

# NRTX-1001: Human inhibitory neuron cell therapy suppresses seizures and reduces histopathology in mouse model of chronic focal epilepsy with high repeatability across multiple studies and manufacturing lots



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Neurona Therapeutics, 170 Harbor Way, South San Francisco, CA 94080, USA, [www.neuronatherapeutics.com](http://www.neuronatherapeutics.com) **Poster #4012**

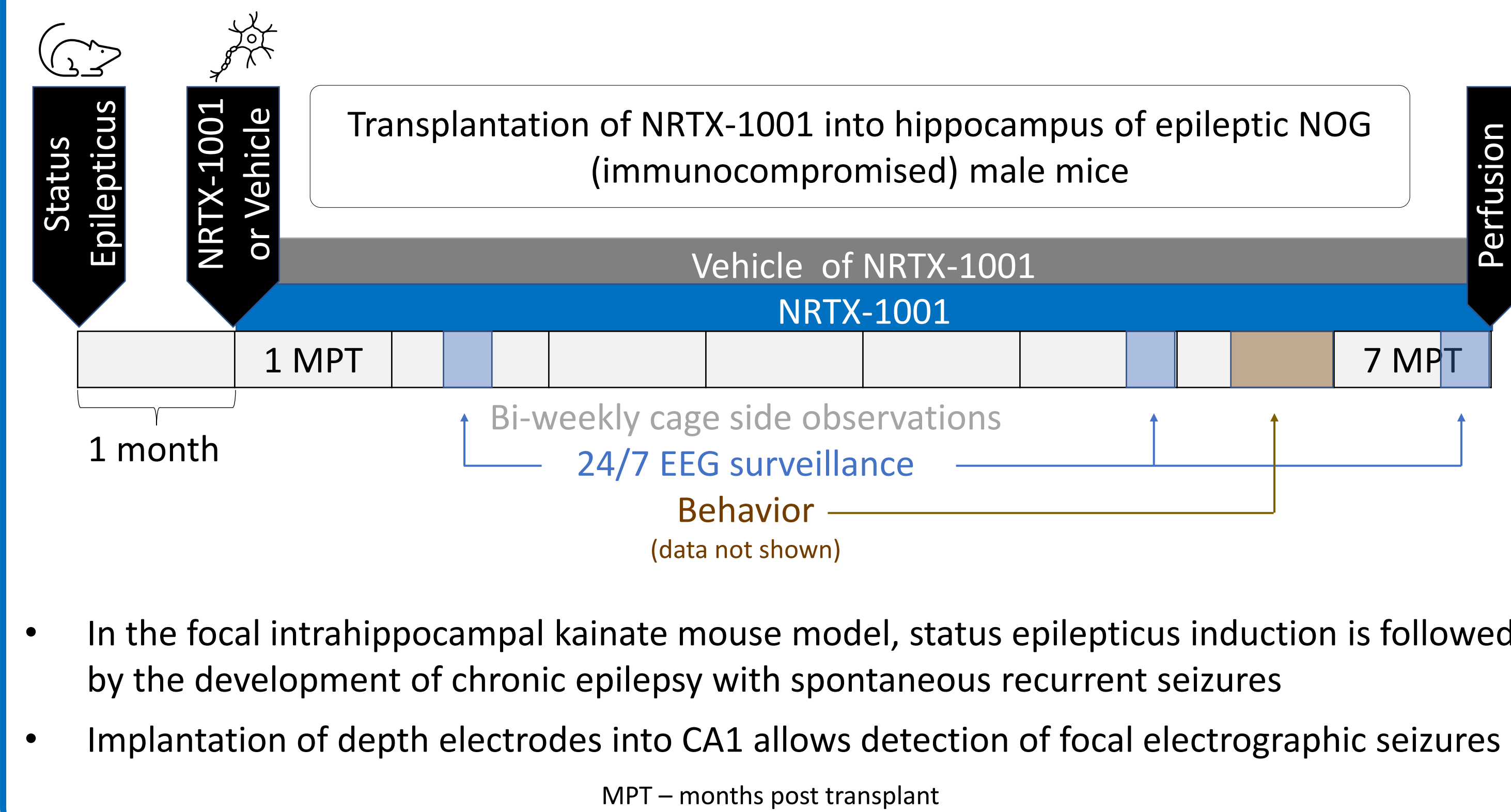
## INTRODUCTION

- Many people with mesial temporal lobe epilepsy continue to have seizures despite anti-seizure drug therapy
- Inhibitory interneuron cell therapy is a novel therapeutic strategy to provide targeted inhibition to hyperexcitable neural networks in the epileptic brain
- NRTX-1001 is composed of pallial-type medial ganglionic eminence (MGE) post-mitotic interneurons that release GABA and consistently reduce focal electrographic seizures after transplantation in the intrahippocampal kainate mouse model

## MGE-type pallial GABAergic interneuron production from a single human embryonic stem cell line

- Allogeneic, cryopreserved cellular therapeutic intended for single administration and long-term persistence
- High purity: >98% MGE pallial-type GABAergic interneurons
- Post-mitotic stage-specific: No proliferation or cycling cells detected
- Reproducible: 3 of 3 lots of cGMP clinical product passed release criteria and support dosing of all subjects in Phase I/II epilepsy trial [ClinicalTrials.gov Identifier: NCT05135091]

## Study design



- In the focal intrahippocampal kainate mouse model, status epilepticus induction is followed by the development of chronic epilepsy with spontaneous recurrent seizures
- Implantation of depth electrodes into CA1 allows detection of focal electrographic seizures

