UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 10, 2022

PRAXIS PRECISION MEDICINES, INC.
(Exact name of registrant as specified in its charter)

Delaware	001-39620	47-5195942
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

Praxis Precision Medicines, Inc.
99 High Street, 30th Floor
Boston, Massachusetts 02110
(Address of principal executive offices, including zip code)

(617) 300-8460
(Registrant's telephone number, including area code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trade Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	PRAX	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

On January 10, 2022, Praxis Precision Medicines, Inc. (the "Company") posted a revised corporate slide presentation in the "Investors + Media" portion of its website at investors.praxismedicines.com. The presentation has been updated to include, among other things, that, in the first quarter of 2022, the Company plans to initiate the PRAX-114 Phase 2, placebo-controlled, crossover study for daytime treatment of essential tremor ("ET") to evaluate safety, pharmacokinetics and efficacy of 10 or 20 mg of PRAX-114 and the PRAX-562 Phase 2 trial in the U.S. for treatment of patients with rare adult cephalgias, including a cohort of participants with Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing and Short-lasting Unilateral Neuralgiform headache with Autonomic symptoms, and a cohort of participants with Trigeminal Neuralgia. The expected timing for topline results from the PRAX-114 Phase 2 trial crossover study for daytime treatment of ET has not changed from the timing previously announced by the Company, and the Company continues to expect topline results in the second half of 2022. A copy of the revised corporate slide presentation is attached to this Current Report on Form 8-K (the "Form 8-K") as Exhibit 99.1. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.1.

The information contained in Item 7.01 of this Form 8-K shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly provided by specific reference in such a filing.

Item. 8.01 Other Information.

The information contained in the first paragraph of Item 7.01 of this Form 8-K (excluding Exhibit 99.1) is incorporated by reference into this Item 8.01.

Forward-Looking Statements

This Form 8-K contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995 and other federal securities laws, including express or implied statements regarding the Company's future expectations, plans and prospects, including, without limitation, statements regarding expectations, plans and timing for clinical data and clinical trials. The express or implied forward-looking statements included in this Form 8-K are only predictions and are subject to a number of risks, uncertainties and assumptions, including, without limitation: uncertainties inherent in clinical trials; the expected timing of submissions for regulatory approval or review by governmental authorities; regulatory approvals to conduct trials; risks, uncertainties and assumptions regarding the impact of the continuing COVID-19 pandemic on the Company's business, operations, strategy, goals and anticipated timelines, the Company's ongoing and planned preclinical activities, the Company's ability to initiate, enroll, conduct or complete ongoing and planned clinical trials and the Company's timelines for regulatory submissions; and other risks concerning the Company's programs and operations described in additional detail in its Annual Report on Form 10-K for the year ended December 31, 2020, its Quarterly Reports on Form 10-Q and other filings made with the Securities and Exchange Commission from time to time. Although the Company's forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by the Company. As a result, you are cautioned not to rely on these forward-looking statements. Any forward-looking statement made in this Form 8-K speaks only as of the date on which it was made. The Company undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future developments or otherwise.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	**Description**
99.1	Praxis Precision Medicines, Inc. January 2022 Corporate Presentation
104	Cover page from this Current Report on Form 8-K, formatted in Inline XBRL

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

PRAXIS PRECISION MEDICINES, INC.

Date: January 10, 2022

By: /s/ Marcio Souza
Marcio Souza
Chief Executive Officer

Exhibit 99.1

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, fu 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 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 o 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, dis 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 fortl 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 anticipa 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 pl publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Altho 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, re are cautioned not to place undue reliance on these forward-looking statements.

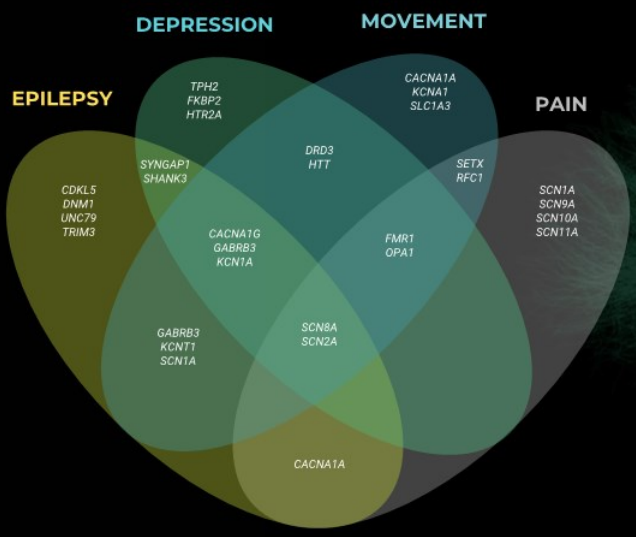
For further information regarding the risks, uncertainties and other factors that may cause differences between Praxis' expectations and actual results, you should review the "Risk Factors" section of our Annual Report on Form 10-K filed for the year ended December 31, 2020, our Quarterly Reports on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

