



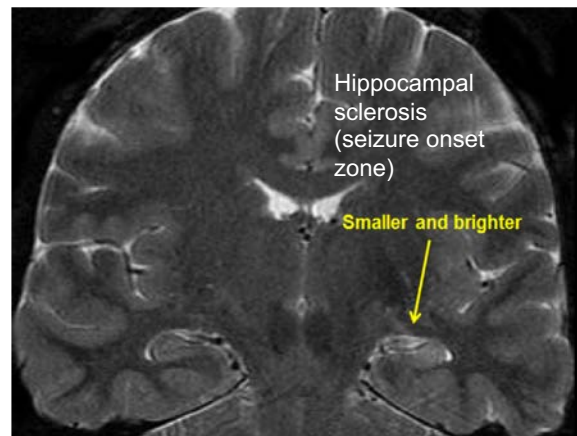
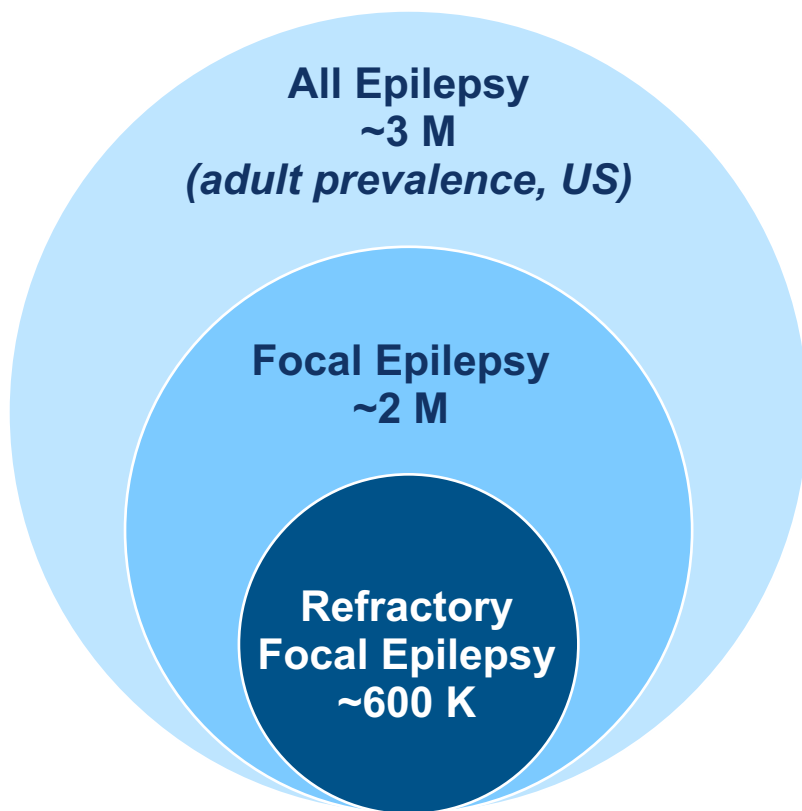
NEURONA
THERAPEUTICS



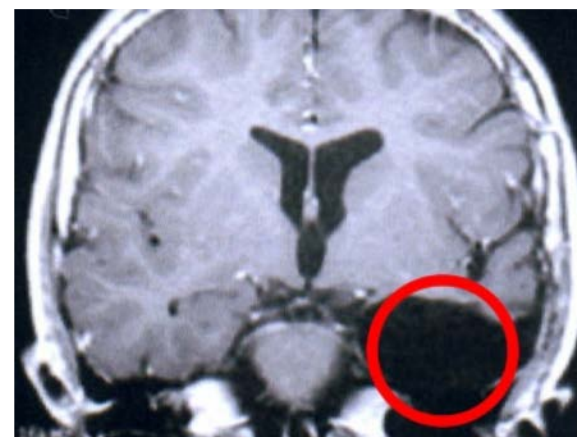
**A PHASE I/II CLINICAL TRIAL OF NRTX-1001
HPSC-DERIVED INHIBITORY INTERNEURON
CELL THERAPY FOR CHRONIC FOCAL EPILEPSY**

Cory Nicholas, PhD
CEO, Co-founder
Neurona

- I am an employee and shareholder of Neurona Therapeutics.



