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Pivotal Phase I/II AMT-130 Huntington's Disease Update

September 24, 2025

uniQure Disclaimer

This presentation 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. All statements other than statements of historical fact are forward-looking statements, which are often indicated by terms such as “anticipate,” “believe,” “could,” “estimate,” “expect,” “goal,” “intend,” “look forward to,” “may,” “plan,” “potential,” “predict,” “project,” “should,” "will,” “would” and similar expressions and the negatives of those terms. Forward-looking statements are based on management's beliefs and assumptions and on information available to management only as of the date of this presentation. Examples of these forward-looking statements include, but are not limited to, statements concerning: the timing of our planned meeting and discussions with regulatory authorities, including with respect to the anticipated pre-BLA meeting for AMT-130; our plans to submit a BLA for AMT-130 in the first quarter of 2026; our ability to continue accumulating long-term patient data; the potential clinical and functional effects of AMT-130; the potential for accelerated regulatory pathways, including priority review, for AMT-130; our enrollment of a fourth cohort studying AMT-130 in patients with higher striatal volumes compared to patients in prior cohorts; the utility of NfL in CSF as an effective biomarker and indicator of clinical severity; and the potential commercialization of AMT-130 and statements related thereto, including our potential addressable market and potential treatment centers. Because these statements are subject to risks and uncertainties, our actual results could differ materially from those expressed in these forward-looking statements. These risks and uncertainties include, among others: risks related to our clinical trials of AMT-130, including the risk that such trials will be unable to demonstrate data sufficient to support further clinical development and the risk that interim or topline data from the trials may not be predictive of later data readouts; risks related to our planned interactions with regulatory authorities, which may affect the initiation, timing and progress of clinical trials and pathways to regulatory approval; whether the measurements that we are evaluating continue to be viewed as robust and sensitive measurements of disease progression; whether Regenerative Medicine Advance Therapy designation, Breakthrough Therapy designation, or any accelerated pathway, if granted, will lead to regulatory approval; our ability to conduct and fund a Phase III or confirmatory study for AMT-130 if needed; our ability to continue to build and maintain the infrastructure and personnel needed to achieve our goals; our effectiveness in managing current and future clinical trials and regulatory processes; our ability to demonstrate the therapeutic benefits of our gene therapy candidates in clinical trials; the continued development and acceptance of gene therapies; our ability to obtain, maintain and protect our intellectual property; and our ability to fund our operations and to raise additional capital as needed and on acceptable terms. These and other risks and uncertainties are described more fully under the heading “Risk Factors” in our periodic filings with the U.S. Securities and Exchange Commission (“SEC”), including in our Annual Report on Form 10-K filed with the SEC on February 27, 2025, our Quarterly Reports on Form 10-Q filed with the SEC on May 9, 2025 and July 29, 2025, and other filings that we make with the SEC from time to time.

Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements and, except as required by law, we assume no obligation to update these forward-looking statements to reflect events that occur or circumstances that exist after the date on which they were made.

The ongoing Phase I/II AMT-130 clinical trials, from which the data herein are derived, are supplemented by two additional protocols, each with a statistical plan that was discussed with and submitted to the FDA. The new protocols, among other things, provide for the pooling of data across the ongoing U.S. and EU studies, and also prespecified the pivotal comparison of AMT-130 clinical end points compared to a propensity score-matched external control from the Enroll-HD natural history data set.

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third -party sources. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

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Opening Remarks

Matt Kapusta
Chief Executive Officer

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

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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 well-tolerated**

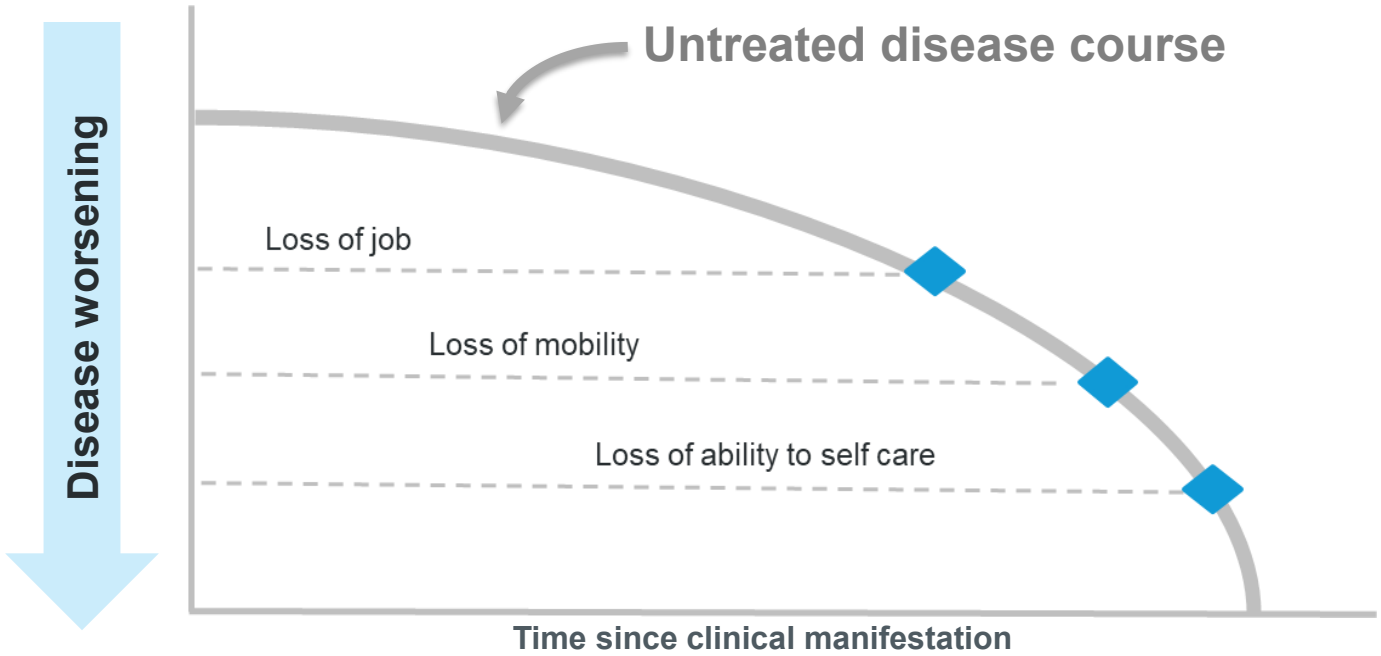
All data presented here in is as of the data cut off date of June 30, 2025, unless otherwise indicated
Abbreviations: cUHDRS, composite Unified Huntington's Disease Rating Scale; TFC total functional capacity, CSF, Cerebrospinal fluid; NfL Neurofilament light chain
References: Data on file. September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

