

# PRAX-562 and Praxis pipeline updates

*Kris Kahlig, PhD*

*Senior Director, Biology*

*Praxis Precision Medicines*

# Imperatives which guide our epilepsy portfolio build

**Focus directly on  
underlying genetic defects  
in rare epilepsy**

**PRAX-222\***  
ASO

**PRAX-020**  
SMALL MOLECULE

**PRAX-080\***  
ASO

**PRAX-090\***  
ASO

**PRAX-100\***  
ASO

**PRAX-030**  
SMALL MOLECULE

**Focus on implicated  
genes in common  
diseases**

**PRAX-114**  
SMALL MOLECULE

**PRAX-944**  
SMALL MOLECULE

**Focus on nodes of  
pathophysiological convergence  
informed by genetics**

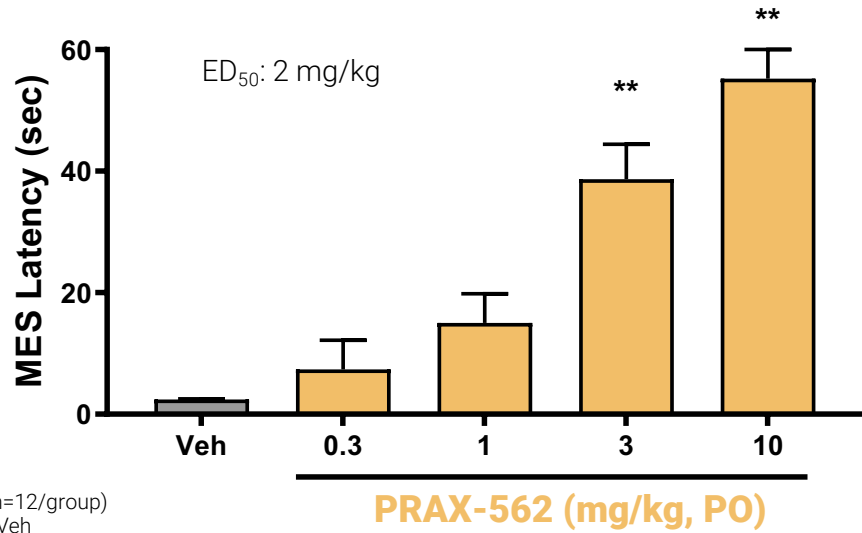
**PRAX-562**  
SMALL MOLECULE

**PRAX-628**  
SMALL MOLECULE

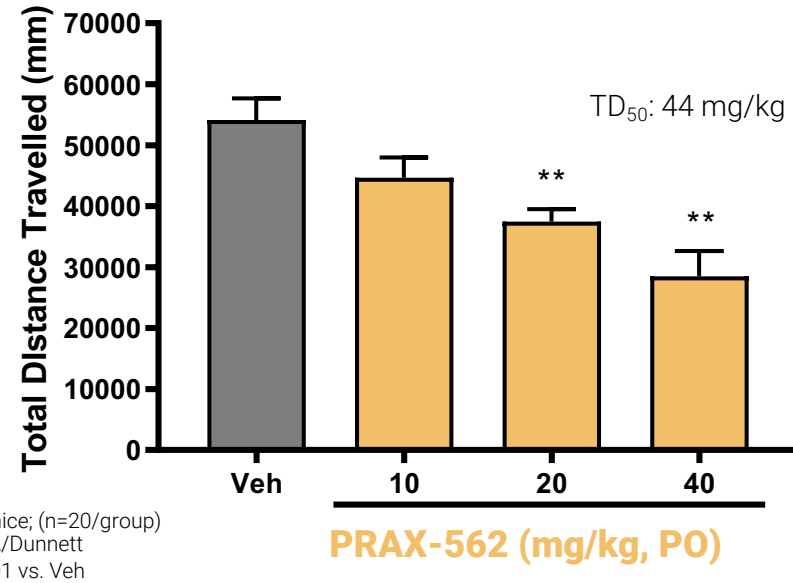
\*PRAX-222 in collaboration with Ionis. PCDH19 (PRAX-080), SYNGAP1 (PRAX-090), SCN2A-LOF (PRAX-100) ASOs are a collaboration with The Florey Institute of Neuroscience and Mental Health.

