PRA

CORPORATE OVERVIEW

December 2021

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. Words such as, but not limited to, "look forward to," "believe," "expect," "anticipate," "estimate," "intend," "plan," "would," "should" and "could," and similar expressions or words, identify forward-looking statements. 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' ongoing and planned clinical trials, (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 collaboration partners' abilities to manufacture our product candidates and scale production, (viii) our ability to meet any specific milestones set forth herein, and (ix) uncertainties 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

For further information regarding the risks, uncertainties and other factors that may cause differences between Praxis' expectations and actual results, you should review the "Risk Factors" section of our Annual Report on Form 10-K filed for the period ended December 31, 2020, our Quarterly Reports on Form 10-Q and other subsequent 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.

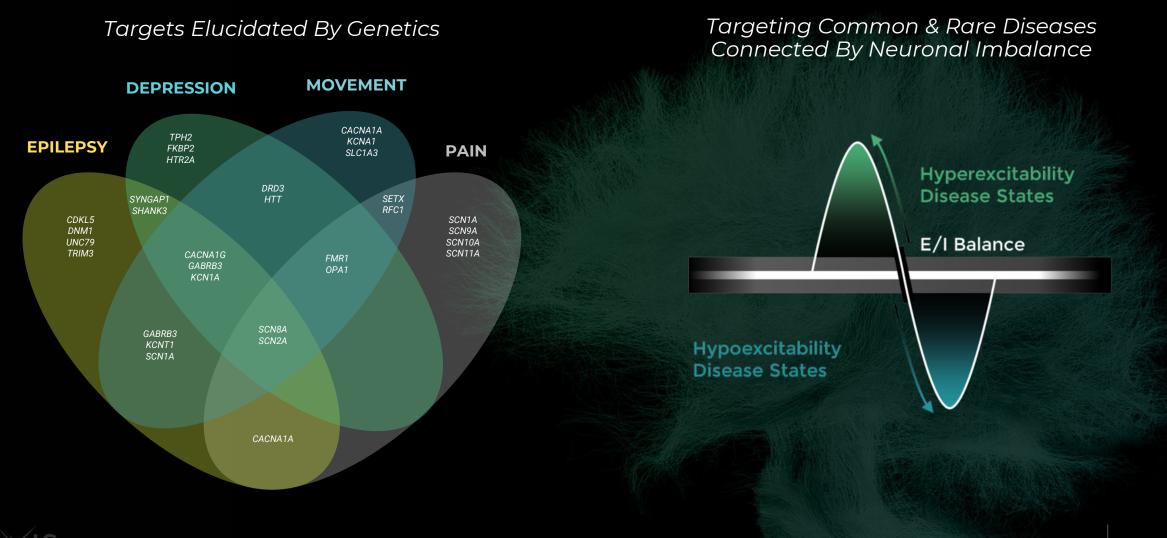
PRAXIS

A PATIENT-GUIDED CNS COMPANY DEVELOPING NEW CLASSES OF TREATMENTS

INSPIRED BY HUMAN GENETICS



The biology of epilepsy offers insights into brain function for CNS disorders



Leveraging genetics to efficiently translate insights into therapies



Targets identified through genetics

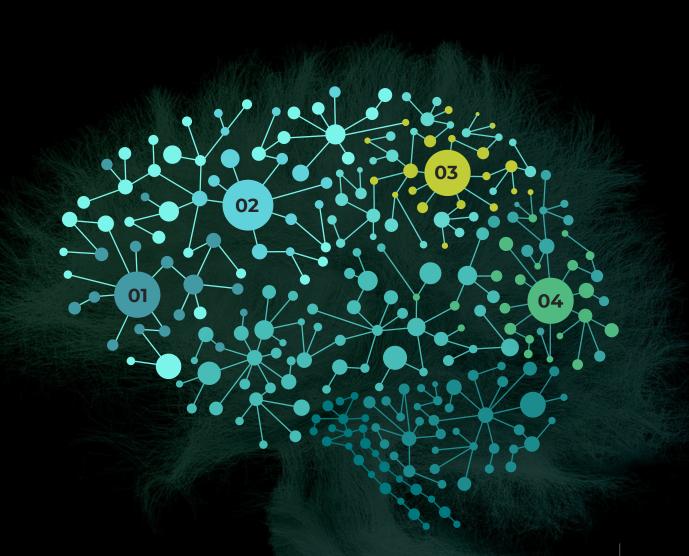
D2 Translational tools to inform development