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**



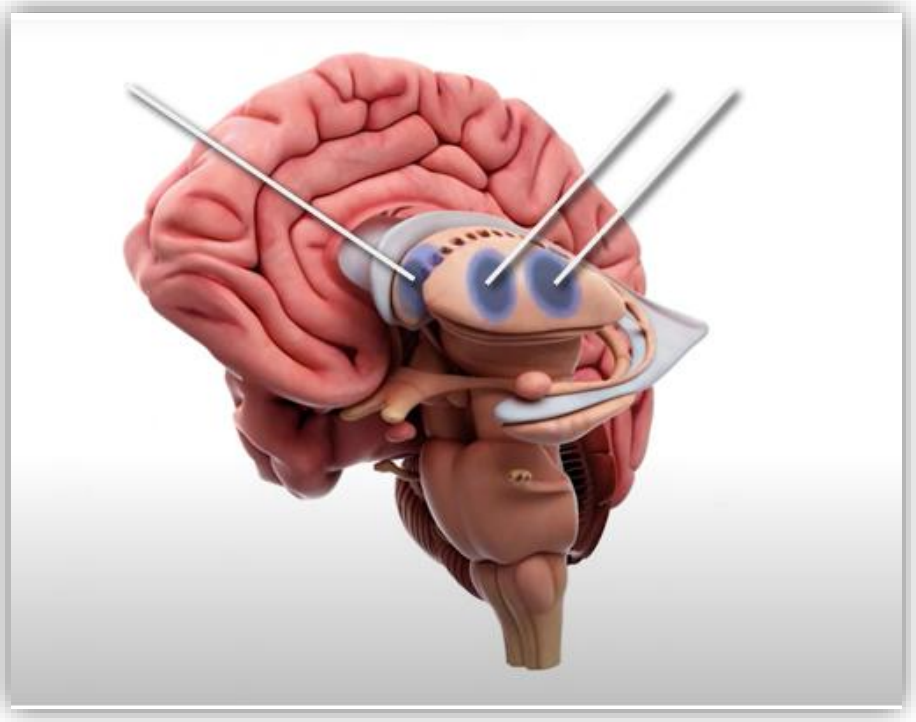
Abbreviations: HD, Huntington's Disease.
References: Ross CA, *et al. Nat Rev Neurol*. 2014; 10(4): 204-16.

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

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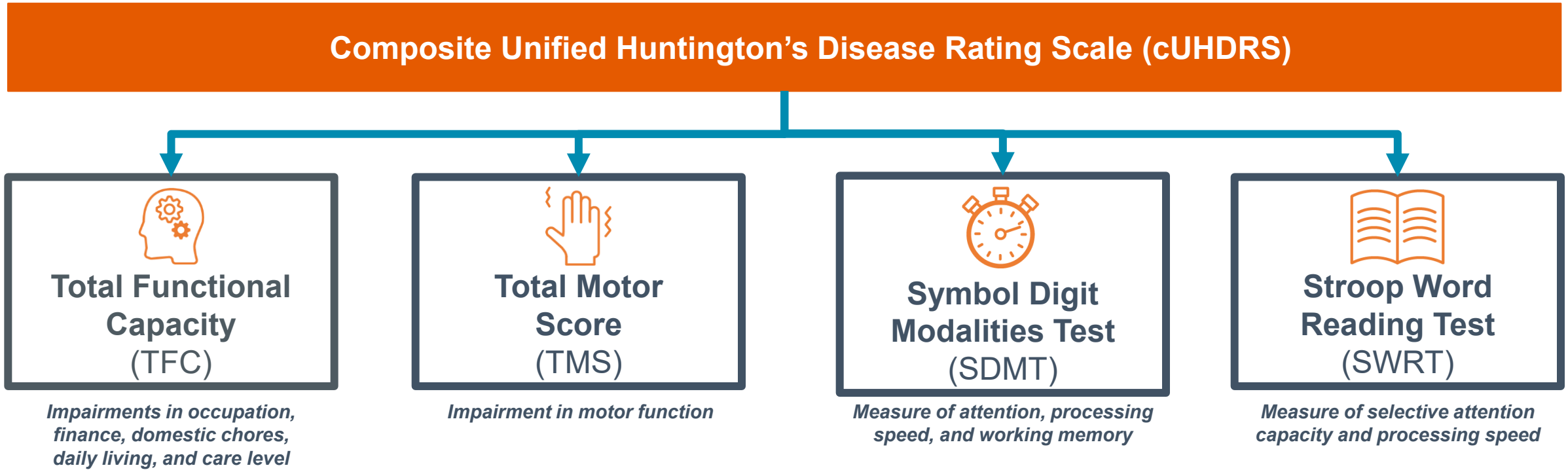
The Composite Unified Huntington's Disease Rating Scale is a widely used efficacy outcome measure