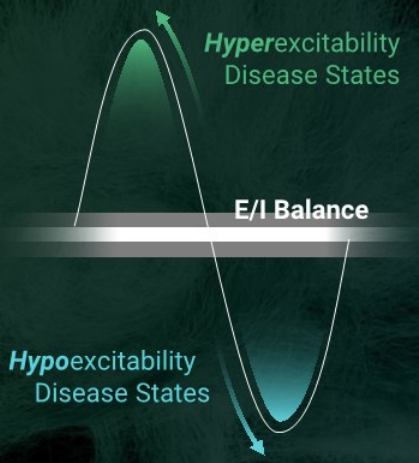

A PATIENT-GUIDED CNS COMPANY
DEVELOPING NEW CLASSES OF TREATMENTS
INSPIRED BY HUMAN GENETICS
PRAXIS

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

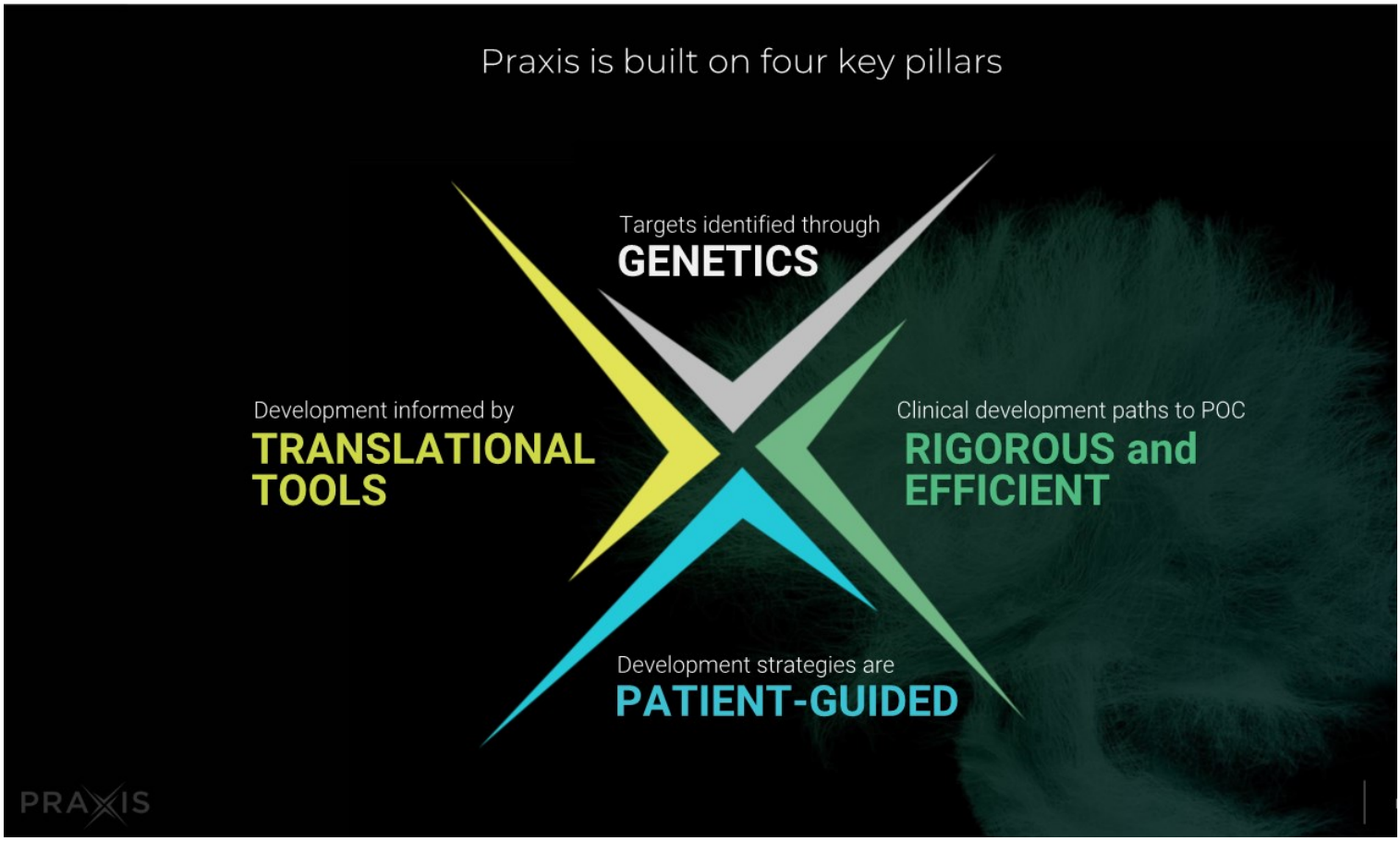
Targets Elucidated By Genetics

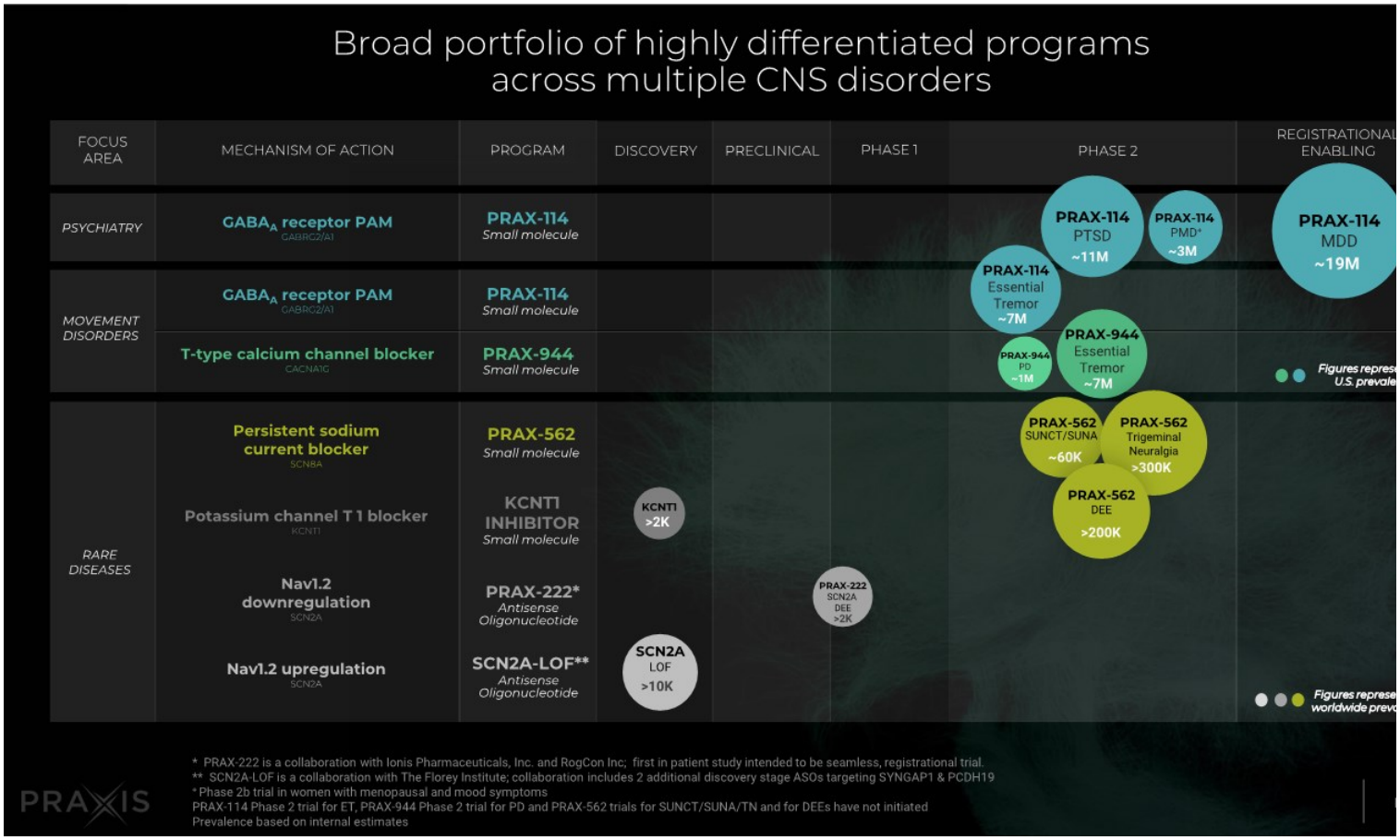


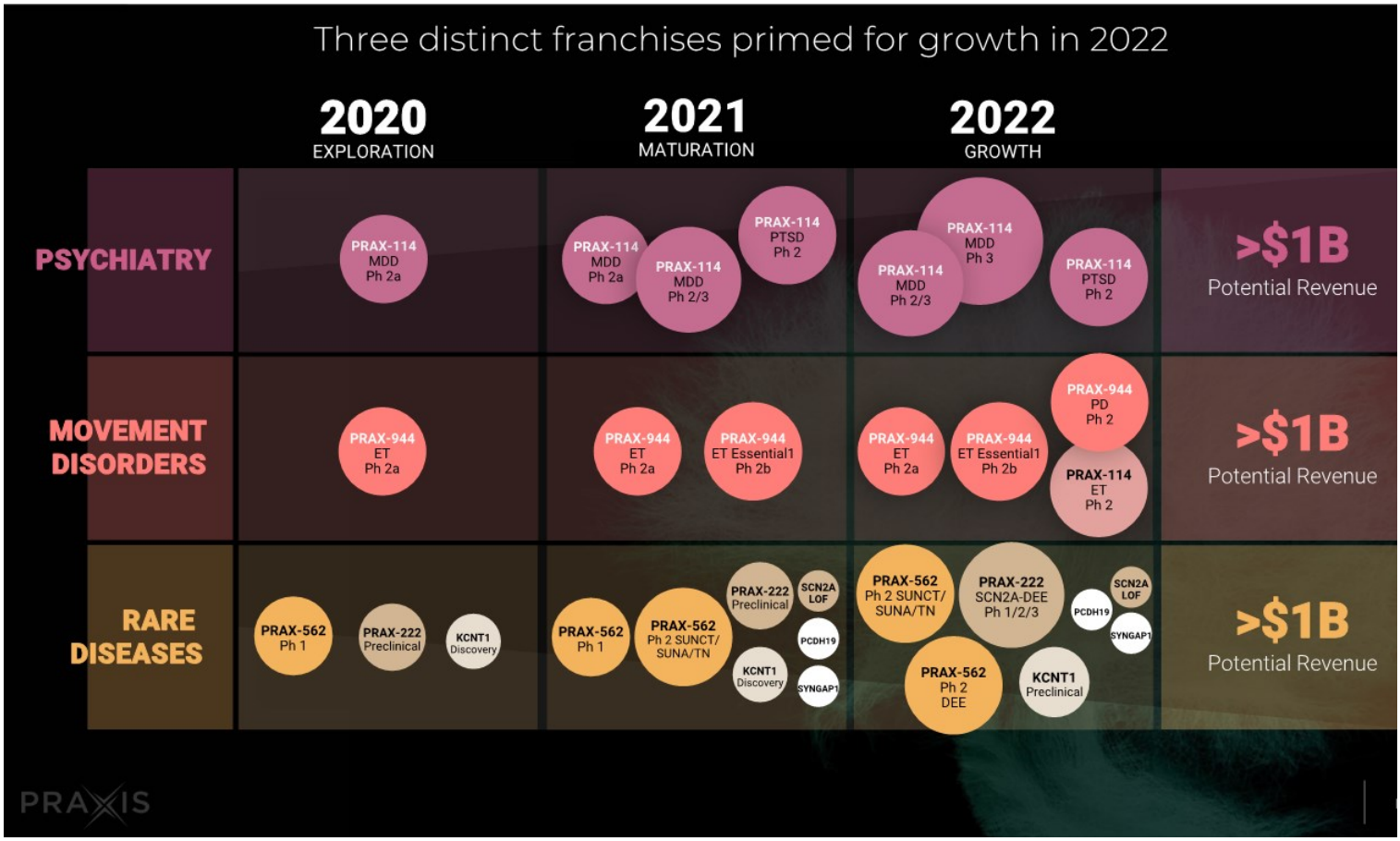
Targeting Common & Rare Diseases Connected By Neuronal Imbalance

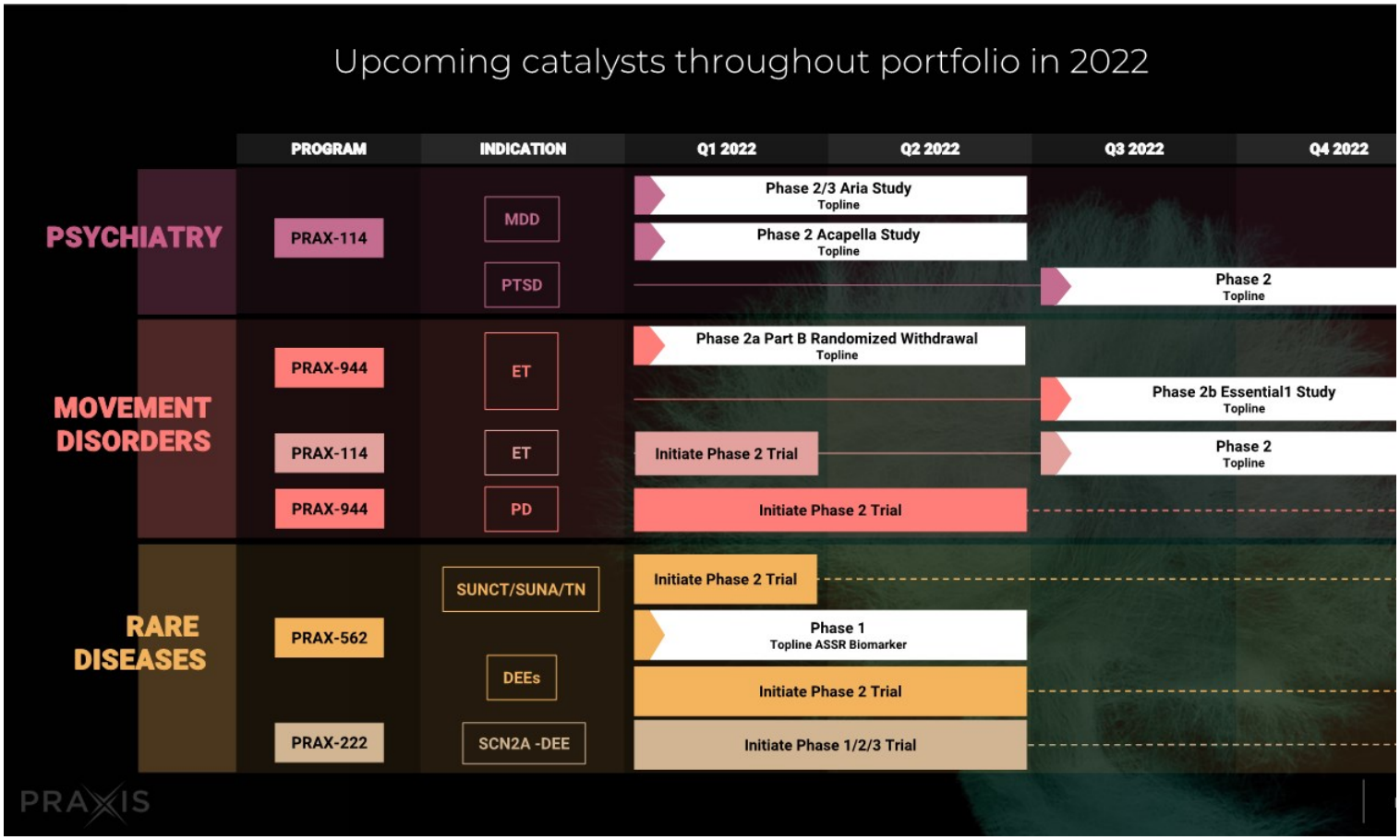


PRAXIS


Praxis is built on four key pillars
Targets identified through
GENETICS
Development informed by
TRANSLATIONAL TOOLS
Clinical development paths to POC
RIGOROUS and EFFICIENT
Development strategies are
PATIENT-GUIDED
PRAXIS


Broad portfolio of highly differentiated programs across multiple CNS disorders
FOCUS AREA
MECHANISM OF ACTION
PROGRAM
DISCOVERY
PRECLINICAL
PHASE 1
PHASE 2
REGISTRATIONAL ENABLING
PSYCHIATRY
GABA$_A$ receptor PAM
GABRG2/A1
PRAX-114
Small molecule
PRAX-114 PTSD ~11M
PRAX-114 PMD* ~3M
PRAX-114 MDD ~19M
MOVEMENT DISORDERS
GABA$_A$ receptor PAM
GABRG2/A1
PRAX-114
Small molecule
PRAX-114 Essential Tremor ~7M
T-type calcium channel blocker
CACNA1G
PRAX-944
Small molecule
PRAX-944 PD ~1M
PRAX-944 Essential Tremor ~7M
RARE DISEASES
Persistent sodium current blocker
SCN8A
PRAX-562
Small molecule
PRAX-562 SUNCT/SUNA ~60K
PRAX-562 Trigeminal Neuralgia >300K
PRAX-562 DEE >200K
Potassium channel T 1 blocker
KCNT1
KCNT1 INHIBITOR
Small molecule
KCNT1 >2K
Nav1.2 downregulation
SCN2A
PRAX-222*
Antisense Oligonucleotide
PRAX-222 SCN2A DEE >2K
Nav1.2 upregulation
SCN2A
SCN2A-LOF**
Antisense Oligonucleotide
SCN2A LOF >10K
Figures represe U.S. prevale
Figures represe worldwide preva
* PRAX-222 is a collaboration with Ionis Pharmaceuticals, Inc. and RogCon Inc; first in patient study intended to be seamless, registrational trial.
** 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 and mood symptoms
PRAX-114 Phase 2 trial for ET, 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
PRAXIS


Three distinct franchises primed for growth in 2022
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
SCN2A LOF
PCDH19
SYNGAP1
PRAX-562 Ph 2 DEE
KCNT1 Preclinical
>$1B
Potential Revenue
PRAXIS


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


DARE for MORE
PRAXIS

PSYCHIATRY

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

KEY UPCOMING MILESTONES

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

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

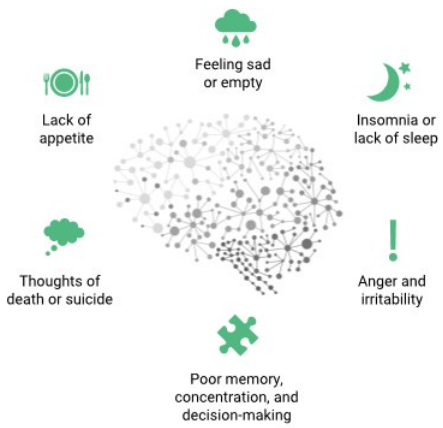
2H 2022
Ph 2 PTSD Topline

PRAXIS

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

MAJOR DEPRESSIVE DISORDER (MDD)

~19 million Americans and an estimated 300 million people worldwide affected by MDD

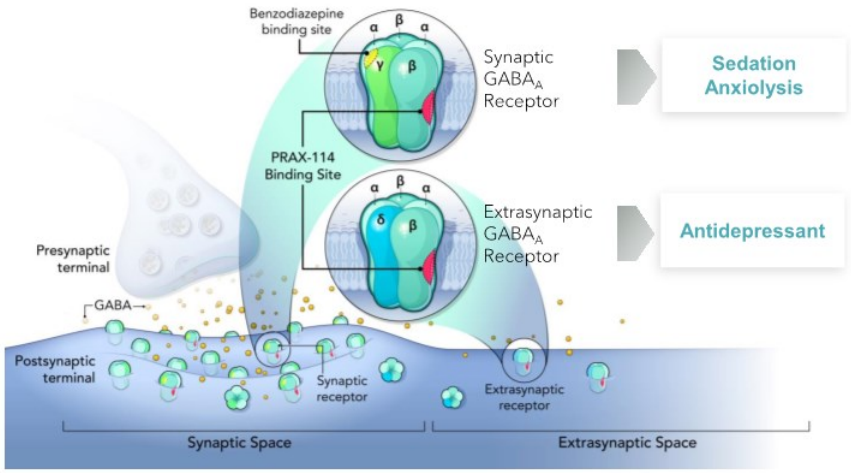


1. **Slow onset** of action for existing treatment options
2. **Low response rate**
3. **Limiting safety profile** can lead to discontinuation of treatment

PRAXIS

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



GABA: Gamma-aminobutyric acid; $GABA_A$ PAMs: $GABA_A$ receptor positive allosteric modulators

PRAX-114 shows 10.5-Fold greater potentiation of extrasynaptic than synaptic $GABA_A$ receptors

		Potentiation		Fold Potentia
	Dosing	$\alpha_4\beta_3\delta$ %*	$\alpha_1\beta_2\gamma_2$ %	$\alpha_4\beta_3\delta$ / $\alpha_1\beta_2\gamma$
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 **$\alpha1\beta_2\gamma_2$:** synaptic $GABA_A$ rece