Temporal Lobe Sclerosis



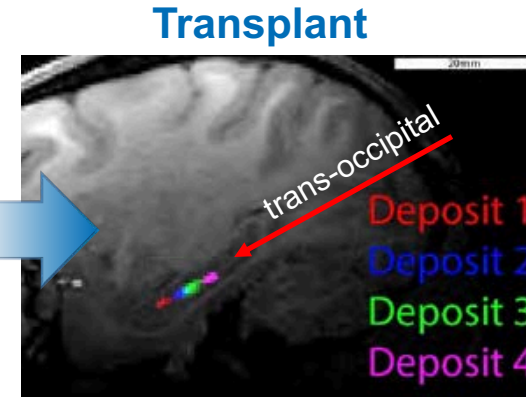
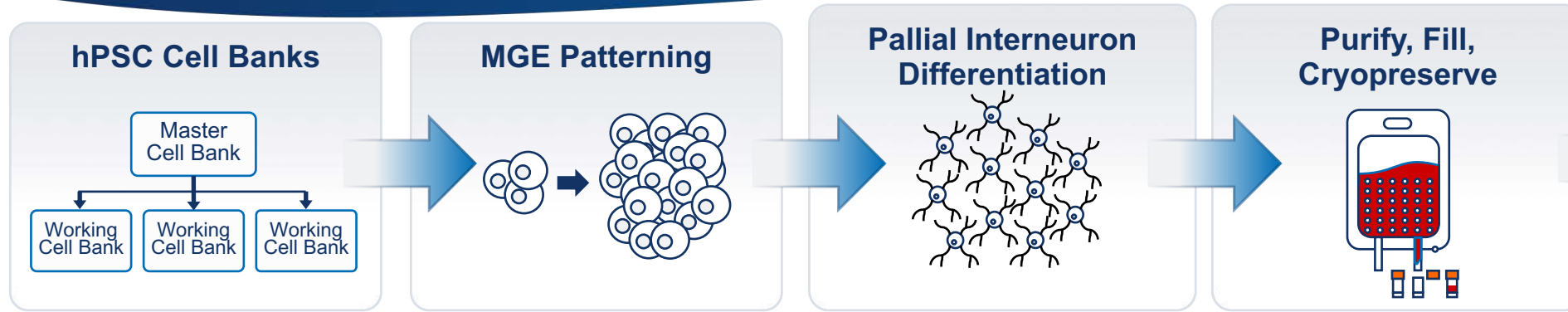
Temporal Lobectomy

- Temporal lobe epilepsy (TLE) is the most common type of adult focal epilepsy
 - ~30% are drug-resistant
- Lobectomy/ablation surgery to destroy the temporal lobe can be an option but risks irreversible adverse effects on cognition
 - Many not inclined due to safety risk (eg. memory loss)
 - Many not eligible (eg. dominant lobe or bilateral TLE)

Regenerative cell therapy could potentially provide:

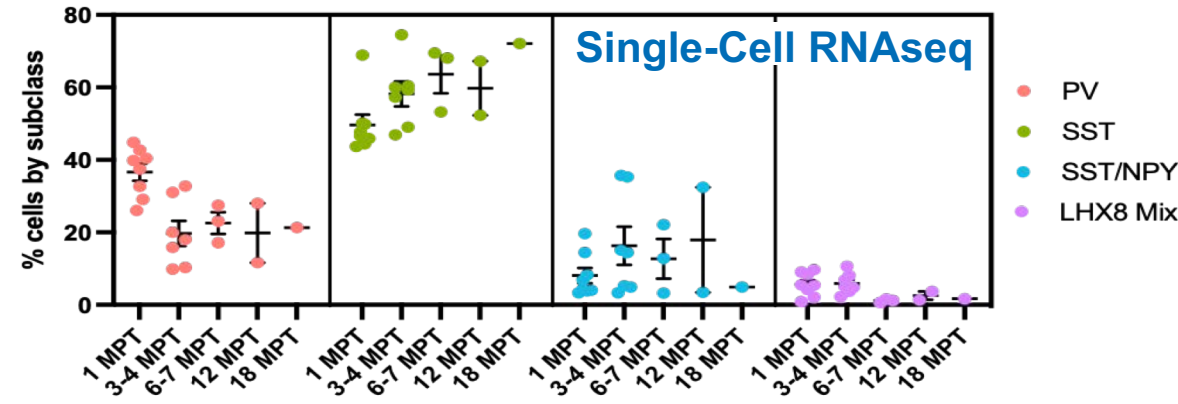
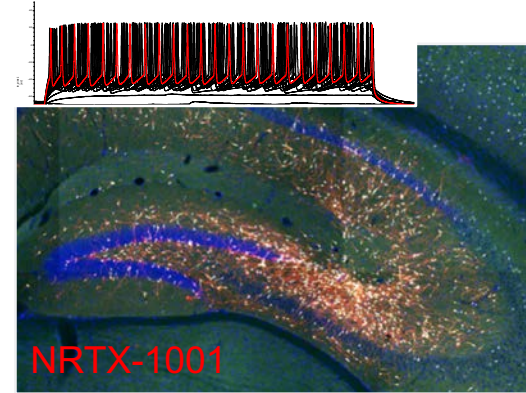
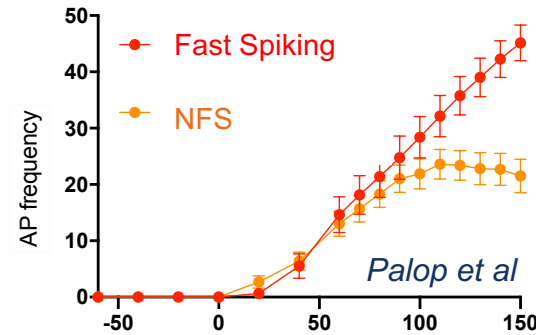
- Safer, non-destructive alternative to lobectomy
- A first disease-modifying option for those not eligible for lobectomy

NRTX-1001: MGE Pallial-type GABAergic Interneurons derived from Human Pluripotent Stem Cells



- **Allogeneic & Cryopreserved:**
MRI-guided intracerebral delivery (single-dose)
- **Lineage-Specific:**
MGE pallial-type GABAergic interneurons (SST/PV)
- **Stage-Specific:**
Post-mitotic migratory stage, no proliferation
- **Functional Integration:**
Form synapses & fire action potentials

Electrophysiology



Preclinical Efficacy: NRTX-1001 is Disease-modifying in a Mouse Model of Chronic Mesial Temporal Lobe Epilepsy (MTLE)

Intra-Hippocampal Kainate MTLE Model



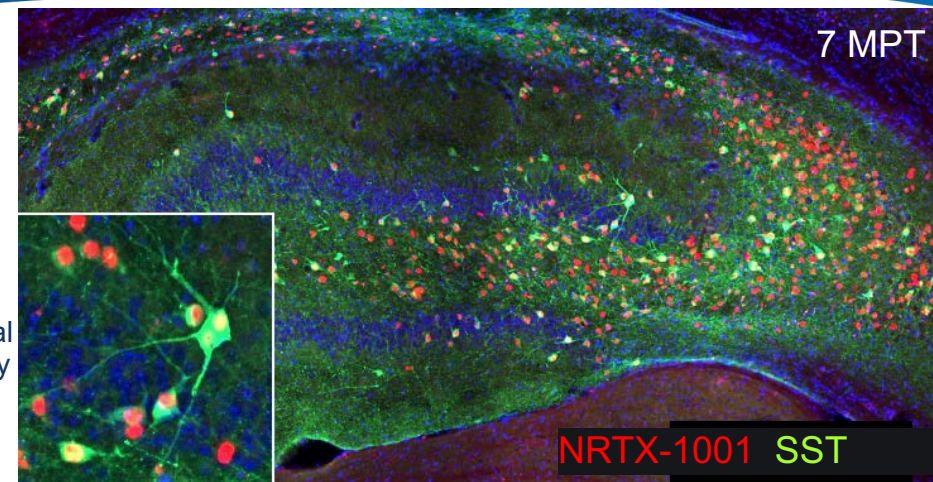
1 month

Intra-Hippocampal EEG Detects Focal Seizures (20-30 seizures/hr)



Mesial Temporal Sclerosis (MTS)