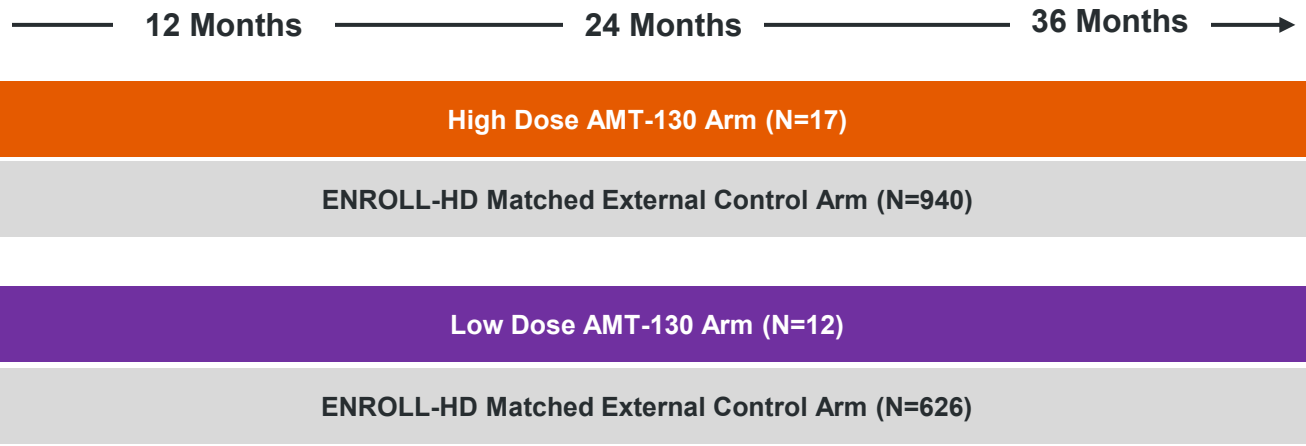


References Neurology 2017;89:2495–2502

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



***N=12** patients with 36-months of follow-up as of June 30, 2025*

Propensity score-matched to AMT-130 high-dose arm

***N=12** patients with 36-months of follow-up as of June 30, 2025*

Propensity score-matched to AMT-130 low-dose arm

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	

uniQure 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.

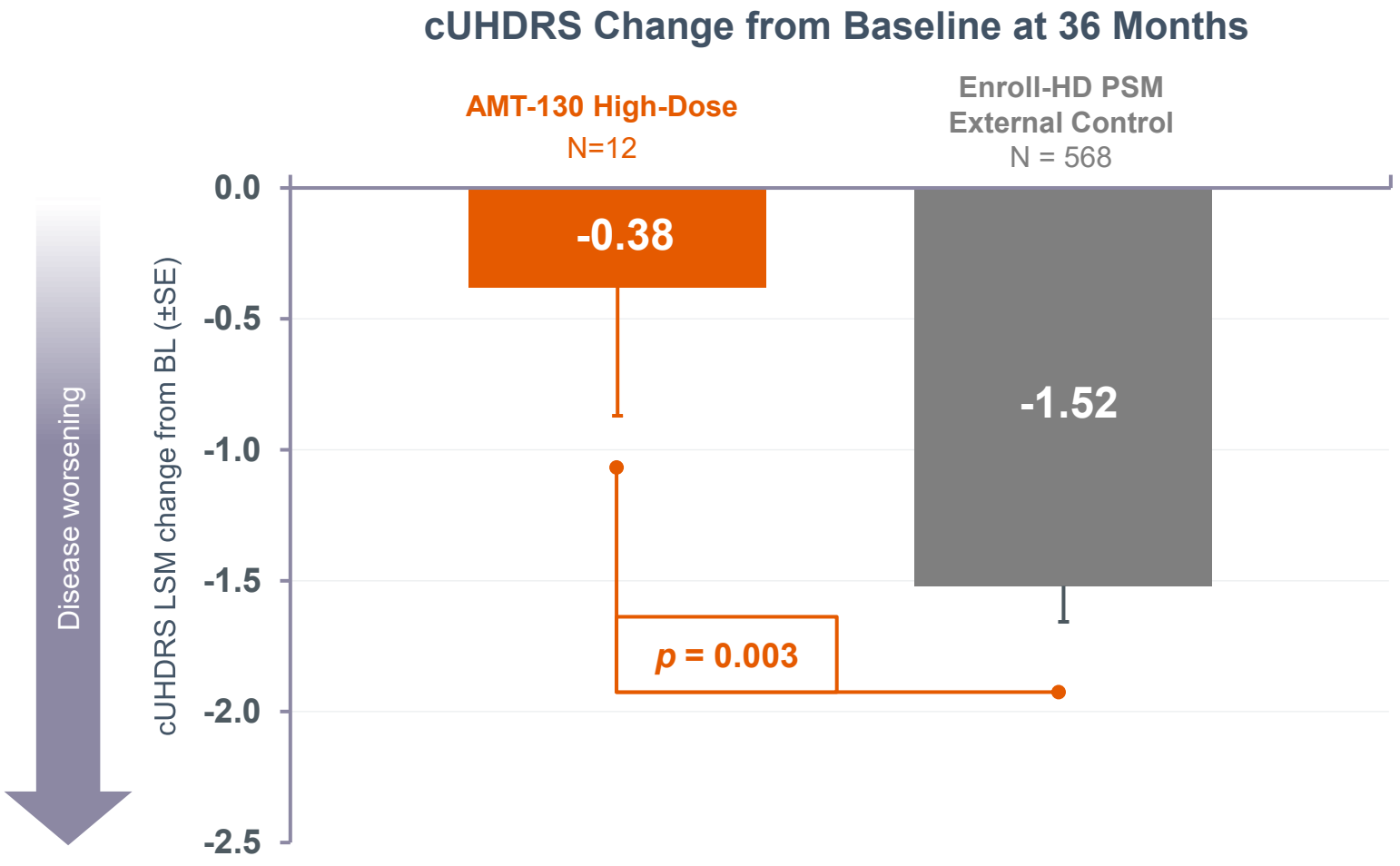
Demographics and Baseline Disease Characteristics Mean (SD)	**AMT-130 High-Dose (N=17)**	**PSM External Control (Enroll-HD) (N=940)**
Sex, Males (%)	47.1	55.6
Age	45.8	45.2
CAG repeats	42.4	42.8
CAP100 score	86.2	86.8
DCL = 3, 4 (%)	35.3, 64.7	30.5, 69.5
PIN Score	0.77	0.81
cUHDRS	14.9	14.7
TFC	12.2	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

