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): February 28, 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 2.02. Results of Operations and Financial Condition.

On February 28, 2022, Praxis Precision Medicines, Inc. (the "Company") announced its financial results for the quarter and full year ended December 31, 2021. A copy of the press release is being furnished as Exhibit 99.1 to this Current Report on Form 8-K.

Item 7.01. Regulation FD Disclosure.

On February 28, 2022, the Company updated its corporate presentation for use in meetings with investors, analysts and others. The presentation is available in the "Investors + Media" portion of the Company's website at investors.praxismedicines.com and a copy is furnished as Exhibit 99.2 to this Current Report on Form 8-K.

The information in this Current Report on Form 8-K under Items 2.02 and 7.01, including Exhibit 99.1 and Exhibit 99.2 attached hereto, is intended to be furnished and 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 set forth by specific reference in such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release, dated February 28, 2022
99.2	Praxis Precision Medicines, Inc. February 2022 Corporate Presentation
104	Cover Page Interactive Data File (embedded within the inline XBRL document)

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: February 28, 2022

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

Praxis Precision Medicines Provides Corporate Update and Reports Fourth Quarter and Full Year 2021 Financial Results

PRAX-114 Phase 2/3 monotherapy MDD Aria Study topline results expected in June 2022

PRAX-944 Phase 2a ET topline results expected in May 2022; to include open-label and placebo-controlled withdrawal data

PRAX-222 seamless study in SCN2A-DEE expected to initiate in 2Q22

Cash and investments of $275.9 million as of December 31, 2021 supports runway into 2Q23

BOSTON, Mass., February 28, 2022 — Praxis Precision Medicines, Inc. (NASDAQ: PRAX), a clinical-stage biopharmaceutical company translating genetic insights into the development of therapies for central nervous system (CNS) disorders characterized by neuronal excitation-inhibition imbalance, today provided a corporate update, including a video highlighting recent business and pipeline progress, and reported financial results for the fourth quarter and full year 2021.

“With screening now closed in all sites in the PRAX-114 Aria Study, we are emboldened by the progress in our psychiatry franchise, and broadly across our pipeline,” said Marcio Souza, president and chief executive officer of Praxis. “There is a clear unmet need for a fast-acting, durable depression treatment with a differentiated tolerability profile relative to both existing treatment options and other drugs in development, which allows patients to remain on drug throughout an episode of depression. We look forward to reporting topline results from the Aria Study in June, followed shortly thereafter by results from the Acapella Study, and intend to initiate a Phase 3 trial in MDD later this year. With additional topline data expected from PRAX-114 studies for PTSD and ET, as well as from PRAX-944 for ET, 2022 is shaping up to be a transformative year for Praxis and we are eager to share our continued progress and growth.”

Recent Business Highlights and Upcoming Milestones:

Psychiatry

- Praxis expects topline results from the PRAX-114 Phase 2/3, placebo-controlled Aria Study for monotherapy treatment of Major Depressive Disorder (MDD) in the second quarter of 2022, in June. The Aria Study is intended to serve as one of two trials required by the U.S. Food and Drug Administration (FDA) to demonstrate clinical efficacy to support registration of PRAX-114 for monotherapy treatment of MDD.

- The Company expects topline results from the PRAX-114 Phase 2, placebo-controlled, dose-ranging Acapella Study for treatment of MDD in mid-2022. The Acapella Study is intended to provide additional understanding of the dose range and to evaluate the safety and efficacy of PRAX-114 at doses of 10, 20, 40 and 60 mg.

- Praxis initiated a PRAX-114 Phase 2, placebo-controlled study for treatment of post-traumatic stress disorder (PTSD) in the fourth quarter of 2021 and has started dosing participants. Topline results are expected in the second half of 2022. The trial is designed to evaluate the safety, tolerability and efficacy of a nightly dose of 40 mg of PRAX-114 for 4 weeks in approximately 80 participants with PTSD, using the CAPS-5 total score as the primary endpoint.

