CORPORATE OVERVIEW

May 2022

Forward-looking statements

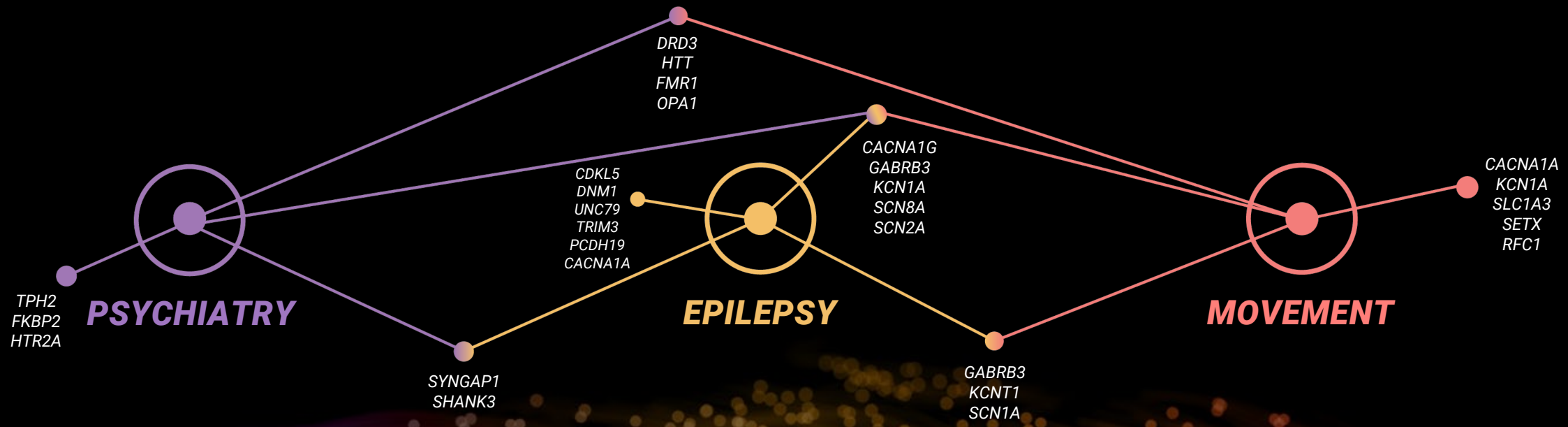
This presentation may contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial conditions, including but not limited to express or implied statements regarding the current beliefs, expectations 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, (viii) our ability to meet any specific milestones set forth herein, and (ix) uncertainties and assumptions regarding the impact of the COVID-19 pandemic on our business, operations, clinical trials, supply chain, strategy, goals and anticipated timelines. 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 filed for the year ended December 31, 2021, our Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission.

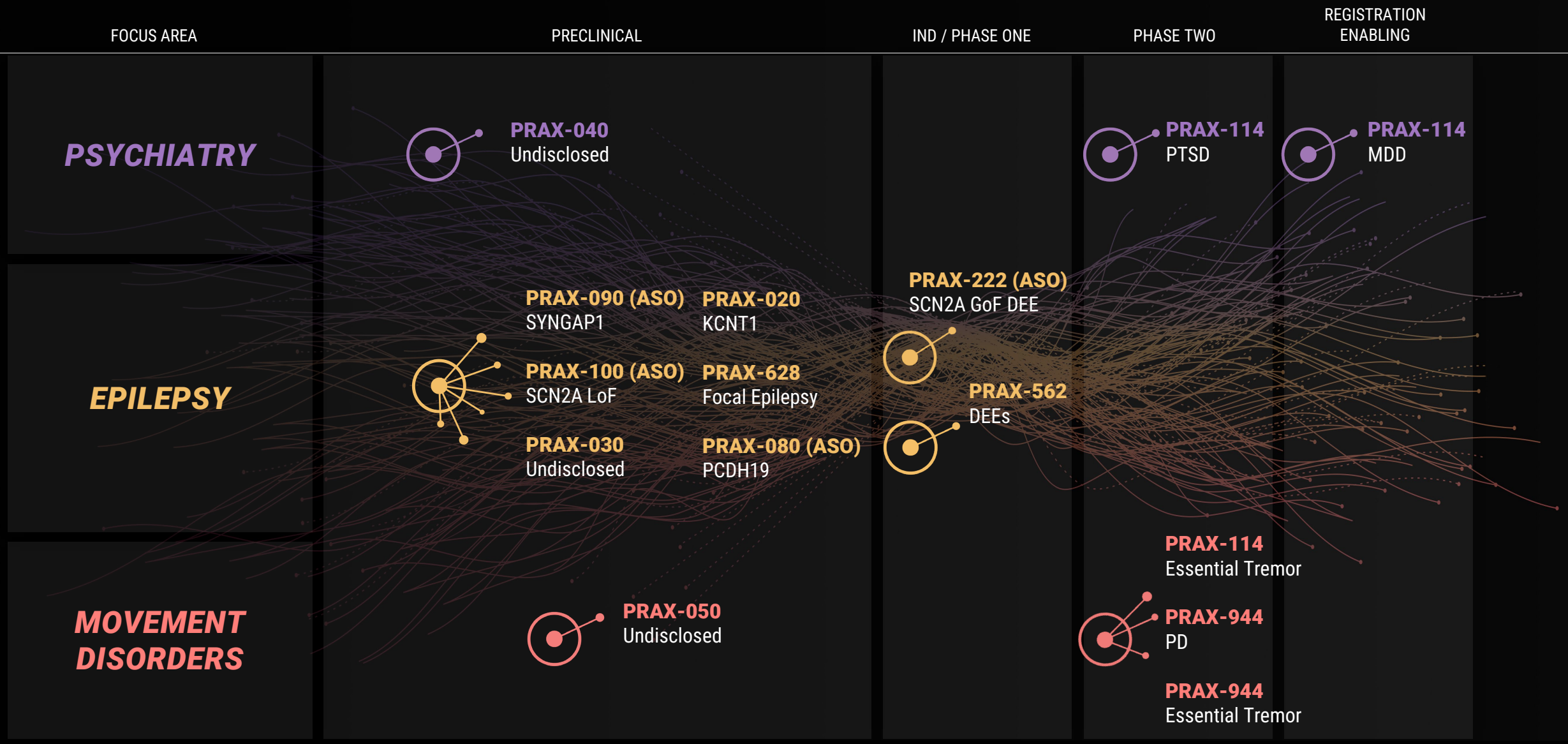
Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, we have 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 New Classes of Treatments

INSPIRED BY THE GENETICS OF EPILEPSY

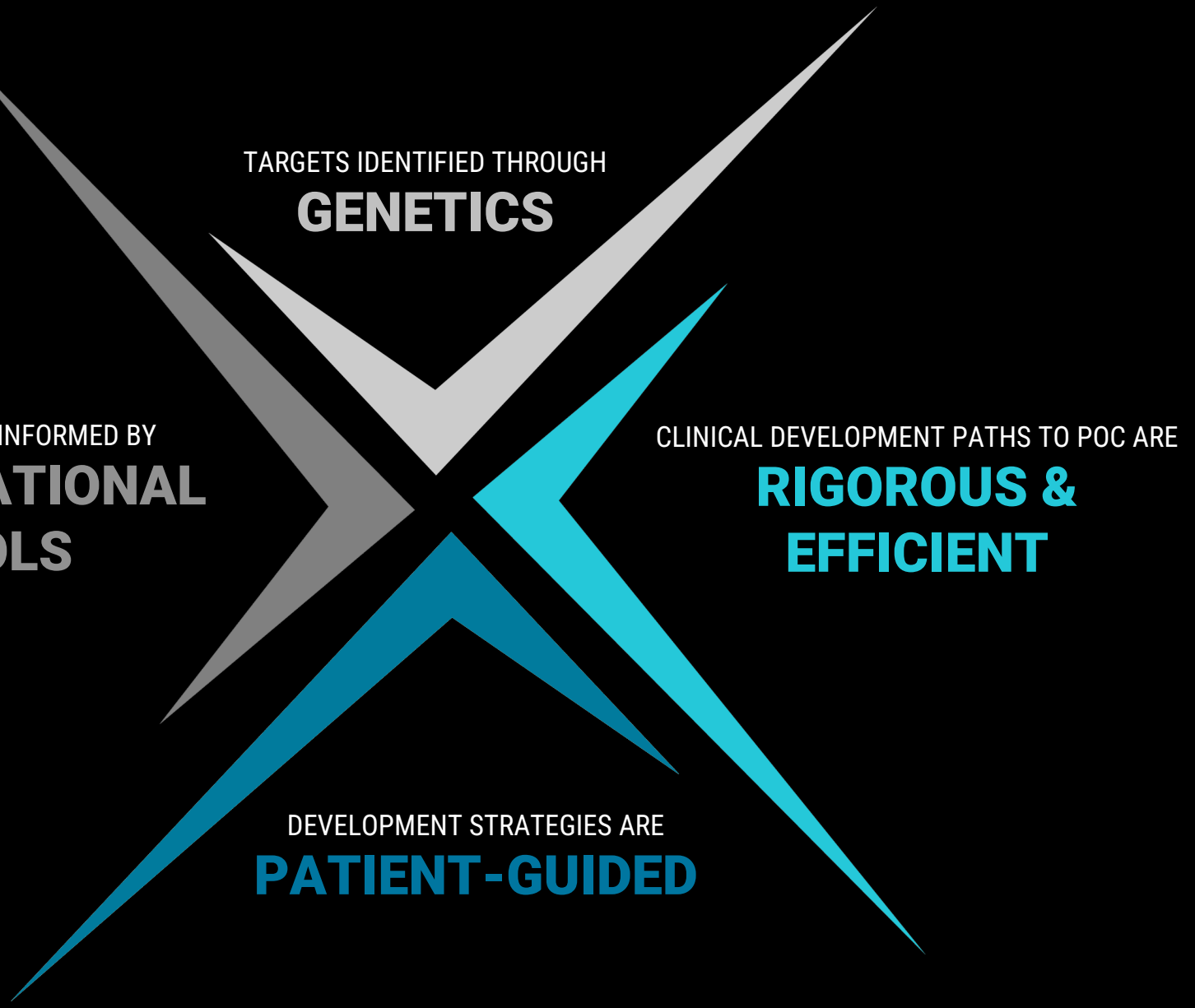


Targeting diseases connected by neuronal imbalance across three franchises



*PRAX-222 in collaboration with Ionis Pharmaceuticals, Inc. and RogCon, Inc.; SCN2A-LOF, SYNGAP1 & PCDH19 ASOs are a collaboration with The Florey Institute of Neuroscience and Mental Health.