## NRTX-1001 transplantation stably reduces focal electrographic seizure frequency in epileptic mice

**Responder rate to NRTX-1001 product lots:**  
Animals with >75% seizure reduction at 7 MPT

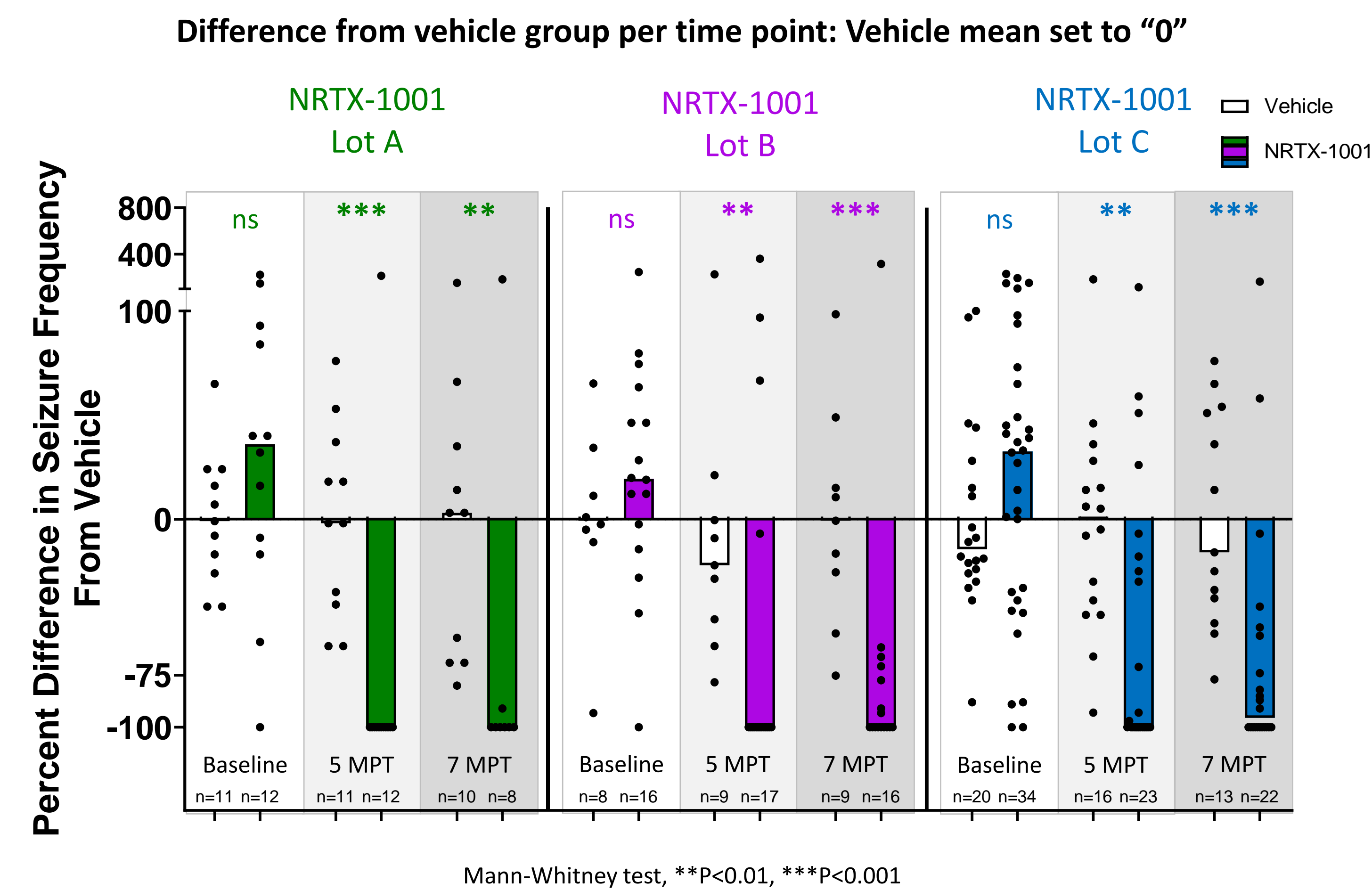
	Lot A	Lot B	Lot C	Lot D	Lot E	Lot F	Lot G	Lot H	Total
Responder/ Total animals treated	7/8 88%	12/16 75%	15/22 68%	10/12 83%	4/5 80%	6/7 86%	31/37 84%	6/10 60%	91/117 78%

Across multiple independent manufacturing lots:

- 78% of epileptic animals that receive NRTX-1001 have > 75% seizure reduction
- 64% (75/117) of epileptic animals that receive NRTX-1001 are seizure free

