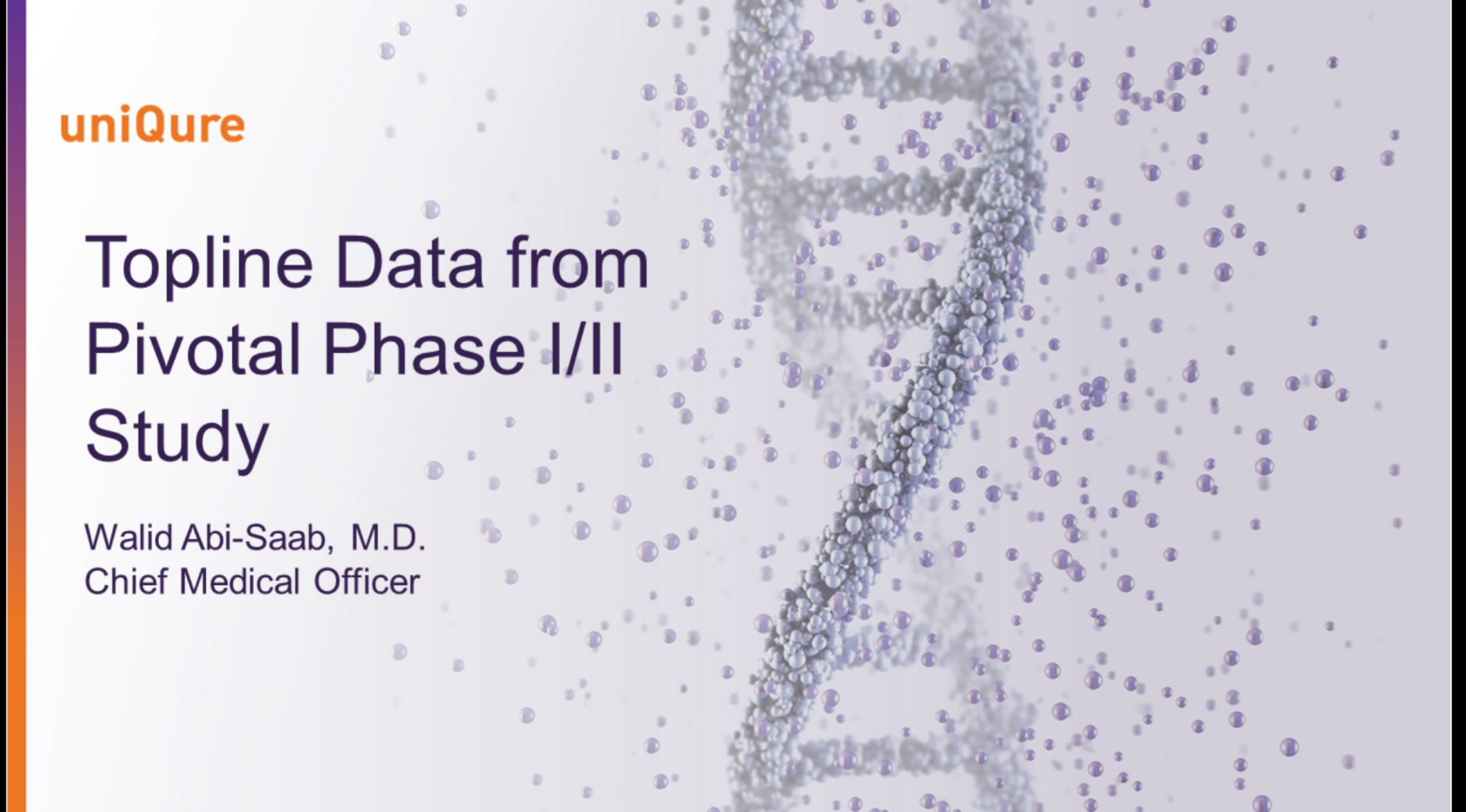
Topline Data from Pivotal Phase I/II Study

