



PRA~~X~~IS

**Movement
Disorder Day**

FRIDAY, DECEMBER 17, 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 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 Praxis’ 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, 2020, our Quarterly Reports on Form 10-Q and our 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.

PRAXIS 2021 MOVEMENT DISORDER DAY

DECEMBER 17, 2021

- Praxis - A Leader in CNS & Movement Disorders
- Essential Tremor (ET) - More Than Tremor
- Daring for More for People Living with ET
- Daring for More Beyond ET
- Praxis - The Year Ahead
- Q&A

Today's Speakers



MARCIO SOUZA

President &
Chief Executive Officer



NICOLE SWEENY

Chief Commercial Officer



BERNARD RAVINA

Chief Medical Officer



TIM KELLY

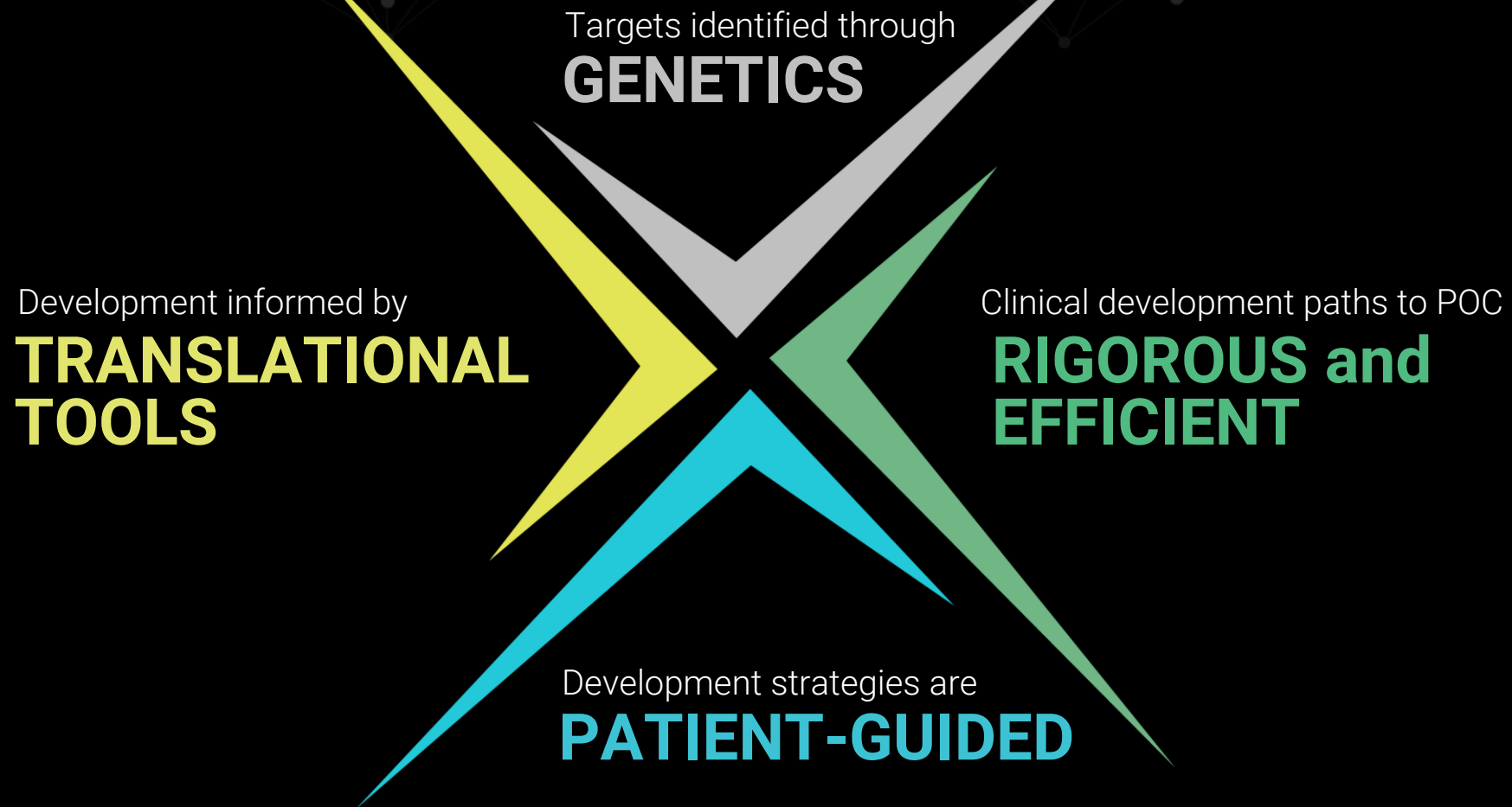
Chief Financial Officer



Praxis – A Leader in CNS and Movement Disorders

The needs of patients with CNS disorders are devastatingly urgent. Our **mission** is to help patients by delivering life-altering treatments faster and more effectively than has ever been done before – and to do it again and again.

Praxis is built on four key pillars



THREE DISTINCT FRANCHISES PRIMED FOR GROWTH IN 2022

PSYCHIATRY

**MOVEMENT
DISORDERS**

RARE DISEASE

2020
EXPLORATION

2021
MATURATION

2022
GROWTH

PSYCHIATRY

PRAX-114
MDD
Ph 2a

PRAX-114
MDD
Ph 2a

PRAX-114
MDD
Ph 2/3

PRAX-114
PTSD
Ph 2

PRAX-114
MDD
Ph 2/3

PRAX-114
MDD
Ph 3

PRAX-114
PTSD
Ph 2

>\$1B
Potential Revenue

MOVEMENT DISORDERS

PRAX-944
ET
Ph 2a

PRAX-944
ET
Ph 2a

PRAX-944
ET Essential1
Ph 2b

PRAX-944
ET
Ph 2a

PRAX-944
ET Essential1
Ph 2b

PRAX-944
PD
Ph 2

PRAX-114
ET
Ph 2

>\$1B
Potential Revenue

RARE DISEASES

PRAX-562
Ph 1

PRAX-222
Preclinical

KCNT1
Discovery

PRAX-562
Ph 1

PRAX-562
Ph 2 SUNCT/
SUNA/TN

PRAX-222
Preclinical

SCN2A
LOF

PCDH19

KCNT1
Discovery

SYNGAP1

PRAX-562
Ph 2 SUNCT/
SUNA/TN

PRAX-222
SCN2A-DEE
Ph 1/2/3

PCDH19

SCN2A
LOF

SYNGAP1

PRAX-562
Ph 2
DEE

KCNT1
Preclinical

>\$1B
Potential Revenue

Movement Disorder franchise focus for 2022

PRAX-944:

for Essential Tremor

Identify dose for
registrational study

Essential1 Study
Topline Data: 2H2022

PRAX-114:

for Essential Tremor

Demonstrate well-
tolerated GABA_A-PAM
with daytime dosing

Ph2 Study
Topline Data: 2H2022

PRAX-944:


for Parkinson's disease

Demonstrate motor
improvement

Initiate Ph2 Study
1H2022



Essential Tremor (ET) – More Than Tremor



0

Medications developed specifically for Essential Tremor patients



1

Medication approved for Essential Tremor over 50 years ago based on a 2-week study of nine patients



7

Million people in the US with daily symptoms of Essential Tremor need better and more options

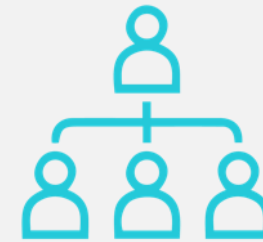
A dark teal background with a faint, light-colored network of interconnected nodes and lines, resembling a molecular or data structure.

DARE *for* MORE

Why Essential Tremor matters



Most common movement disorder ~7x the prevalence of Parkinson's disease¹



~ 50% of patients have a family history^{2,3}



Daytime action tremor that primarily affects the hands^{3,4}



Heterogeneous condition with progressive disability³

ET burden of disease extends beyond the tremor



Social

embarrassed by their
tremor^{1,2}



Self

feel negative about
themselves¹



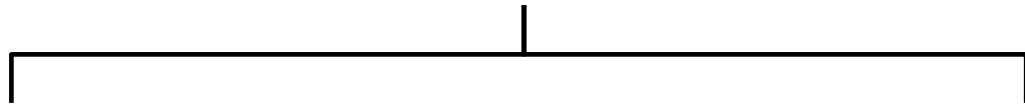
Mood

symptoms of social isolation,
depression, and anxiety¹⁻⁵

Current management of ET is based on trial and error



Pharmacologic initiation



As needed

OR



Chronic

PHARMACOLOGIC TREATMENT IS DETERMINED BY:

- severity of tremor
- body part affected
- occupation of the patient
- degree of disability
- comorbidities

As needed treatment options offer minimal utility

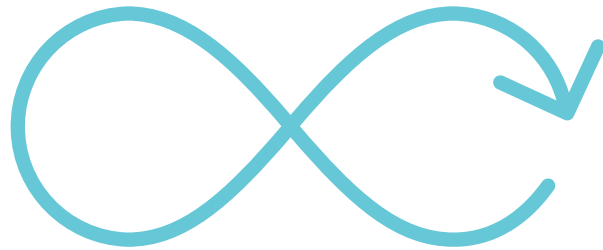


As needed

CURRENT MANAGEMENT

- Alcohol use 10-15 min before event
- Propranolol one hour before event

Chronic use options increase tolerability concerns



Chronic

CURRENT MANAGEMENT

- Propranolol
- Primidone
- Topiramate



What have we learned?

The ET market today: immediate addressable U.S. market

COMPREHENSIVE CLAIMS ANALYSIS 2019 SNAPSHOT

~1M patients
On-treatment

Patients are
coping with
Treatment Burden

~1M patients
Not on-treatment

Patients are
coping with
Disease Burden

Currently, there is an equilibrium between patients who discontinue treatment and those who initiate treatment

**Each year 200K patients
discontinue treatment**

~1M patients
On-treatment

~1M patients
Not on-treatment

Patients not on treatment could (re)join the on-treatment pool which increases treatment utilization



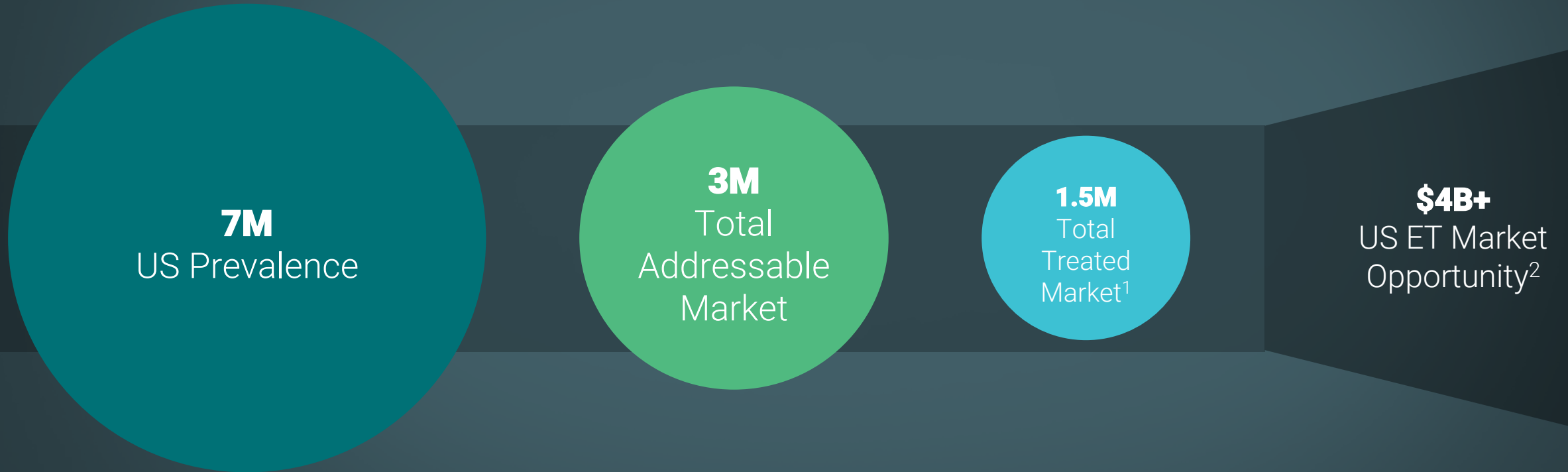
Newly diagnosed patients initiate treatment earlier which increases the total addressable patient market

**Potential to expand
on-treatment patients
to 2M**



**Each year 200K new
patients are diagnosed**

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



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 will allow patients to fit the right therapy to their needs to realize improved outcomes

