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Ashley, Huntington's disease patient advocate

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Leadership in Gene Therapy

Corporate Presentation
May 2024

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 potential clinical and functional effects of AMT-130, including as an effective treatment option for patients with Huntington's disease; the utility of CSF mHTT or NfL as an effective biomarkers of target engagement with respect to AMT-130; the design and engineering of AMT-130 to maximize clinical and functional benefit; the potential that volumetric data yielded from the AMT-130 clinical trial will be clinically significant; our use of a natural history cohort as a basis for comparison with respect to the efficacy of AMT-130; the initiation of the third cohort in our ongoing Phase I/II clinical trial of AMT-130 and the timing and release of additional clinical data; and our plans to request regulatory interactions with the relevant authorities in the U.S. and Europe and the potential for accelerated regulatory pathways. 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 ongoing Phase I/II clinical trial of AMT-130, including the risk that such trial will be unable to demonstrate efficacy data sufficient to support further clinical development and the risk that interim data from the trial may not be predictive of later data readouts; risks related to our financial position and share price, including our ability to raise sufficient capital to support further development of our clinical programs, as needed and on acceptable terms; risks related to our reliance on third parties to conduct, supervise, and monitor our preclinical studies and clinical trials and to manufacture components of our drug product, including the clinical trial for AMT-130; and our ability to obtain, maintain and protect our intellectual property. 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 28, 2024, our Quarterly Reports on Form 10-Q filed with the SEC on August 1, 2023, November 7, 2023, and May 7, 2024, and other filings that we make with the SEC from time to time.

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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.

— Rob
Clinical trial patient for etranacogene dezaparvovec, Toledo, Ohio

uniQure

Our mission is to reimagine the future of medicine by delivering innovative cures that transform lives.

uniQure corporate investment highlights: 2024

1. Pioneer in AAV gene therapy with successful track record
2. Validated and established technology platform
3. Strong pipeline including 4 clinical-stage programs
4. Multiple value drivers over next 12-24 months
5. Leading commercially licensed manufacturing capabilities
6. World-class R&D and CMC organizations
7. Strong financial position and prudent capital allocation

uniQure our history of innovation

A gene therapy pioneer with more than 25-years of history and deeply engrained culture of innovation across an increasingly validated platform

First approved AAV gene therapy in the world

First commercially licensed AAV manufacturing facility

First AAV-delivered gene silencing for HD to enter clinic

First AAV vector demonstrated effective in patients with NABs

First Gene therapy approved for hemophilia B

uniQure a case study in delivering value through innovation

- Leapfrogging hemophilia B with a first and best-in-class gene therapy

HEMGENIX®
etranacogene dezaparvovec-drlb

5 years!

2008
Licensed wtFIX gene cassette

2015
Initiated Phase 1/2 study of AMT-060

2017
Announced transition to AMT-061

2018
Initiated Ph 2b dose-confirmation study and HOPE-B pivotal study

2020
Completed dosing in HOPE-B pivotal study

2020
Announced $2 billion CSL license and collaboration agreement

2022
BLA approved

key milestones for 2024

Huntington's	• Initiate interactions with the regulatory authorities for ongoing development • Present longer-term follow-up data from U.S./European Ph I/II trial • Complete enrollment in third cohort of U.S./European Phase I/II clinical trial
Mesial Temporal Lobe Epilepsy	• Initiate patient enrollment and dosing in third quarter of 2024
SOD1-ALS	• Initiate patient enrollment and dosing in third quarter of 2024
Fabry Disease	• Initiate patient enrollment and dosing in second quarter 2024
Research Pipeline	• IND enabling studies for C9orf72 ALS and autosomal dominant Alzheimer's disease • Continue to advance other undisclosed research and discovery programs

Our Research and Development Pipeline

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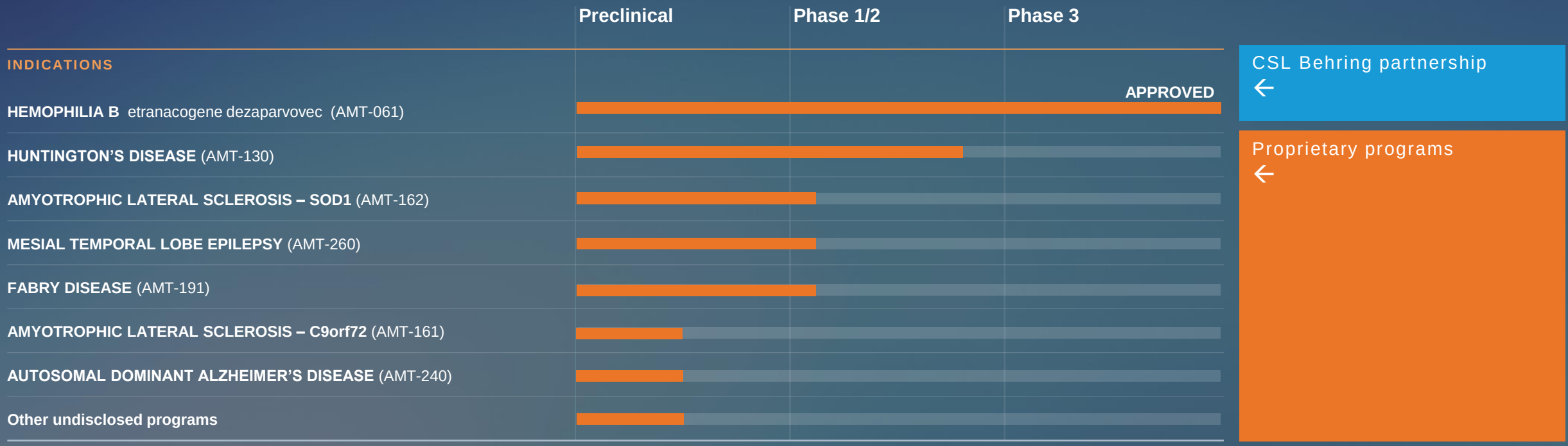


uniQure our leading three-pillar technology platform

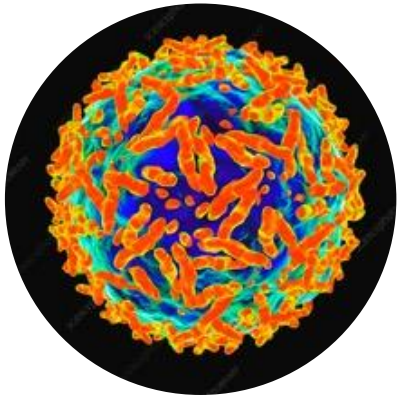
Cargo

miQURE® - Safe and effective miRNA delivery platform

linQURE™ - Multiple miRNAs delivered in a single AAV

goQURE™ - Gene replacement platform

Delivery



AAV5 & AAV9 – Naturally-occurring serotypes

Next-gen AAVs - Novel engineered capsids

BrainX™ - Library of novel capsids for CNS indications

Manufacturing

GMP manufacturing - Safe and reliable commercial manufacturing

DuoBac - Large scale, low cost of goods manufacturing

iREP - Modern high productivity cell lines

uniQure manufacturing excellence for global, commercial opportunities

Establishing larger scale and highly cost-effective capabilities to address more prevalent disorders

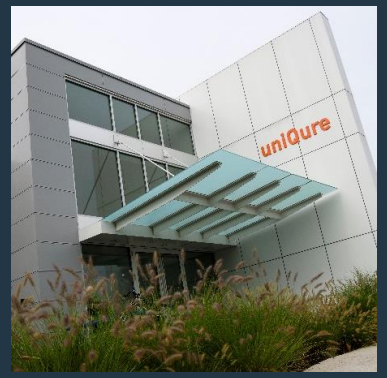
uniQure commercial product manufacturing and research capabilities

Consolidation of all cGMP commercial product manufacturing in Lexington, Massachusetts, process and analytical development housed in Amsterdam, the Netherlands and research & development in Basel, Switzerland

Amsterdam, NL

- Research
- Process Development
- Analytical Development
- Quality

Lexington, MA



- cGMP Manufacturing
- Quality

Basel, CH

- Research & Development

uniQure company well funded to meet future needs

Significant cash runway to advance our pipeline

~$556M* of cash, cash equivalents and investment securities > Runway into 2Q 2026 2026

+$180M from recent strategic restructuring > Extends runway into 2Q 2027 2027

+$1.4B in potential other milestones + royalties > Extends runway through 2027 and beyond 2027+

*Cash as of March 31, 2024

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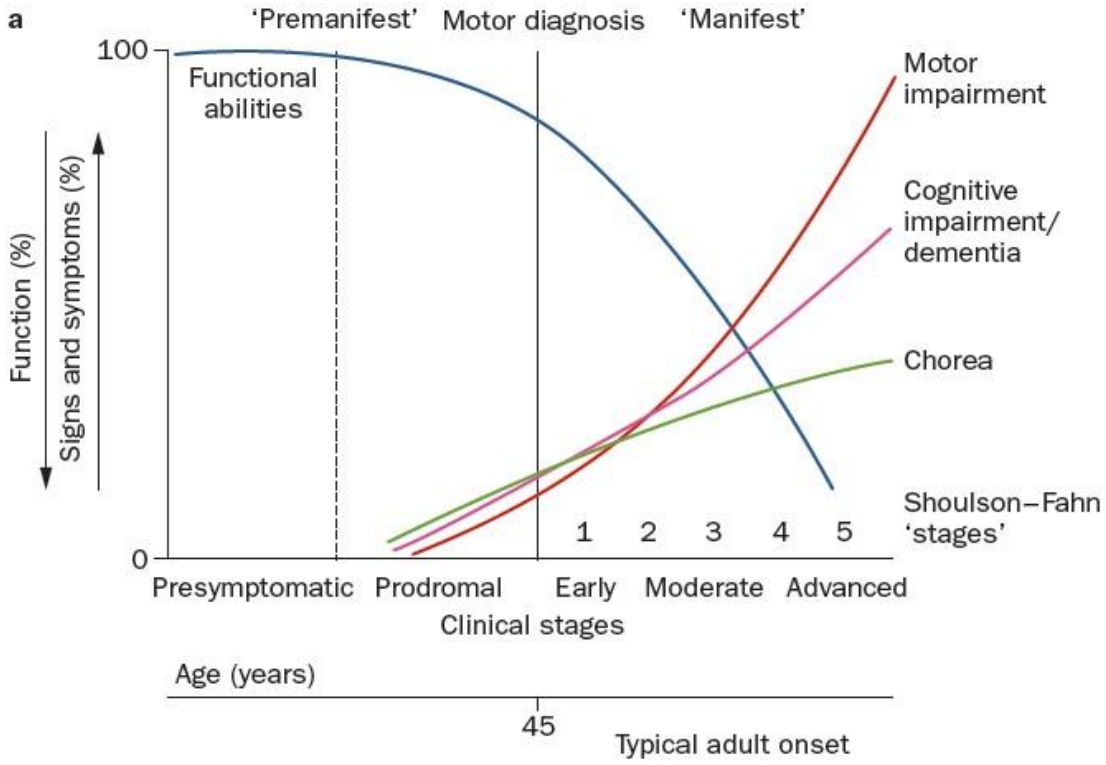
Huntington's Disease