Walid Abi-Saab, M.D.
Chief Medical Officer



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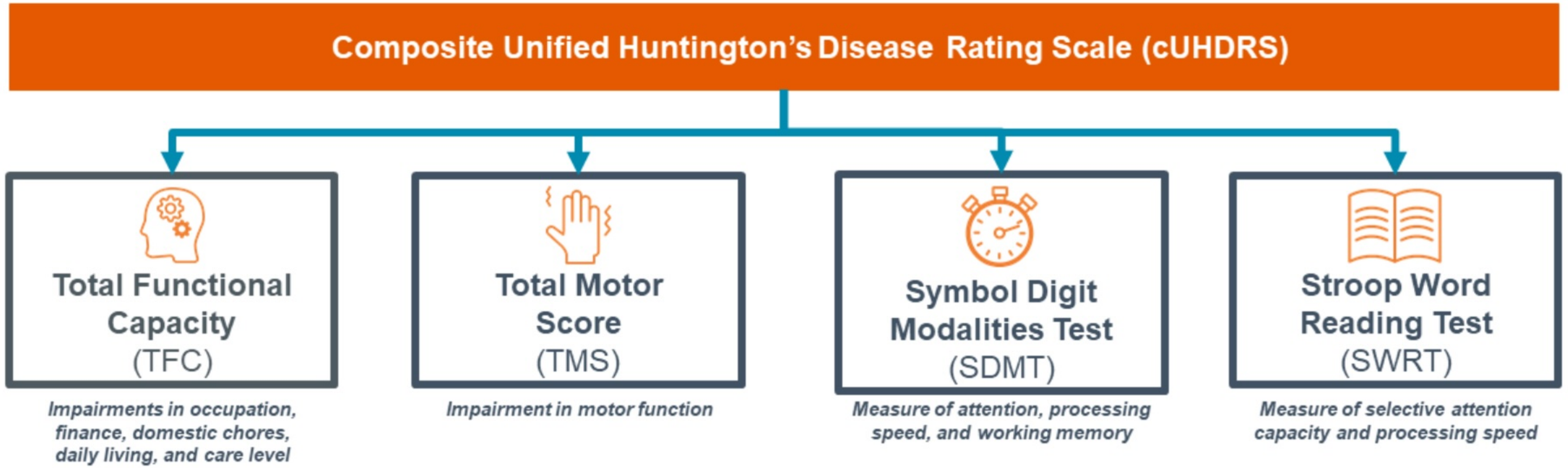
The Composite Unified Huntington's Disease Rating Scale is a widely used efficacy outcome measure



References Neurology 2017;89:2495–2502

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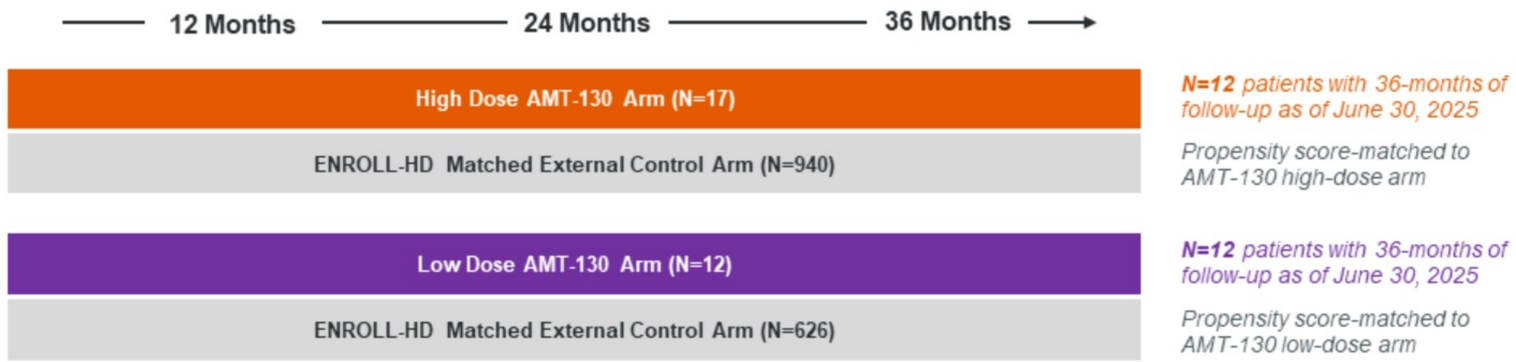
Pivotal Phase I/II Study of AMT-130

Prespecified statistical analysis plan

Prespecified statistical analysis plan was **aligned with and submitted** to the FDA in advance of database lock



PRIMARY ENDPOINT	• **Composite Unified Huntington's Disease Rating Scale (cUHDRS)**	Change from baseline at 36-months vs Enroll-HD propensity score-matched external control
SECONDARY ENDPOINTS	• **Total Functional Capacity (TFC)** • **Symbol Digit Modalities Test (SDMT)** • **Stroop Word Reading Test (SWRT)** • **Total Motor Score (TMS)**	
SUPPORTIVE ENDPOINT	• **Cerebrospinal fluid (CSF) Neurofilament light chain (NfL)** change from baseline at 36-months	

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Demographic and baseline characteristics of high-dose cohort