MPT – months post transplant

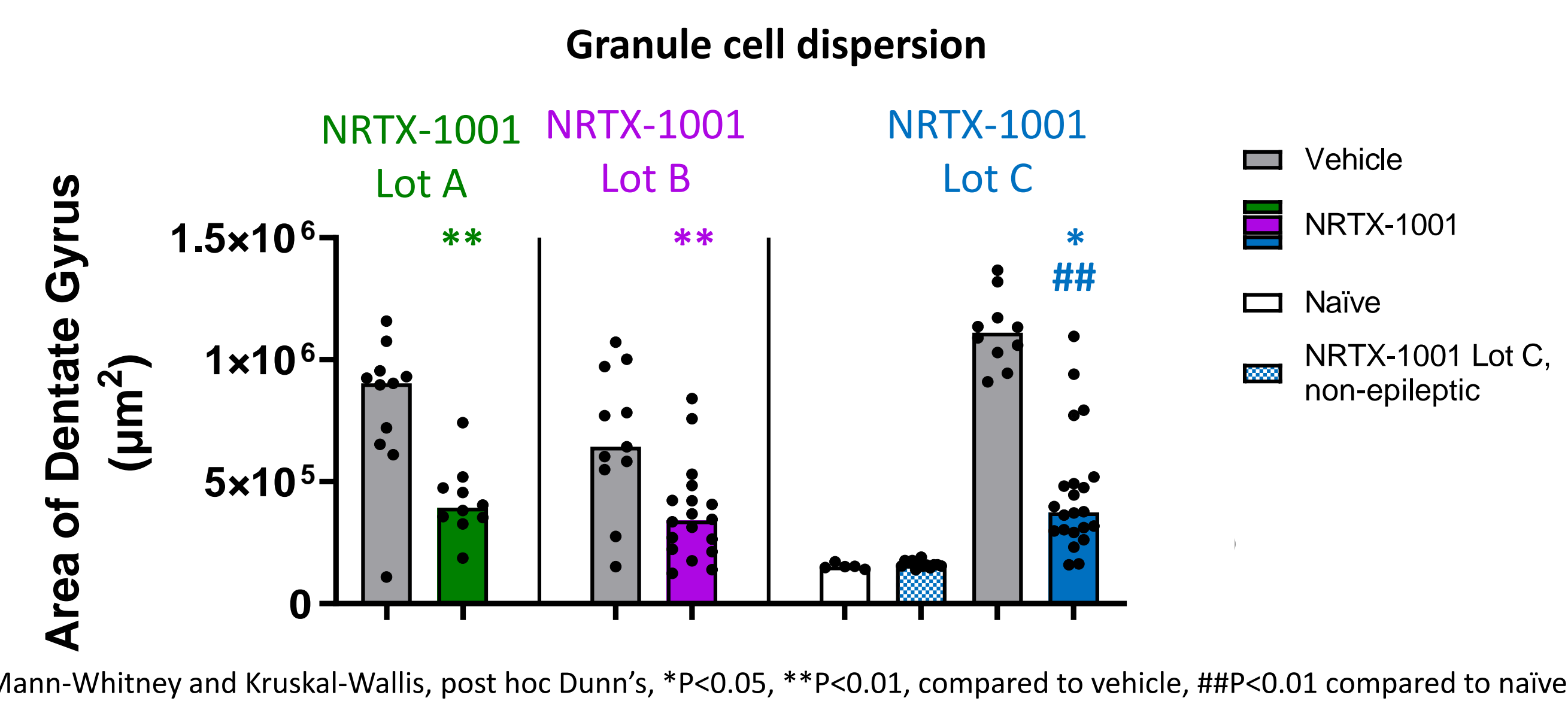
## NRTX-1001 transplantation stably reduces focal electrographic seizure frequency in epileptic