03

Efficient, rigorous clinical development paths to PoC

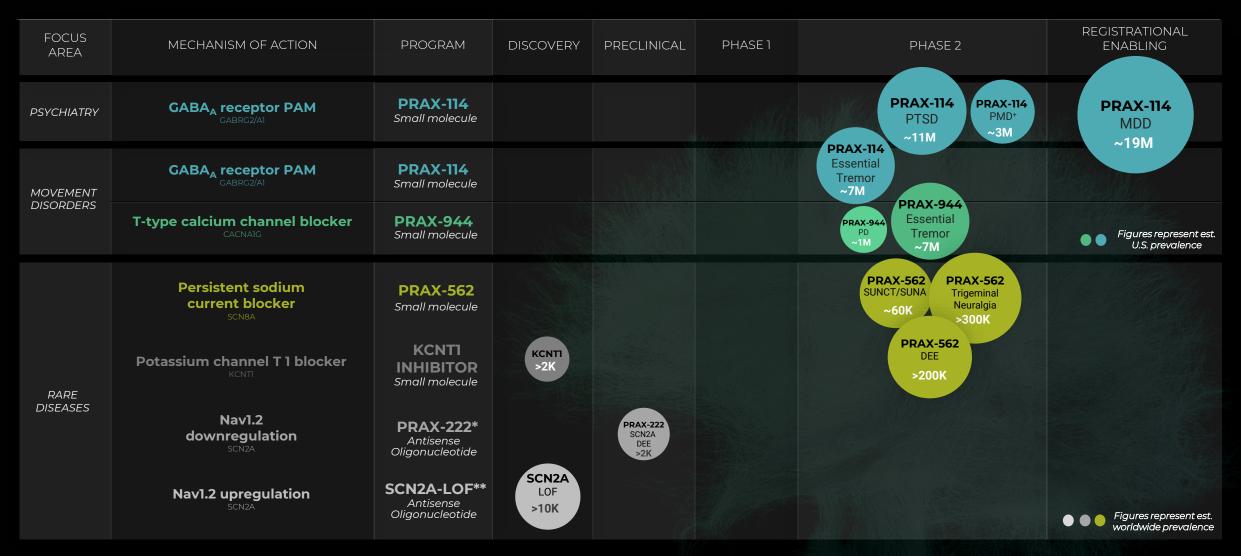


Patient-guided development strategies





Broad portfolio of highly differentiated programs across multiple CNS disorders

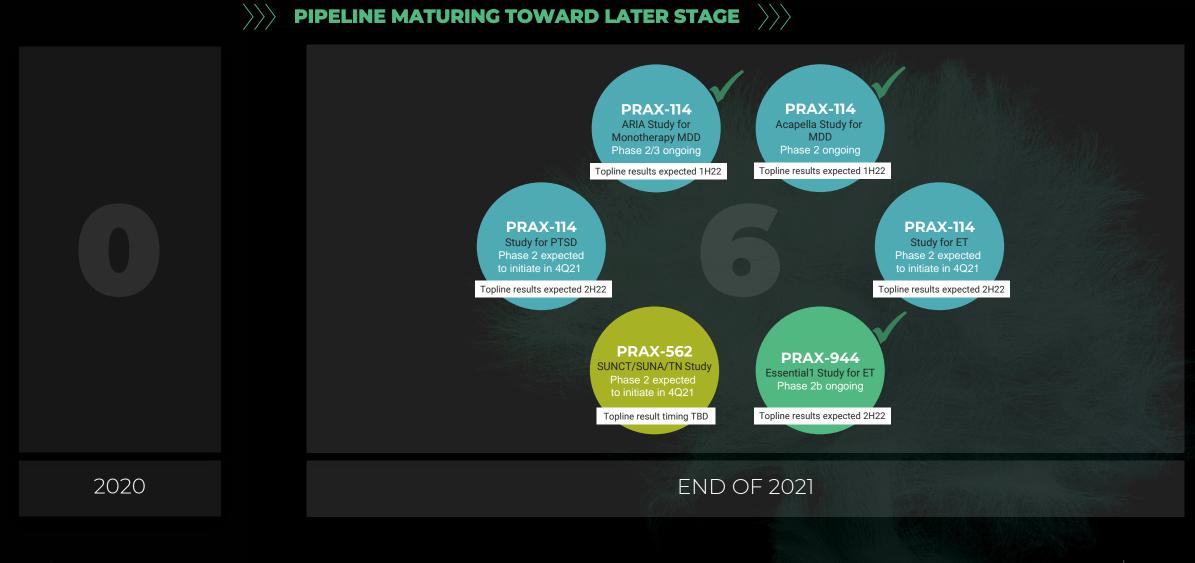


* PRAX-222 is a collaboration with Ionis Pharmaceuticals, and RogCon Inc; Ionis is eligible to receive double-digit royalties on net product sales worldwide.

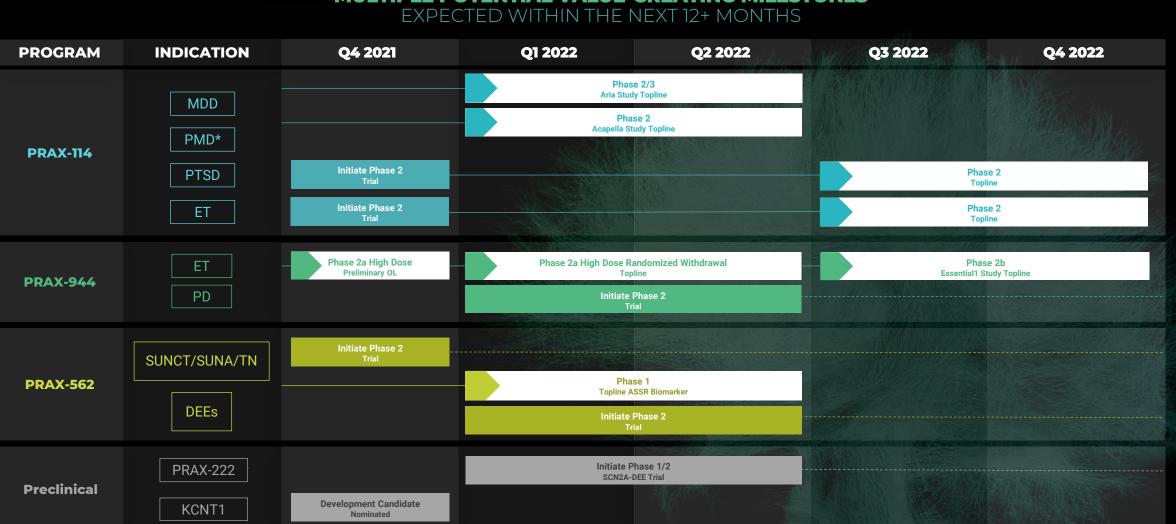
- ** SCN2A-LOF is a collaboration with The Florey Institute; collaboration includes 2 additional discovery stage ASOs targeting SYNGAP1 & PCDH19
- *Phase 2b trial in women with menopausal & mood symptoms

PRAX-114 Phase 2 trials for ET and PTSD, PRAX-944 Phase 2 trial for PD and PRAX-562 trials for SUNCT/SUNA/TN and for DEEs have not initiated Prevalence based on internal estimates

Six placebo-controlled trials across three clinical programs by end of 2021



PRAXIS



MULTIPLE POTENTIAL VALUE-CREATING MILESTONES



DARE for MORE



PRAX-114 GABA_A Receptor PAM

PSYCHIATRY & MOVEMENT DISORDERS

Depression Post-traumatic Stress Disorder Essential Tremor

KEY UPCOMING MILESTONES

1H 2022 Ph 2/3 Monotherapy MDD Aria Study Topline

1H 2022 Ph 2 MDD Dose-Ranging Acapella Study Topline

> 2H 2O22 Ph 2 PTSD Topline

2H 2022 Ph 2 ET Topline

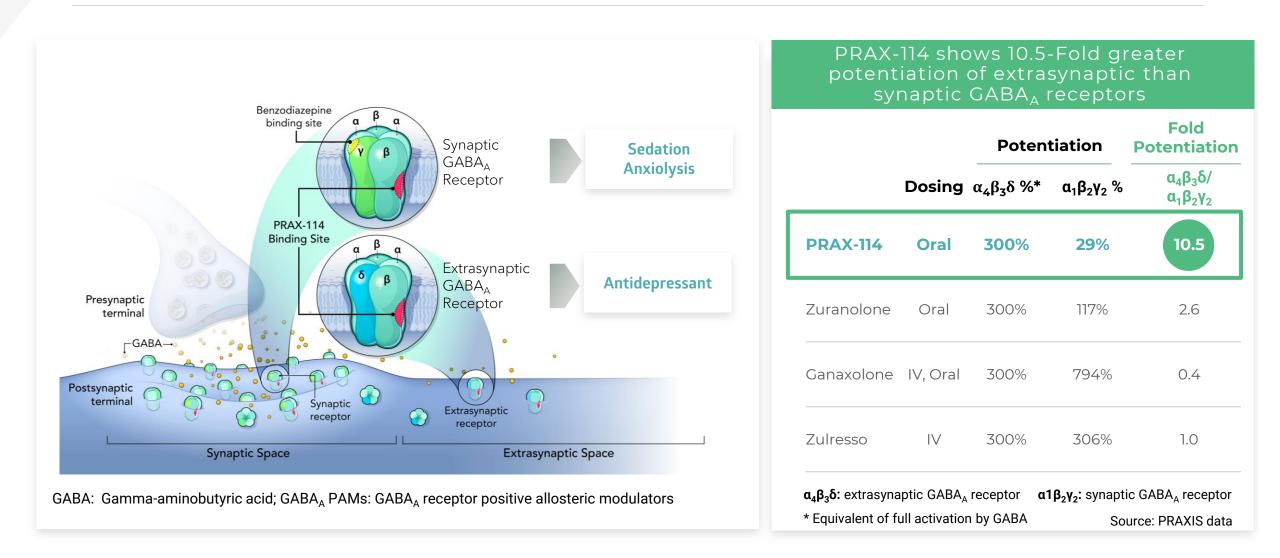


Major depressive disorder is a growing and debilitating disorder with substantial unmet need despite numerous treatment options