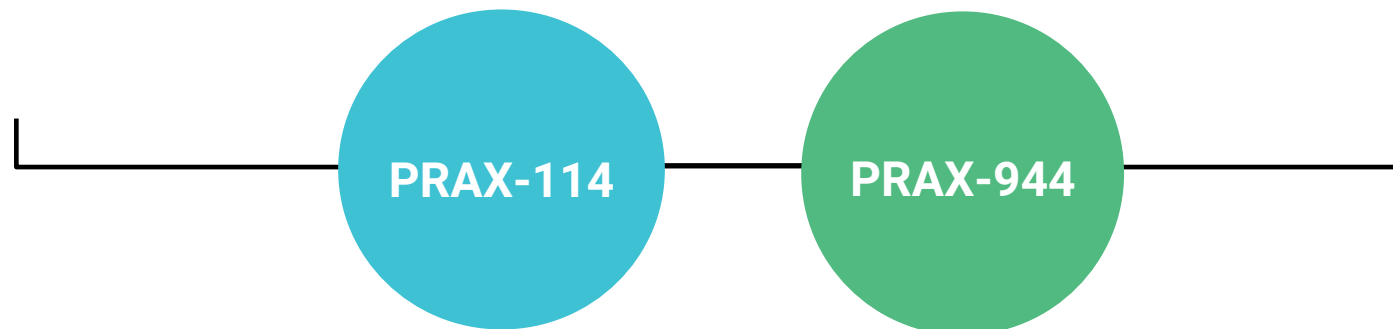


As needed

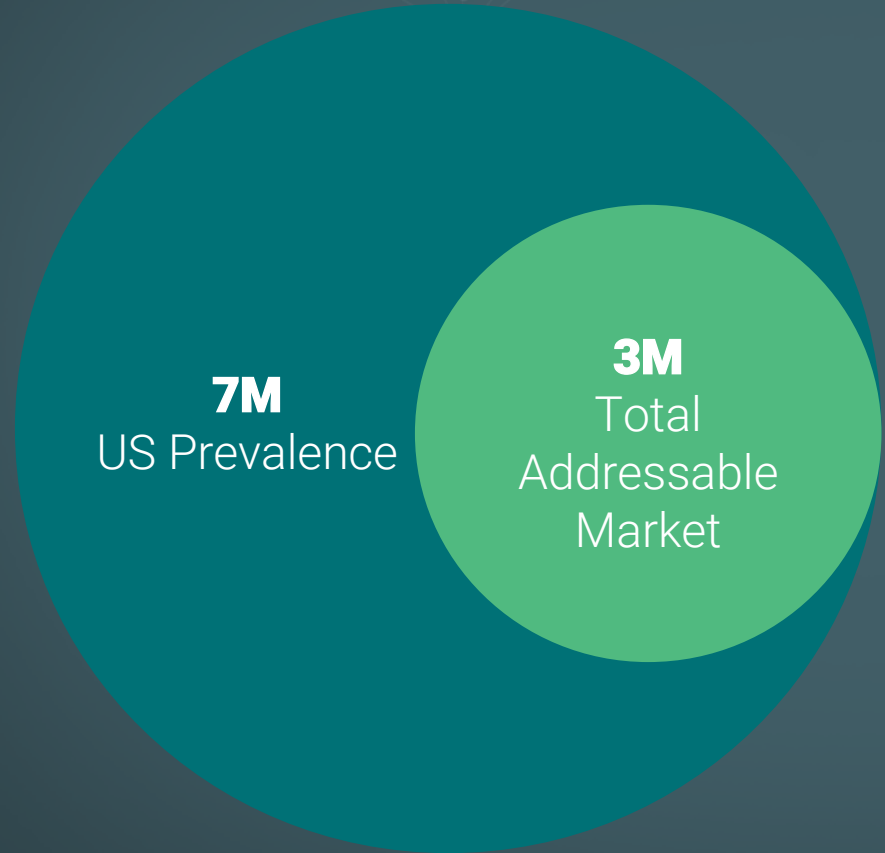


Chronic

- Patients will initiate ET treatment sooner
- Patients will treat as needed
- Patients will maintain ET therapy



Longer-term opportunity extends into capturing the undiagnosed



- Disease awareness
- Earlier adoption of treatment in disease course
- Access
- Multiple effective, well-tolerated therapies



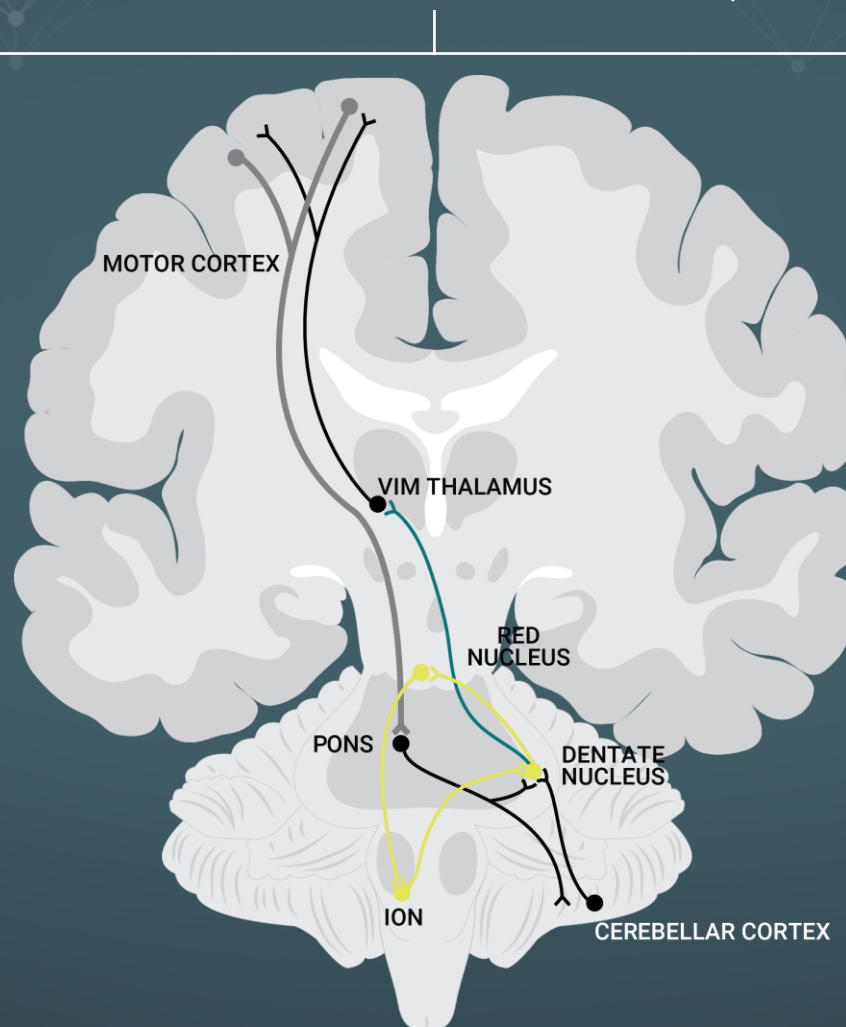
Daring for More for People Living with Essential Tremor

Tackling Movement Disorders through two mechanisms of action

CEREBELLO-THALAMO-CORTICAL (CTC) CIRCUIT

T-TYPE CALCIUM CHANNELS

PRAX-944



GABA_A RECEPTORS

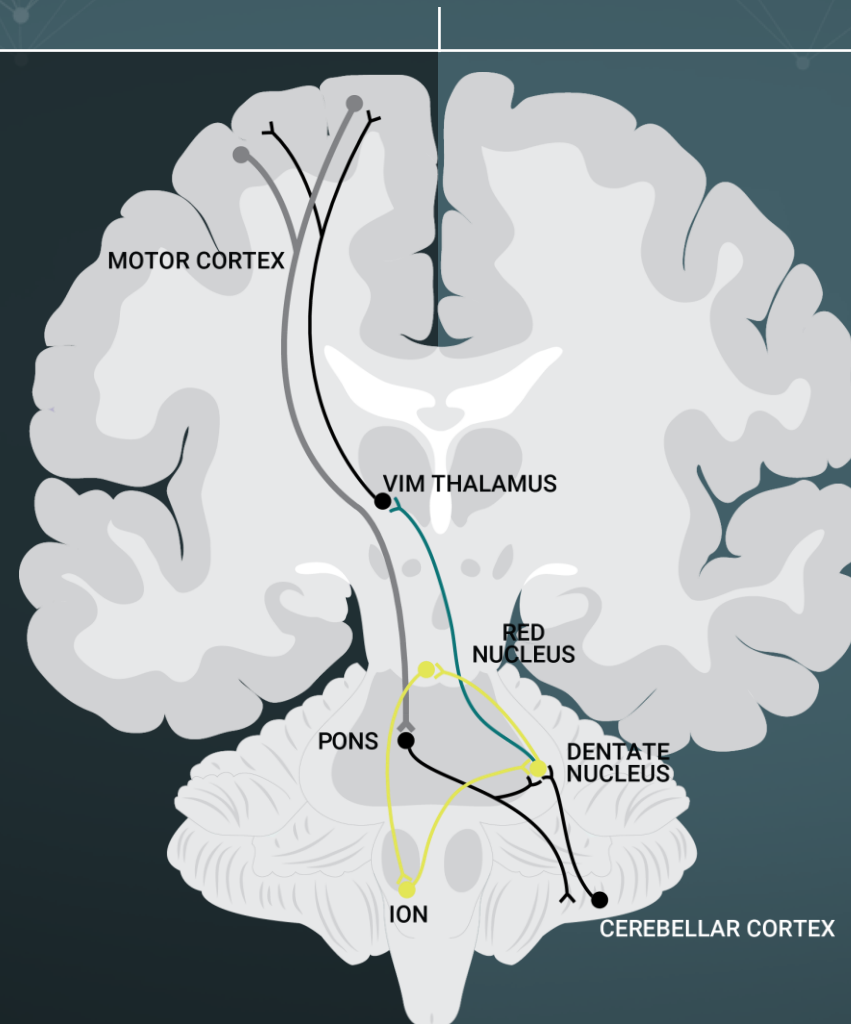
PRAX-114

Tackling Movement Disorders through two mechanisms of action

CEREBELLO-THALAMO-CORTICAL (CTC) CIRCUIT

T-TYPE CALCIUM CHANNELS

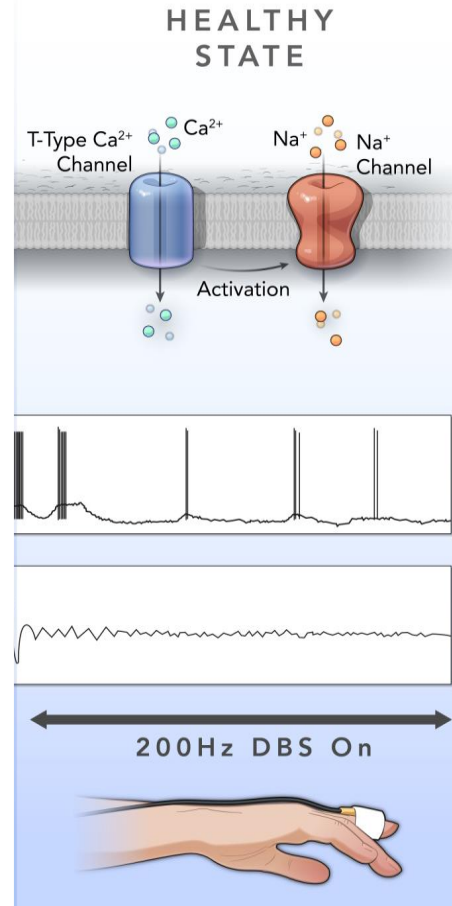
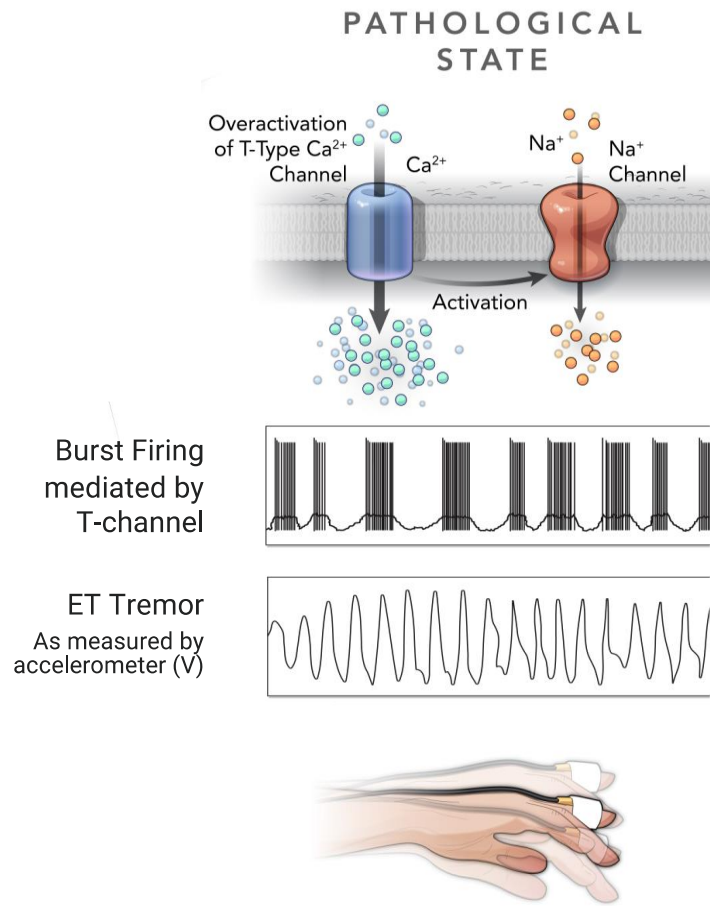
PRAX-944



GABA_A RECEPTORS

PRAX-114

T-Type calcium channels are gatekeepers of neuronal firing patterns in the CTC circuit