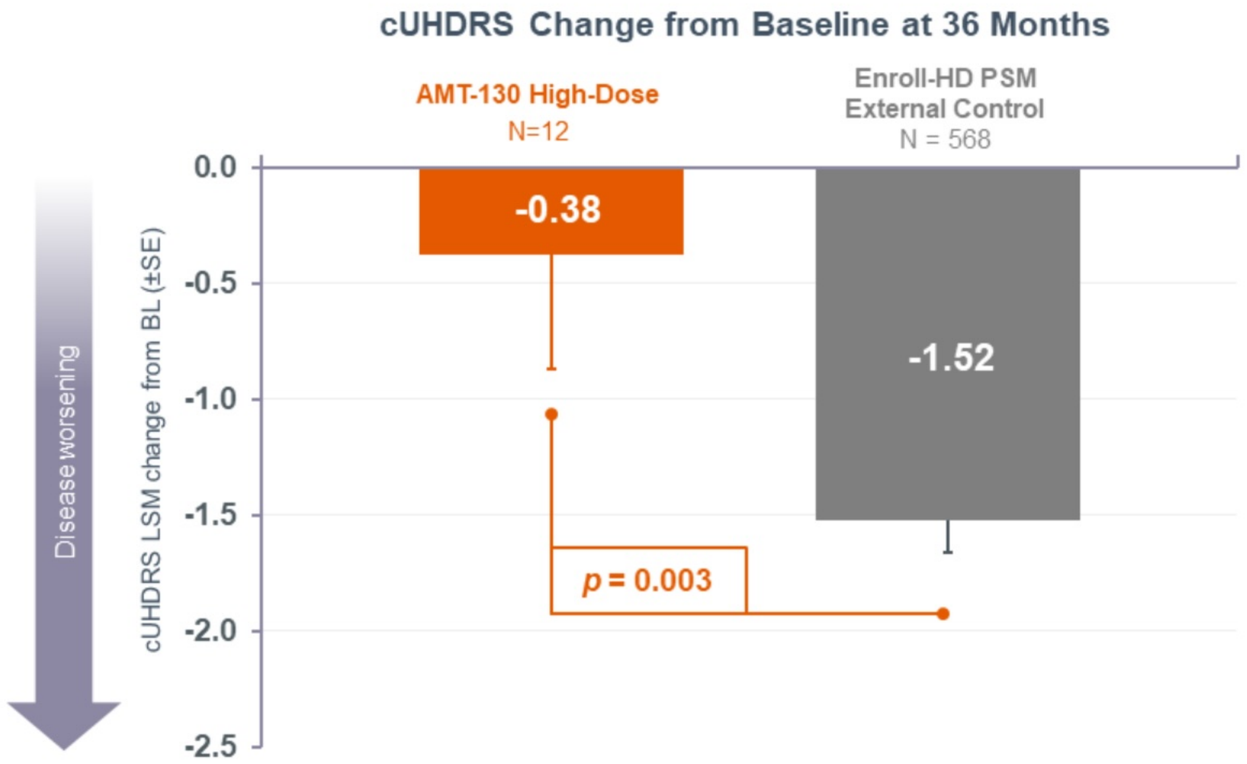
The propensity score-matched external control has **well-matched baseline characteristics** to the patients treated with high-dose AMT-130.

Demographics and Baseline Disease Characteristics Mean (SD)	**AMT-130 High-Dose (N=17)**	**PSM External Control (Enroll-HD) (N=940)**
Sex, Males (%)	47.1	55.6
Age	45.8	45.2
CAG repeats	42.4	42.8
CAP100 score	86.2	86.8
DCL = 3, 4 (%)	35.3, 64.7	30.5, 69.5
PIN Score	0.77	0.81
cUHDRS	14.9	14.7
TFC	12.2	12.1
SDMT	46.1	45.3
SWRT	89.9	87.6
TMS	12.1	11.6
HD-ISS Stage 2, 3 (%)	47.1, 52.9	51.6, 48.4
Region; No. America, Other (%)	58.8, 41.2	28.9, 71.1

Abbreviations: CAG, cytosine-adenine-guanine; CAP, CAG-Age-Product; cUHDRS, composite Unified Huntington's Disease Rating Scale; DCL, diagnostic confidence level; PIN, Prognostic Index; TFC, Total Function Capacity; SDMT, symbol digit modalities test; SWRT, Stroop word reading test; TMS, total motor score; HD-ISS, Huntington's disease Integrated Staging System; SD, standard deviation
References: Data on file. September 2025.

uniQure Study met primary endpoint of cUHDRS at 36 months

AMT-130 high-dose **significantly reduced HD progression by 75% based on cUHDRS** at 36 months

