CORPORATE OVERVIEW

April 2023

Forward-looking statements

This presentation may contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial conditions, including but not limited to express or implied statements regarding the current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our preclinical and clinical results and other future conditions. Any forward-looking statements in this presentation are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, risks relating to: (i) the success and timing of our ongoing clinical trials, (ii) the success and timing of our product development activities and initiating clinical trials, (iii) the success and timing of our collaboration partners' product development activities, (iv) our ability to obtain and maintain regulatory approval of any of our product candidates, (v) our plans to research, discover and develop additional product candidates, (vi) our ability to enter into collaborations for the development of new product candidates, (vii) our ability to establish manufacturing capabilities, and our and our collaboration partners' abilities to manufacture our product candidates and scale production, and (viii) our ability to meet any specific milestones set forth herein. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements.

For further information regarding the risks, uncertainties and other factors that may cause differences between our expectations and actual results, you should review the "Risk Factors" section of our Annual Report on Form 10-K for the year ended December 31, 2022 and other filings with the Securities and Exchange Commission.

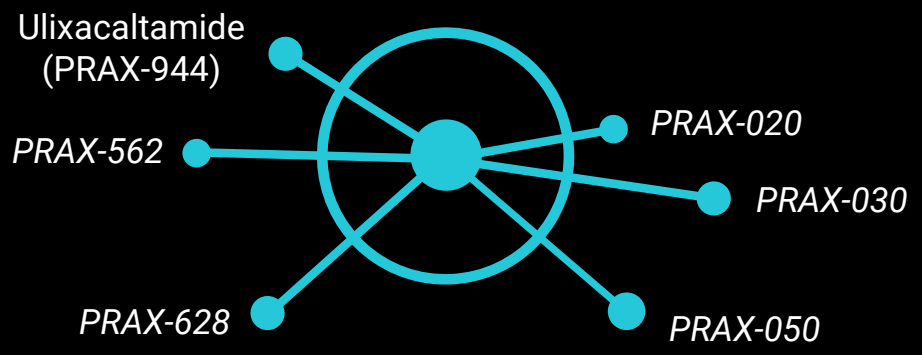
Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

Developing Treatments Inspired By The Genetics of Epilepsy

ENABLED BY TWO PLATFORMS

CEREBRUM™

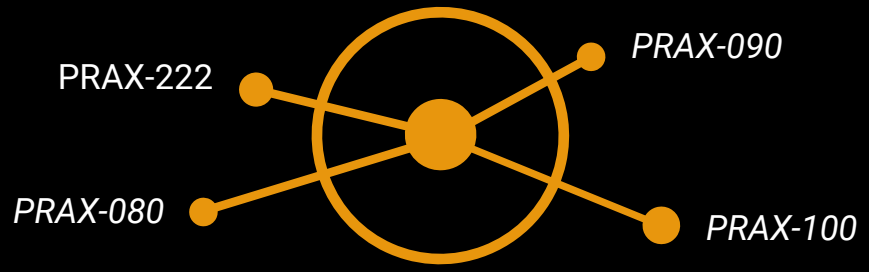
SMALL MOLECULE PLATFORM



Cerebrum™ utilizes deep understanding of neuronal excitability and neuronal networks and applies a series of computational and experimental tools to develop orally available precision therapies

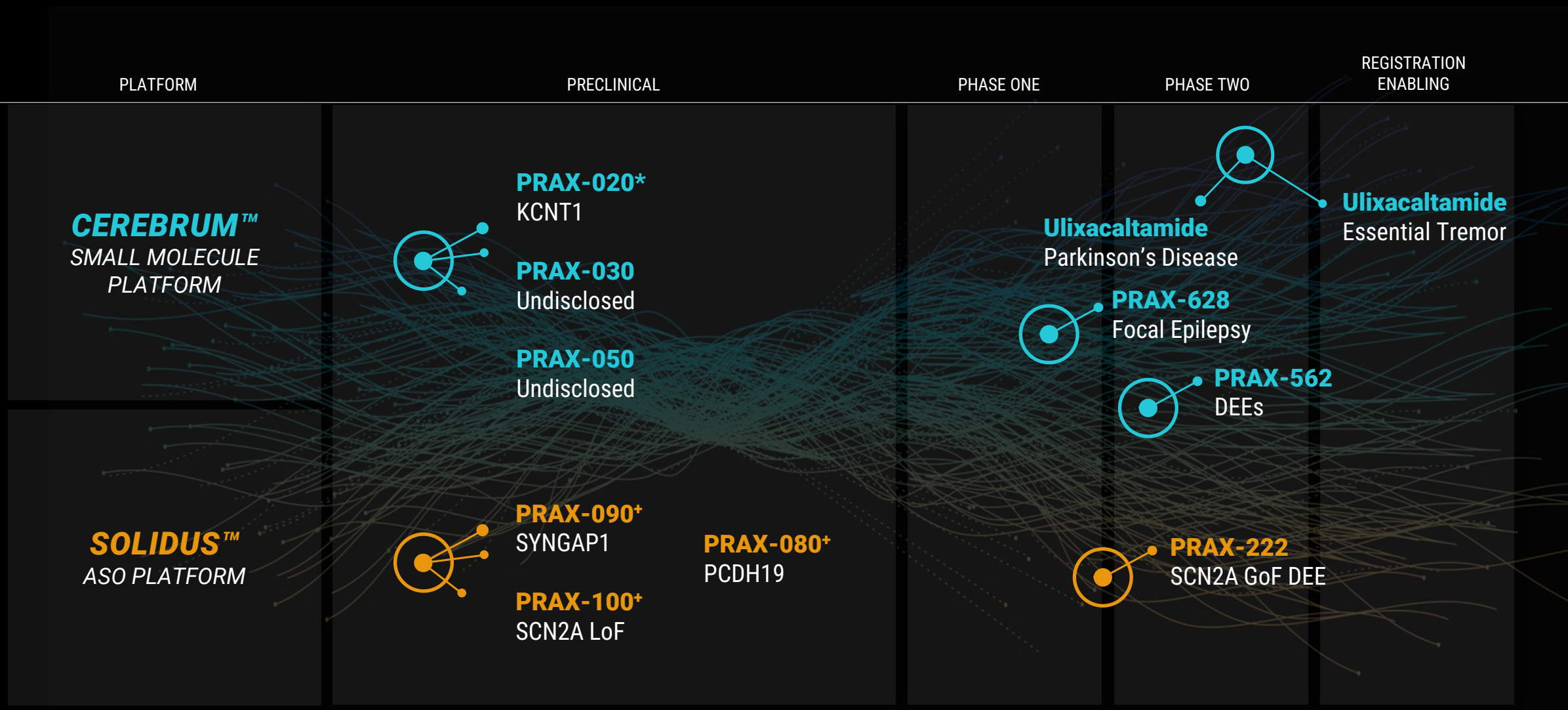
SOLIDUS™

ANTISENSE OLIGONUCLEOTIDE (ASO) PLATFORM



Solidus™ is an efficient, targeted precision medicine discovery and development engine for ASOs anchored on proprietary, computational methodology

Targeting movement disorders & epilepsies connected by neuronal imbalance



*PRAX-020 (KCNT1) is a research collaboration with UCB

+PRAX-080 (PCDH19), PRAX-090 (SYNGAP1) & PRAX-100 (SCN2A-LoF) ASOs are a collaboration with The Florey Institute of Neuroscience and Mental Health

Leveraging genetics to efficiently translate insights into therapies

GENETICS

Focus on therapeutic targets identified through human genetics

TRANSLATIONAL TOOLS

Translational tools validate potential of target and product candidate and can provide early proof of biology

EFFICIENT & RIGOROUS

Efficient, rigorous clinical development paths to proof-of-concept in humans

PATIENT-GUIDED

Patient-guided development strategies to deliver on what patients actually need

What to expect from Praxis in 2023

PLATFORM	1Q23	2Q23	MID YEAR	3Q23	4Q23
CEREBRUM™ *SMALL MOLECULE PLATFORM*	**Ulixacaltamide Ph 2b Essential1 Study Topline Results** Essential Tremor	**Ulixacaltamide End of Ph 2 FDA Meeting*** Essential Tremor		**Ulixacaltamide Ph 3 Initiation** Essential Tremor	
		PRAX-628 Ph 1 Topline Results		**PRAX-562 Ph 2 EMBOLD Study Topline Results** DEEs	**PRAX-628 Initiate Ph 2 Study** Focal Epilepsy
SOLIDUS™ *ASO PLATFORM*		**PRAX-222 EMBRAVE Study First Dose Cohort (Part 1) Topline Safety Results** SCN2A GoF DEE			

*Ulixacaltamide EOP2 meeting with FDA scheduled for June 2023

CEREBRUM™

SMALL MOLECULE PLATFORM

Ulixacaltamide (PRAX-944)

Essential Tremor and Parkinson's Disease

KEY UPCOMING MILESTONES

Mid-2023
ET End-of-Phase 2 FDA Meeting

2H 2023
ET Phase 3 Initiation

Essential Tremor (ET) is the most common movement disorder…

Up to 7 million people in the United States may have ET[1]

Action tremors significantly disrupt daily living for people with ET

Hallmark feature is action tremor that primarily affects the hands[2,3]

Almost all ET patients suffer from at least one comorbid condition (e.g. depression, anxiety, sleep disorders, cognitive dysfunction)[4]

SOURCE: 1. GHOSH (2016) (P.231, C.1, PH.1, L.1-2), 2. Elble RJ. Curr Neurol Neurosci Rep. 2013 Jun;13(6):353. 3. Putzke JD, et al. J Neurol Neurosurg Psychiatry. 2006 Nov;77(11):1235-7. 4. Vetterick, C., Lyons, K.E., Matthews, L.G. et al. The Hidden Burden of Disease and Treatment Experiences of Patients with Essential Tremor: A Retrospective Claims Data Analysis. Adv Ther (2022). https://doi.org/10.1007/s12325-022-02318-8

PRAXIS

…but ET often remains undiagnosed, misdiagnosed, undertreated and untreated

Approximately 1 million people are diagnosed with ET and on treatment, while another 1 million patients are estimated to remain untreated

Of patients who seek treatment, ~40% discontinue within 2 years, or 200,000 patients annually

0 medications have been developed specifically for ET & only 1 medication was approved for ET >50 years ago

Many ET patients are frequently misdiagnosed, leading to ET diagnosis about 1.5 years after an initial movement disorder diagnosis

SOURCE: Vetterick, C., Lyons, K.E., Matthews, L.G. et al. The Hidden Burden of Disease and Treatment Experiences of Patients with Essential Tremor: A Retrospective Claims Data Analysis. Adv Ther (2022). https://doi.org/10.1007/s12325-022-02318-8

PRAXIS

Ulixacaltamide is a differentiated, selective T-type calcium channel blocker in development for ET and Parkinson's disease

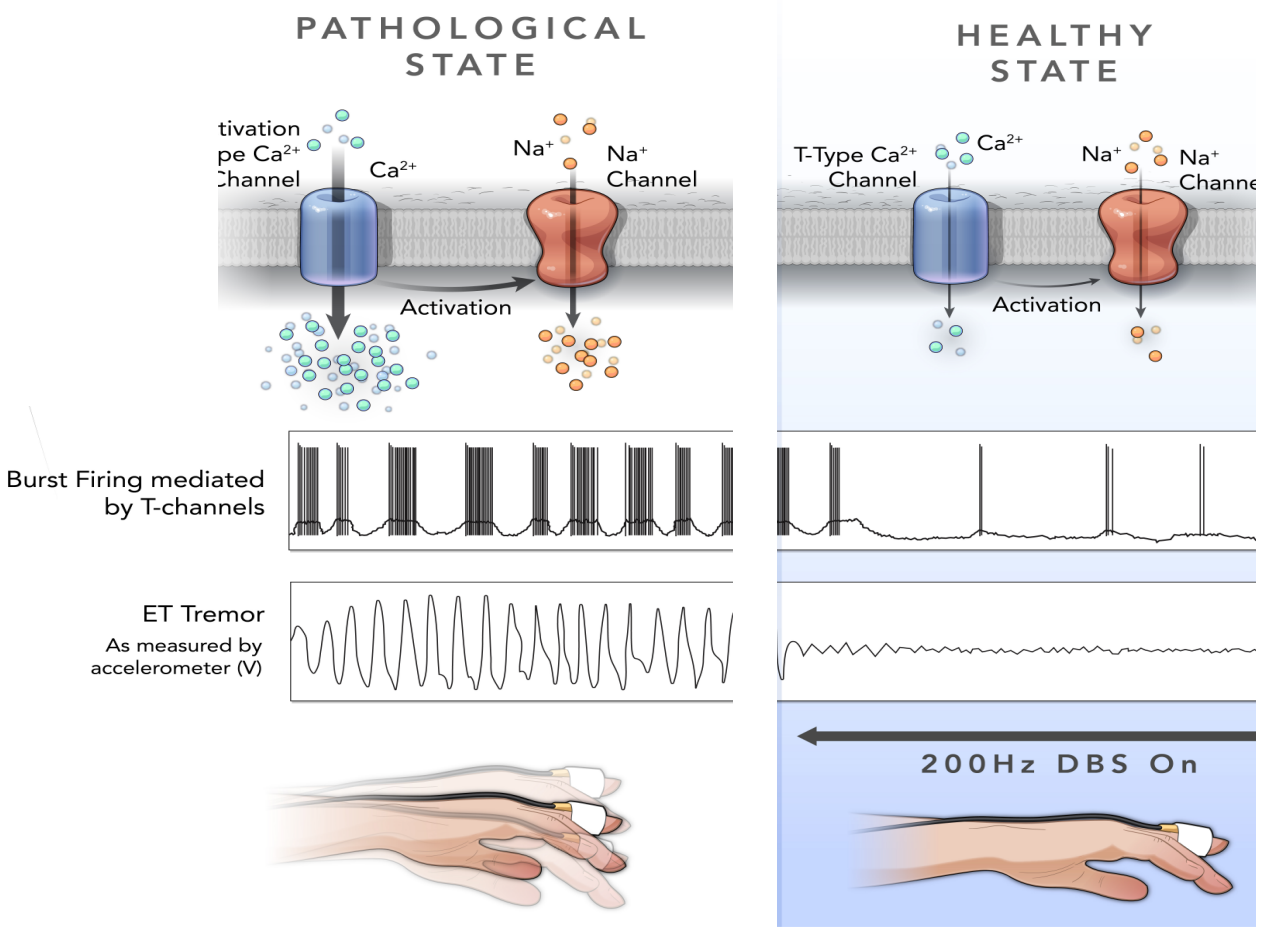
Highly selective for T-type calcium channels