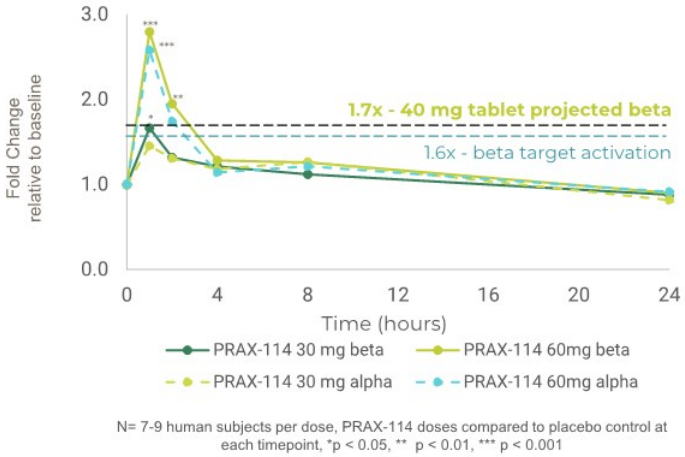
* Equivalent of full activation by GABA

Source: PRAXIS

PRAXIS Source: Praxis Data on file

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



N= 7-9 human subjects per dose, PRAX-114 doses compared to placebo control at each timepoint, *p < 0.05, ** p < 0.01, *** p < 0.001

No MTD identified up to 80mg

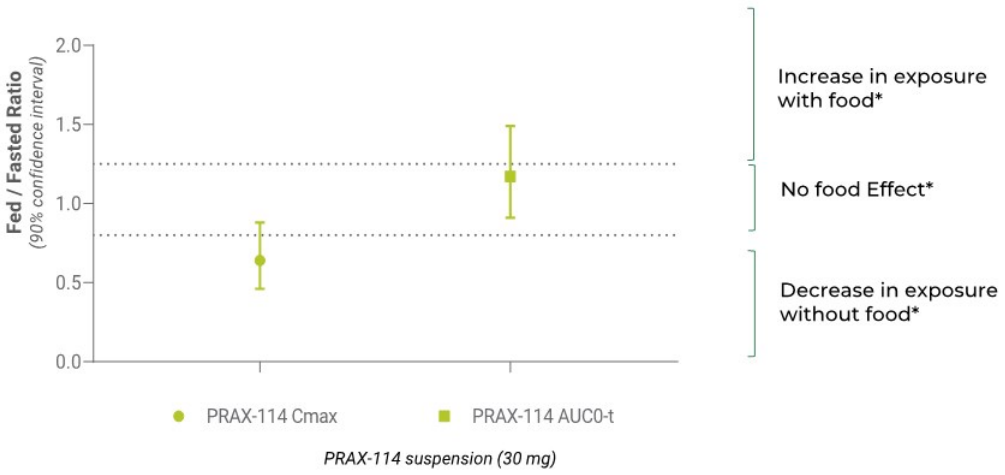
Tolerability profile maintained throughout dos escalation

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

PRAXIS

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

Effect of high-fat meal on pharmacokinetics



PRAX-114 suspension (30 mg)

*FDA Guidance for Industry: Food-Effect Bioavailability and Fed Bioequivalence Studies

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PRAX-114 Phase 2a: rapid and marked 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)

Phase 2a combined* HAM-A anxiety and HAM-D insomnia item results

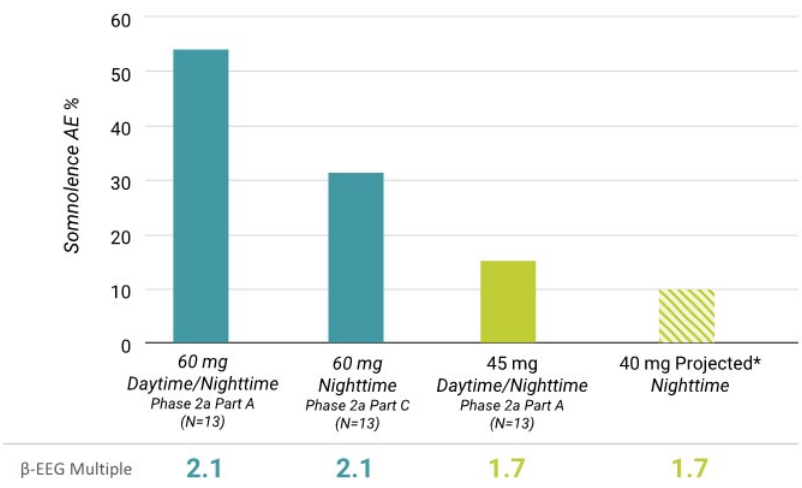
Visit	HAM-A *Anxiety Rating Scale* Mean (SD) N=52	HAM-D *Insomnia Item Total (max score of 6)* Mean (SD) N=52
Day 1 (BL)	22.4 (4.16)	4.2 (1.3)
Day 8 (CFB)	-12.4 (7.55)	-2.8 (1.9)
Day 15 (CFB)	-11.6 (6.67)	-3.1 (1.7)

PRAXIS

*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

Low rates of somnolence with PRAX-114 at targeted exposure level

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



β-EEG Multiple	2.1	2.1	1.7	1.7

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

PRAXIS

*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

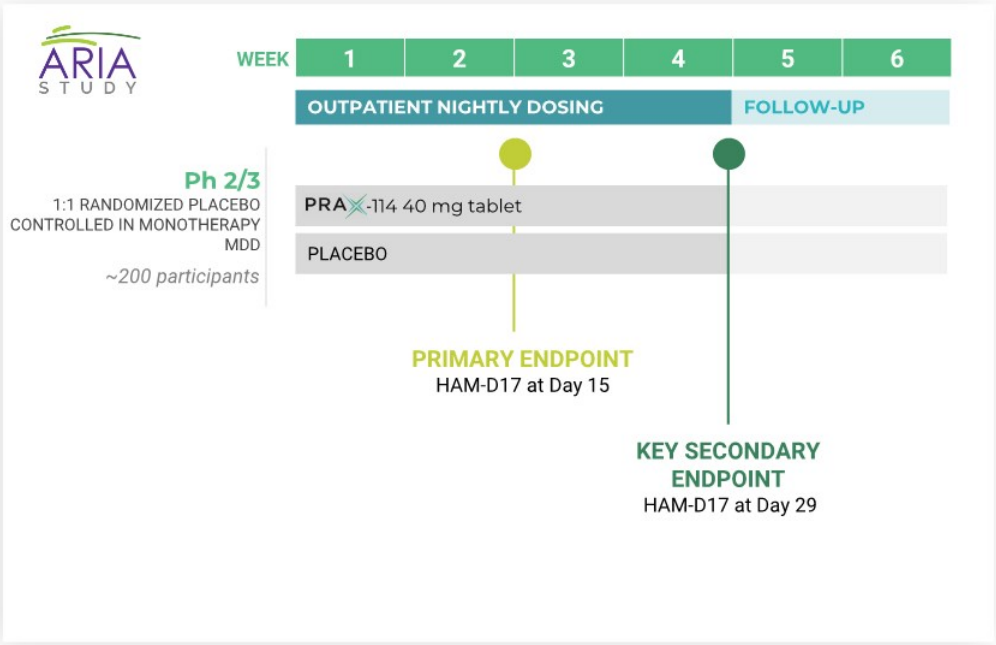
Key Operational Controls

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]

PRAXIS

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/

PRAX-114 monotherapy MDD Phase 2/3 Aria Study topline data expected 1H 202



PHASE 2/3

First of two registrational trials for monotherapy MDD

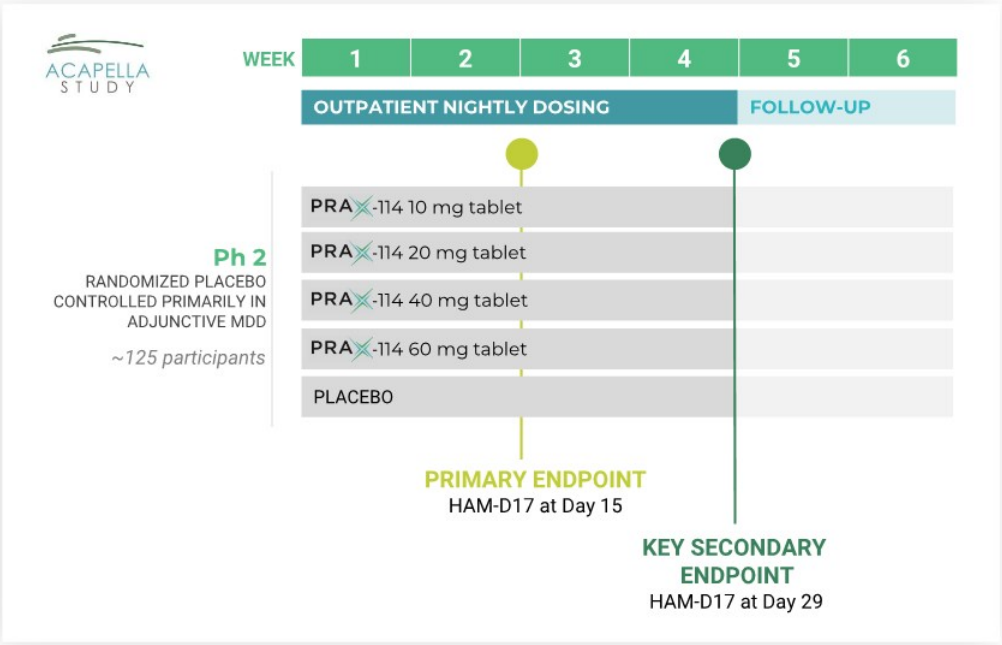
KEY INCLUSION CRITERIA

Ages 18-65
HAM-D17 ≥ 23
At least one prior episode of MDD

KEY EXCLUSION CRITERIA

Treatment-resistant depression
Current antidepressant treatment

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, 2 40 and 60 mg

KEY INCLUSION CRITERIA

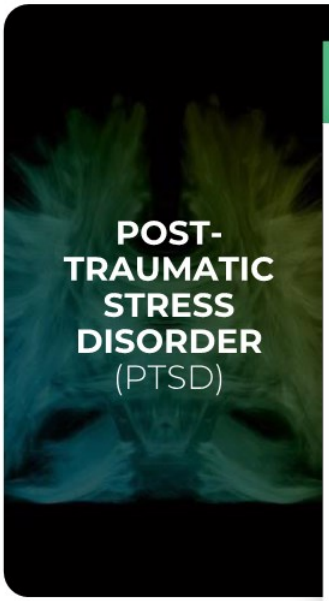
Ages 18-65
HAM-D17 ≥ 20
At least one prior episode of MDD
Inadequate response to treatment i current episode of at least 12 weeks

KEY EXCLUSION CRITERIA

Treatment-resistant depression

PRAXIS clinicaltrials.gov/ct2/show/NCT04969510

PRAX-114 has broad potential in psychiatry disorders



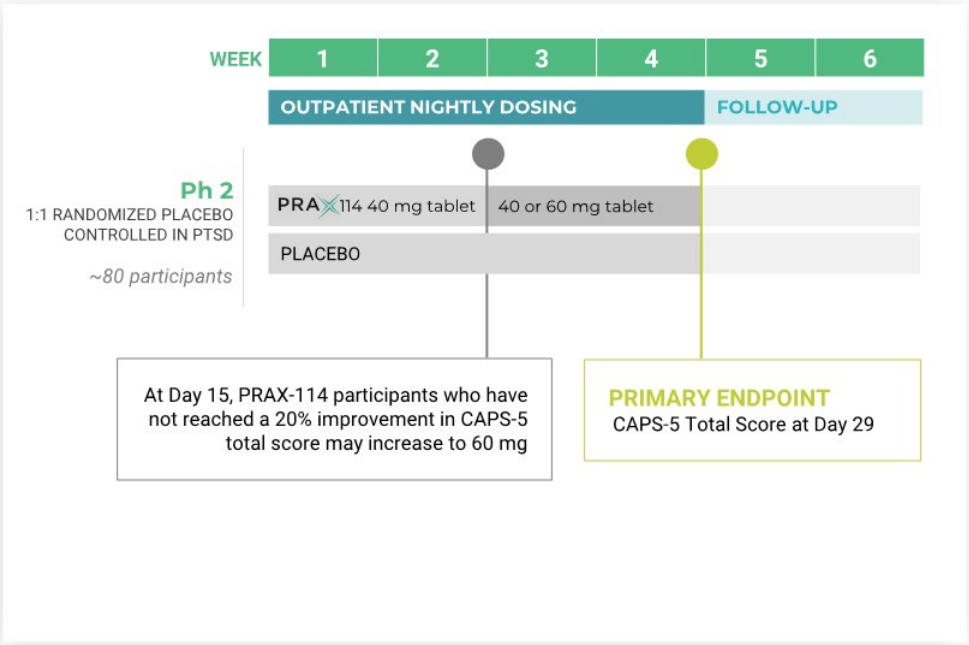
Dysfunction of GABA pathway is associated with chronic stress and symptoms of PTS

11M
ADULT PTSD
ESTIMATED US PREVALENCE

Flashbacks
Insomnia & Nightmares
Anxiety
Negative cognition
Mood symptoms
Intrusive thoughts