AMT-130

Ashley, Huntington's disease patient advocate

Huntington's disease (HD): an overview

- Autosomal dominant inherited disorder (50% risk if your parent has HD)
- Affects ~25,000 patients each in U.S./EU[1]
- Initially described based upon characteristic chorea
- Dystonia, incoordination, ataxia, and later rigidity and bradykinesia contribute to functional impairment
- Cognitive and behavioral symptoms may occur early
- Progressive course from onset ~age 45 to death over 10-15 years[2]



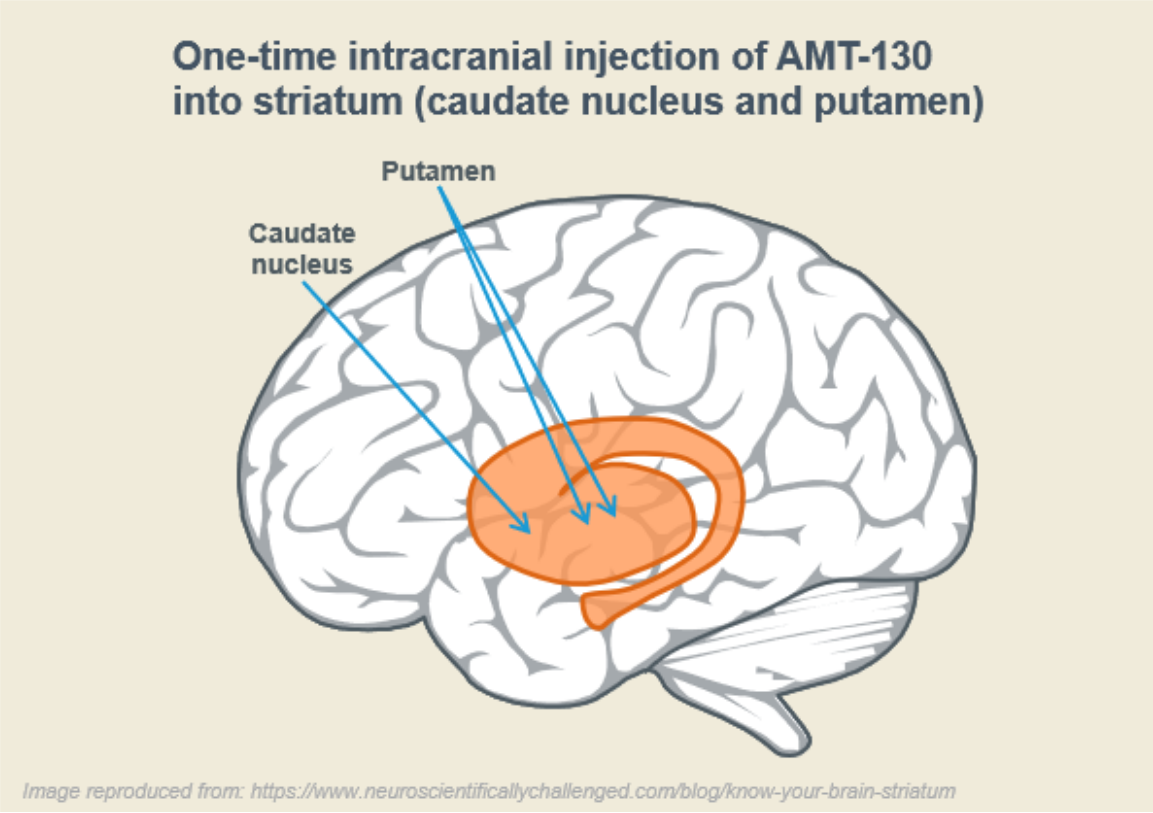
1) Neuroepidemiology 2016; 46:14-153 2) Ross CA, et al Nat Rev Neurol 2014; 10:204-216

AMT-130: a gene therapy approach for early manifest HD

- **AAV5-miHTT (AMT-130)**
  - Replication-deficient adeno-associated viral vector serotype 5 (AAV5)
  - Codes for microRNA (miRNA) that targets the HTT mRNA at exon 1
  - Blocks expression of HTT protein

Extensive preclinical validation

Model	Efficacy	Safety	Distribution
Cultured human neurons	✓	✓	
Rodents (HD rat[4]) (4 types HD mouse[3])	✓	✓	
NHP (Non-human primate[1])	✓	✓	✓
Pig (tgHD Minipig[2])	✓	✓	✓



1) Samaranch L, et al. Gene Ther 2017;24:253-261; 2) Evers M, et al. Mol Ther 2017;5(Suppl. 1):247; 3) Spronck EA, et al. Hum Gene Ther 2017;28:A78; 4) Miniarikova J, et al. Gene Therapy 2017;24:630-639; 5) Evers MM et al. Mol Ther. 2018;26(9):2163-2177; 6) Spronck EA et al. Mol Ther Methods Clin Dev. 2019 Mar 16;13:334-343; 7) Keskin S et al. Mol Ther Methods Clin Dev. 2019 Oct 4;15:275-284; 8) Caron NS et al. Nucleic Acids Res. 2019 Nov 20. pii: gkz976. doi: 10.1093/nar/gkz976

AMT-130: patient enrollment overview

CT-AMT-130-01 (Phase Ia/II)
double-blind sham-controlled

HD-GeneTRX1

26 Patients

- Low-dose 6e12 AMT-130 (6 Drug, 4 Control)
- High-dose 6e13 AMT-130 (10 Drug, 6 Control)
- Cohort 3

20 patients in HD-GTRX1 have received AMT-130
Four patients in the control arm have crossed over and received AMT-130 (1 low-dose, 3 high-dose)

CT-AMT-130-02 (Phase Ib/II)
open-label

HD-GeneTRX2

13 Patients

- Low-dose 6e12 AMT-130 (6 patients)
- High-dose 6e13 AMT-130 (7 patients)
- Cohort 3

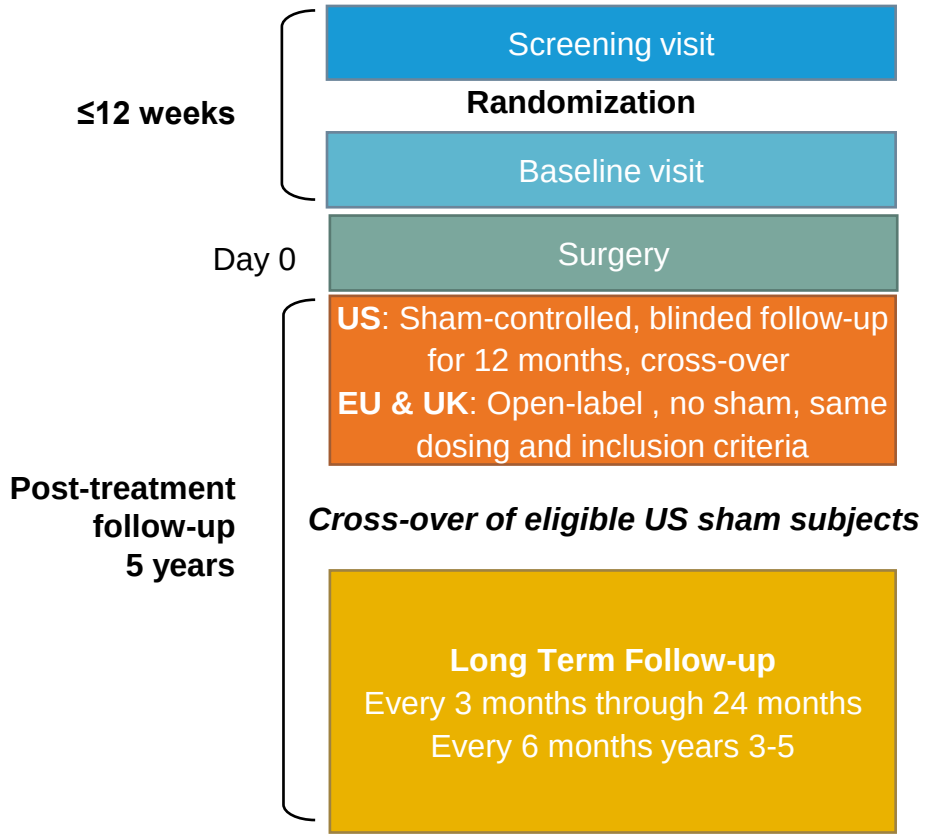
13/13 patients in HD-GTRX2 have received AMT-130

uniQure AMT-130: phase I/II U.S. & European clinical trial design

Inclusion Criteria

- ✓ **≥40 CAG**
- ✓ **25 to 65 years of age**
- ✓ **Total functional capacity** (Cohort 1&2, TFC 9-13; Cohort 3, TFC 11-13)
- ✓ **Diagnostic Classification Level (DCL) 4 (motor manifest) or 3 (multidimensional)**
- ✓ **Putamen volume of ≥2.5 cm³ (per side), and caudate volume of ≥2.0 cm³ (per side)**
- ✓ **Stable concomitant HD medication for 3 months**

United States, European Cohorts 1 and 2



Endpoints and Biomarkers

cUHDRS
Total Functional Capacity
Total Motor Score (TMS)
Symbol Digit Modality Test (SDMT)
Stroop Word Reading Test (SWT)

Volumetric MRI

NfL, mHTT

AMT-130: safety and tolerability

- AMT-130 was generally well-tolerated across both dose cohorts
- Surgical and drug-related adverse events were manageable
  - CNS inflammation, seen in several SAEs, improved with glucocorticoid medication; a short course of perioperative steroid prophylaxis has been added to the treatment regimen for Cohort 3
- There were no clinically relevant differences between treatment groups in vital signs, ECG, or clinical chemistry and hematology laboratory values

uniQure AMT-130: safety and tolerability

	Control (n=10)		Low-dose AMT-130 (n=13)		High-dose AMT-130 (n=20)	
	N	(%)	N	(%)	N	(%)
Any TEAEs	10	100.0	12	92.3	20	100.0
Any SAEs (peri-operative)	1	10.0	2	15.4	5	25.0
Any Drug-Related TEAE	0	0.0	0	0.0	6	30.0
Any Drug-Related SAE	0	0.0	0	0.0	4	20.0
CNS Inflammation					4 *	20.0
Most Common TEAEs (≥30% in at least one group)						
Procedural headache	5	50.0	4	30.8	9	45.0
Headache	3	30.0	3	23.1	9	45.0
Post lumbar puncture syndrome	6	60.0	2	15.4	7	35.0
Procedural complication	4	40.0	4	30.8	5	25.0
Procedural pain	5	50.0	2	15.4	6	30.0
Upper respiratory tract infection	1	10.0	4	30.8	0	0.0

** One SAE reported as "tension headache" was retrospectively recognized by uniQure as a case of CNS inflammation.*

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.