Praxis is built on four key pillars



BROAD CNS PORTFOLIO
Uncorrelated program risk & significant potential for indication expansion

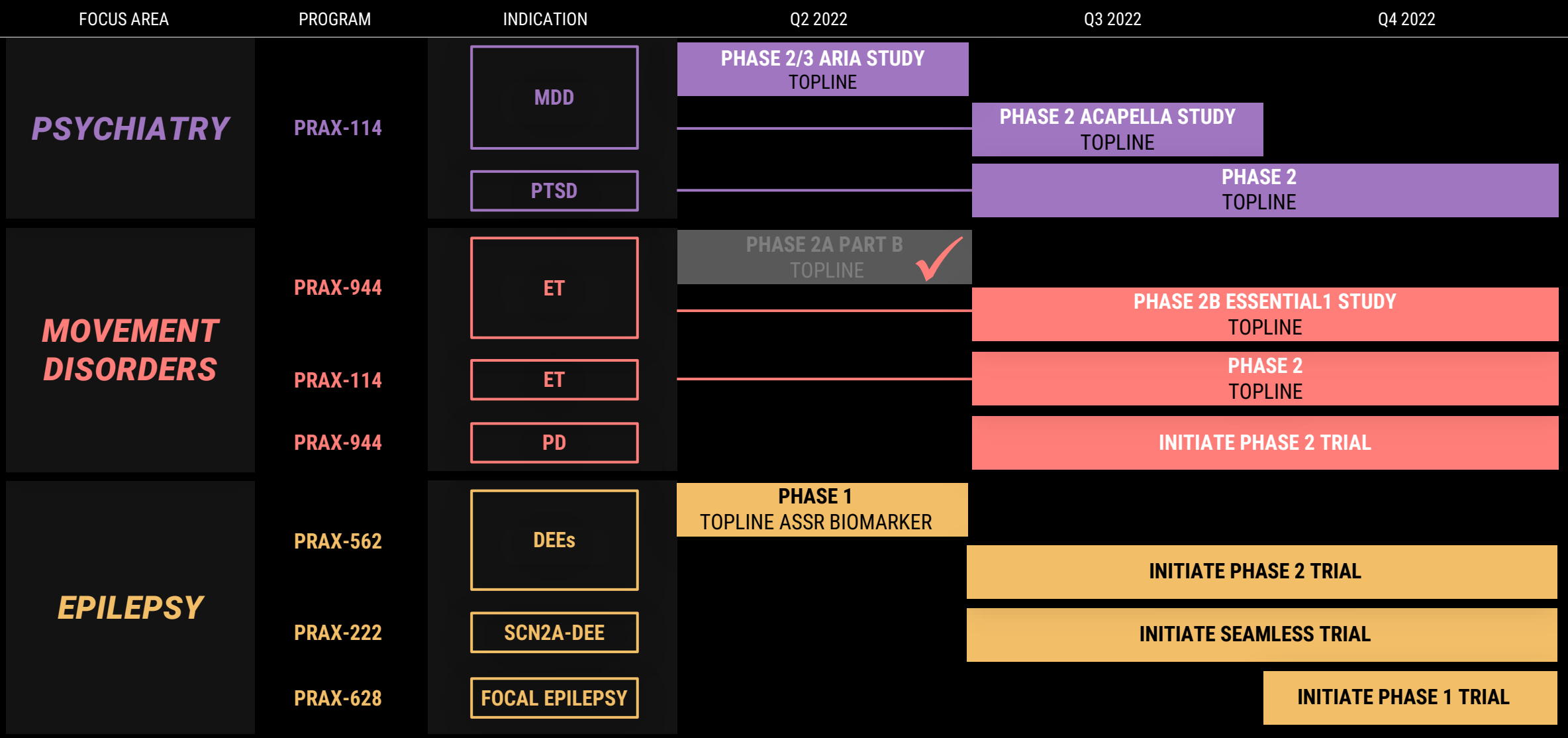
DATA RICH 2022
Topline results from six Phase 2 or registrational studies

DEEP EARLY-STAGE PIPELINE
Enables continuous advancement of new programs

MULTI-BILLION DOLLAR REVENUE POTENTIAL from each of three therapeutic franchises

CASH RUNWAY to advance each program through value inflecting milestones

Six phase 2 or registrational topline readouts in 2022



PRAX-114 Phase 2/3 Aria Study topline results expected in June 2022; PRAX-944 Phase 2a Part B topline results disclosed in May 2022

PSYCHIATRY

PRAX-114
$GABA_A$ Receptor PAM
Depression
Post-traumatic Stress Disorder

KEY UPCOMING MILESTONES

JUNE 2022
Ph 2/3 Monotherapy MDD Aria Study Topline

3Q 2022
Ph 2 MDD Dose-Ranging Acapella Study Topline

2H 2022
Ph 2 PTSD Topline

PRAX-114 is a novel $GABA_A$-PAM ideally suited to address the unmet needs of patients living with major depressive disorder

UNMET NEEDS	*PRAX-114*
Low response rate >50% of treated patients fail first line treatment	**Novel mechanism** Supports differentiated efficacy profile across range of MDD symptoms
Slow onset of action Existing treatment options typically take 1-2 months to take effect	**Rapid and durable** Clinically meaningful response within days maintained while on treatment
Limiting safety profile Unwanted side effects including weight gain & sexual dysfunction can lead to discontinuation of treatment	**Differentiated safety profile** Allows for continuous treatment throughout an episode of depression

Source: Rush et al 2006, Masand et al 2003, Kupfer et 2005, DSM-5 2013, ExpressScripts MDD Report 2020

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

PRAX-114 SHOWS 10.5-FOLD GREATER POTENTIATION OF EXTRASYNAPTIC THAN SYNAPTIC $GABA_A$ RECEPTORS

		POTENTIATION		FOLD POTENTIATION
	DOSING	$\alpha_4\beta_3\delta$ %*	$\alpha_1\beta_2\gamma_2$ %	$\alpha_4\beta_3\delta$/ $\alpha_1\beta_2\gamma_2$
PRAX-114	**Oral**	**300%**	**29%**	**10.5**
Zuranolone	Oral	300%	117%	2.6
Ganaxolone	IV, Oral	300%	794%	0.4
Zulresso	IV	300%	306%	1.0

$\alpha_4\beta_3\delta$: extrasynaptic $GABA_A$ receptor
$\alpha 1\beta_2\gamma_2$: synaptic $GABA_A$ receptor

* Equivalent of full activation by GABA
Source: PRAXIS data

NO MTD IDENTIFIED up to 80 mg

TOLERABILITY PROFILE maintained throughout dose escalation

EXPOSURE-DEPENDENT RATES OF SOMNOLENCE resolved 1 to 3 hours post-dosing, consistent with peak concentrations

Source: Praxis Data on file

PRAX-114 Phase 2a: rapid, marked & durable improvement in depression scores

PHASE 2A COMBINED* HAM-D MONOTHERAPY & ADJUNCTIVE RESULTS

VISIT	**HAM-D** *Monotherapy* **Mean (SD) N=14**	**HAM-D** *Adjunctive* **Mean (SD) N=38**
DAY 1 (BL)	25.2 (1.82)	24.7 (2.90)
DAY 8 (CFB)	-17.6 (4.77)	-13.4 (7.94)
DAY 15 (CFB)	-16.6 (5.23)	-12.2 (7.02)

