Interneuron Cell Therapy For Epilepsy And Other Neurological Disorders

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Co-Founder
CEO

Program Overview

Regenerative Cell Therapy Platform

- Founded in 2015, based on >15 years of research at UCSF.
- Core Technology: Deep developmental understanding of interneuron biology.
- Objective: To develop disease modifying interneuron cell therapies that rebalance dysregulated neural circuits.
- Lead Program: NRTX-1001 interneuron cell therapy for drug-resistant epilepsy, entering Phase 3.

Founders and Key Discoveries

John Rubenstein, MD, PhD

Arturo Alvarez-Buylla, PhD

Arnold Kriegstein, MD, PhD

Cory Nicholas, PhD

1. Anderson SA, Eisenstat DD, Shi L, **Rubenstein JL**. (1997). Interneuron migration from basal forebrain to neocortex: dependence on Dlx genes. Science.
2. Wichterle H, Garcia-Verdugo JM, Herrera DG, **Alvarez-Buylla A**. (1999). Young neurons from medial ganglionic eminence disperse in adult and embryonic brain. Nat Neurosci.
3. Baraban S. C., Southwell D. G., Estrada R. C., et al, **Rubenstein J. L. R.,** and **Alvarez-Buylla A**., Reduction of seizures by transplantation of cortical GABAergic interneuron precursors into Kv1.1 mutant mice. (2009) PNAS.
4. **Nicholas C. R**., Chen J., Tang Y., Southwell D. G., et al, **Alvarez-Buylla A., Rubenstein J. L., Kriegstein A. R**. (2013). Functional maturation of hPSC-derived forebrain interneurons requires an extended timeline and mimics human neural development. Cell Stem Cell.

Timeline and CIRM Support

MGE discovered as the source for most cortical interneurons

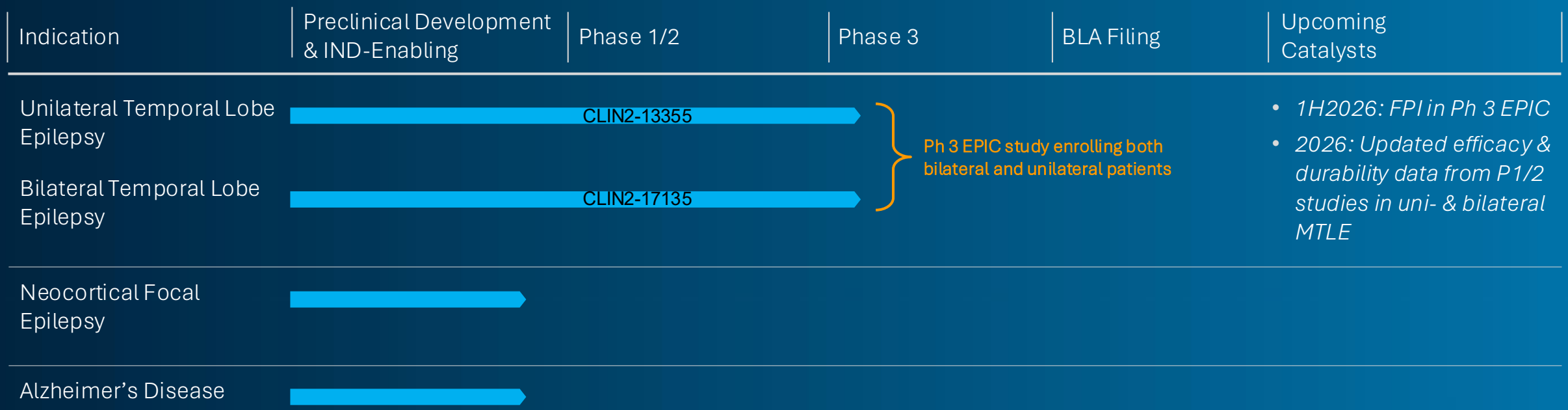
Preclinical POC demonstrated using fetal MGE transplantation

Derivation of MGE interneurons from human ES cells

1;2 RC1-00346 3 RB2-01602 TR2-01749 TR3-05606 4 **Neurona Launch** DISC2-10525 TRAN1-11611 CLIN2-13355 **Phase 1** CLIN2-17135 TRAN1-16225 **Phase 3**

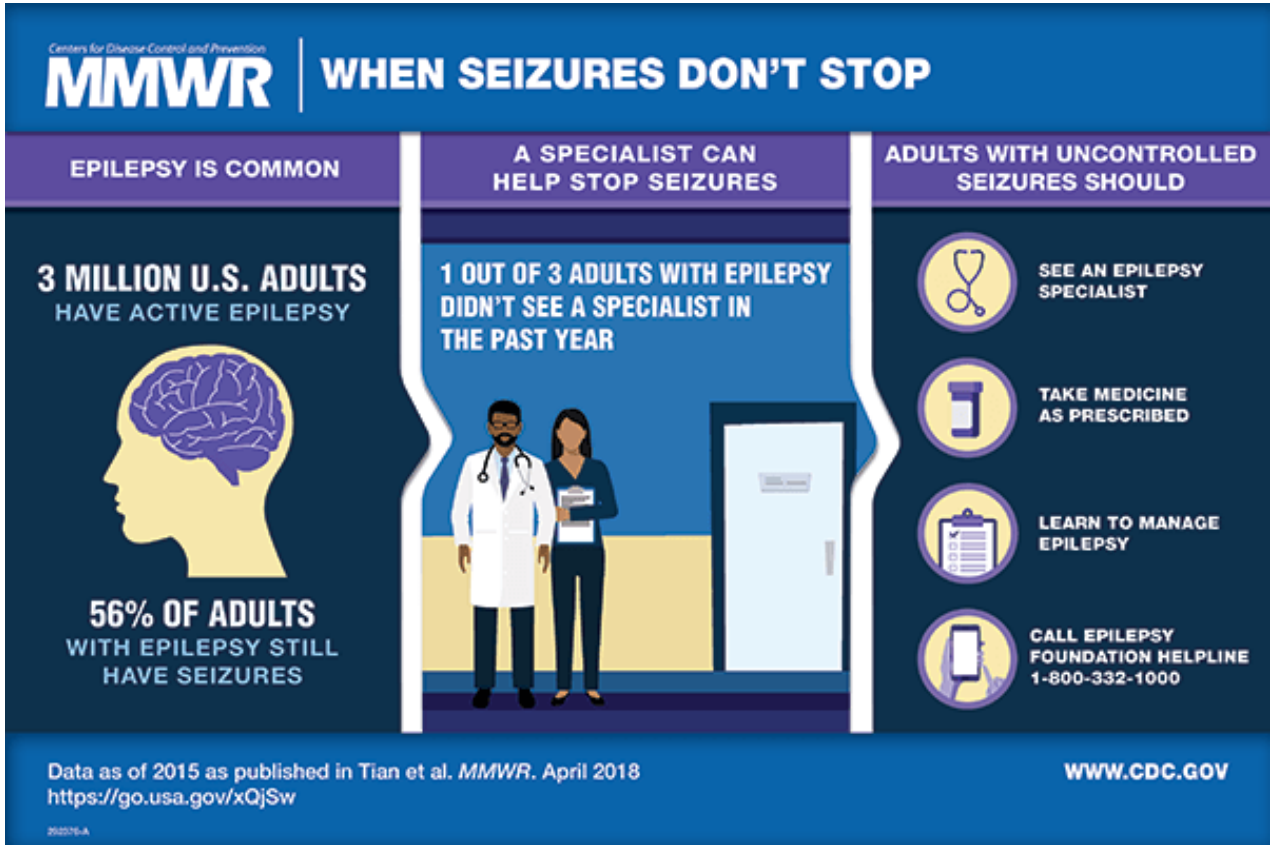
2000 2005 2010 2015 2020 2025

NRTX-1001 Programs



- All programs wholly-owned
- Additional programs in pipeline include preclinical development of other cell types and indications

