uniQure

Leadership in Gene Therapy

January 2026

Sophia –
Huntington's Disease
Community Advocate

Disclaimer

This presentation contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), 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, disease-modifying treatment option for patients with Huntington's disease; our plans with respect to regulatory interactions with the relevant authorities in the U.S. and ex-U.S., including with respect to interactions with the U.S. FDA regarding a potential accelerated approval pathway for AMT-130; the design and engineering of AMT-130 to maximize clinical and functional benefit; our plans for further clinical updates and plans to announce additional data, including with respect to our AMT-191 and AMT-260 programs; and our planned milestones for 2026. 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 the our Phase I/II clinical trials of AMT-130, including the risk that such trials will be unable to demonstrate data sufficient to support further clinical development or regulatory approval; the risk that the FDA ultimately concludes that such trials are not adequate and well-controlled to provide the primary evidence to support a BLA; the risk that more patient data become available that results in a different interpretation than the one derived from the topline AMT-130 data or preliminary data for our other programs; risks related to our 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 are viewed as robust and sensitive measurements of disease progression; whether RMAT 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, July 29, 2025, and November 10, 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.

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 make 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.

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

uniQure – A Leader in Gene Therapy

Gene therapy pioneer with **validated AAV platform** and **successful track record**

Robust clinical pipeline with data readouts in MTLE and Fabry over the next 3-6 months

AMT-130 is the first potential **disease-modifying therapy** for HD **with blockbuster potential**

Focused engagement with FDA to align on a pathway to BLA submission

Leveraging **preferred customer status** for **world-class, commercial-ready manufacturing capabilities**

Strong financial position, with approximately $694.2M of cash as of September 30, 2025*

*Cash, cash equivalents and investment securities.

Abbreviations: AAV, adeno-associated virus; HD, Huntington's disease; BLA, Biologics License Application; FDA, Food & Drug Administration; MTLE, mesial temporal lobe epilepsy

Management Team

Matt Kapusta
Chief Executive Officer

Richard Porter, Ph.D.
Chief Business and Scientific Officer

Kylie O'Keefe
Chief Customer and Strategy Officer

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

Amin Abujoub, Ph.D.
Chief Technology Operations Officer

Erin Boyer
Chief People and Culture Officer

Christian Klemt
Chief Financial Officer

Jeannette Potts, Ph.D., J.D.
Chief Legal and Compliance Officer

History of Innovation

uniQure: A gene therapy pioneer with a 25-year history and deeply ingrained culture of innovation across an increasingly validated platform

First approved gene therapy in the western world

First commercially licensed gene therapy manufacturing facility

First AAV-delivered gene silencing therapy for Huntington's disease to enter clinical development

First AAV vector demonstrated to be clinically shown to be effective in patients with pre-existing NABs

First FDA approval of a gene therapy for adult patients with Hemophilia B

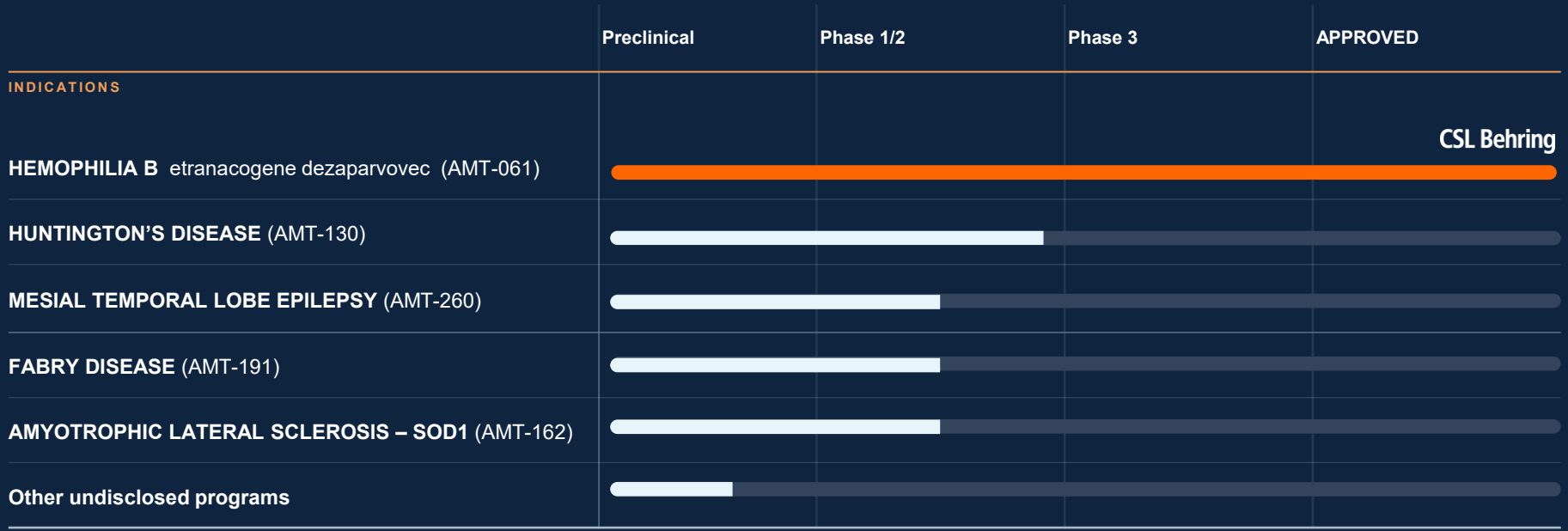
First FDA RMAT designation for a gene therapy treatment for Huntington's disease