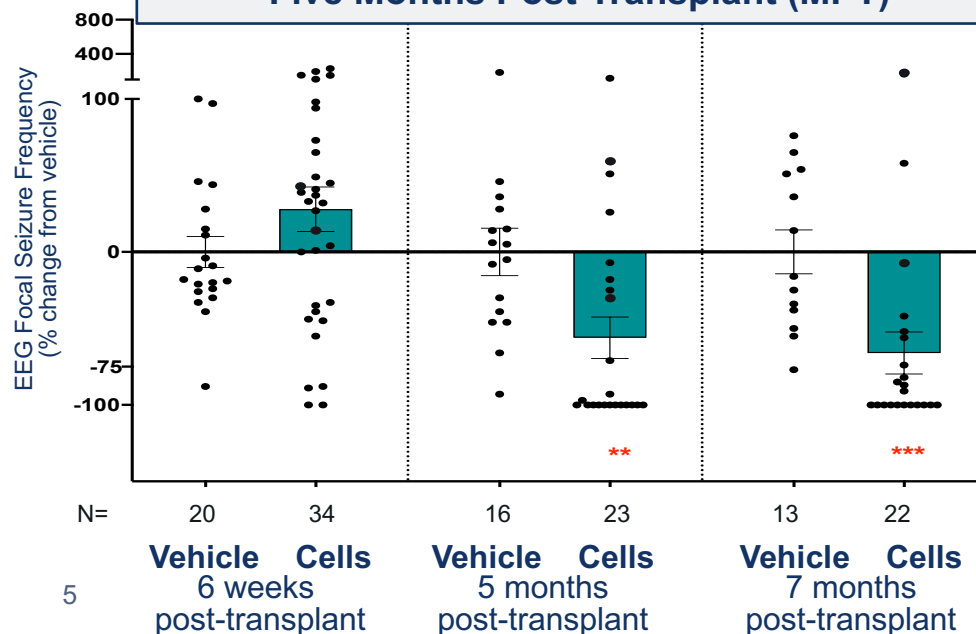
Intra-Hippocampal Cell Delivery



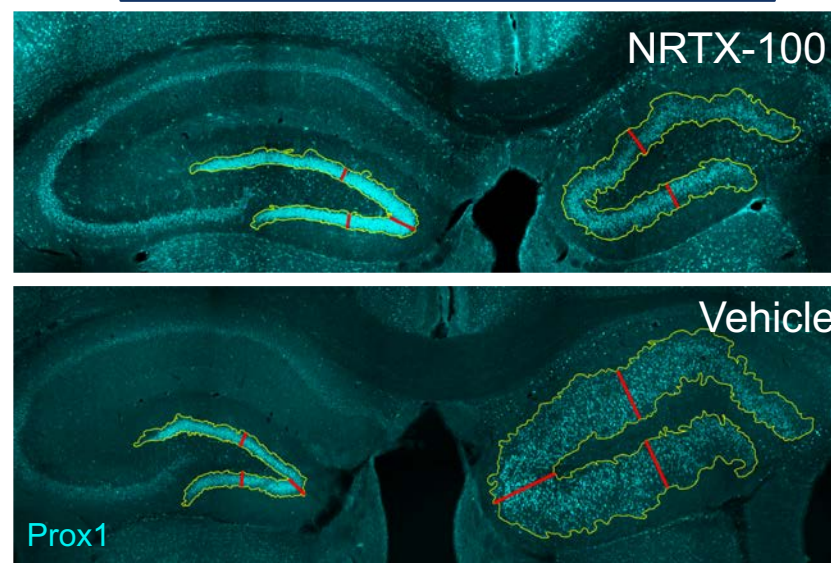
7 MPT

NRTX-1001 SST

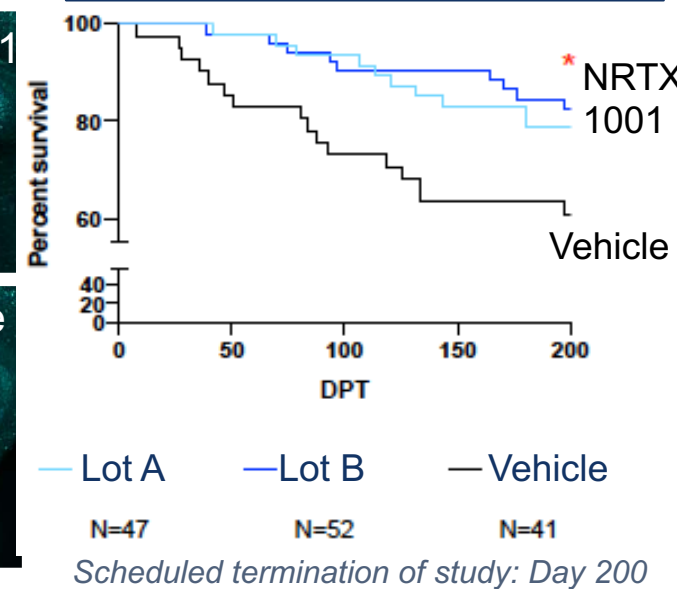
NRTX-1001 Suppresses Seizures by Five Months Post-Transplant (MPT)