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

Enrollment has started for PRAX-114 PTSD Phase 2 study



TOPLINE DATA EXPECTED 2H22

To evaluate safety, tolerabili and efficacy of PRAX-114 fo treatment of adults with PTSD

KEY INCLUSION CRITERIA

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

PRAXIS

MOVEMENT DISORDERS

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

PRAX-114
$GABA_A$ Receptor PAM
Essential Tremor

PRAXIS

KEY UPCOMING MILESTONES

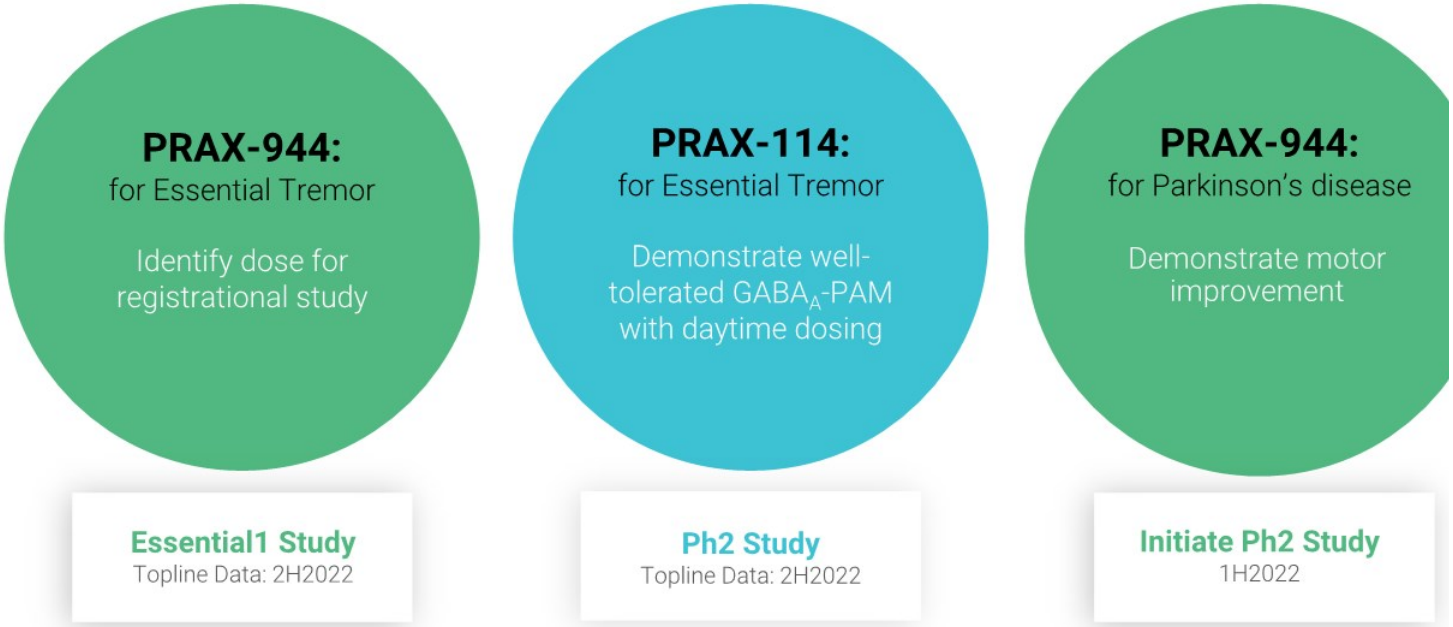
1H 2022
PRAX-944 Ph 2a ET Part B Randomized Withdrawal Topline

1H 2022
Initiate PRAX-944 Ph 2 PD Trial

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

2H 2022
PRAX-114 Ph 2 ET Topline

Movement Disorder franchise focus for 2022



Why Essential Tremor matters

Most common movement disorder ~7x the prevalence of Parkinson's disease[1]

~ 50% of patients have a family history[2,3]

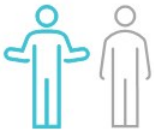
Daytime action tremor that primarily affects the hands[3,4]

Heterogeneous condition with progressive disability[3]

PRAXIS

SOURCE: 1. GHOSH (2016) (P.231, C.1, PH.1, L.1-2), 2. LIU (2016) (P.1009, C.1, PH.2, L.1-3 3.) 3. Elble RJ. Curr Neurol Neurosci Rep. 2013 Jun;13(6):353.
4. Putzke JD, et al. J Neurol Neurosurg Psychiatry. 2006 Nov;77(11):1235-7. 5.

ET burden of disease extends beyond the tremor



Social

embarrassed by their tremor[1,2]

Self

feel negative about themselves[1]

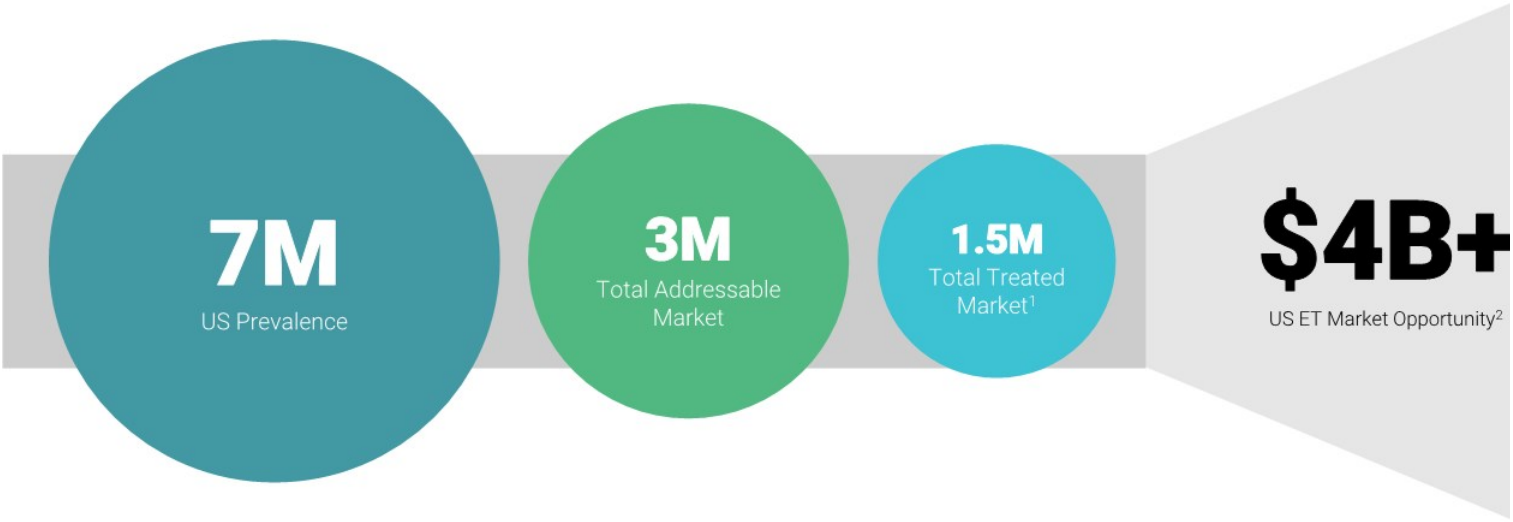
Mood

symptoms of social isolation, depression, and anxiety[1-5]

PRAXIS

1. LOUIS ED, ET AL. PARKINSONISM RELAT DISORD. 2015;21(7):729-735. 2. HOLDING SJ, ET AL. CHRONIC ILLN. 2015 MAR;11(1):69-71. 3.SHALASH AS, ET AL. TREMOR OTHER HYPERKINET MOV (N Y). 2019;9. 4. JANICKI SC,ET AL. THER ADV NEUROL DISORD. 2013;6(6):353-368. 5. LOUIS ED, ET AL. EUR J NEUROL. 2007 OCT;14(10):1138-46.

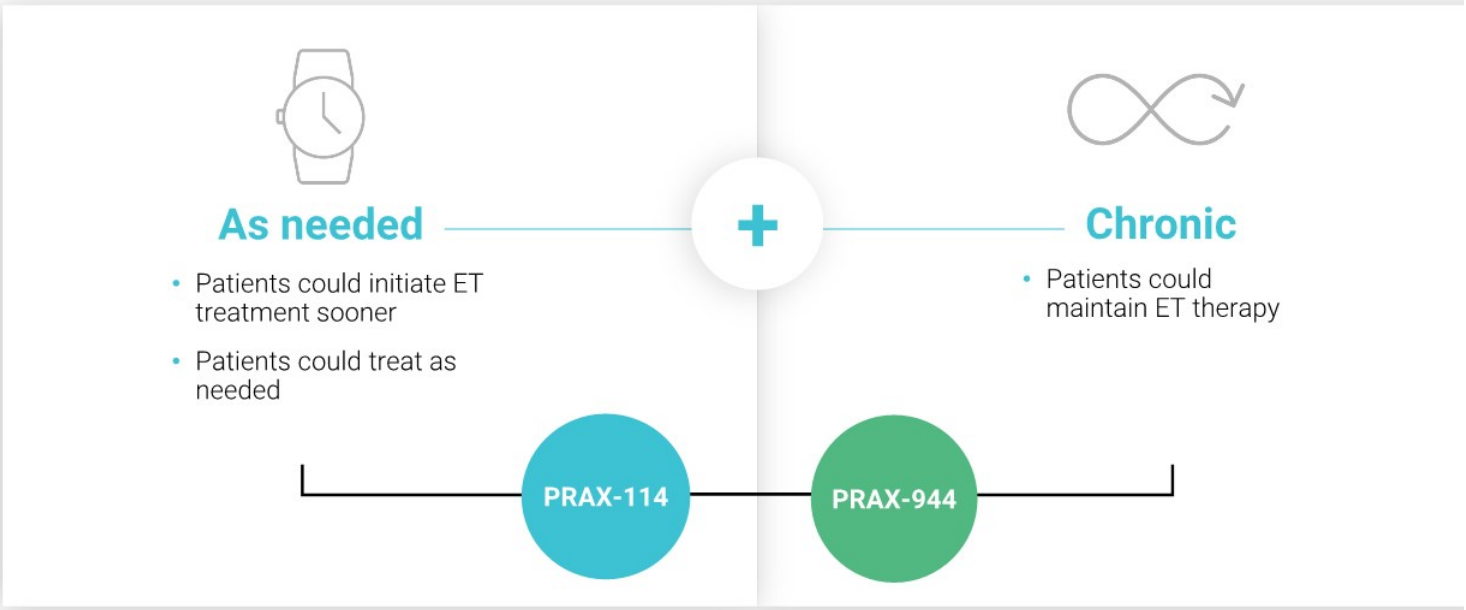
Our focus is on elevating the standard of care to capture the $4B+ US ET marke



PRAXIS

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

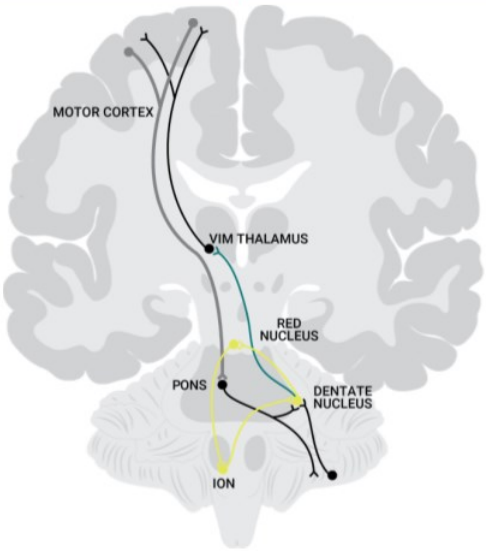


Tackling Movement Disorders through two mechanisms of action

CEREBELLO-THALAMO-CORTICAL (CTC) CIRCUIT

$GABA_A$ RECEPTORS

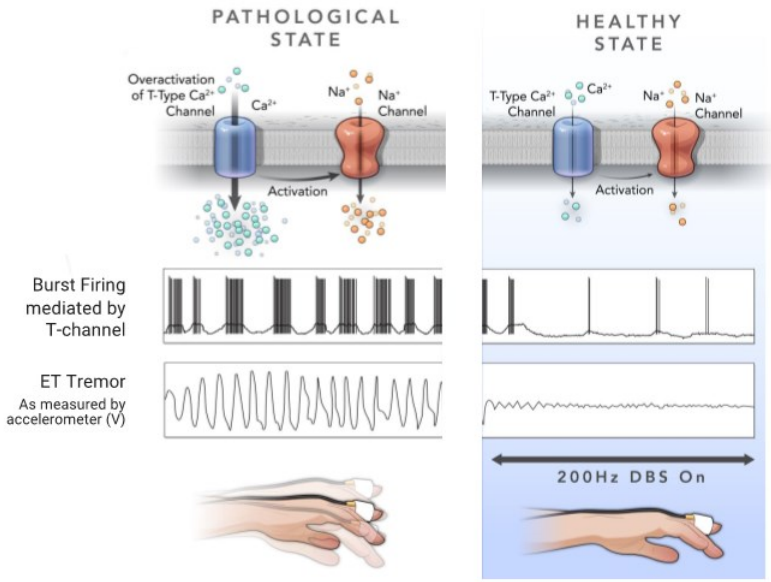
PRAX-114



T-TYPE CALCIUM CHANNELS

PRAX-944

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

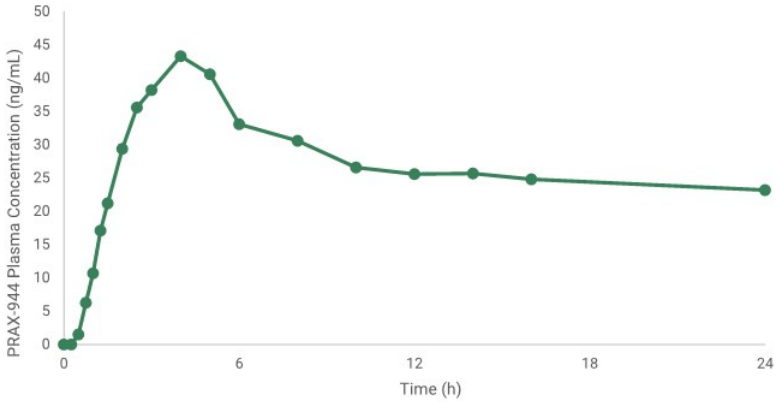
Deep Brain Stimulation reduces burst firing and tremor