Highly potent across all three T-type isoforms

Potential for effectiveness across range of neuronal activity levels

Source: Praxis Data on file, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9310641/

T-Type calcium channels are gatekeepers of neuronal firing patterns in the Cerebello-Thalamo-Cortical (CTC) circuit



Mutations in T-type calcium channels (TTCC) are genetically linked to familial ET

TTCC drive burst firing in the CTC circuit

Burst firing in the CTC circuit correlated with tremor in patients with ET and PD

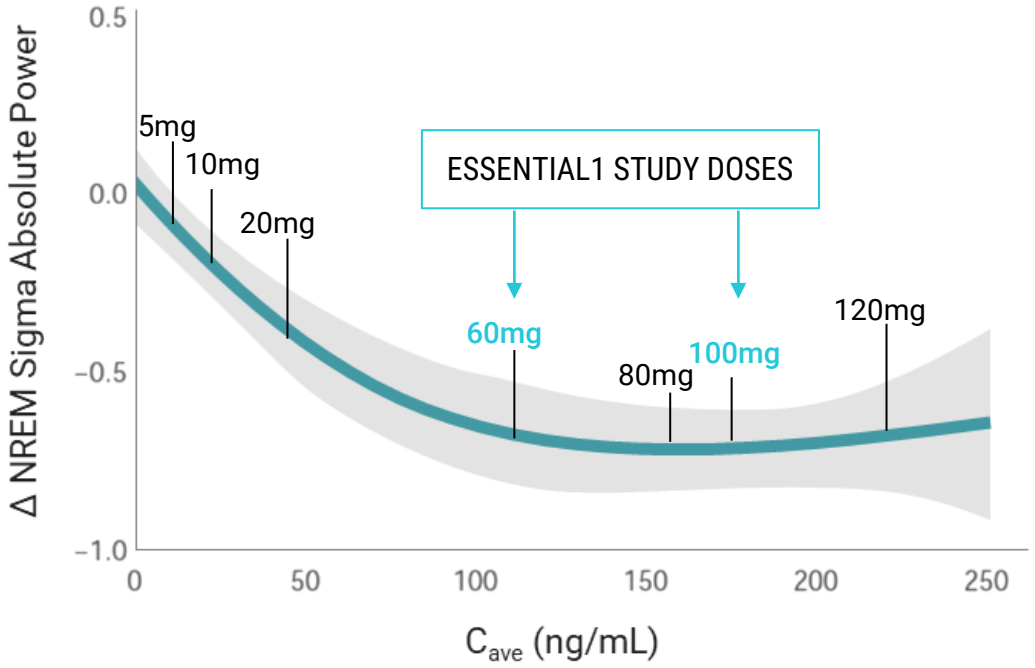
Deep Brain Stimulation reduces burst firing and tremor

Source: Based on Milosevic 2018 figured on actual ET patient intraoperative real-time single-unit recordings of action potentials of individual neurons

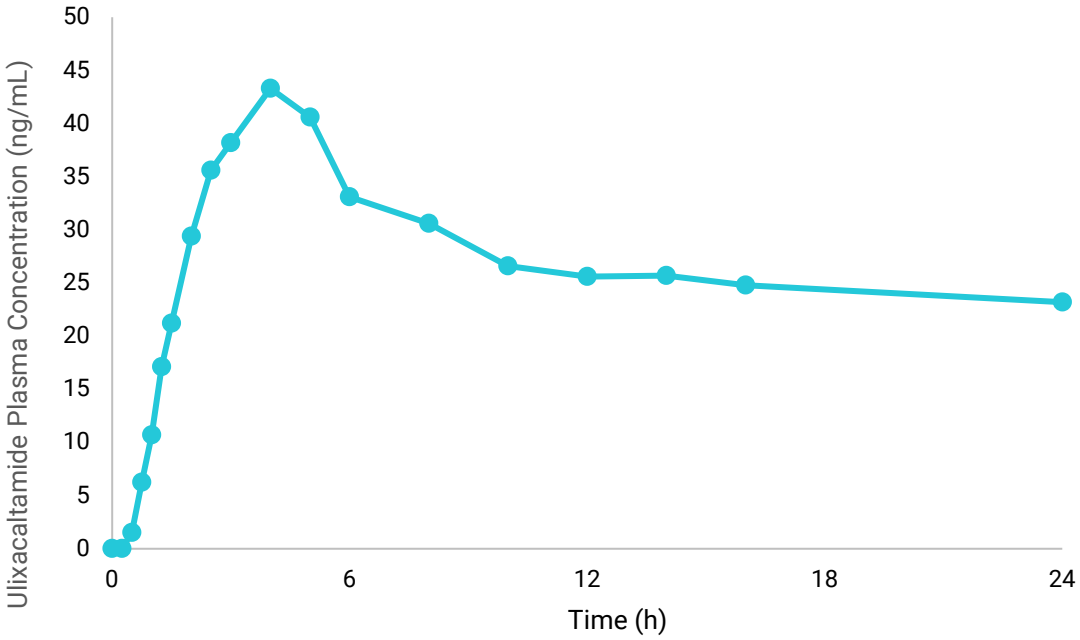
PRAXIS

Ulixacaltamide's wide dosing range and modified release formulation may support tolerability & efficacy profile

PREDICTABLE PK, FLEXIBILITY IN TITRATION & WIDE DOSING RANGE UP TO ~100 MG CONFIRMED IN ESSENTIAL1



SUSTAINED EXPOSURE WITH BLUNTED C_{MAX}



Source: Praxis Data on file

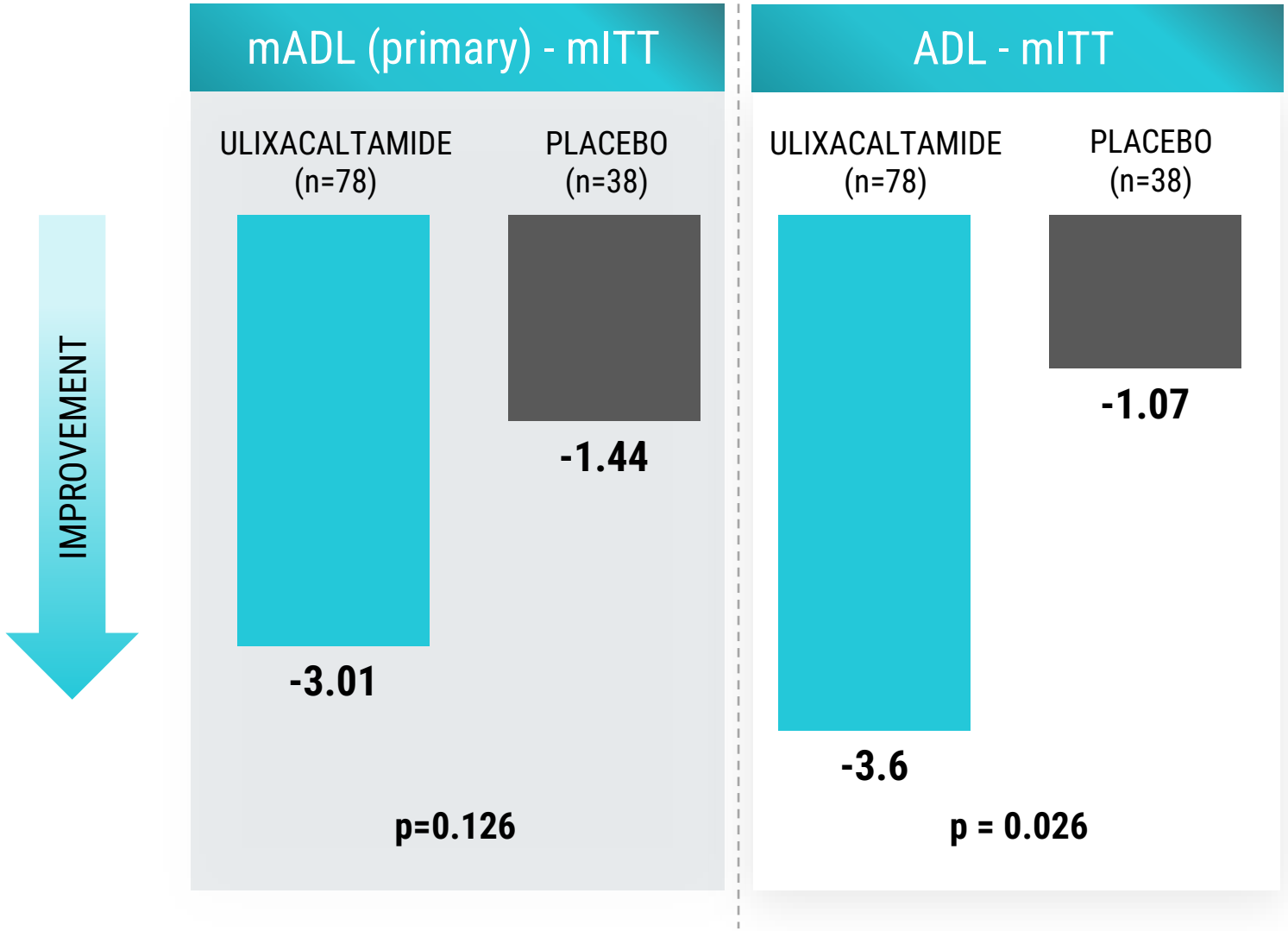
Breaking ground with Essential1 - path forward toward registration

ESSENTIAL1 ENABLES PROGRESS

- Clinically meaningful effect observed in functional outcomes
- Improvement or stabilization in all TETRAS ADL measurements
- Therapeutic drug levels achieved, suggesting individualized exposure response curve consistent with translational data
- Well tolerated safety profile, no new safety signals identified
- TETRAS performance subscale not a reliable measure for clinical studies
- Opportunity to further control for potential confounding factors in subsequent clinical trials, including ET patients with intention tremor

clinicaltrials.gov/ct2/show/NCT05021991

Essential1 topline results show mADL* and ADL improvement over placebo at Day 56 in Phase 2b ET study



No dose related difference in efficacy between 60 mg and 100 mg groups

*Composite sum of items 1 to 11 of TETRAS-ADL subscale and items 6 (bilateral) and 7 of TETRAS-PS; modified ADL score is calculated as the sum of all 13 items and ranges from 0 to 42

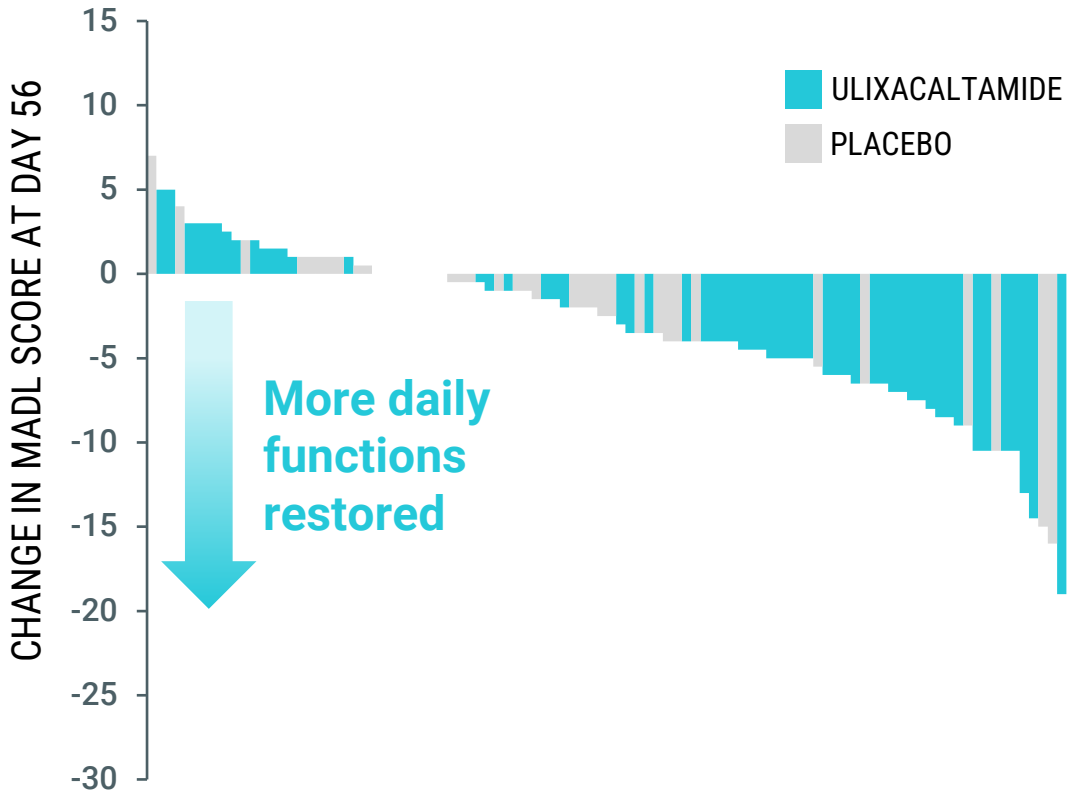
MMRM, Adjusted by baseline value, propranolol use and familial history of ET, all p values are nominal

mITT ANALYSIS: Defined as all patients enrolled under Version 4 of Protocol (or enrolled in prior version and eligible for V4), who were randomized to treatment, and received 1 dose of study drug [n=116]; excluded from mITT analysis are 16 patients enrolled under earlier protocol version that did not meet Version 4 inclusion/exclusion criteria and dose levels