Many with Epilepsy still have Drug-Resistant Seizures

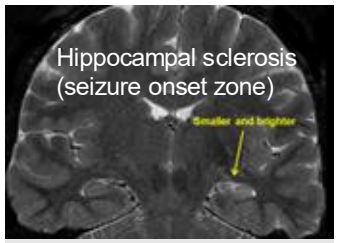


- The most common form of epilepsy in adults is **mesial temporal lobe epilepsy (MTLE)**
- ~600,000 people in USA have drug-resistant TLE
- ~100,000 people in California are affected

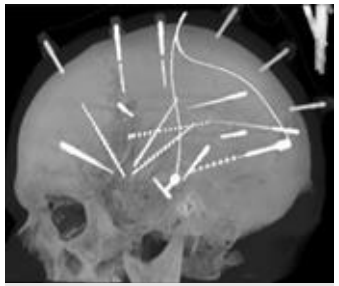
Standard of Care for Refractory Focal Epilepsy is Suboptimal:
Destructive Surgery

People with Drug-Resistant Seizures

Level 3/4 NAEC Center



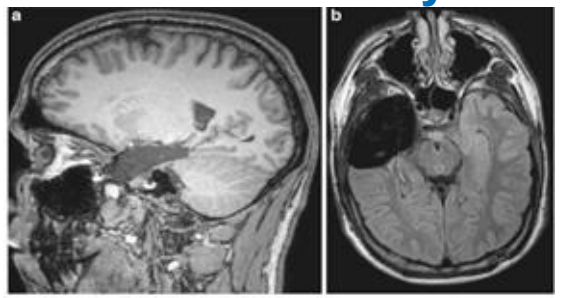
MRI/PET Imaging



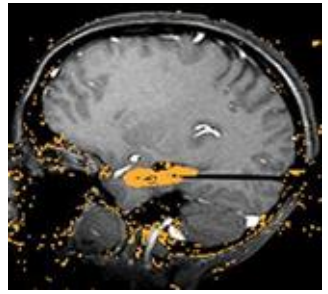
Intra-cranial EEG

Focal Temporal Lobe Onset Confirmed

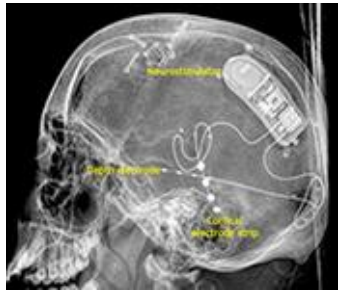
Temporal Lobectomy



Laser Ablation



RNS / DBS Stimulator

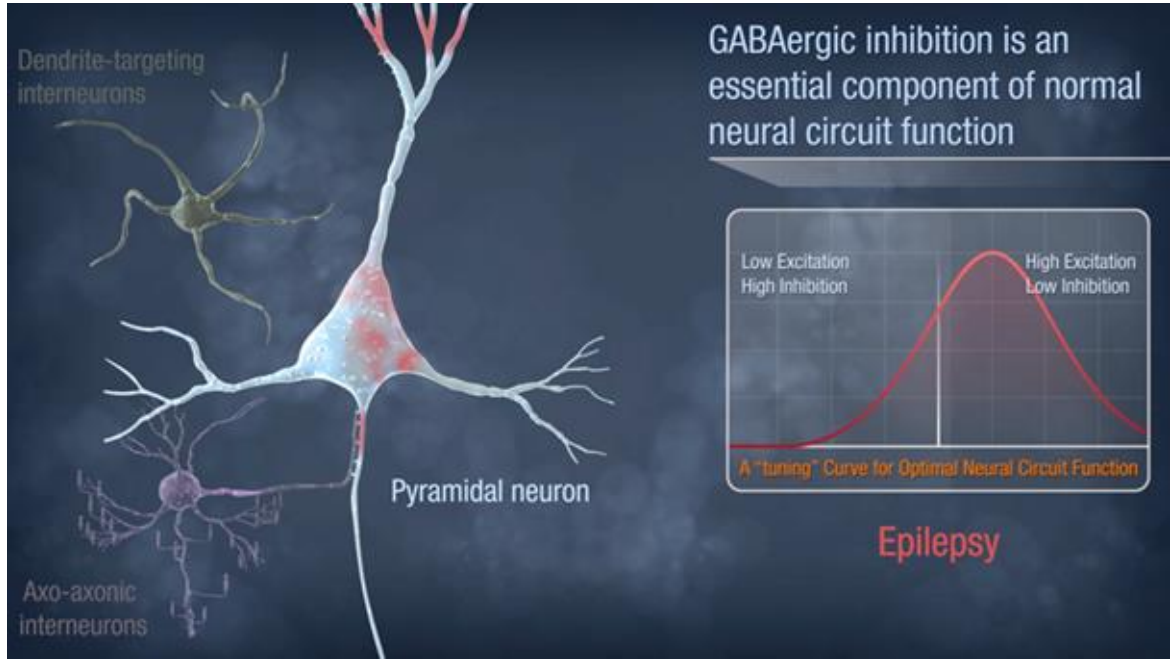


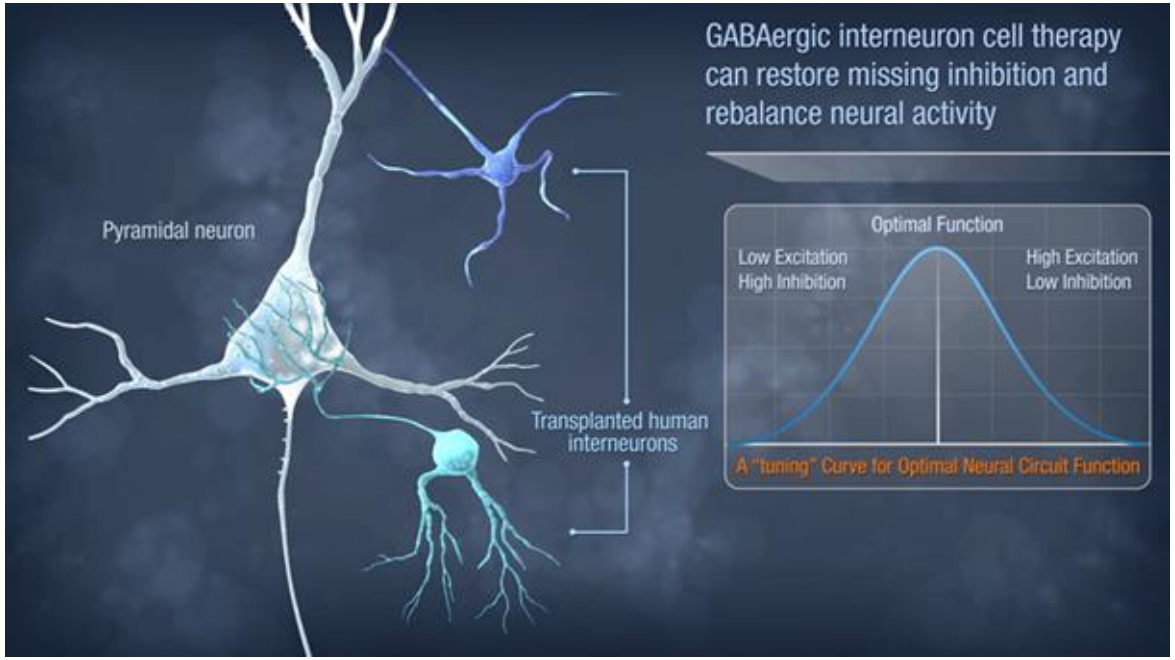
- Most patients are not eligible for lobectomy/ablation due to risk of cognitive impairment and/or are not interested due to brain tissue destruction
- RNS/DBS avoids tissue destruction but is invasive/indwelling and failed to control seizures in 2/3rd of patients in Phase 3