PRAXIS

SOURCE: BASED ON MILOSEVIC 2018 FIGURE ON ACTUAL ET PATIENT INTRAOPERATIVE REAL-TIME SINGLE-UNIT RECORDINGS OF ACTION POTENTIALS OF INDIVIDUAL NEURONS

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

Sustained exposure with blunted MR Cmax allows for potential of sustained efficacy and improved tolerability



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

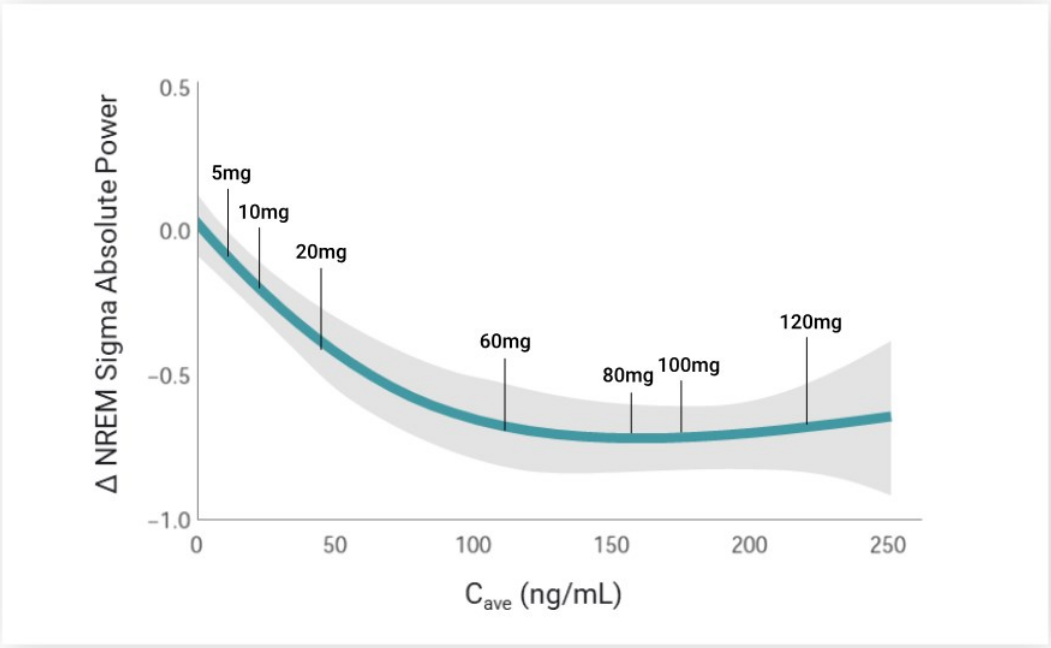
MR formulation is well-tolerated

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

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



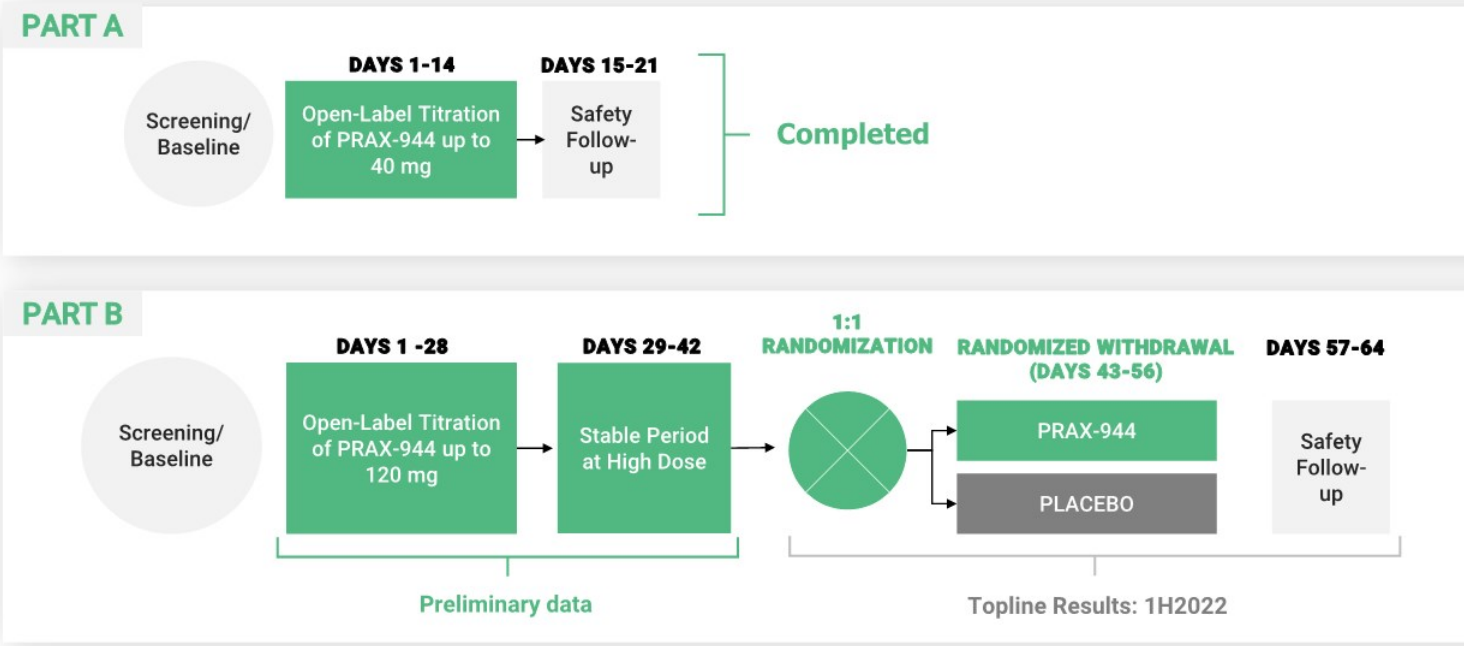
KEY TAKEAWAYS

- 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

PRAXIS

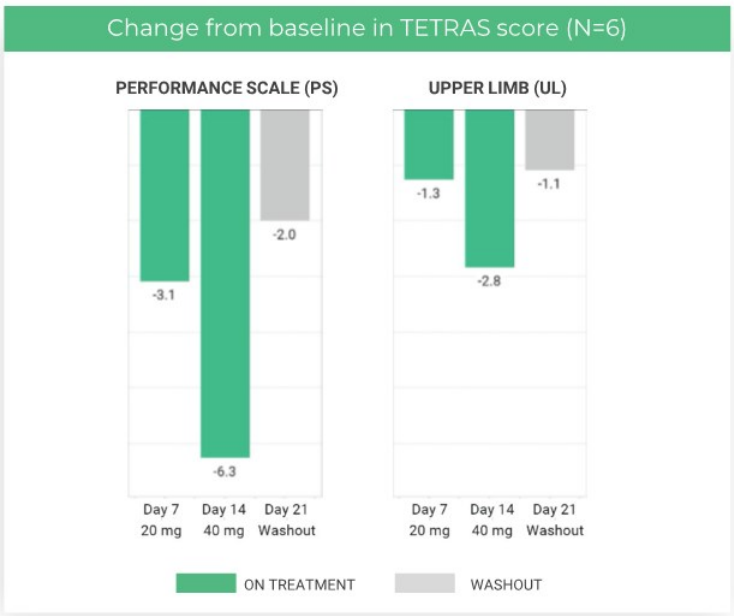
SOURCE: PRAXIS STUDY-944-105; PRAXIS DATA ON FILE

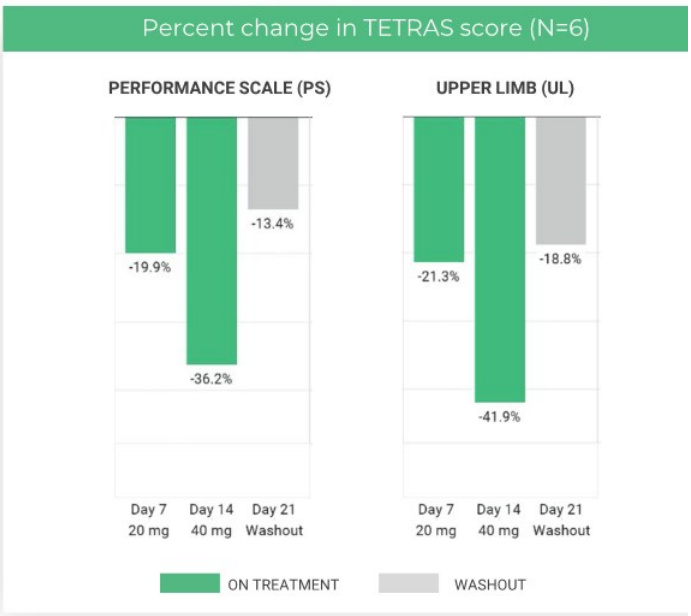
PRAX-944 Phase 2a ET study design



PRAXIS CLINICALTRIALS.GOV/CT2/SHOW/NCT05021978

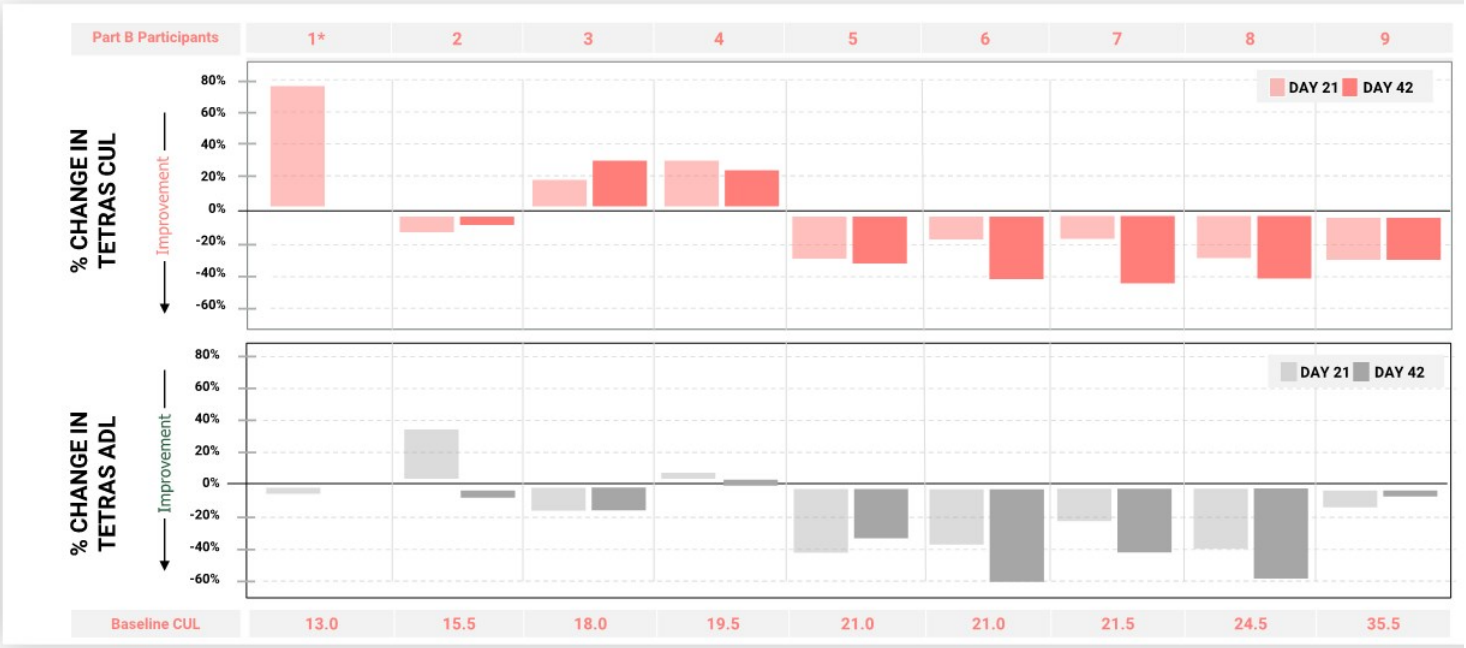
PRAX-944 Phase 2a ET Part A data shows dose dependent reduction in tremor amplitude