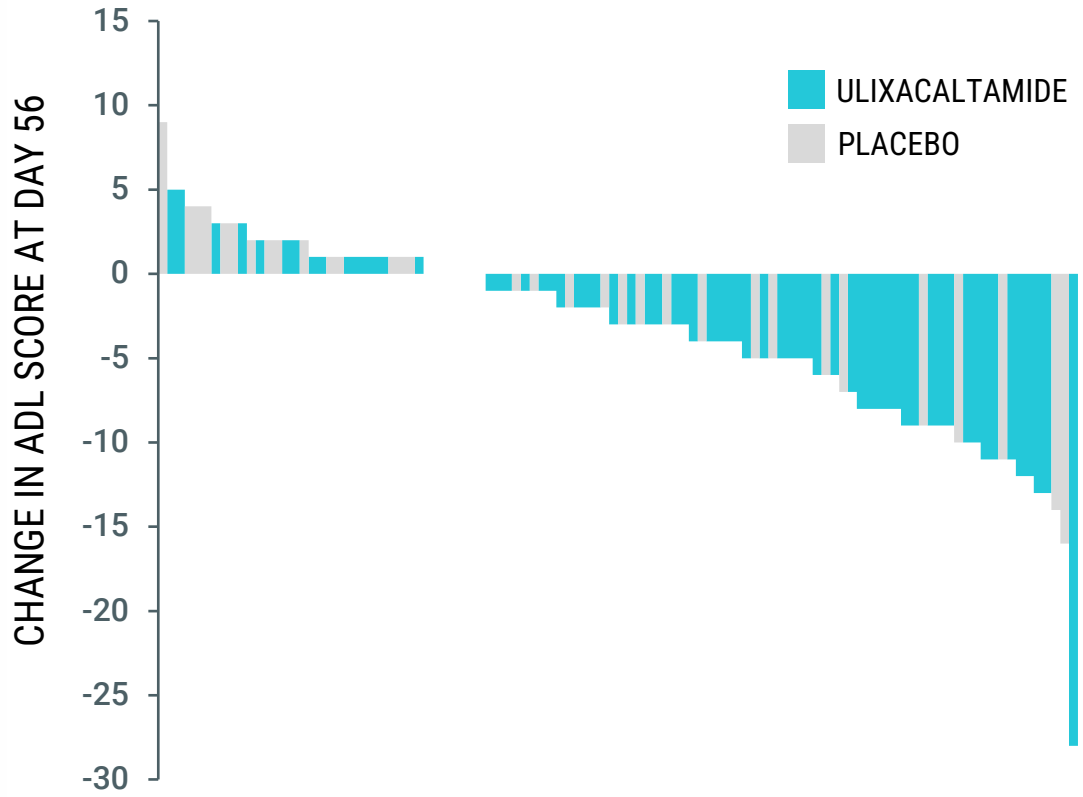
PRAXIS

More patients taking ulixacaltamide showed improvements in ADL scores compared to patients on placebo in Essential1 study

Observed mADL Change - mITT

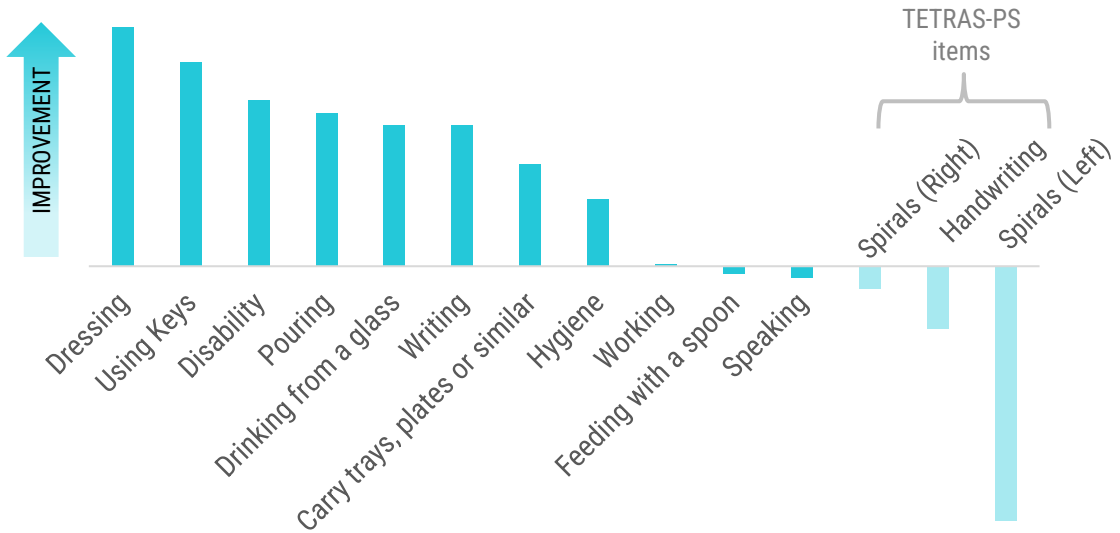


Observed ADL Change - mITT

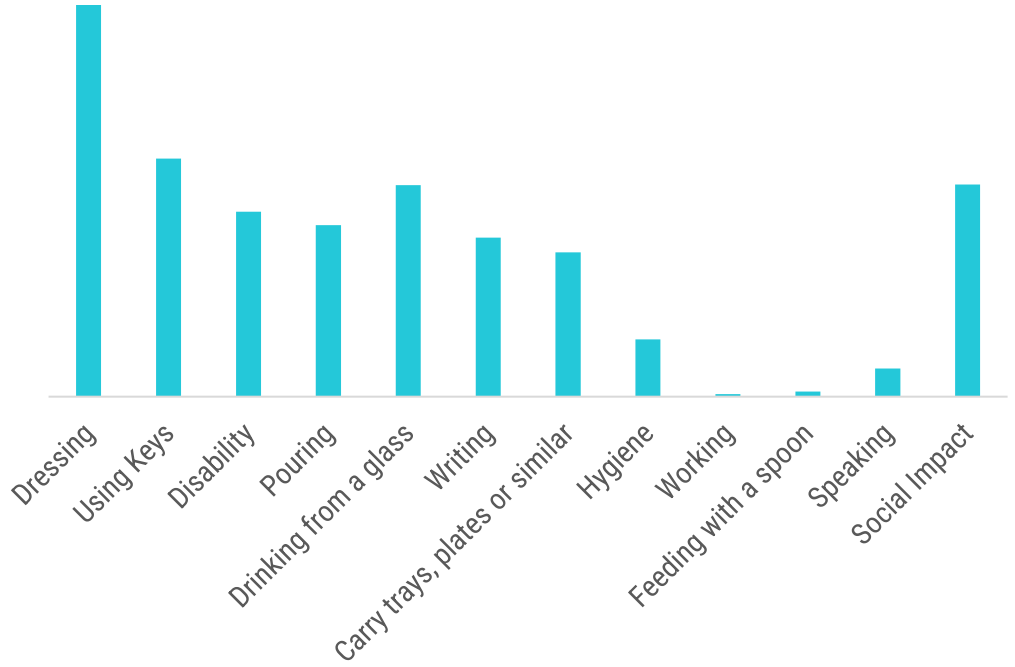


Ulixacaltamide demonstrated consistent effect relative to placebo across ADL scored items in Essential1 study