Data cut-off as of September 30, 2023

AMT-130: non-concurrent natural history comparator cohorts with and without the minimum striatal volume criteria

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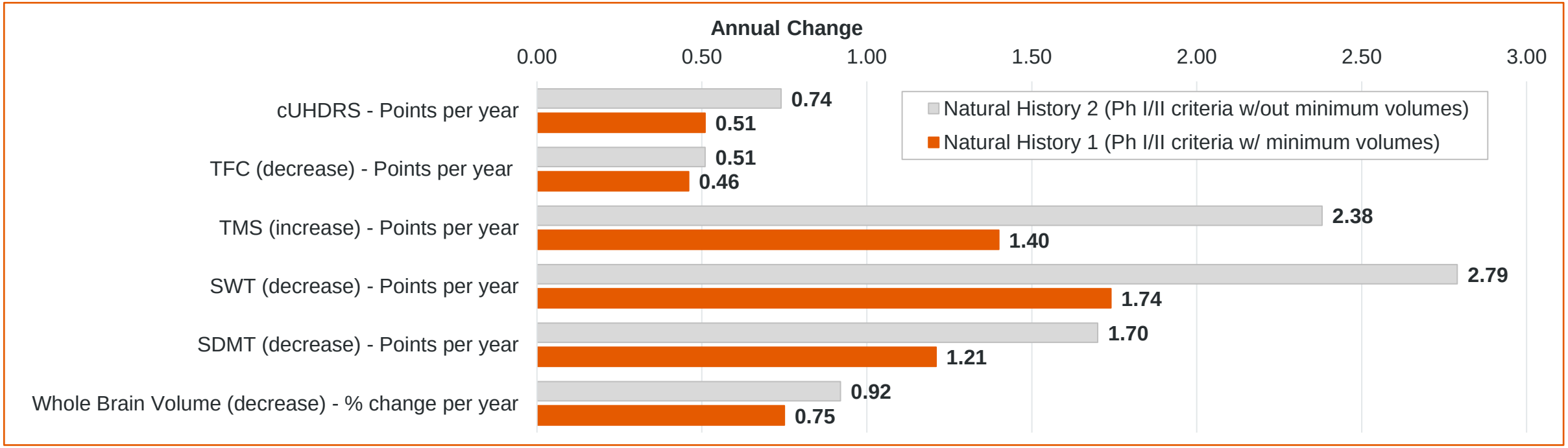
Natural History Cohort 1: subgroup from Natural History cohort 2 that exceed the minimum striatal volumes.

Natural History Cohort 2: TRACK-HD patients that closely match the study's clinical inclusion criteria.



Natural History 1 (Phase I/II inclusion criteria and also exceeds minimum striatal volumes) : N=31; TFC 9-13; DCL 3-4; Putamen volume ≥2.5cm^3; Caudate volume ≥2.0cm^3 per side

Natural History 2 (Phase I/II inclusion criteria without minimum striatal volume) : N=105; TFC 9-13; DCL 3-4

AMT-130: cUHDRS remained favorable in treated patients compared to natural history; high-dose patients preserved cUHDRS relative to baseline

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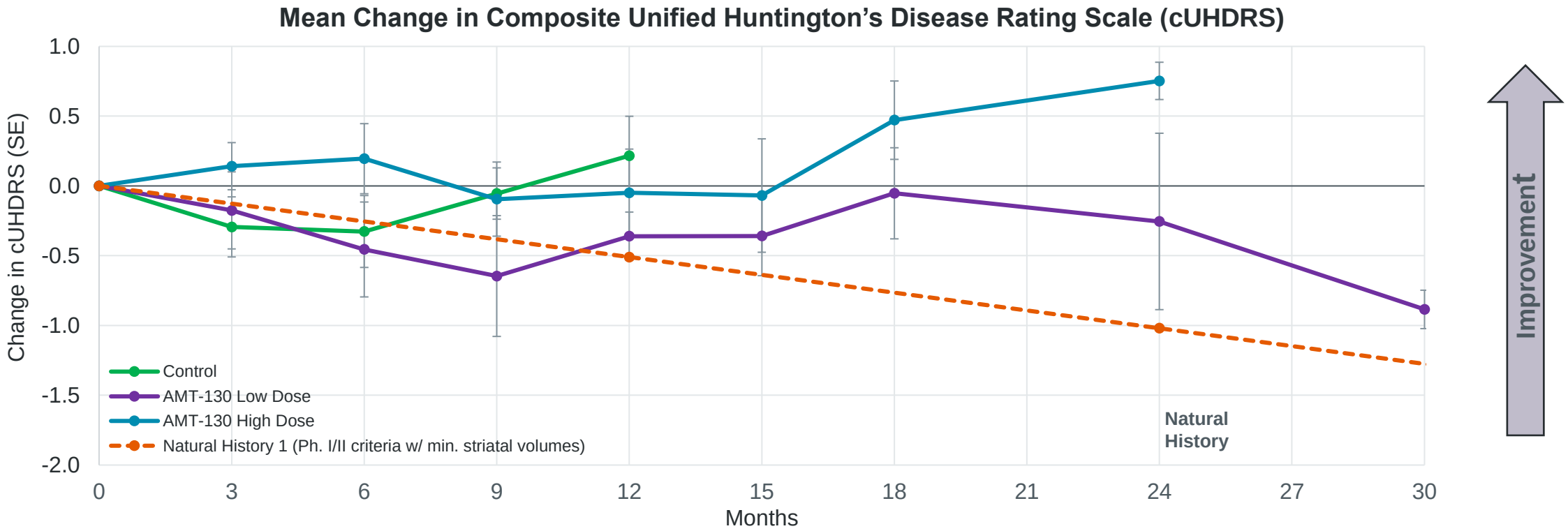

Patients	Base	3M	6M	9M	12M	15M	18M		24M		30M
Low Dose	12	12	12	12	12	12	12		6		5
High Dose	17	17	14	14	14	13	9		2		
Control	10	9	10	10	9						

cUHDRS is a composite endpoint developed to evaluate disease progression in early-to-moderate manifest HD. The scoring algorithm combines four elements: Total Functional Capacity (TFC), Total Motor Score (TMS), Symbol Digit Modalities Test (SDMT) and Stroop Word Reading Test (SWT)

Standard Error (SE); TRACK HD (Poster CHDI 2022)

AMT-130: treated patients showed a favorable difference in TFC when compared to natural history and stabilization relative to baseline

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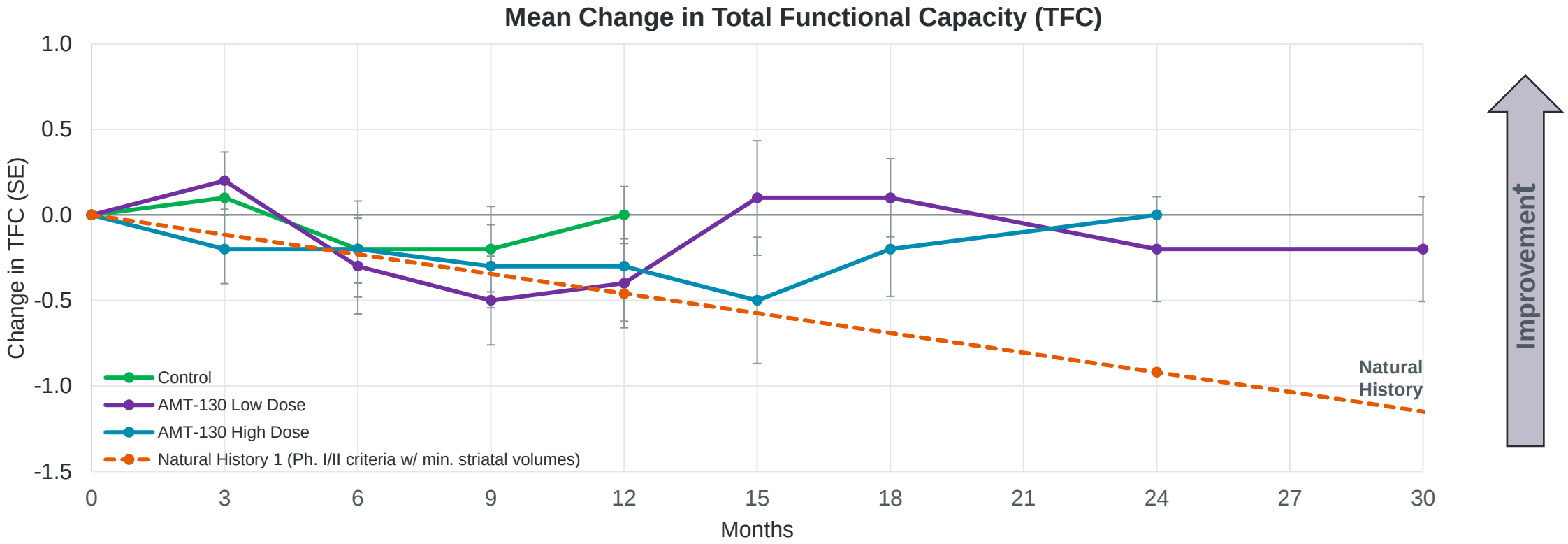

Patients	Base	3M	6M	9M	12M	15M	18M		24M		30M
Low Dose	12	12	12	12	12	12	12		6		6
High Dose	17	17	14	14	14	13	9		2		
Control	10	10	10	10	9						

TFC measures functional abilities in five categories, including occupation, finances, domestic chores, activities of daily living, and care level. Each category is rated on a scale, with higher scores indicating better functioning. The total TFC score ranges from 0 to 13, with lower scores representing greater functional impairment.

Standard Error (SE); TRACK HD (Poster CHDI 2022)

AMT-130: treated patients showed a favorable difference in TMS when compared to natural history and stabilization relative to baseline

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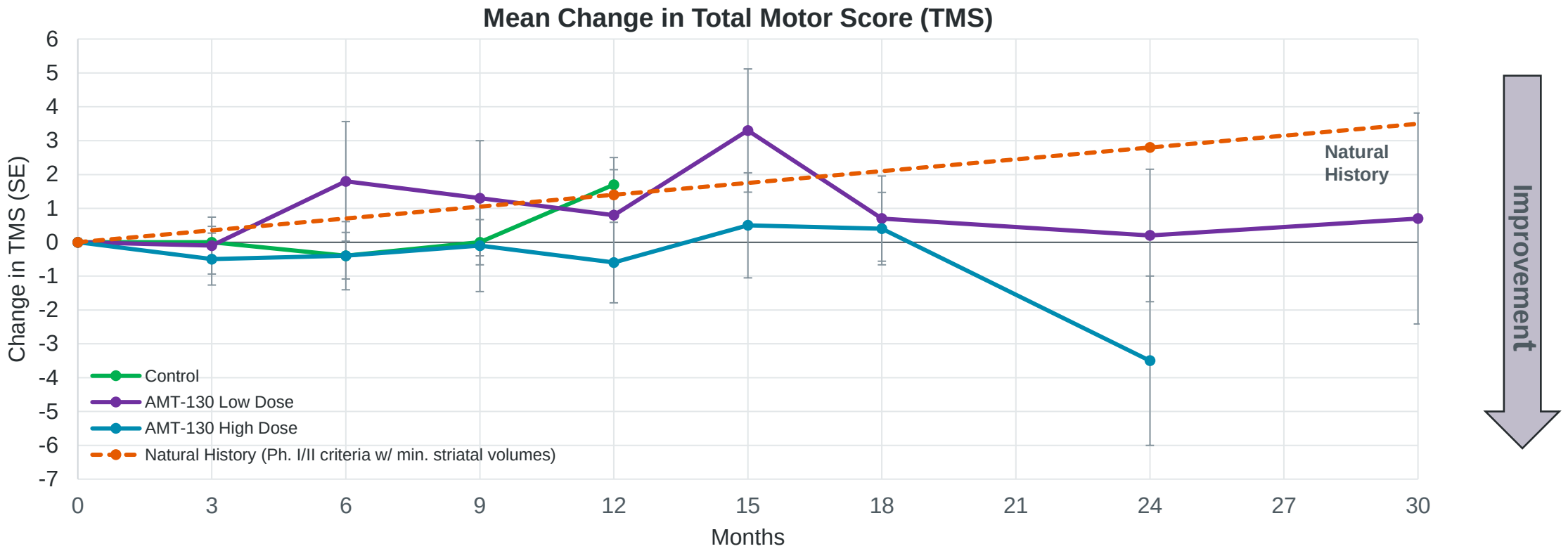

Patients	Base	3M	6M	9M	12M	15M	18M		24M		30M
Low Dose	12	12	12	12	12	12	12		6		6
High Dose	17	17	14	14	14	13	9		2		
Control	10	10	10	10	9						

TMS evaluates the patient's motor function, focusing on involuntary movements (chorea, dystonia), voluntary movements, eye movements, and muscle tone (rigidity). It consists of 31 items, each rated on a 0-4 scale, with higher scores indicating more severe motor impairment. The total motor score ranges from 0 to 124.