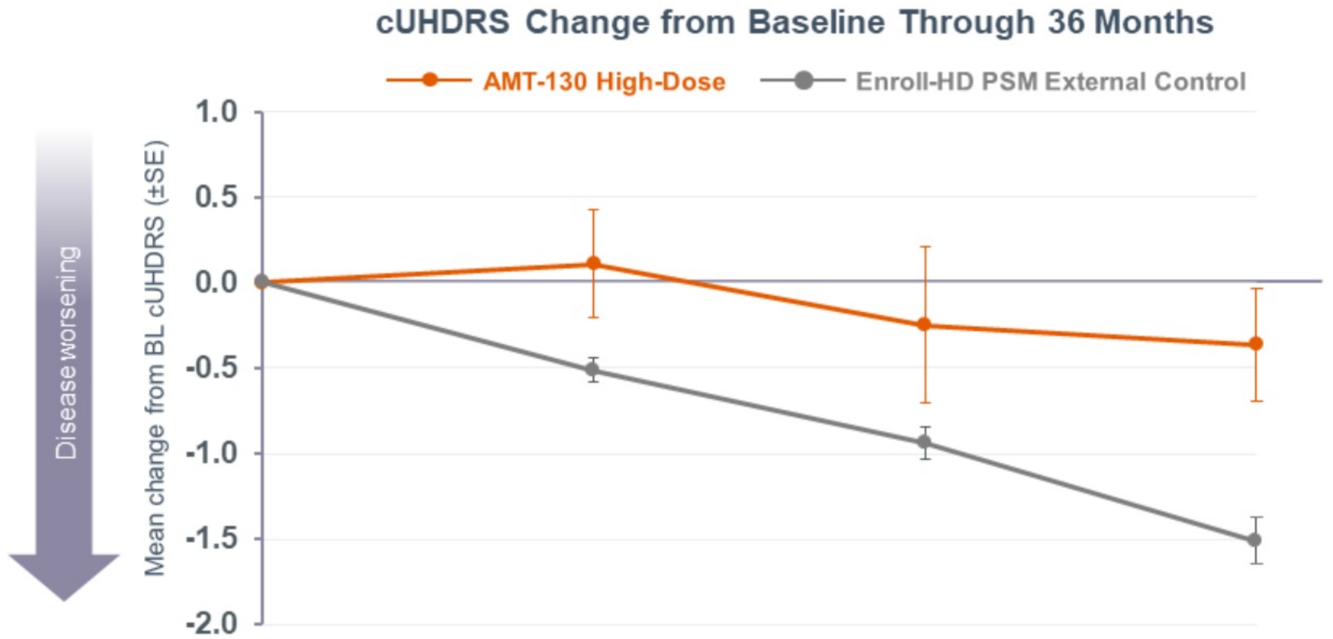


Participants	Baseline	36 months
AMT-130 High-Dose	17	12
PSM External Control	940	568

Abbreviations: cUHDRS, composite Unified Huntington's Disease Rating Scale; HD, Huntington's disease, SE, standard error; PSM, propensity score-matched; LSM, least squares mean; BL, baseline
References: Data on file. September 2025

uniQure Study met primary endpoint of cUHDRS at 36 months

AMT-130 high-dose **significantly reduced HD progression by 75% based on cUHDRS** at 36 months



Participants	Baseline	12 months	24 months	36 months
AMT-130 High-Dose	17	17	15	12
PSM External Control	940	715	586	568