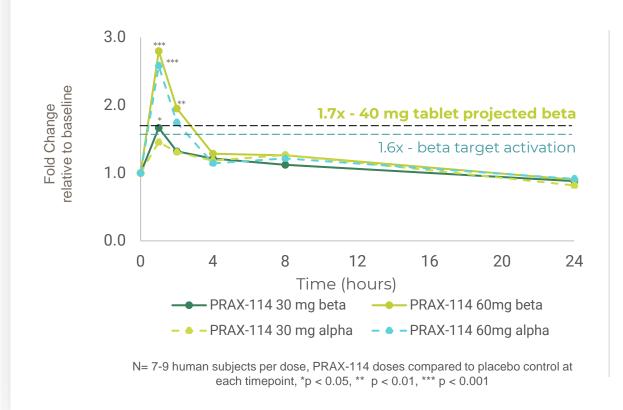
Preference for extrasynaptic GABA_A receptors has the potential of marked antidepressant effect with an improved tolerability profile



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Extrasynaptic GABA_A preference allows PRAX-114 the potential to achieve high-levels of GABAergic activation with improved tolerability

PRAX-114 shows robust qEEG signal and target activation



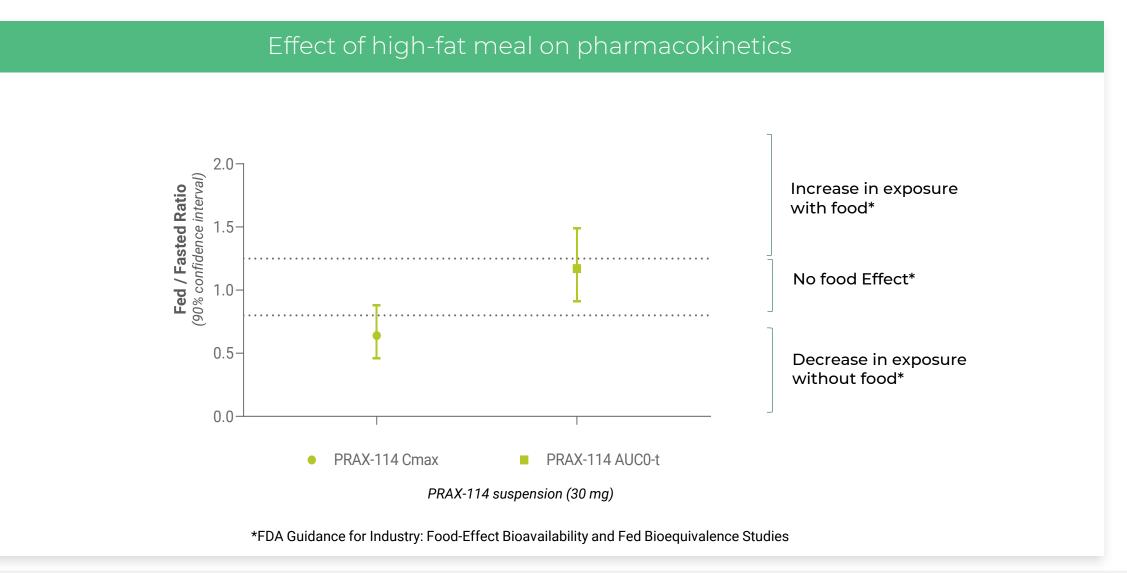
No MTD identified up to 80mg

Tolerability profile maintained throughout dose escalation

Exposure-dependent rates of somnolence resolved 1 to 3 hours post-dosing, consistent with peak concentrations



PRAX-114 can be dosed at bedtime with or without food





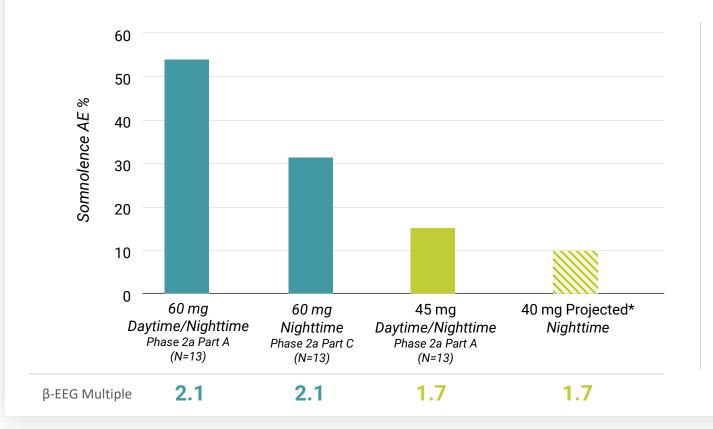
PRAX-114 Phase 2a: rapid and marked improvement in depression scores

Phase 2a combined* HAM-D monotherapy & adjunctive results			Phase 2a combined* HAM-A anxiety and HAM-D insomnia item results		
Visit	HAM-D Monotherapy Mean (SD) N=14	HAM-D Adjunctive Mean (SD) N=38	Visit	HAM-A Anxiety Rating Scale Mean (SD) N=52	HAM-D Insomnia Item Total (max score of 6) Mean (SD) N=52
Day 1 (BL)	25.2 (1.82)	24.7 (2.90)	Day 1 (BL)	22.4 (4.16)	4.2 (1.3)
Day 8 (CFB)	-17.6 (4.77)	-13.4 (7.94)	Day 8 (CFB)	-12.4 (7.55)	-2.8 (1.9)
Day 15 (CFB)	-16.6 (5.23)	-12.2 (7.02)	Day 15 (CFB)	-11.6 (6.67)	-3.1 (1.7)



*Combined results include Part A MDD cohort (N=33; 2-week treatment), Part B PMD cohort (N=6; 2-week treatment) & Part C MDD cohort (N=13; 4-week treatment); results show change from baseline (CFB) at Day 8 & Day 15

Estimated somnolence rate of approximately 10% for 40 mg tablet (1.7x beta power) administered at nighttime