Standard Error (SE); TRACK HD (Poster CHDI 2022)

AMT-130: high-dose treated patients preserved function in SWT relative to baseline

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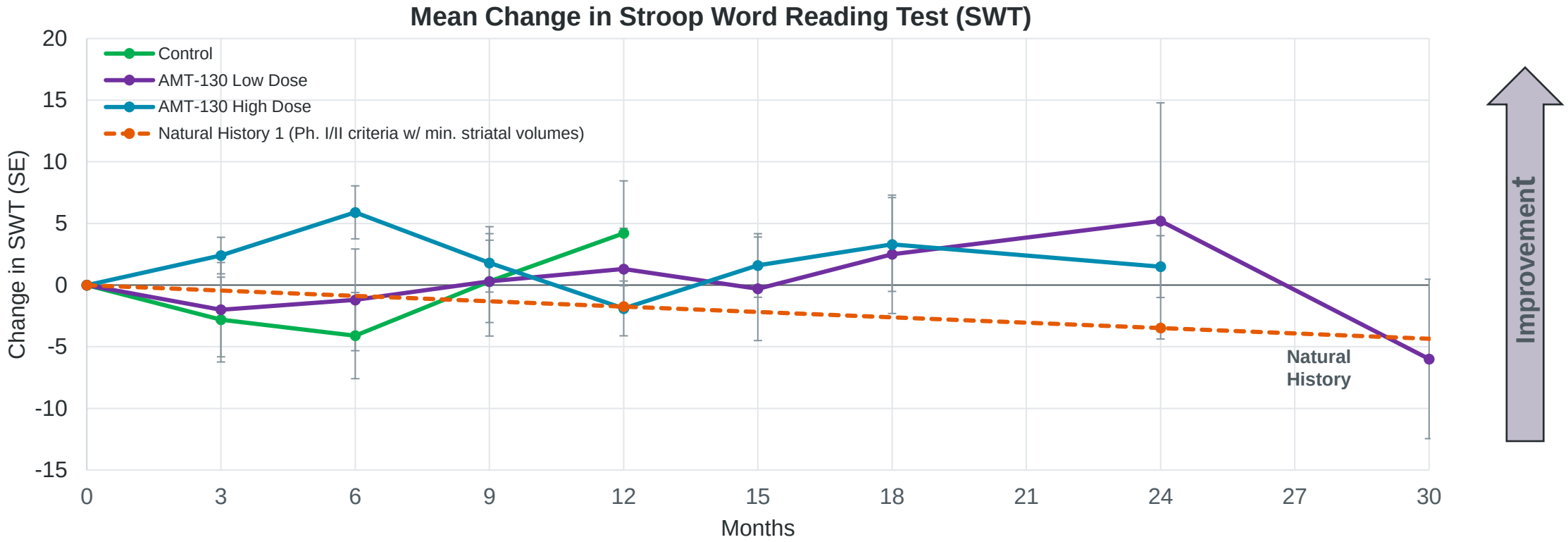

Patients	Base	3M	6M	9M	12M	15M	18M		24M		30M
Low Dose	12	12	12	12	12	12	12		6		6
High Dose	17	17	14	14	14	13	9		2		
Control	10	9	10	10	9						

SWT is scored by measuring the time it takes for an individual to correctly name the ink color of a series of words. The score used to assess performance is typically the difference in time between the word-reading condition and the color-word naming condition (i.e., the interference effect).

Standard Error (SE); TRACK HD (Poster CHDI 2022)

AMT-130: high-dose treated patients preserved baseline with favorable trends to natural history in SDMT

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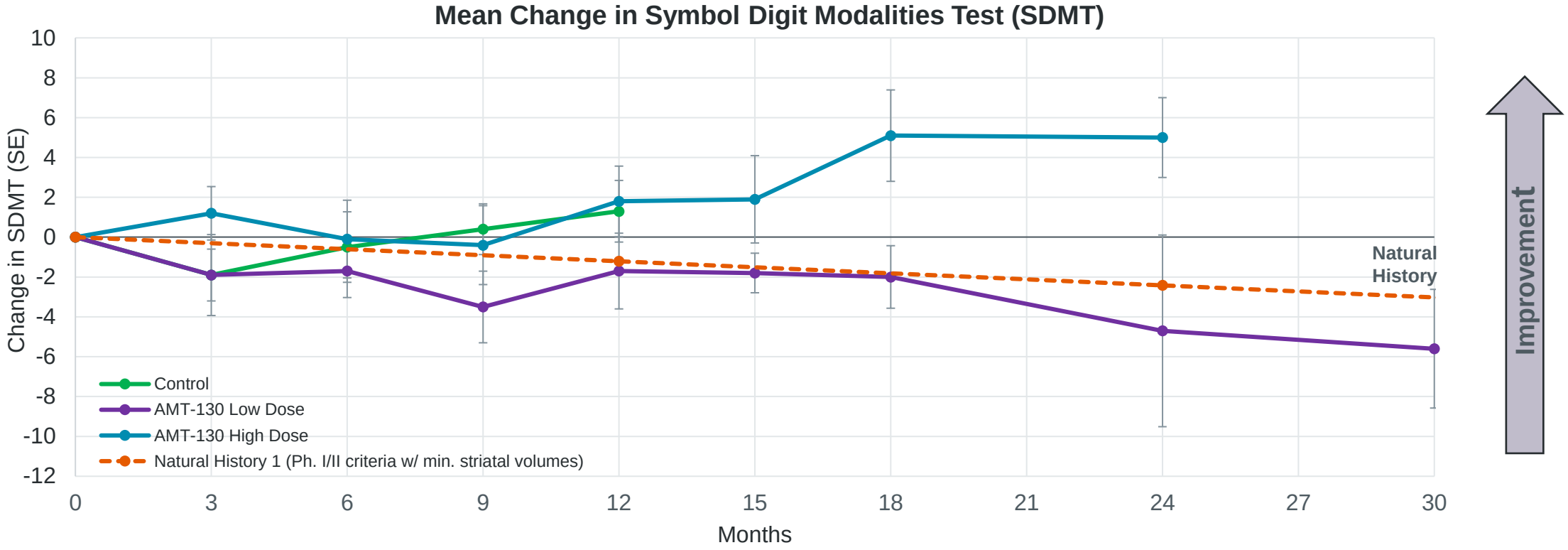

Patients	Base	3M	6M	9M	12M	15M	18M		24M		30M
Low Dose	12	12	12	12	12	12	12		6		5
High Dose	17	17	14	14	14	13	9				
Control	10	10	10	10	9						

SDMT evaluates processing speed, attention, and working memory. Range (0-110) Mean in young adults = 49 +/- 13

Standard Error (SE); TRACK HD (Poster CHDI 2022)

AMT-130: CSF NfL continued favorable trends; low-dose below baseline at month 30 with high-dose near baseline at month 18

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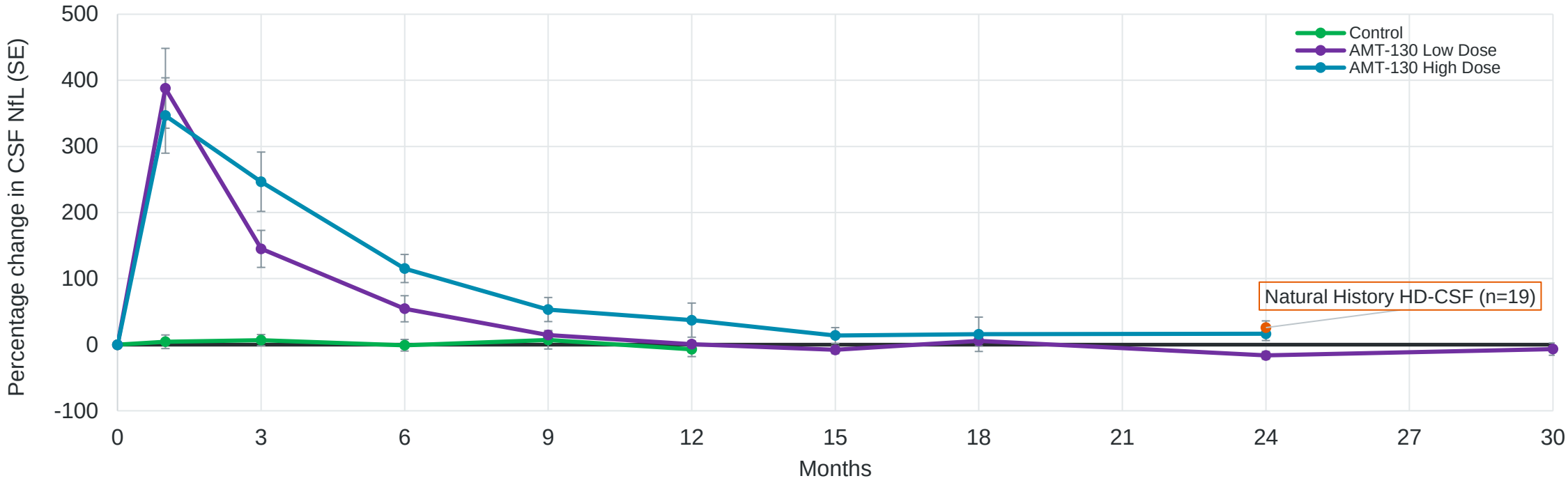
CSF NfL percentage change from baseline