mice



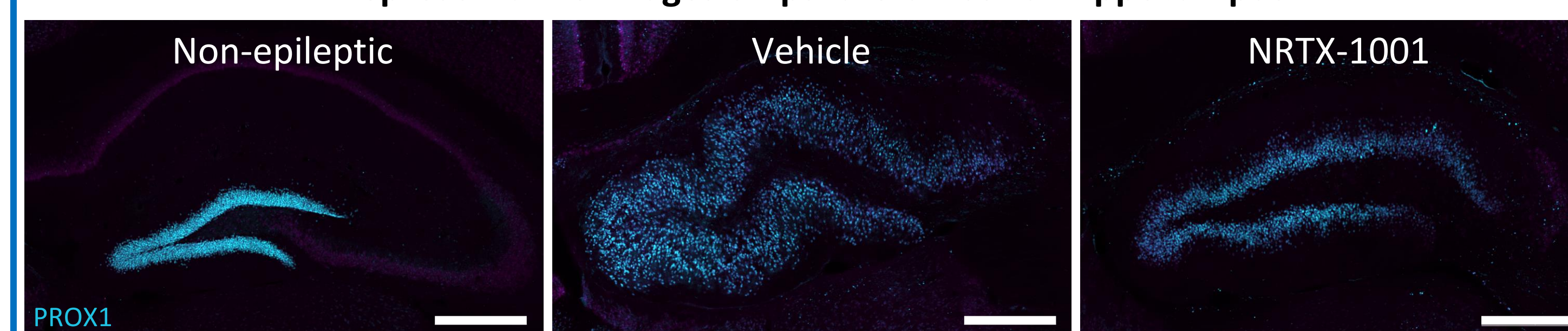
- Frequency of electrographic seizures is significantly reduced after NRTX-1001 transplantation across multiple studies