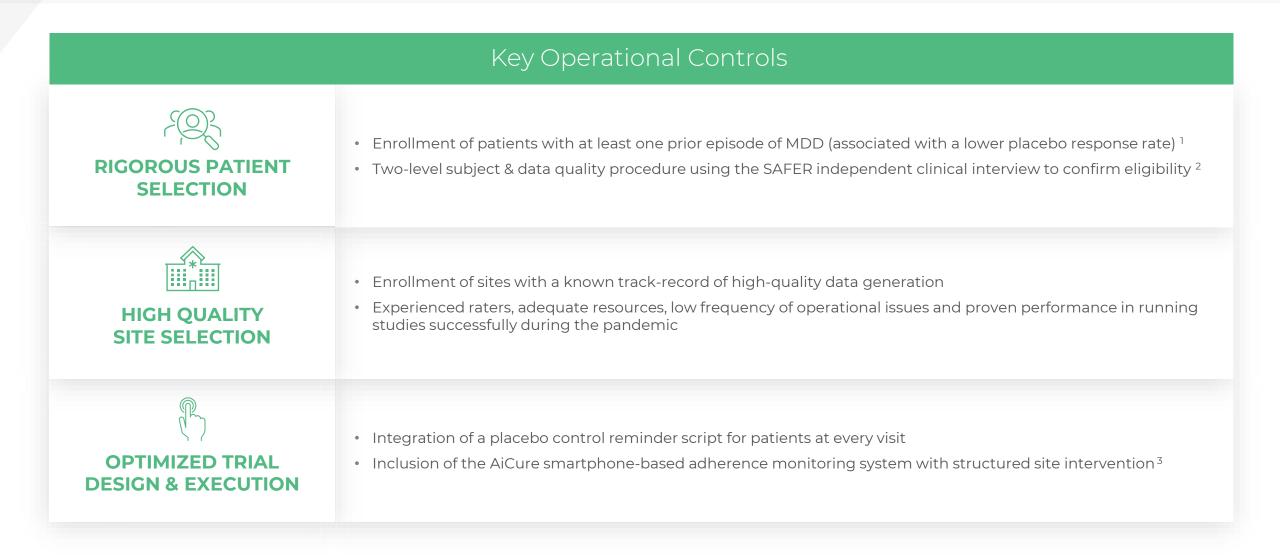
No evidence of decreased alertness in the morning after administration of PRAX-114 in Phase 2a trial in MDD patients**



*Estimated somnolence rate for PRAX-114 40 mg tablet is derived by combining somnolence AE data from all 45 mg nighttime dosing cohorts. This estimate does not reflect data from any patients dosed at the 40 mg level and there is no guarantee that actual data for patients dosed at the 40 mg level will reflect such estimates.

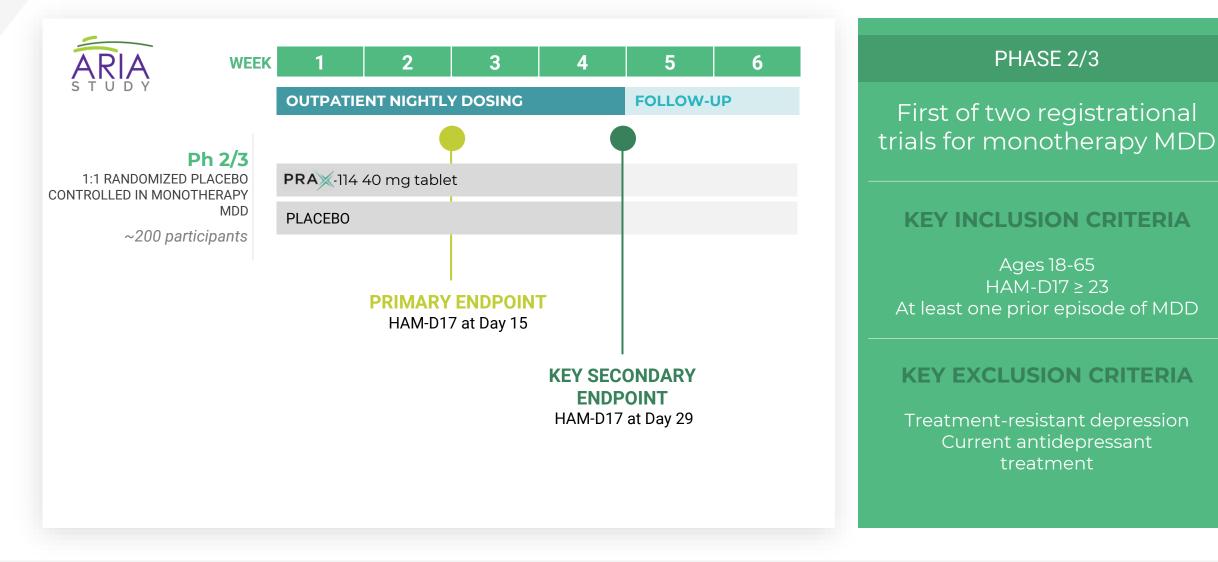
**Modified Observer's Assessment of Alertness/Sedation Scale (MOAA/S) was administered during the inpatient phase of Part A of the Phase 2a to assess potential for daytime somnolence; one participant in PMD cohort of Phase 2a study discontinued treatment due to AEs of moderate daytime sedation and mild feeling abnormal

PRAX-114 clinical program leverages best practices in conduct of MDD trials



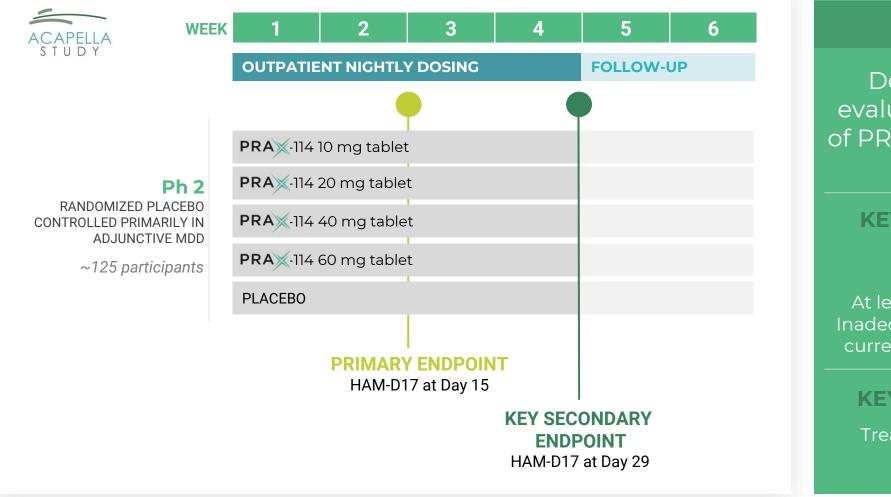


1: Sonawalla SB, Rosenbaum JF. Placebo response in depression. Dialogues Clin Neurosci. Mar 2002;4(1):105-13. 2: Freeman MP, Pooley J, Flynn MJ, et al. Guarding the Gate: Remote Structured Assessments to Enhance Enrollment Precision in Depression Trials. J Clin Psychopharmacol. Apr 2017;37(2):176-181. doi:10.1097/JCP.000000000000669 3: https://ajoure.com/ PRAX-114 monotherapy MDD Phase 2/3 Aria Study topline data expected 1H 2022





PRAX-114 MDD Phase 2 Acapella Study topline data expected 1H 2022



PHASE 2

Dose-ranging study to evaluate safety and efficacy of PRAX-114 at doses of 10, 20, 40 and 60 mg