Key Unmet Need for Drug-Resistant Focal Epilepsy:

Seizure control without tissue-destruction and cognitive impairment

Therapeutic Strategy:
Restore balanced activity with GABA interneuron cell therapy

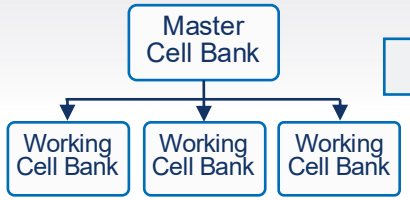




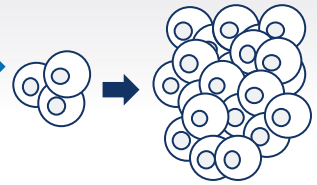
NRTX-1001 Manufacturing:
GABAergic Interneurons derived from a Human Pluripotent Stem Cell Line (hPSC)

NEURONA THERAPEUTICS

Cell Bank

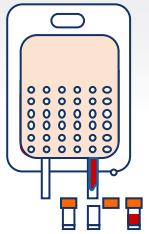


MGE Patterning



Cortical Interneuron Differentiation

NRTX-1001: Cryopreserved GABAergic Interneurons



- **>98% purity**
- **Post-mitotic stage**

NRTX-1001 Attributes:

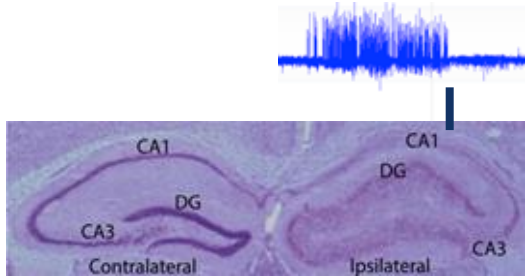
- Reproducible and robust process
- No genetic modification
- Manufactured in-house
- Phase 3 manufacturing completed

NRTX-1001 Efficacy:
Model of Chronic Mesial Temporal Lobe Epilepsy (MTLE)

Drug-Resistant Model of MTLE

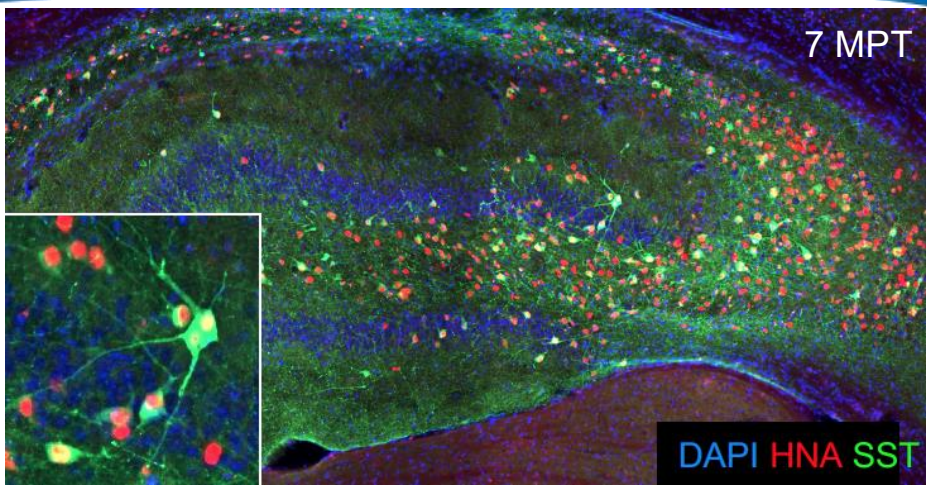
Intra-Hippocampal Kainate

1 month

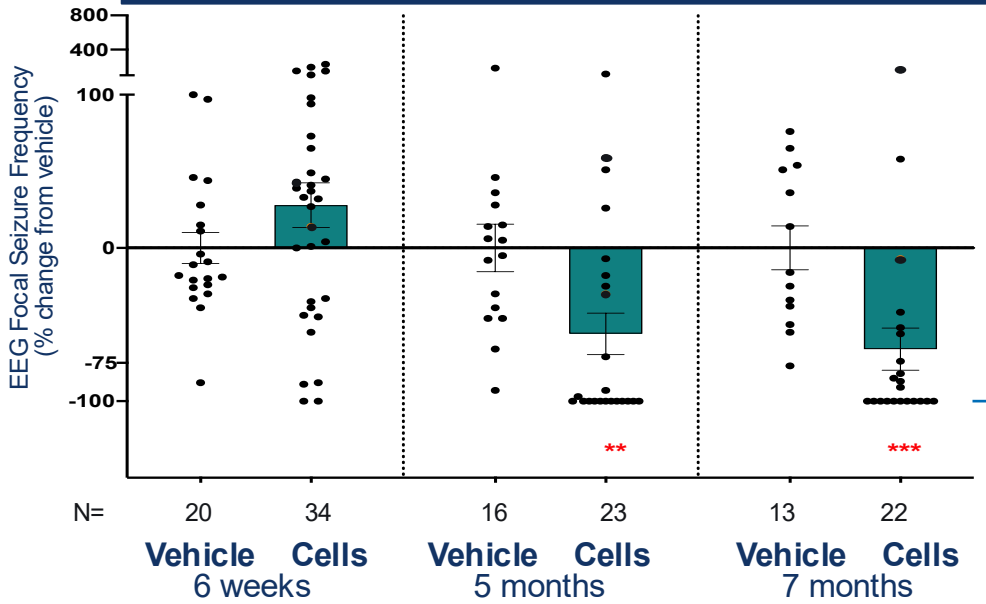


Intra-Hippocampal EEG Electrode Detects Seizures (20 seizures/hr)