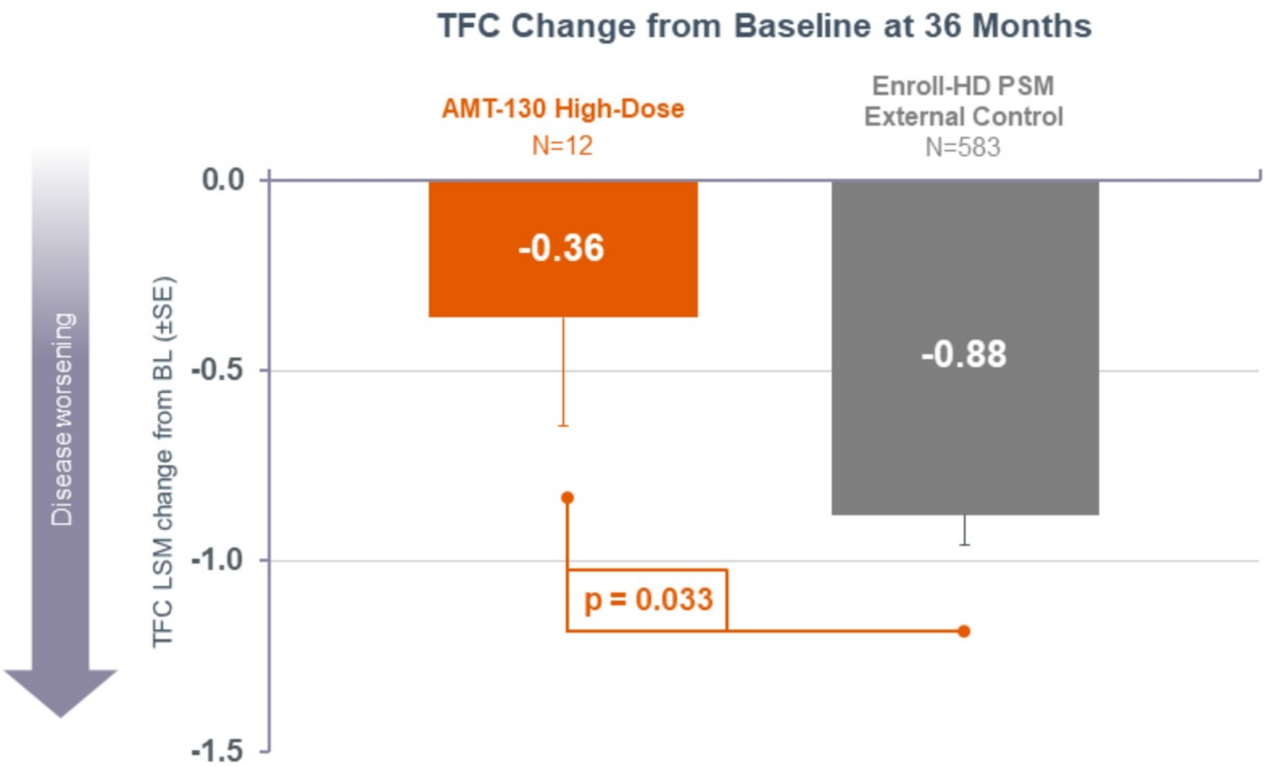
Above graph represents observed data

Abbreviations: cUHDRS, composite Unified Huntington's Disease Rating Scale; HD, Huntington's disease; SE, standard error; PSM, propensity score-matched; BL, baseline

References: Data on file. September 2025

uniQure Study met key secondary endpoint of TFC at 36 months

AMT-130 high-dose **significantly reduced HD progression by 60% based on TFC** at 36 months

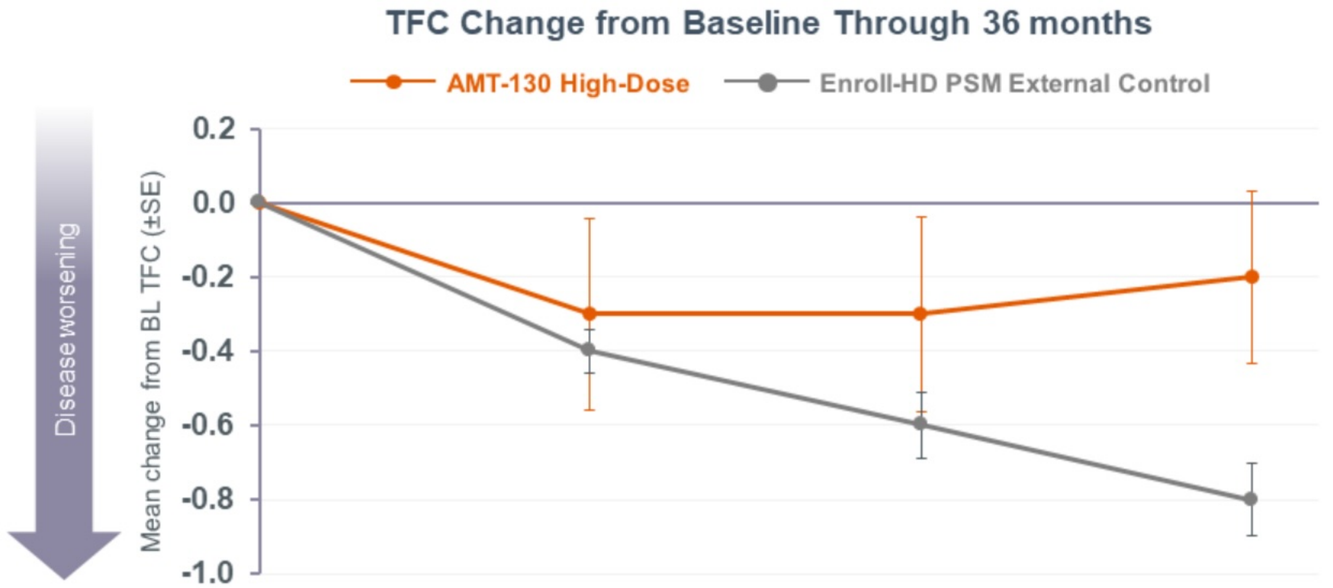


Participants	Baseline	36 months
AMT-130 High-Dose	17	12
PSM External Control	940	583

Abbreviations: TFC, Total Functional Capacity; HD, Huntington's disease; SE, standard error; LSM, least squares mean; BL, baseline; PSM, propensity score-matched
References: Data on file. September 2025.

uniQure Study met key secondary endpoint of TFC at 36 months

AMT-130 high-dose **significantly reduced HD progression by 60% based on TFC** at 36 months



Participants	Baseline	12 months	24 months	36 months
AMT-130 High-Dose	17	17	15	12
PSM External Control	940	725	597	583

Above graph represents observed data

Abbreviations: TFC, Total Functional Capacity; HD, Huntington's disease; SE, standard error; PSM, propensity score-matched; BL, baseline

References: Data on file. September 2025.