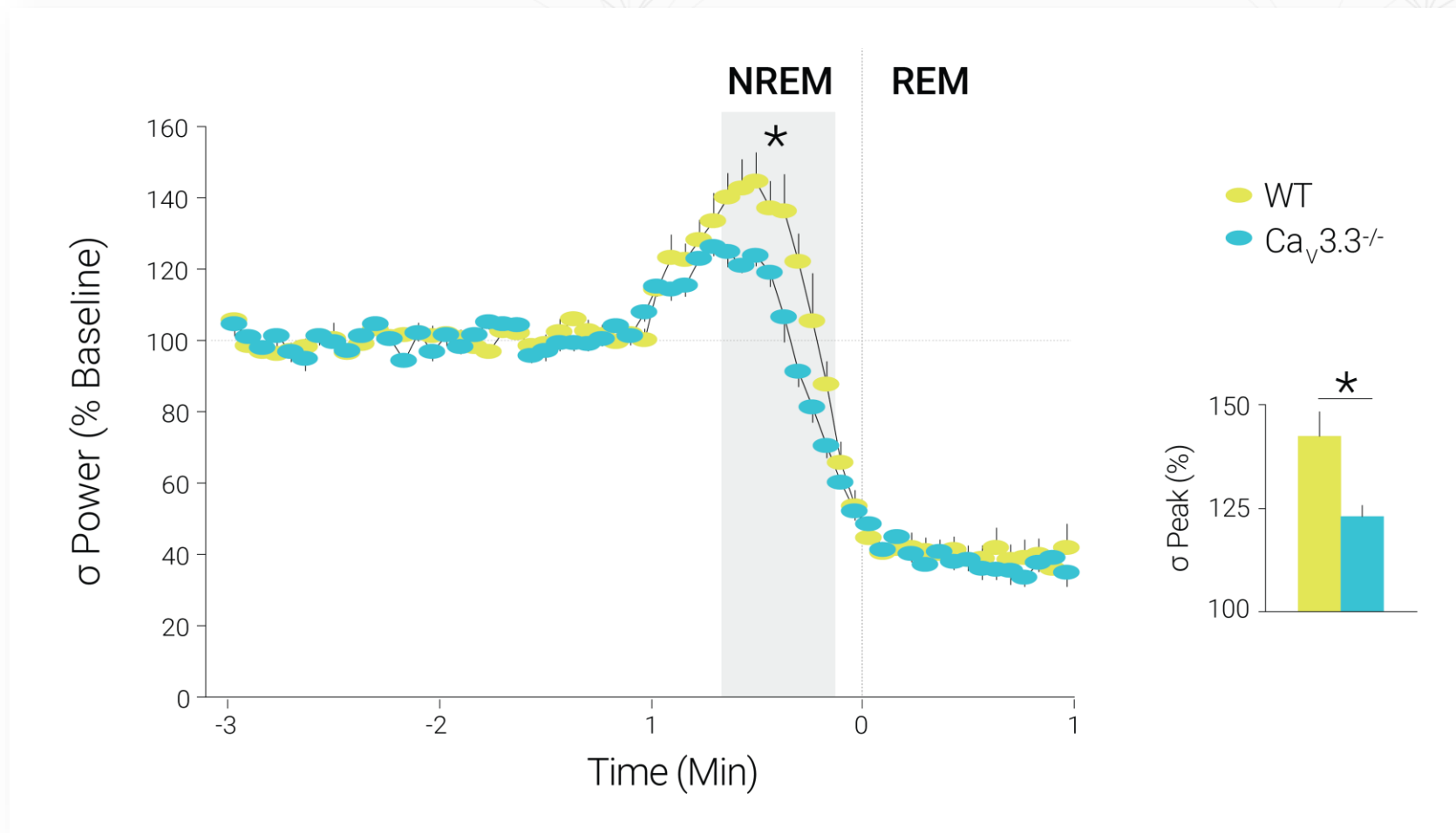
Mutations in T-type calcium channels (TTCC) are genetically linked to familial ET

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

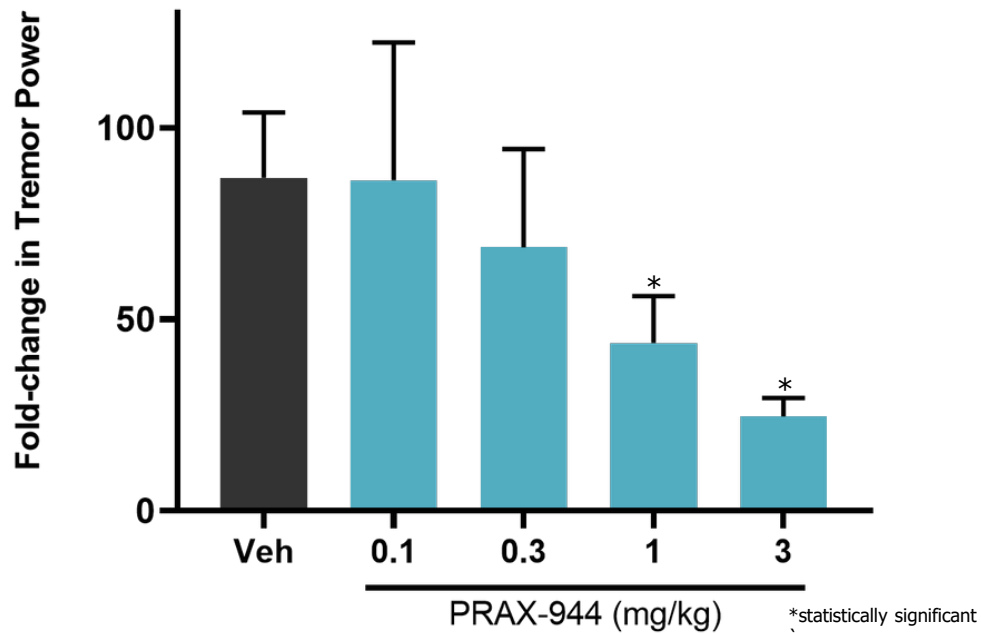
EEG biomarker of T-Type calcium channels: sigma frequency



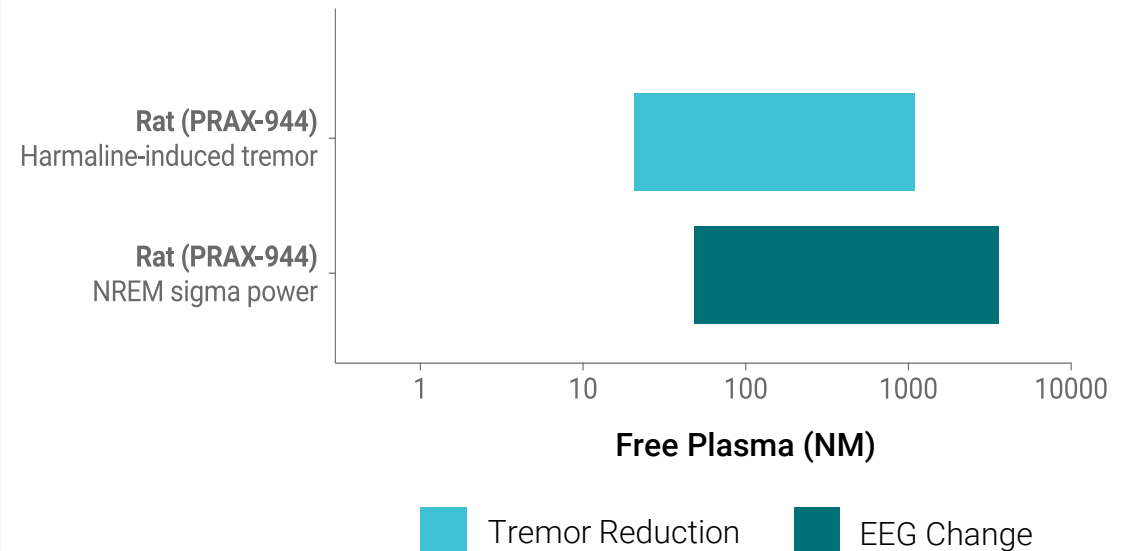
- Sigma frequency (10-14 Hz) occurs during NREM sleep
- Thought to be generated by thalamic-cortical pathways
- Reduced with Ca_v3.3 knock-out of T-type Calcium Channels

PRAX-944 dose-dependently reduced rat harmaline-induced tremor and sigma band EEG

Rat harmaline-induced tremor



Strong preclinical correlation between EEG change and tremor reduction



PRAX-944 is a differentiated, selective T-Type calcium channel blocker

**HIGHLY POTENT ON
ALL 3 ISOFORMS**

HIGHLY SELECTIVE

**NO ACTIVE
METABOLITES**

Extensive safety and PK data from > 165 Healthy Volunteers

Predictable PK

**Wide dosing range up to
120mg**

Flexibility in titration

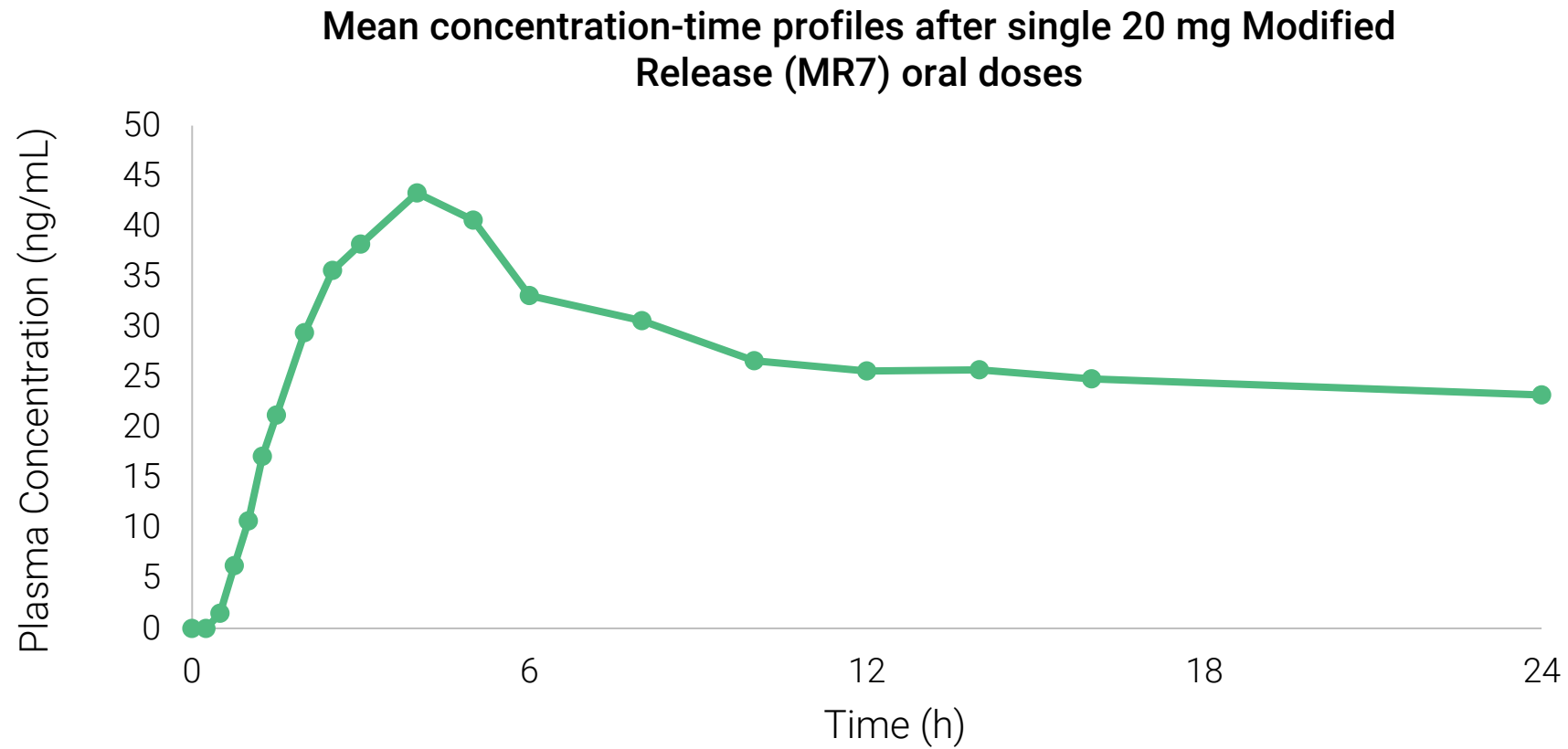
SAFETY SUMMARY

- Studied multiple IR, MR formulations
- Most common AEs included:
 - CNS: dizziness, headache, euphoric mood, illusion, disturbed attention
 - GI: nausea
- AEs generally transient and C_{Max} related