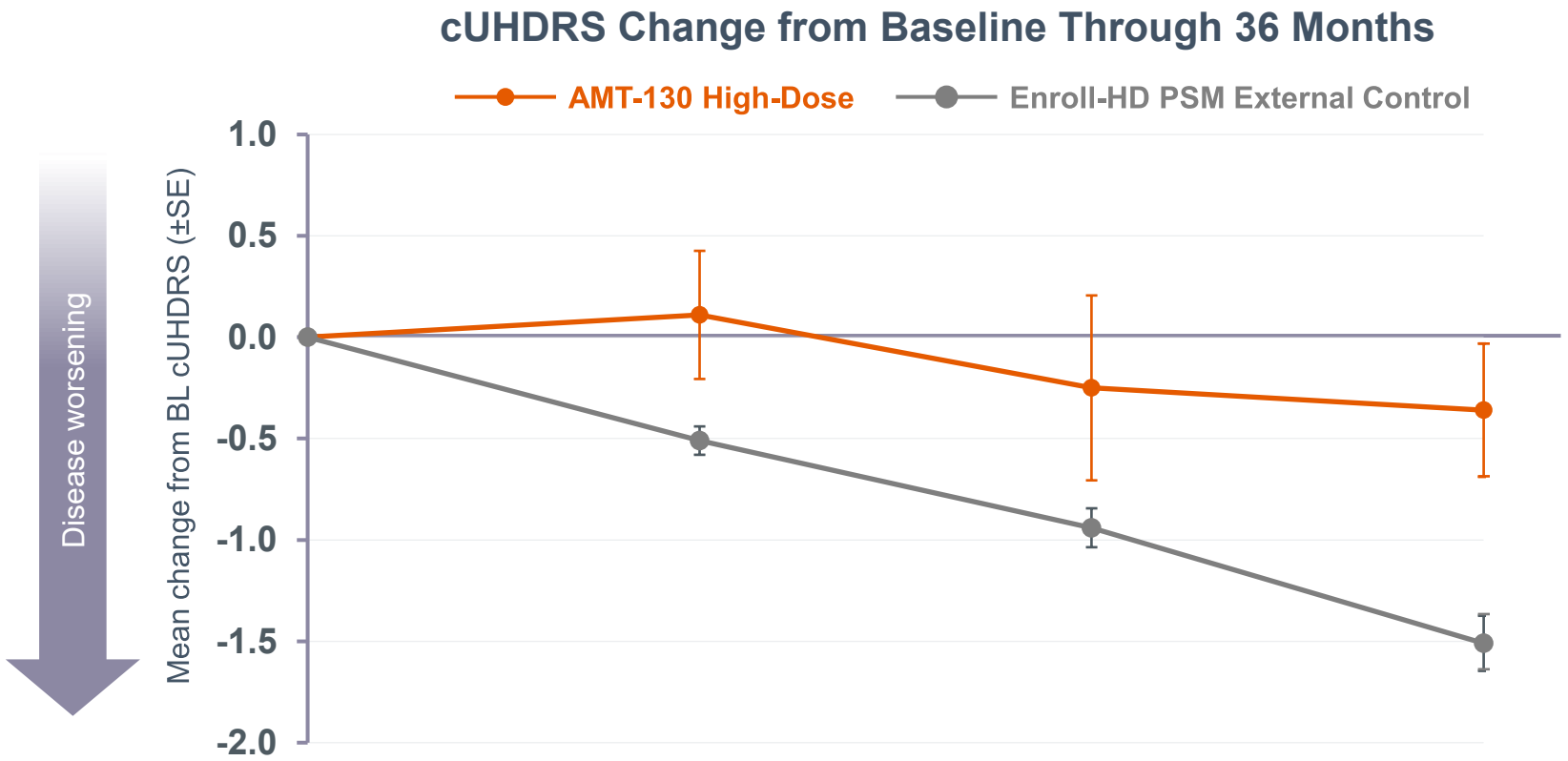


Participants	Baseline	36 months
AMT-130 High-Dose	17	12
PSM External Control	940	568