Intra-Hippocampal Cell Delivery



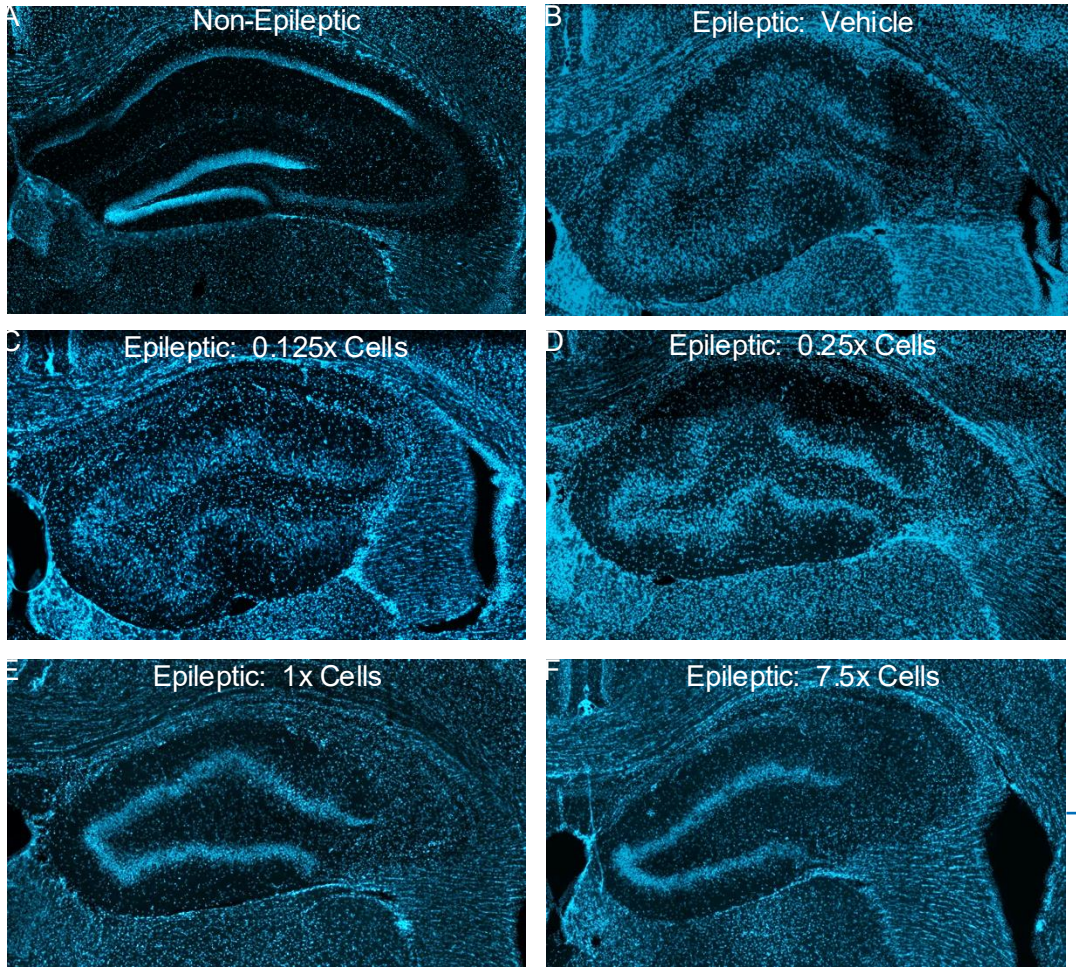
Single Dose of NRTX-1001 Durably Suppresses Hippocampal Seizures

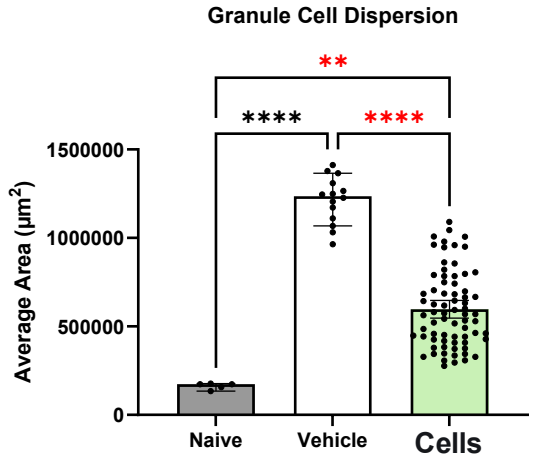


Seizure-free

- 92% median seizure reduction across product lots
- 64% of animals with >75% seizure reduction
- 50% of animals are seizure-free

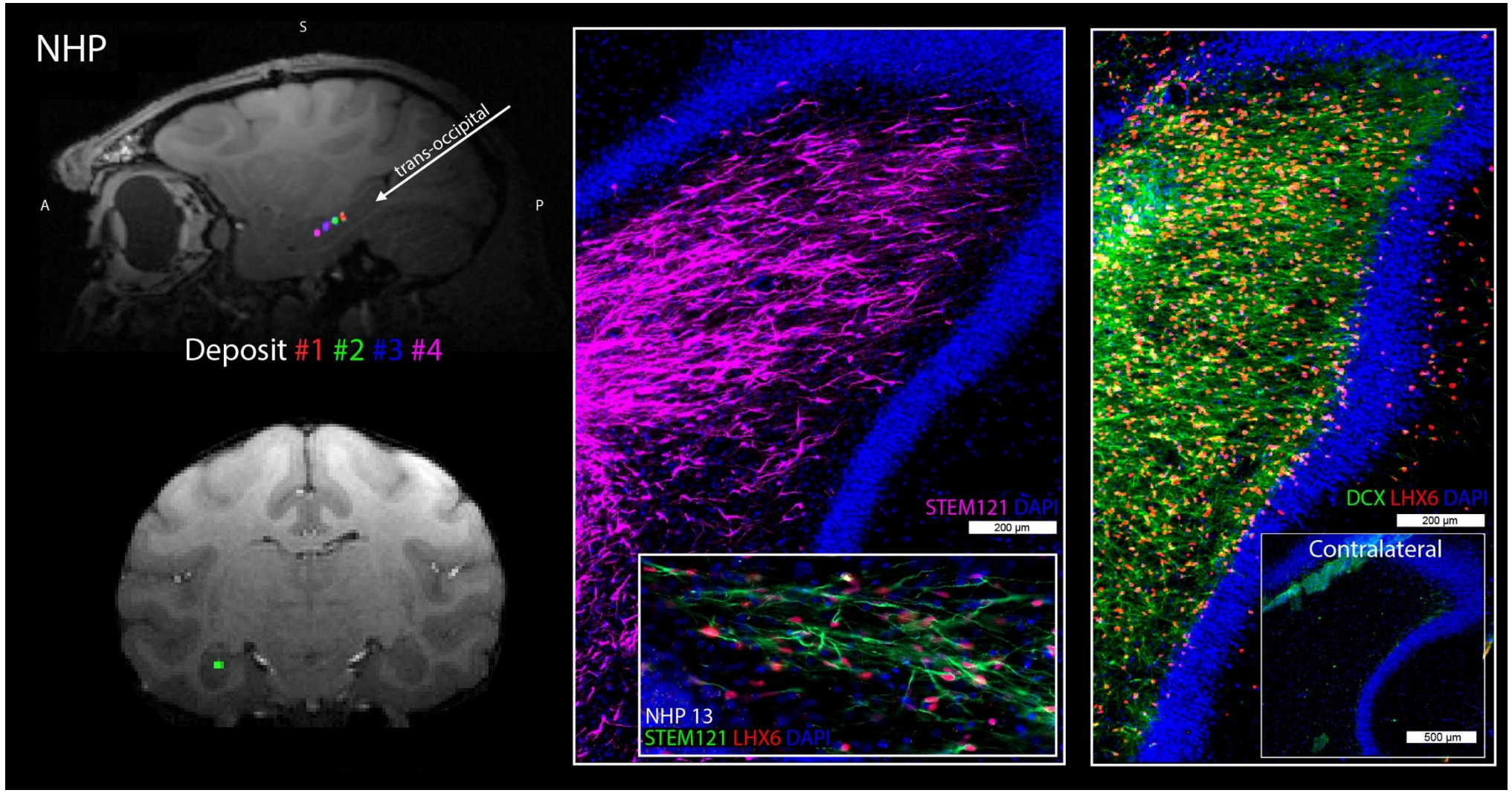
NRTX-1001 Disease Modifying Activity:
Dose-Dependent Reduction of Hippocampal Pathology