First FDA Breakthrough Therapy designation for a gene therapy treatment for Huntington's disease

Commercial manufacturing facility sold to Genezen in 2024

Abbreviations: AAV, adeno-associated virus; HD, Huntington's disease; NAB, neutralizing antibody; FDA, Food & Drug Administration; RMAT, Regenerative Medicine Advanced Therapy

Our Research and Development Pipeline



AMT-130: Huntington's disease

Charles –
Huntington's Disease
Community Advocate

AMT-130: Huntington's disease

- HD is a progressive neurodegenerative disease with no disease-modifying treatments available
- Autosomal dominant inherited disorder (50% risk if a parent has HD)
- Estimated ~100K[1] genetically identifiable patients in US with HD

Ashley –
Huntington's Disease
Community Advocate

Abbreviations: HD, Huntington's Disease.
References: 1. Fisher et al., 2014; Yohrling et al. 2020

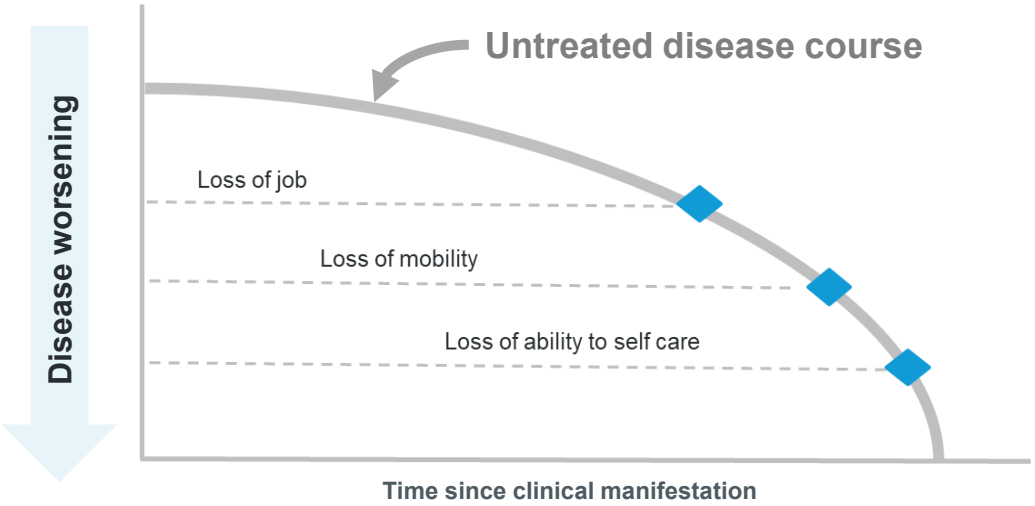
Slowing Progression of Huntington's Disease Could Extend Patients' Quality of Life