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

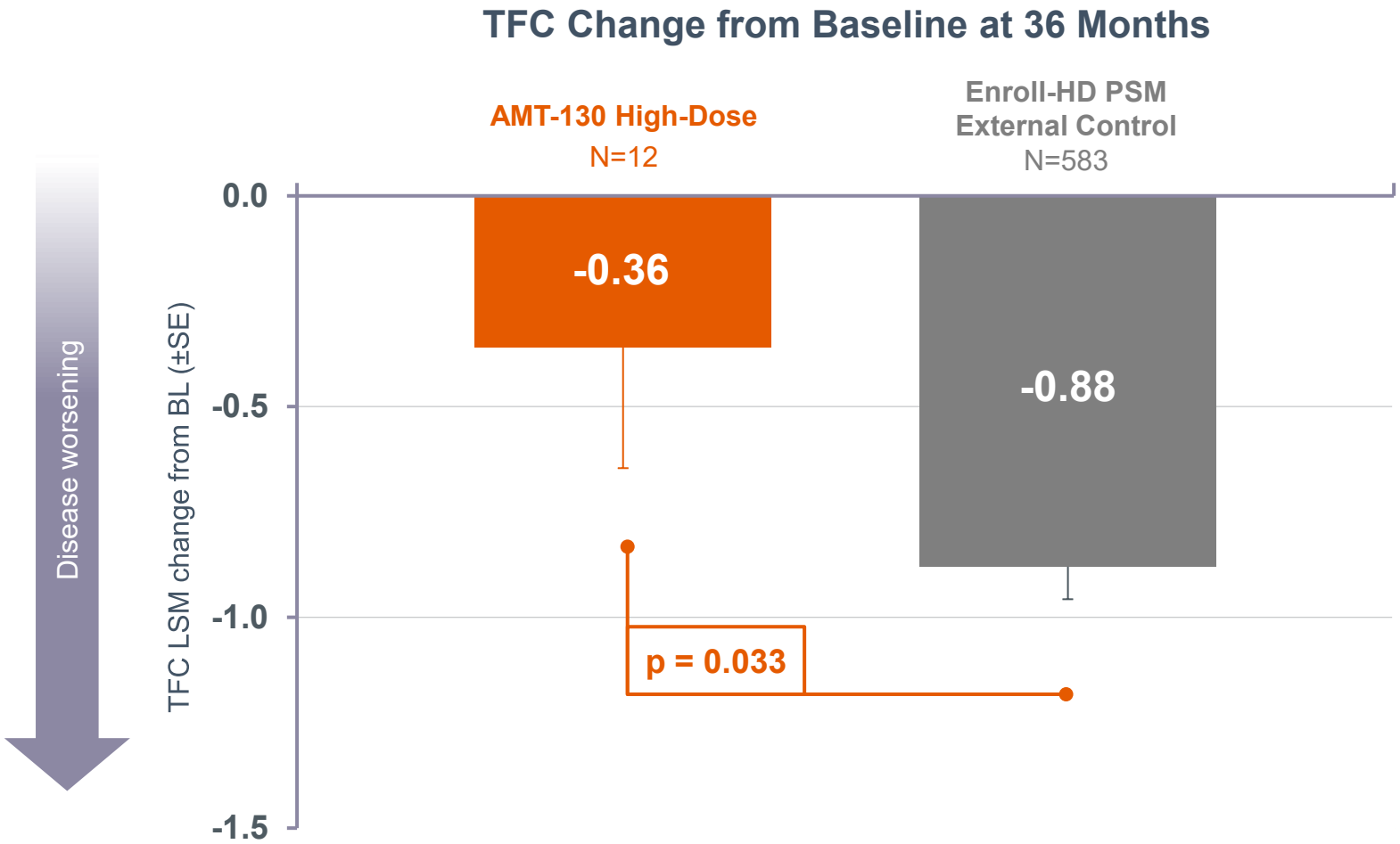
Above graph represents observed data

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

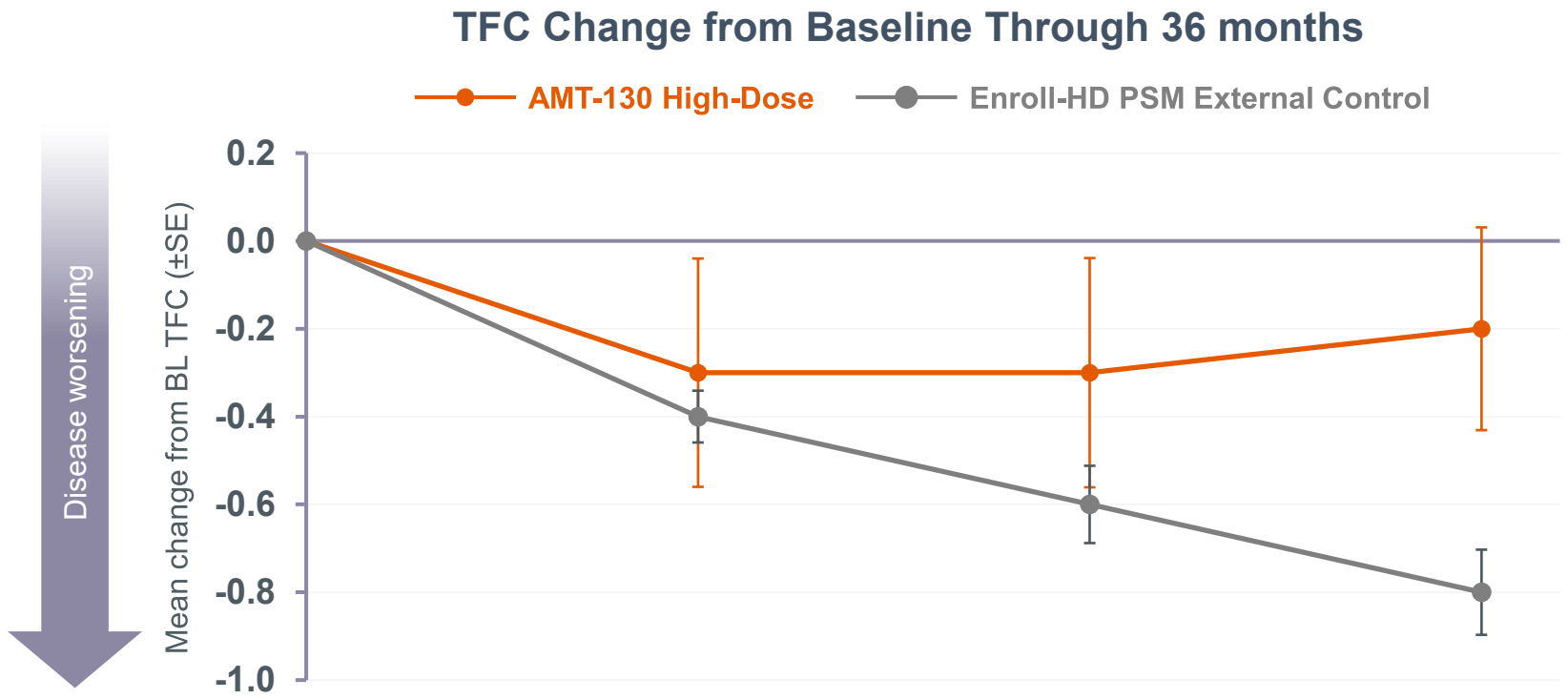


Participants	Baseline	36 months
AMT-130 High-Dose	17	12
PSM External Control	940	583

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

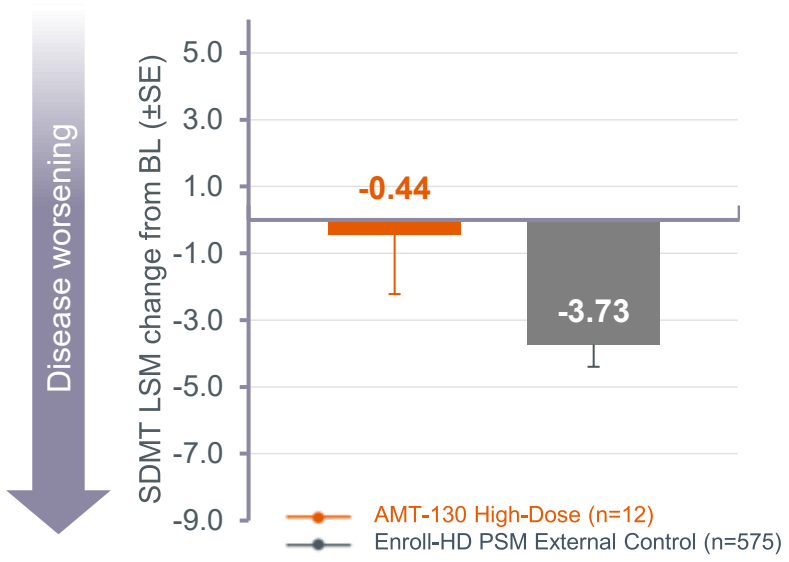
Abbreviations: TFC, Total Functional Capacity; HD, Huntington's disease; SE, standard error; PSM, propensity score-matched; BL, baseline

References: Data on file. September 2025.