Difference from Placebo in mADL Items - mITT

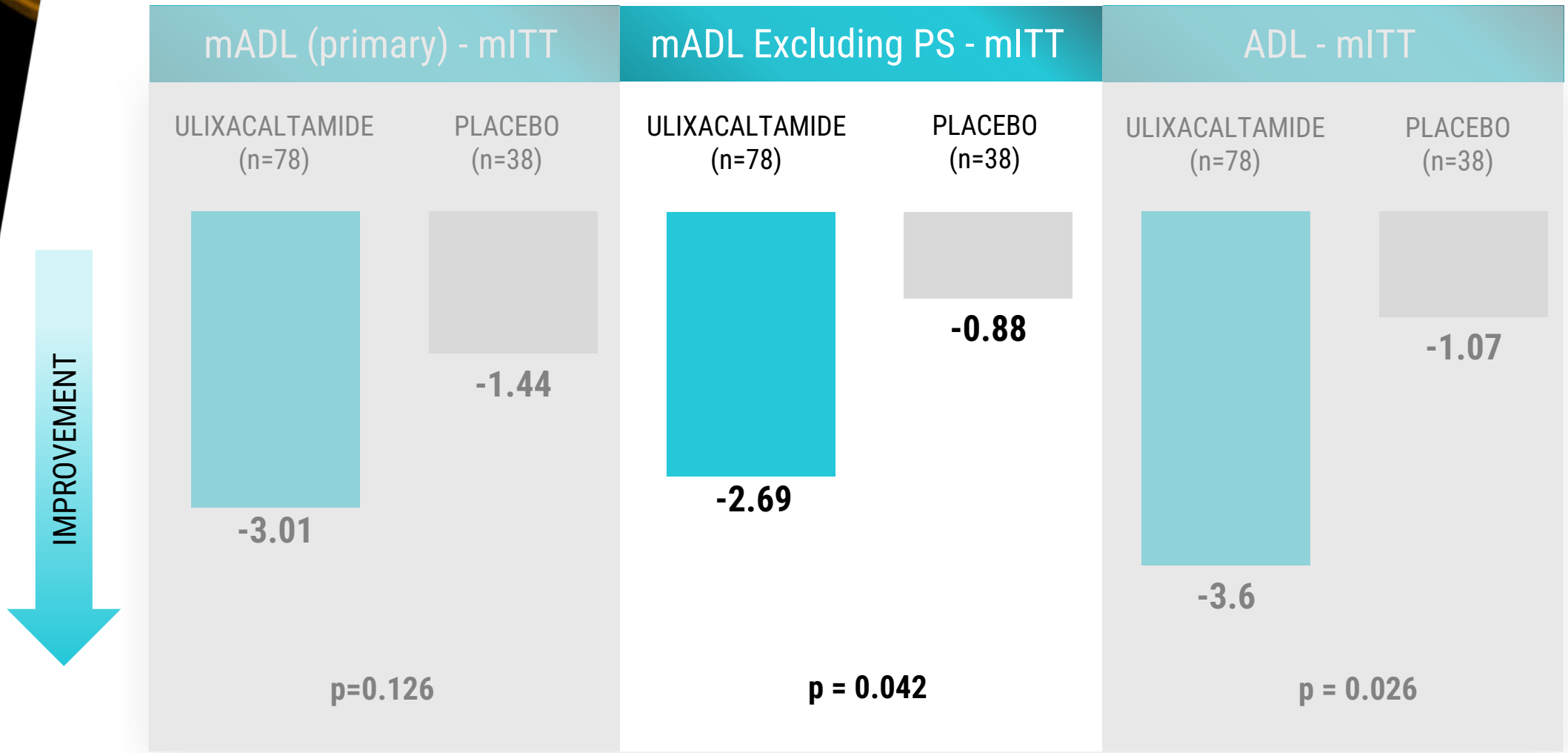


Difference from Placebo in ADL Items - mITT



PRAXIS

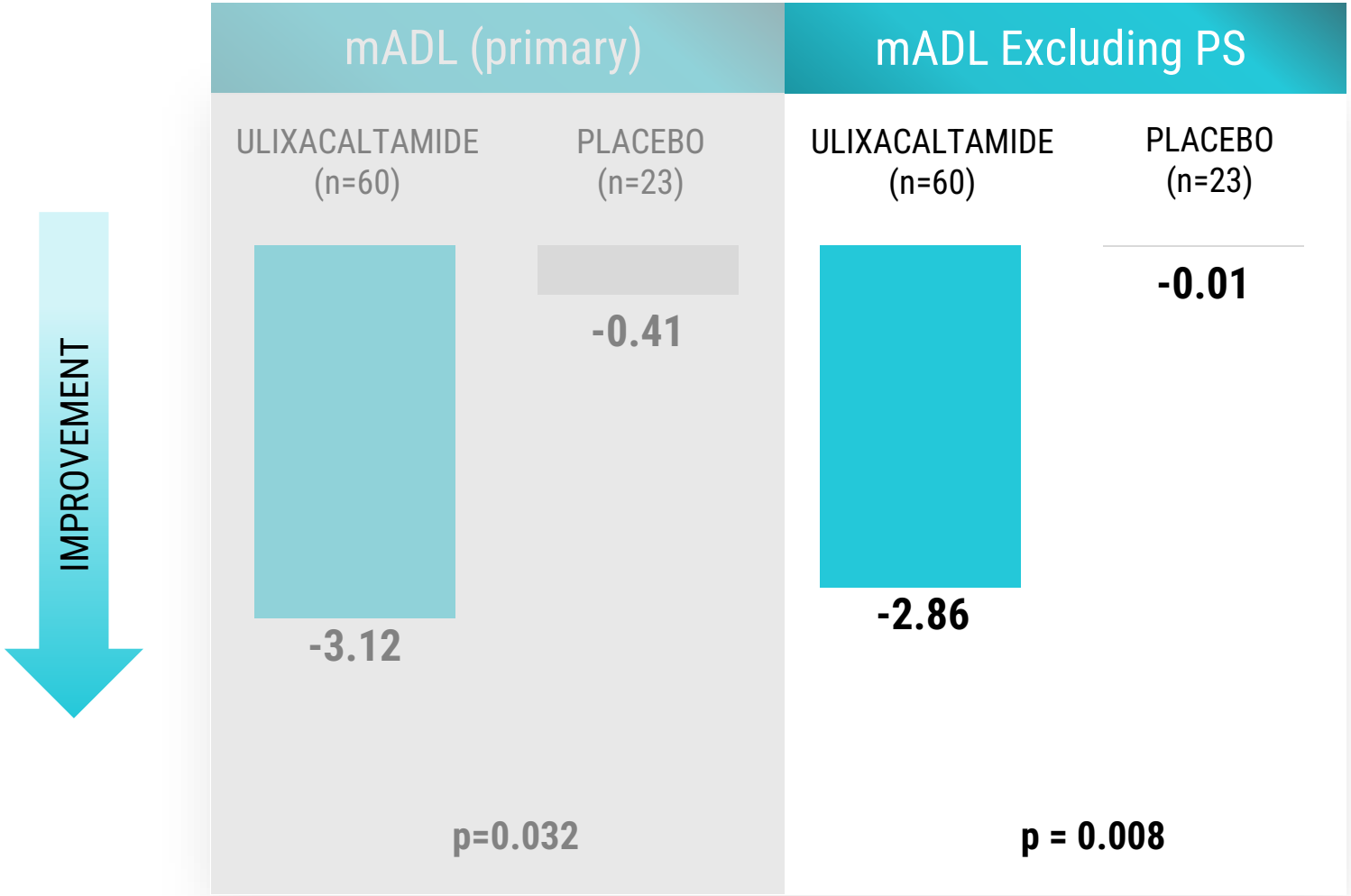
Ulixacaltamide demonstrated improvement over placebo in the mADL excluding PS at Day 56 in Essential1 study



MMRM, Adjusted by baseline value, propranolol use and familial history of ET, all p values are nominal

mADL and mADL excluding PS improvement over placebo at Day 56

mITT Excluding ET Patients with Intention Tremor



We intend to control for the presence of ET participants with intention tremor in future trials

MMRM, Adjusted by baseline value, propranolol use and familial history of ET, all p values are nominal

PRAXIS

Breaking ground with Essential1 - path forward toward registration

ESSENTIAL1 ENABLES PROGRESS

- Clinically meaningful effect observed in functional outcomes
- Improvement or stabilization in all TETRAS ADL measurements
- Therapeutic drug levels achieved, suggesting individualized exposure response curve consistent with translational data
- Well tolerated safety profile, no new safety signals identified
- TETRAS performance subscale not a reliable measure for clinical studies
- Opportunity to further control for potential confounding factors in subsequent clinical trials, including ET patients with intention tremor

NEXT STEPS

- End of Phase 2 meeting with the FDA scheduled for June 2023

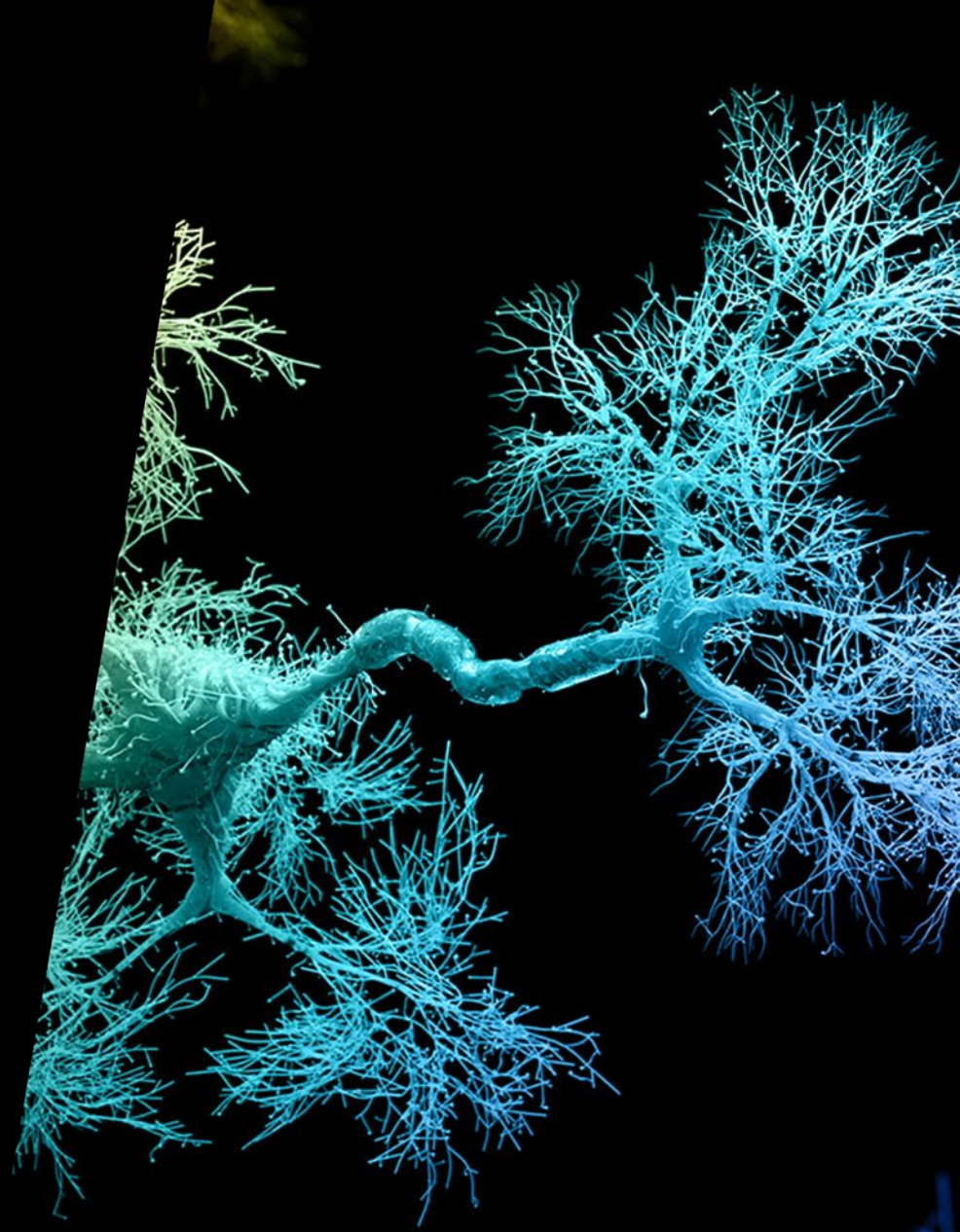
- Preliminary elements of Phase 3 program planned to start in 2H23:
  - Parallel design with 60 mg and placebo treatment arms
  - Primary endpoint of mADL excluding PS
  - 6-week treatment duration

PRAX-562

SCN2A, SCN8A & OTHER DEEs

KEY UPCOMING MILESTONES

2H 2023
Ph 2 EMBOLD Study Topline Results



Preclinical and emerging clinical data demonstrate PRAX-562 has the potential to be a first- and best- in-class Na_V blocker for DEEs

PRAX-562

SCN2A, SCN8A
+ OTHER DEEs

PAN-NA_V BLOCKER

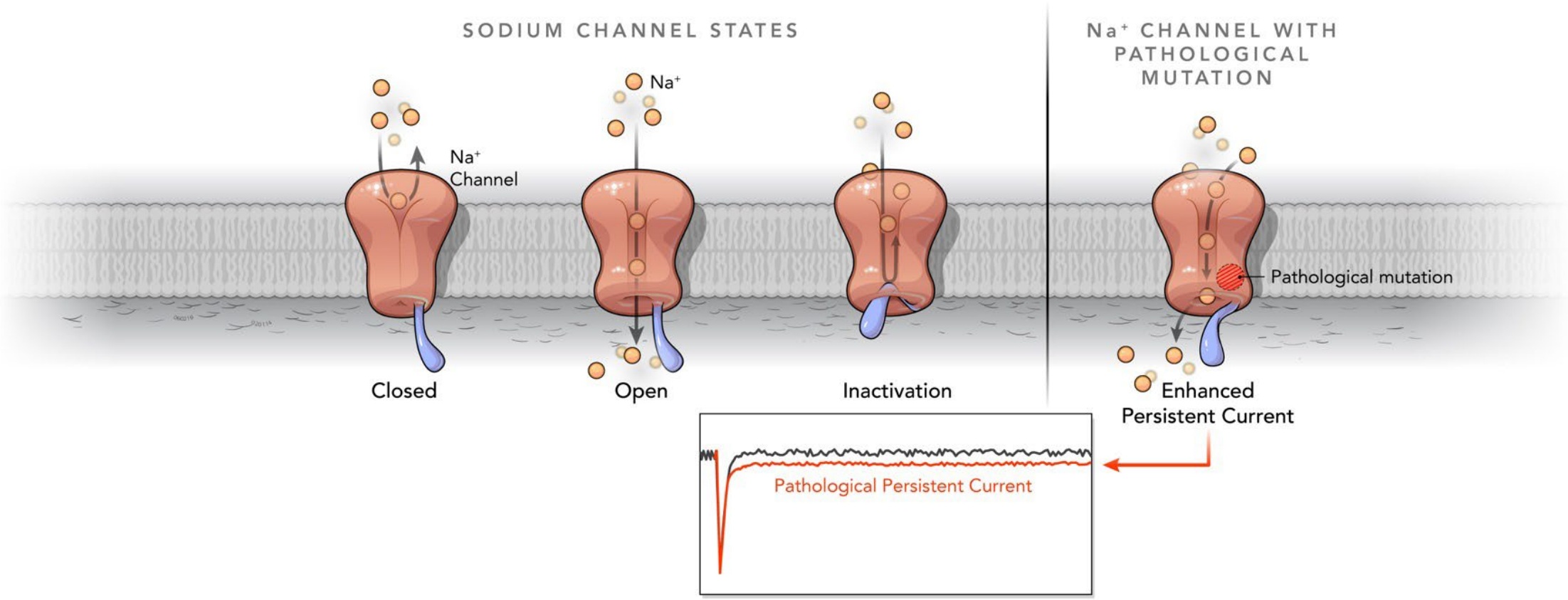
SMALL MOLECULE

Superior selectivity for disease-state Na_V channel hyperexcitability

Unprecedented therapeutic window with potential for superior safety and efficacy

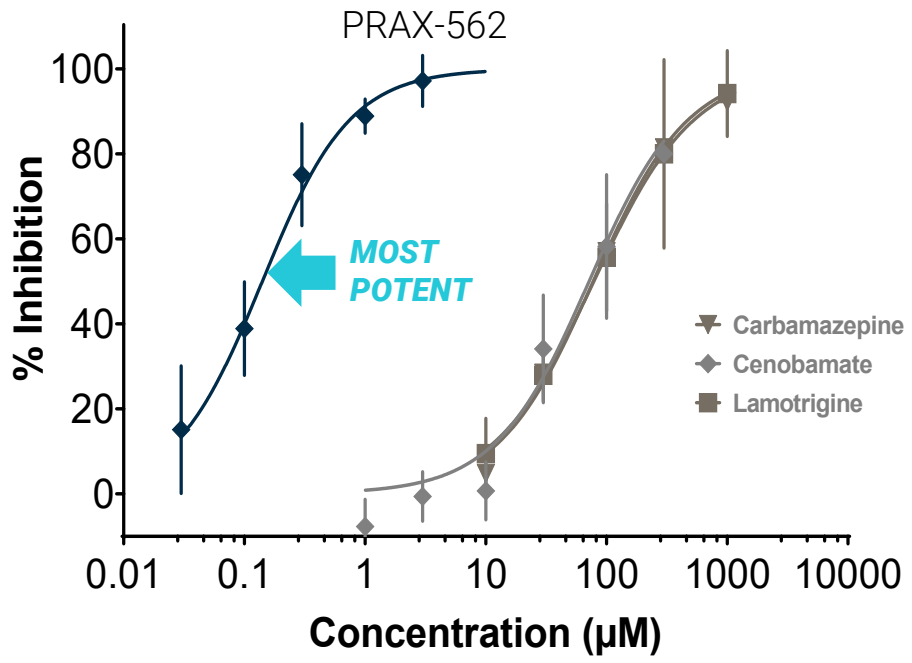
Convenient auto-titration regimen with stable PK

Persistent sodium current (I_{Na}) is a critical driver of pathological hyperexcitability in CNS disorders