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

AMT-130 aims…

To **slow the rate of disease progression**

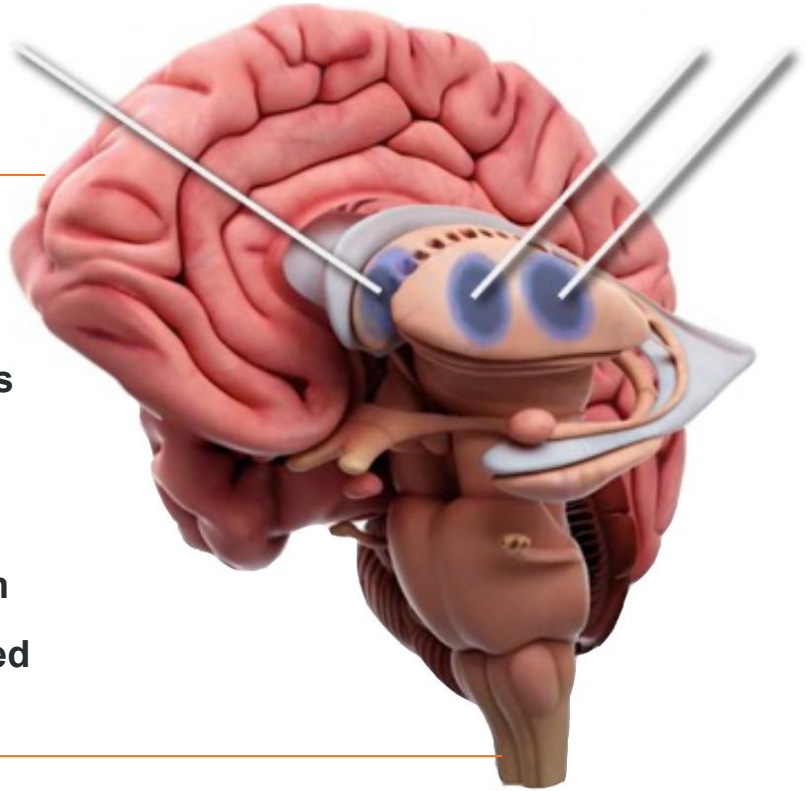
To provide HD patients with an **improved quality of life**



Abbreviations: HD, Huntington's Disease.

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

AMT-130: A Promising Approach to Treat Huntington's Disease



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

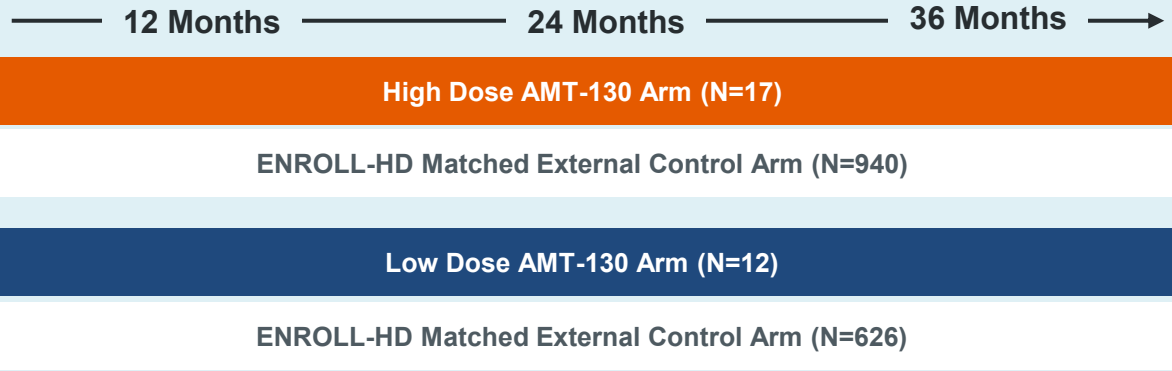
- **One-time administration** with potentially **long-term effects**
- **Precision-delivery** directly to diseased areas of the brain
- **Minimizes systemic exposure** of drug
- Suppresses both **HTT** and the **highly toxic exon-1 isoform**
- Standard stereotactic **procedure can be broadly performed**

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

AMT-130 Phase I/II 36-Month Data

AMT-130: Pivotal Phase I/II Study Design

Prespecified statistical analysis plan



***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	

AMT-130: A Promising Approach to Treat Huntington's Disease

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

Clinical Measures

Statistically significant slowing of disease progression as measured by **cUHDRS** (primary endpoint) and **TFC** (secondary endpoint)