PRAXIS

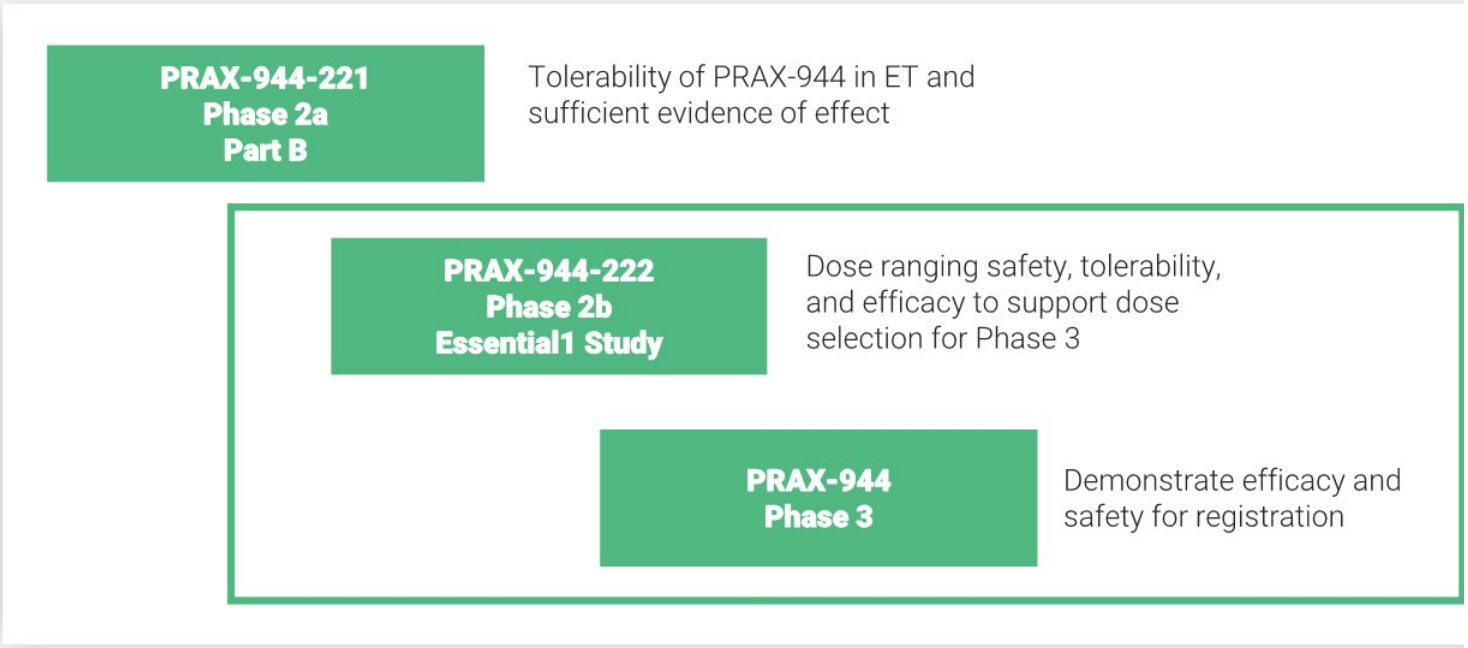
Preliminary Part B data: TETRAS Combined Upper Limb (CUL) and TETRAS Activities of Daily Living (ADL)



PRAXIS

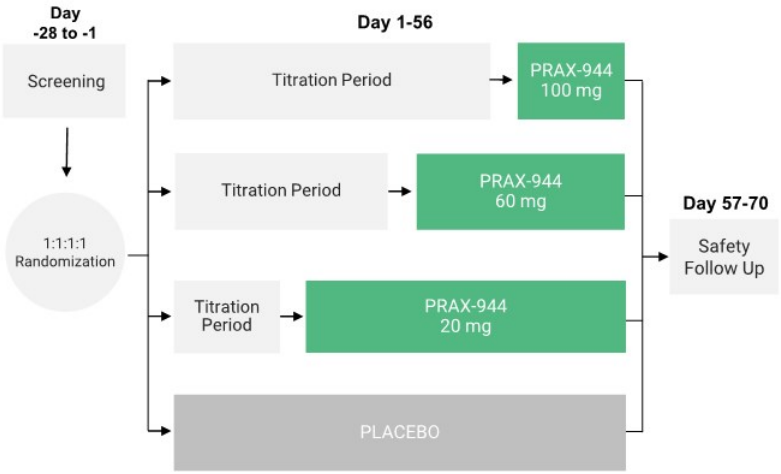
Preliminary data as of 10-Dec-2021 cutoff; ongoing CLINICALTRIALS.GOV/CT2/SHOW/NCT05021978
* 8 of 12 patients enrolled and dosed completed per protocol ; Part B Patient 1 discontinued after Day 21 assessment, 2 participants discontinued due to protocol violations, 1 participant discontinued due to an AE

Key PRAX-944 development questions in ET



Enrollment ongoing for PRAX-944 ET Phase 2b Essential1 Study

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



TOPLINE DATA EXPECTED 2H22

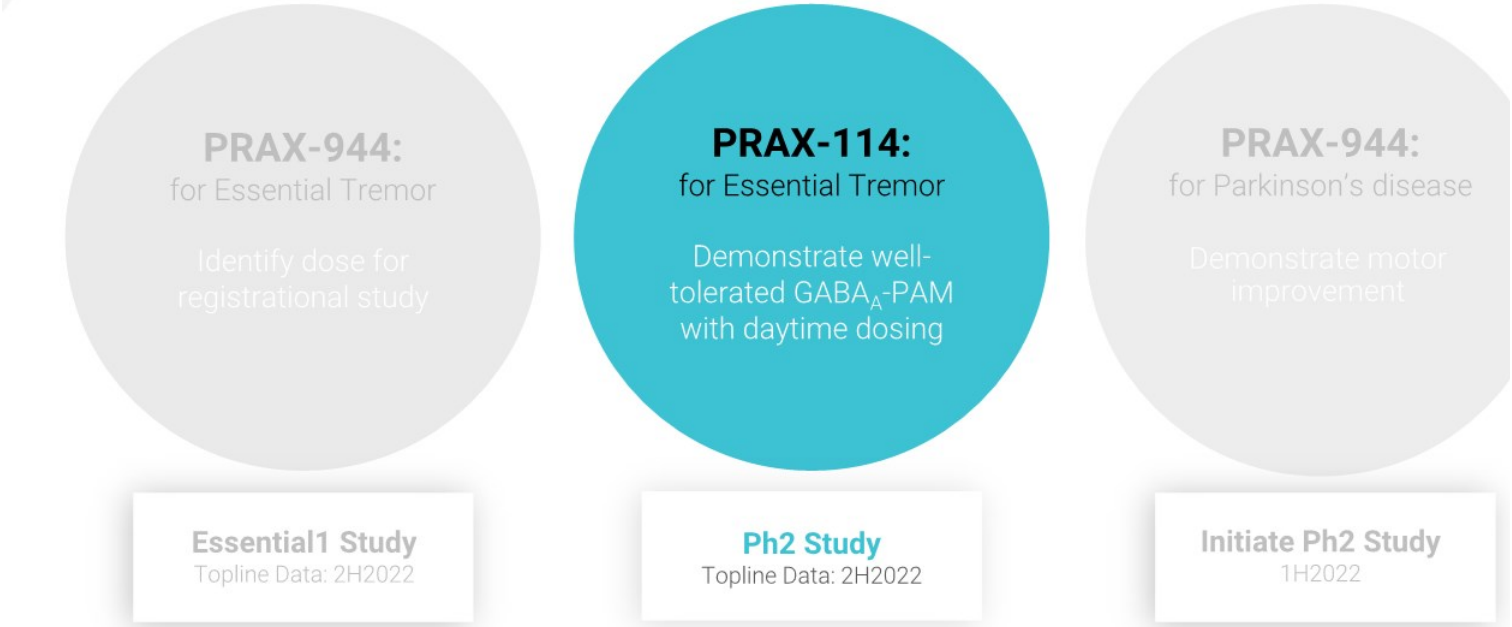
Dose-ranging study to evaluate safety, tolerability and efficacy of PRAX-944 f treatment of adults with E

KEY INCLUSION CRITERIA

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

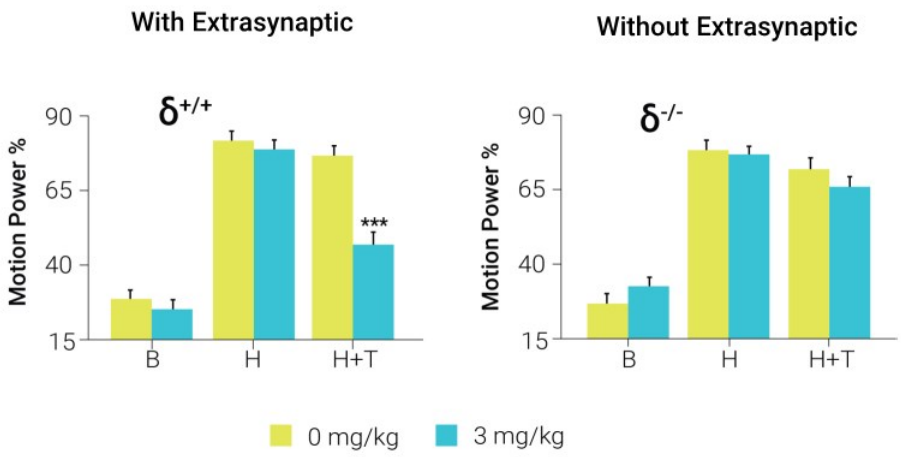
PRAXIS clinicaltrials.gov/ct2/show/NCT05021991

Movement Disorder franchise focus for 2022



Essential1 Study	Ph2 Study	Initiate Ph2 Study
Topline Data: 2H2022	Topline Data: 2H2022	1H2022

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



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

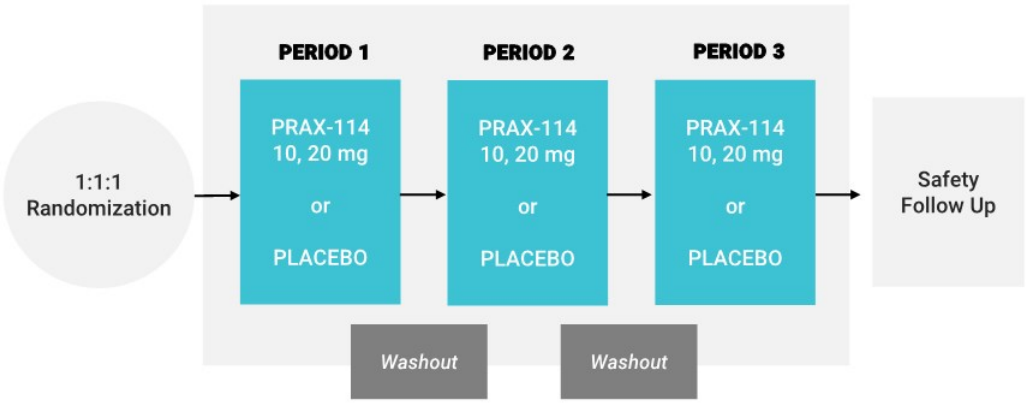
Potentiation		Fold Potentiation
$\alpha_4\beta_3\delta$ %*	$\alpha_1\beta_2\gamma_2$ %	$\alpha_4\beta_3\delta$/ $\alpha_1\beta_2\gamma_2$
300%	29%	10.5

PRAXIS

$A_4B_3\Delta$: EXTRASYNAPTIC $GABA_A$ RECEPTOR; $A1B_2\Gamma_2$: 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