KEY INCLUSION CRITERIA

Ages 18-65 HAM-D17 ≥ 23 At least one prior episode of MDD Inadequate response to treatment in current episode of at least 12 weeks

KEY EXCLUSION CRITERIA

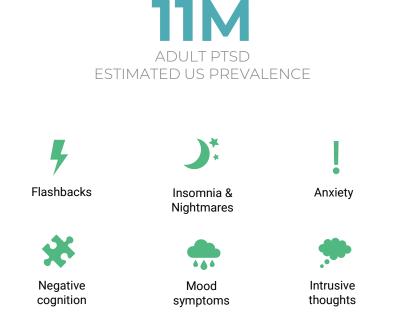
Treatment-resistant depression



PRAX-114 has broad potential in psychiatry and movement disorders

Dysfunction of GABA pathway is associated with chronic stress and symptoms of PTSD

POST-TRAUMATIC STRESS DISORDER (PTSD)

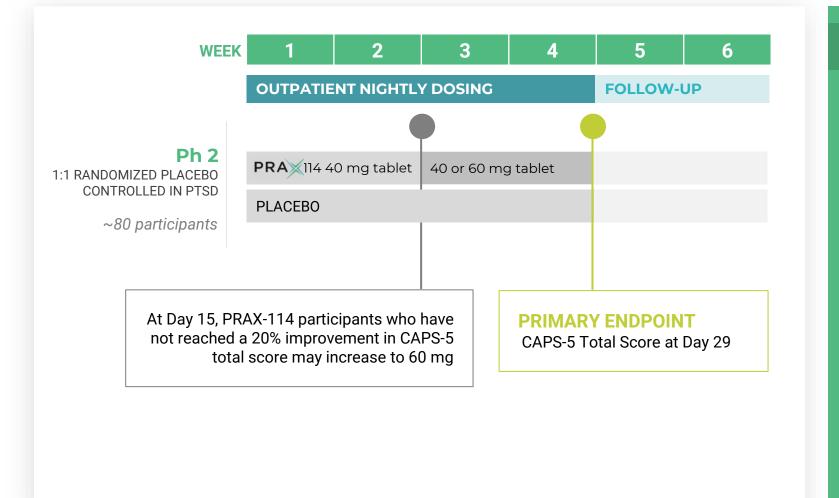


Post-traumatic Stress Disorder is a debilitating psychiatric disorder that leads to social, occupational and interpersonal dysfunction

2 **Profound unmet need**, meaningful link to PRAX-114 MOA, and complementarity to MDD program



PRAX-114 PTSD Phase 2 study expected to initiate in 4Q21



TOPLINE DATA EXPECTED 2H22

To evaluate safety, tolerability and efficacy of PRAX-114 for treatment of adults with PTSD

KEY INCLUSION CRITERIA

Ages 18-65 CAPS-5 ≥ 30 PTSD diagnosis with duration of >6 months



PRAX-114 has broad potential in psychiatry and movement disorders

Extrasynaptic GABAA receptors are associated with anti-tremor activity in ET



ESSENTIAL TREMOR ESTIMATED US PREVALENCE GABA_A PAM neuroactive steroids are **clinically validated** for the treatment of essential tremor

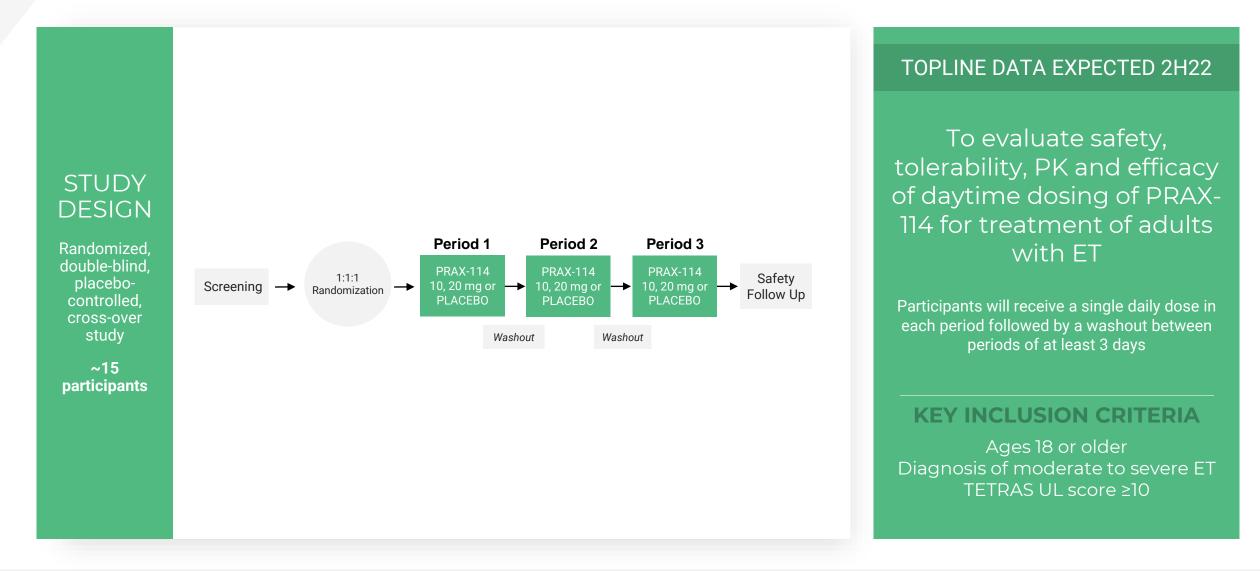
PRAX-114 extrasynaptic GABA_A preference has demonstrated a wide therapeutic window and welltolerated safety profile relative to other GABA_A PAMs in the class

³ Reducing **daytime**, **action-based tremors** without significant somnolence could provide meaningful impact to quality of life for people living with ET

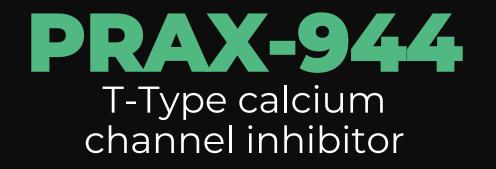
4 Potential **complementarity with PRAX-944** for essential tremor



PRAX-114 ET Phase 2 study expected to initiate in 4Q21







MOVEMENT DISORDERS

Essential Tremor Parkinson's Disease

KEY UPCOMING MILESTONES

Q4 2021 Ph2a ET High Dose Cohort Preliminary OL

1H 2022

Ph2a ET High Dose Cohort Randomized Withdrawal Topline

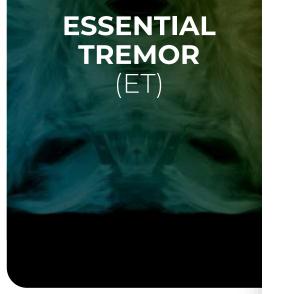
> **1H 2022** Initiate Ph2 PD Trial

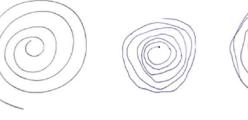
2H 2022 Ph2b Essential1 Study Topline



PRAX-944 is a selective T-type calcium channel inhibitor for the treatment of Essential Tremor

ET is the most common movement disorder







Up to 7 million patients in the U.S.