Neurodegeneration

CSF **NfL below baseline**

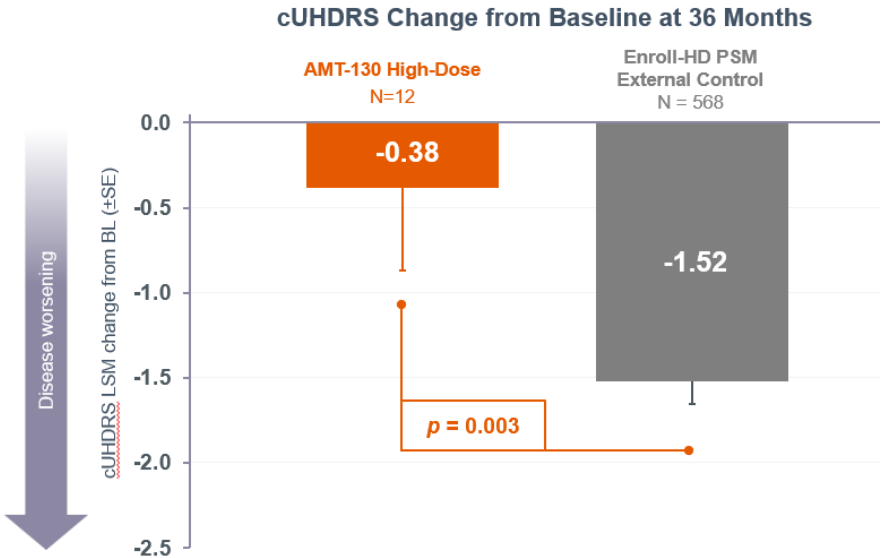
Safety Profile

Generally well-tolerated with **no new SAEs** related to AMT-130

Data cutoff date of June 30, 2025
Abbreviations: cUHDRS, composite Unified Huntington's Disease Rating Scale; TFC total functional capacity, CSF, Cerebrospinal fluid; NfL Neurofilament light chain; SAE, serious adverse event
References: Data on file. September 2025

AMT-130: A Promising Approach to Treat Huntington's Disease

Demonstrated statistically significant slowing of disease progression at 36 months



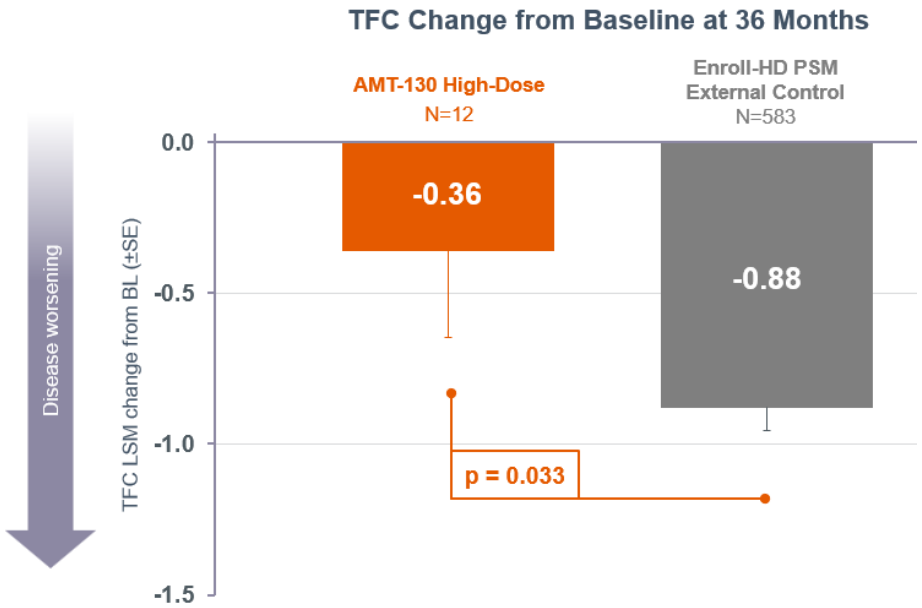
AMT-130 high-dose **significantly reduced disease progression by 75% based on cUHDRS** compared to a propensity score-matched external control. (p=0.003)

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

Data cutoff date of June 30, 2025
Abbreviations: cUHDRS, composite Unified Huntington's Disease Rating Scale; TFC, Total Functional Capacity; HD, Huntington's disease, SE, standard error; PSM, propensity score-matched; LSM, least squares mean; BL, baseline
References: Data on file. September 2025

AMT-130: A Promising Approach to Treat Huntington's Disease

Demonstrated statistically significant slowing of disease progression at 36 months



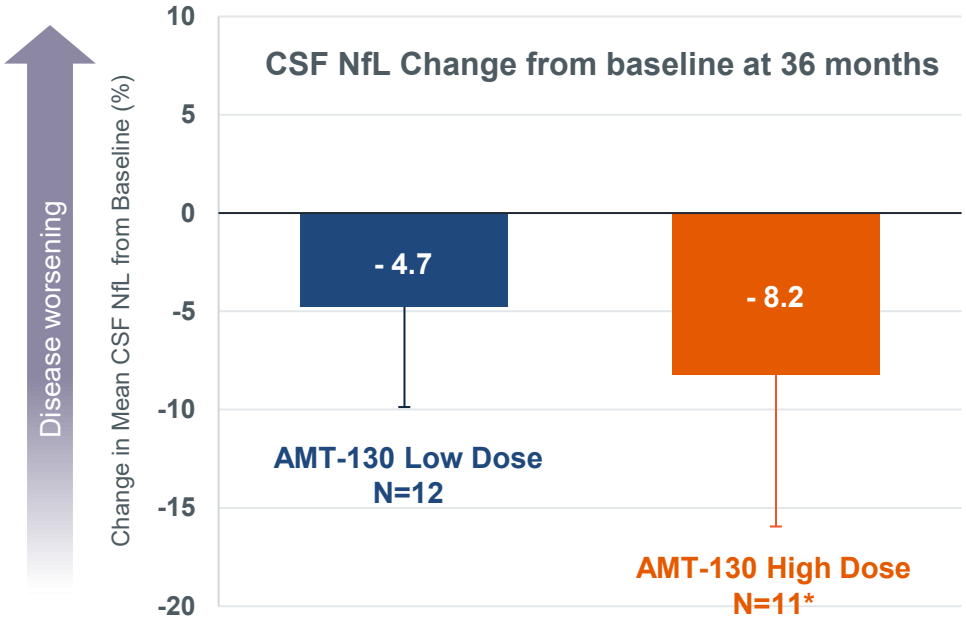
AMT-130 high-dose **significantly reduced disease progression by 60% based on TFC** compared to a propensity score-matched external control. (p=0.033)