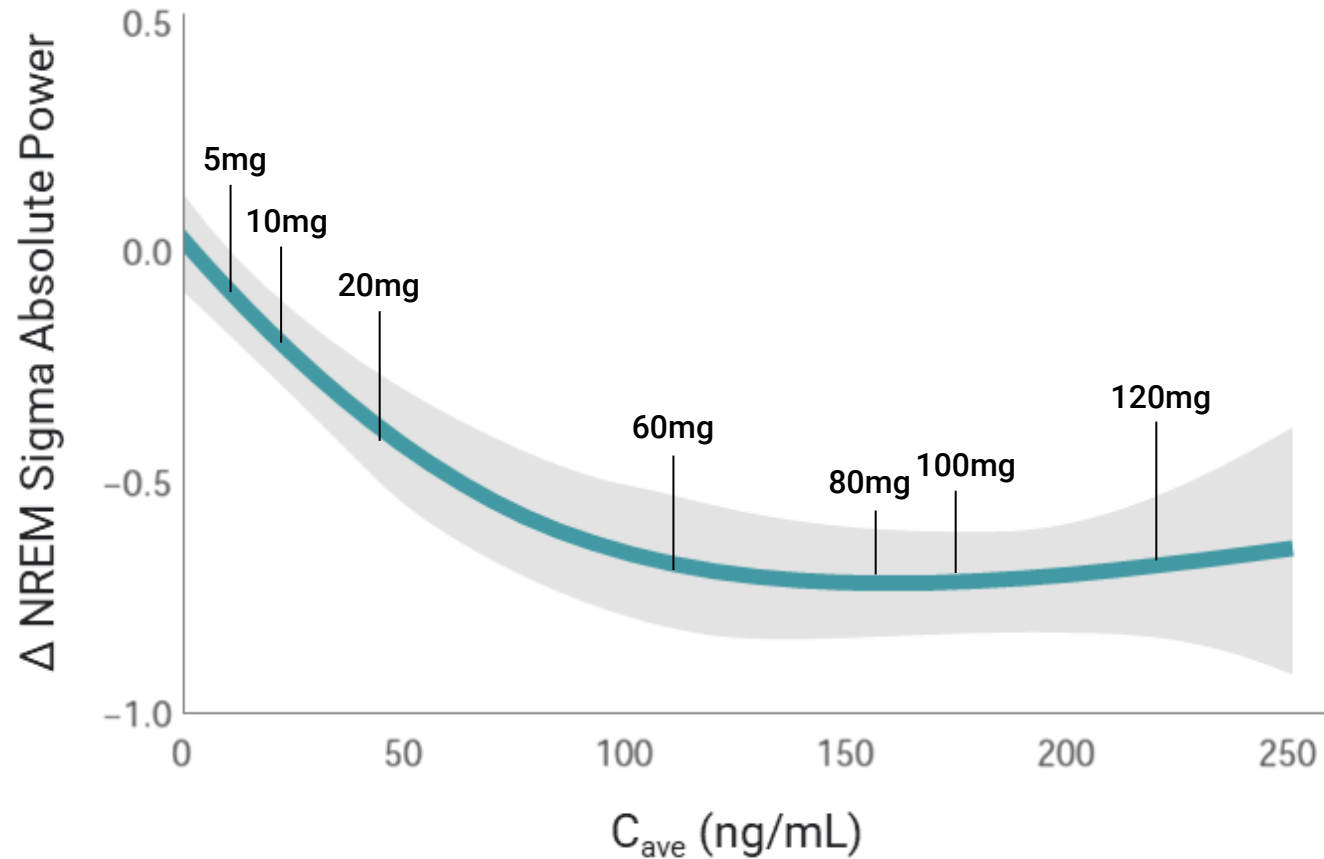
SAFETY SUMMARY – MR7 FORMULATION

- MR7 titrated to 120mg in HV
 - No MTD
 - No SAE
 - Most common CNS AEs: dizziness and headache

PRAX-944 modified release is optimized to enable once daily daytime dosing with a well-tolerated safety profile



PRAX-944 showed robust PK:PD relationship to guide dosing



KEY TAKEAWAYS

- Dose-dependent reduction in sigma-band power
- Effect observed over >20x dose range
- Provides confidence that PRAX-944 is reaching functionally relevant brain concentrations and targets

Key PRAX-944 development questions in ET

PRAX-944-221 **Phase 2a**

Tolerability of PRAX-944 in ET and sufficient evidence of effect

PRAX-944-222 **Phase 2b** **Essential1 Study**

Dose ranging safety, tolerability, and efficacy to support dose selection for Phase 3

PRAX-944 **Phase 3**

Demonstrate efficacy and safety for registration

Study 221 design

PART A



DAYS 1-14

Open-Label Titration
of PRAX-944 up to
40 mg

DAYS 15-21

Safety
Follow-
up

Part A data shared previously

PART B



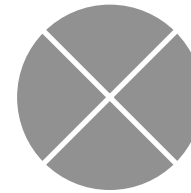
DAYS 1 -28

Open-Label Titration
of PRAX-944 up to
120 mg

DAYS 29-42

Stable Period
at High Dose

**1:1
RANDOMIZATION**



**RANDOMIZED WITHDRAWAL
(DAYS 43-56)**

PRAX-944

PLACEBO

DAYS 57-64

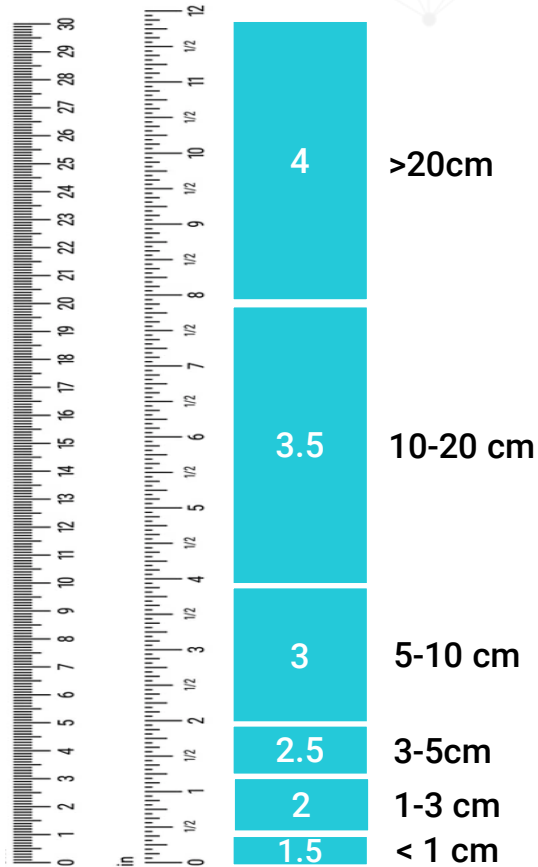
Safety
Follow-
up

**Preliminary data
shared today**

**Topline Results:
1H2022**

Examples of clinical measures used in Study 221

- TETRAS Upper Limb – Performance Scale



Barely Visible = 1
No Tremor = 0

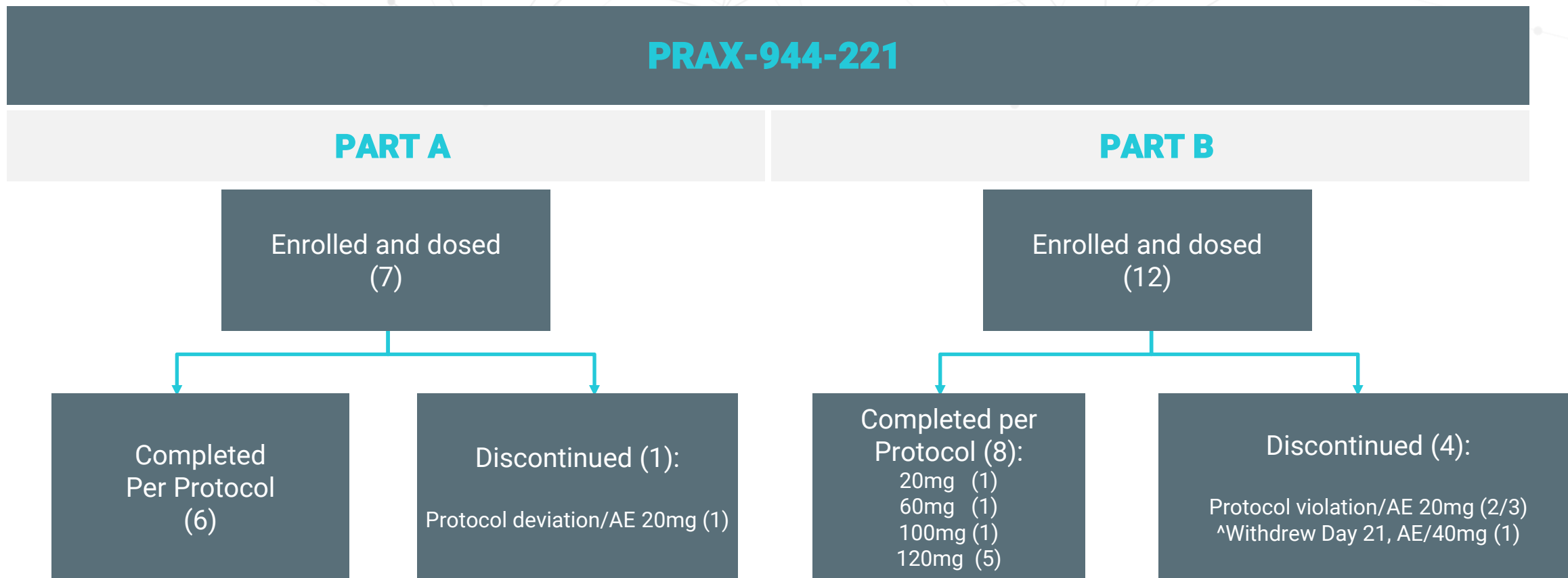
- TETRAS Activities of Daily Living (ADL)



POURING A GLASS OF WATER

4	Cannot pour
3	Must use two hands or use other strategies to avoid spilling
2	Must be very careful to avoid spilling, but may spill occasionally
1	Tremor is present but does not interfere with pouring
0	Normal

Current patient disposition



All discontinuations included in safety data set

^ Discontinuation with evaluable post dose efficacy

Study 221 demographics representative of the ET population

BASELINE DEMOGRAPHICS	PART A (N = 7)	PART B (N = 12)	OVERALL (N = 19)
Age, mean (range)	68 (58-75)	59 (43-75)	62 (43-75)
Disease Duration, mean (range)	42 (14-57)	32 (11-52)	36 (11-57)
Gender (Male/Female) (n, %)	5 / 2 (71%/29%)	11 / 1 (92%/8%)	16/3 (84%/16%)
# presently on Propranolol (n, %)	6 (86%)	2 (17%)	8 (42%)
# previously on ET medication (n, %)	3 (43%)	9 (75%)	12 (63%)
Family History – First-degree relative with ET (n, %)	2 (29%)	8 (67%)	10 (53%)
TETRAS Combined Upper Limb (CUL), mean (SD)	22.2 (4.5)	20.9 (5.5)	21.4 (5.1)
TETRAS ADL, mean (SD)	--	26.3 (3.5)	26.3 (3.5)
TETRAS Modified ADL, mean (SD)	--	16.2 (3.7)	16.2 (3.7)

TEAEs are mild to moderate and consistent with safety profile for the program

NUMBER OF PARTICIPANTS WITH CNS RELATED TREATMENT EMERGENT ADVERSE EVENTS *		
Preferred Term	Part A	Part B
Any TEAE**	6	10
Dizziness	4	3
Headache	3	1
Cognitive disorder		3
Fatigue		2
Insomnia		2
Paraesthesia		2

*Preferred terms reported by ≥ 2 ET participants in the OL period; all reported events to date have been mild to moderate in intensity

**Any participant who experienced a TEAE

TEAEs leading to dose down-titration or discontinuation were mild-moderate

TEAEs LEADING TO DOWN TITRATION IN 4 PARTICIPANTS*

Preferred Term	Part B
Confusional state	1
Disturbance in attention	1
Dizziness postural	1
Paraesthesia	1
Somnolence	1

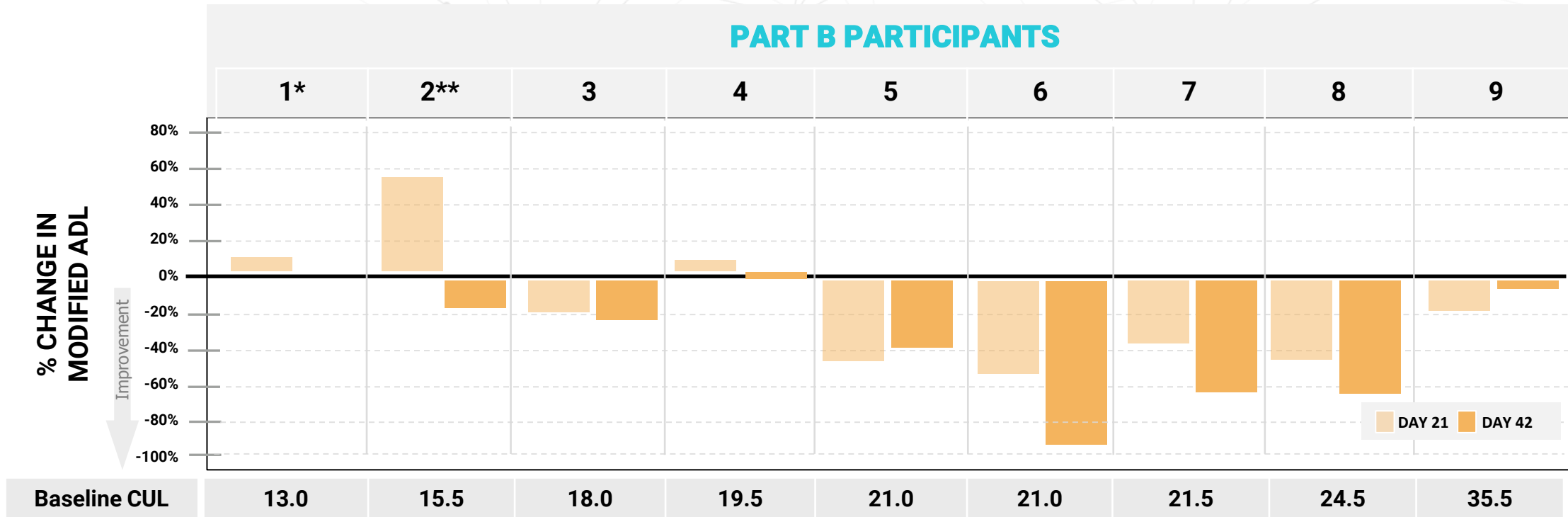
*Protocol permitted patients to dose titrate down once during Part B

TEAEs ASSOCIATED WITH STUDY DRUG DISCONTINUATION IN 5 PARTICIPANTS*

Preferred Term	Part A	Part B
Anxiety	1	
Cognitive disorder		2
Confusional state		1
Disturbance in attention		1
Dizziness		1
Hallucinations		1