1-2% of the world population lives with essential tremor

3 **80% estimated discontinuation rate** for available therapies due to limited efficacy and poor tolerability

Last option is invasive brain surgery



- Parkinson's disease
- Essential tremor



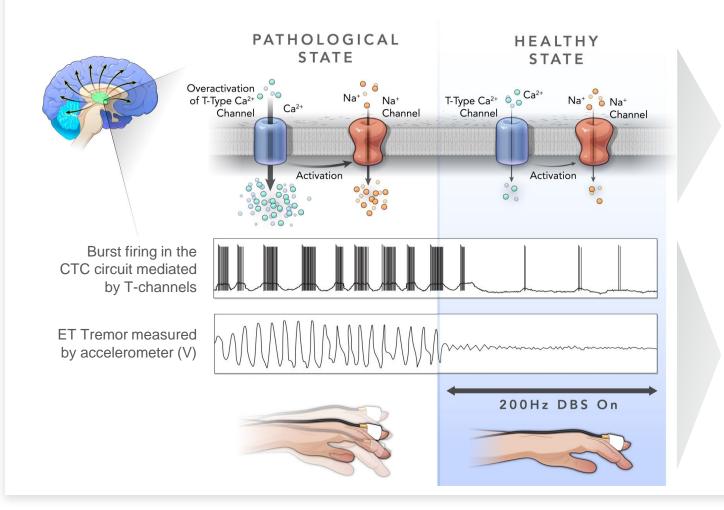
Characterized by involuntary progressive tremor especially in the hands

Tremor markedly impairs activities of daily living (ADL), including eating, dressing, and speaking



Large body of clinical, preclinical and human genetic evidence supporting key role of T-type calcium channels in ET

T-Type calcium channels are gatekeepers of neuronal firing patterns



T-type calcium channels drive burst firing in the cerebello-thalamo-cortical (CTC) circuit

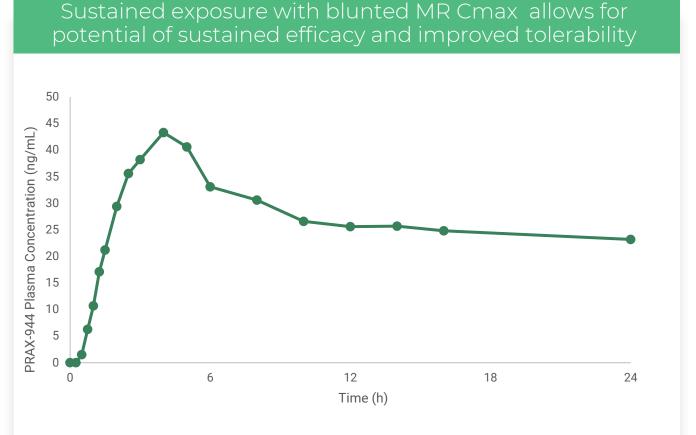
Mutations in T-type calcium channels are genetically linked to early onset familial ET

Abnormal neuron burst firing in the CTC circuit correlated with tremor activity in ET patients

Deep Brain Stimulation (DBS) leads to near complete silencing of bursting firing and significant tremor reduction



PRAX-944 is designed to enable once daily dosing and a well-tolerated safety profile



Mean PRAX-944 Concentration-Time Profiles after single 20 mg Modified Release (MR) oral dose

MR formulation is well-tolerated

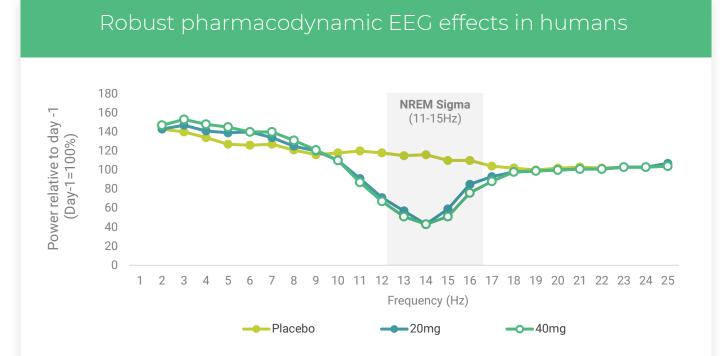
Titration and fit for purpose formulation are key to tolerability profile

No MTD identified up to 120 mg per day

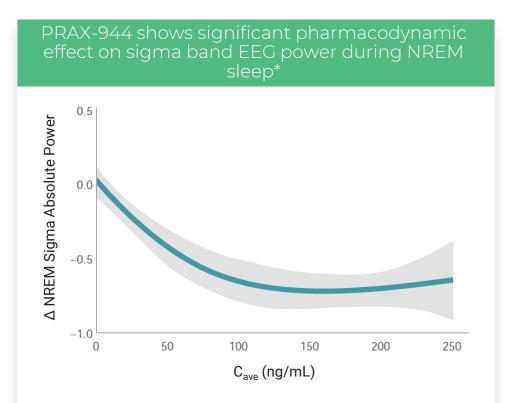
Majority of AEs have been mild, transient and resolved without intervention



PK-PD analysis suggests that doses of PRAX-944 of up to ~120 mg/day may achieve additional pharmacodynamic effect



- NREM sigma EEG biomarker is relevant to T-type calcium channel inhibitor mechanism
- Clinically, PRAX-944 demonstrated robust reduction in NREM sigma at 20 mg and 40 mg



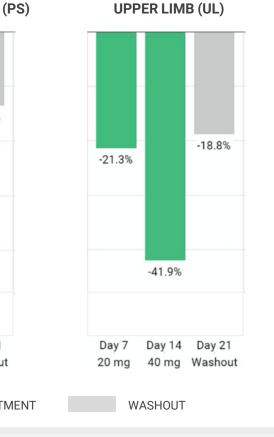
- Effect observed over wide, well-tolerated dose range from 5 mg to 120 mg
- Dose/concentration response effect justifies assessing dose levels up to 120 mg



PRAX-944 Phase 2a ET Part A data shows dose dependent reduction in tremor amplitude



Percent change in TETRAS score (N=6)





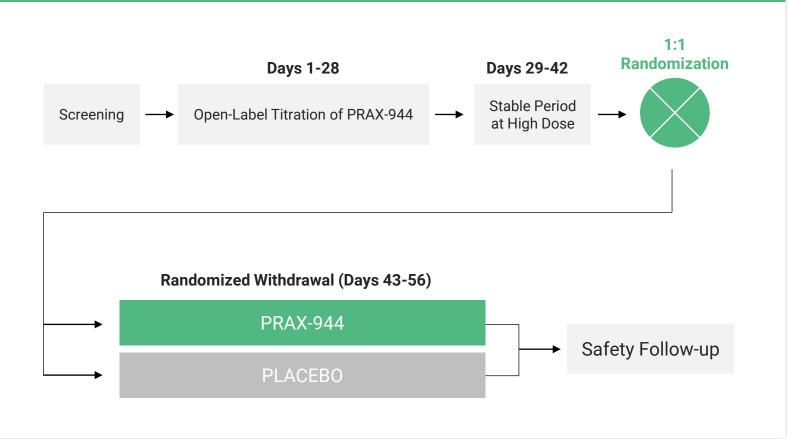
PRAX-944 Phase 2a ET Part A Archimedes spiral data indicates functional improvement