NRTX-1001 reduced hippocampal pathology

NRTX-1001 Delivery Strategy:
On-Target and Safe Intracerebral MRI- or CT-guided Delivery



NRTX-1001 Clinical Studies:
Two Ongoing Phase 1/2 Trials for Uni- and Bi-lateral MTLE

Design: Adults with drug-resistant MTLE

Key Eligibility Criteria:

- Drug-resistant focal seizures from hippocampus
- >2 disabling focal seizures/mo at baseline
  - Focal aware with objective component
  - Focal impaired awareness
  - Focal to bilateral tonic-clonic

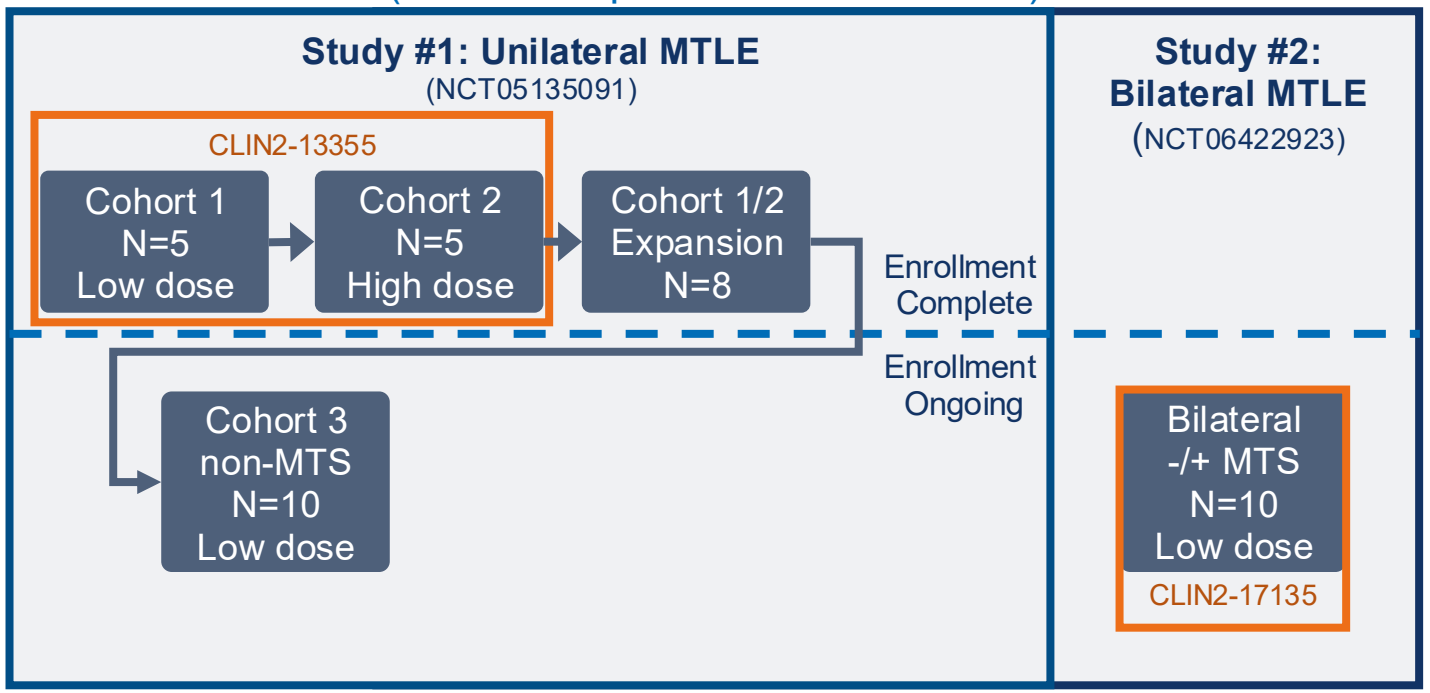
Delivery: Single image-guided cell delivery

Immunosuppression: 1 year

Objectives:

- **Primary**
  - Safety during months 1-12
- **Secondary**
  - Reduction in seizure frequency during months 7-12

Two phase-1/2: open-label, multicenter studies in USA
(N=38 total patients to be enrolled)