NRTX-1001 Reduces Dentate Granule Cell Dispersion by 7 MPT



NRTX-1001 Increases Epileptic Animal Survival



Phase I/II Clinical Study: NRTX-1001 for Drug-resistant MTLE (NCT05135091)

Design: Safety and efficacy study in adult subjects with chronic unilateral MTLE (lobectomy candidates)

Delivery: Single MRI-guided administration of cells into hippocampus

Immunosuppression: 1 year

Primary Endpoint (1yr Safety):

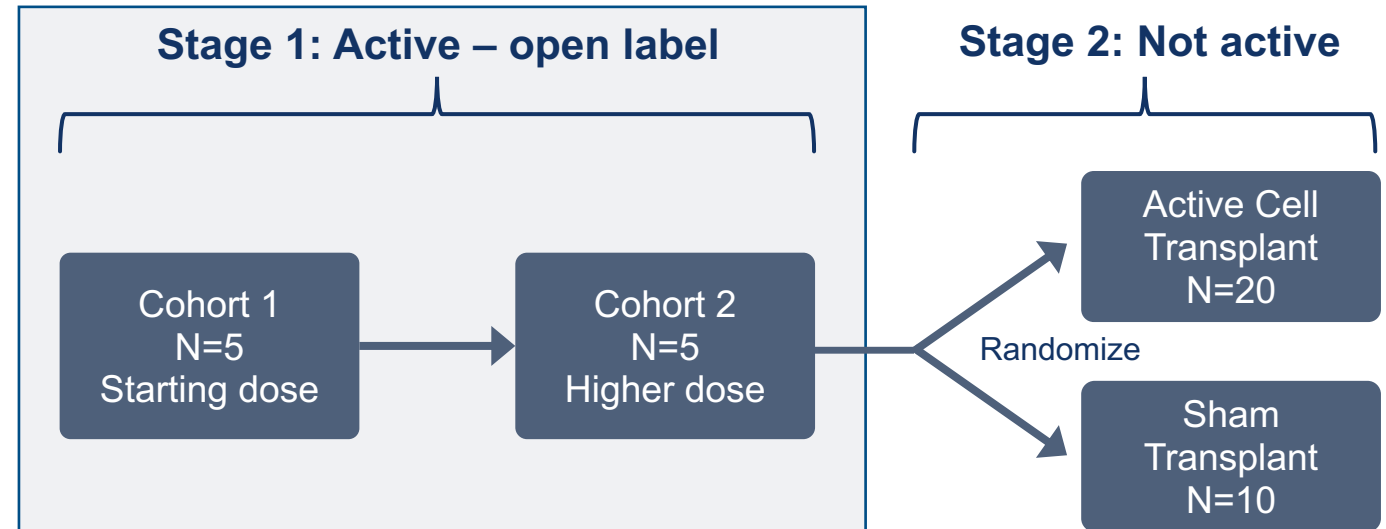
- Frequency of adverse events

Secondary Endpoint (1yr Efficacy):

- Reduction in seizure frequency
- Responder rate

Other Endpoints:

- Neurocognitive outcomes
- EEG, imaging, and blood biomarkers
- Anti-seizure drug dose reduction

