

uniQure

GenTLE

GenTLE Clinical Study of AMT-260

AAV9-microRNA based therapy for the treatment of refractory MTLE

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on behalf of the entire AMT-260 Global Project Team*

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.

AMT-260: Mechanism of Action

AAV9 investigational gene therapy targeting GluK2

- **Kainate receptors** are ionotropic glutamate receptors which modulate excitatory neurotransmission, synaptic plasticity, and network excitability
- Aberrant KAR expression and function are implicated in **chronic TLE**
- KARs are composed of subunits GluK1 - 5, encoded by genes GRIK1- 5

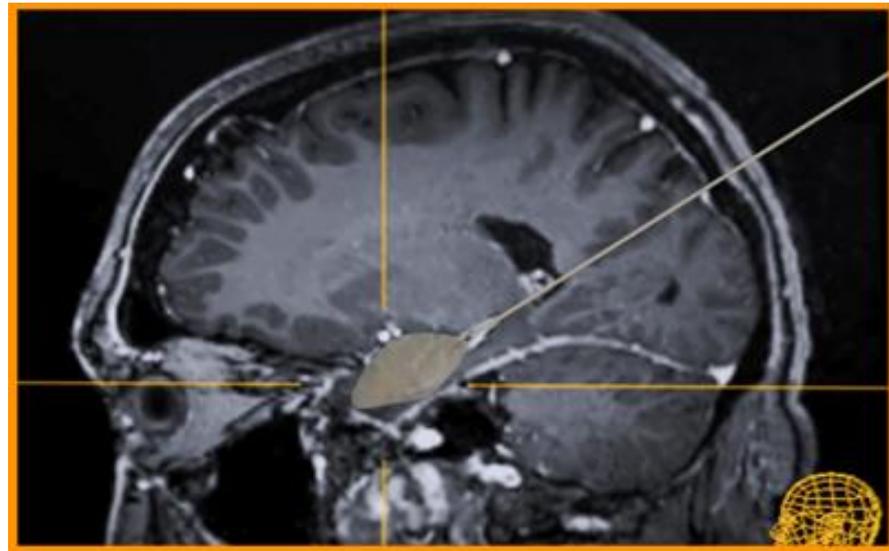
- **AMT-260** is a recombinant AAV9 coding for two engineered miRNAs which interfere with GRIK2 mRNA
- Interference reduces the expression of the GluK2 glutamate receptor subunit
- This leads to a reduced expression of Kainate receptors containing the GluK2 subunit



AMT-260: Route of Administration

Single administration into the affected hippocampus

- AMT-260 is delivered via stereotactic surgery into the hippocampus
- Single administration
- Single trajectory
- MRI-guided Convection-Enhanced Delivery (CED)





A Multi-center, Phase 1/2a, First-in-human (FIH) Study Investigating the Safety, Tolerability, and Efficacy of AMT-260 in Adults with Unilateral Refractory Mesial Temporal Lobe Epilepsy (MTLE) Administered via Magnetic Resonance Imaging (MRI)-guided Convection-enhanced Delivery (CED)

Screening Period

3 months retrospective data
≥30 days prospective data

Cohort 1

Subj. 1

Subj. 2-3

Subj. 4-6

DSMB

DSMB

Cohort 2 (*adapted dose*)

Subj. 7

Subj. 8-9

Subj. 10-12

DSMB

DSMB

DSMB



Participants

18-65 years old
12 males/females
(2 cohorts/2 doses)



Population

Diagnosis of
unilateral
refractory MTLE

(average ≥ 2 focal onset
impaired awareness
seizures/month)



Locations

12 + US sites



Study duration

2024 to ~2031



NCT06063850

P

Primary

Safety and tolerability

(Adverse events)

S

Secondary

**Vector & miRNA
biodistribution, Vector
shedding**

Early signs of efficacy

Neuropsych

**PROs (QoL, Depression,
Anxiety, Sleep)**

**Add'l Safety Endpoints
(MRI, laboratory tests)**

E

Exploratory

**Changes in
interictal activity
(EEG recording)**

**Changes in
wearable
biosensor data
(activity and sleep
phases)**

GenTLE: Preliminary Data from the First Participant Dosed with AMT-260 (n=1)



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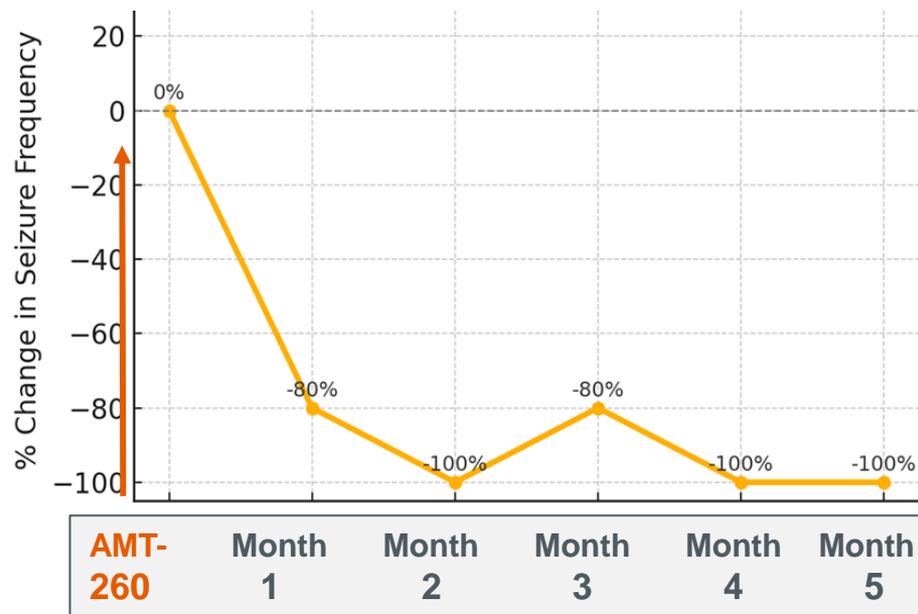
• Safety data

- No SAE
- 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

% Change in 30 day Seizure Frequency from Screening Baseline



As of 4/17/25 (5 mo data preliminary)

uniQure Where to find out more information about the GenTLE study:

GenTLE

Please visit our web page
[uniQure AMT-260 GenTLE](#)



You can search on [GenTLE on CT.gov](#) **NCT06063850**



You are also welcome to
email us at:

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Questions