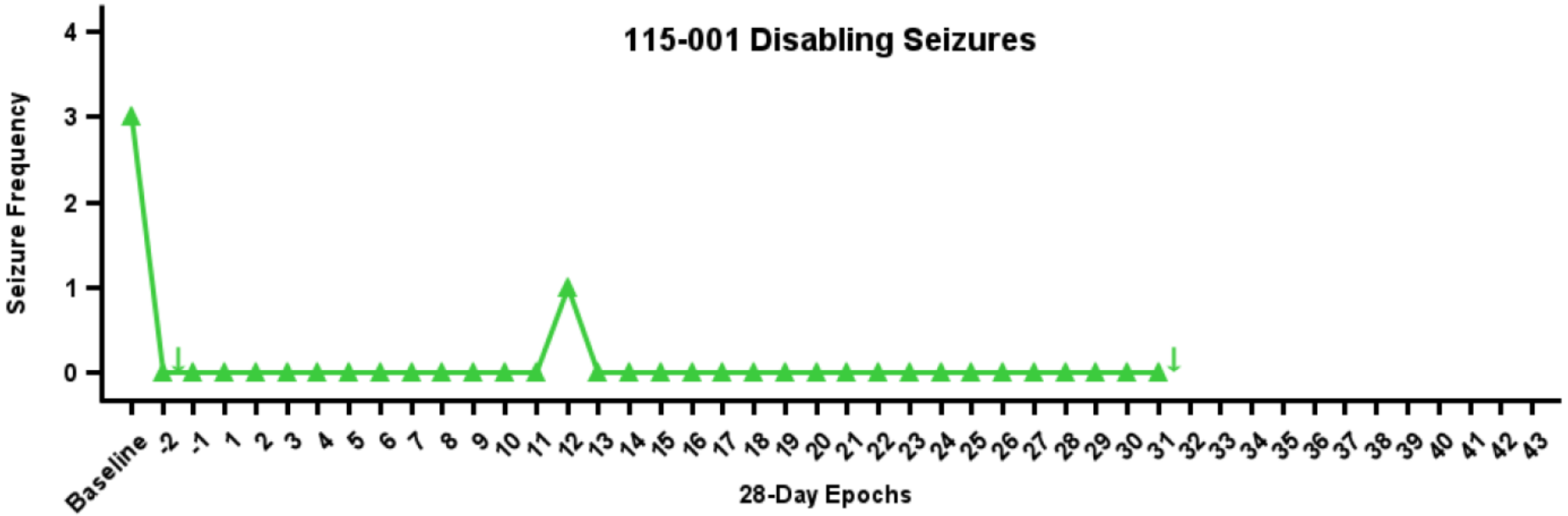


- 30 patients treated to date
  (8 patients treated in CA)
- 32 clinical centers are active
  (19 centers have treated patients; 7 centers in CA)
- Data cut presented here from October 27, 2025 (N=26 patients)

Safety Overview

- **No serious adverse events attributed to NRTX-1001**
- No serious surgical complications
- Non-serious events related to procedure & immunosuppression
  - Procedural AEs resolved post-implantation
  - Immunosuppression AEs resolved in 9 of 10 subjects who have discontinued immunosuppression
- No group decline in cognitive performance over long-term follow up, including word retrieval, verbal memory, and visuospatial memory batteries

Seizure Count:
First Unilateral MTLE Patients (low dose)



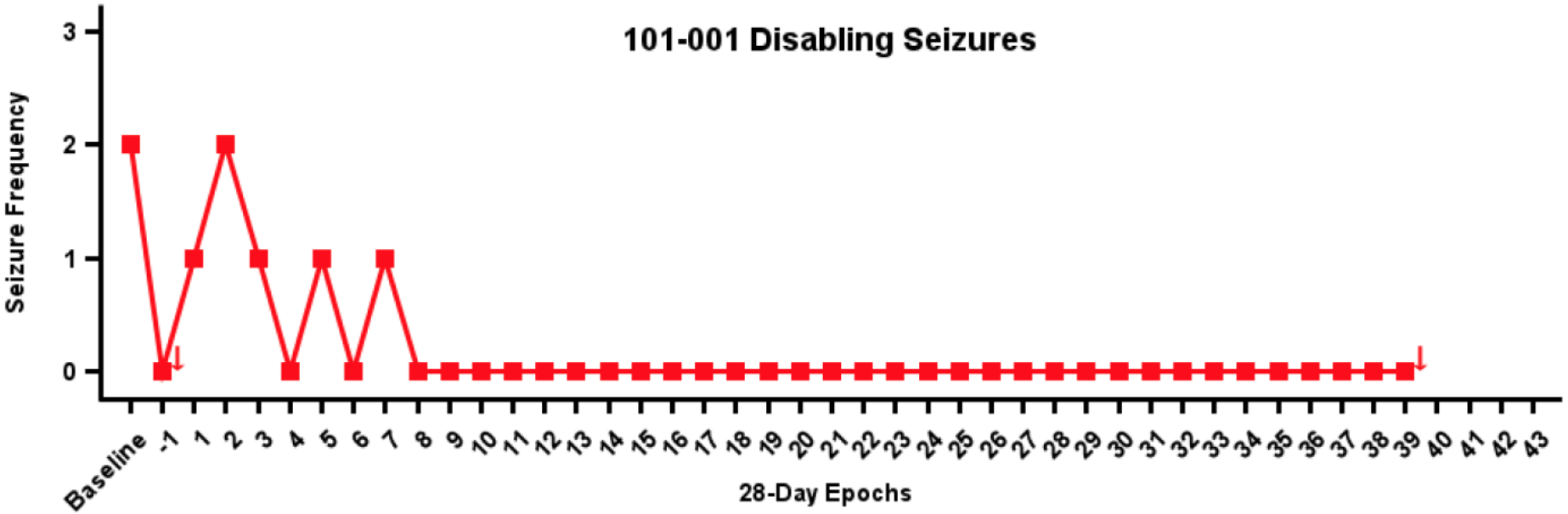
Before NRTX-1001: ”passed out while managing scuba store”

- Passion was swimming and open-water diving
- Had to stop due to seizures
- Quit his dream job
- Can’t drive
- Drank heavily to cope
- When offered to be the 3rd person to receive cell therapy; said:
  “Yes, but I didn’t understand the magnitude of it”

After NRTX-1001:

- Seizures have decreased
- Loves the idea of being able to help people all over the world
- Had only one disabling seizure since treatment with cells
  “Hasn’t changed anything else, what else could it be?”

Seizure Count:
First Unilateral MTLE Patients (low dose)



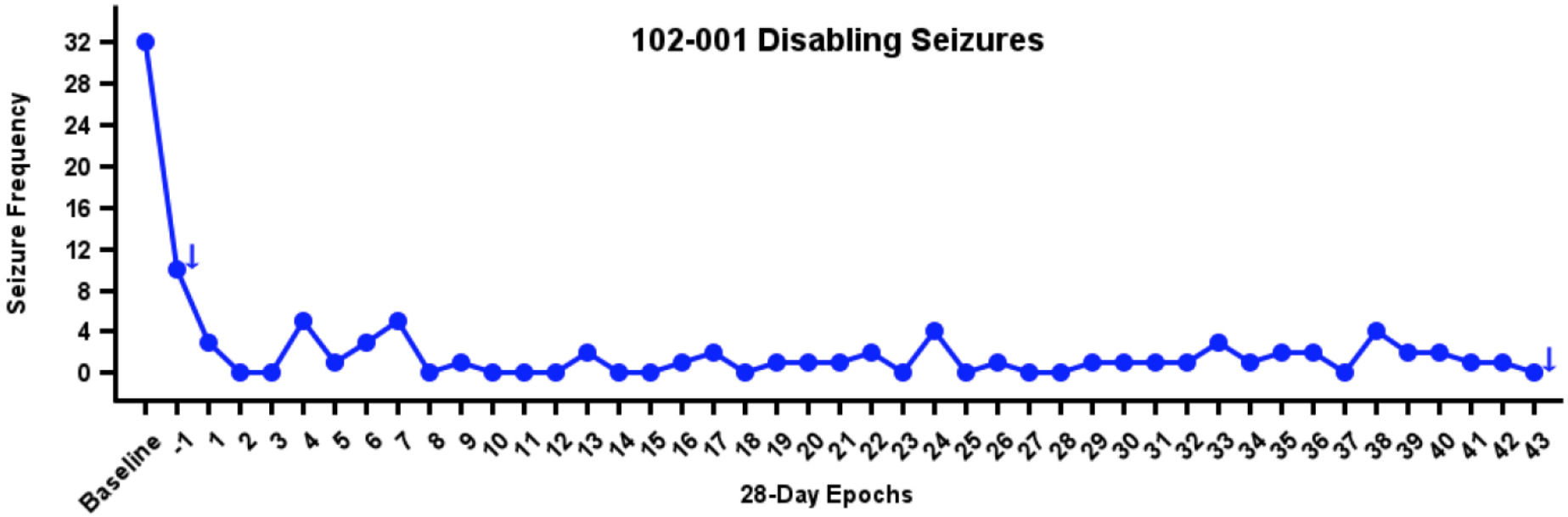
Before NRTX-1001: ”it happened in my sleep”