# PRAX-562 preclinical data

## MES EFFICACY



## sLMA TOLERABILITY



Therapeutic Index = TC<sub>50</sub> / EC<sub>50</sub>  
MES, maximal electroshock  
sLMA, spontaneous locomotor activity

**Molecule**

**PRAX-562**

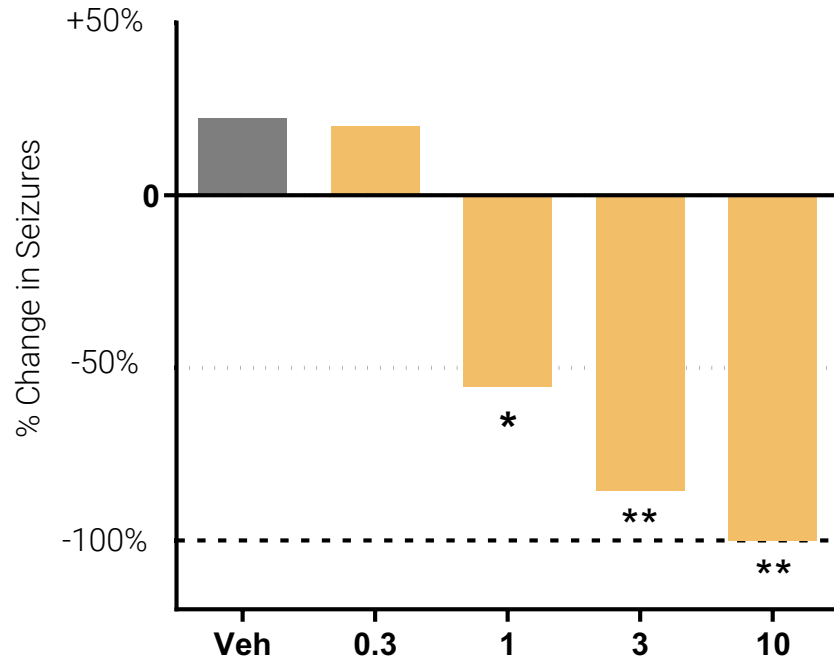
**Plasma Therapeutic Index**

**16.2x**

Kahlig KM et al. Epilepsia. 2022;00:1–12.