Broader in vitro panel indicates PRAX-562 has best-in-class preferences

% INHIBITION OF $hNa_V1.6$ PERSISTENT I_{Na}

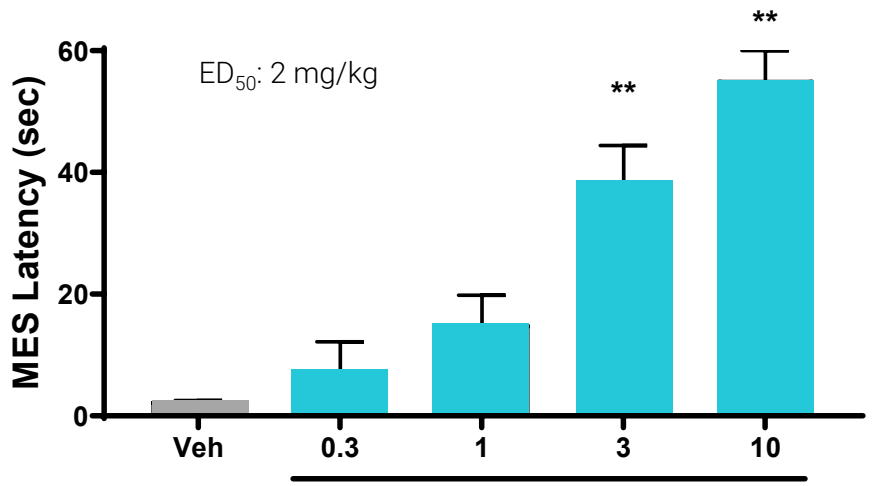


COMPARISON OF POTENCY AND SELECTIVITY

	Persistent I_{Na} IC50 (nM)	Ratio of persistent to peak inhibition	
PRAX-562	***141***	***60***	***MOST SELECTIVE***
Carbamazepine	77,520	30	
Cenobamate	73,263	23	
Lidocaine	68,230	19	
Lamotrigine	78,530	16	
Vixotrigene (BIIB074)	3,676	14	
Lacosamide	833,100	n/a*	
Valproic Acid	<10% @ 1 mM	No inhibition	

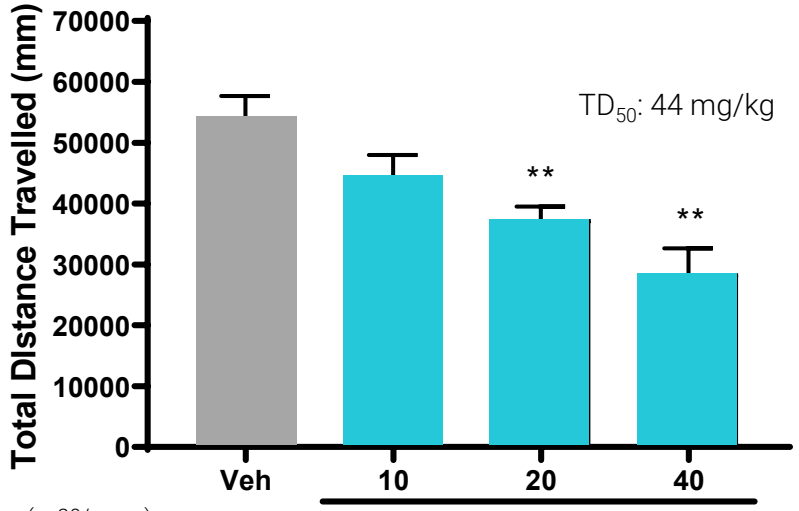
Our mechanistic hypothesis translates to a wide therapeutic index in vivo for PRAX-562

MES EFFICACY



CD-1 mice; (n=12/group)
**p<0.01 vs. Veh

sLMA TOLERABILITY



CD-1 mice; (n=20/group)
ANOVA/Dunnett
**p<0.01 vs. Veh

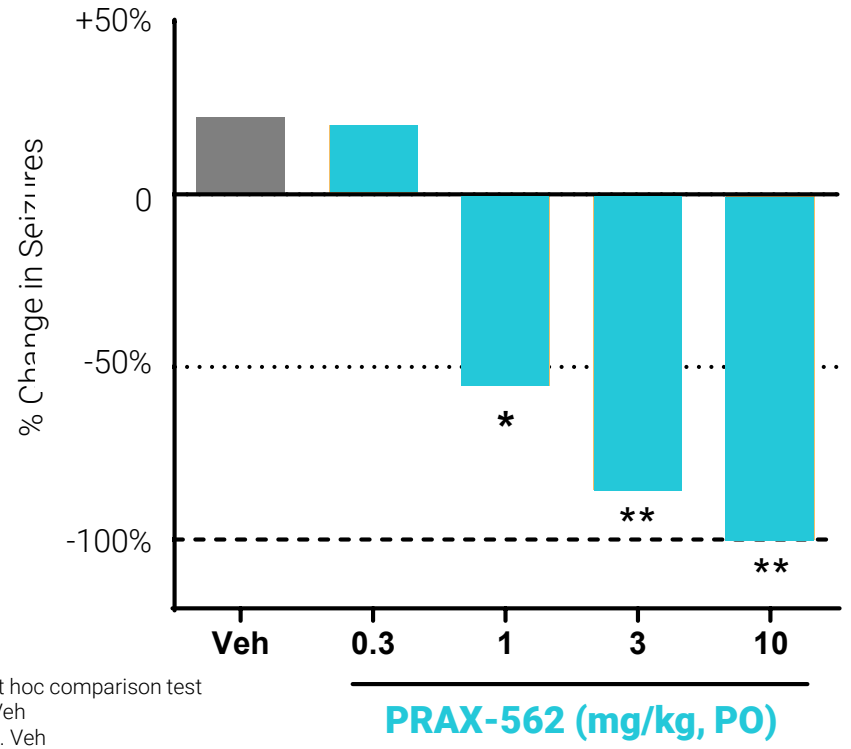
Molecule	Plasma Therapeutic Index
PRAX-562	17.2x

Therapeutic Index (TI) = TC50 / EC50

PRAXIS

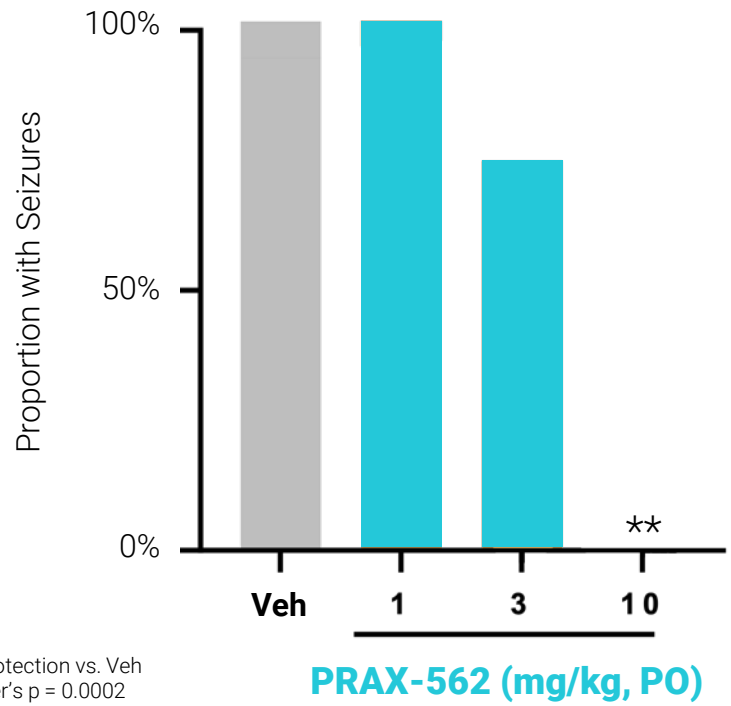
PRAX-562 completely inhibits seizures in SCN2A and SCN8A GoF mutation mouse models

IN VIVO POC IN SCN2A SPONTANEOUS SEIZURES[1]



Sidack's post hoc comparison test
*p<0.05 vs. Veh
**p<0.001 vs. Veh

IN VIVO POC IN SCN8A AUDIOGENIC EVOKED SEIZURES[2]



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

[1] PRAX-562 inhibition of spontaneous seizures in Q54 GoF mice.
[2] PRAX-562 inhibition of audiogenic seizures in N1768D D/+ mice

PRAX-562 Phase 1 summary

PRAX-562 has been generally well tolerated in over 130 healthy volunteers

No MTD at exposures multiple fold above therapeutic range indicates potential for superior therapeutic index

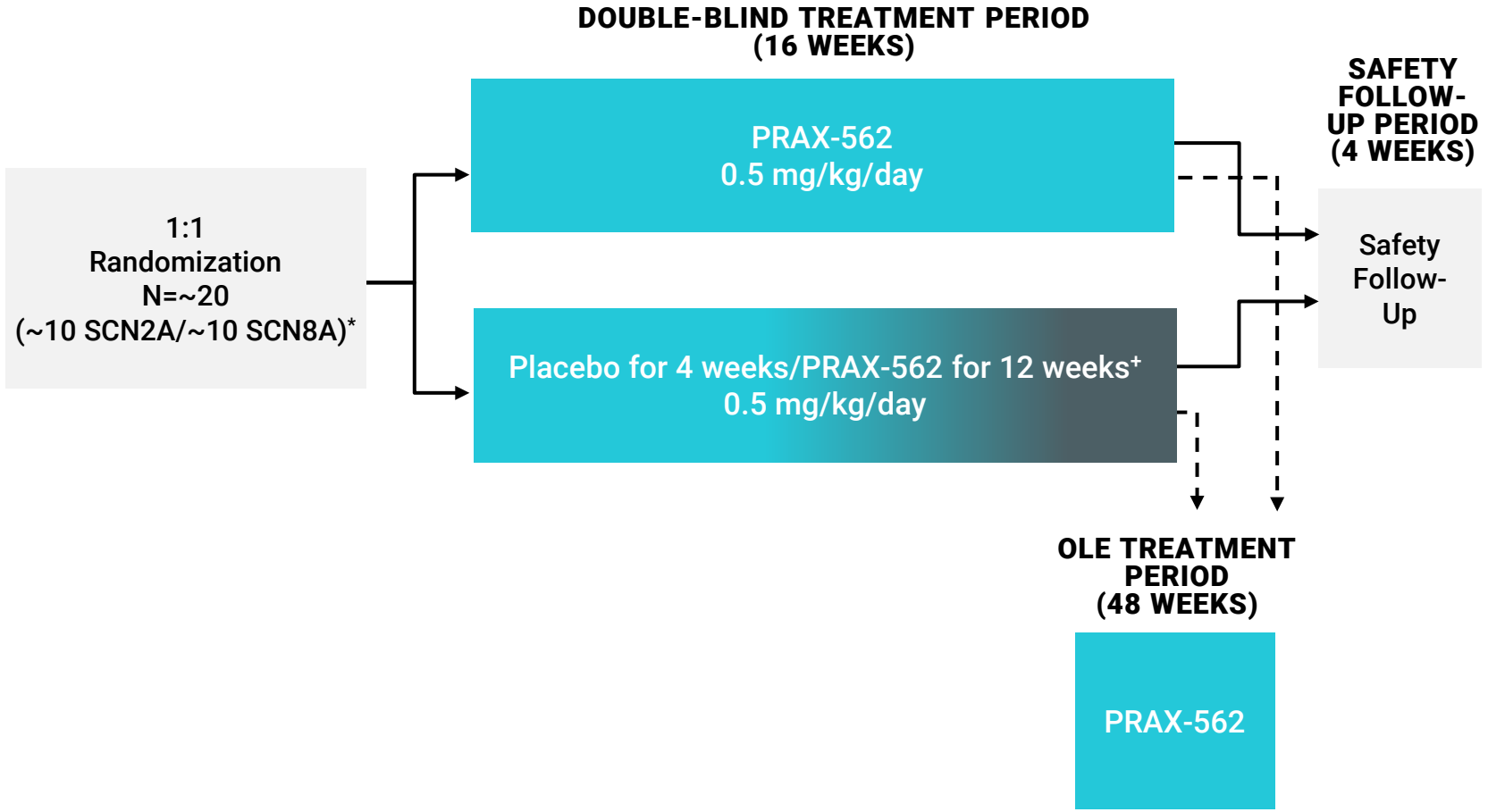
All TEAEs mild to moderate as stand-alone therapy*, with headache & dizziness most common TEAEs

Significant changes observed between placebo and 90 mg of PRAX-562 on qEEG and on ASSR biomarkers

Source: Praxis data on file; https://investors.praxismedicines.com/news-releases/news-release-details/praxis-precision-medicines-provides-corporate-update-and-5
* Co-administration of supra-therapeutic doses of PRAX-562 and oxcarbazepine led to additive sodium blocking effects, including resulting in SAEs

PRAXIS

PRAX-562 Phase 2 EMBOLD Study topline data expected 2H23



PRIMARY ENDPOINT:

Incidence and severity of treatment-emergent adverse events (TEAEs)

KEY SECONDARY:

Change from baseline in monthly (28 day) motor seizure frequency

* Two distinct cohorts in early-onset SCN2A-DEE and SCN8A-DEE patients

\+ Participants receive either 0.5 mg/kg/day PRAX-562 QD for 16 weeks or 0.5 mg/kg/day PRAX-562 QD for 12 weeks & matching placebo QD for 4 weeks. Participants in the PRAX-562/placebo arm will receive placebo for 4 consecutive weeks during the 16-week treatment period, with timing of placebo administration blinded for both participants and investigator. Dose adjustment is permitted to a max of 1.0 mg/kg/day and a min of 0.25 mg/kg/day.