Movement Disorders

- In December 2021, Praxis reported preliminary open-label data from the second of two cohorts of its PRAX-944 Phase 2a trial for daytime treatment of essential tremor (ET), evaluating safety and efficacy in participants titrated up to 120 mg per day. Enrollment of study participants was subsequently completed. Topline open-label and placebo-controlled, randomized withdrawal results are expected in the second quarter of 2022, in May.

- The Company expects topline results from the PRAX-944 Phase 2b Essential1 Study for daytime treatment of ET in the second half of 2022. Essential1 is a placebo-controlled, dose-ranging clinical trial designed to evaluate the safety, tolerability and efficacy of PRAX-944 at 20, 60 or 100 mg per day.

- Praxis expects to initiate a PRAX-114 Phase 2, placebo-controlled, crossover study for daytime treatment of ET to evaluate safety, pharmacokinetics (PK) and efficacy of 10 and 20 mg of PRAX-114 in the first quarter of 2022. Topline results are expected in the second half of 2022.

- Praxis intends to initiate a Phase 2, placebo-controlled trial to evaluate the safety, PK and efficacy of PRAX-944 as a non-dopaminergic treatment for the motor symptoms of Parkinson's disease in the second quarter of 2022.

Epilepsy

- Praxis plans to initiate a PRAX-562 Phase 2, placebo-controlled trial for treatment of developmental epileptic encephalopathies (DEEs) in the second quarter of 2022.

- Praxis intends to initiate a seamless study of PRAX-222, its lead antisense oligonucleotide (ASO) candidate, for the treatment of SCN2A-DEE in the second quarter of 2022.

- In January 2022, the European Medicines Agency (EMA) Committee for Orphan Medicinal Products (COMP) granted Orphan Drug Designation (ODD) to PRAX-222 for the treatment of SCN2A-DEE. Previously, in January 2021, the FDA granted both ODD and Rare Pediatric Disease (RPD) designation to PRAX-222 for the treatment of SCN2A-DEE.

- In December 2021, the EMA COMP granted ODD to PRAX-562 for the treatment of SCN8A-DEE and SCN2A-DEE. Previously, in January 2021, the FDA granted both ODD and RPD designation to PRAX-562 for the treatment of SCN8A-DEE and SCN2A-DEE.

- In December 2021, Praxis presented data from two of its rare epilepsy programs, PRAX-562 and its KCNT1 inhibitor, at the American Epilepsy Society 2021 Annual Meeting. Presentations on PRAX-562 focused on its potent anticonvulsant activity in SCN2A-DEE and SCN8A-DEE mouse models and its mechanistic distinction relative to standard-of-care sodium channel inhibitors, with greater potency and selectivity for persistent sodium current. The presentation on KCNT1 focused on the compound's in vitro and in vivo profiling, including its efficacy in a KCNT1 gain-of-function mouse model.

- In December 2021, Praxis entered into a research collaboration with Cerebral Therapeutics, Inc., with an exclusive option to in-license delivery technology for intracerebroventricular administration of its ASOs.

- Praxis intends to develop PRAX-628, a small molecule with unique NaV channel binding kinetics that favor inhibition of pathological neuronal activity underlying aberrant brain function, such as that seen in the initial indication of focal onset seizures. The Company anticipates use in other common forms of epilepsy and CNS excitability disorders more generally. PRAX-628 is currently in IND-enabling toxicology studies.

Other Exploratory CNS Indications

- Praxis plans to initiate a PRAX-562 Phase 2, placebo-controlled trial for treatment of rare adult cephalgias in the first quarter of 2022, including a cohort of participants with Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing (SUNCT) and Short-lasting Unilateral Neuralgiform headache with Autonomic symptoms (SUNA), and a cohort of participants with Trigeminal Neuralgia (TN).