PRAX-944 Phase 2a high dose cohort preliminary results expected in 4Q 2021





To evaluate safety, tolerability and efficacy of PRAX-944 in patients treated up to 120 mg per day

4Q21

Preliminary open-label safety, tolerability and efficacy results

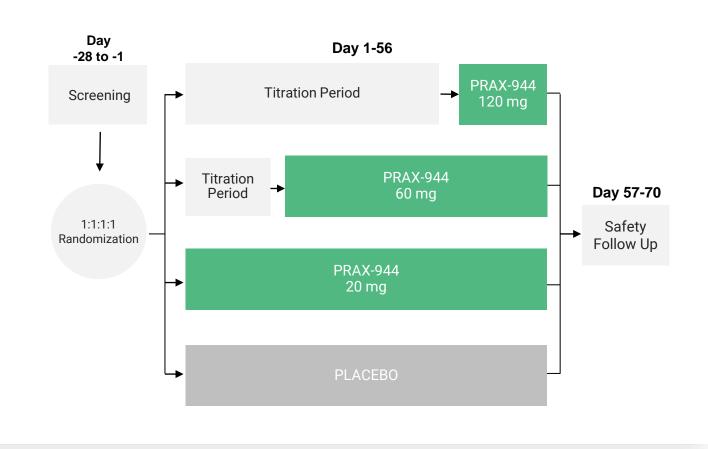
1H22

Complete open-label and placebocontrolled randomized withdrawal results



Enrollment has initiated for PRAX-944 ET Phase 2b Essential Study

Randomized, double-blind, placebo-controlled study in ~112 participants



TOPLINE DATA EXPECTED 2H22

Dose-ranging study to evaluate safety, tolerability and efficacy of PRAX-944 for treatment of adults with ET

KEY INCLUSION CRITERIA

Ages 18 or older Diagnosis of ET for at least 3 years TETRAS UL score ≥10





RARE DISEASES

Adult Cephalgias Pediatric Epilepsies (DEEs)

KEY UPCOMING MILESTONES

Q4 2021 Initiate Ph 2 Adult Cephalgias Trial

1H 2022 Topline Ph 1 ASSR Biomarker

> **1H 2022** Initiate Ph 2 DEE Trial



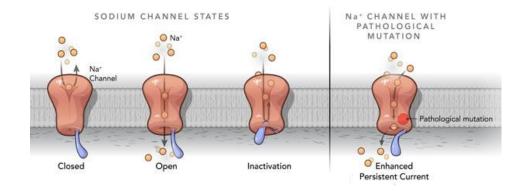
Block of persistent sodium current can reduce neuronal hyperexcitability and impact multiple disease states

Standard sodium channel blockers target peak sodium current and disrupt AP, leading to side effects

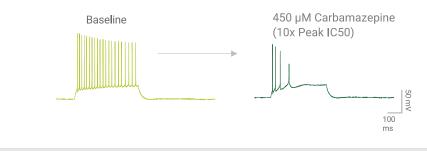
- Standard sodium channel blockers are an important class of medicines in neurology and psychiatry, broadly used in epilepsy, pain, migraine, and bipolar disorder
- All standard NaV blockers target peak sodium current
- In general, efficacy is limited by side effects



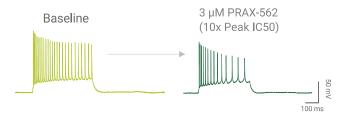
Modulation of persistent sodium current reduces hyperexcitability without disrupting AP



Carbamazepine Representative AP Traces



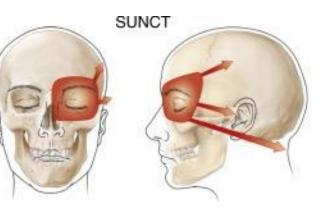
PRAX-562 Representative AP Traces





PRAX-562 has broad potential in rare CNS conditions

SUNCT, SUNA & TN are devastating headache disorders with limited treatment options



SUNCT and SUNA Cephalgias are devastating primary headaches highly responsive to IV sodium channel blockers

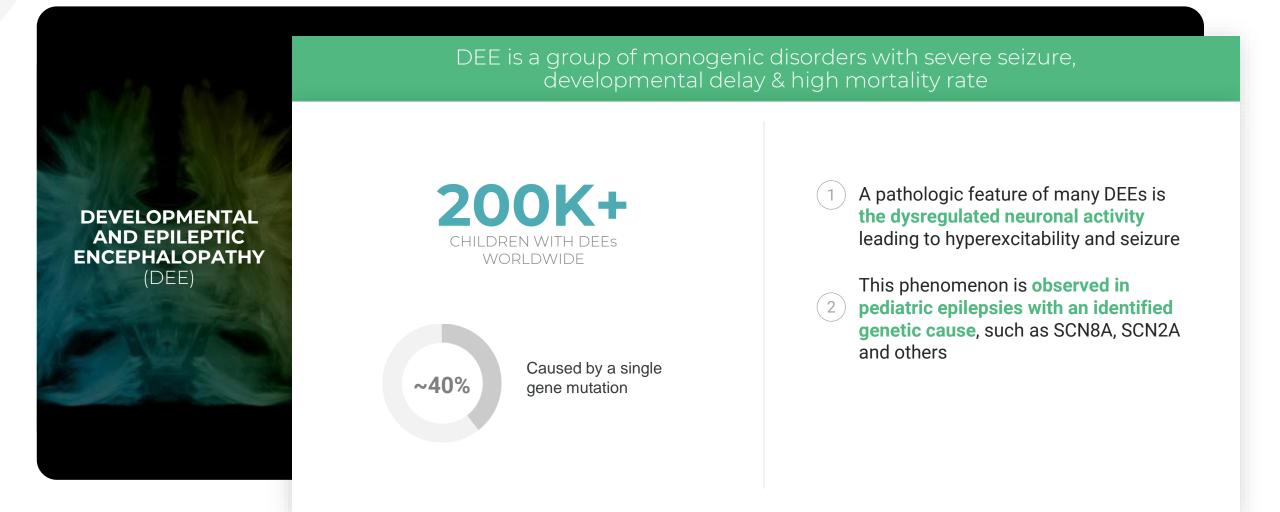
2 **Trigeminal Neuralgia** is characterized by intense, stabbing, electric-shock pain typically in the lower face and jaw, usually on one side of the face



SUNCT,

SUNA & TN

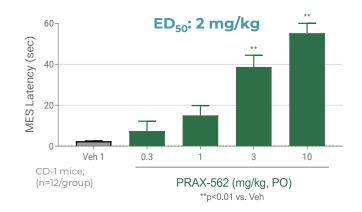
PRAX-562 has broad potential in rare CNS conditions