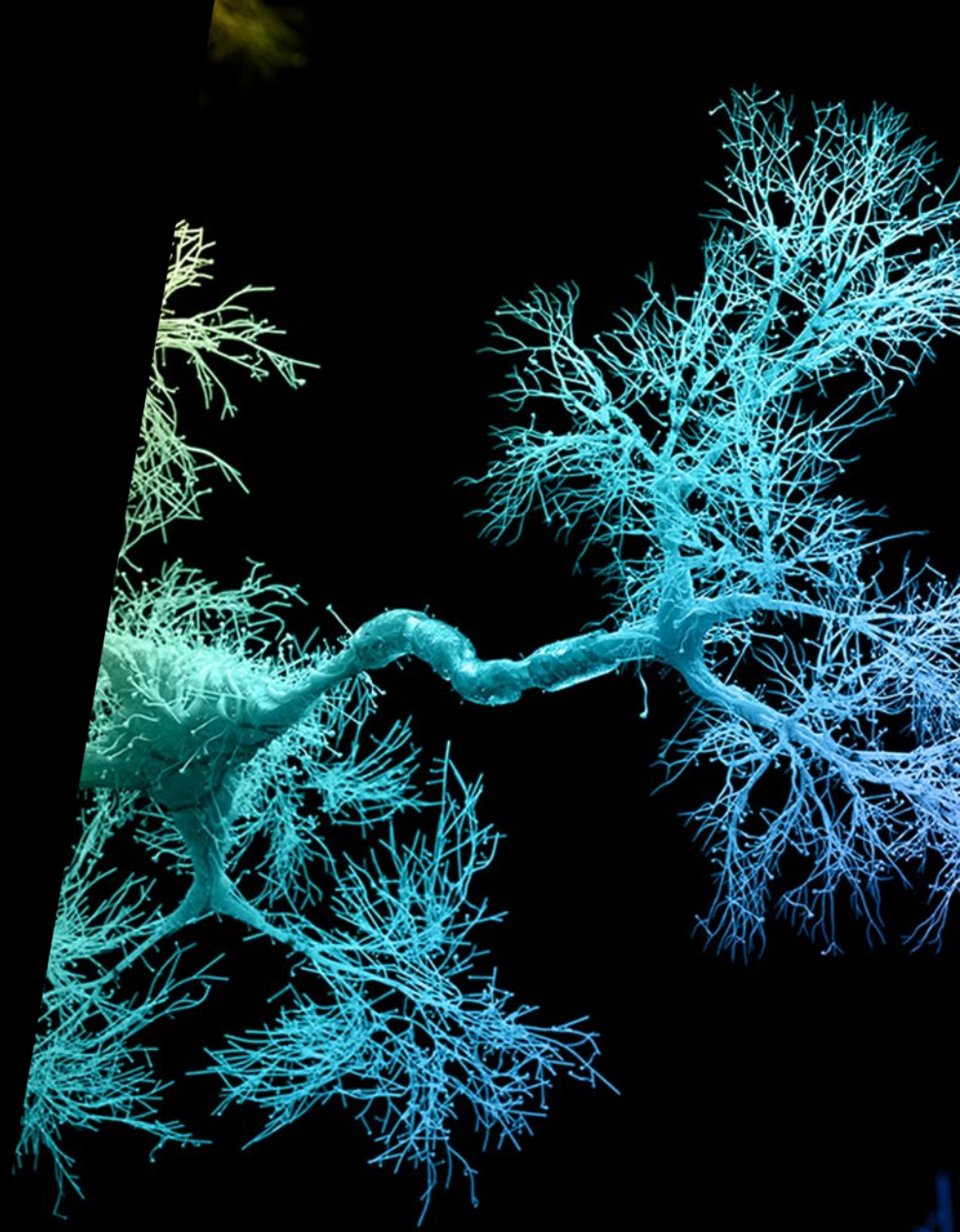
PRAX-628

Focal Epilepsy

KEY UPCOMING MILESTONES

2Q 2023
Ph 1 Topline Results

4Q 2023
Initiate Focal Epilepsy Study



Preclinical data demonstrates PRAX-628 may be a best-in-class Na_V blocker for focal epilepsy

PRAX-628

FOCAL EPILEPSY

PAN-NA_V
ACTIVITY DEPENDENT
BLOCKER

SMALL MOLECULE

Superior selectivity for disease-state Na_V channel hyperexcitability

Unprecedented therapeutic window translating to superior safety and efficacy

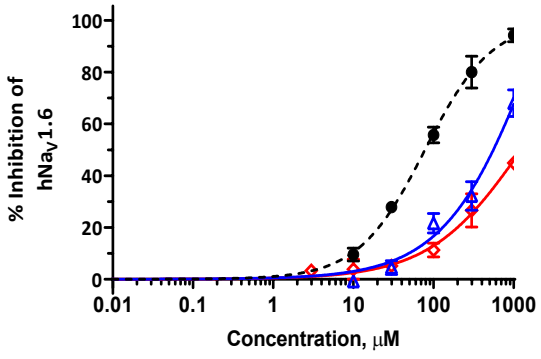
PK differentiated for broad epilepsy population

PRAXIS

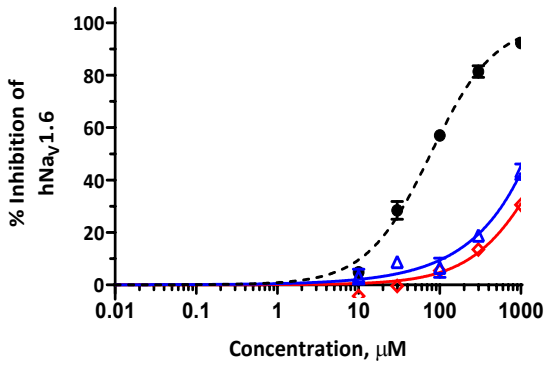
Our internal discovery effort focused on developing a Na_V blocker with high disease-state dependence and consequent wide therapeutic index

LOW DISEASE-STATE DEPENDENCE THIN THERAPEUTIC INDEX

LAMOTRIGINE



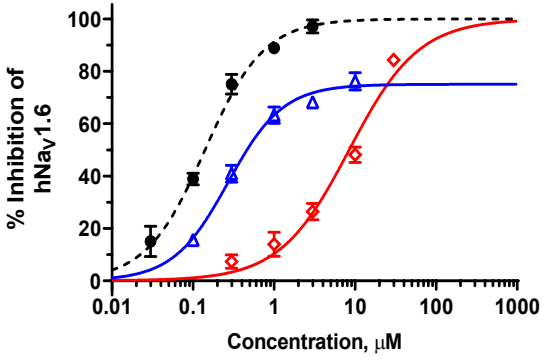
CARBAMAZEPINE



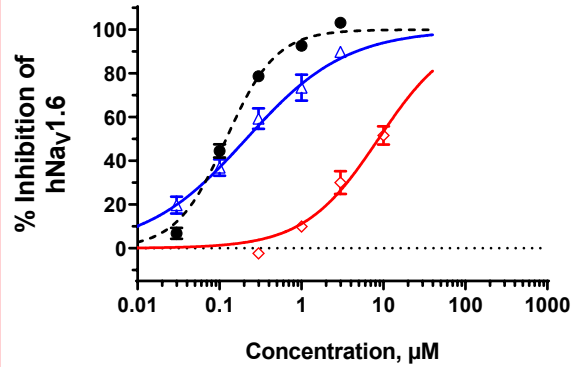
"Na_V Fingerprint"
Persistent I_{Na} Inhibition
Peak I_{Na}, UDV-10Hz (Disease-State Dependence) Inhibition
Peak I_{Na}, Tonic Block Inhibition

HIGH DISEASE-STATE DEPENDENCE WIDE THERAPEUTIC INDEX

PRAX-562

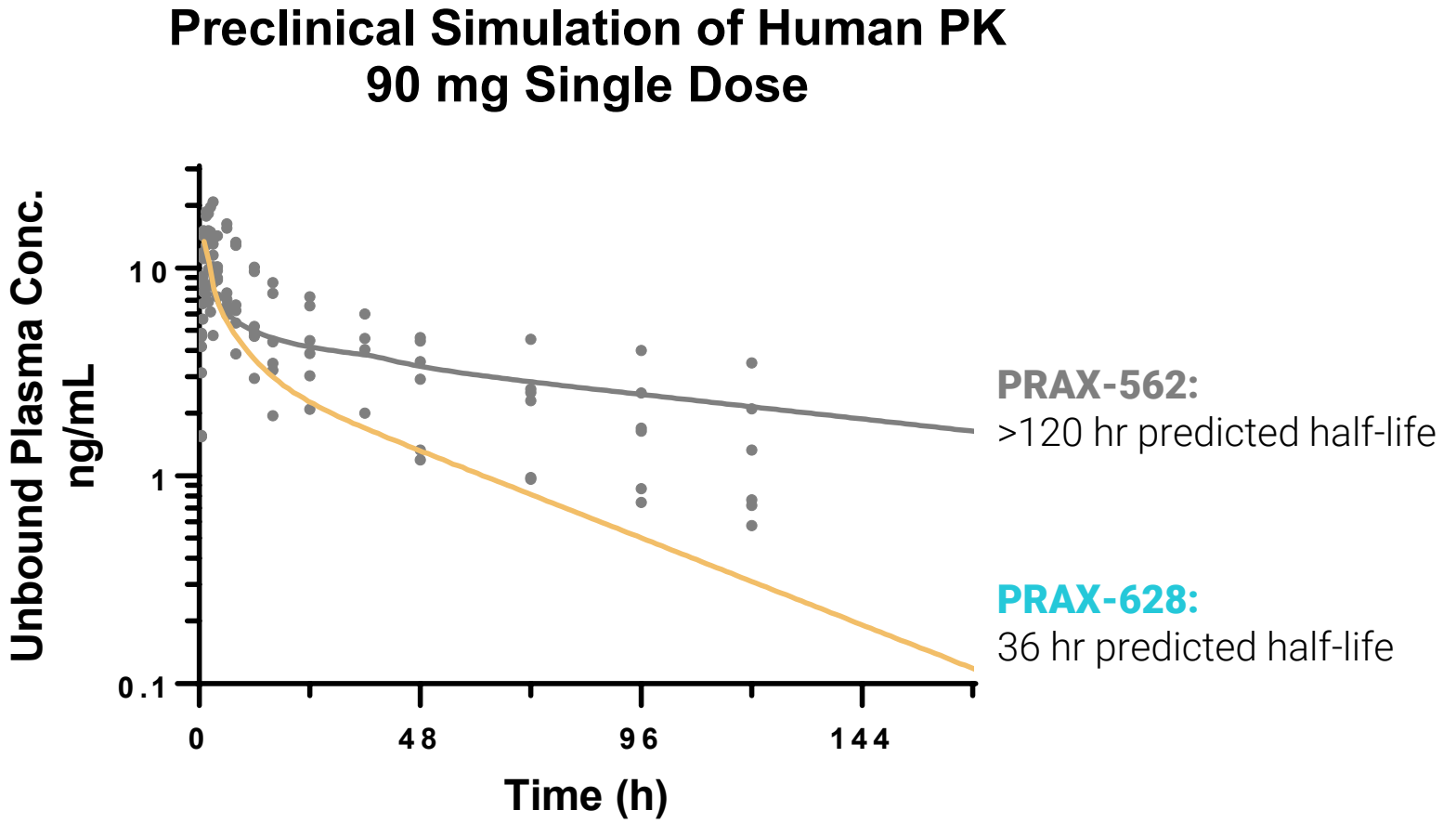


PRAX-628



Source: Praxis data on file

PRAX-628 has unique pharmacological properties that enable acute dosing in a broader patient population

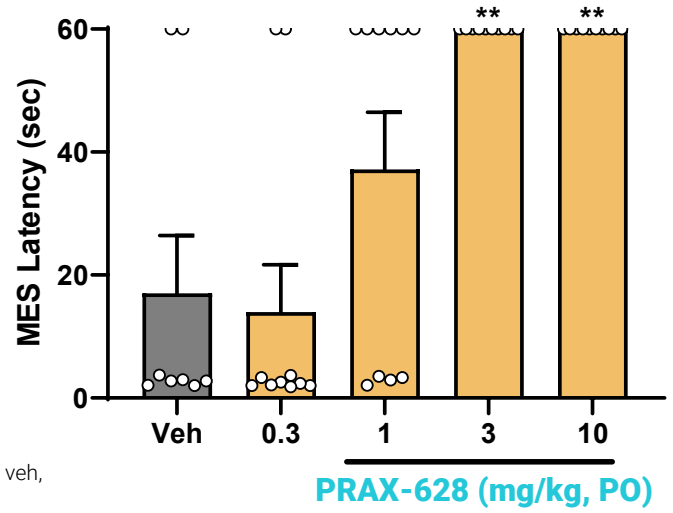


Modeling 90mg, single dose of PRAX-628 or PRAX-562. Preclinical simulation recapitulates PRAX-562 clinical data.