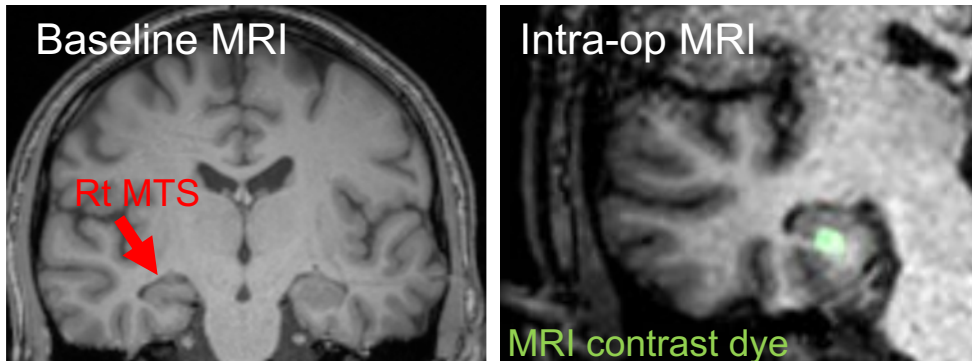


12 clinical sites active in US

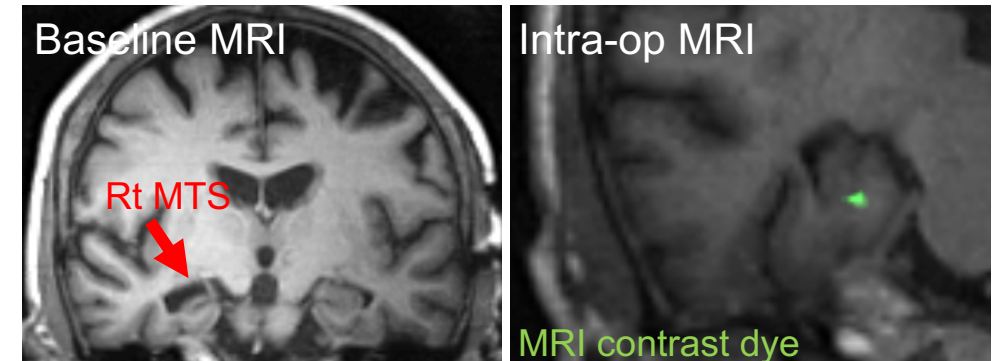
SUNY Upstate
OHSU
UCSD
Rush
NYU
Jefferson

Duke
Stanford
UWisconsin
UUtah
UColorado
UCLA

Subject #1: 26yr old male



Subject #2: 59yr old female



- **Averaging 32 seizures/month** in the 6 months prior to dosing
- 7-year history of seizures with right MTS
- Clobazam, lacosamide, levetiracetam, lorazepam, oxcarbazepine
- **Averaging 14 seizures/month** in the 6 months prior to dosing
- 9-year history of seizures with right MTS
- Clobazam, lacosamide, levetiracetam, lorazepam, midazolam

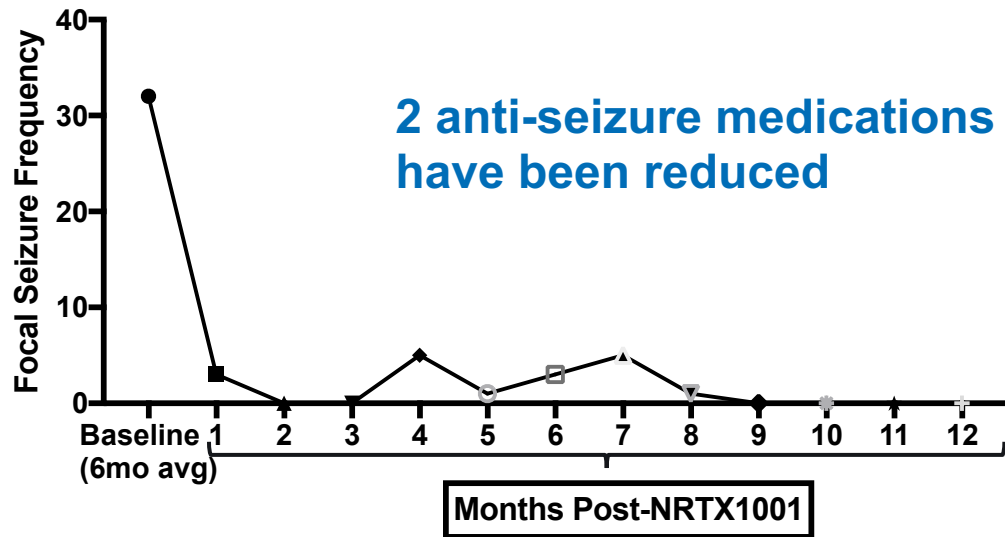
- NRTX-1001 delivered on-target
- No structural abnormalities or inflammation by MR
- No SAEs to date