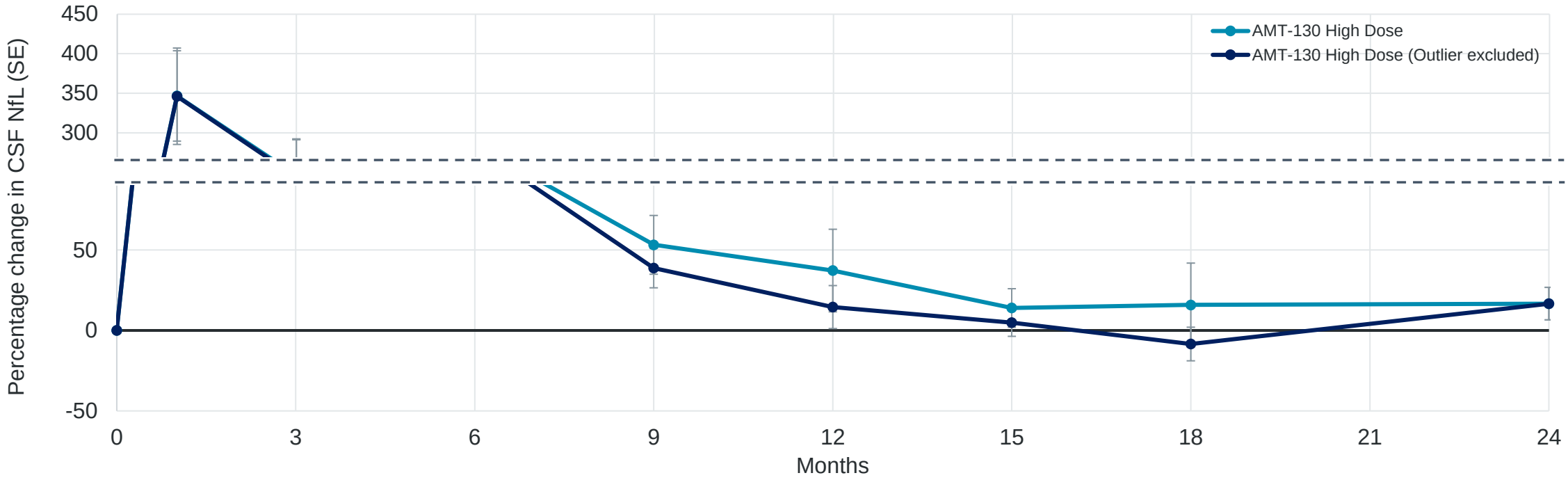


Patients	Base	1M	3M	6M	9M	12M	15M	18M		24M		30M
Low-Dose	12	12	11	12	12	12	12	12		6		6
High-Dose	17	17	16	13	13	11	11	9		2		
Control	10	9	9	9	7	7						

CSF, Cerebrospinal fluid; NfL Neurofilament light chain; Standard Error (SE)

AMT-130: excluding single high-dose outlier*, CSF NfL trended below baseline at month 18 with tighter error bars

CSF NfL percentage change from baseline



Patients	Base	1M	3M	6M	9M	12M	15M	18M		24M
High-Dose	17	17	16	13	13	11	11	9		2
High-Dose (Outlier excluded)	16	16	15	12	12	10	10	8		2

* Single patient experienced a late-onset serious adverse event of central nervous system inflammation around Month 12 with CSF NfL levels approximately 2 to 3-fold higher relative to baseline until their last measurement at Month 18

CSF, Cerebrospinal fluid; NfL Neurofilament light chain; Standard Error (SE)

AMT-130: promising trends in clinical assessments and CSF NfL support continuing development

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- AMT-130 was generally well-tolerated, with a manageable safety profile;
  SAE cases of CNS inflammation have clinically responded to glucocorticoids
- Patients treated with both doses of AMT-130 show evidence of preserved neurologic function relative to baseline, and potential clinical benefit relative to a non-concurrent natural history
- CSF NfL trends are favorable following the post treatment spike with the low-dose crossing baseline at approximately 12 months with relative stability through month 30, and the high-dose near baseline at month 18
- Brain volumetric changes do not appear to be clinically meaningful in light of the surgical intervention and promising clinical and biomarker data
- CSF mHTT values are close to the lower-limit of quantification, and may not be an effective measure of target engagement for a striatally-administered HTT-lowering therapy

AMT-130: next steps in clinical development

- ✓ Q4 2023: Initiated Cohort 3 in Phase I/II trials in the U.S. and Europe to investigate the effects of immune suppression on perioperative safety
- ✓ Q1 2024: Request regulatory interactions to discuss the U.S. and European data and potential regulatory strategies for ongoing development
- Mid 2024: Clinical update on Phase I/II trials out to three years in the US study and two years in the European study

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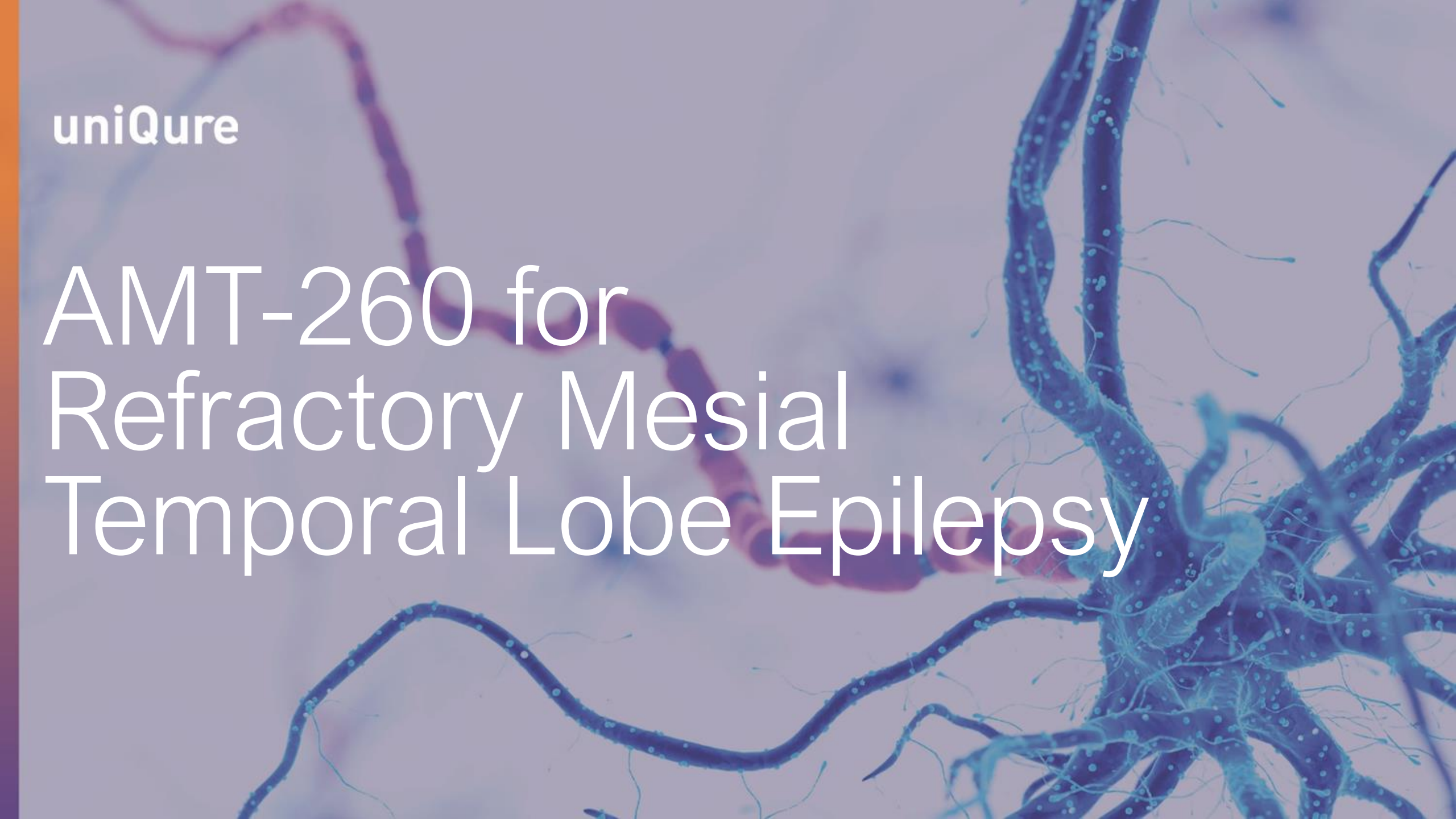
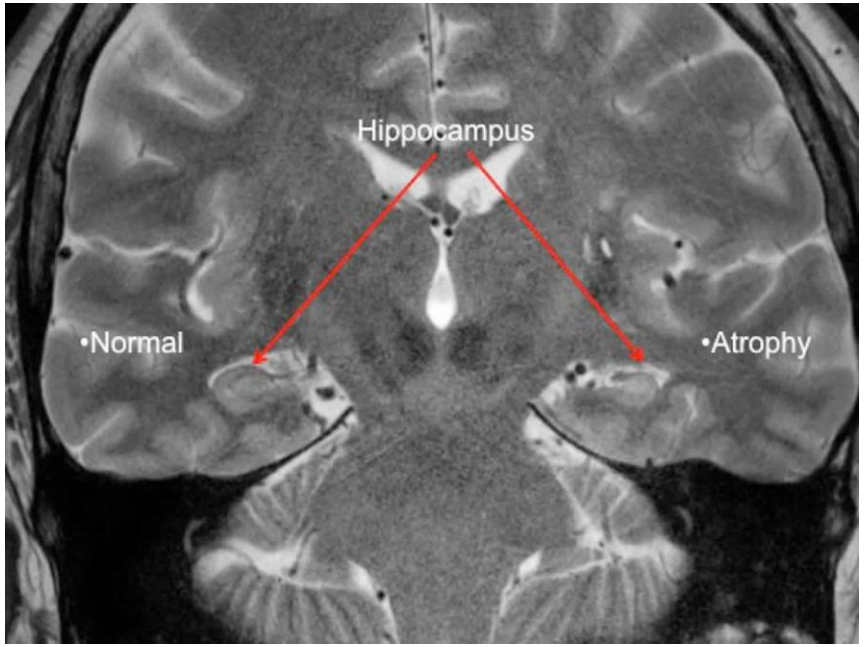
AMT-260 for Refractory Mesial Temporal Lobe Epilepsy



uniQure refractory mesial temporal lobe epilepsy (MTLE)

- TLE is the **most common type** of focal epilepsy[1] and affects approximately 1 million people in the U.S. and Europe[2]
- **~300,000 U.S. TLE patients are inadequately treated** through anti-seizure medications and are considered **refractory**[3]
- **~240,000 of U.S. refractory TLE patients** have a lesion in the **mesial** temporal lobe (hippocampus), which is expressed as sclerosis, atrophy or scarring[4]
- MTLE is often caused by brain injury, infections or prolonged febrile seizures which can lead to **hyperexcitability of the hippocampus** and repeated seizures which can further **damage the hippocampus over time**
- Refractory MTLE patients have a poor quality of life and a reduced lifespan
- Surgical treatment for refractory patients is lobectomy or laser tissue ablation but **only 1-2% of eligible patients undergo surgery**[5]