MPT – months post transplant

## NRTX-1001 transplantation ameliorates granule cell dispersion



## Representative images of ipsilateral rostral hippocampus

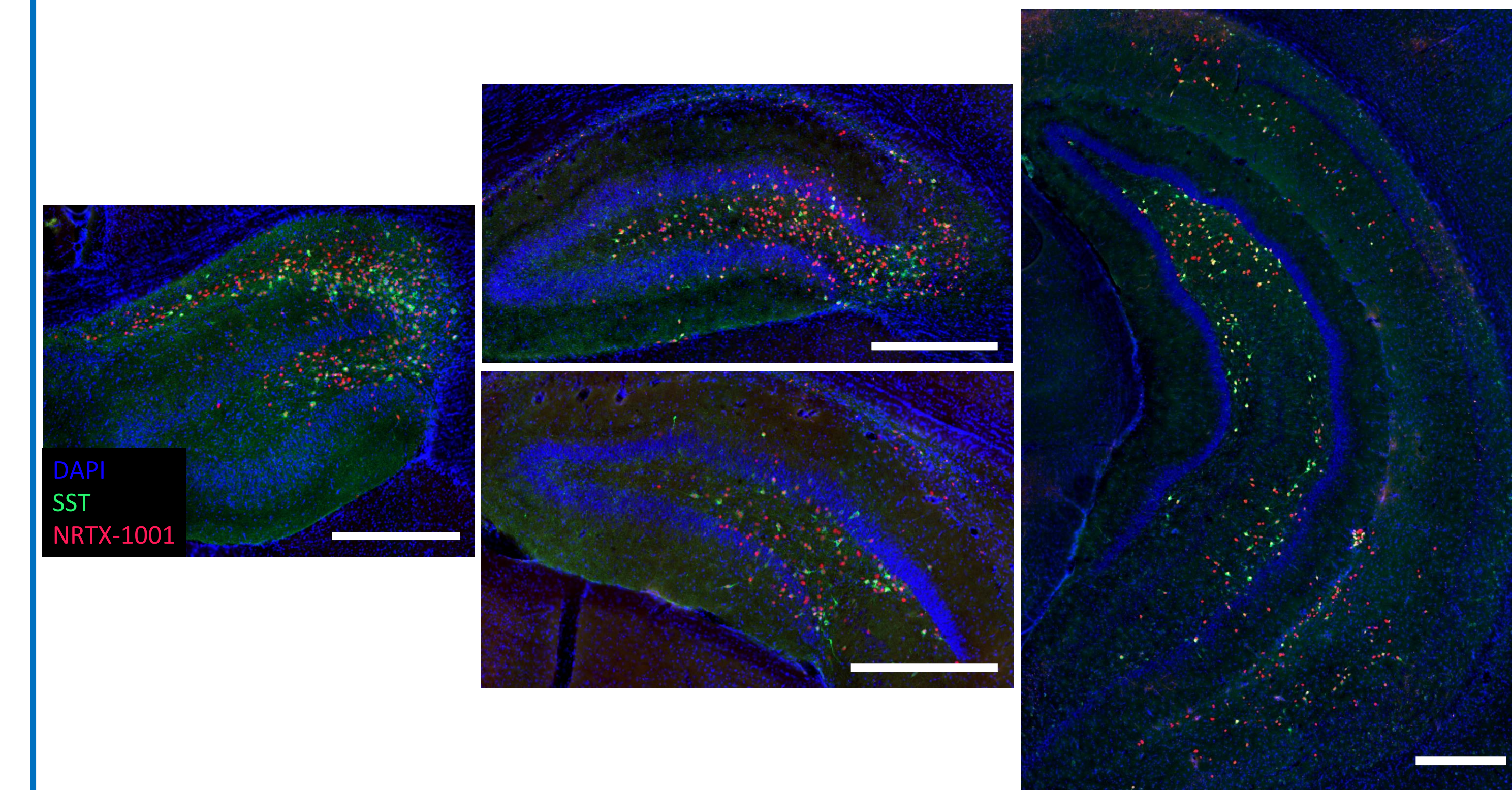


Scale bars indicate 500 µm

- Granule cell dispersion in the focal kainate model mirrors an aspect of hippocampal sclerosis that can be seen in people with temporal lobe epilepsy
- Granule cell dispersion is significantly reduced in the ipsilateral rostral hippocampus in NRTX-1001-transplanted epileptic mice