General Corporate Updates

- In December 2021, Praxis announced the appointment of Megan Sniecinski as chief business officer, the promotions of Alyssa Wyant to chief regulatory and quality officer and Karl Hansen, Ph.D., to chief technical operations officer, and the decision by chief scientific officer and co-founder, Steven Petrou, Ph.D., to fully dedicate his time to Praxis upon stepping down from his role as Director of the Florey Institute of Neuroscience and Mental Health and Head of the Florey Department at The University of Melbourne.

Fourth Quarter and Full Year 2021 Financial Results:
As of December 31, 2021, Praxis had $275.9 million in cash, cash equivalents and marketable securities, compared to $296.6 million in cash and cash equivalents as of December 31, 2020. This decrease of $20.7 million primarily reflects cash used in operations of $124.6 million during the year ended December 31, 2021, partially offset by $105.7 million in net proceeds from the follow-on public offering of shares of the Company's common stock in May 2021 and at-the-market offerings during the fourth quarter of 2021. The company's cash, cash equivalents and marketable securities as of December 31, 2021 are expected to fund operations into the second quarter of 2023.

Research and development expenses were $43.5 million for the fourth quarter of 2021, compared to $16.3 million for the fourth quarter of 2020. Research and development expenses were $120.3 million for the year ended December 31, 2021, compared to $45.0 million for the year ended December 31, 2020. The increase in research and development expenses for full year 2021 of $75.3 million was primarily attributable to $43.6 million in increased expenses related to the Company's franchises, $17.6 million in increased personnel-related costs due to increased headcount and $8.8 million in increased expenses for other exploratory CNS indications.

General and administrative expenses were $15.1 million for the fourth quarter of 2021, compared to $9.4 million for the fourth quarter of 2020. General and administrative expenses were $47.1 million for the year ended December 31, 2021, compared to $17.0 million for the year ended December 31, 2020. The increase in general and administrative expenses for full year 2021 of $30.1 million was primarily attributable to $14.6 million in increased personnel-related costs due to increased headcount, $9.9 million in increased professional fees and a $5.6 million increase in other general and administrative expenses.

Praxis reported a net loss of $58.6 million for the fourth quarter of 2021, including $6.1 million of stock-based compensation expense, compared to $25.7 million for the fourth quarter of 2020, including $3.8 million of stock-based compensation expense. Praxis reported a net loss of $167.1 million for the year ended December 31, 2021, including $22.7 million of stock-based compensation expense, compared to a net loss of $61.8 million for the year ended December 31, 2020, including $5.2 million of stock-based compensation expense.

As of December 31, 2021, Praxis had 45.3 million shares of common stock outstanding.

Conference Call and Webcast
Praxis will host a Q&A session focused on today's corporate update and financial results for the fourth quarter and full year 2021 via a conference call and webcast today, February 28, 2022, at 8:30 a.m. ET. To access the conference call, please dial (833) 398-1037 (local) or (914) 987-7735 (international) at least 10 minutes prior to the start time and refer to conference ID 8993704. A live audio webcast of the event may also be accessed through the Events & Presentations page of the Investors + Media section of the company's website at https://investors.praxismedicines.com/events-and-presentations. A replay of the webcast will be available on Praxis' website approximately two hours after the completion of the event and will be archived for 30 days following the event.

About Praxis
Praxis Precision Medicines is a clinical-stage biopharmaceutical company translating genetic insights into the development of therapies for CNS disorders characterized by neuronal excitation-inhibition imbalance. Praxis is applying insights from genetic epilepsies to both rare and more prevalent neurological and psychiatric disorders, using our understanding of shared biological targets and circuits in the brain. Praxis has established a broad portfolio with multiple programs, including product candidates across psychiatric disorders, movement disorders, epilepsy and other exploratory CNS indications, with three clinical-stage product candidates. For more information, please visit www.praxismedicines.com and follow us on LinkedIn and Twitter.