- Sudden grand mal seizure, was foaming at the mouth
- Anti-seizure drugs have not helped
- Had to quit job – very hard. Important part of her life.
- Avid hiker – backpacking several miles/day – had to stop
- EEG showed 11 seizures over 2 days
- Didn’t want laser ablation due to risks of brain tissue destruction
- When offered to be the 2nd person to receive cell therapy; said: “Let’s go for it!”

After NRTX-1001:

- “Delivery procedure was a piece of cake!”
- Seizure-free since month-7
- Fatigue has improved
- Able to hike again up to 3 miles per day
- Able to get on with her retirement plans, traveling, seeing her grandchild

Seizure Count:
First Unilateral MTLE Patients (low dose)




Mother of first patient (26-yr old)

Before NRTX-1001: ”an epilepsy hostage situation”

- Taking 4 different anti-seizure drugs at high doses
- Multiple debilitating seizures daily
- Had to quit two jobs and unable to live alone/function
- Mother had to stop working to care for son
- Memory impaired; poor quality of life
- EEG showed 200 seizures over 7 days
- Didn’t want lobectomy due to risks of brain tissue removal
- When offered to be the first to receive cell therapy; told his mom: “Someone has to be first!”

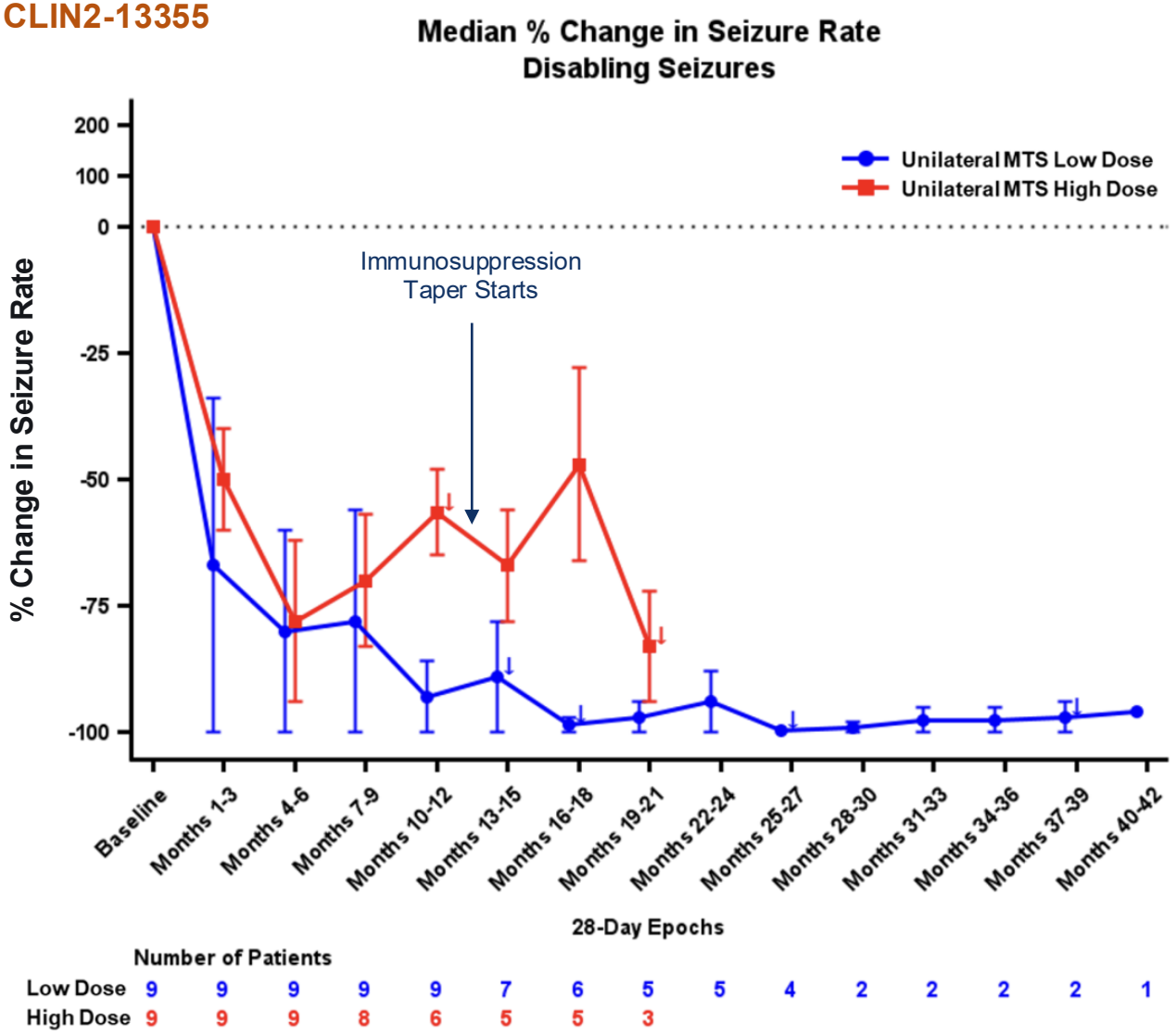
After NRTX-1001:

- Noticed improvements by month-3
- Improvements continued to date
- Hasn’t had a loss-of-consciousness seizure since month-1
- Coherence and balance have improved
- Able to decrease anti-seizure drugs
- Regaining independence
- Spirit has improved
- Told that patient and his mom are working again

First Unilateral MTLE Patient Treated with NRTX-1001

Aggregated Efficacy Data for Cohorts 1 and 2:
Unilateral MTLE with MTS

CLIN2-13355



Cohort 1 Low Dose

Months 7-12 (n=9):

- 89% median disabling seizure reduction
- 78% (7/9 subjects) with ≥50% responder rate