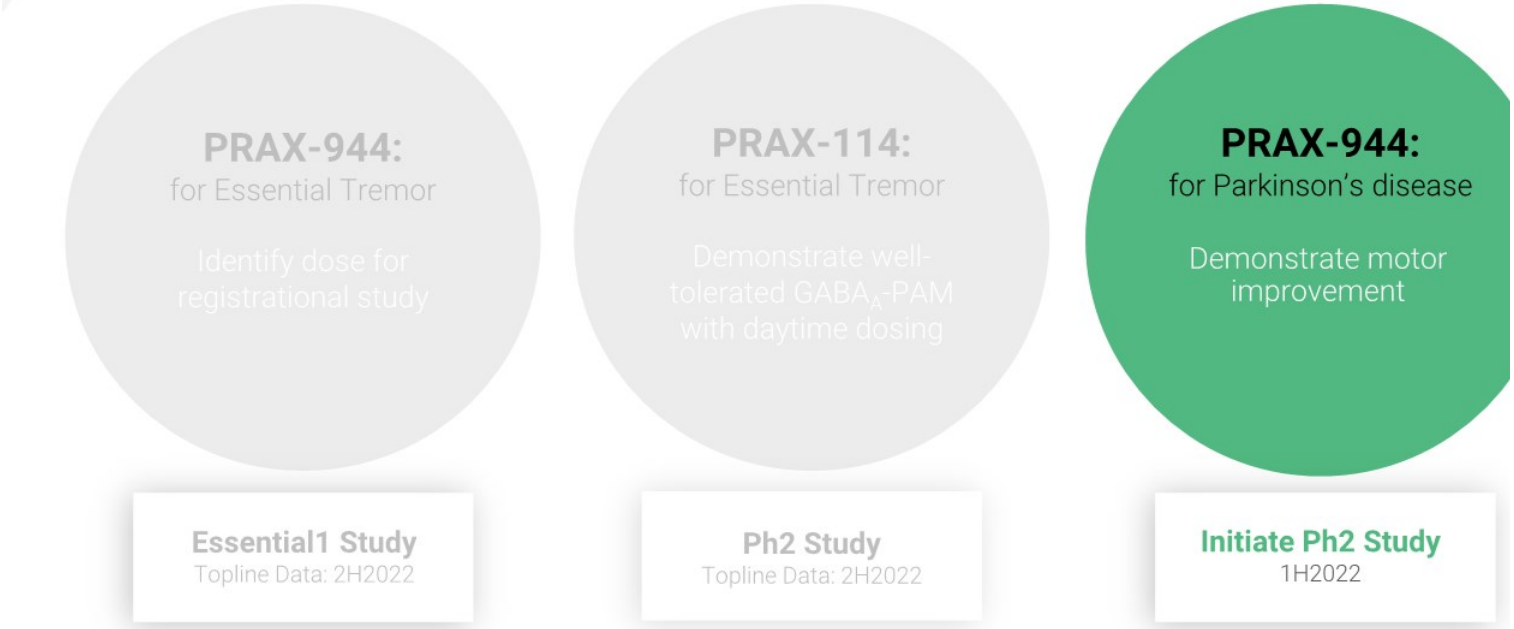
KEY QUESTION:

Is there a dose that enabl
reduction in tremor witho
somnolence or sedation

TOPLINE DATA:

2H2022

Movement Disorder franchise focus for 2022



Essential1 Study
Topline Data: 2H2022

Ph2 Study
Topline Data: 2H2022

Initiate Ph2 Study
1H2022

Why Parkinson's disease matters?

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

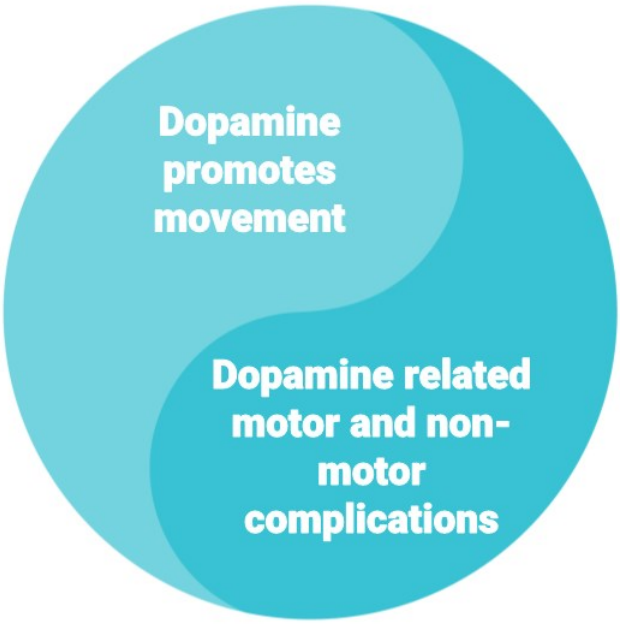
Incidence is age related. Average age of onset is early 60s. High risk in men.

Progressive disability motor and non-motor symptoms

PRAXIS

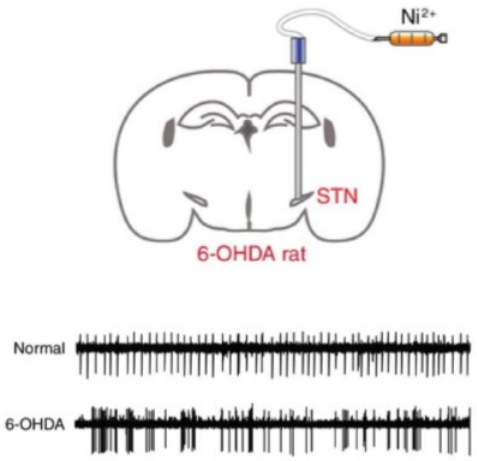
1. HTTPS://WWW.PARKINSON.ORG/UNDERSTANDING-PARKINSONS/STATISTICS 2. GLOBAL DATA REPORT: PARKINSON'S DISEASE - GLOBAL DRUG FORECAST AND MARKET ANALYSIS TO 2029, APRIL 2021 3.CLAIMS ANALYSIS; SECONDARY RESEARCH

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

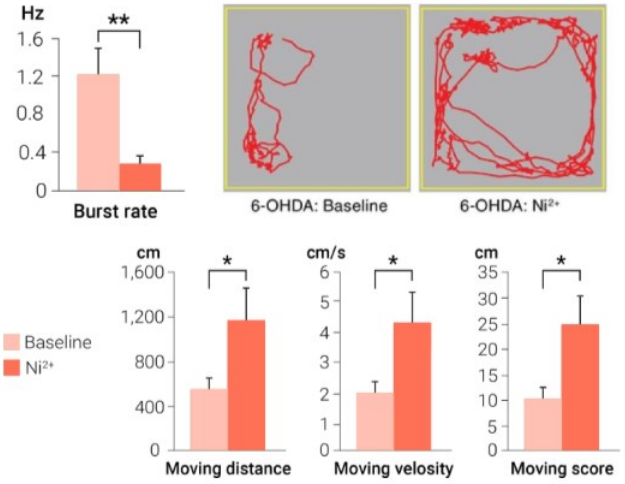


Blocking T-type Calcium Channels improves motor activity in 6-OHDA model of Parkinson's disease

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

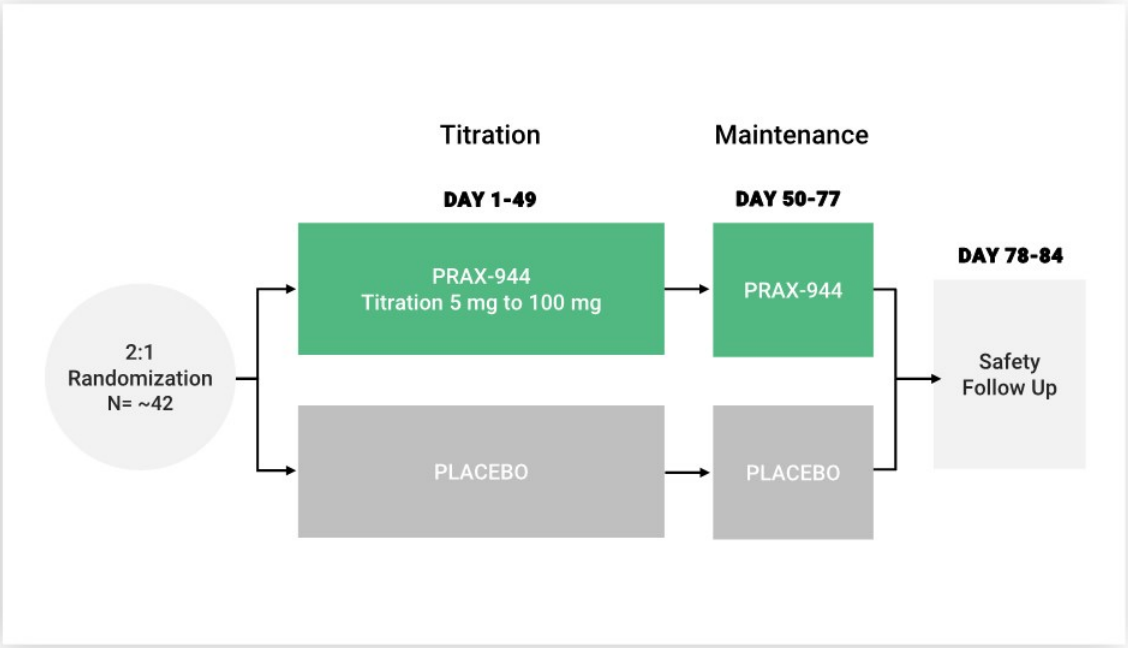


BLOCK OF BURST FIRING IMPROVES MOVEMENT IN 6-OHDA PARKINSON'S MODEL



PRAXIS PAN ET AL (2016) J CLIN INVEST DOI: 10.1172/JCI88170

PRAX-944 study to evaluate motor function in Parkinson's disease patients expected to initiate in 1H22



CLINICAL MEASUREMENTS:

Motor function

KEY QUESTION:

Does PRAX-944 demonstrate motor improvement in patients?

RARE DISEASES

PRAX-562
Persistent Sodium Channel Blocker
Adult Cephalgias
Pediatric Epilepsies (DEEs)

PRAX-222 (ASO)
Nav1.2 downregulation
SCN2A-DEE

KEY UPCOMING MILESTONES

1Q 2022
Initiate PRAX-562 Ph 2 SUNCT/SUNA/TN Trial

1H 2022
PRAX-562 Ph 1 ASSR Biomarker Topline

1H 2022
Initiate PRAX-562 Ph 2 DEE Trial

1H 2022
Initiate PRAX-222 Ph 1/2/3 SCN2A-DEE Trial

PRAXIS

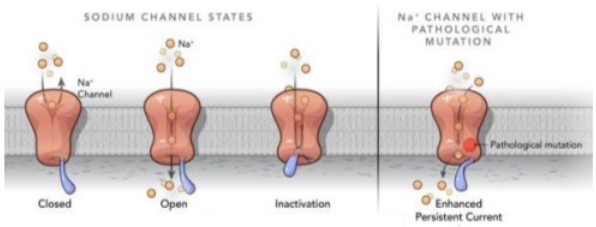
PRAX-562: Block of persistent sodium current can reduce neuronal hyperexcitability and impact multiple disease states

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

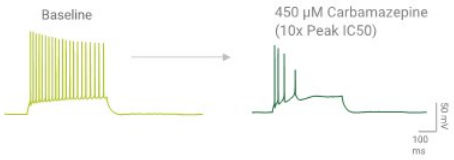
- Standard sodium channel blockers are an important class of medicines in neurology and psychiatry, broadly used in epilepsy, pain, migraine and bipolar disorder
- All standard NaV blockers target peak sodium current
- In general, efficacy is limited by side effects

Depakote divalproex sodium
Tegretol-XR carbamazepine extended-release tablets
Lidoderm lidocaine patch 5%
Oxtellar XR
Dilantin
EXPAREL
lamictal

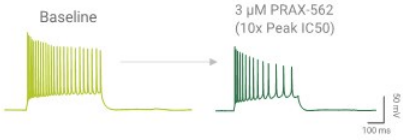
Modulation of persistent sodium current reduces hyperexcitability without disrupting AP



Carbamazepine Representative AP Traces



PRAX-562 Representative AP Traces



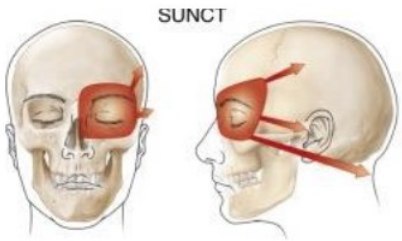
PRAXIS

Source: Schachter et al. antiseizure drugs UptoDate 2020, Praxis data

PRAX-562 has broad potential in rare CNS conditions

SUNCT, SUNA AND TRIGEMINAL NEURALGIA (TN)