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

Data cutoff date of June 30, 2025
Abbreviations: cUHDRS, composite Unified Huntington's Disease Rating Scale; TFC, Total Functional Capacity; HD, Huntington's disease, SE, standard error; PSM, propensity score-matched; LSM, least squares mean; BL, baseline
References: Data on file. September 2025

AMT-130: A Promising Approach to Treat Huntington's Disease

Demonstrated reductions of CSF NfL at 36 months



AMT-130 low and high dose **CSF NfL at 36 months were below baseline.**

*1 of 12 patients declined to undergo a lumbar puncture procedure
Data cutoff date of June 30, 2025
Abbreviations: CSF, cerebrospinal fluid; NfL, neurofilament light chain
References: Data on file. September 2025.

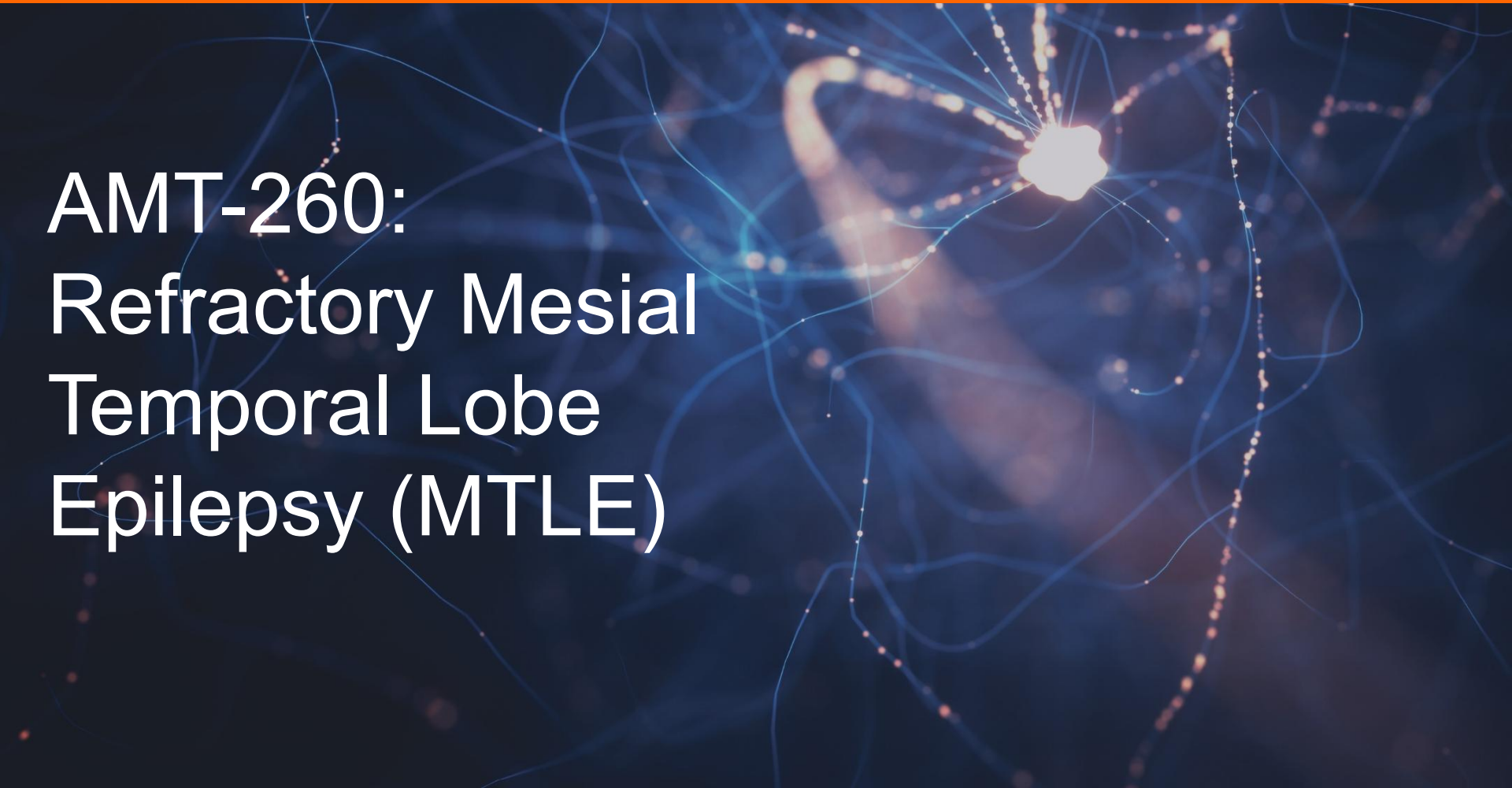
Safety Summary: AMT-130 Remained Generally Well Tolerated