Forward-Looking Statements
This press release 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 Praxis' future expectations, plans and prospects, including, without limitation, statements regarding expectations, plans and timing for our clinical data, the anticipated timing of our clinical trials and regulatory filings, the development of our product candidates, including the design of our clinical trials and the treatment potential of our product candidates, and the sufficiency of our cash, cash equivalents and marketable securities, and as well as other statements containing the

words “anticipate,” “believe,” “continue,” “could,” “endeavor,” “estimate,” “expect,” “anticipate,” “intend,” “may,” “might,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will” or “would” and similar expressions that constitute forward-looking statements under the Private Securities Litigation Reform Act of 1995.

The express or implied forward-looking statements included in this press release 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 Praxis’ business, operations, strategy, goals and anticipated timelines, Praxis’ ongoing and planned preclinical activities, Praxis’ ability to initiate, enroll, conduct or complete ongoing and planned clinical trials and Praxis’ timelines for regulatory submissions; and other risks concerning Praxis’ programs and operations are described in additional detail in its Annual Report on Form 10-K for the year ended December 31, 2021 to be filed and other filings made with the Securities and Exchange Commission. Although Praxis’ forward-looking statements reflect the good faith judgment of its management, these statements are based only on information and factors currently known by Praxis. As a result, you are cautioned not to rely on these forward-looking statements. Any forward-looking statement made in this press release speaks only as of the date on which it is made. Praxis undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future developments or otherwise.

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PRAXIS PRECISION MEDICINES, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(Amounts in thousands)
(Unaudited)

	December 31,	
	2021	**2020**
Assets		
Cash and cash equivalents	$ 138,704	$ 296,608
Marketable securities	137,207	—
Prepaid expenses and other current assets	11,498	5,718
Property and equipment, net	1,213	82
Operating lease right-of-use assets	3,653	754
Other non-current assets	472	15
Total assets	$ 292,747	$ 303,177
Liabilities and stockholders' equity		
Accounts payable	$ 10,780	$ 4,088
Accrued expenses	26,844	10,869
Operating lease liabilities	4,311	763
Common stock	5	4
Additional paid-in capital	567,598	437,007
Accumulated other comprehensive loss	(176)	—
Accumulated deficit	(316,615)	(149,554)
Total liabilities and stockholders' equity	$ 292,747	$ 303,177

PRAXIS PRECISION MEDICINES, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(Amounts in thousands, except share and per share amounts)
(Unaudited)

	Three Months Ended December 31,		Year Ended December 31,	
	2021	2020	2021	2020
Operating expenses:				
Research and development	$ 43,511	$ 16,272	$ 120,257	$ 44,976
General and administrative	15,146	9,440	47,075	16,992
Total operating expenses	58,657	25,712	167,332	61,968
Loss from operations	(58,657)	(25,712)	(167,332)	(61,968)
Other income:				
Other income, net	70	6	271	140
Total other income	70	6	271	140
Loss before benefit from income taxes	(58,587)	(25,706)	(167,061)	(61,828)
Benefit from income taxes	5	—	—	8
Net loss	$ (58,582)	$ (25,706)	$ (167,061)	$ (61,820)
Accretion and cumulative dividends on redeemable convertible preferred stock	—	(950)	—	(8,996)
Gain on repurchase of redeemable convertible preferred stock	—	—	—	493
Net loss attributable to common stockholders	$ (58,582)	$ (26,656)	$ (167,061)	$ (70,323)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.30)	$ (0.87)	$ (3.94)	$ (7.86)
Weighted average common shares outstanding, basic and diluted	44,964,580	30,703,886	42,454,055	8,950,152