*1 participant discontinued in Part A and 4 in Part B

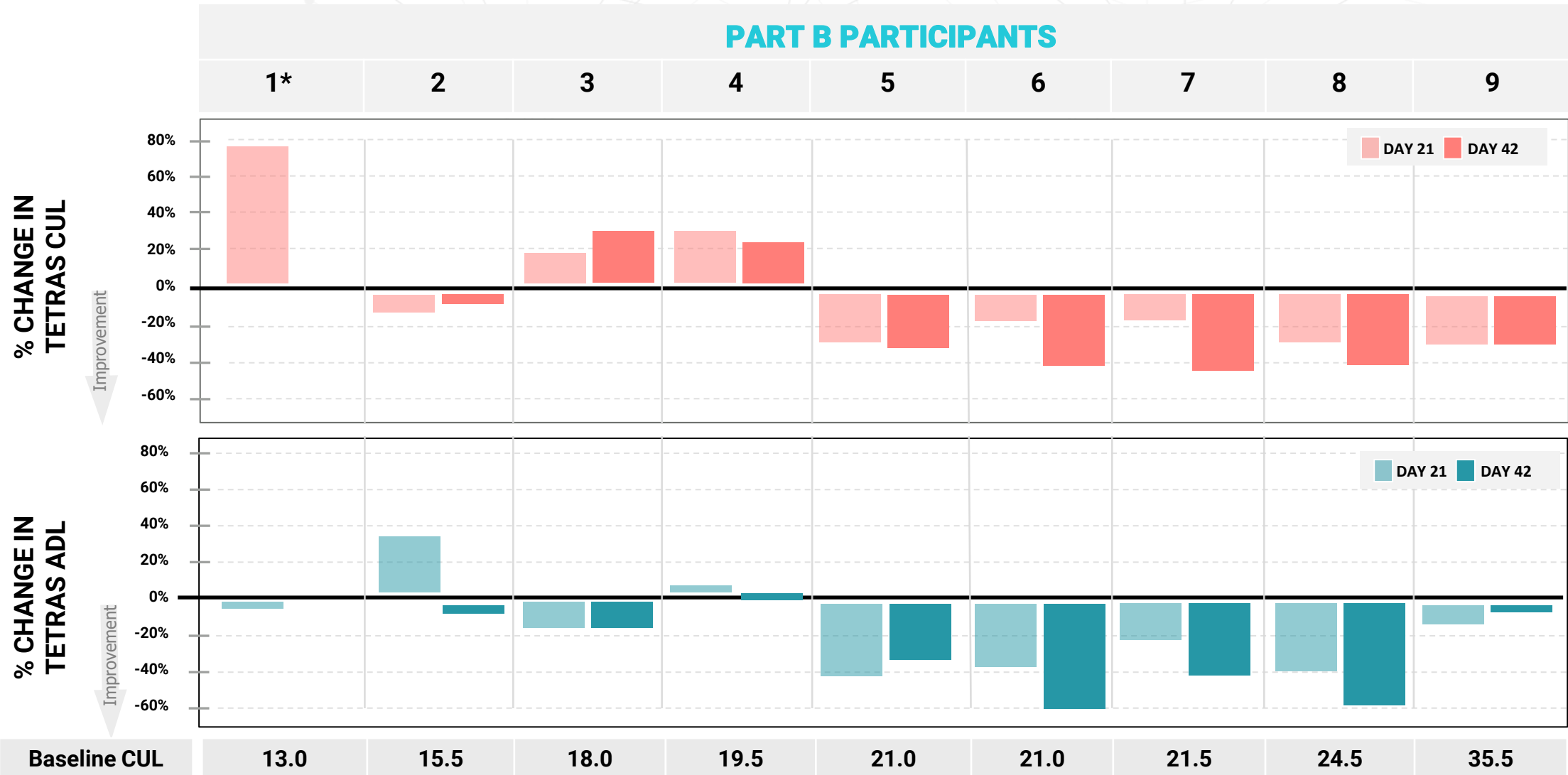
Preliminary Part B data: modified ADL by baseline CUL score



Modified ADL as suggested by FDA:

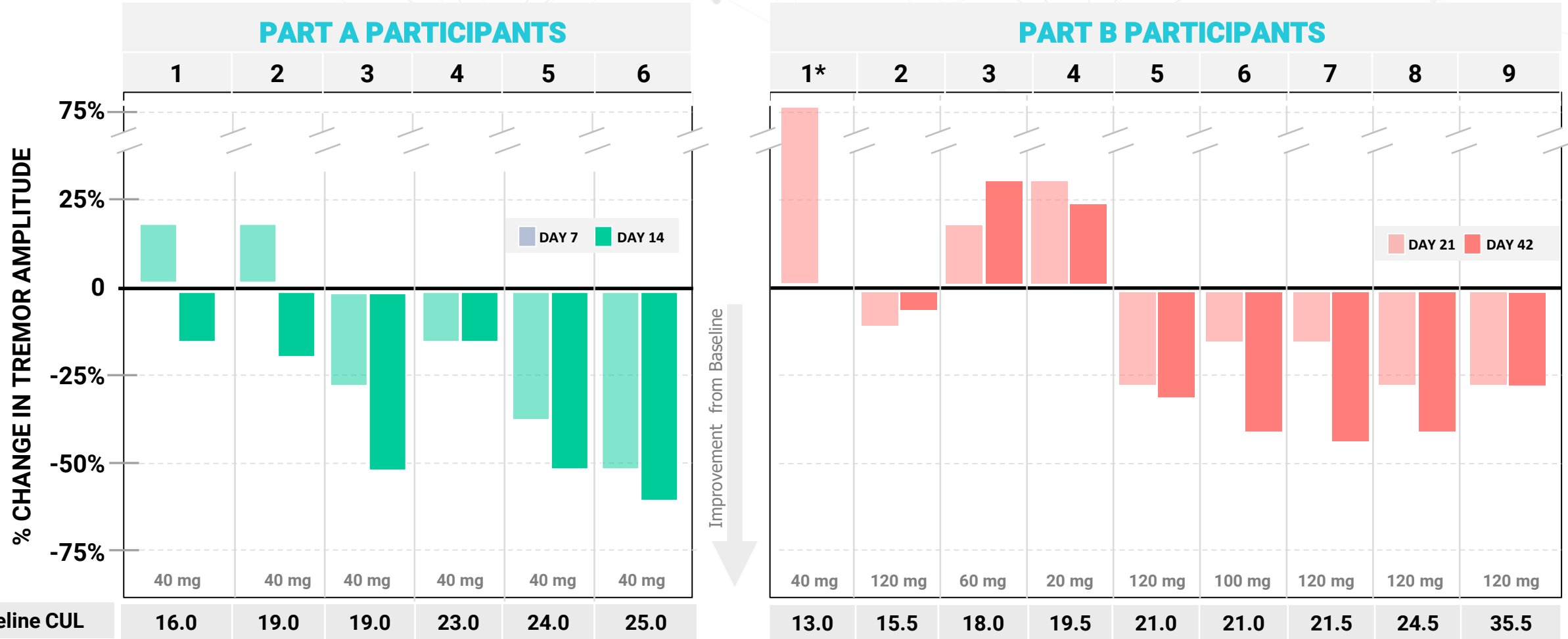
- Score of 1 re-coded as 0; highest score of 3
- Exclude social impact
- Include: handwriting and spirals

Preliminary Part B data: TETRAS CUL and TETRAS ADL



PRELIMINARY DATA AS OF 10-DEC-2021 CUTOFF; ONGOING CLINICALTRIALS.GOV/CT2/SHOW/NCT05021978
 *PART B PATIENT 1 DISCONTINUED AFTER DAY 21 ASSESSMENT.

Preliminary data: PRAX-944-221 TETRAS CUL



PRELIMINARY DATA AS OF 10-DEC-2021 CUTOFF; ONGOING CLINICALTRIALS.GOV/CT2/SHOW/NCT05021978

*PART B PATIENT 1 DISCONTINUED AFTER DAY21 ASSESSMENT; FINAL DOSE LEVEL NOTED IN CHART

Key learnings from Part A/Part B: implications to Essential1 and program

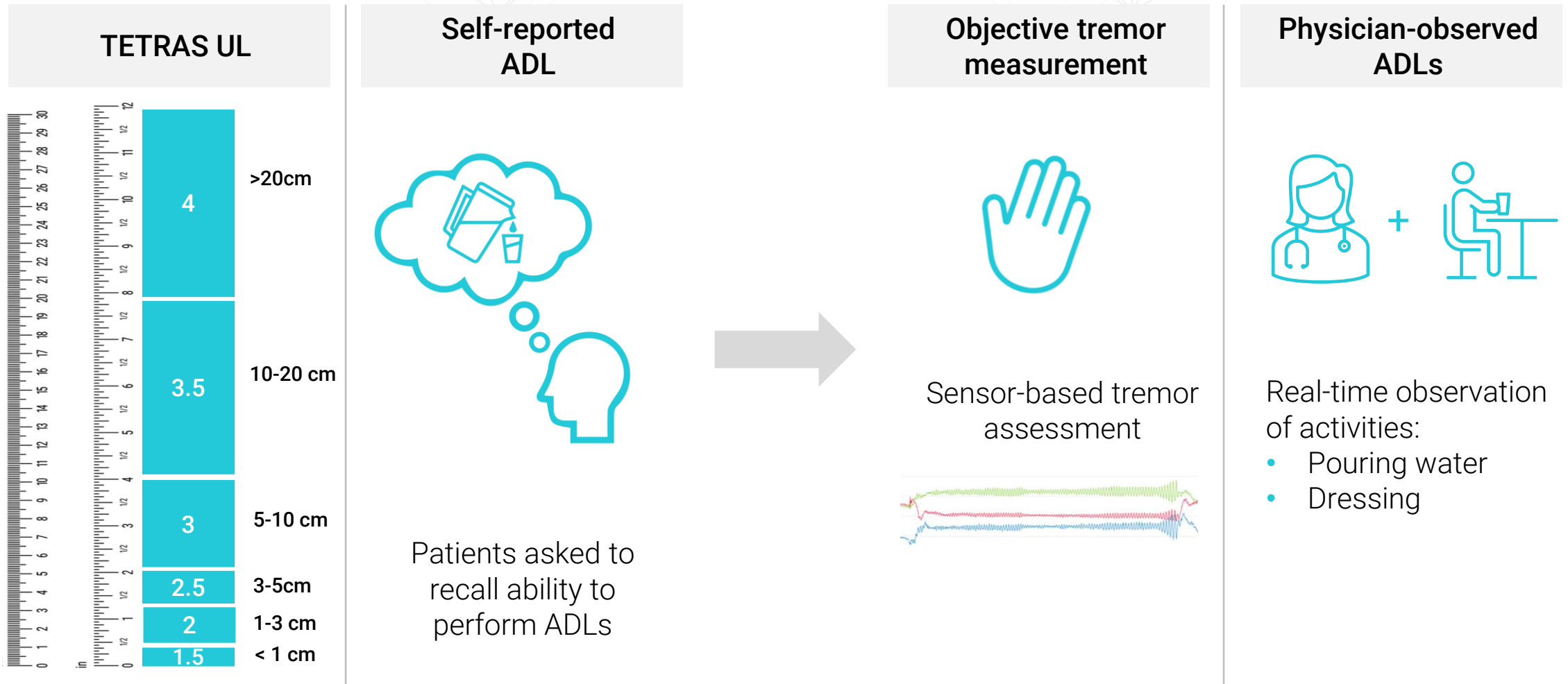
PRAX-944-221 Phase 2a Part B

- Safety and tolerability
- Efficacy: consistency, plausibility, magnitude, dose response

PRAX-944-222 Phase 2b Essential1 Study

- Titration: planning 5-100 mg, increase weekly
- Dose: parallel dose group
- Patient selection: baseline severity/variability
- Endpoint evolution