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

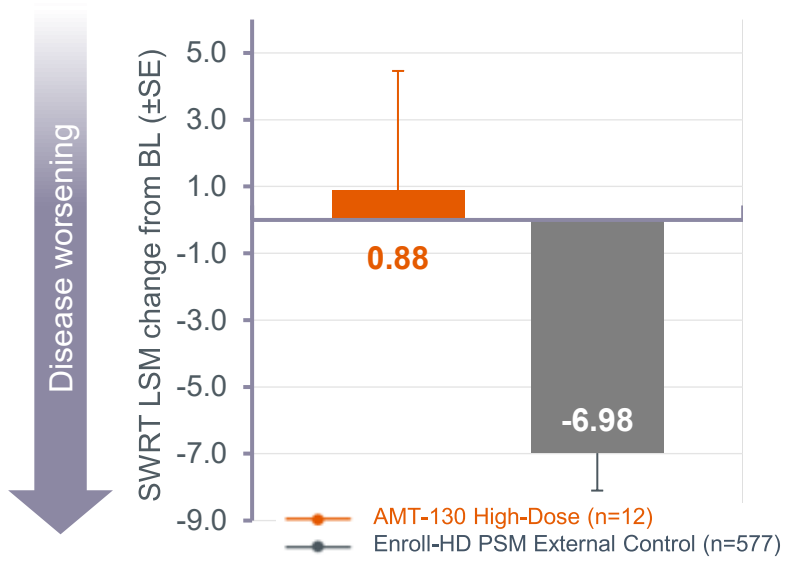
AMT-130 high-dose showed trends supportive of disease slowing **across all other clinical subdomains of cUHDRS**

SDMT Change from Baseline at 36 Months



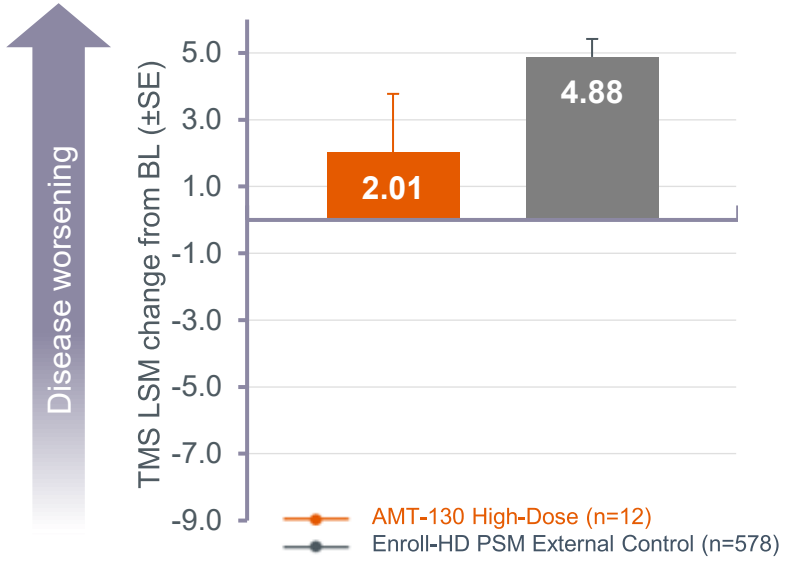
Reduced HD progression by 88% based on SDMT at 36 months (p=0.057)

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

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

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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