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**

Data cutoff date of June 30, 2025



AMT-260: Refractory Mesial Temporal Lobe Epilepsy (MTLE)

AMT-260: Refractory Mesial Temporal Lobe Epilepsy (MTLE)

- Most common form of epilepsy
- ~240K[1] are treatment-resistant
- AAV9-GRiK2 (miRNA) investigational gene therapy

Lena - Temporal Lobe Epilepsy (TLE) Community Advocate

References: 1 Yang L *et al.* Long-term prognosis in temporal lobe epilepsy. *Ann Palliat Med.* 2020.

AMT-260: Refractory Mesial Temporal Lobe Epilepsy (MTLE)

Ph 1/2 Overview

- Full enrollment of Cohort 1, First patient enrolled in Cohort 2
- Objective: assess safety, tolerability and signs of efficacy
- Part I: U.S., multicenter, open-label, dose-finding study in a total of 12 patients
- Part II: Randomized, controlled trial for additional safety and proof of concept

Observation Period

12 Subjects
3 months retrospective data
≥30 days prospective data

Cohort 1

Patient 1 → DSMB → Patients 2 - 3 → DSMB → Patients 4 – 6

Cohort 2

Patient 7 → DSMB → Patients 8 - 9 → DSMB → Patients 10 –12

Patients 1-3 and 7-9 required to be MRI positive with non-dominant hemisphere lesions only

Patients 4-6 and 10-12 can include dominant hemisphere lesions and not required to be MRI positive

Enrollment as of Jan 1, 2026
Abbreviations: DSMB; data safety monitoring board; MRI, magnetic resonance imaging

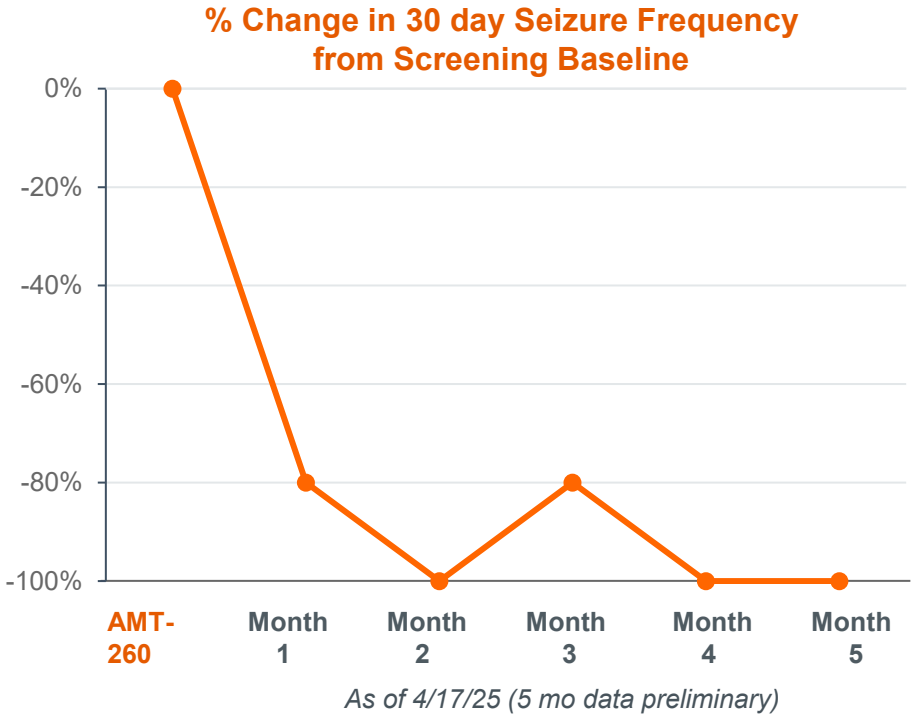
Case Study from the First Participant Dosed with AMT-260 Through Five Months of Follow Up

Safety data:

- No SAEs
- No AE of neuroinflammation or neuroimaging abnormalities
- No worsening seizures or new seizure type