Moving towards more objective assessments for clinical endpoints



Barely Visible = 1
No Tremor = 0

We are testing innovative, objective ways of measuring tremor

Sensor Locations

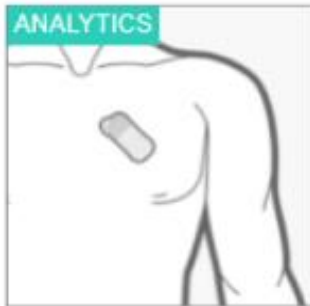


Dorsal Hand
Dominant Side

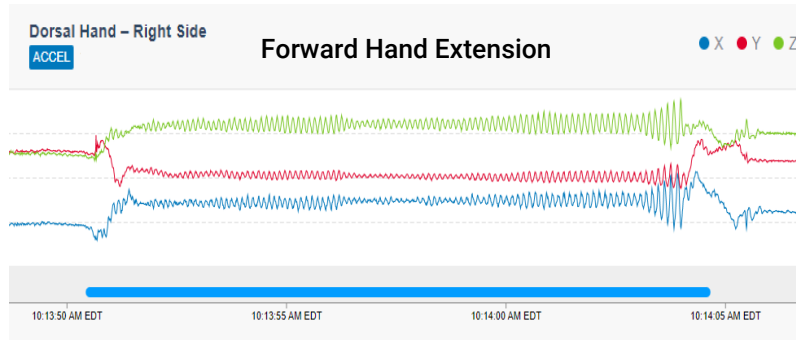
ACCEL



Anterior Thigh
Any Side



Heart II
No Side



Key PRAX-944 development questions in ET

PRAX-944-221
Phase 2a
Part B

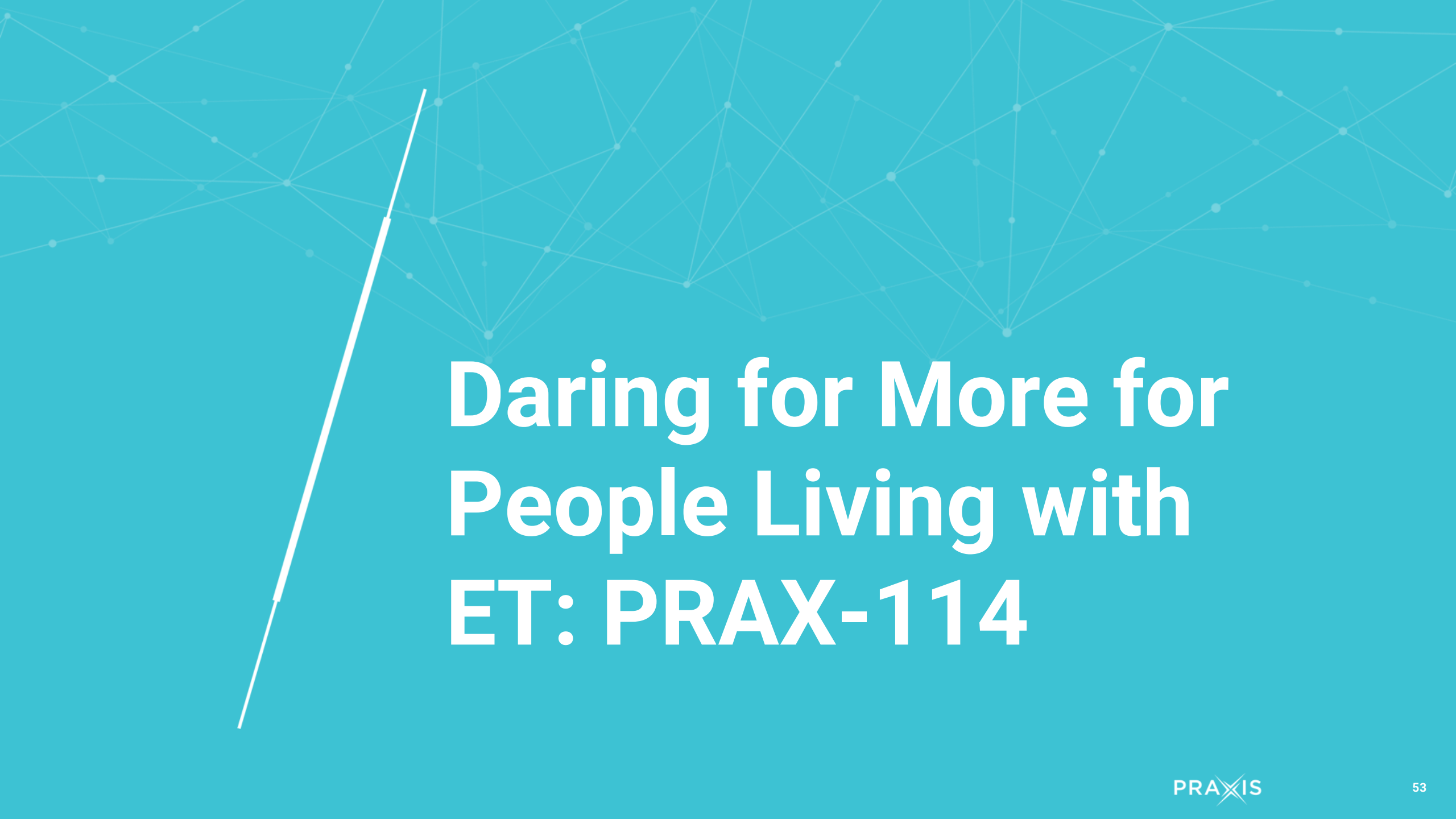
Tolerability of PRAX-944 in ET and sufficient evidence of effect

PRAX-944-222
Phase 2b
Essential1 Study

Dose ranging safety, tolerability, and efficacy to support dose selection for Phase 3

PRAX-944
Phase 3

Demonstrate efficacy and safety for registration



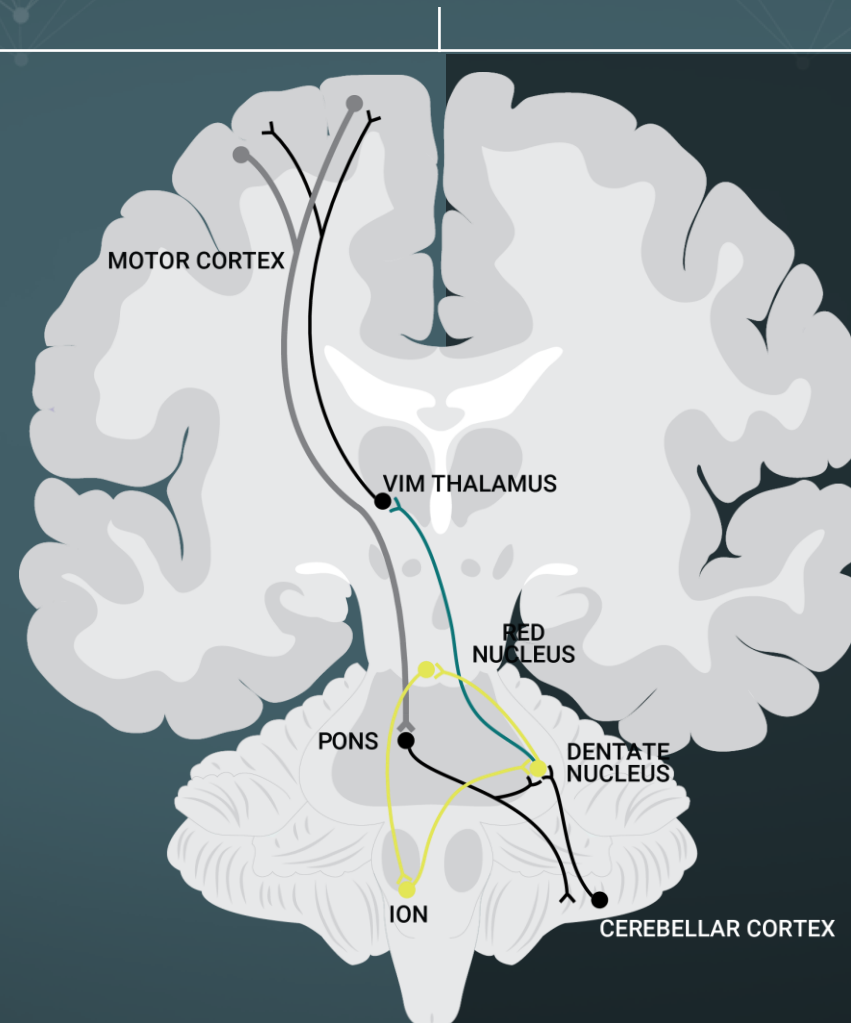
Daring for More for People Living with ET: PRAX-114

Tackling Movement Disorders through two neuronal systems

CEREBELLO-THALAMO-CORTICAL (CTC) CIRCUIT

T-TYPE CALCIUM CHANNELS

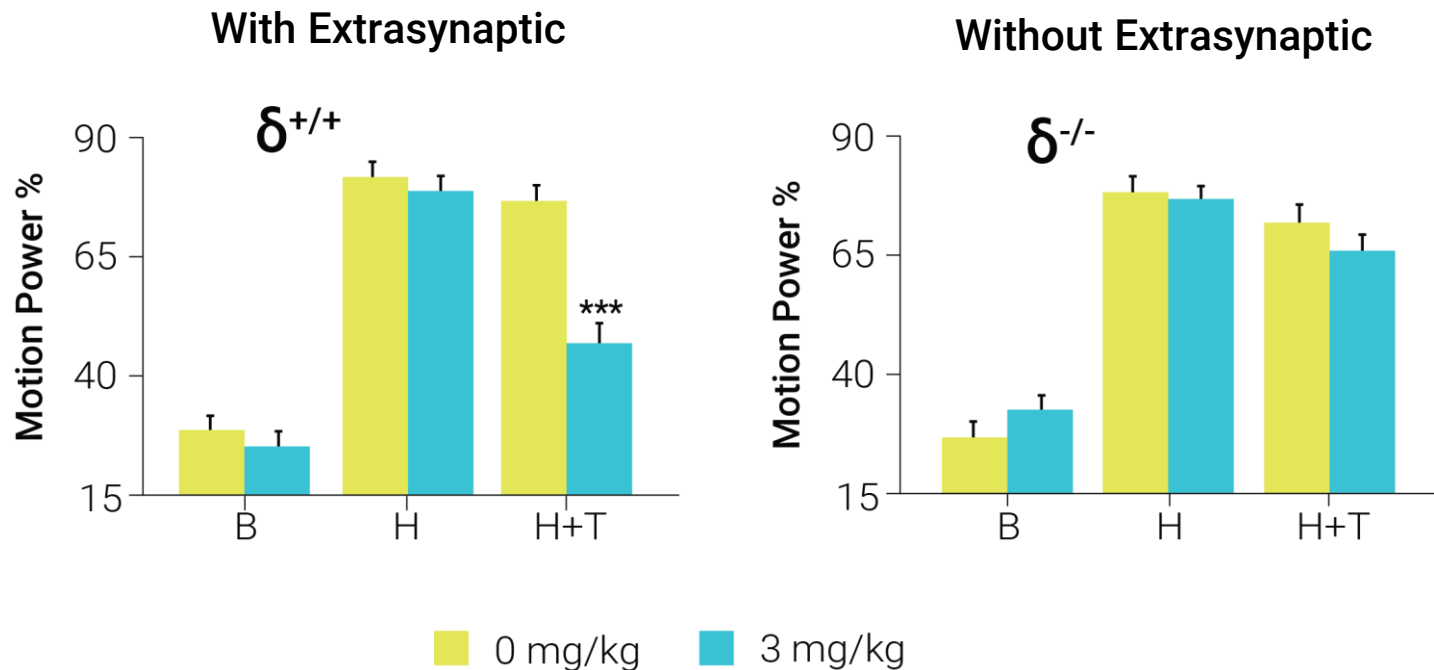
PRAX-944



GABA_A RECEPTORS

PRAX-114

Evidence suggests central role of extrasynaptic GABA_A receptors targeting tremor pathophysiology

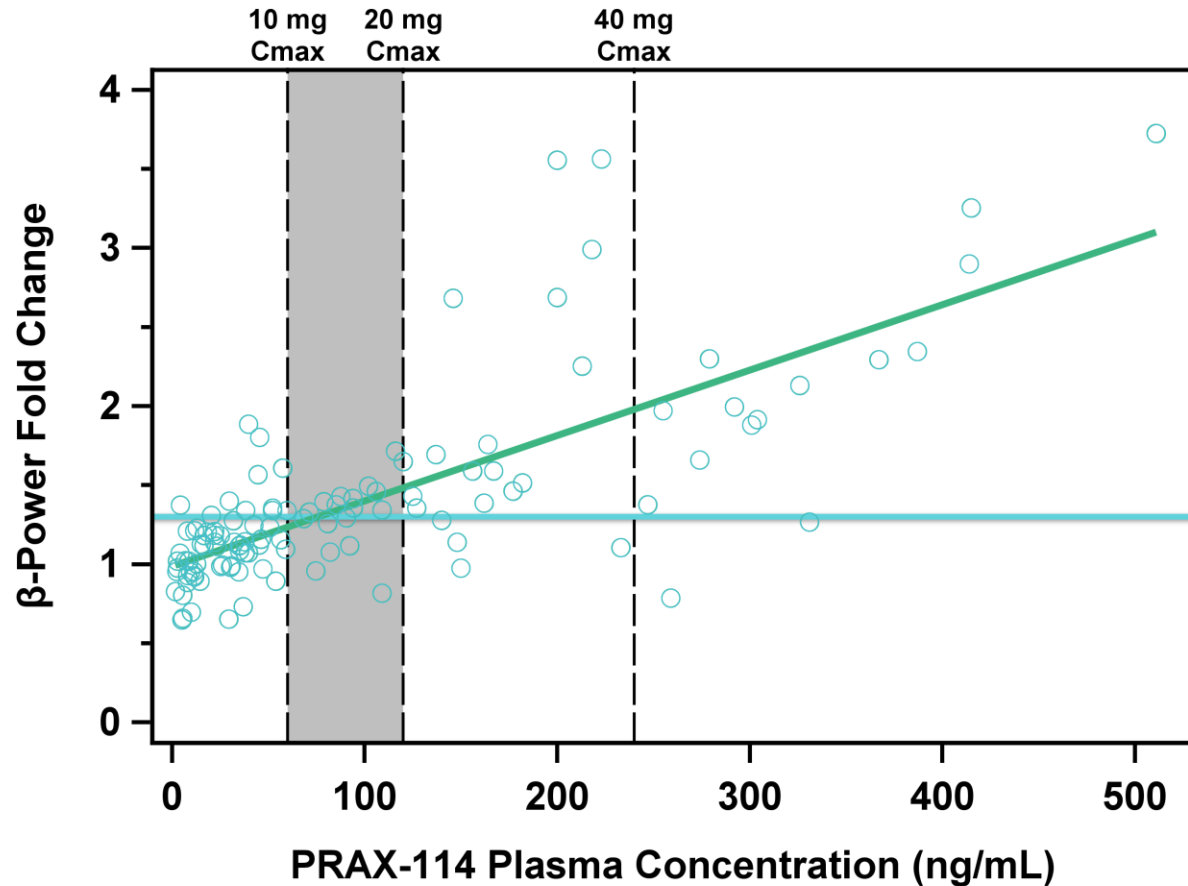


PRAX-114 has greater potentiation of extrasynaptic GABA_A receptors

Potentiation		Fold Potentiation
$\alpha_4\beta_3\delta$ %*	$\alpha_1\beta_2\gamma_2$ %	$\frac{\alpha_4\beta_3\delta}{\alpha_1\beta_2\gamma_2}$
300%	29%	10.5