PRAXIS
CORPORATE
OVERVIEW
FEBRUARY 2022
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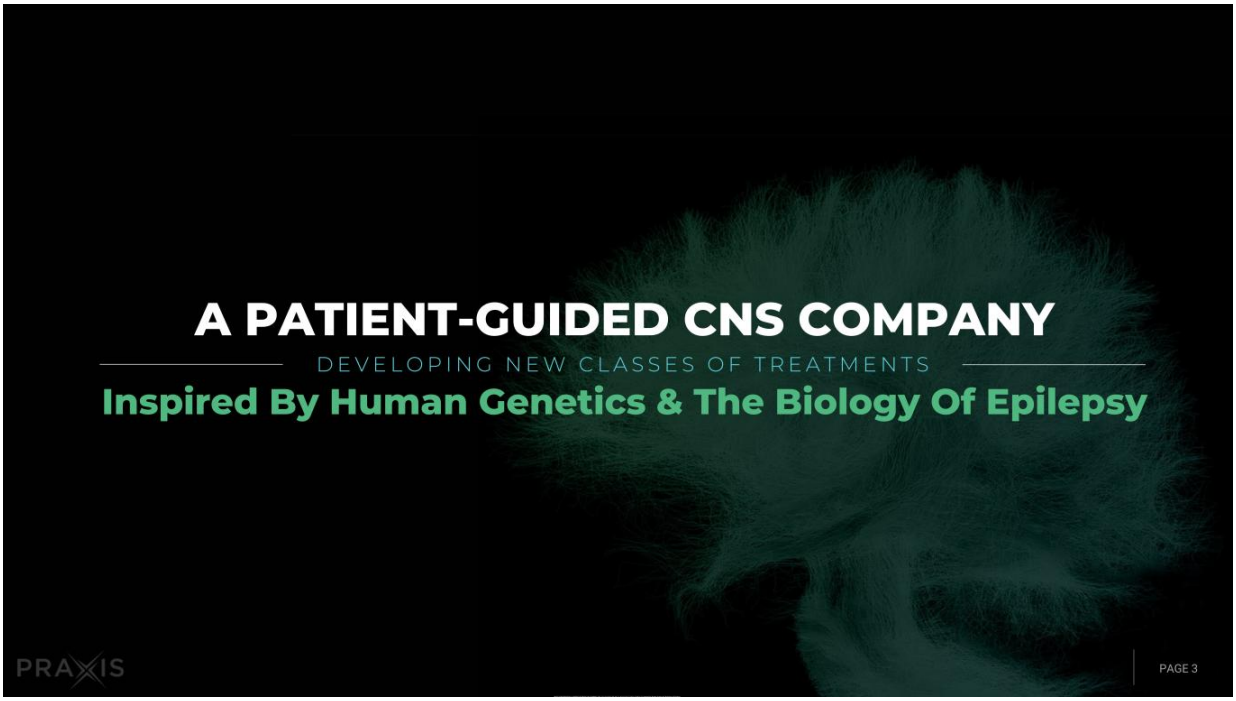
Forward-looking statements

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.

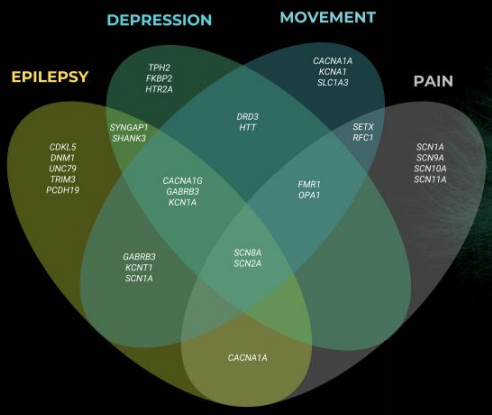
For further information regarding the risks, uncertainties and other factors that may cause differences between our expectations and actual results, you should review the "Risk Factors" section of our Annual Report on Form 10-K filed for the year ended December 31, 2021 and other filings with the Securities 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.