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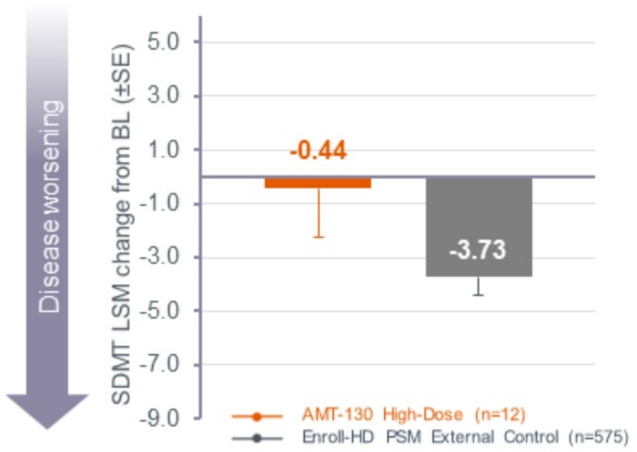
Other Secondary Endpoints: High-dose AMT-130 showed favorable trends across other key clinical subdomains

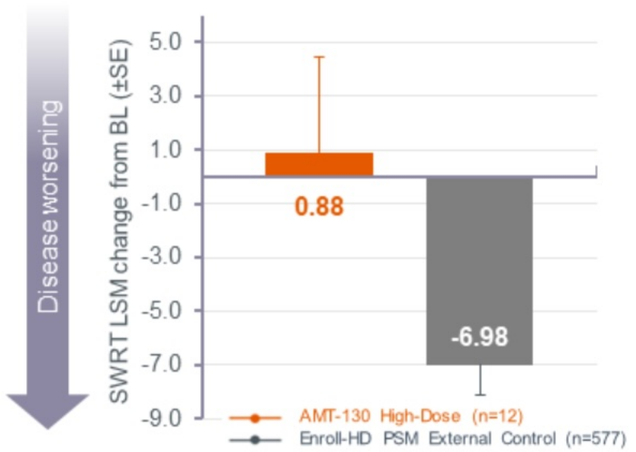
AMT-130 high-dose showed trends supportive of disease slowing **across all other clinical subdomains of cUHDRS**

SDMT Change from Baseline at 36 Months



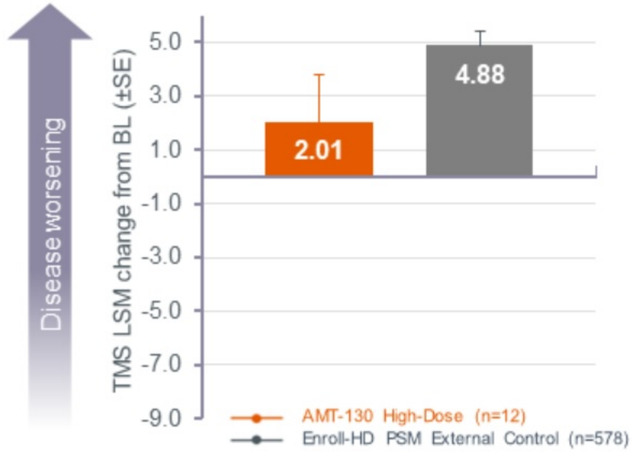
Reduced HD progression by 88% based on SDMT
at 36 months (p=0.057)

SWRT Change from Baseline at 36 Months



Reduced HD progression by 113% based on SWRT
at 36 months (p=0.002*)

TMS Change from Baseline at 36 Months



Reduced HD progression by 59% based on TMS
at 36 months (p=0.174*)

Abbreviations: cUHDRS, composite Unified Huntington's Disease Rating Scale; SDMT, Symbol Digit Modalities Test; SWRT, Stroop Word Reading Test; TMS, Total Motor Score; PMS, propensity score-matched; LSM, least squares mean; BL, baseline; SE, standard error

References: Data on file. September 2025; * P-value is nominal

uniQure Low-dose AMT-130 results at 36-months

Patients receiving low-dose AMT-130 showed variable trends in functional, motor and cognitive endpoints, suggestive of a **dose-dependent effect**

Low-Dose	AMT-130 Low-Dose (N=12) LSM Change (SE)	Enroll-HD PSM External Control LSM Change (SE)	LSM Difference in Change from Baseline, AMT-130 vs. Enroll-HD PSM External Control Mean [95% CI]	Slowing of Disease Progression (%)	P-value
cUHDRS	-1.65 (0.411)	-1.72 (0.151) N=383	0.07 [-0.75, 0.88]	3.9	0.871∞
TFC	-0.33 (0.296)	-1.04 (0.120) N=392	0.71 [0.12, 1.31]	68.1	0.019 ∞
SDMT	-6.44 (1.532)	-3.35 (0.503) N=387	-3.09 [-6.14, -0.05]	-92.3	0.046 ∞
SWRT	-3.67 (4.134)	-5.20 (1.373) N=387	1.44 [-7.45, 10.33]	27.7	0.751 ∞
TMS	8.64 (2.039)	5.61 (0.688) N=392	3.02 [-1.23, 7.28]	-53.9	0.163 ∞

∞ P-value is nominal; hierarchical testing was discontinued for p-value >0.05

Abbreviations: cUHDRS, composite Unified Huntington's Disease Rating Scale; TFC, Total Functional Capacity; SDMT, Symbol Digit Reading Modalities Test; SWRT, Stroop Word Reading Test; TMS, Total Motor Score; LSM, least squares mean; PMS; propensity score-matched; SE, standard error; CFB, change from baseline

References: Data on file. September 2025

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Natural history data show NfL levels correlate with the severity of Huntington's Disease

An independent study has confirmed a **strong association between CSF NfL levels and the clinical severity of HD**

The study demonstrated early-manifest HD patients will experience **increases in CSF NfL of ~10% to 15% per year**

Recent data from HD-CSF study where CSF NfL levels were measured in 71 patients over a two-year period showed an increase over time and a sigmoid trajectory with age.