EFFICACY MAINTAINED WHILE ON TREATMENT

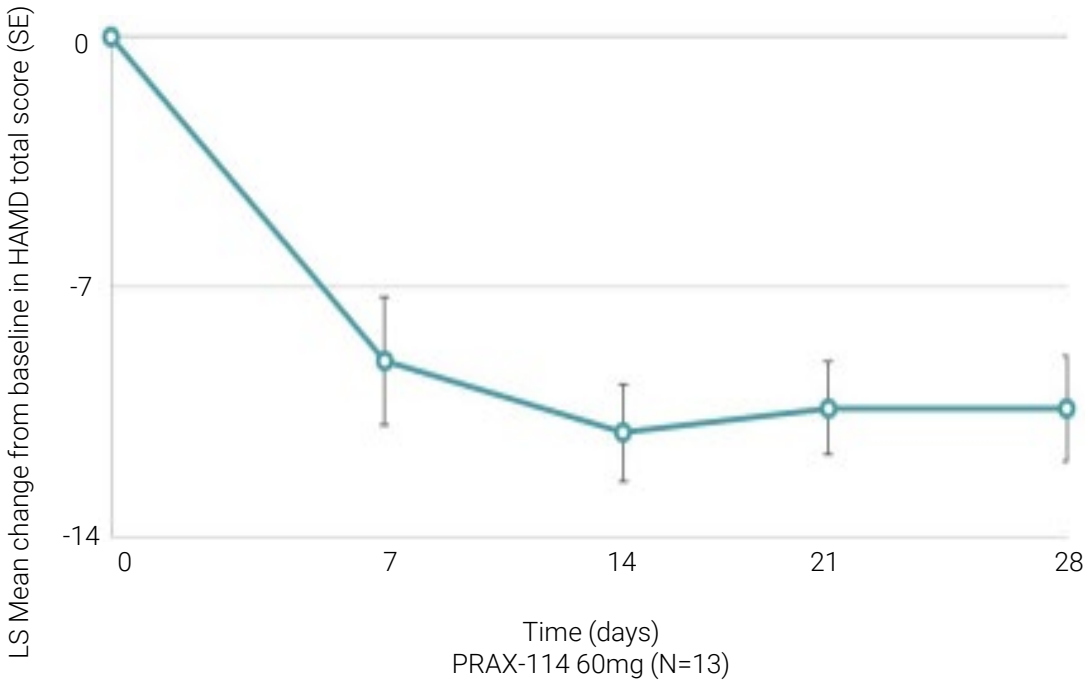
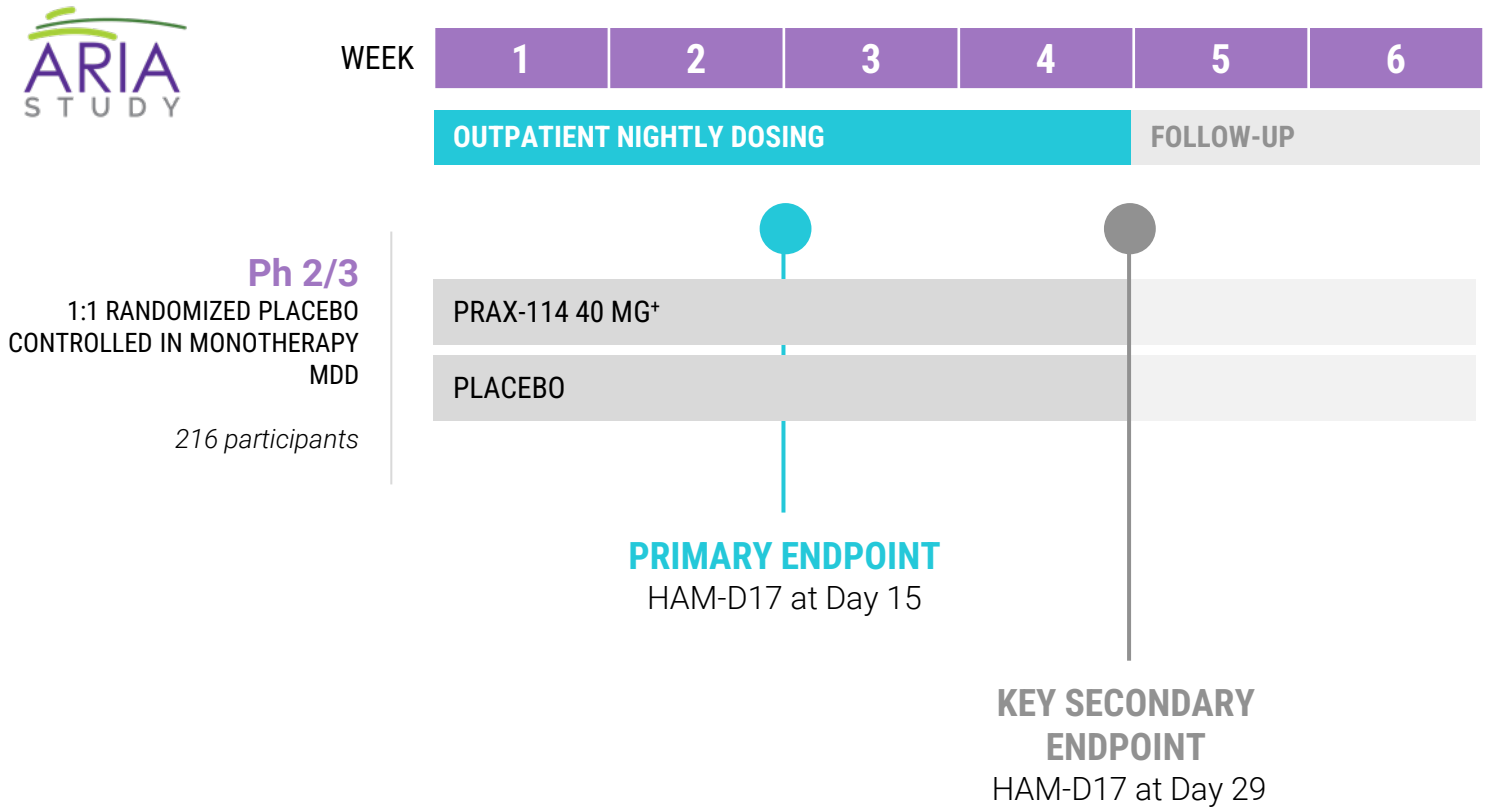


Figure 10. Reduction of HAM-D total score observed in MDD patients treated with PRAX-114 for 28 days in Part C.

*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

PRAX-114 monotherapy MDD Phase 2/3 Aria Study completed; topline data expected June 2022



PHASE 2/3
First of two registrational trials for monotherapy MDD

KEY ASSUMPTION
80% powered for 0.4 effect size

+PRAX-114 administered in tablet formulation
clinicaltrials.gov/ct2/show/NCT04832425; https://theariastudy.com/

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

KEY OPERATIONAL CONTROLS

RIGOROUS PATIENT SELECTION

- Enrollment of patients with at least one prior episode of MDD (associated with a lower placebo response rate) [1]
- Two-level subject & data quality procedure using the SAFER independent clinical interview to confirm eligibility [2]

HIGH QUALITY SITE SELECTION

- Enrollment of sites with a known track-record of high-quality data generation
- Experienced raters, adequate resources, low frequency of operational issues and proven performance in running studies successfully during the pandemic

OPTIMIZED TRIAL DESIGN & EXECUTION

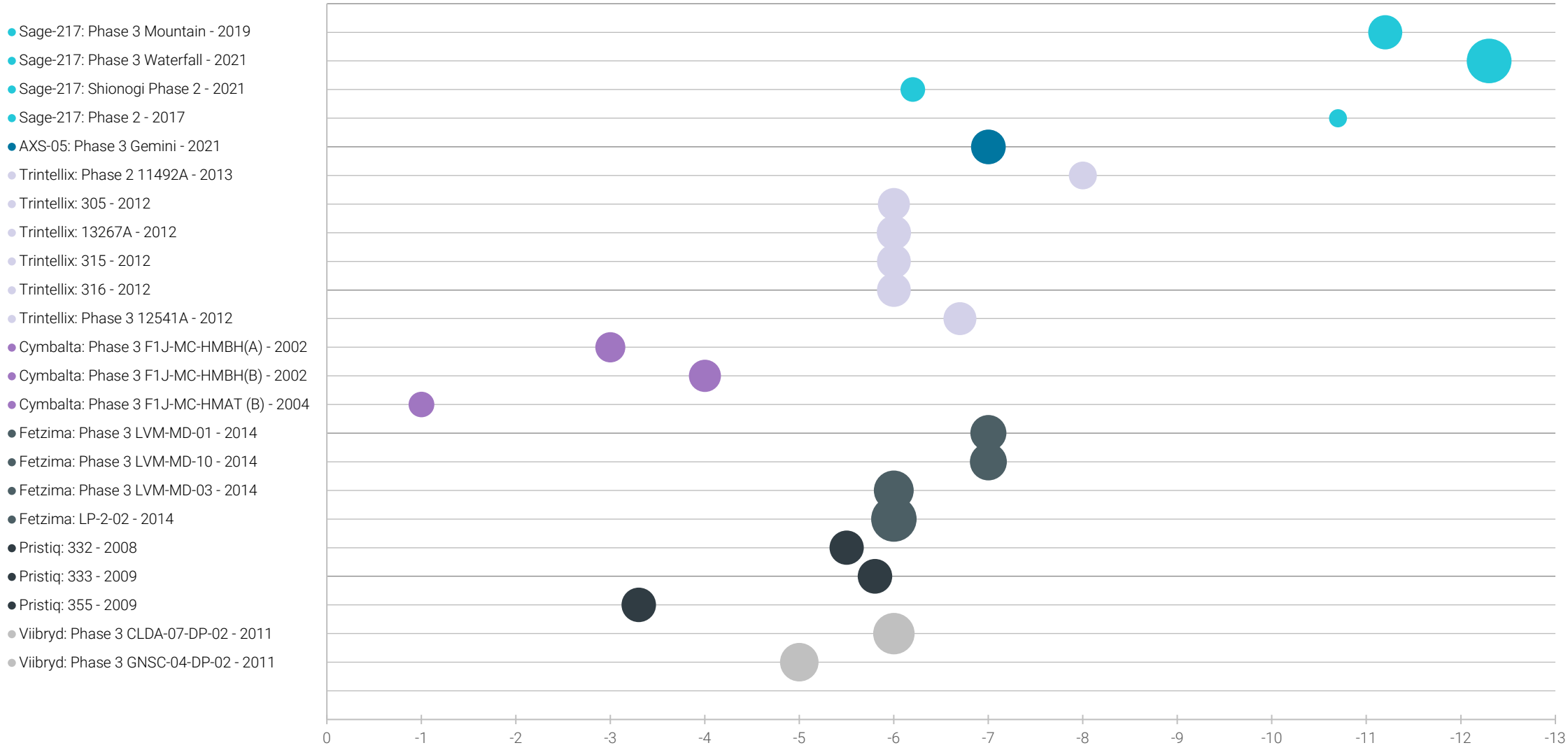
- Integration of a placebo control reminder script for patients at every visit
- Inclusion of the AiCure smartphone-based adherence monitoring system with structured site intervention [3]

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.0000000000000669

3: https://aicure.com/

HAM-D⁺ placebo change trends toward 6-8 points reduction at 2 weeks in MDD trials



⁺Based on HAM-D or conversion of MADRS to HAM-D (Leucht et al. 2017, Table 2)
*Bubble size correlates to N population size