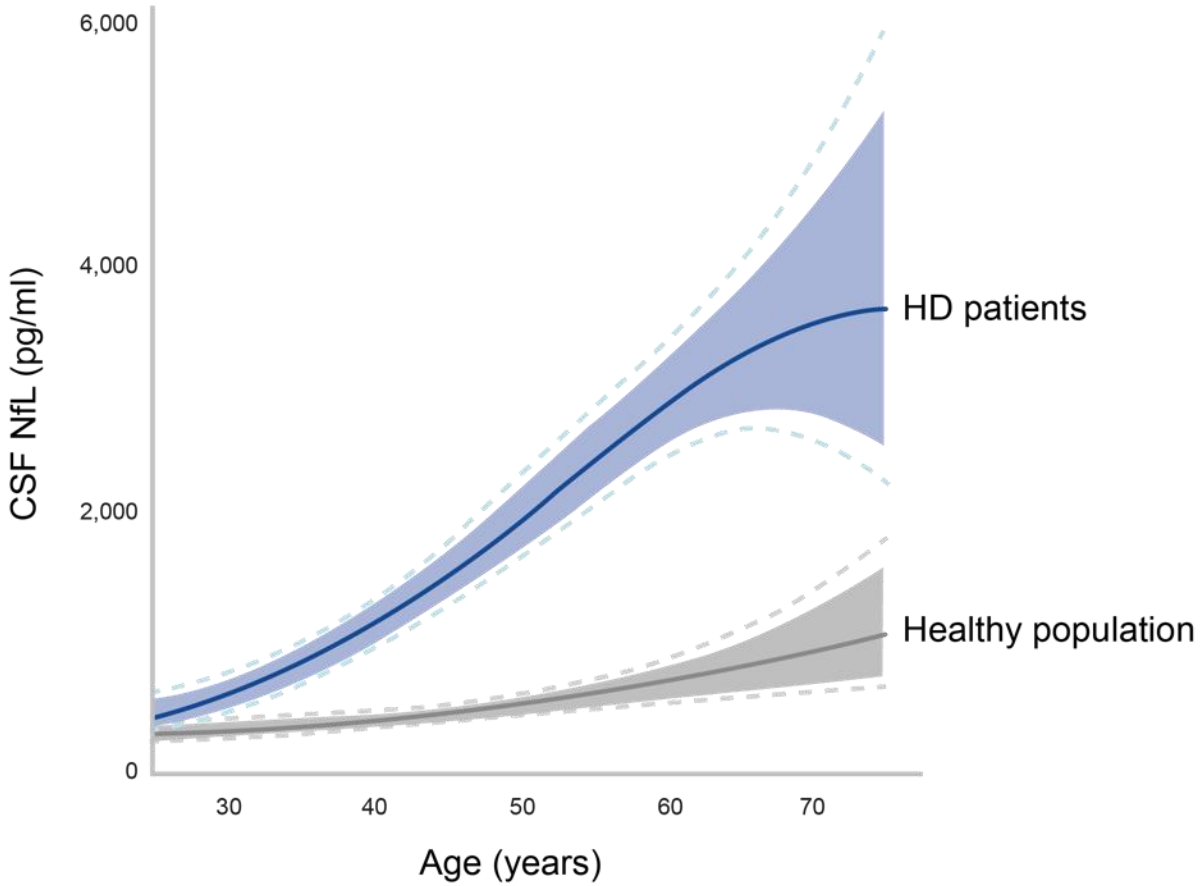
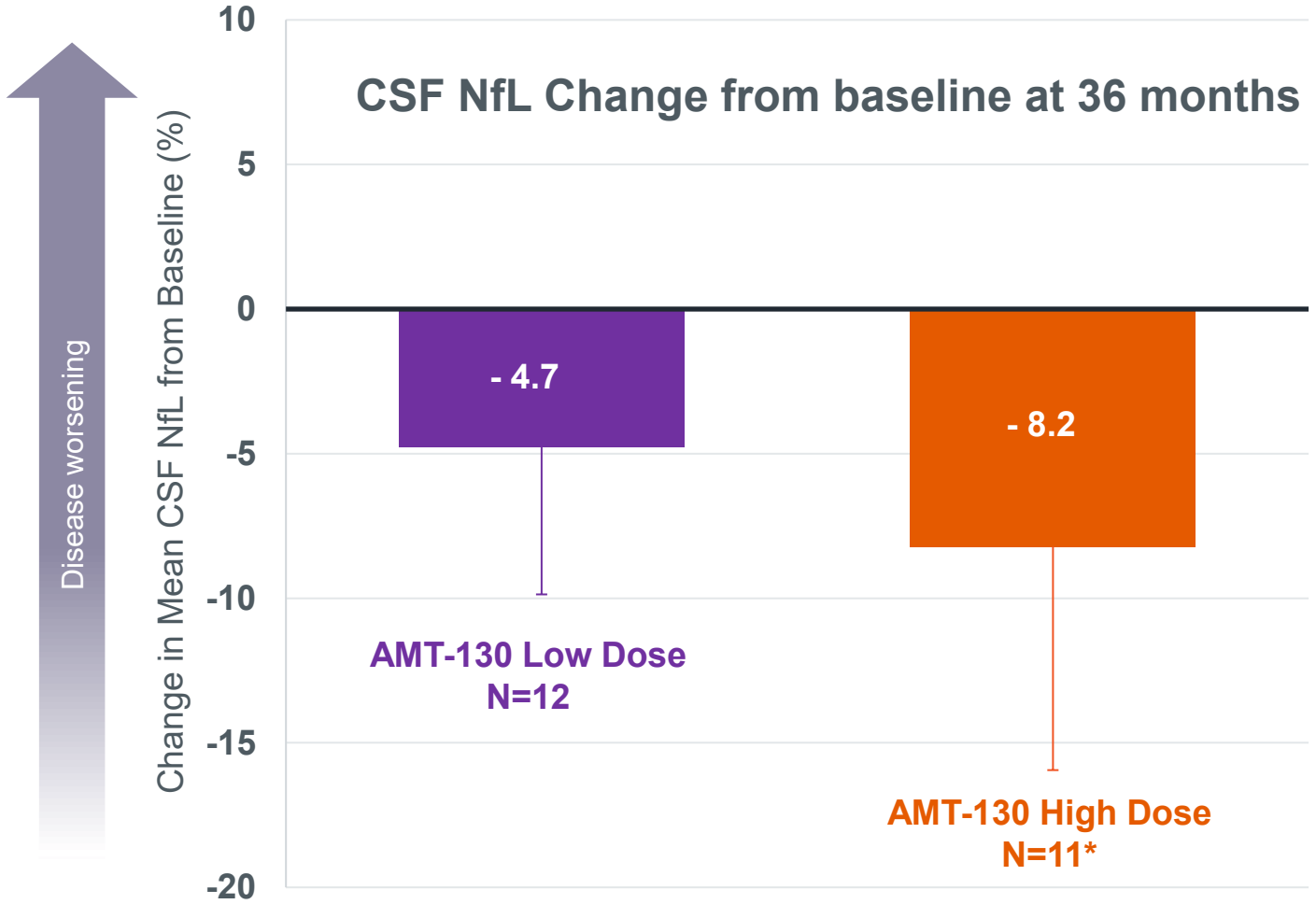


Image reproduced and modified from Rodrigues et al. Sci. Transl. Med. 2021

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 supportive 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***

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

Sarah Tabrizi, M.D., FRCP, FRS, FMedSci, Ph.D.,
University College London

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Commercialization

Kylie O'Keefe
Chief Customer & Strategy Officer

Large anticipated total addressable US market at time of launch, with potential for further growth

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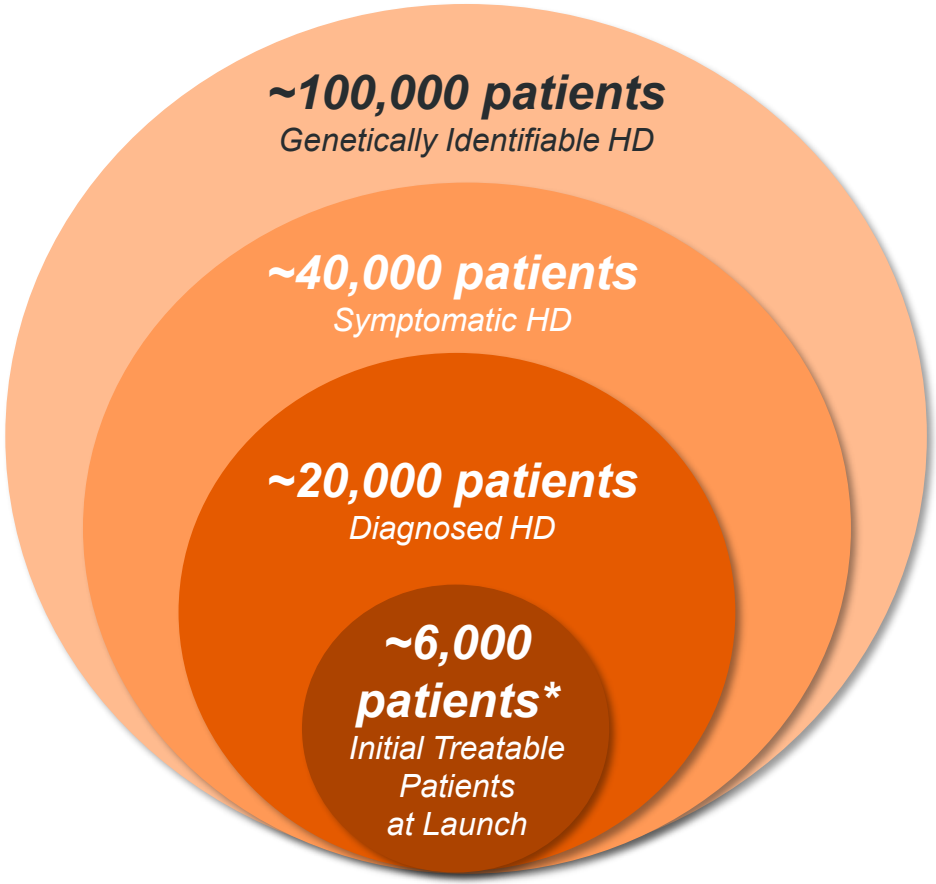