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

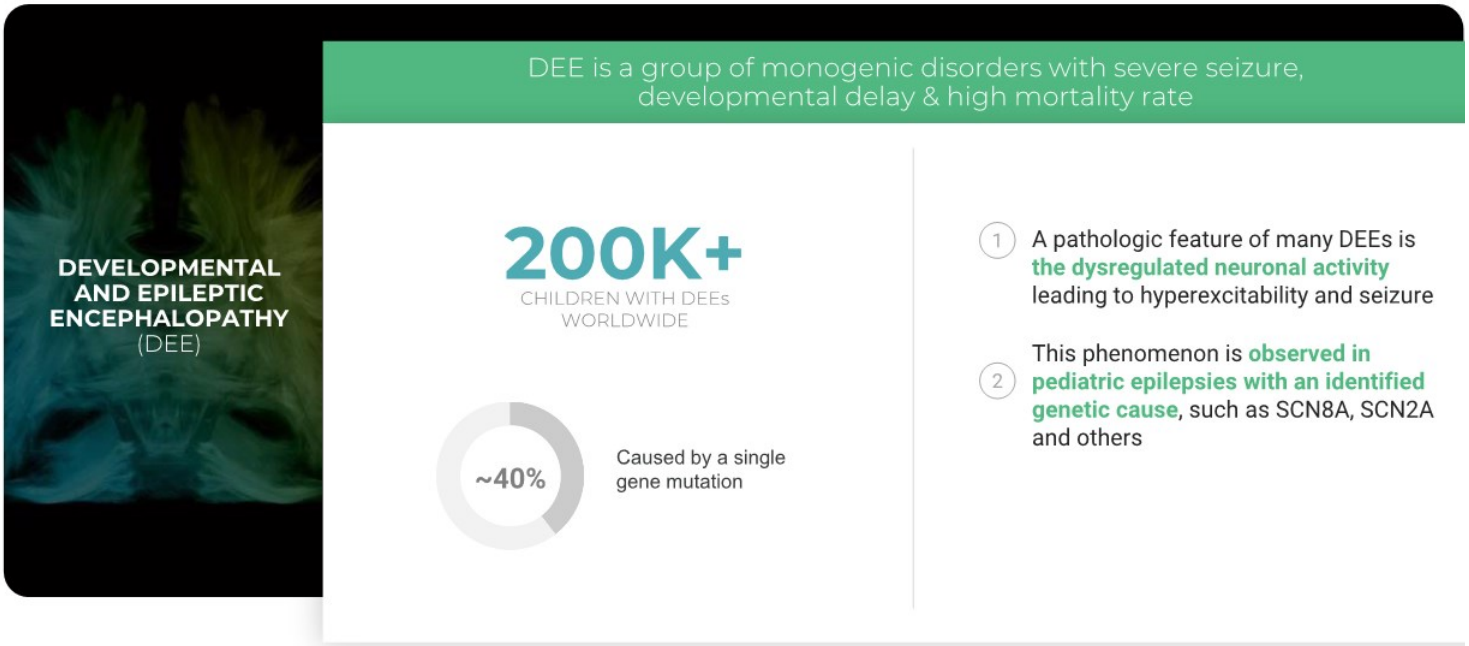


1. **SUNCT and SUNA Cephalgias** are devastating primary headaches highly responsive to IV sodium channel blockers
2. **Trigeminal Neuralgia** is characterized by intense, stabbing, electric-shock pain typically in the lower face and jaw, usually on one side of the face

PRAXIS

Source: Eltze et al. 2013 ; Howell et al 2018

PRAX-562 has broad potential in rare CNS conditions

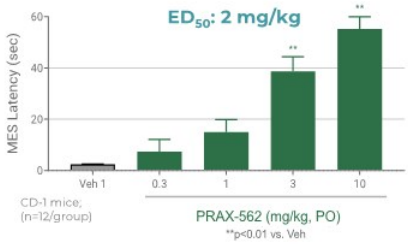


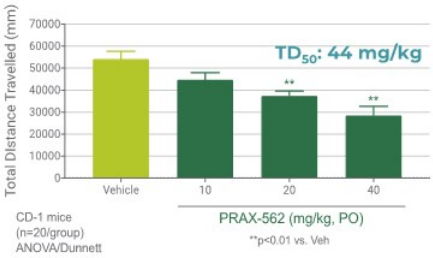
PRAXIS

Source: Eltze et al. 2013 ; Howell et al 2018

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
PRAX-562	**16.4x**
Carbamazepine	5.9x
Lamotrigine	4.6x

Therapeutic Index (TI) = TC_{50} / EC_{50}

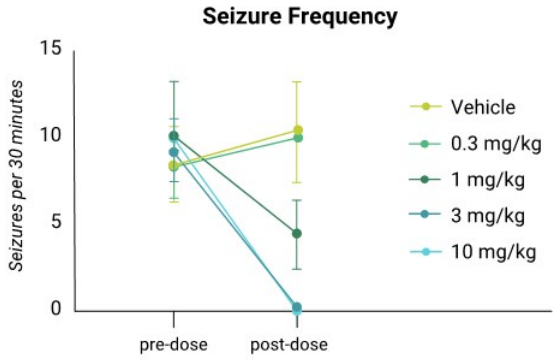
PRAX-562 had an increased ratio between drug levels that demonstrated preclinical anti-seizure activity versus those that caused toxicity

PRAXIS

Source: Praxis Data as of Sept. 3, 2020

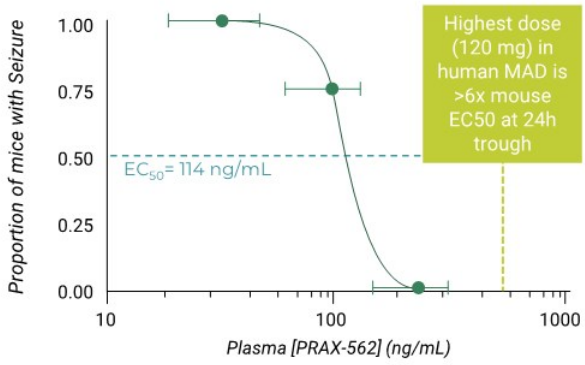
Treatment with PRAX-562 has shown significant reduction of seizures in geneti pediatric epilepsy animal models

PRAX-562 elicited dose-dependent prevention of seizures in SCN2A* 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 ± SEM, n=6-10 per symbol.

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



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

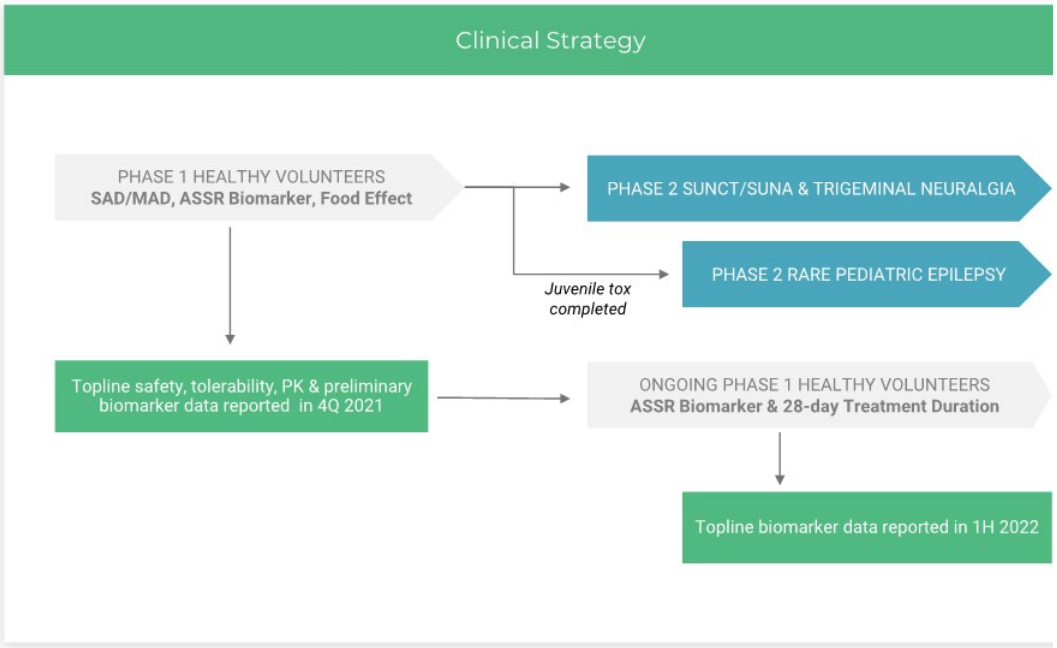
PRAXIS

*FDA granted orphan drug and rare pediatric designation for PRAX-562 for treatment of SCN2A-DEE and SCN8A-DEE

PRAX-562 development strategy in rare cephalgias and pediatric epilepsies

OBJECTIVE

Identify PoC and safety in SUNCT/SUNA & Trigeminal Neuralgia while continuing efforts to expand to rare pediatric epilepsies



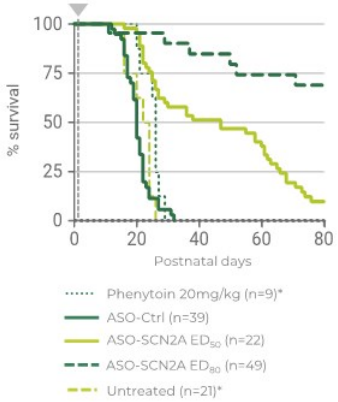
PRAX-222 is expected to initiate seamless, registrational first-in-patient trial in 1H

PRAX-222: ASO to treat SCN2A GoF Epilepsy

- Severe early onset epilepsy estimated to affect thousands of patients worldwide
- Antisense oligonucleotide (ASO) to down-regulate SCN2A expression

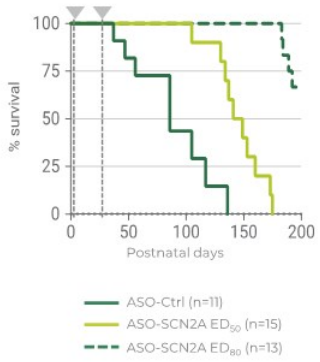
Increased Survival with Single ASO Dose at PN Day 1

ASO injection (icv)



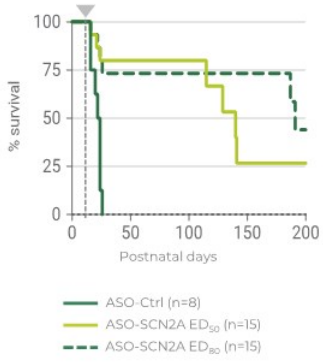
Redosing Significantly Extends Survival

ASO injections (icv)



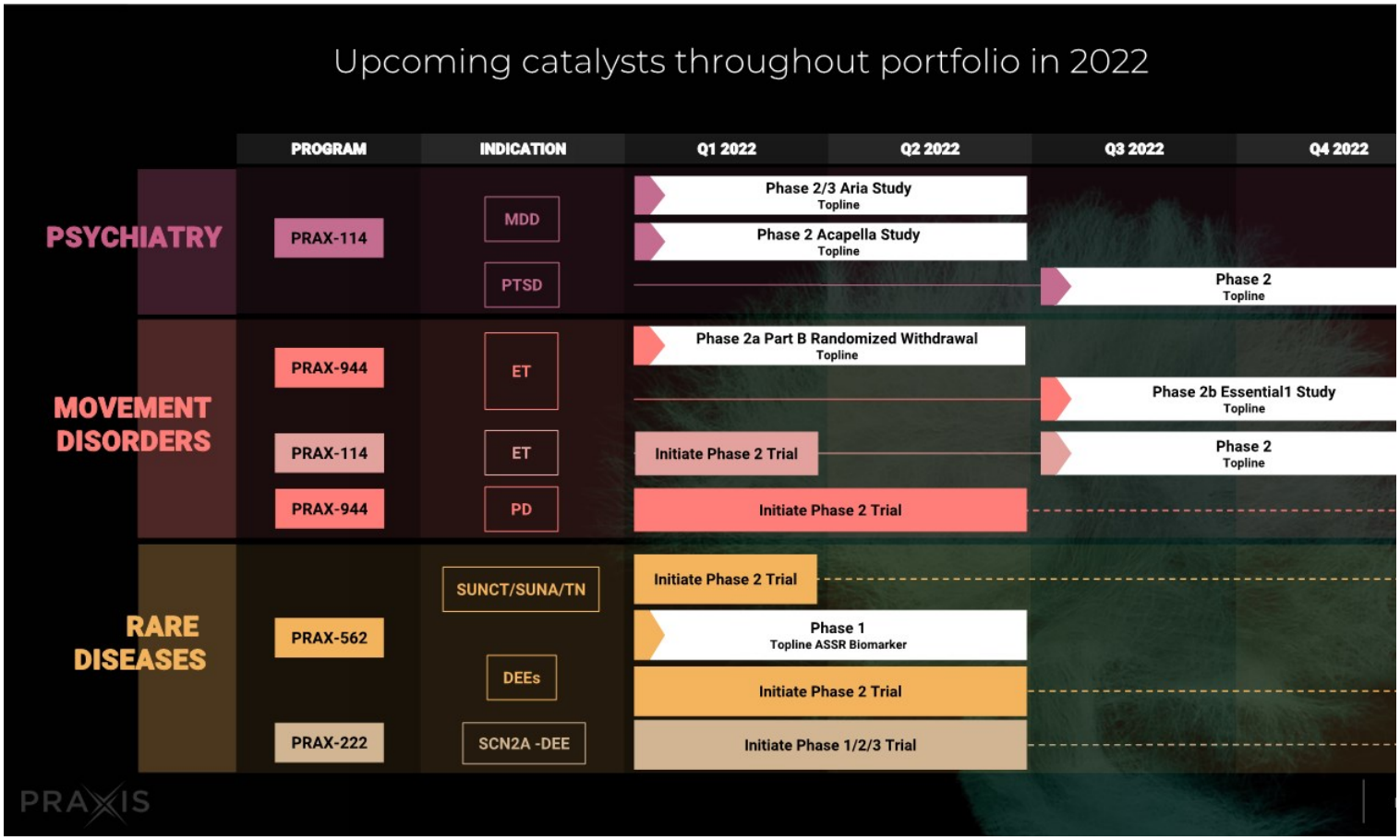
Administration Post-Disease Onset Also Extends Survival

ASO injection (icv, P15)



PRAXIS

Source: Praxis Data; *Data separate from experiment **All mice with zero seizure at baseline were excluded from the analysis; If all mice were included, would be 273%, -80%, -87%, -83% for vehicle, 30mg/kg, 75mg/kg and 150mg/kg group


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