PRAXIS

PRAX-628 protects mice from seizures with a wide therapeutic window

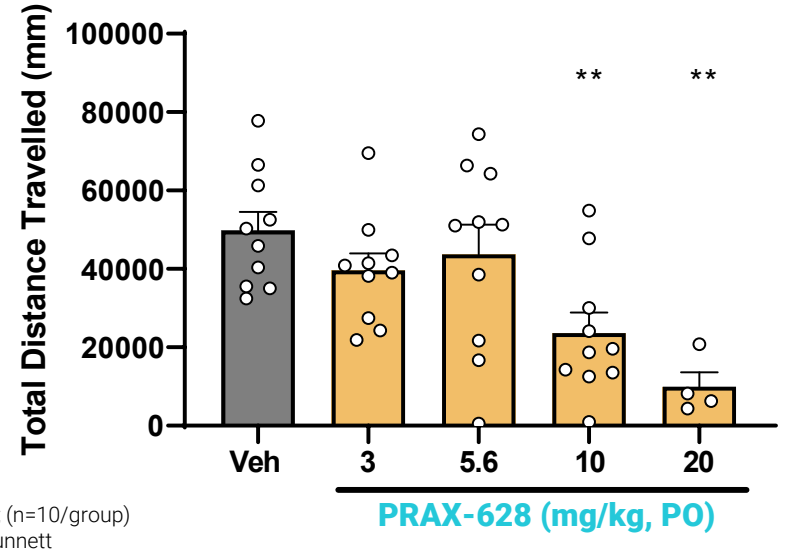
MES EFFICACY



CD-1 mice; (n=8/group veh, n=10 PRAX)
ANOVA/Dunnett (PRAX)
**p<0.01 vs. Veh

ED_{50}: 0.67 mg/kg

sLMA TOLERABILITY



CD-1 mice; (n=10/group)
ANOVA/Dunnett
**p<0.01 vs. Veh

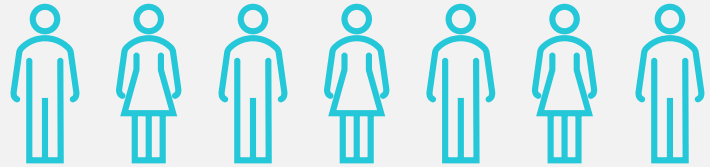
TD_{50}: 10.3 mg/kg

Molecule	Plasma Therapeutic Index
PRAX-628	**16.7x**

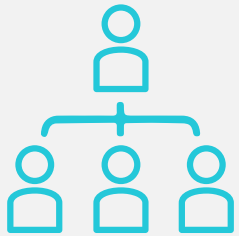
Therapeutic Index (TI) = TC50 / EC50

Focal epilepsy affects ~2 million people in the US alone

Defined as epilepsy that originates in one side or area of the brain and affects one side of the body



Most common type of epilepsy in adults and children - occurs in 60% of epilepsy cases



~ 50% have family history but genetics is not well understood

Most common age of onset is in the first year of life and in the 6th and 7th decade

PRAXIS

SOLIDUS™

ASO PLATFORM

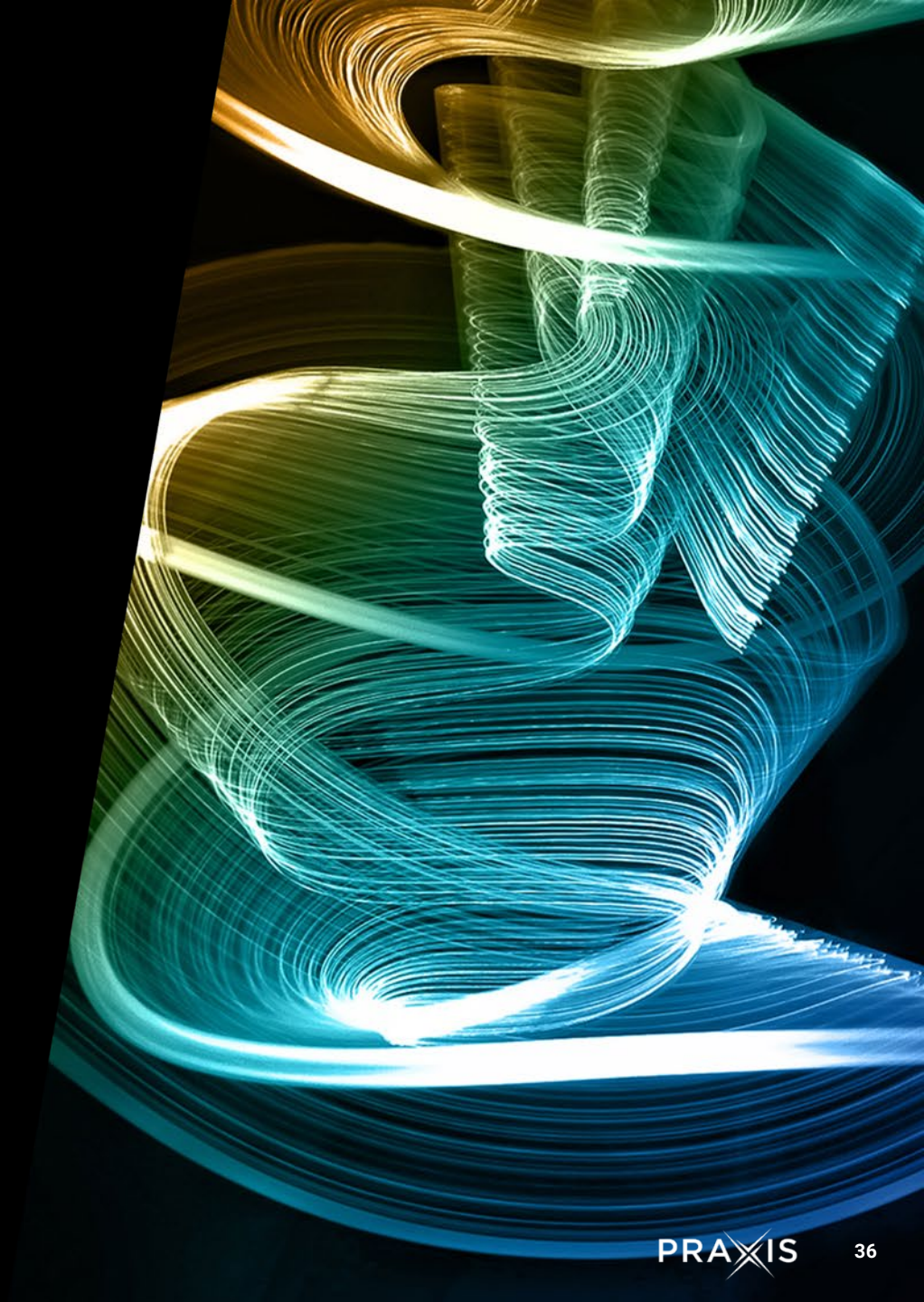
PRAX-222

SCN2A-GoF ASO

KEY UPCOMING MILESTONES

Mid-2023

EMBRAVE Study First Dose Cohort (Part 1)
Topline Safety Results



Preclinical data suggest PRAX-222 has potential to be disease-modifying for early onset SCN2A gain-of-function DEE

PRAX-222

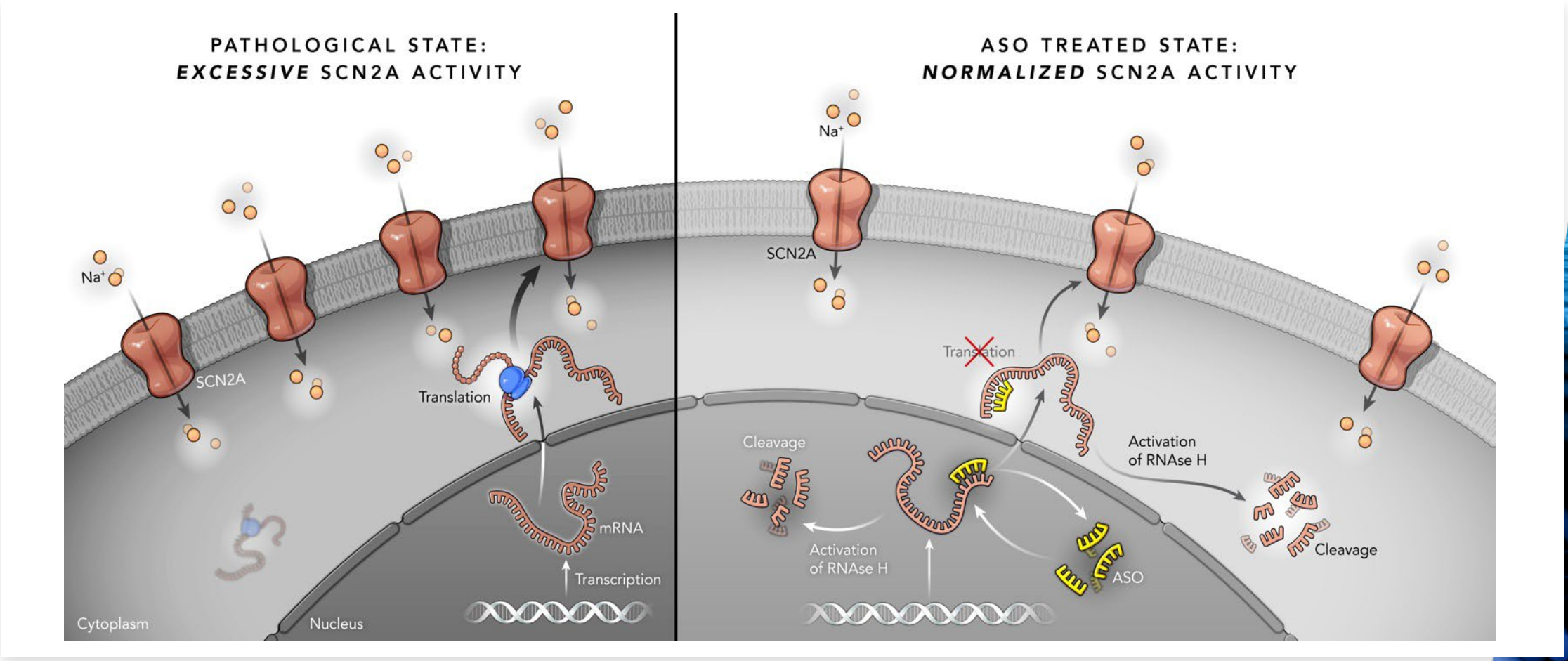
INTRATHECALLY-ADMINISTERED ASO for SCN2A GoF DEE

Dose-dependent reduction in interictal spikes, seizures and increased survival

Improvement in behavioral and locomotor activity

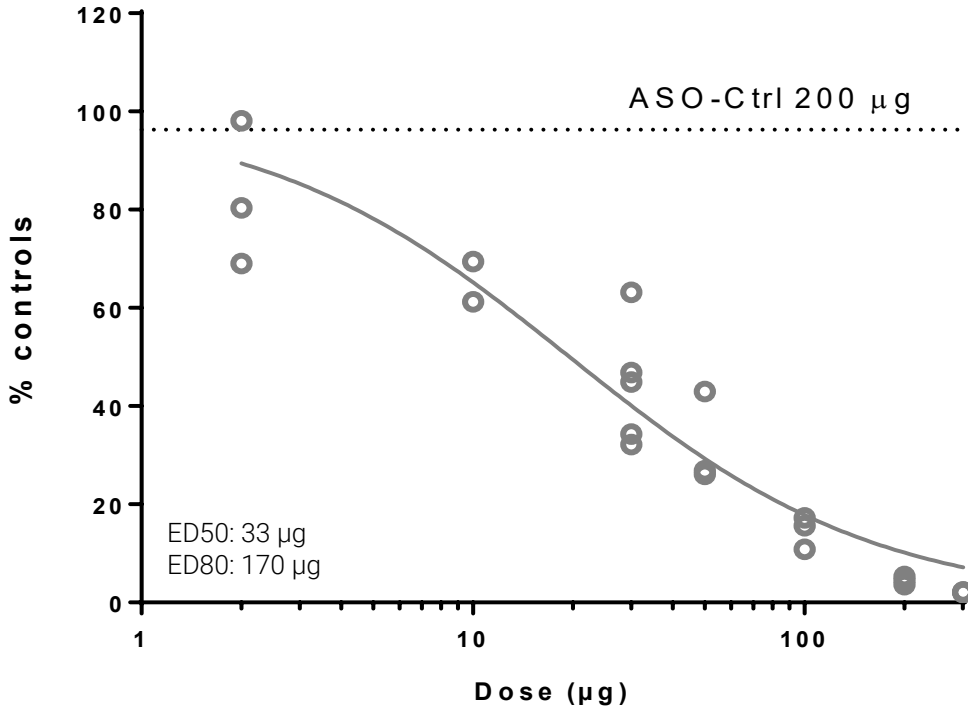
Survival benefit extended with repeat dosing

PRAX-222 is an ASO designed to down-regulate SCN2A expression in patients with gain-of-function mutation

