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GenTLE Phase 1/2a Clinical Study of AMT-260: Preliminary Results of an Investigational Gene Therapy for Refractory MTLE

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AMT-260 is an investigational agent currently being studied in the treatment of mesial temporal lobe epilepsy. Its safety and efficacy have not been established, and it has not been approved by the United States Food and Drug Administration, European Medicines Agency, or any other regulatory body. There is no guarantee that investigational agents will receive health authority approval or become commercially available.

Background

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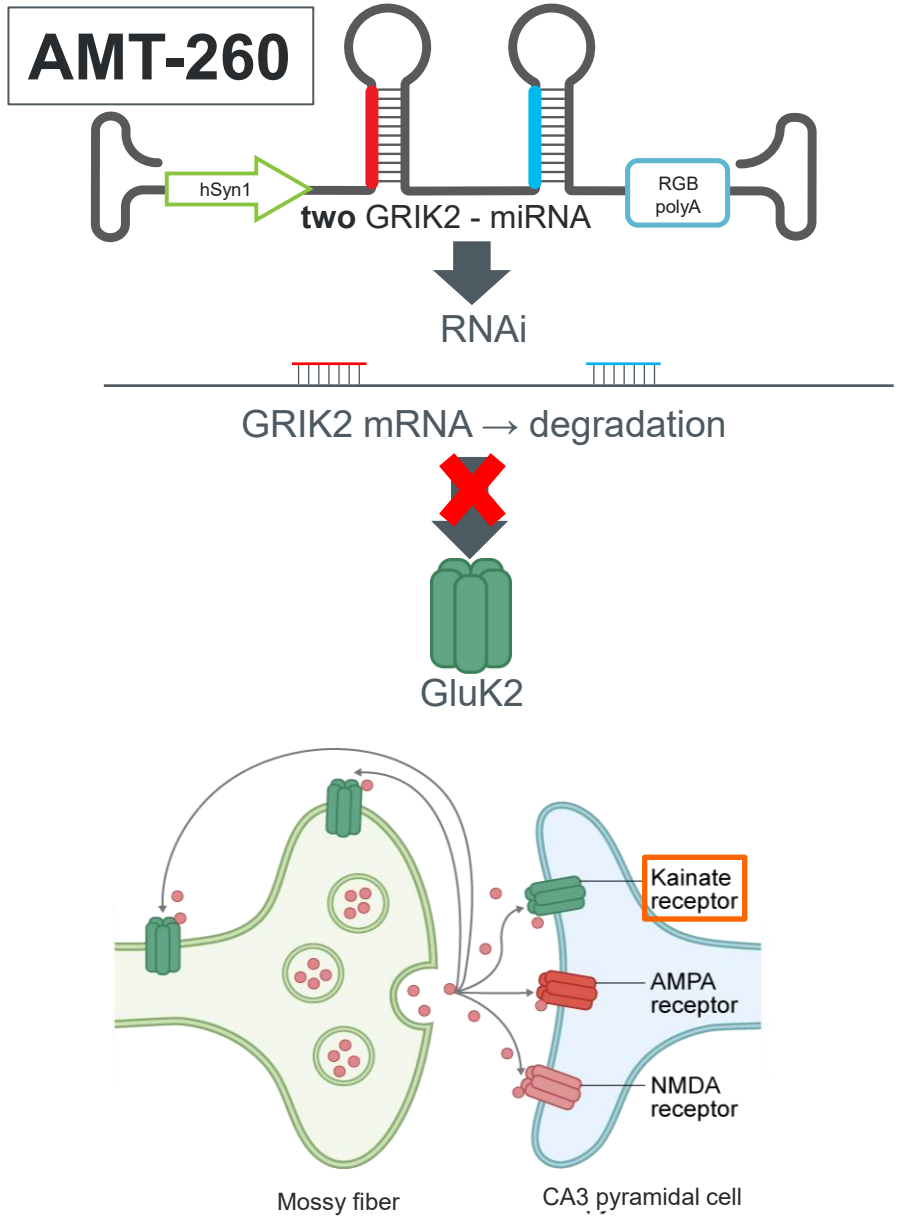
- Mesial temporal lobe epilepsy (MTLE) is the most common form of focal epilepsy in adults[1]
- AMT-260 is a gene therapy candidate under investigation intended to reduce or eliminate seizures in people with refractory MTLE
  - AAV9 encoding 2 engineered miRNAs targeting GRIK2 mRNA
  - Designed to reduce expression of the *GluK2* subunit of kainate-type glutamate receptors (KARs)



AAV9, adeno-associated virus serotype 9; AMPA, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; GluK2, glutamate ionotropic receptor kainite type subunit 2; GRIK2, glutamate ionotropic receptor kainite type subunit 2; KAR, kainate-type glutamate receptor; miRNA, microRNA; mRNA, messenger RNA; MTLE, mesial temporal lobe epilepsy; NDMA, N-methyl-D-aspartate; RNAi, RNA interference.