# PRAX-562 preclinical data

## IN VIVO POC IN SCN2A SPONTANEOUS SEIZURES<sup>1</sup>



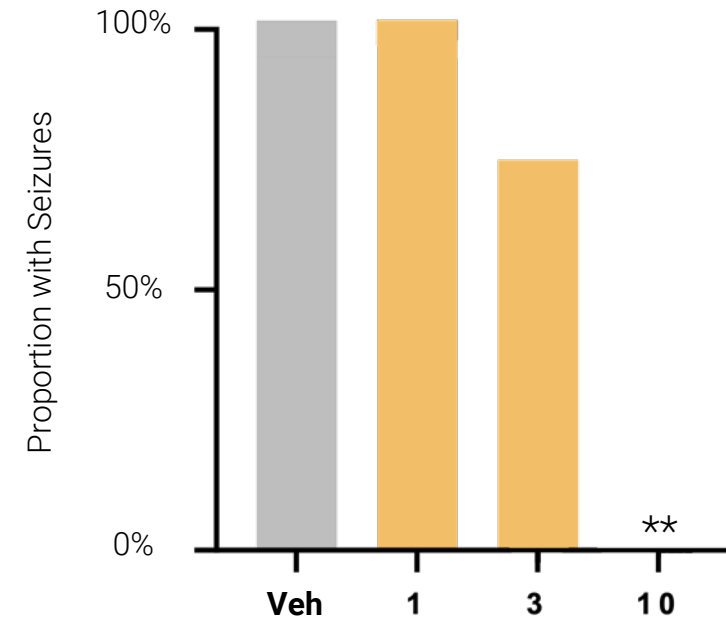
Sidak's post hoc comparison test

\*p<0.05 vs. Veh

\*\*p<0.001 vs. Veh

**PRAX-562 (mg/kg, PO)**

## IN VIVO POC IN SCN8A AUDIOGENIC EVOKED SEIZURES<sup>2</sup>



\*\*Significant protection vs. Veh  
 $\chi^2_2 = 16.0$ , Fisher's p = 0.0002

**PRAX-562 (mg/kg, PO)**

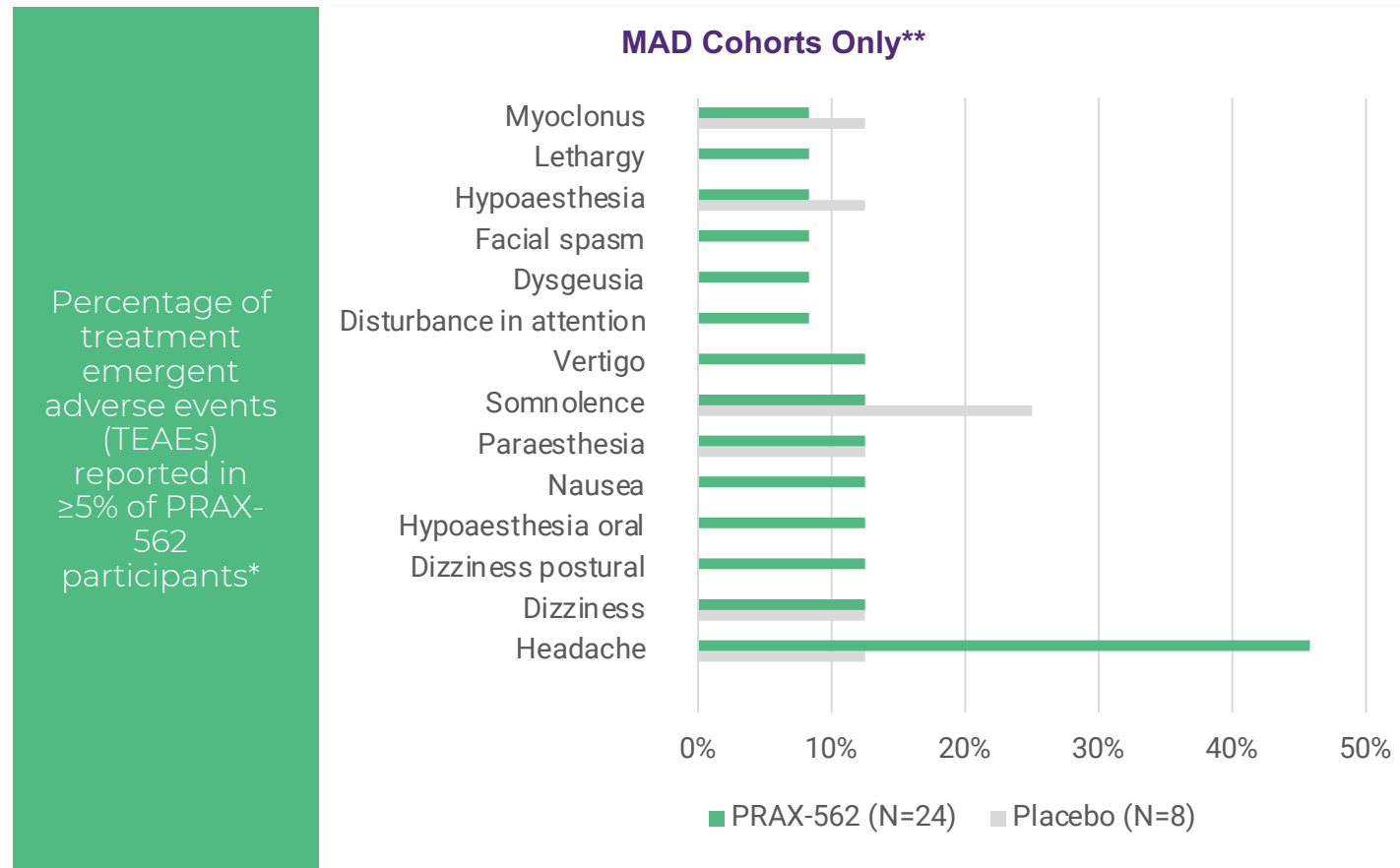
<sup>1</sup> PRAX-562 inhibition of spontaneous seizures in Q54 GoF mice.