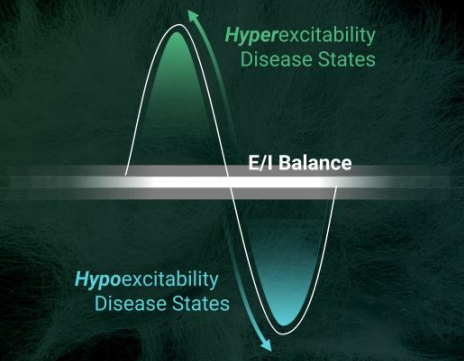

A PATIENT-GUIDED CNS COMPANY
DEVELOPING NEW CLASSES OF TREATMENTS
Inspired By Human Genetics & The Biology Of Epilepsy
PRAXIS
PAGE 3

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

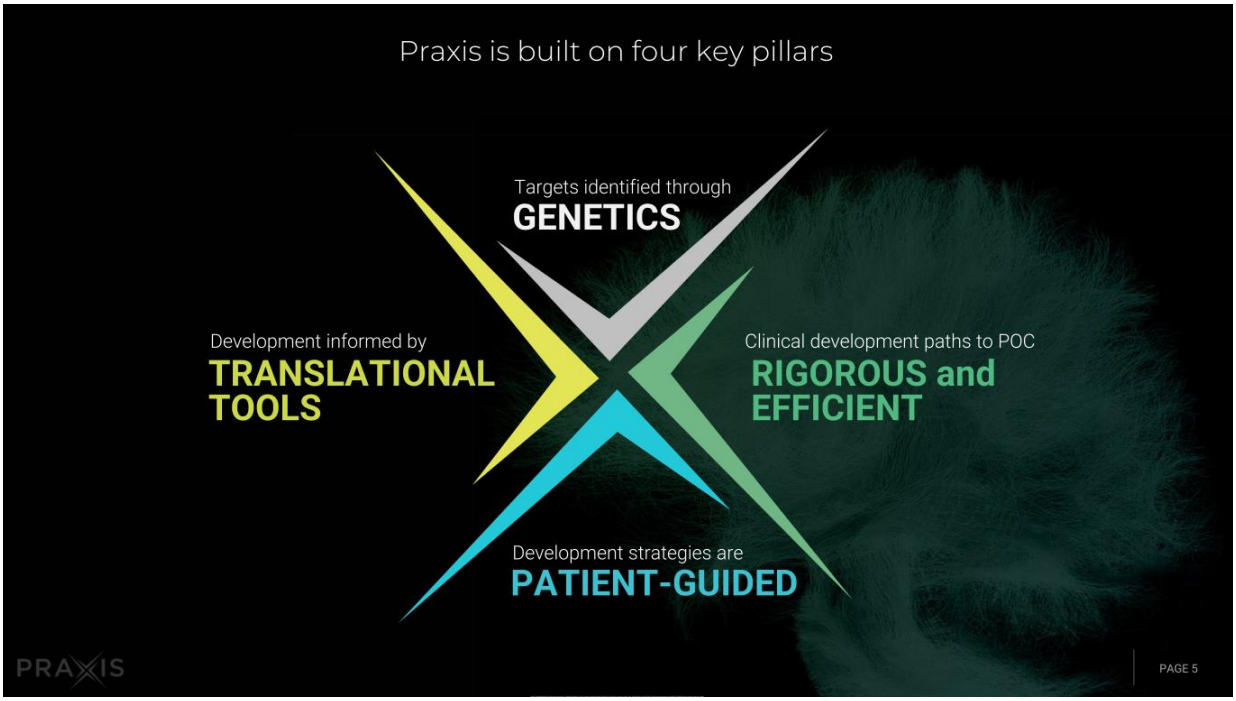
Targets Elucidated By Genetics



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
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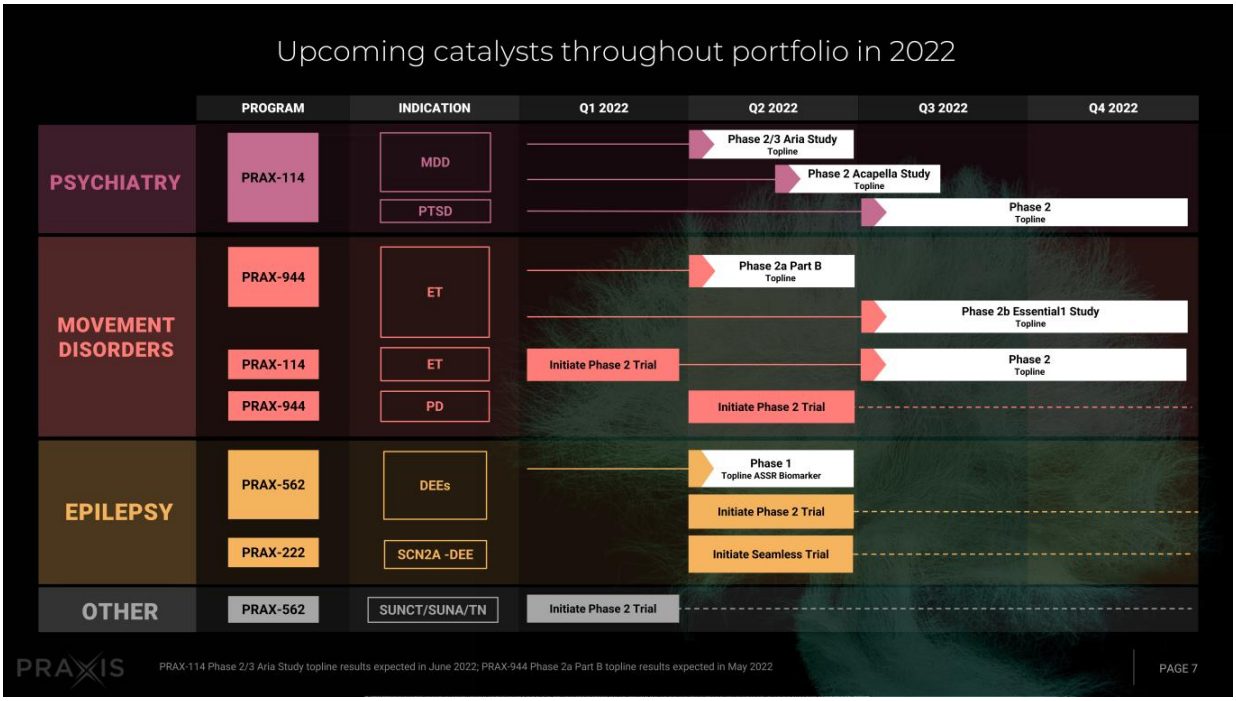
Broad portfolio of highly differentiated programs across multiple CNS disorders

FRANCHISE	MECHANISM OF ACTION	PROGRAM	PRECLINICAL	PHASE 1	PHASE 2	REGISTRATIONAL ENABLING
PSYCHIATRY	$GABA_A$ receptor PAM	PRAX-114 *Small molecule*			PRAX-114 PTSD	PRAX-114 MDD
	Undisclosed	PRAXIS-040 *Small molecule*	PRAXIS-040 UNDISCLOSED PSYCHIATRY TARGET			
MOVEMENT DISORDERS	$GABA_A$ receptor PAM	PRAX-114 *Small molecule*			PRAX-114 Essential Tremor	