Exploratory Efficacy Data:

- Encouraging signs of seizure reduction from screening and retrospective periods
- The patient previously averaged 7 seizures/month in retrospective period, and 5 seizures/month in screening period, despite multiple ASDs



Data cutoff date of April 17, 2025

References: Data on file. **Abbreviations:** SAE, serious adverse event; ASD, anti-seizure drug

AMT-191:
Fabry Disease

AMT-191: Fabry Disease

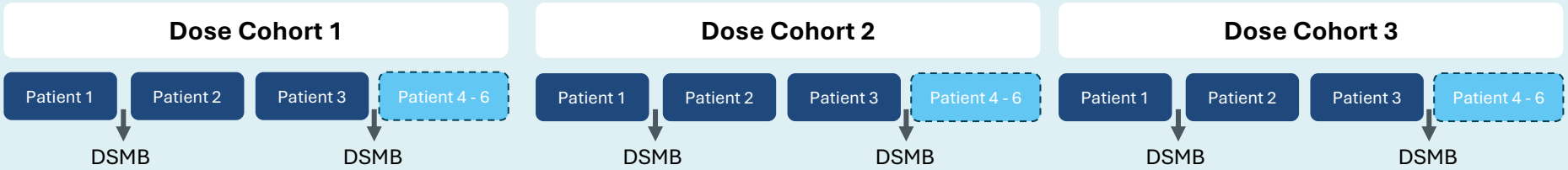
- ~15,000[1] people in US+EU5
- ERT – poor uptake in heart/kidneys
- AAV5-GLA investigational gene therapy

Reference: 1. Spada, et al, Am. J. Hum. Gent. 2006:79, 31-40 **Abbreviations:** EU5, Germany, France, Italy, Spain United Kingdom; ERT, enzyme replacement therapy

AMT-191: Fabry Disease

Ph 1/2 Overview

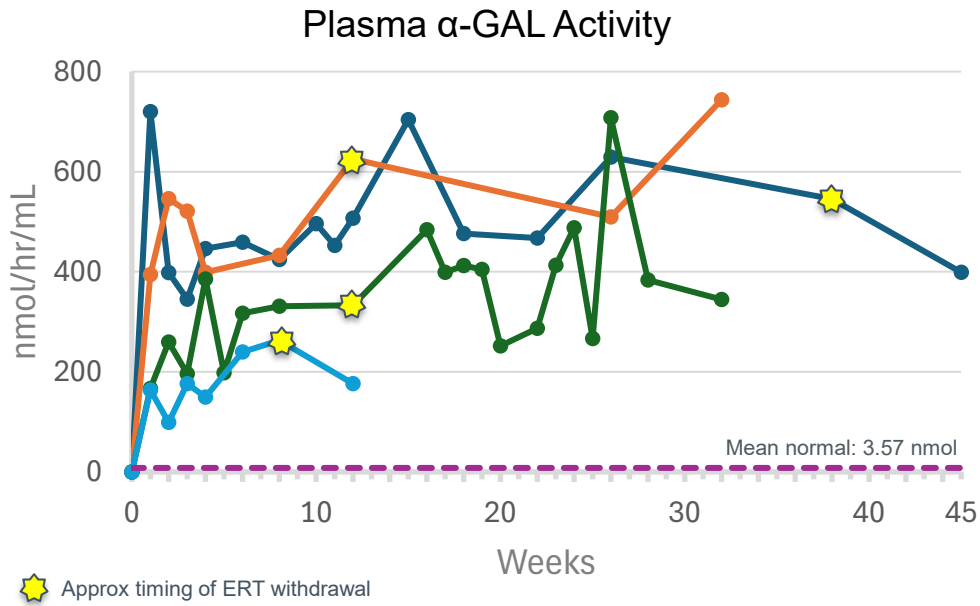
- Cohorts 1, 2 and 3 are fully enrolled
- Objective: assess safety, tolerability and signs of efficacy
- U.S., open-label, multi-center study
- Dose-ranging in up to 12 patients