PRAXIS

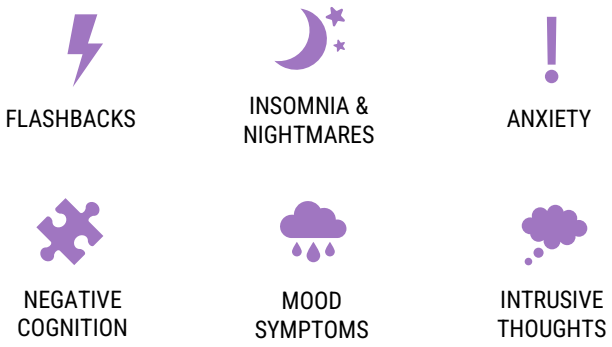
PRAX-114 has broad potential in psychiatry disorders such as PTSD

DYSFUNCTION OF GABA PATHWAY IS ASSOCIATED WITH CHRONIC STRESS AND SYMPTOMS OF PTSD

POST-TRAUMATIC STRESS DISORDER (PTSD)

11M

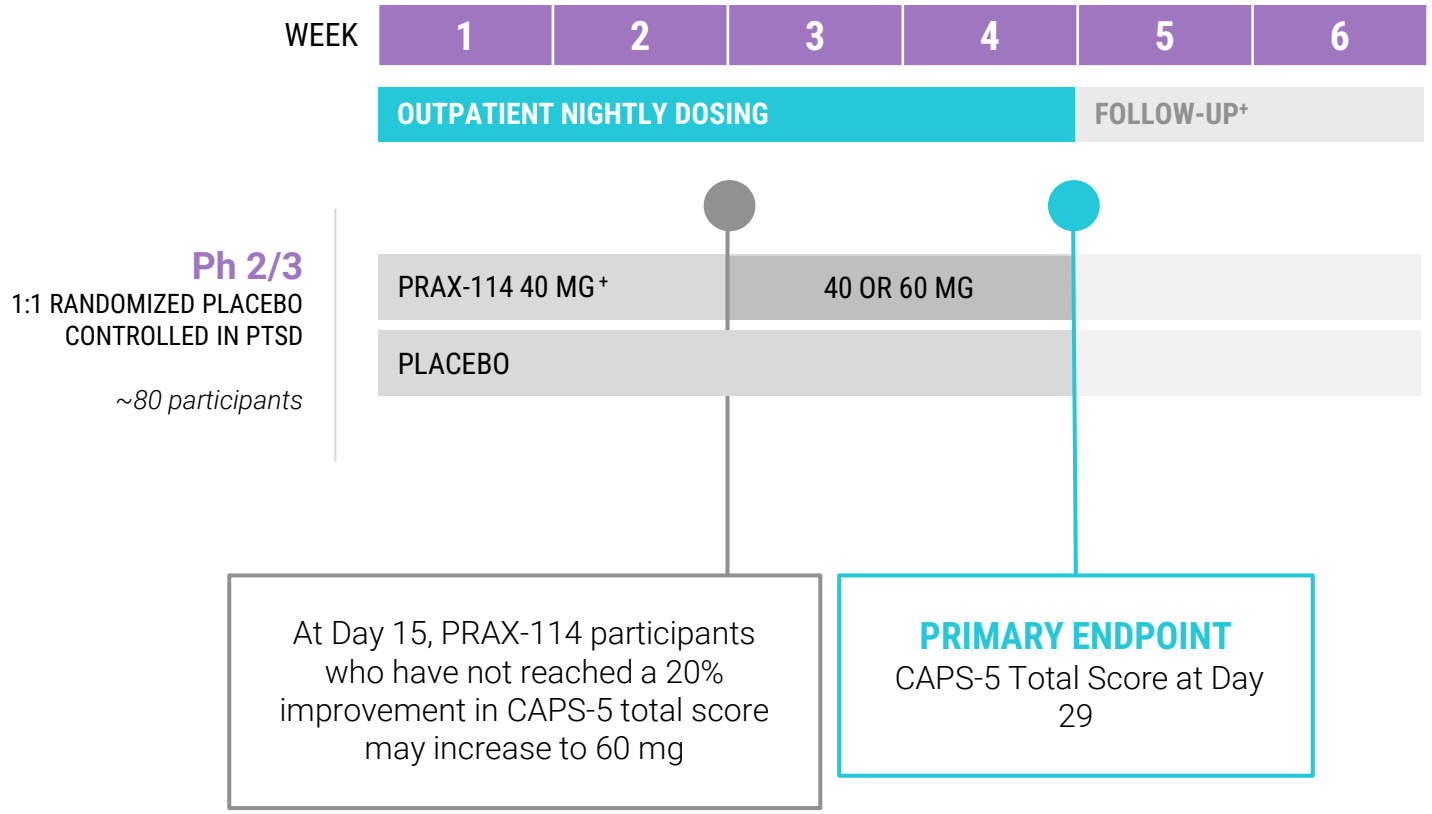
ADULT PTSD
ESTIMATED US PREVALENCE



1. **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 topline data expected 2H22



To evaluate safety, tolerability and efficacy of PRAX-114 for treatment of adults with PTSD, followed by 8-week OLE

KEY INCLUSION CRITERIA

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

+PRAX-114 administered in tablet formulation
clinicaltrials.gov/ct2/show/NCT04969510

MOVEMENT DISORDERS

PRAX-944
T-Type Calcium Channel Inhibitor
Essential Tremor
Parkinson's disease

PRAX-114
$GABA_A$ Receptor PAM
Essential Tremor

KEY UPCOMING MILESTONES

2Q 2022
PRAX-944 Ph 2a ET Part B Randomized Withdrawal Topline ✓

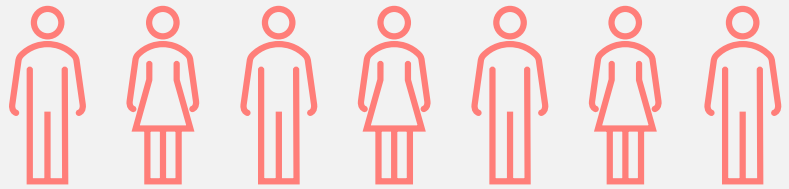
2H 2022
PRAX-944 Ph 2b ET Essential1 Study Topline

2H 2022
PRAX-114 Ph 2 ET Topline

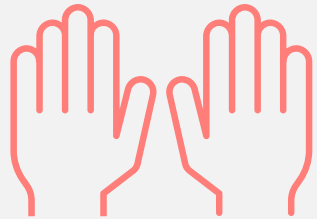
2H 2022
Initiate PRAX-944 Ph 2 PD Trial

PRAX-944 Phase 2a Part B topline results disclosed in May 2022

Daring for more for people living with essential tremor

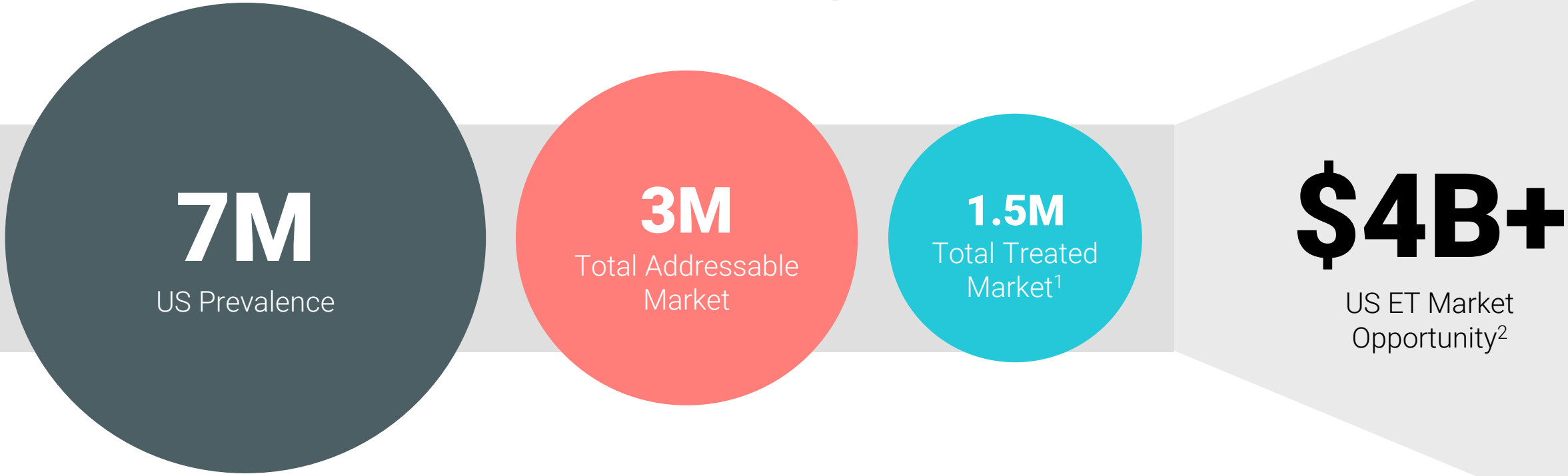


0 medications developed specifically for ET & only 1 medication approved for ET >50 years ago



~50% of patients that seek treatment discontinue medication due to limited efficacy & poor tolerability

Our focus is on elevating the standard of care to capture the $4B+ US ET market



Source: Primary market research and praxis internal modeling and projections

1. Claims analysis indicates that 50% of diagnosed patients are on treatment; 2. Based on minimum of range for net price estimates from praxis covering analysts as of 16-december-2021- $3.6k

Praxis treatments could allow patients to fit the right therapy to their needs to realize improved outcomes