1. Semah F. *Neurology*. 1998;51(5):1256-62.

Study Objective and Design

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GenTLE

Phase 1/2a clinical trial

NCT06063850

Objective: To evaluate the safety, tolerability, and exploratory signs of efficacy of AMT-260 in adults with unilateral refractory MTLE and a baseline mean of ≥2 focal impaired awareness seizures per month

Screening period

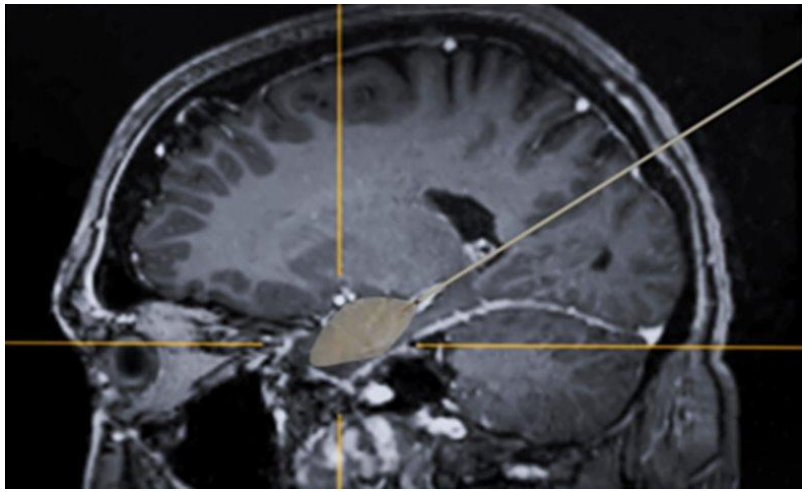
Treatment & evaluation period (12 months)

Cohort 1: Low dose (n=6)

Cohort 2: High dose (n=6)

LTFU (+4 years)

Delivery:
Single administration via stereotactic surgery into the hippocampus



Endpoints	
Primary:	Incidence of TEAEs; tolerability
	Vector and miRNA biodistribution, vector shedding
Secondary:	Early signs of efficacy
	Neuropsychology

LTFU, long-term follow-up; miRNA, microRNA; MTLE, mesial temporal lobe epilepsy; TEAE, treatment-emergent adverse event.

Results: Primary Endpoints for Cohort 1

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Baseline Characteristics

Characteristics	Cohort 1: Low dose (n=6)
Age (years), median (range)	52 (36, 61)
Male, n (%)	4 (67)
BMI (kg/m^2), median (range)	30 (19, 32)
Dominant TLE, n (%)	3 (50)
Mesial temporal sclerosis, n (%)	3 (50)
Duration of epilepsy (years), median (range)	16 (8, 55)
Baseline disabling seizures per 28 days, median (range)	7 (5, 14)
Baseline antiseizure medications, median (range)	3 (2, 4)

AE, adverse event; BMI, body mass index; CNS, central nervous system; DLE, dose-limiting event; MRI, magnetic resonance imaging; SAE, serious adverse event; TLE, temporal lobe epilepsy.

Safety Outcomes*

- AEs were reported in 4 of 6 participants; 16 were Grade 1 and 5 were Grade 2 severity, with headache most common (n=2)
- AEs were considered by investigators to be related to the AMT-260 neurosurgical procedure (48%) or AMT-260 (19%) in a minority of cases
- No SAEs, DLEs, or AEs leading to study discontinuation