Abbreviations: DSMB; data safety monitoring board

AMT-191: Cohort 1 - Exploratory Efficacy Biomarkers

Initial individual patient data: α-GAL **

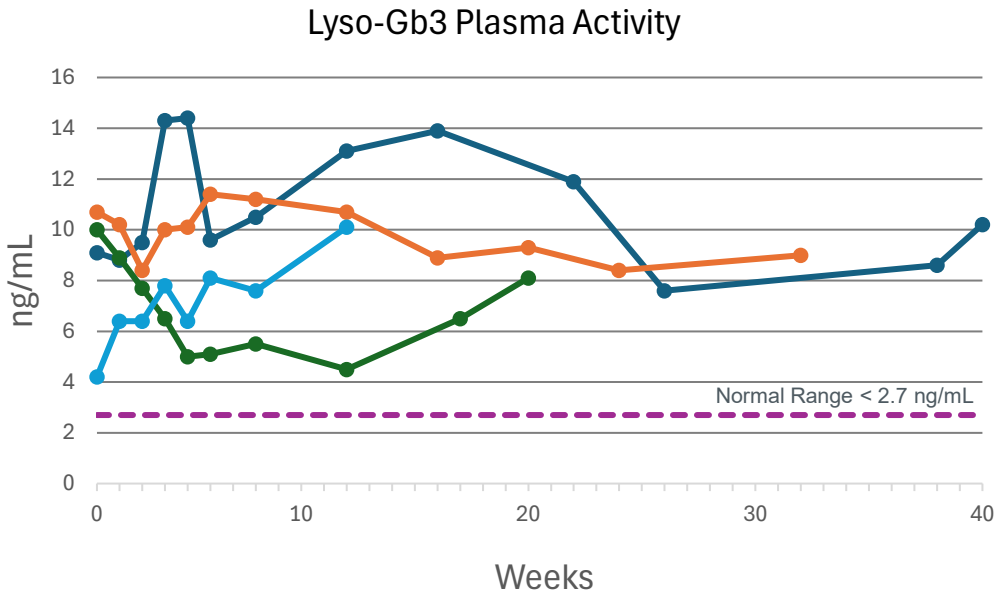


- Achievement of supraphysiological* α-GAL activity observed after 1-week post-treatment
- Sustained elevated α-GAL levels for up to 45 weeks
- Therapeutic levels maintained post-ERT discontinuation

* Normal α-GAL range: 1.38-8.66 nmol, Mean normal 3.57 nmol
** Data cutoff date of July 24, 2025

AMT-191: Cohort 1 - Exploratory Efficacy Biomarkers

Initial individual patient data: plasma lyso-Gb3 levels**



- Lyso-Gb3 levels were higher than normal range* however in line with patients receiving ERT
- Lyso-Gb3 levels remained stable post AMT-191 administration

* Normal lyso-Gb3 range: < 2.7 ng/mL
** Data cutoff date of July 24, 2025
Abbreviations: ERT, enzyme replacement therapy

AMT-191: Cohort 1 – Safety Data

Manageable Safety Profile at $6.0x10^{13}$ gc/kg Dose

Treatment-emergent adverse events: Majority Grade 1-2 laboratory values.

A single Grade 3 laboratory value (LFT elevation) – resolved with corticosteroids

Of TEAEs reported, 5 were SAEs:
1 possibly related to treatment,
2 considered related and
2 not related to treatment

No infusion-related reactions reported

Data cutoff date of July 24, 2025
Abbreviations: SAE, serious adverse event; LFT, Liver Function Tests; TEAE, treatment emergent adverse event
References: Data on file. September 2025

Key Milestones

Ashley –
Huntington's Disease
Community Advocate

Key Milestones Achieved in 2025

AMT-130: Huntington's Disease

- ✓ Initiated BLA-readiness activities
- ✓ Met with FDA on primary statistical analysis plan and CMC requirements in 1H 2025
- ✓ Provided Phase I/II 36-month follow-up in 3Q2025
- ✓ Held pre-BLA meeting in 4Q25

Other Programs

- ✓ Presented case study from first patient dosed with AMT-260 MTLE in 2Q25
- ✓ Presented initial data from AMT-191 Fabry study in 3Q25

Abbreviations: BLA, Biologics License Application; FDA, Food & Drug Administration; MTLE, mesial temporal lobe epilepsy; CMC, Chemistry, Manufacturing and Controls

Planned Milestones for 2026

AMT-130: Huntington's Disease

- Complete CMC requirements for BLA submission
- Engage with FDA on Accelerated Approval pathway
- Prepare for potential commercialization
- Define pathway in ex-US markets

Other Programs

- Present additional clinical data in AMT-260 MTLE in 1H26
- Complete enrollment of Cohort 2 in Phase I/II trial of AMT-260 for MTLE
- Present additional clinical data in AMT-191 Fabry in 1Q26

Abbreviations: BLA, Biologics License Application; FDA, Food & Drug Administration; MTLE, mesial temporal lobe epilepsy; CMC, Chemistry, Manufacturing and Controls

Strong Financial Position with Prudent Capital Allocation

In September 2025, **completed an upsized $300 million** public offering with gross proceeds of $345 million.

Also in September 2025, **refinanced existing $50 million debt** and secured up to an **additional $125 million** of non-dilutive funding

$694.2M

cash on hand as of 30th September 2025

*Cash, cash equivalents and investment securities

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uniQure