As needed

- Patients could initiate ET treatment sooner
- Patients could treat as needed

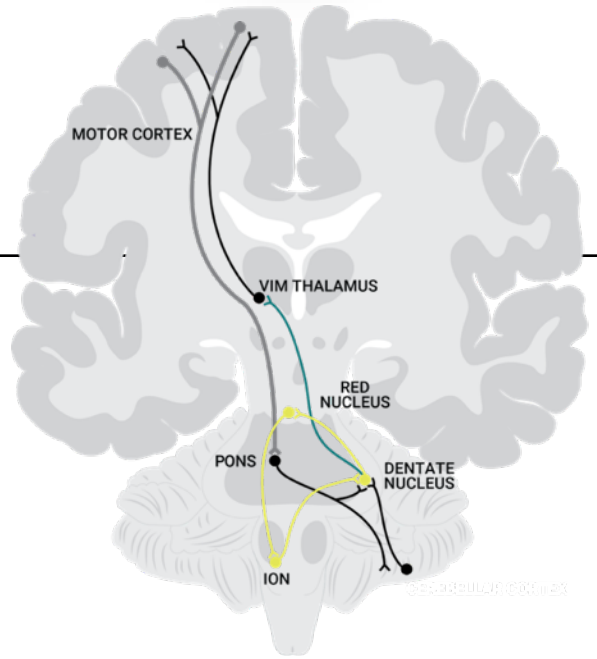
+

Chronic

- Patients could maintain ET therapy

PRAX-114

$GABA_A$ RECEPTORS



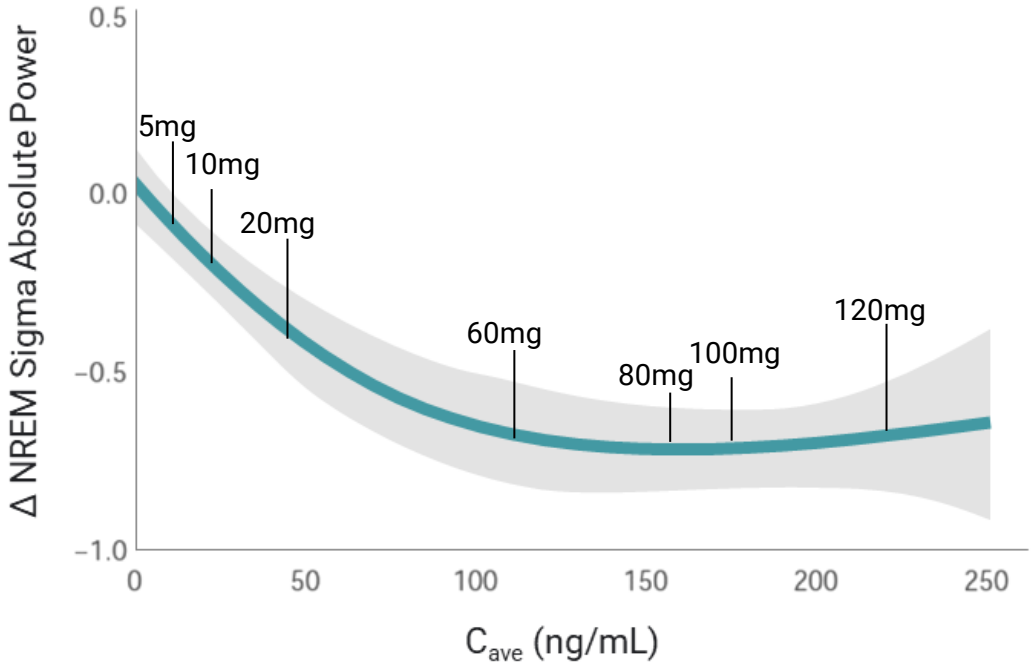
PRAX-944

T-TYPE CALCIUM CHANNELS

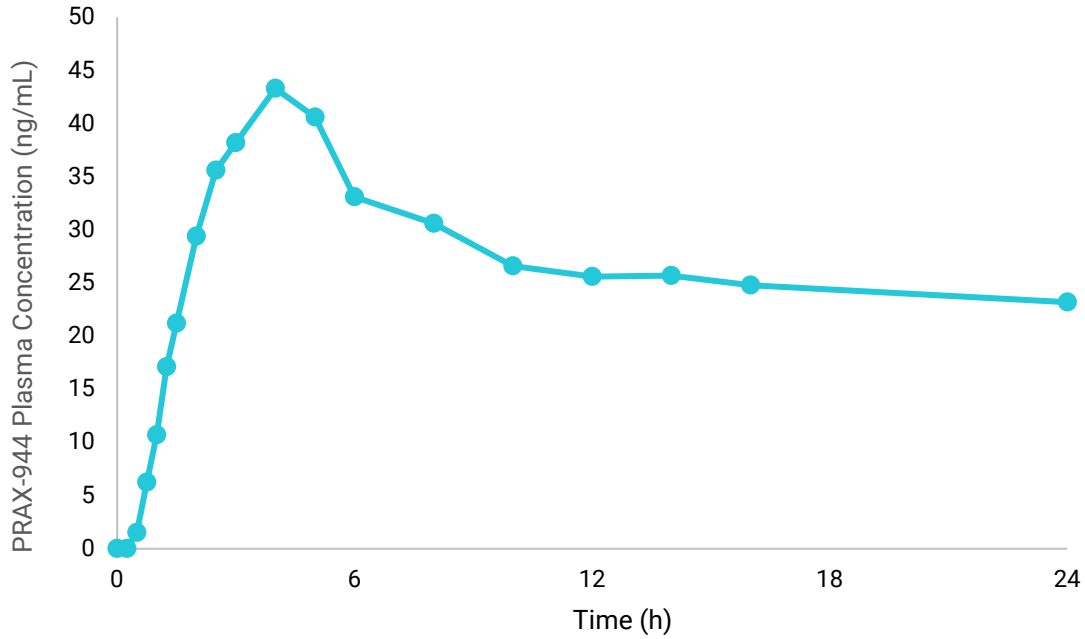
CEREBELLO-THALAMO-CORTICAL (CTC) CIRCUIT

Wide dosing range and modified release formulation for PRAX-944 may support improved tolerability & efficacy profile

PREDICTABLE PK, WIDE DOSING RANGE UP TO 120 MG & FLEXIBILITY IN TITRATION



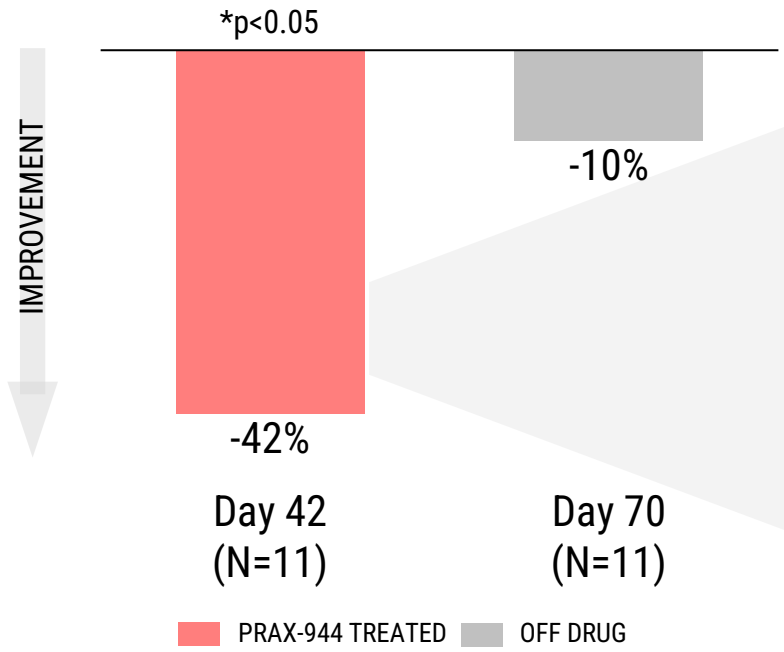
SUSTAINED EXPOSURE WITH BLUNTED MR CMAX



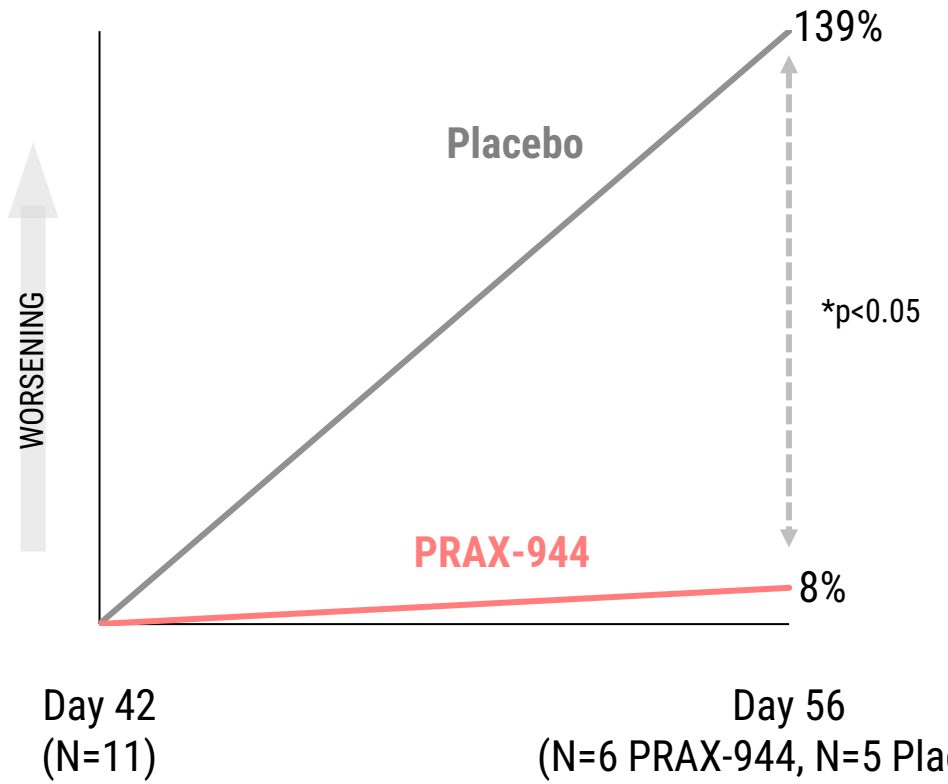
Source: Praxis Data on file

Marked functional benefit observed while on PRAX-944 in Part B of Phase 2a study while withdrawal results in regression to baseline severity