<sup>2</sup> PRAX-562 inhibition of audiogenic seizures in N1768D D/+ mice

# PRAX-562 emerging clinical data

- Superior selectivity for disease-state NaV channel hyperexcitability
- Unprecedented therapeutic window with potential for superior safety and efficacy
- Convenient auto-titration regimen with stable PK

# PRAX-562 well tolerated in Phase 1 study in healthy adults



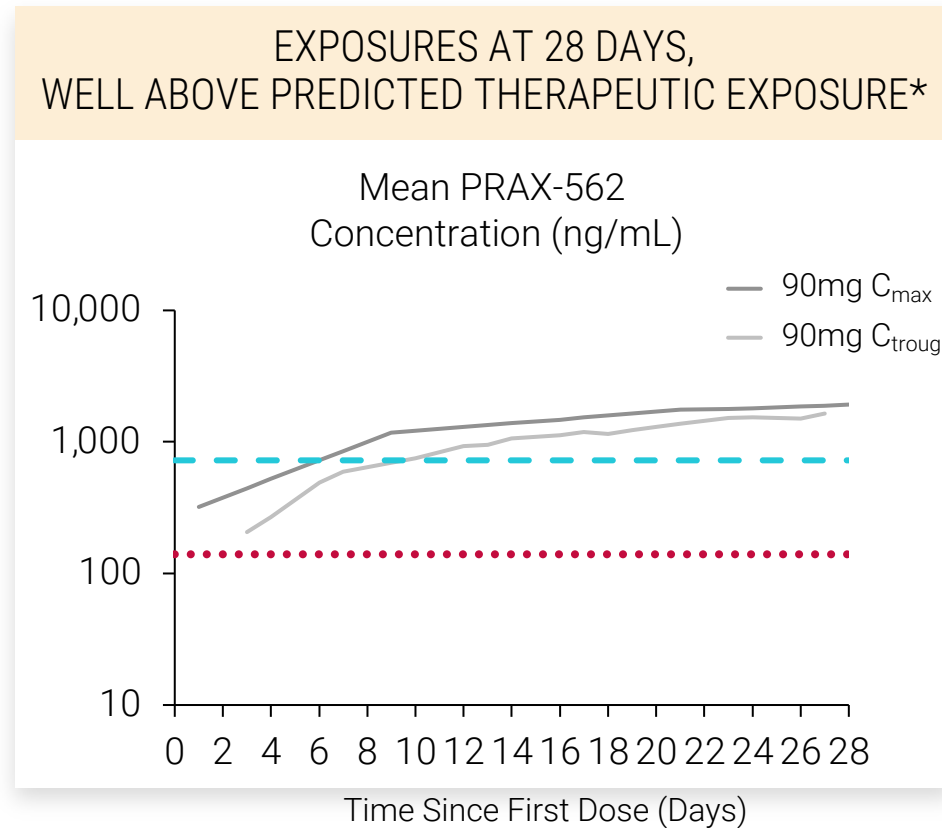
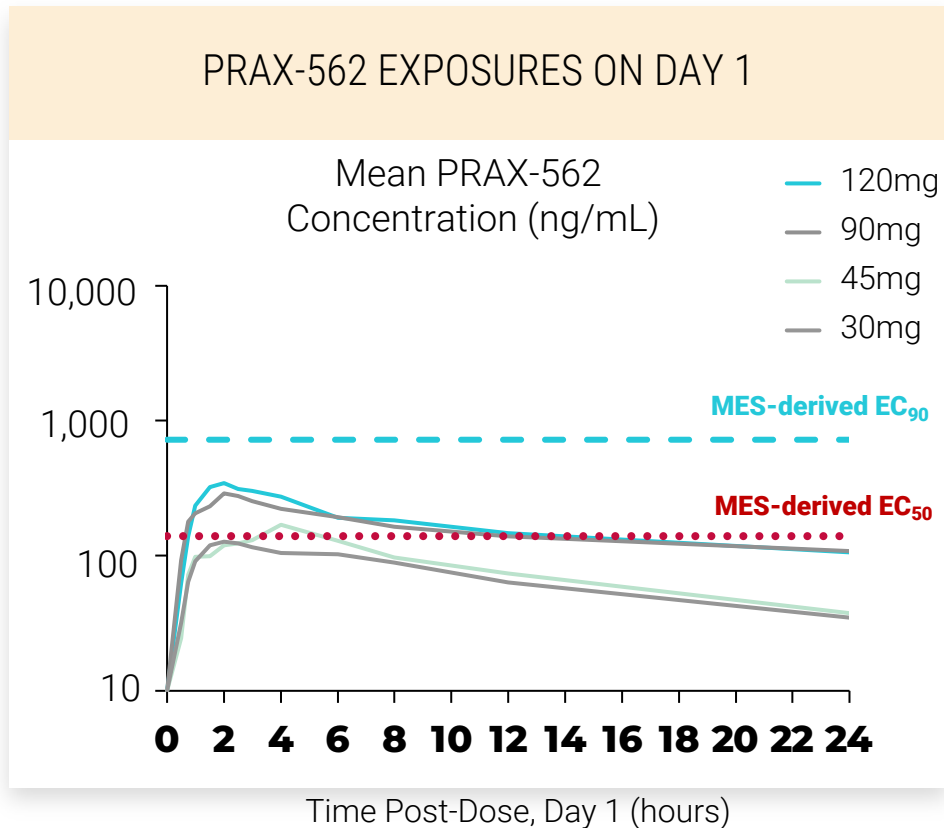
- All TEAEs mild to moderate in severity
- No drug-related SAEs or severe AEs
- No significant aberrations in clinical safety labs, ECGs, or assessments of suicide

MAD, multiple ascending dose

\*TEAEs related to blood sample collection excluded

\*\*112 people have been exposed to PRAX-562 across the SAD, MAD, and food effect cohorts in PRAX-562-101.

# PRAX-562 in healthy volunteers safely exceeds projected therapeutic exposure



\*Preliminary data from 562-102 study from first 12 participants enrolled in the study; C<sub>max</sub> is representative of concentration at 2.5 hours post-dose. Source: Praxis data on file.

# Three epilepsy drugs in clinic by end of 2022

**PRAX-562**

*(SCN2A, SCN8A, TSC)*

**Initiate Phase 2 Study:  
2H22**

**PRAX-628**

*(FOCAL EPILEPSY)*

**Initiate Phase 1 Study:  
4Q22**

**PRAX-222**

*(SCN2A)*

**Initiate Seamless Study:  
2H22\***

**PRAX-222 and PRAX-562 received Orphan Drug Designations for severe pediatric epilepsy indications from the FDA and EMA, and Rare Pediatric Disease designation from the FDA**

\*In April 2022, the FDA placed the first-in-patient study of PRAX-222 on clinical hold. The letter detailing the reasons for the hold is expected to be received from the FDA within 30 days of April 28, 2022