Relationship Between NfL and Age in HD

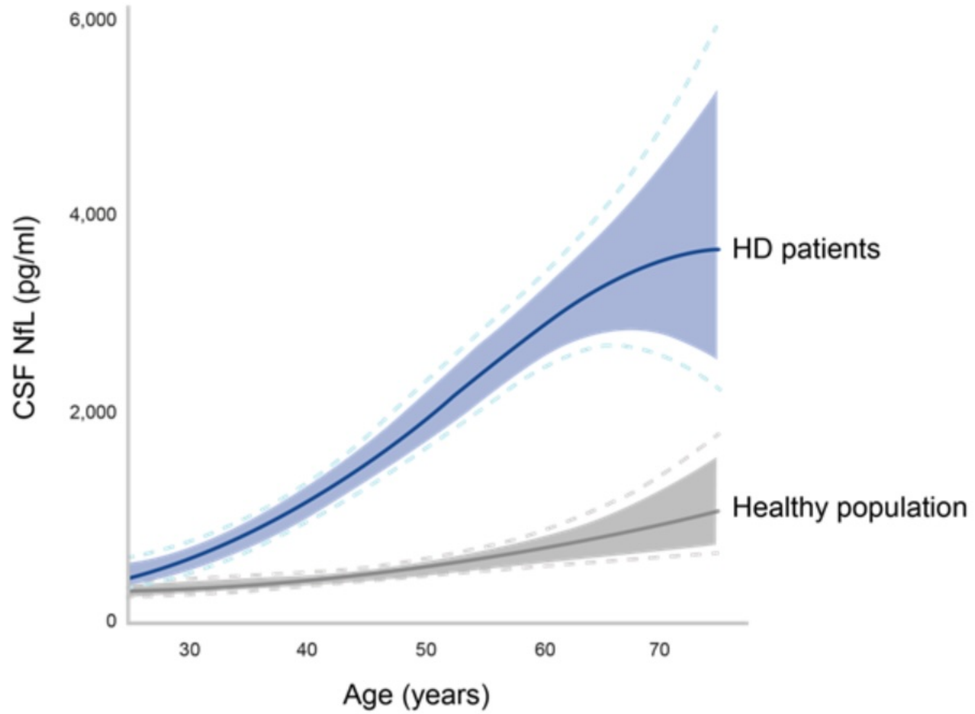
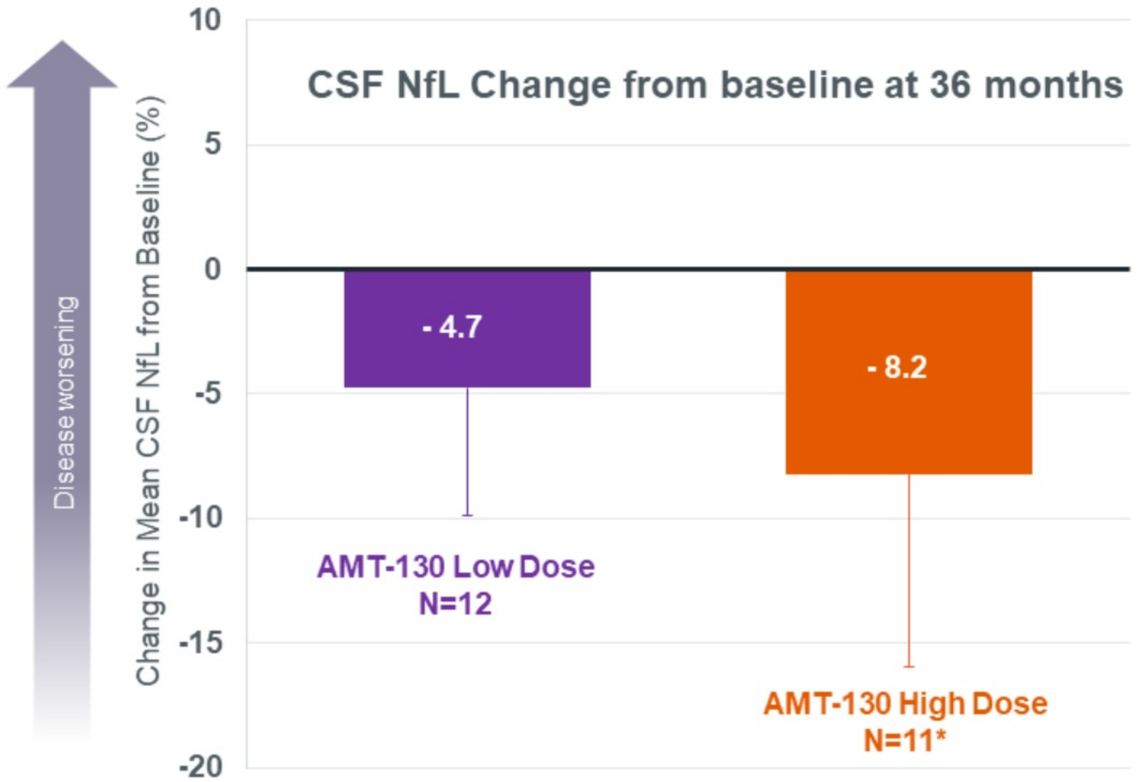