	T-type calcium channel blocker	PRAX-944 *Small molecule*			PRAX-944 PD; PRAX-944 Essential Tremor	
	Undisclosed	PRAXIS-050 *Small molecule*	PRAXIS-050 UNDISCLOSED MOVEMENT TARGET			
EPILEPSY	Persistent sodium current blocker	PRAX-562 *Small molecule*			PRAX-562 DEEs	
	Nav1.2 downregulation	PRAX-222 *ASO*	PRAX-222 SCN2A-DEE			
	Potassium channel T 1 blocker	PRAX-020 *Small molecule*	PRAX-020 KCNT1			
	Activity dependent sodium current blocker	PRAX-628 *Small molecule*	PRAX-628 Focal Epilepsy			
	Nav1.2 upregulation	SCN2A-LOF* *ASO*	SCN2A LoF ASO SCN2A-DEE			
	RAS GTPase activating protein (SynGAP) upregulation	SYNGAP1* *ASO*	SYNGAP1 ASO SYNGAP1			
	Protocadherin-19 downregulation	PCDH19* *ASO*	PCDH19 ASO PCDH19			
	Undisclosed	PRAXIS-030 *Small molecule*	PRAXIS-030 UNDISCLOSED EPILEPSY TARGET			
OTHER CNS	Persistent sodium current blocker SCN8A	PRAX-562 *Small molecule*			PRAX-562 SUNCT/SUNA/TN	