$\alpha_4\beta_3\delta$: EXTRASYNAPTIC GABA_A RECEPTOR
 $\alpha_1\beta_2\gamma_2$: SYNAPTIC GABA_A RECEPTOR
 * EQUIVALENT OF FULL GABA ACTIVATION
 SOURCE: PRAXIS DATA ON FILE

Targeting doses that activate the system without expected sedation

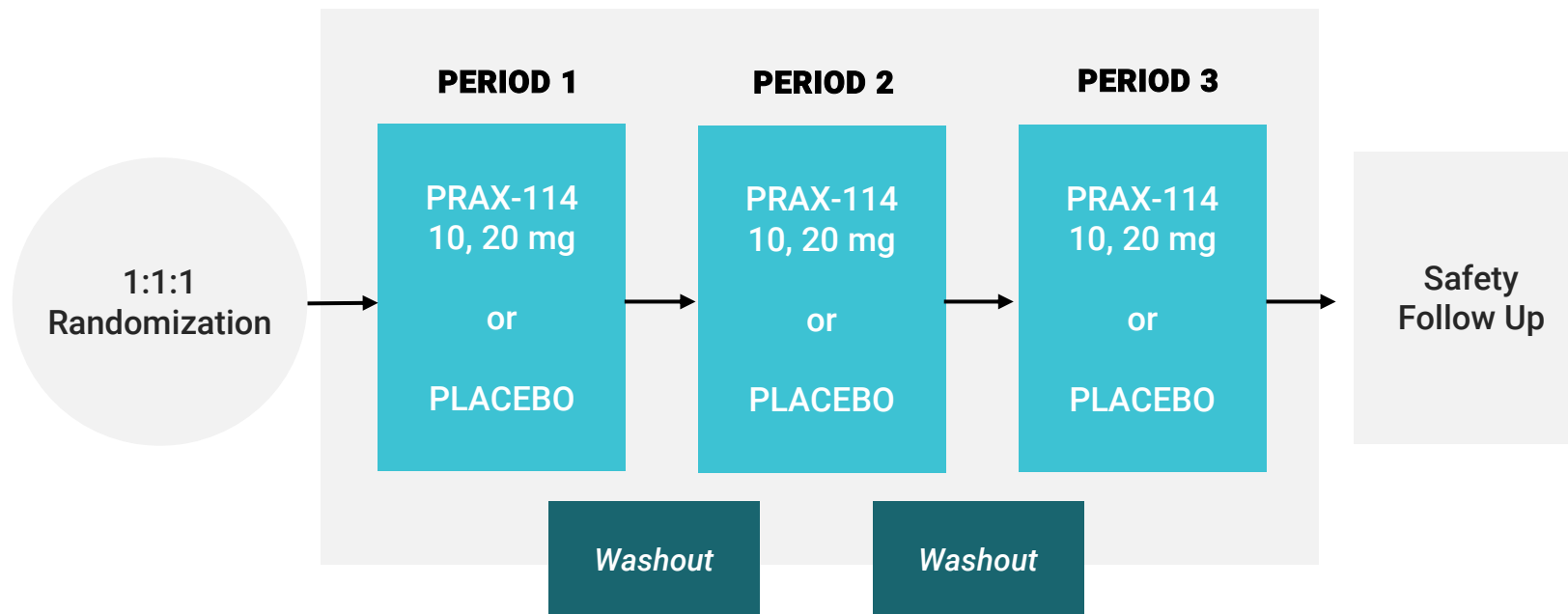


KEY LEARNINGS:

- β -Power of ~ 1.3 corresponds to efficacy in harmaline tremor model with PRAX-114
- In HV studies β -Power achieved with 10-20mg at Cmax
- This dose range showed no AE of somnolence or sedation with day-time dosing in HV

PRAX-114 ET Phase 2 study initiated 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

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

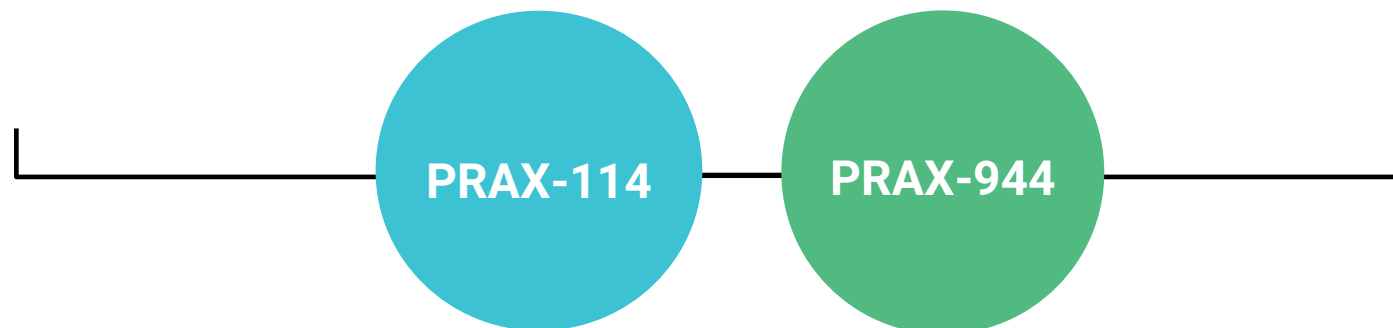


As needed



Chronic

- Patients will initiate ET treatment sooner
- Patients will treat as needed
- Patients will maintain ET therapy





Daring for More Beyond ET

Why Parkinson's disease matters?



Affects ~1 million people in the US, with 85% of patients treated pharmacologically



Incidence is age related. Average age of onset is early 60s. High risk in men.

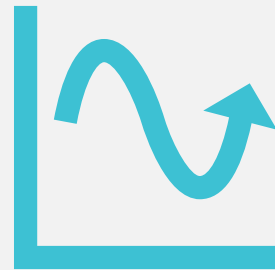


Progressive disability motor and non-motor symptoms

Current treatment adds to the burden of Parkinson's disease



Progressive &
debilitating



Inconsistent
therapeutic effect
over time



High treatment
burden

Limitations of dopaminergic therapy

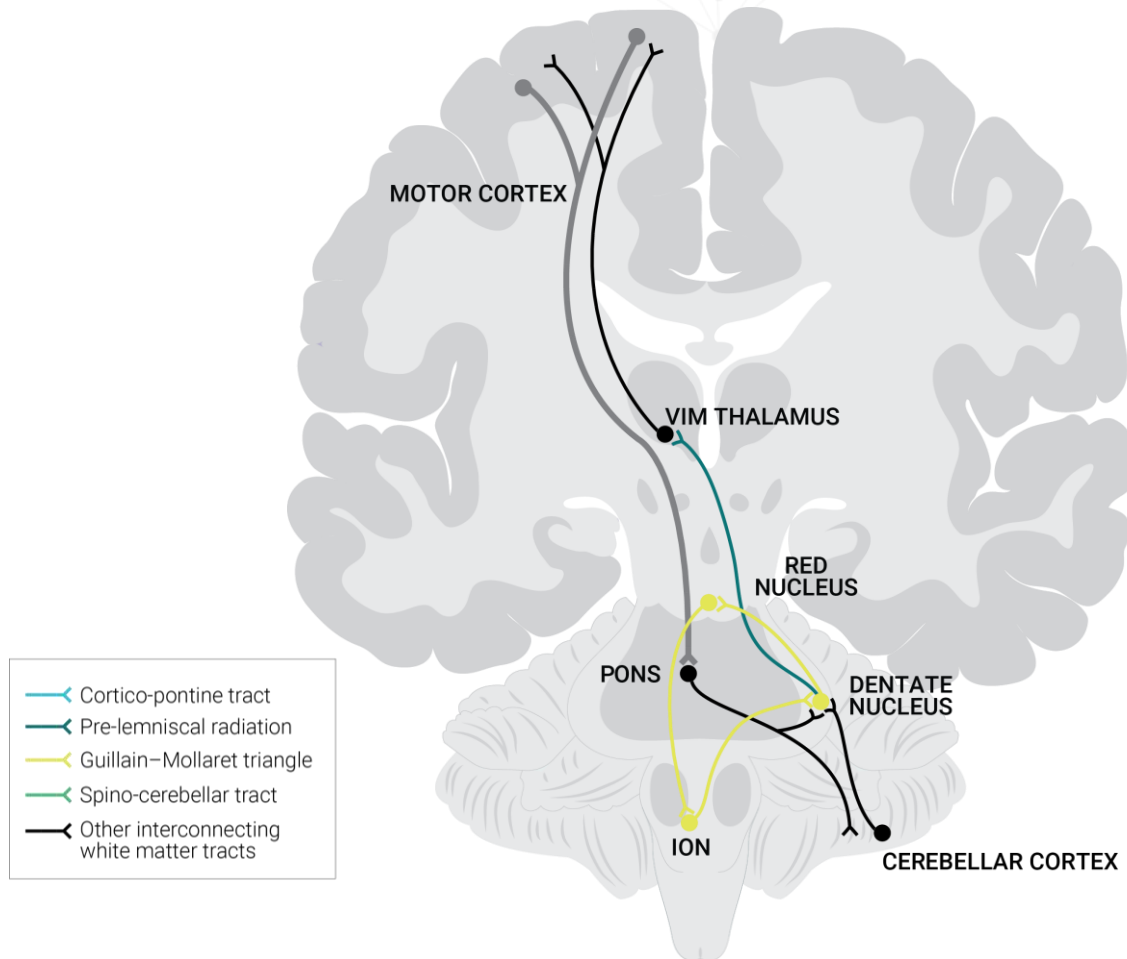
**Dopamine
promotes
movement**

**Dopamine related
motor and non-
motor
complications**

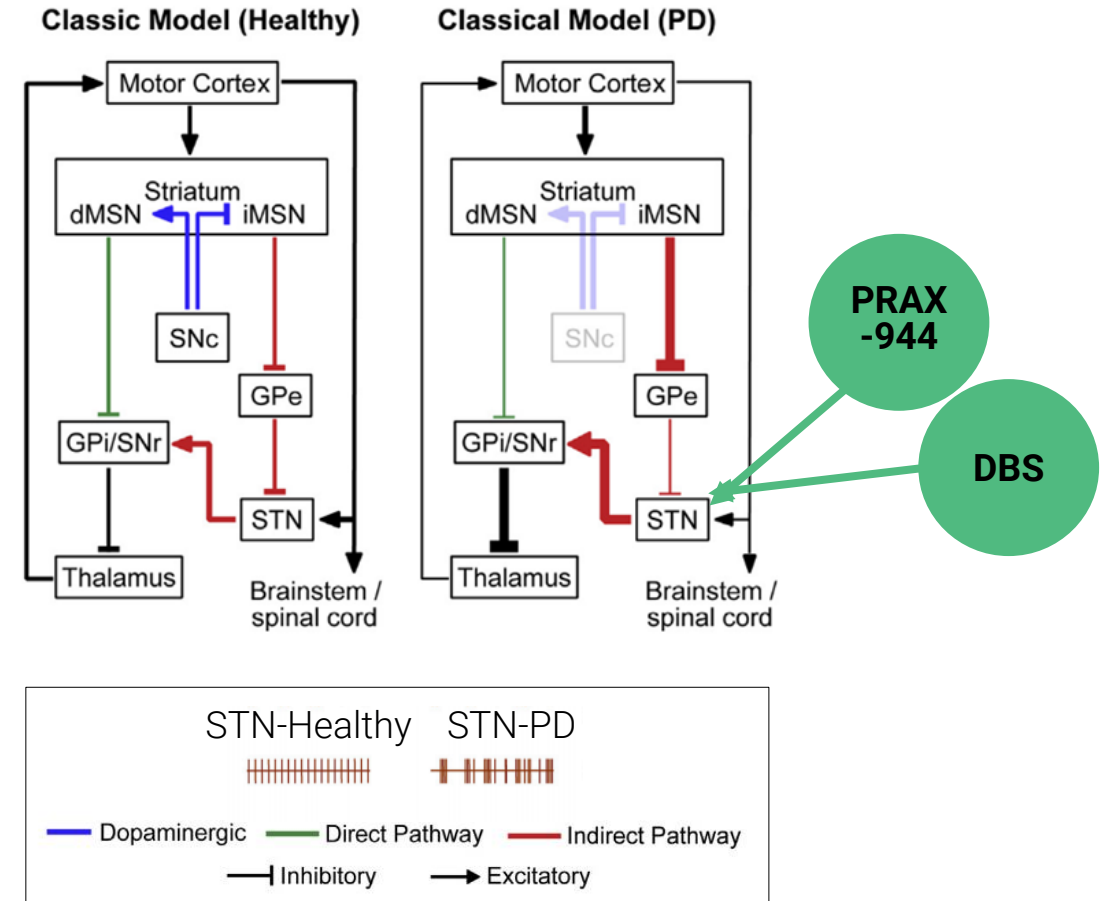
**PRAX-944 has potential to
be a non-dopaminergic
therapy for
Parkinson's disease**

T-type Calcium Channels modulate the motor circuit in Parkinson's disease and overlap with target for Deep Brain Stimulation