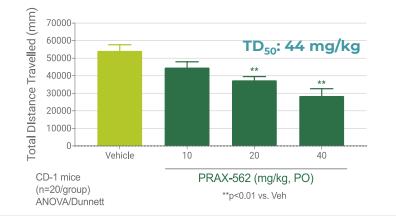




PRAX-562 mediated persistent current block protects mice from seizure with a wide therapeutic window *in-vivo*

PRAX-562 shows robust anti-seizure activity without impairment of locomotor activity





PRAX-562 showed significantly improved TI as compared to currently prescribed sodium channel blockers

Molecule	Brain Therapeutic Index 16.4x		
PRAX-562			
Carbamazepine	5.9x		
Lamotrigine	4.6x		
	Therapeutic Index (TI) = TC ₅₀ / EC ₅₀		

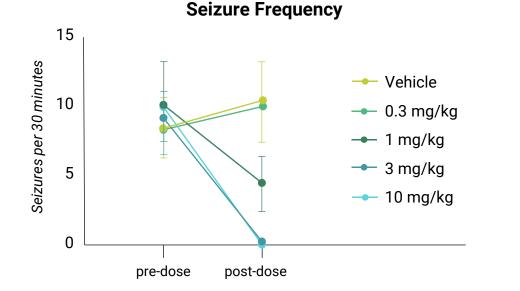
PRAX-562 had an increased ratio between drug levels that demonstrated preclinical anti-seizure activity versus those that caused toxicity



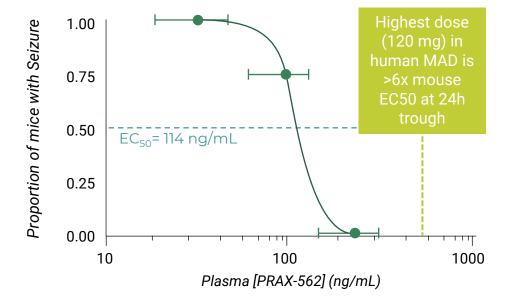
Treatment with PRAX-562 has shown significant reduction of seizures in genetic pediatric epilepsy animal models

PRAX-562 elicited dose-dependent prevention of seizures in SCN2A* mouse model

PRAX-562 elicited dose-dependent prevention of seizures in SCN8A* mouse model



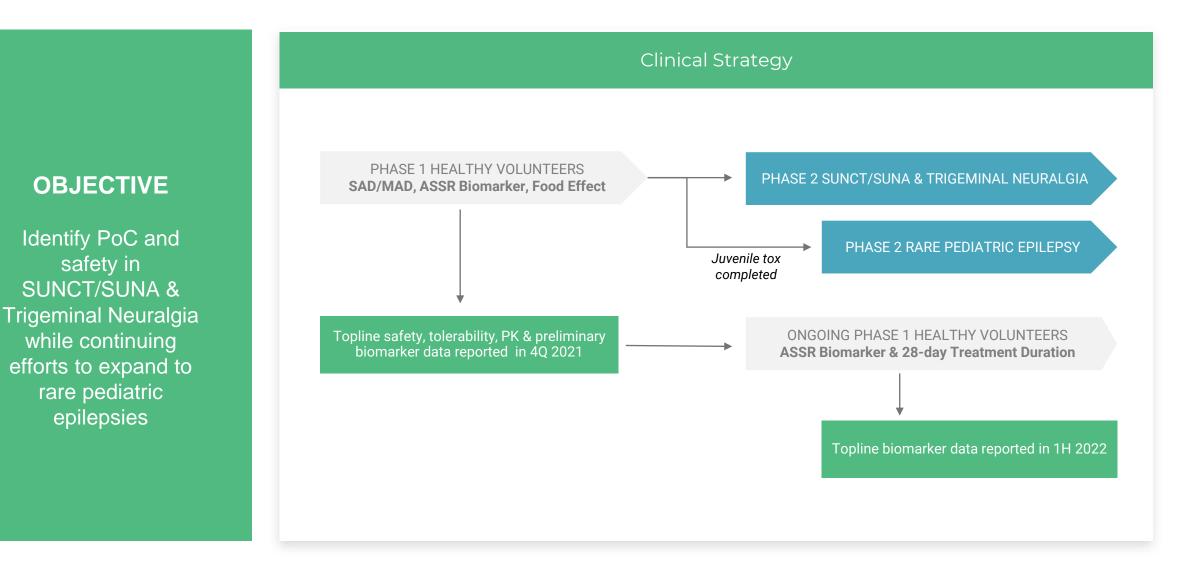
Baseline seizure frequency was measured for 30 minutes prior to treatment (Pre) and then again 30 minutes after treatment (Post). Symbols represent mean \pm SEM, n=6-10 per symbol.



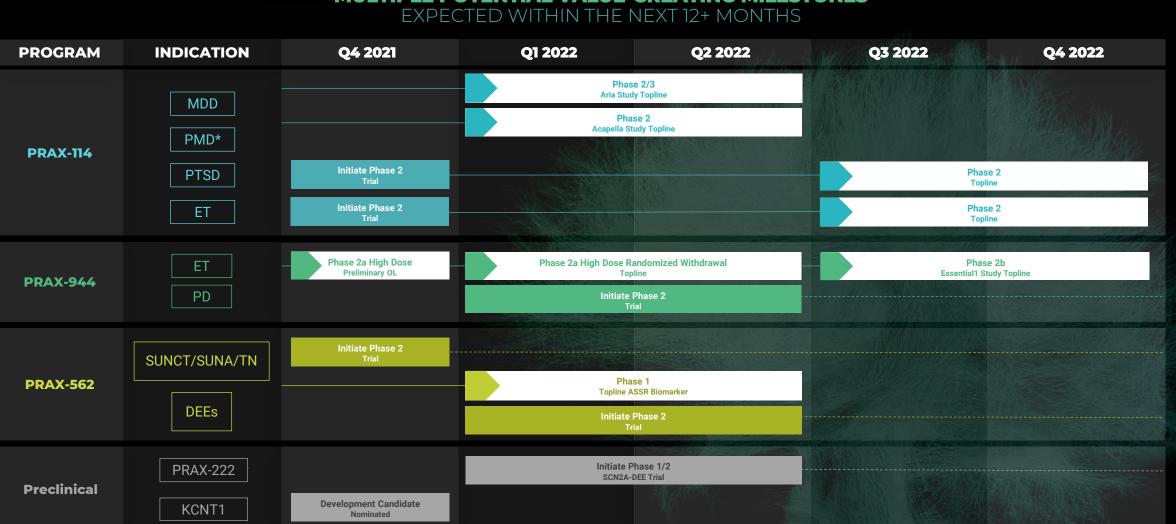
PRAX-562 inhibition of audiogenic seizures in D/+ mice



PRAX-562 development strategy in rare cephalgias and pediatric epilepsies







MULTIPLE POTENTIAL VALUE-CREATING MILESTONES

* Plans for upcoming PRAX-114 Phase 2b study in women with menopausal and mood symptoms to be disclosed by end of 2021