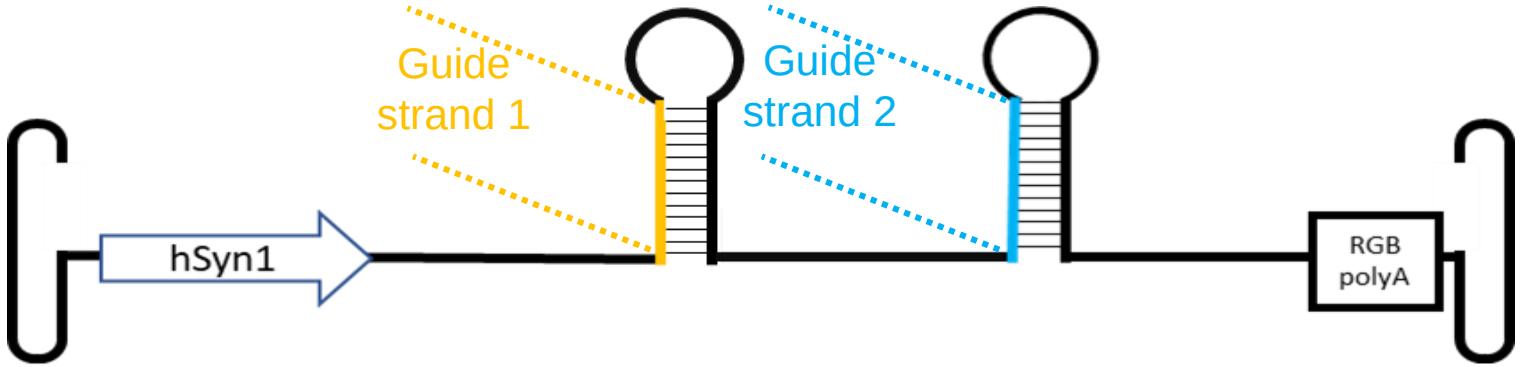


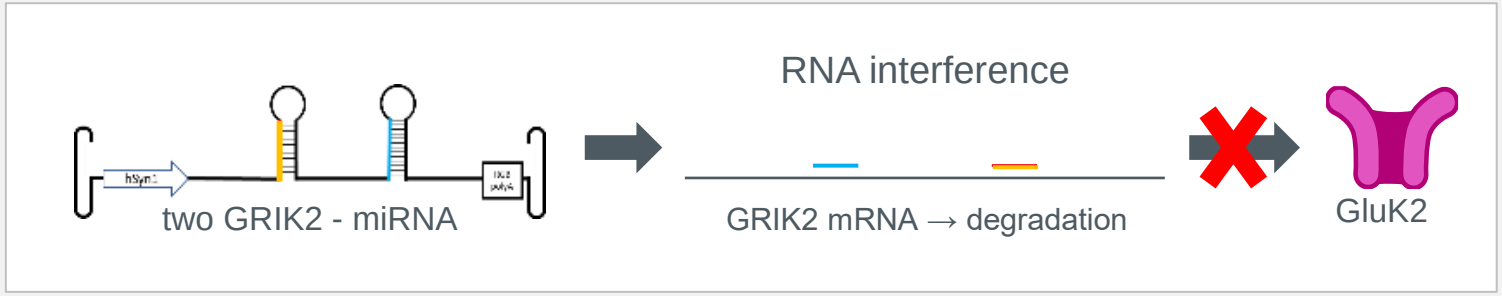
Left temporal lobe lesion expressed as atrophy

1. "Epilepsy: Hope Through Research", NINDS, Publication date April 2015. NIH Publication No. 15-15
2. Mesraoua B, Deleu D, Al Hail HJ, et al. Prevalence and Incidence of Drug-Resistant Temporal Lobe Epilepsy in Qatar. *J Cent Nerv Syst Dis*. 2020;12:1179573520935031. Published 2020 Jun 27.
3. Yang L, Zhang R, Zhu H, Chen F, Yu N, Di Q. Factors influencing the long-term prognosis of patients with temporal lobe epilepsy: a single center study. Ann Palliat Med 2020;9(5):3194-3203. doi: 10.21037/apm-20-1415
4. https://www.epilepsy.com/what-is-epilepsy/syndromes/temporal-lobe-epilepsy#:~:text=Mesial%20temporal%20lobe%20epilepsy%20(MTLE,of%20all%20temporal%20lobe%20seizure
5. Engel J Jr: The current place of epilepsy surgery. Curr Opin Neurol. 2018; 31(2):192–7.

AMT-260: an AAV9 targeting GRIK2, the kainate glutamate receptor

- AAV9 delivery of engineered miRNAs to reduce the expression of a glutamate receptor subtype that triggers seizures in focal epilepsies
- AMT-260 targets the GluK2 subunit of the kainate receptors





AMT-260: route of administration demonstrated focal biodistribution

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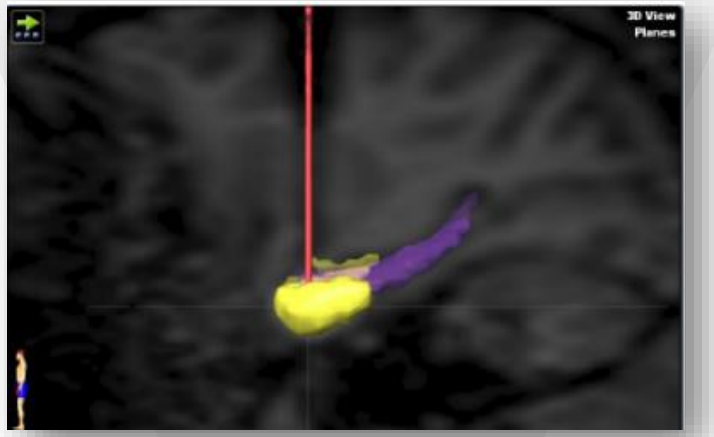
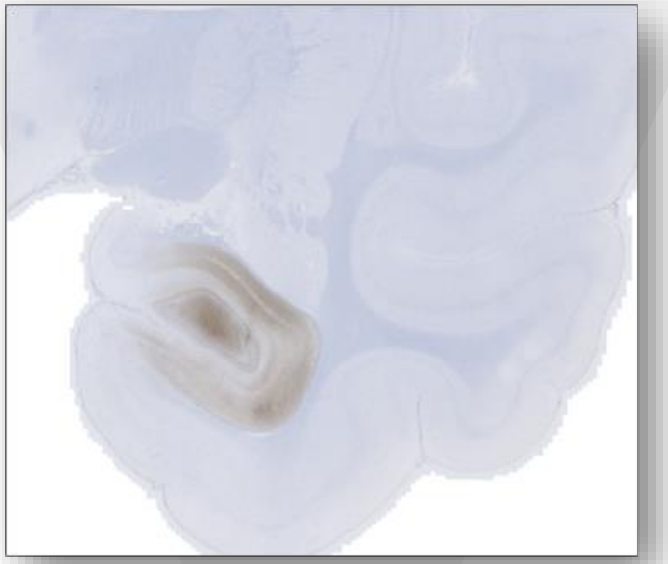
Injection accuracy in NHPs



Purple – Hippocampus
Yellow – Gadoteridol
Red - Trajectory

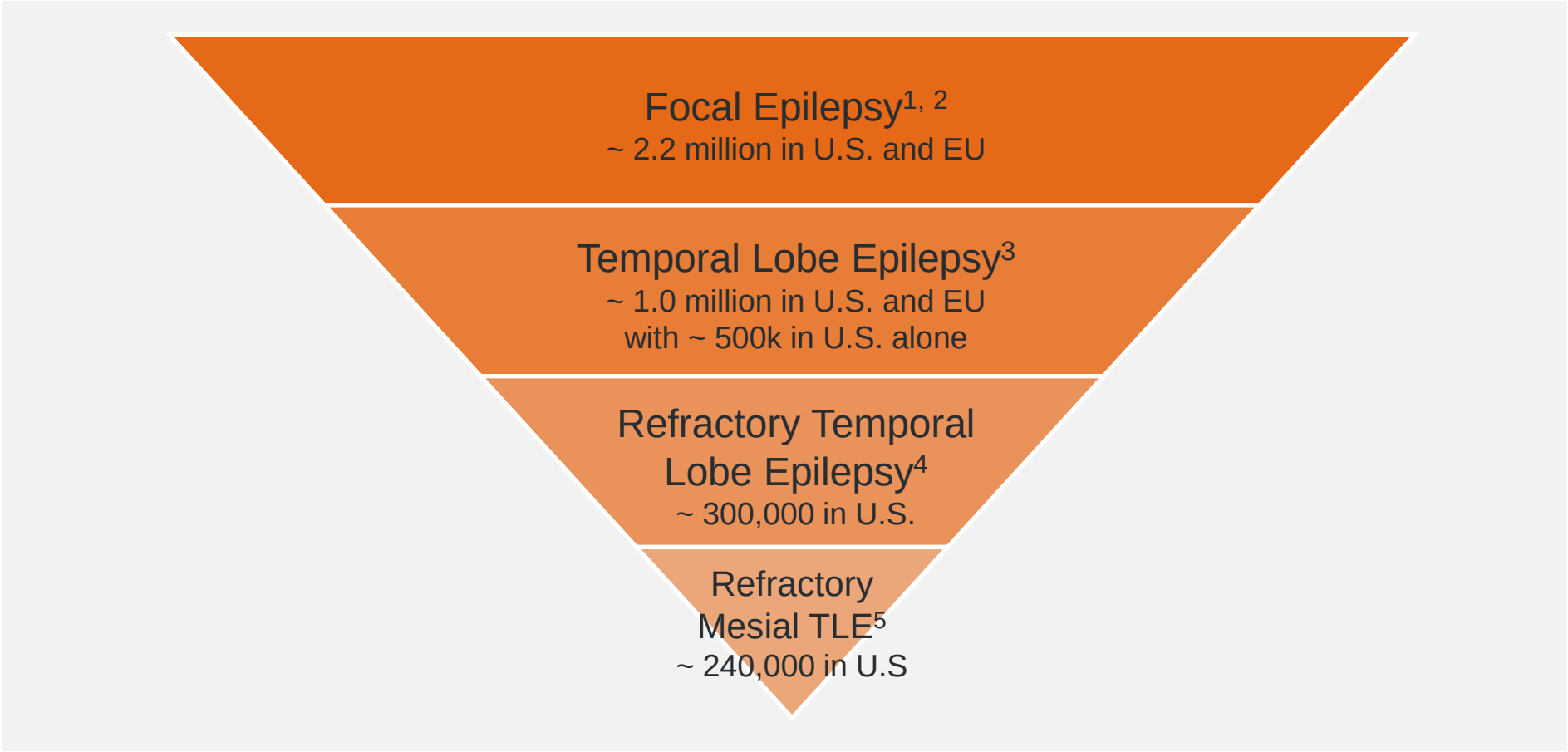
Injection into effected brain areas is targeted and accurate