Potential Long-term Growth Levers

- *Continued Disease Progression In Presymptomatic And Incident Patients*
- *Increased Diagnosis Rate Due To Genetic Testing And Disease Modifying Treatment Availability*
- *Increase In Addressable Patient Segments*

Sources: Fisher et al. 2014, Yohrling et al. 2020, *Management Estimate.

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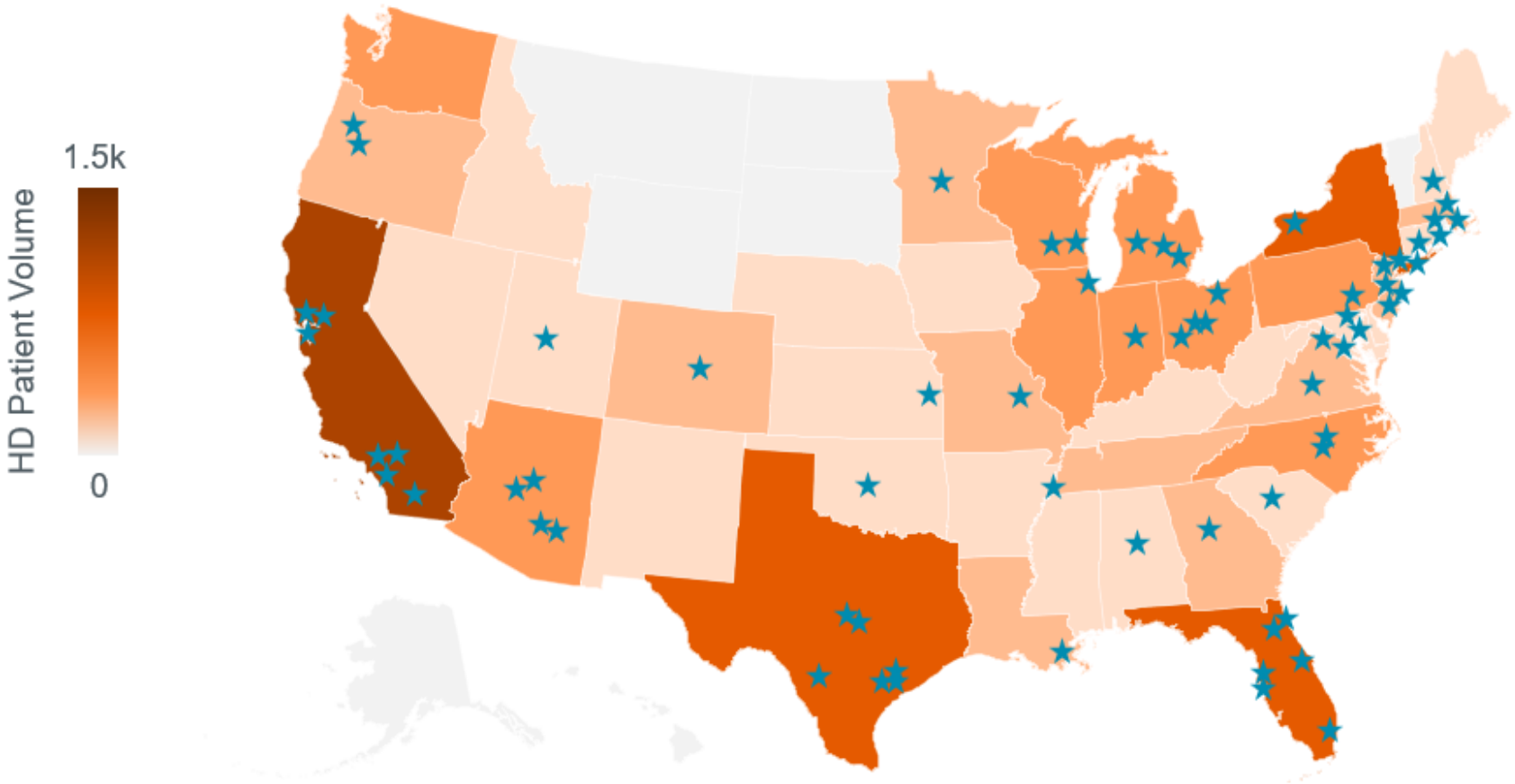
Established HDSA COEs and surgical infrastructure are well positioned to serve HD patients, with ongoing efforts to prioritize key treatment centers for launch

Heat Map of Clearpoint Neuro Capable Facilities and HDSA COEs by Patient Volume



Huntington's Disease Society of America
Center of Excellence

60 HD COEs and 9 Partner centers in the US

CLEARPOINT NEURO

*~68 Institutions**

Abbreviations: HDSA, Huntington's disease Society of America; COE, center of excellence .

Source: Komodo Dataset, HD patient volume determined by the presence of 1 claim between 2024 and the present for respective HCO; HD patient volume rolled up to individual COEs but may represent volume across multiple facilities. *CLEARPOINT NEURO Corporate Presentation August 2025. Non-Pediatric Institutions

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Research Analyst Questions

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Closing Remarks

Matt Kapusta
Chief Executive Officer

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