MODIFIED ADLs IN OPEN LABEL MEAN % CHANGE FROM BASELINE



MODIFIED ADLs IN RANDOMIZED WITHDRAWAL MEAN % CHANGE FROM DAY 42



*Nominal p-value based on ANCOVA
Source: Praxis Data on file

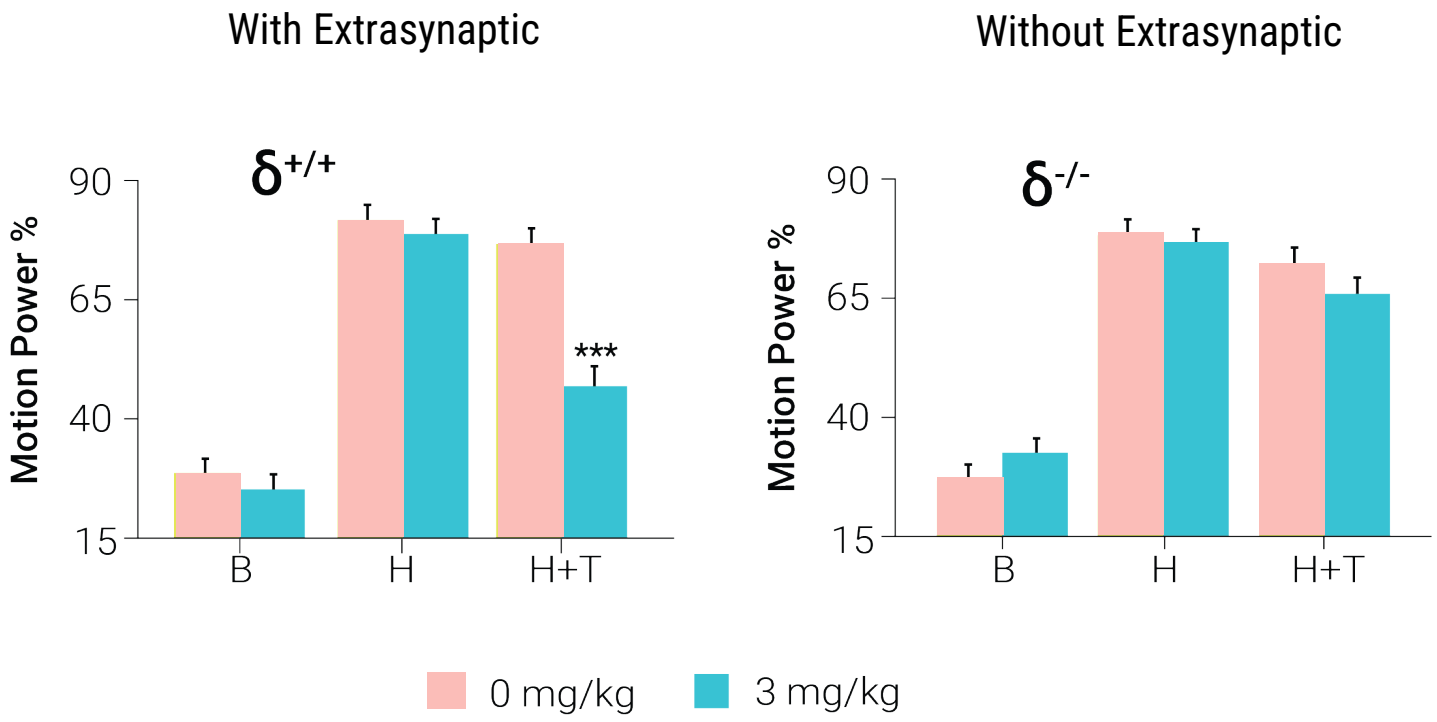
PRAX-944 was generally well tolerated in Part B of Phase 2a study

SAFETY SUMMARY

- Safety profile in study consistent with previous experience with PRAX-944
- 8 of 11 participants completed open-label period at highest dose of 120 mg
- 3 of 14 evaluable participants discontinued, with 1 discontinuation unrelated to study drug[1]
- All TEAEs leading to down-titration or discontinuation were mild to moderate[2]

[1] Participant had a pre-existing condition which was unrelated to study drug and required a medical procedure
[2] One severe AE of essential tremor reported while on placebo following withdrawal of PRAX-944; all other AEs mild to moderate
Source: Praxis Data on file

PRAX-114: Evidence suggests central role of extrasynaptic $GABA_A$ receptors targeting tremor pathophysiology



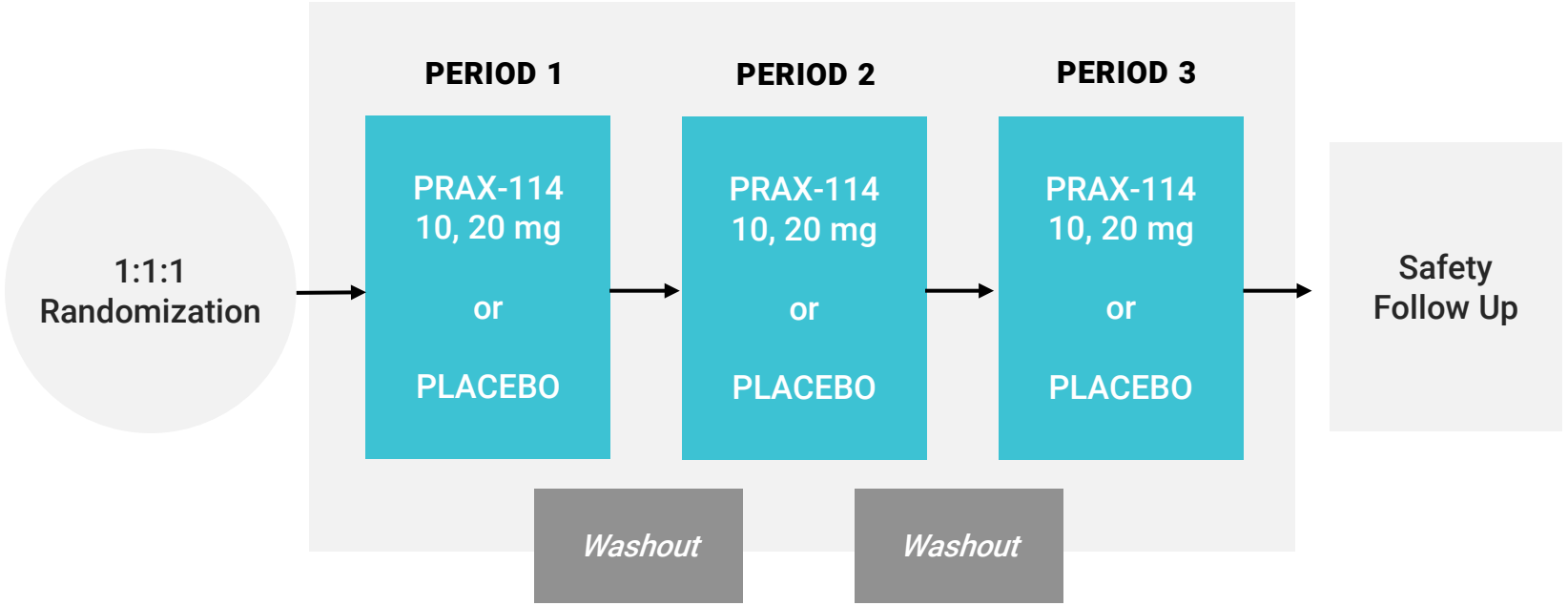
PRAX-114 has greater potentiation of extrasynaptic $GABA_A$ receptors

POTENTIATION		FOLD POTENTIATION
$\alpha_4\beta_3\delta$ %*	$\alpha_1\beta_2\gamma_2$ %	$\alpha_4\beta_3\delta$/ $\alpha_1\beta_2\gamma_2$
300%	29%	10.5

$A_4\beta_3\delta$: extrasynaptic $gaba_a$ receptor; $\alpha1\beta_2\gamma_2$: synaptic $gaba_a$ receptor; * equivalent of full gaba activation
Source: Praxis Data on file

PRAX-114 ET Phase 2 study designed to evaluate safety, tolerability, PK and efficacy of daytime dosing

STUDY DESIGN: RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, CROSS-OVER STUDY
N = ~15 PARTICIPANTS



KEY QUESTION:
Is there a dose that enables reduction in tremor without somnolence or sedation?

TOPLINE DATA:
2H2022

EPILEPSY

PRAX-562 (DEEs)

PRAX-222 (SCN2A-GOF ASO)

PRAX-020 (KCNT1)

PRAX-628 (Focal Epilepsy)

PRAX-100 (SCN2A-LOF ASO)

PRAX-090 (SYNGAP1 ASO)

PRAX-080 (PCDH19 ASO)

PRAX-030 (Undisclosed)

KEY UPCOMING MILESTONES

2Q 2022
PRAX-562 Ph 1 ASSR Biomarker Topline

2H 2022
Initiate PRAX-562 Ph 2 DEE Trial

2H 2022
Initiate PRAX-222 Seamless SCN2A-DEE Trial

4Q 2022
Initiate PRAX-628 Ph 1 Trial

TARGETS IDENTIFIED THROUGH
GENETICS

Three key imperatives guide our epilepsy portfolio build

Focus on nodes of pathophysiological convergence informed by genetics

- **PRAX-562** *SMALL MOLECULE*
- **PRAX-628** *SMALL MOLECULE*

Focus directly on underlying genetic defects in rare epilepsy

- **PRAX-222*** *ASO*
- **KCNT1 INHIB.** *SMALL MOLECULE*
- **PCDH19*** *ASO*
- **SYNGAP1*** *ASO*
- **SCN2A-LOF *** *ASO*
- **PRAXIS-030** *SMALL MOLECULE*