Transduction efficacy in NHP hippocampus



Post-administration demonstrated full transduction within the hippocampus

uniQure AMT-260: targeted MTLE patient population for phase I/IIa study



1. Asadi-Pooya AA, Stewart GR, Abrams DJ, Sharan A. Prevalence and Incidence of Drug-Resistant Mesial Temporal Lobe Epilepsy in the United States. *World Neurosurg*. 2017;99:662-666. doi:10.1016/j.wneu.2016.12.074
2. Ioannou P, Foster DL, Sander JW, et al. The burden of epilepsy and unmet need in people with focal seizures. *Brain Behav*. 2022;12(9):e2589. doi:10.1002/brb3.2589
3. Mesraoua B, Deleu D, Al Hail HJ, et al. Prevalence and Incidence of Drug-Resistant Temporal Lobe Epilepsy in Qatar. *J Cent Nerv Syst Dis*. 2020;12:1179573520935031. Published 2020 Jun 27.
4. Yang L, Zhang R, Zhu H, Chen F, Yu N, Di Q. Factors influencing the long-term prognosis of patients with temporal lobe epilepsy: a single center study. Ann Palliat Med 2020;9(5):3194-3203. doi: 10.21037/apm-20-1415
5. https://www.epilepsy.com/what-is-epilepsy/syndromes/temporal-lobe-epilepsy#:~:text=Mesial%20temporal%20lobe%20epilepsy%20(MTLE,of%20all%20temporal%20lobe%20seizure

uniQure AMT-260: anticipated phase I/IIa clinical study

Study Overview

- Objective: assess safety, tolerability and first signs of efficacy
  - Part 1: U.S., multicenter, open-label, 1-month baseline period, dose-finding of two cohorts with a total of 12 patients
  - Part 2: Randomized, controlled trial for additional safety and proof of concept

Patient enrollment criteria

- Adult subjects, age 18-65
- Clinical diagnosis of refractory mesial temporal lobe epilepsy
- Confirmed disease severity based on seizure frequency

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Amyotrophic Lateral Sclerosis (SOD1 ALS)

AMT-162

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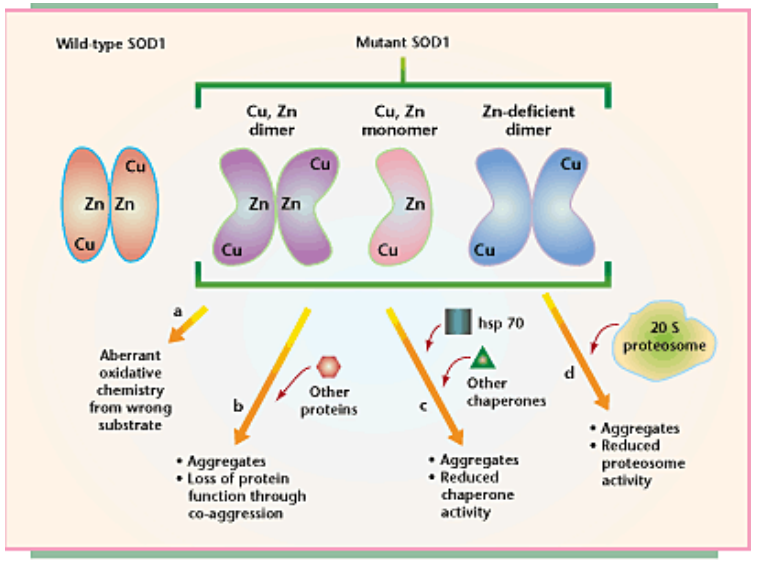
SOD1 Amyotrophic Lateral Sclerosis (ALS)

- **ALS** (aka Lou Gehrig's disease) is a progressive neurodegenerative disease that results in loss of motor neurons, involuntary movement, and death
- Average age of diagnosis is mid 50's; average lifespan of 2-4 years[1]
- Most cases are sporadic but ~10% are found to have a dominant genetic causation (familial), e.g., C9orf72*, SOD1, TPD42, FUS
- Mutations in SOD1 are found in ~20% of familial and up to 2% of sporadic cases of ALS[2]
- Approx 300 incident cases / year in US/EU5[2]

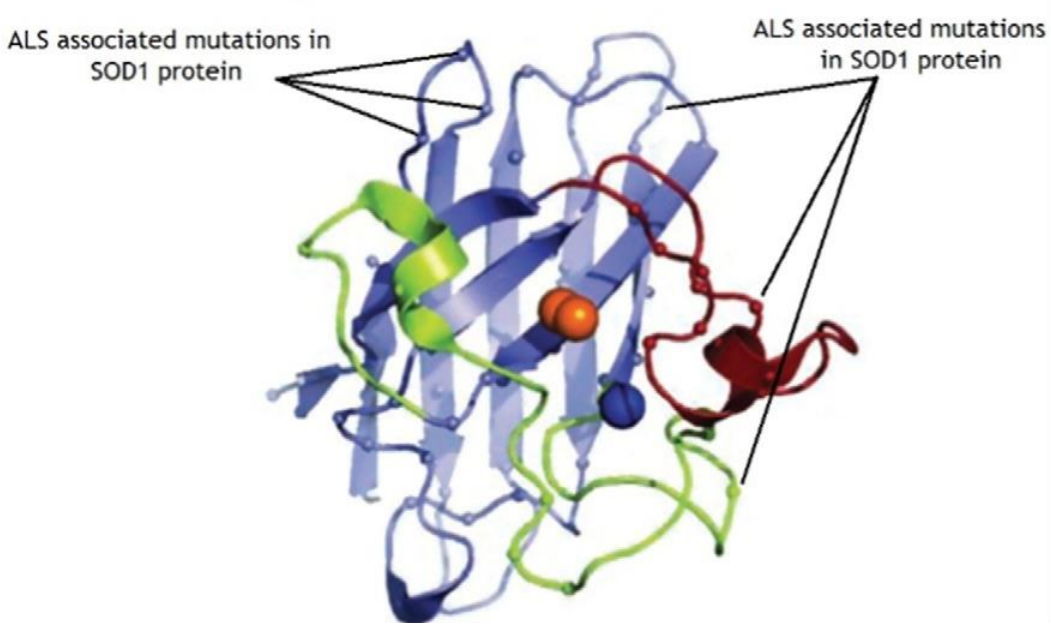


- **SOD1** (superoxide dismutase) is an enzyme that is responsible for catalyzing toxic superoxide to hydrogen peroxide and dioxygen
- While the exact mechanism for disease is not known, it is believed that a toxic gain of function in SOD1 results in oxidative stress and cell death of motor neurons

1) Brown RH, Al-Chalabi A. Amyotrophic Lateral Sclerosis. N Engl J Med. 2017 Jul 13

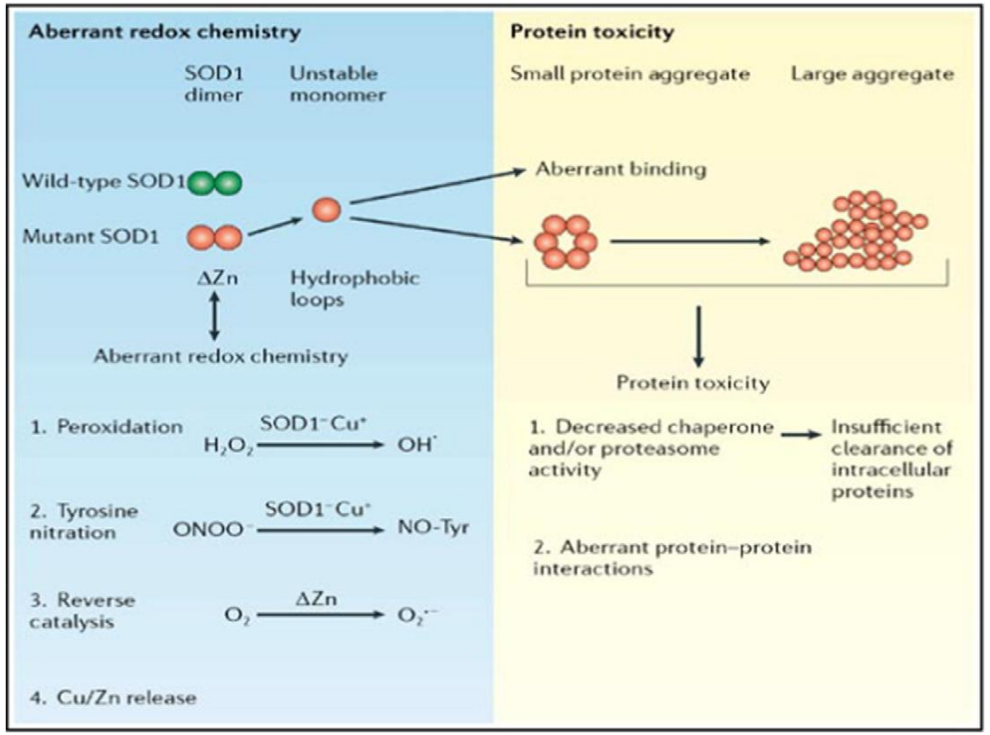
2) Brown CA, Lally C, Kupelian V, Flanders WD. Estimated Prevalence and Incidence of Amyotrophic Lateral Sclerosis and SOD1 and C9orf72 Genetic Variants. Neuroepidemiology. 2021

SOD1 genetics and pathophysiology



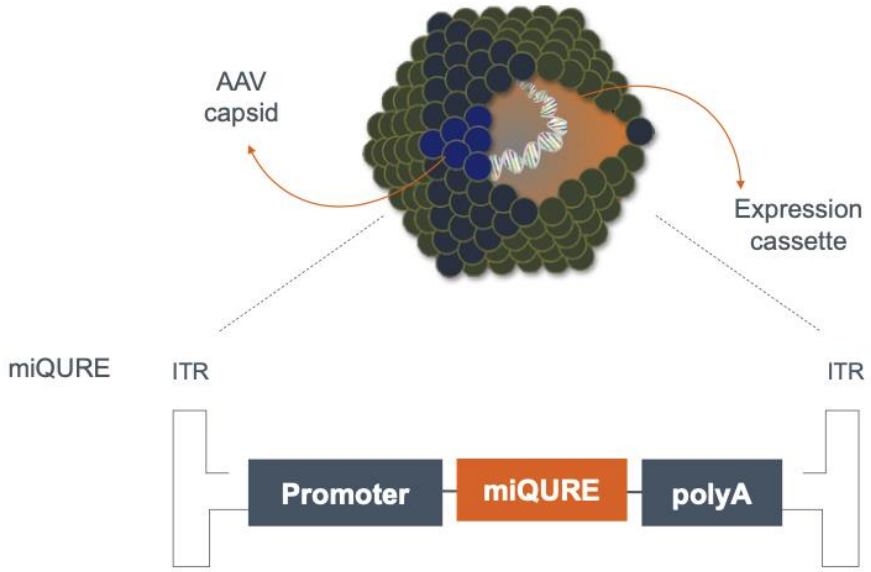
- More than 100 Pathogenic SOD-1 have been identified.
- Mutations are concentrated in a few regions of the protein.
- Mutations can be both dominant and recessive.
- Most common mutations: D90A, G93A, A4H, D46R
- Patients with different mutations progress at different rates

Mutations in SOD1 are a toxic gain of function that can affect many aspects of neuronal biology



uniQure AMT-162 for SOD1-ALS

- Recombinant AAVrh10 vector expresses an artificial micro ribonucleic acid (miRNA) designed to knock down the expression of SOD1
- Intrathecally administered
- *In vivo* mouse data demonstrates greatly enhanced survival
- *In vivo* mouse and NHP data supports biodistribution with SOD1 reduction in spinal cord motor neurons



uniQure AMT-162: anticipated phase I/II clinical study

Study Overview

- Objective: assess safety, tolerability and first signs of efficacy
  - Part 1: U.S., multicenter, open-label, three ascending doses with 2-4 patients per dosing level
  - Part 2: Randomized 1:1, controlled trial of ~30 patients for additional safety and proof of concept