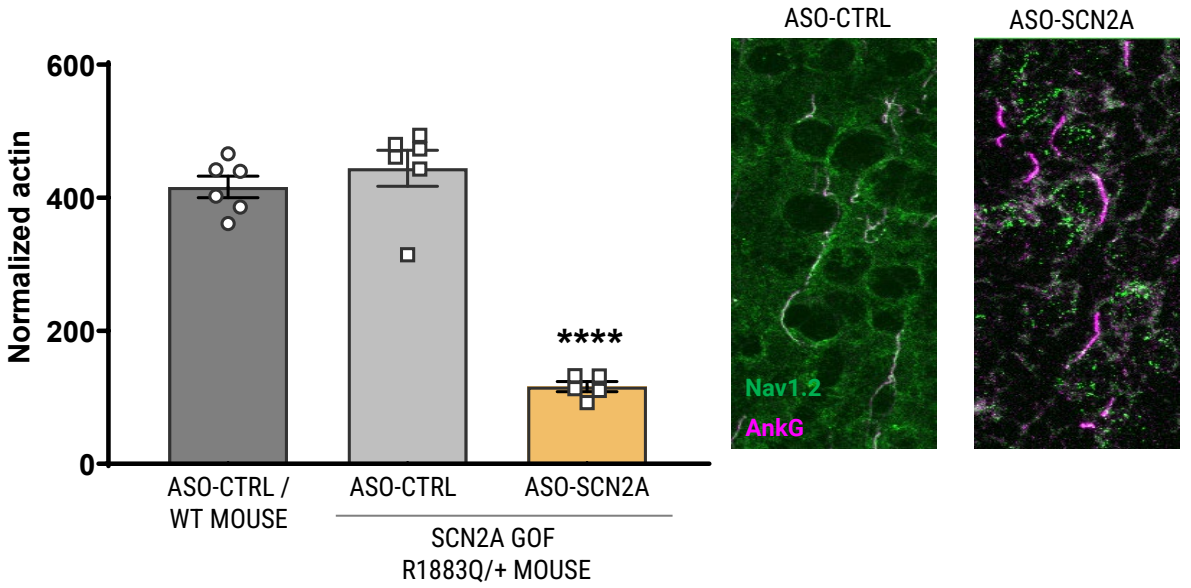


In vitro, PRAX-222 down-regulates both mRNA and protein

SCN2A mRNA KNOCKDOWN



SCN2A PROTEIN KNOCKDOWN

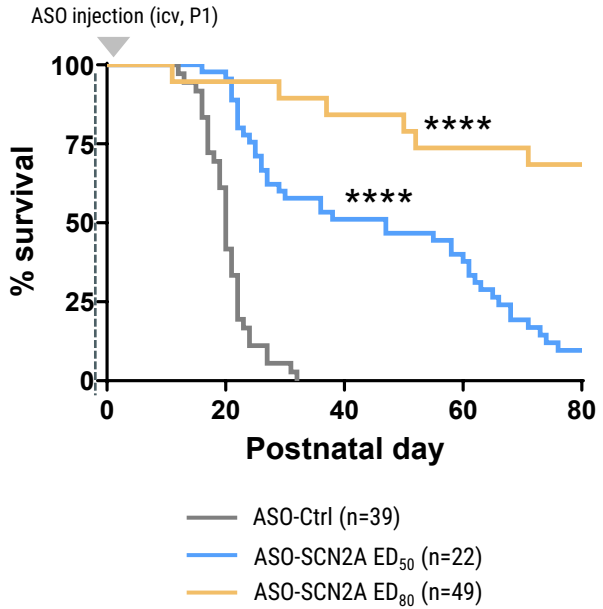


ASOs were administered at P30 and brains were collected 14 days post-ICV for qPCR analysis

PRAX-222 increases survival in SCN2A GoF mice

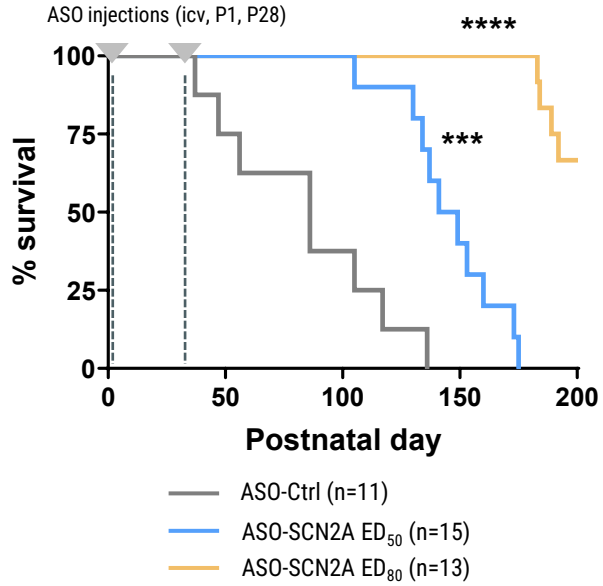
SCN2A ASO INCREASES SURVIVAL WITH A SINGLE DOSE INJECTION

SCN2A GOF model



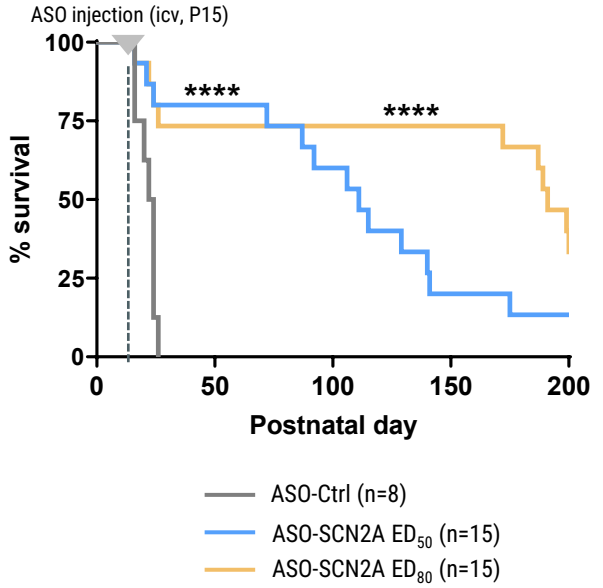
RE-DOSING SIGNIFICANTLY EXTENDS SURVIVAL

SCN2A GOF model



ADMINISTRATION POST-DISEASE ONSET ALSO EXTENDS SURVIVAL

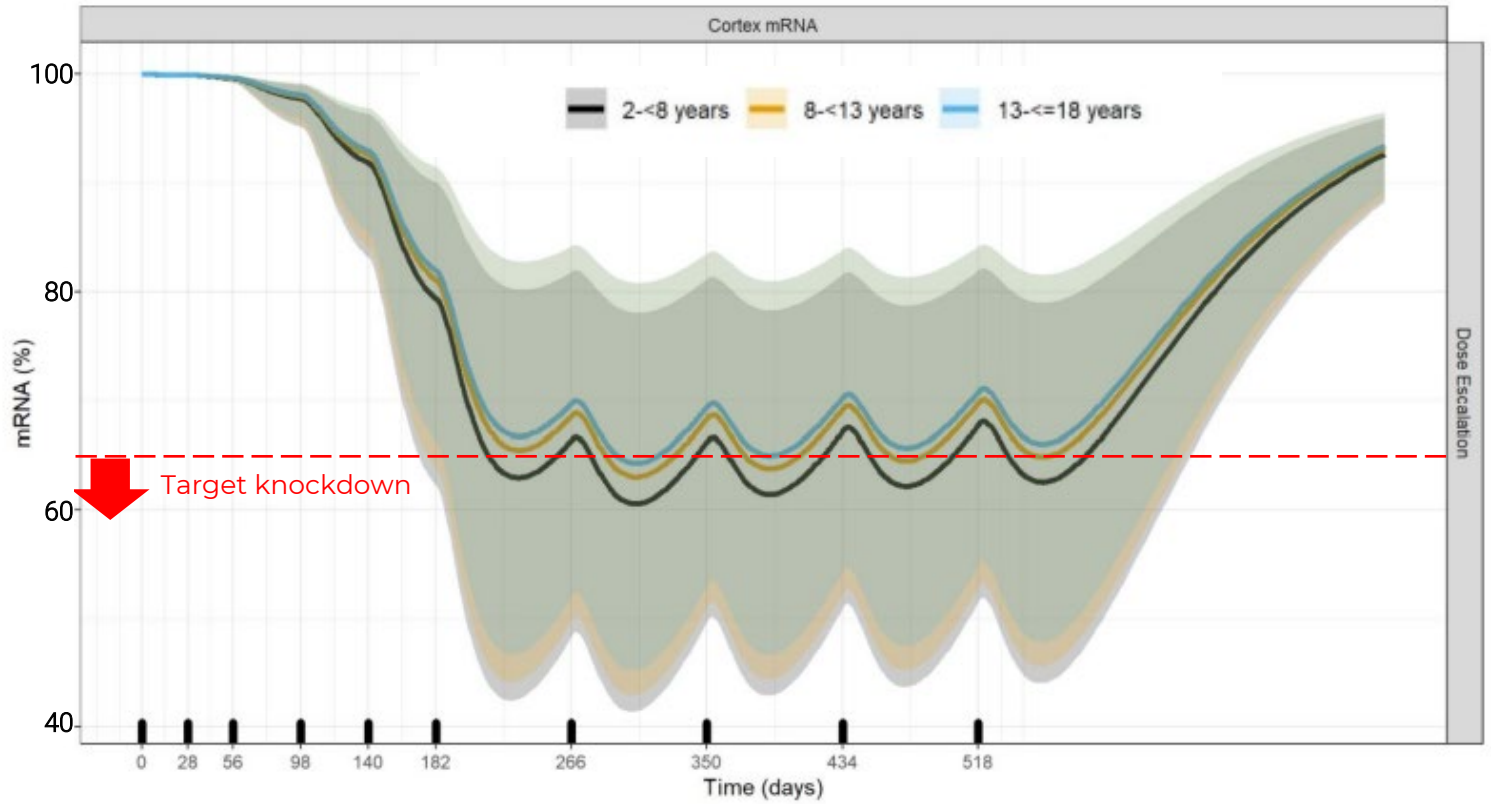
SCN2A GOF model



***p<0.001
****p<0.0001
All experiments conducted with SCN2A R1882Q mouse model

PRAXIS

PRAX-222 PK/PD modeling informs starting dose and proposed escalation based on level of knockdown anticipated to achieve clinical benefit and tolerability



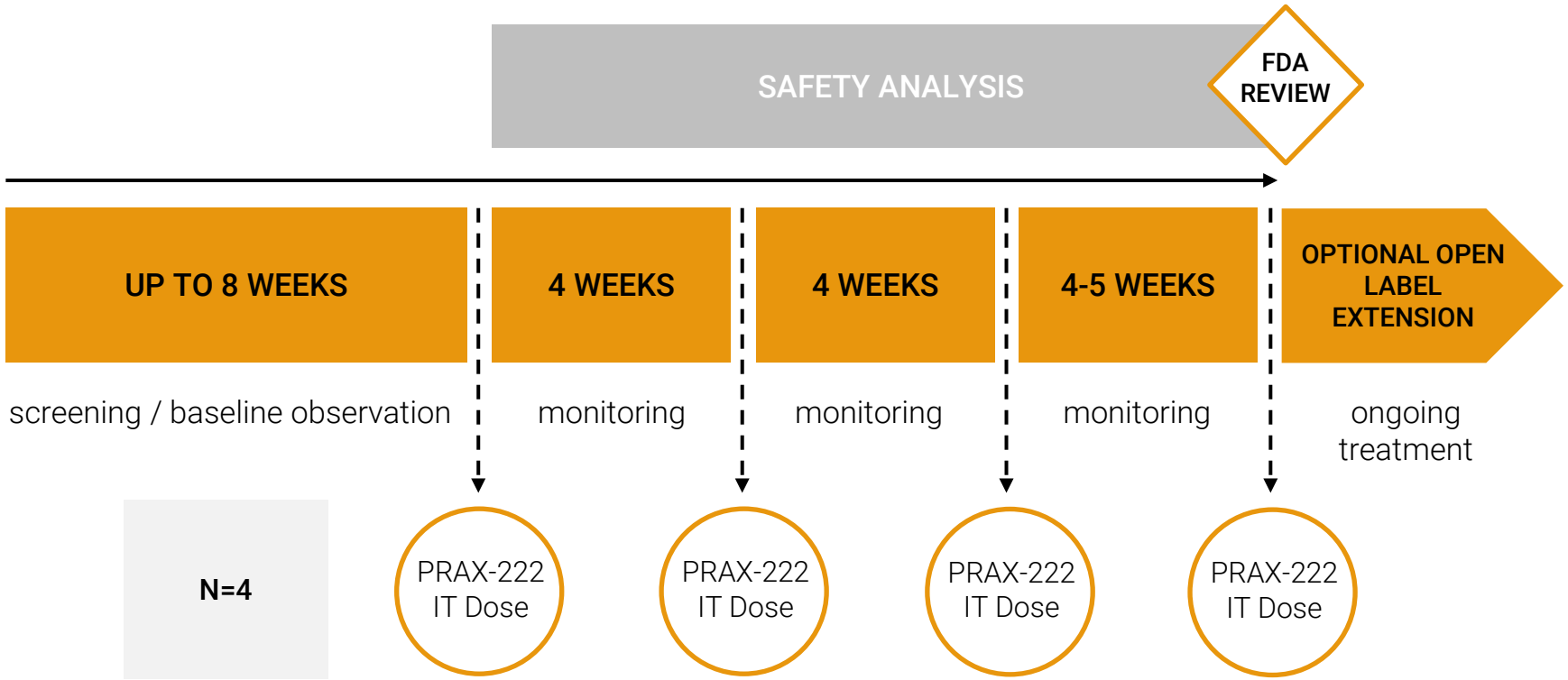
Median and 95% prediction interval illustrated

Simulated mRNA knockdown in human cortex in pediatric patients

Achieves distribution in key areas of brain based on NHP data

Source: Praxis data on file.

PRAX-222 EMBRAVE study initial dose cohort (Part 1)



GOAL:
Assess preliminary safety of PRAX-222

21-week study

Open label design

PRAXIS


PRAXIS
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