Thalamo-Cortical Pathway

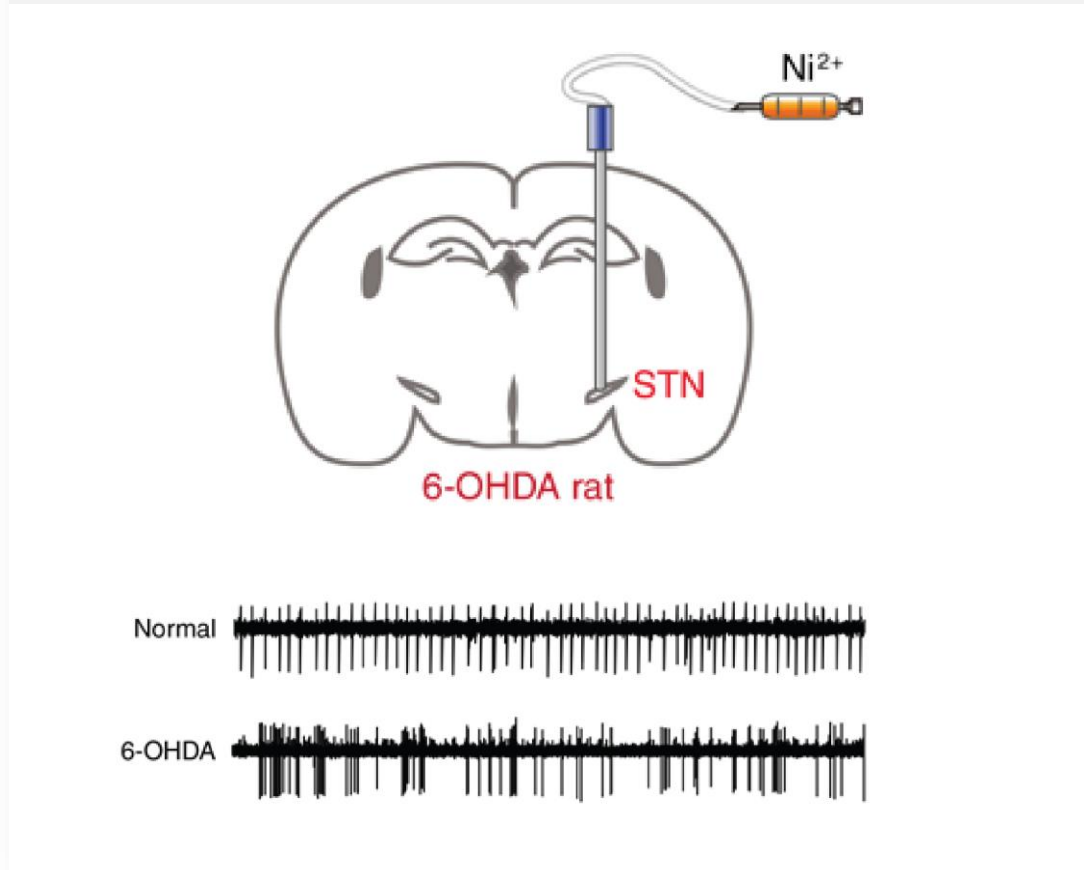


Thalamo-Cortical Pathway Imbalance in PD

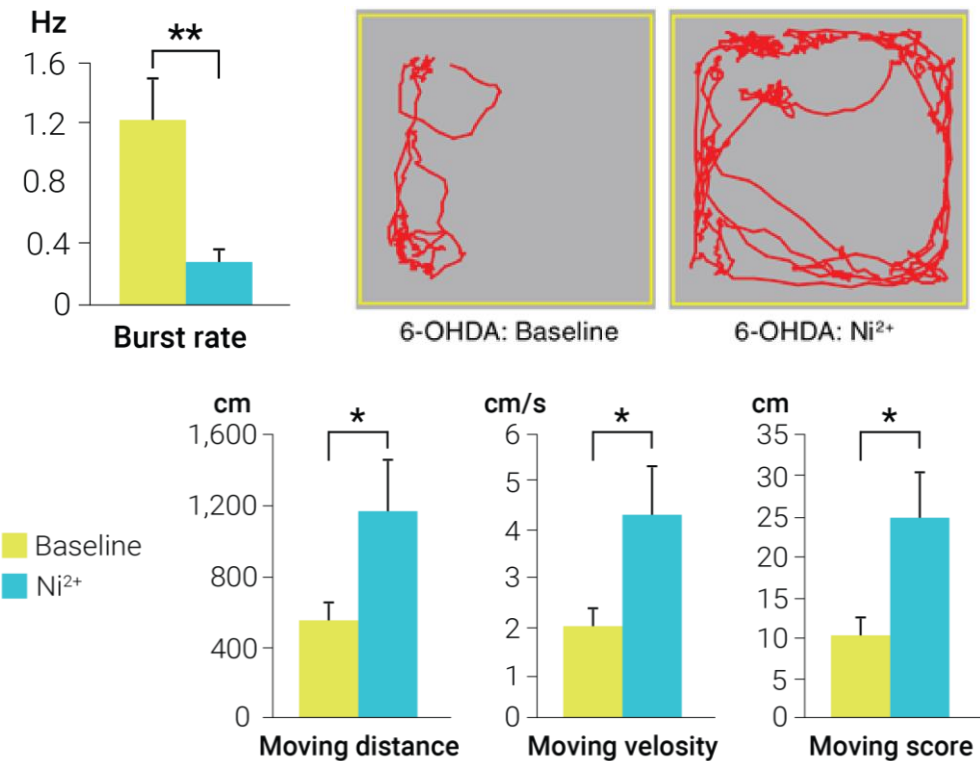


Blocking T-type Calcium Channels improves motor activity in 6-OHDA model of Parkinson's disease

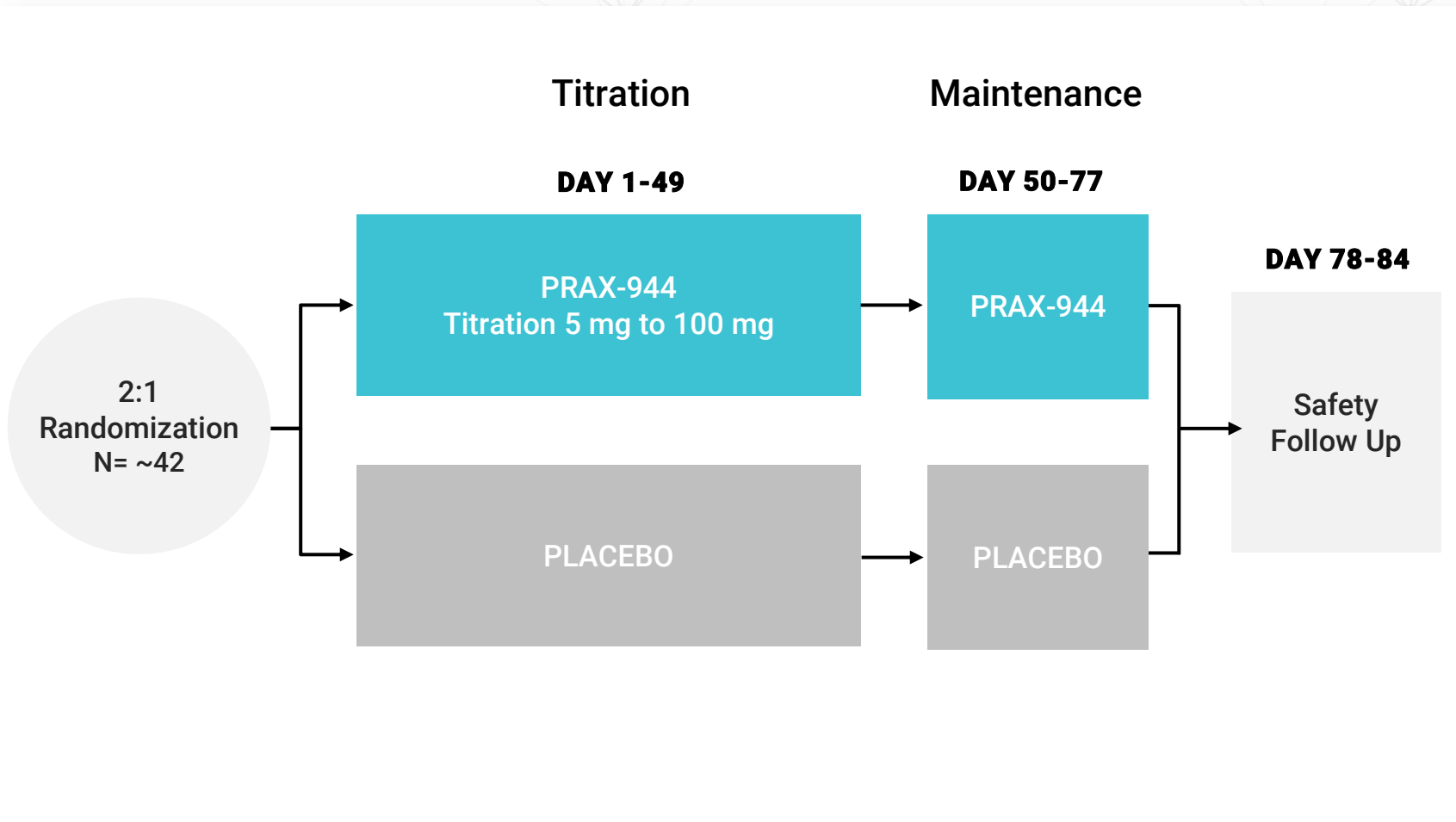
BURST FIRING IN STN OF 6-OHDA PARKINSON'S MODEL



BLOCK OF BURST FIRING IMPROVES MOVEMENT IN 6-OHDA PARKINSON'S MODEL



PRAX-944 in Parkinson's disease - study design



CLINICAL MEASUREMENTS:

Motor function

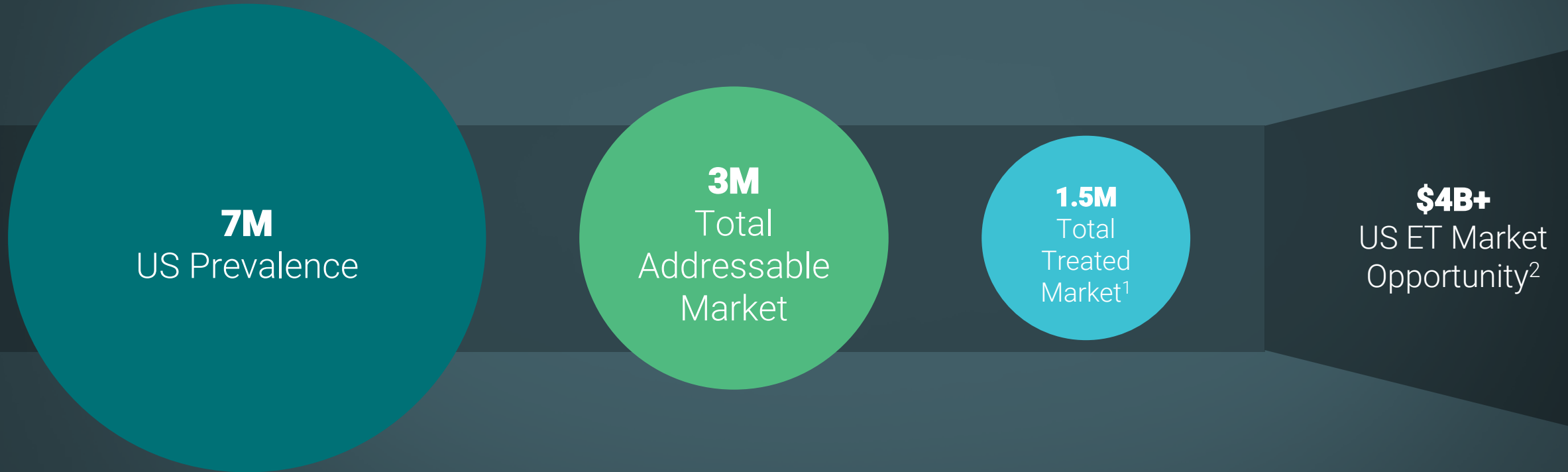
KEY QUESTION:

Does PRAX-944 demonstrate motor improvement in patients?



Daring for More The Year Ahead

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



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

Upcoming catalysts for Movement Disorders in 2022

MOVEMENT DISORDERS

PROGRAM	INDICATION	Q1 2022	Q2 2022	Q3 2022	Q4 2022
PRAX-944	ET	Phase 2a Part B Randomized Withdrawal Topline	Phase 2b Essential1 Study	Phase 2b Essential1 Study Topline	
PRAX-114	ET	Phase 2 Trial		Phase 2 Topline	
PRAX-944	PD	Initiate Phase 2 Trial			

Upcoming catalysts throughout portfolio in 2022

	PROGRAM	INDICATION	Q1 2022	Q2 2022	Q3 2022	Q4 2022
PSYCHIATRY	PRAX-114	MDD	Phase 2/3 Aria Study Topline			
		PTSD	Phase 2 Acapella Study Topline			
			Phase 2 Trial		Phase 2 Topline	
MOVEMENT DISORDERS	PRAX-944	ET	Phase 2a Part B Randomized Withdrawal Topline			
			Phase 2b Essential1 Study		Phase 2b Essential1 Study Topline	
	PRAX-114	ET	Phase 2 Trial		Phase 2 Topline	
	PRAX-944	PD	Initiate Phase 2 Trial			
RARE DISEASES	PRAX-562	SUNCT/SUNA/TN	Phase 2 Trial			
		DEEs	Phase 1 Topline ASSR Biomarker			
	PRAX-222	SCN2A - DEE	Initiate Phase 2 Trial			
			Initiate Phase 1/2/3 Trial			

Upcoming portfolio events in 1H 2022

RARE DISEASE DAY

- PRAX-562: Cephalgias and DEEs
- PRAX-222: SCN2A-DEE
- Preclinical Portfolio
 - KCNT1
 - SYNGAP1
 - PCDH19
 - SCN2A (LoF)

PSYCHIATRY DAY

- PRAX-114: Major Depressive Disorder
- PRAX-114: Post Traumatic Stress Disorder



DARE *for* MORE