Image reproduced and modified from Rodrigues et al. Sci. Transl. Med. 2021

Abbreviations: CSF, cerebrospinal fluid; NfL, neurofilament light chain; HD, Huntington's Disease.
References: Rodrigues et al. *Sci Transl Med* 2021, Dr. Ed Wild, personal communication

uniQure AMT-130 demonstrated reductions of CSF NfL at 36 months

AMT-130 high dose **demonstrated a reduction of CSF NfL at 36 months vs. baseline.**



*1 of 12 patients declined to undergo a lumbar puncture procedure
Abbreviations: CSF, cerebrospinal fluid; NfL, neurofilament light chain
References: Data on file. September 2025.

uniQure AMT-130 remained generally well-tolerated

AMT-130 remained **generally well-tolerated**, with a **manageable safety profile** at both doses

The **majority** of drug-related serious adverse events occurred within the **first weeks** post treatment and **fully resolved** with steroids or palliative care

No new drug-related serious adverse events have been observed since **December of 2022**

References: Data on file. September 2025.

uniQure AMT-130 remained generally well-tolerated

	Sham Surgery (n=10)		Low-dose AMT-130 (Cohort 1) (n=13[&])		High-dose AMT-130 (Cohort 2) (n=20[&])		Dose -Blinded (Cohort 3) (n= 12)		All AMT-130 (Cohorts 1, 2 and 3) (n=45[&])	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Any TEAEs	10	100.0	12	92.3	20	100.0	12	100	44	97.8
Any SAEs	1	10.0	3	23.1	9	45.0	3	25	15	33.3
Any SAEs (peri-operative)	1	10.0	2	15.4	6	30.0	0	0.0	8	17.8
Any Drug-Related TEAE	0	0.0	0	0.0	6	30.0	3	25.0	9	20.0
Any Drug-Related SAE	0	0.0	0	0.0	4	20.0	0	0.0	4	8.8
Most Common TEAEs (≥30% in at least one group)										
Headache	3	30.0	3	23.1	9	45.0	6	50.0	18	40.0
Procedural headache	5	50.0	4	30.8	10	50.0	2	16.7	16	35.6
Procedural pain	6	60.0	2	15.4	7	35.0	2	16.7	11	24.4
Post lumbar puncture syndrome	6	60.0	2	15.4	5	25.0	2	16.7	10	22.2
Procedural complication	4	40.0	4	30.8	5	25.0	0	0.0	9	20.0
Anxiety	0	0.0	0	0.0	4	20.0	4	33.3	8	17.8
Constipation	0	0.0	0	0.0	2	10.0	6	50.0	8	17.8
Insomnia	0	0.0	1	7.7	1	5.0	6	50.0	8	17.8
Back pain	1	10.0	0	0.0	0	0.0	5	41.7	5	11.1

AE, adverse event; N, number of patients; TEAE, treatment-emergent adverse event; SAE, serious adverse event. TEAEs are defined as AEs after Day 0. Perioperative AEs had onset Day 0 to 13. ***Safety data as of June 30, 2025; [&]1 low dose and 3 high dose cross-over patients included***

uniQure Regulatory next steps

4Q 25 - Hold pre-BLA meeting with the FDA

1Q 26 - Expected BLA submission for AMT-130 with a request for priority review

Abbreviations: FDA, Food & Drug Administration; BLA, Biologics License Application.

uniQure Positive topline data from pivotal Phase I/II study

High-dose AMT-130 met its primary and key secondary endpoints at 36 months, with favorable trends observed across additional clinical and supportive endpoints

1. Statistically-significant **75%** slowing of disease progression based on **cUHDRS**
2. Statistically-significant slowing of disease progression based on **TFC**
3. Favorable **trends in disease slowing observed across all other clinical subdomains** of cUHDRS
4. CSF **NfL below baseline**
5. Results from **sensitivity analyses were generally consistent** with the primary statistical analysis
6. Continued to be **generally well tolerated** with manageable safety profile; **no new treatment-related SAEs**

Abbreviations: cUHDRS, composite Unified Huntington's Disease Rating Scale; TFC, total functional capacity, CSF, cerebrospinal fluid; NfL, neurofilament light chain, SAE, serious adverse events

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Key Opinion Leader Perspective

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