Safety board cleared study to continue enrolling both dominant and non-dominant lobe MTLE

Seizure Counts after Single-dose Administration of NRTX-1001

Subject #1: 26yr old male

All Seizure Events per Month

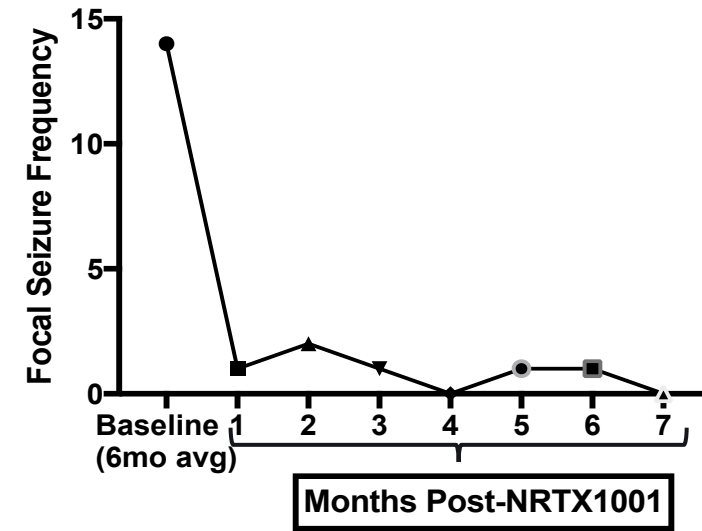


95% overall monthly seizure reduction post-NRTX1001:

- 95% reduction of focal aware
- 95% reduction of focal impaired awareness

Subject #2: 59yr old female

All Seizure Events per Month



94% overall monthly seizure reduction post-NRTX1001:

- 100% reduction of focal aware
- 57% reduction of focal impaired awareness

No Detectable Cognitive Decline, and Potential Improvement, after Single-dose Administration of NRTX-1001



Subject #1: 26yr old male

Subject #2: 59yr old female

	<i>Normal Adult</i>	Base line	6-month	9-month	
Boston (total)	54 +/- 4	50	57	55	Word Retrieval
RAVLT (sum trials 1-5)	46 +/- 10	27	34	34	Verbal Memory
RAVLT (trial 6)	5 +/- 2	3	5	3	
RAVLT (delayed recall 7)	9 +/- 3	2	7	7	
RAVLT (delayed recall 8)	9 +/- 3	2	6	4	
BVMT delayed recall	10 +/- 2	6	10	10	Visuo-Spatial Memory
BVMT % retained	93 +/- 10%	67%	91%	100%	

	<i>Normal Adult</i>	Base line	6-month	
Boston (total)	54 +/- 4	58	54	Word Retrieval
RAVLT (sum trials 1-5)	46 +/- 10	36	36	Verbal Memory
RAVLT (trial 6)	5 +/- 2	2	4	
RAVLT (delayed recall 7)	9 +/- 3	4	8	
RAVLT (delayed recall 8)	9 +/- 3	4	3	
BVMT delayed recall	10 +/- 2	6	6	Visuo-Spatial Memory
BVMT % retained	93 +/- 10%	67%	75%	

Red = outside of normal adult range

Red = outside of normal adult range

Neurocognitive scores increased at 6 and 9 months post-NRTX-1001

Select neurocognitive scores numerically increased by 6 months post-NRTX-1001

NRTX-1001: Next Clinical Studies Planned

Indication	2023				2024				2025
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	
#1 NRTX-1001: Unilateral MTLE <i>Ongoing Trial</i>	[Dark blue bar spanning all quarters]								
#2 NRTX-1001: Bilateral MTLE					[Dark blue bar spanning Q1-Q4 2024]				
#3 NRTX-1001: Neocortical Focal Epilepsy									[Dark blue bar in Q4 2025]
#4 NRTX-1001: Alzheimer's + Hyperactive EEG									[Dark blue bar in Q4 2025]



- Robert Beach, MD, PhD
- Harish Babu, MD, PhD



- David Spencer, MD
- Kim Burchiel, MD