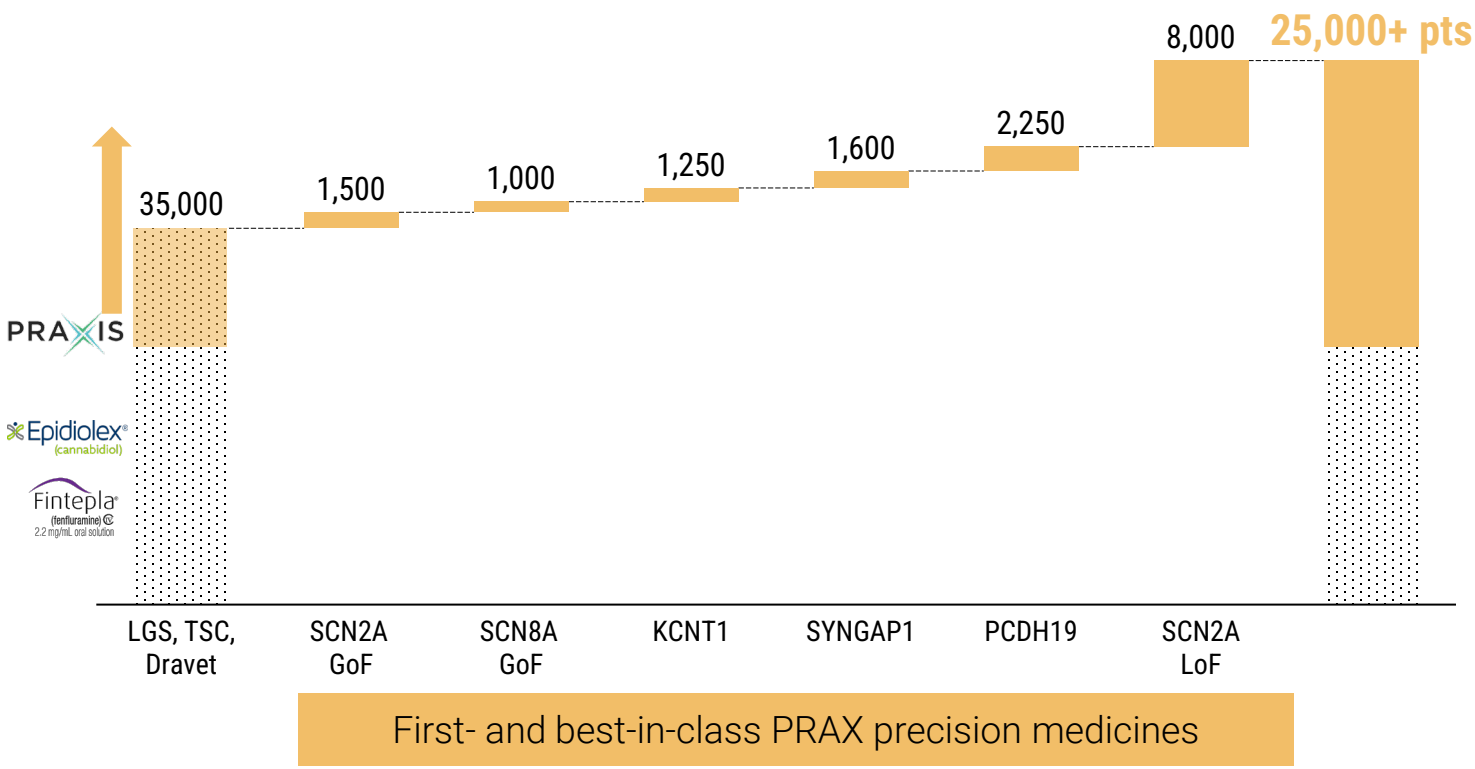
Focus on implicated genes in common diseases

- **PRAX-114** *SMALL MOLECULE*
- **PRAX-944** *SMALL MOLECULE*
- **TARGET ID BY POLYGENIC RISK VARIANTS** *SMALL MOLECULE*

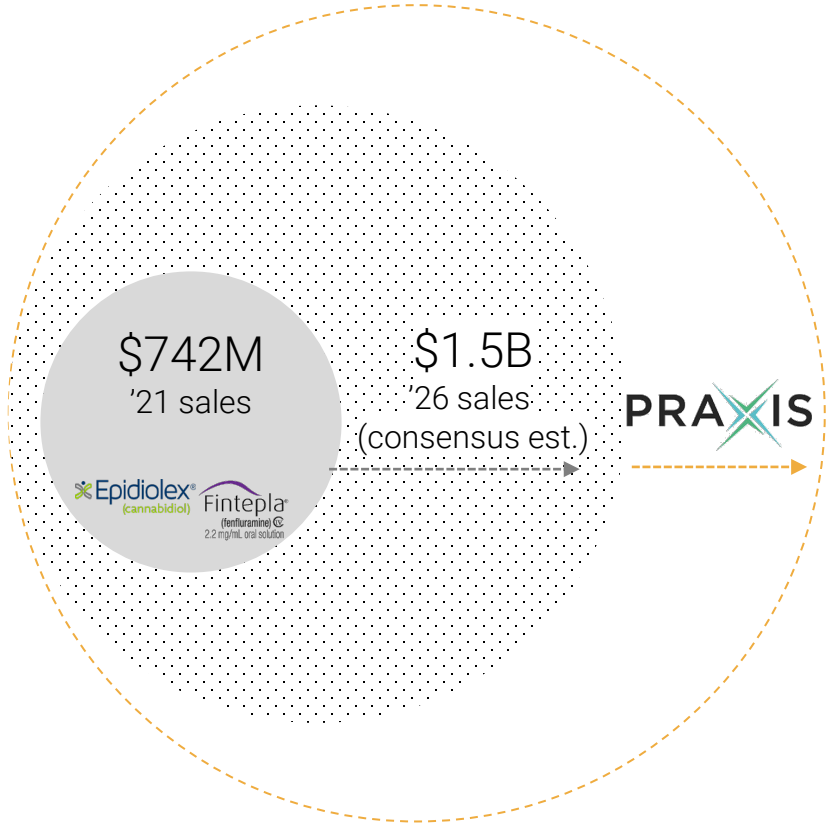
*PRAX-222 in collaboration with Ionis Pharmaceuticals, Inc. and RogCon, Inc.. PCDH19 (PRAX-080), SYNGAP1(PRAX-090), SCN2A-LOF(PRAX-100) ASOs are a collaboration with The Florey Institute of Neuroscience and Mental Health.

Delivering first and best-in-class precision medicines for 25,000+ rare epilepsy patients

U.S. Diagnosed Prevalence for Rare Epilepsy Programs
(patients ≤20 years of age)



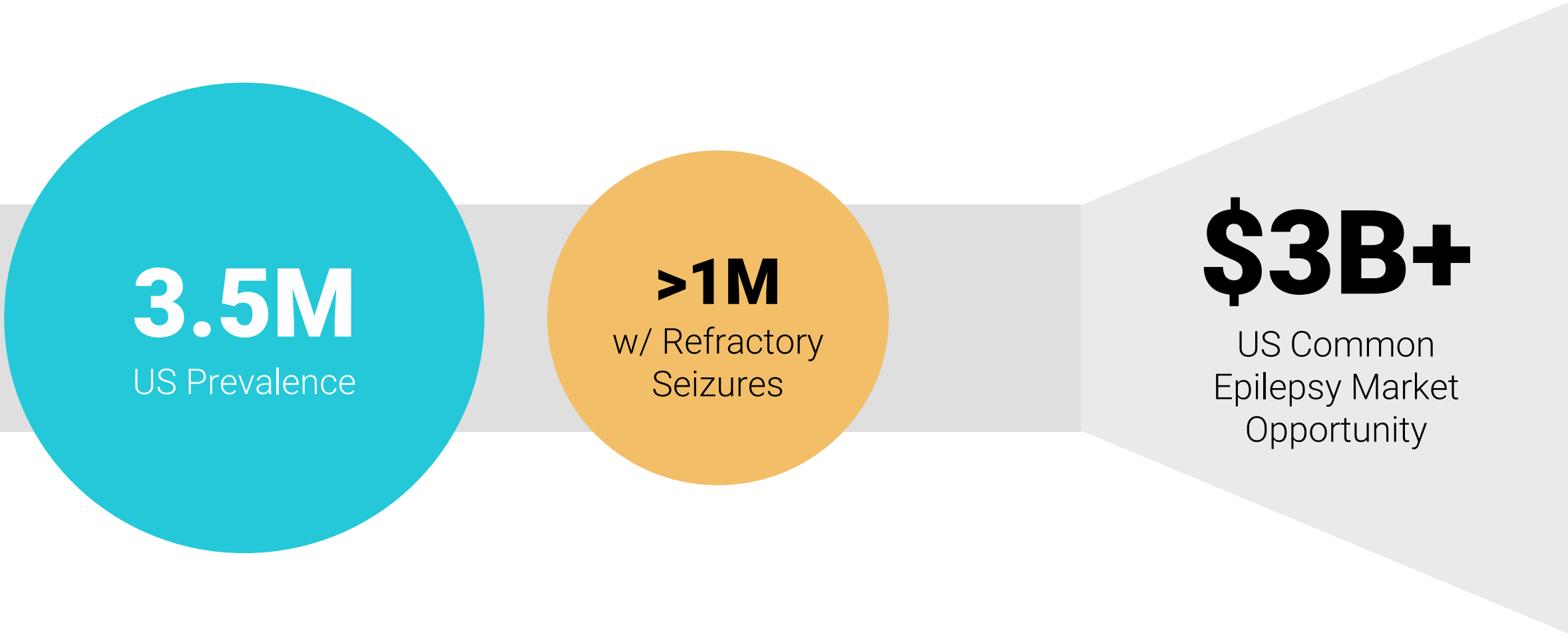
U.S. Market Size



LGS: Lennox-Gastaut Syndrome; TSC: Tuberous Sclerosis Complex

Source: Ambit Genetic Testing and Claims Data Analysis; EvaluatePharma; Sanders S. J. *et al. Trends Neurosci.* (2018); Wolff M. *et al* Brain (2017);

We aim to address unmet need in the $3B+ US common epilepsy market



Source: CDC, EvaluatePharma; Tang F. et al. Front. Neurol. (2017)

Preclinical and emerging clinical data demonstrate PRAX-562 will be a first- and best-in-class NaV blocker for DEEs