## NRTX-1001 persists and disperses throughout the hippocampus

### Representative images of NRTX-1001 distribution

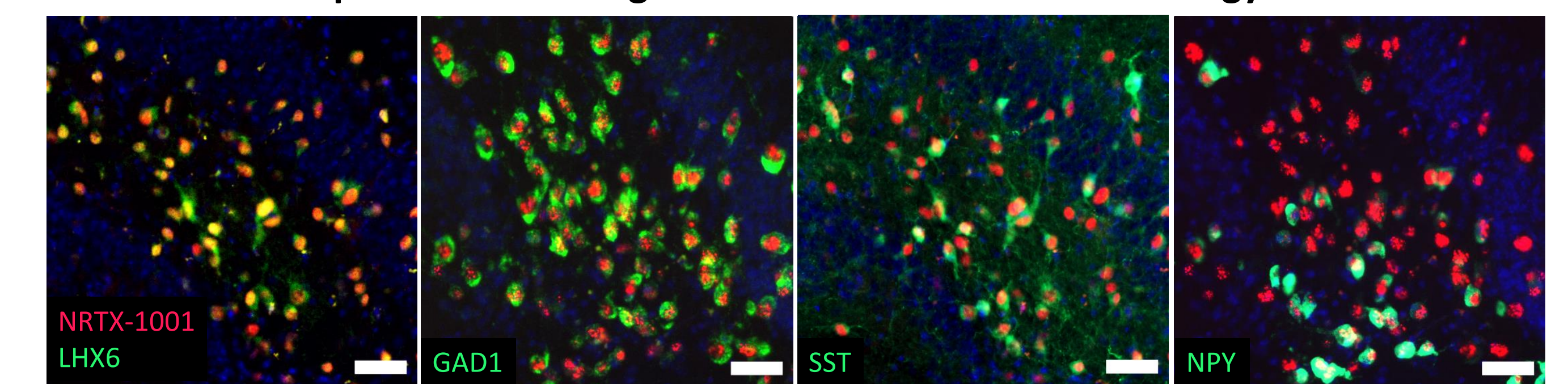


Scale bars indicate 500 µm

- NRTX-1001 interneurons distribute throughout CA1-3 and the dentate gyrus
- Across multiple studies, transplanted NRTX-1001 interneurons persist up to 12 months

## NRTX-1001 expresses markers of inhibitory interneurons

### Representative images of NRTX-1001 cells in dentate gyrus



Scale bars indicate 50 µm

- NRTX-1001 cells express LHX6 (MGE lineage), GAD1 (GABAergic), somatostatin (SST – interneuron subtype), and NPY (interneuron subtype)
- NRTX-1001 cells do not express proliferative marker KI67, nor do they cause formation of ectopic tissue or teratomas.

MGE – medial ganglionic eminence

## CONCLUSIONS

- NRTX-1001 transplantation consistently reduces focal electrographic seizures in the intrahippocampal kainate mouse model of mesial temporal lobe epilepsy as early as 5 months post transplantation
- NRTX-1001 consists of MGE-type GABAergic interneurons that persist and distribute in the hippocampus
- NRTX-1001 transplantation into epileptic mice significantly reduces hippocampal pathology

NRTX-1001 persisted in the epileptic mouse hippocampus, was well tolerated, and resulted in significant mesiotemporal seizure suppression. These findings support an ongoing Phase I/II clinical trial in people with mesiotemporal lobe epilepsy [ClinicalTrials.gov Identifier: NCT05135091]