* As of 29May2026 data cut date

Results: Secondary Endpoint for Cohort 1

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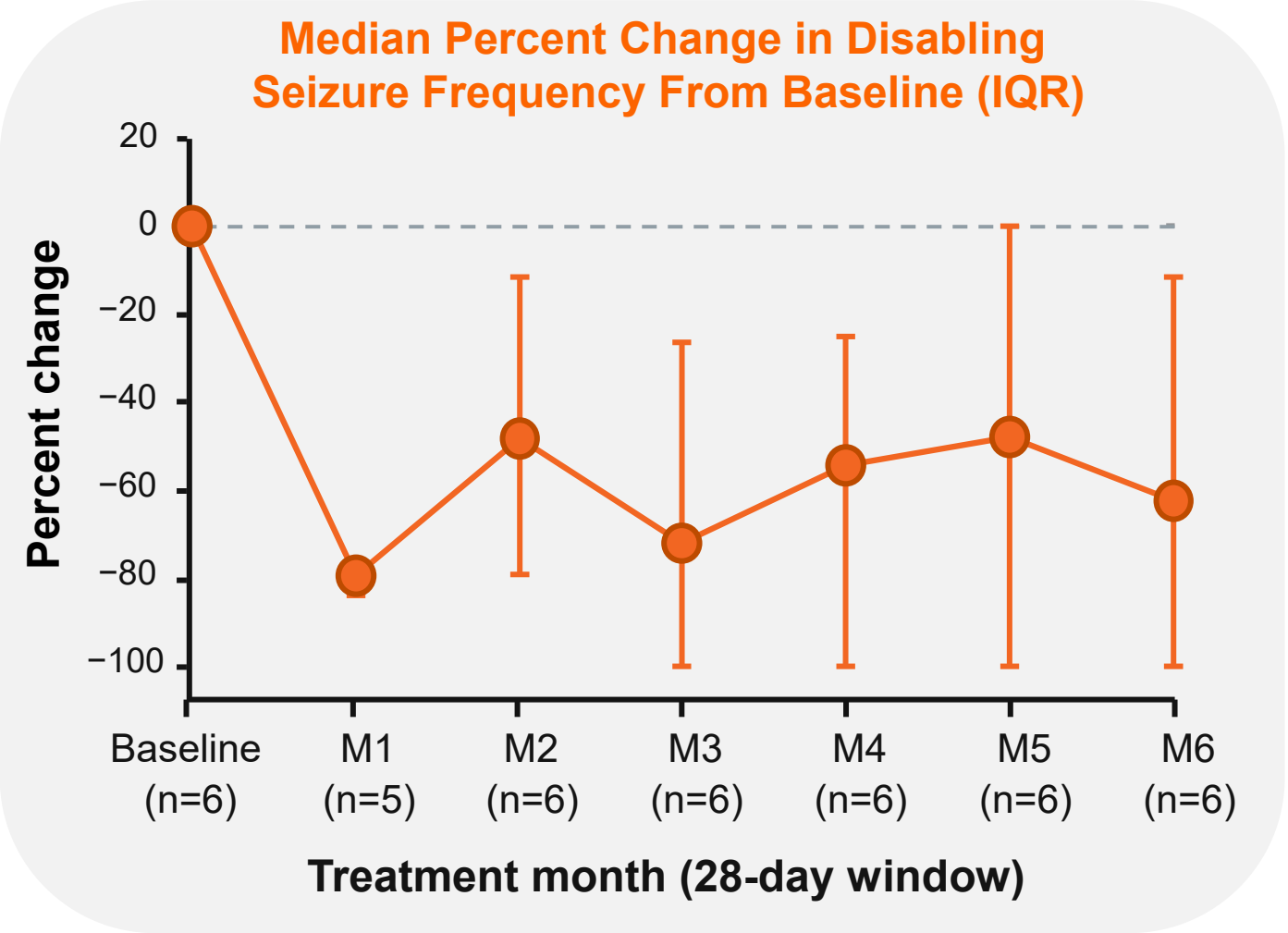
- During months 4 to 6, 3 of 6 participants achieved reduction in disabling seizures (ranging from 79-100%)
- The remaining three participants experienced variable changes in seizure frequency ranging from a 33% decrease to a 36% increase



Summary

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Safety Profile:

- AEs reported in Cohort 1 were Grade 1 or 2 in severity
- No SAEs or DLEs in any participant to date across the study

Initial Clinical Data, Cohort 1:

- During months 4 to 6, 3 of 6 participants achieved reduction in disabling seizures (ranging from 79-100%)
- The remaining three participants experienced variable changes in seizure frequency ranging from a 33% decrease to a 36% increase

Looking Ahead:

- Cohort 2 (high dose) is currently enrolling

AE, adverse event; DLE, dose-limiting event; SAE, serious adverse event.