PRAX-562

SCN2A, SCN8A, TSC,
+ OTHER DEEs
PAN-NA_V BLOCKER
SMALL MOLECULE

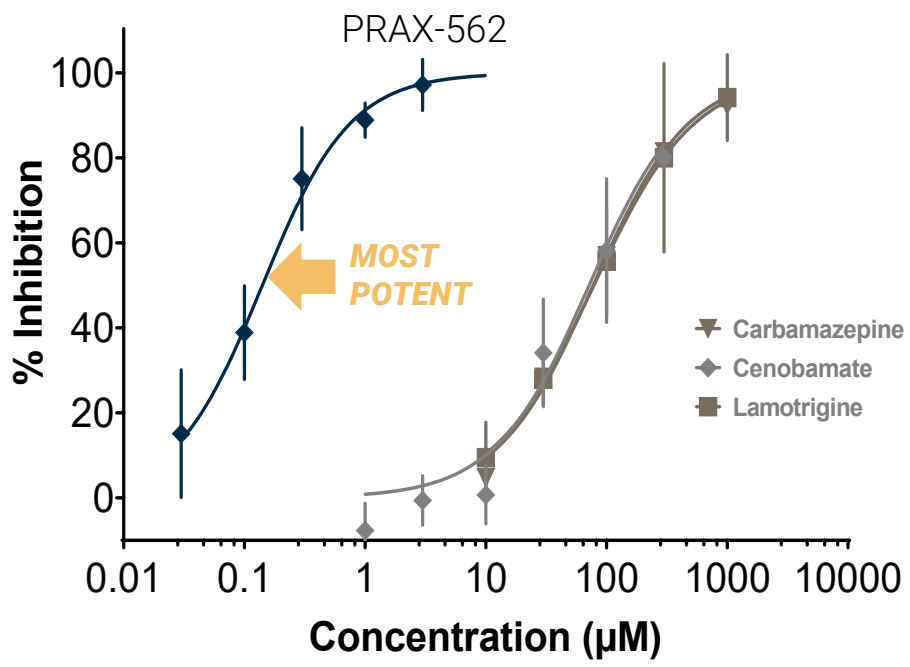
Superior selectivity for disease-state Na_V channel hyperexcitability

Unprecedented therapeutic window translating to superior safety and efficacy

Convenient auto-titration regimen with stable PK

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

% INHIBITION OF hNa$_V$1.6 PERSISTENT I$_{Na}$ (SAME DATA AS ON PRIOR SLIDE)



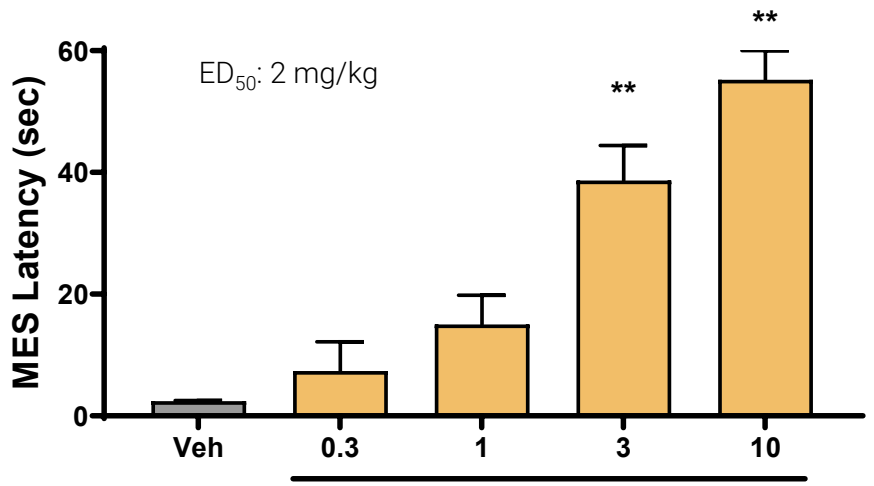
COMPARISON OF POTENCY AND SELECTIVITY

	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	

*solubility concerns

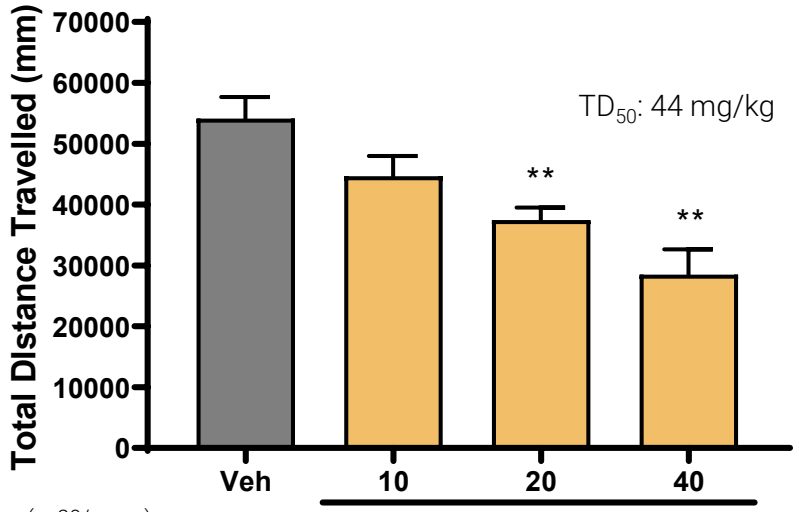
Our mechanistic hypothesis translates to a wide therapeutic index in vivo

MES EFFICACY



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

sLMA TOLERABILITY



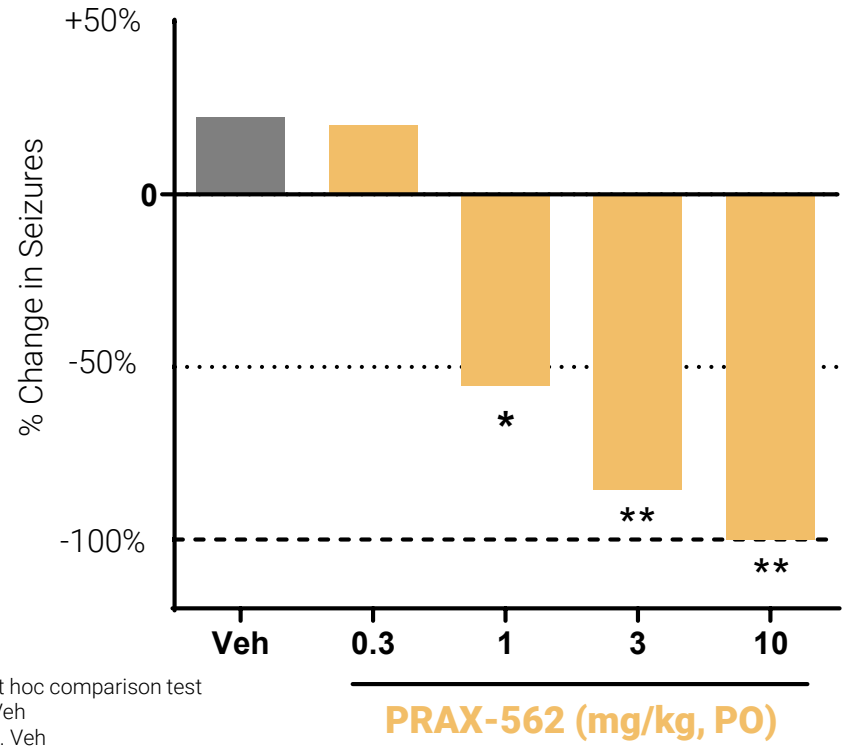
CD-1 mice; (n=20/group)
ANOVA/Dunnett
**p<0.01 vs. Veh

Molecule	Plasma Therapeutic Index
PRAX-562	17.2x

Therapeutic Index (TI) = TC50 / EC50

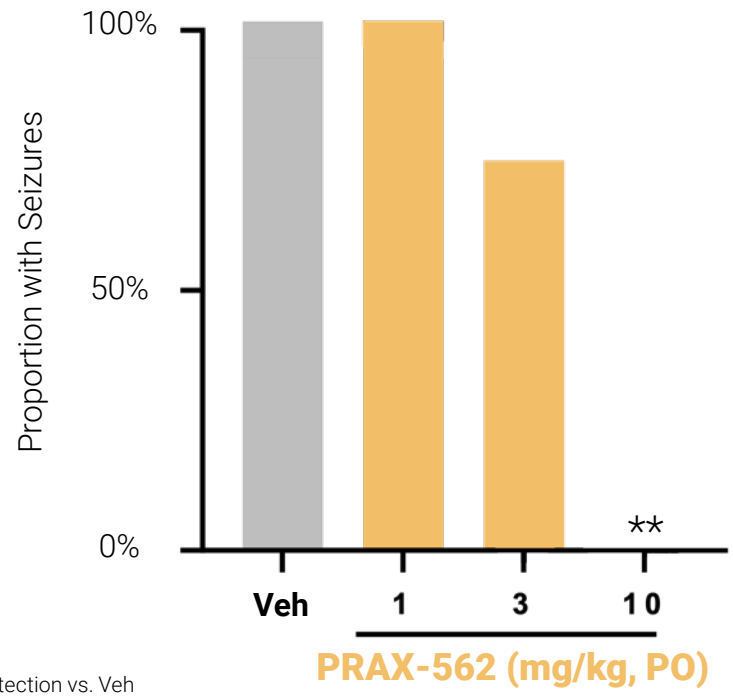
PRAX-562 completely blocks seizures in SCN2A and SCN8A GoF mutation mouse models

IN VIVO POC IN SCN2A SPONTAEOUS 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

Three epilepsy drugs in clinic by end of 2022

PRAX-222
(SCN2A)

Initiate Seamless Study: 2H22*

PRAX-562
(SCN2A, SCN8A, TSC)

Initiate Phase 2 Study: 2H22

PRAX-628
(FOCAL EPILEPSY)

Initiate Phase 1 Study: 4Q22

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

PRAXIS


PRAXIS
DARE for MORE™