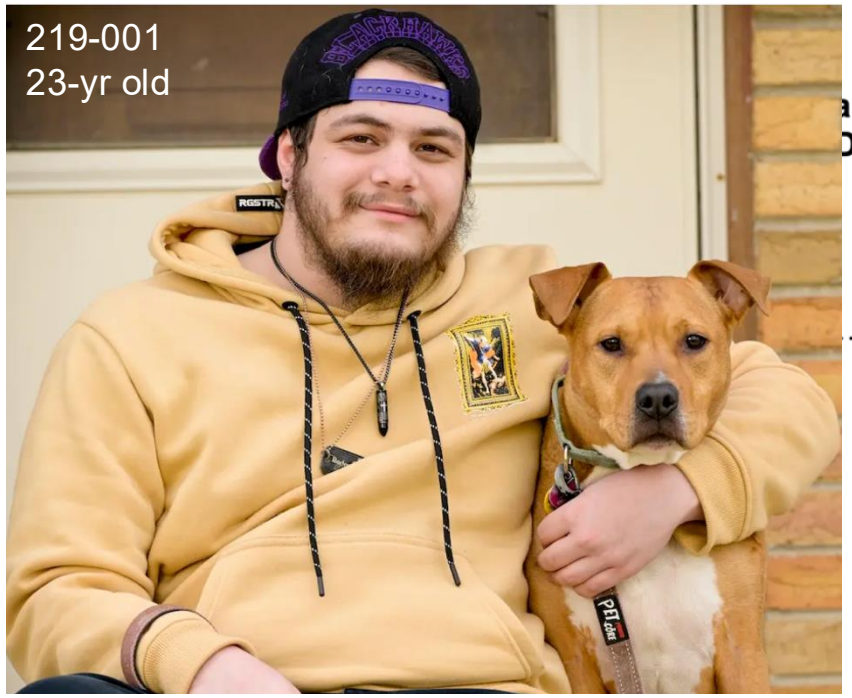
Cohort 2 High Dose

Months 7-12 (n=5)[a] :

- 58% median disabling seizure reduction
- 80% (4/5 subjects) with ≥50% responder rate

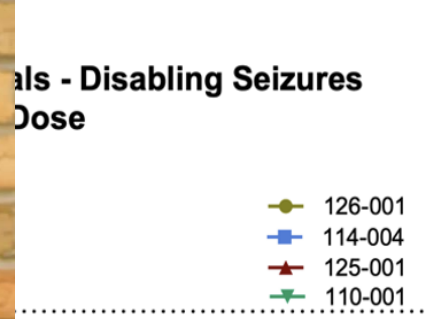
[a] 4 High Dose subjects have yet to complete 12-month endpoint

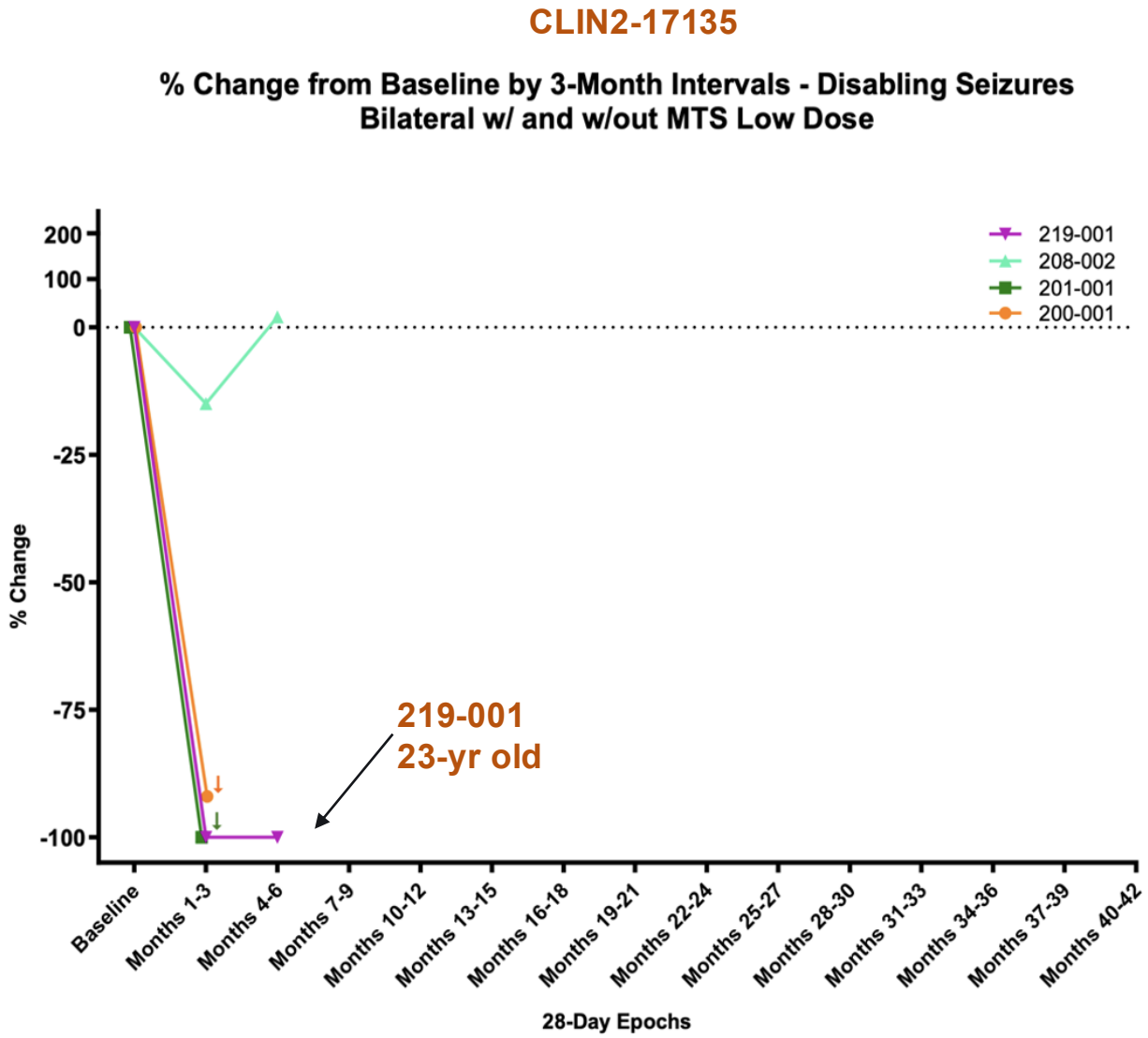
Individual Efficacy Data for Cohort 3 and Bilateral Trial:
Unilateral MTLE (-MTS), and Bilateral MTLE (-/+ MTS)



Before NRTX-1001:
- Seizures broke spine twice
- Unable to drive
- Stays home, depressed
- Feels he is a burden
- Medications not working
- Not eligible for lobectomy

After NRTX-1001:
- So far has been seizure-free
- "Just maybe we can get a cure for epilepsy"





Summary

- NRTX-1001 has been well-tolerated to date
- Significant and durable control of drug-resistant seizures across MTLE patient populations
- No neurocognitive impairments detected, with trend to cognitive improvement, and improved quality-of-life
- RMAT designation granted by FDA in 2024; PRIME granted by EMA in 2025
- Single pivotal Phase 3 EPIC double-blind trial to dose first patients in 1H 2026

Thank You!

CIRM

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