Patient enrollment criteria

- Adult subjects
- Confirmed mutant SOD1-mediated ALS experiencing signs and/or symptoms of lower motor neuron dysfunction with or without upper neuron symptoms

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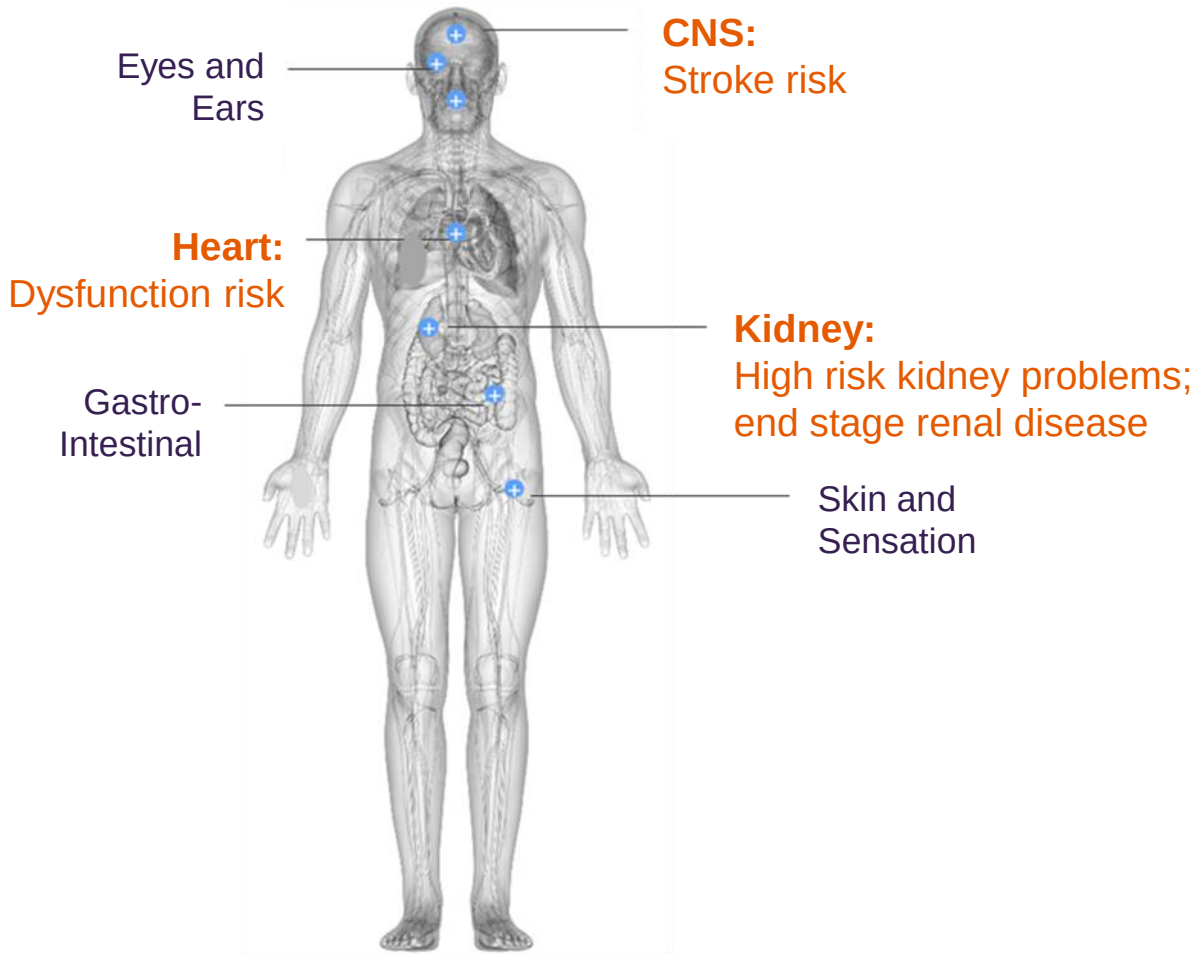
Fabry Disease
AMT-191

Fabry disease: a lysosomal storage disease

- X-linked genetic disorder
- Deficiency of α-galactosidase A (GLA)
- Incidence: 1:3,700 – 80,000 live births*
- Population: ~15,000 in US and Europe

Symptoms:

- Fatigue and hearing loss
- Neuropathic pain
- Angiokeratomas
- Corneal opacity
- Cardiac disease
- Renal failure
- Stroke risk



* Spada, et al, Am. J. Hum. Gent. 2006:79, 31-40

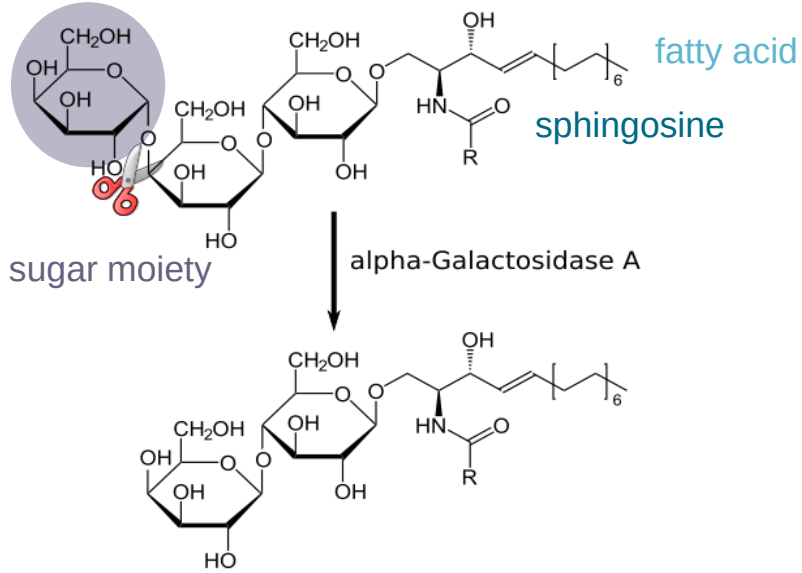
Fabry disease: unmet need with current enzyme replacement therapy (ERT)

- α-galactosidase A (GLA) degrades:
  - Globotriaosylceramide (Gb3)
  - Lyso-Gb3
- Systemic accumulation of substrate in lysosomes of endothelial cells in the kidney, heart and brain

The standard of care is bi-weekly enzyme replacement therapy (ERT)

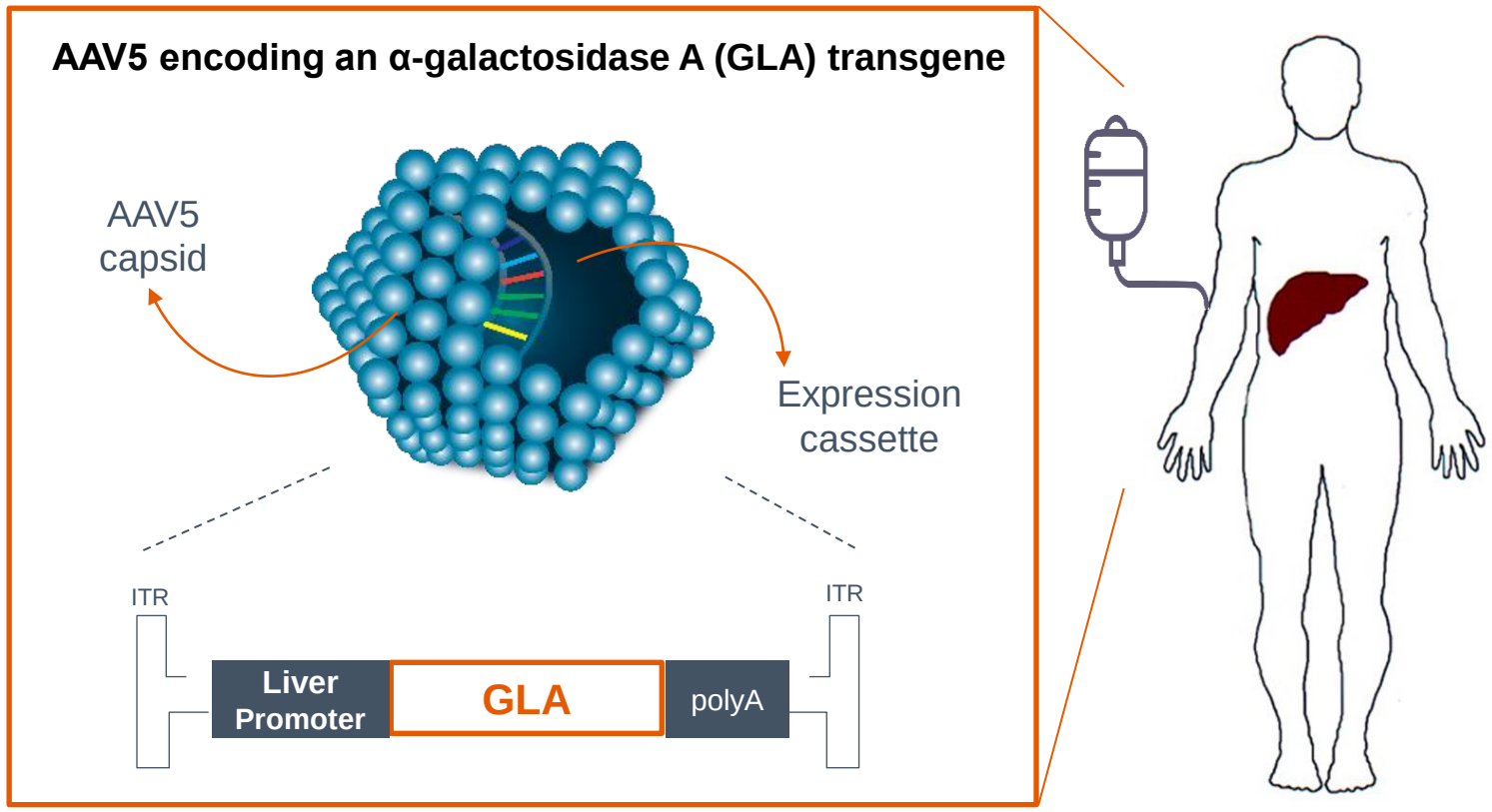
- ERT has limited tissue penetration and biodistribution
- Results in poor substrate clearance in the heart and kidney
- Disease progresses despite ERT

Globotriaosylceramide



Desnick and Schuchman Annu. Rev. Genomics Hum. Gent. 2012; 13:307-35

uniQure AMT-191: AAV5-GLA Gene Therapy for Fabry disease



Gene therapy

- One-time long-term treatment
- GLA transgene delivery

AAV5-vector

- Low immunogenicity*
- Excellent liver distribution

Liver specific promoter

- Potent and specific proprietary promoter

* Majowicz A. et al. Haemophilia 2020; 26:20-20

uniQure AMT-191: anticipated phase I/IIa clinical study

Study Overview

- Objective: assess safety, tolerability and initial signs of efficacy
  - Open-label, 3+3 dose escalation design
    - Three patients will be dosed. If not dose-limiting toxicology (DLT) is identified, the dose will be escalated
    - If DLT occurs in one of the three initial patients, three additional patients will be enrolled at the same dose level
    - If no additional patients experience a DLT, the dose will be escalated.
  - Assessments will be made a three- and six-months post-treatment

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