PRAXIS

* SCN2A-LOF, SYNGAP1 & PCDH19 ASOs are a collaboration with The Florey Institute
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


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
Topline
Phase 2b Essential1 Study
Topline
PRAX-114
ET
Initiate Phase 2 Trial
Phase 2
Topline
PRAX-944
PD
Initiate Phase 2 Trial
EPILEPSY
PRAX-562
DEEs
Phase 1
Topline ASSR Biomarker
Initiate Phase 2 Trial
PRAX-222
SCN2A -DEE
Initiate Seamless Trial
OTHER
PRAX-562
SUNCT/SUNA/TN
Initiate Phase 2 Trial
PRAXIS
PRAX-114 Phase 2/3 Aria Study topline results expected in June 2022; PRAX-944 Phase 2a Part B topline results expected in May 2022
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DARE for MORE
PRAXIS
PAGE 8

PSYCHIATRY

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

KEY UPCOMING MILESTONES

2Q 2022
Ph 2/3 Monotherapy MDD Aria Study Topline

MID-2022
Ph 2 MDD Dose-Ranging Acapella Study Topline

2H 2022
Ph 2 PTSD Topline

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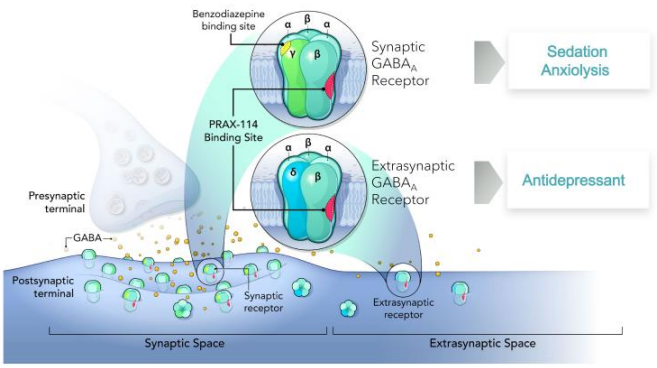
Major depressive disorder is a growing and debilitating disorder with substantial unmet need despite numerous treatment options

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 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

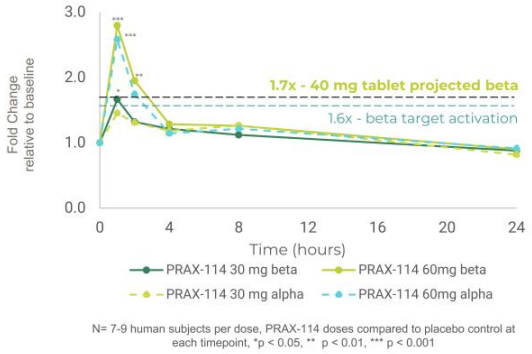
$\alpha_4\beta_3\delta$: extrasynaptic $GABA_A$ receptor **$\alpha1\beta_2\gamma_2$:** synaptic $GABA_A$ receptor

* Equivalent of full activation by GABA

Source: PRAXIS data

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

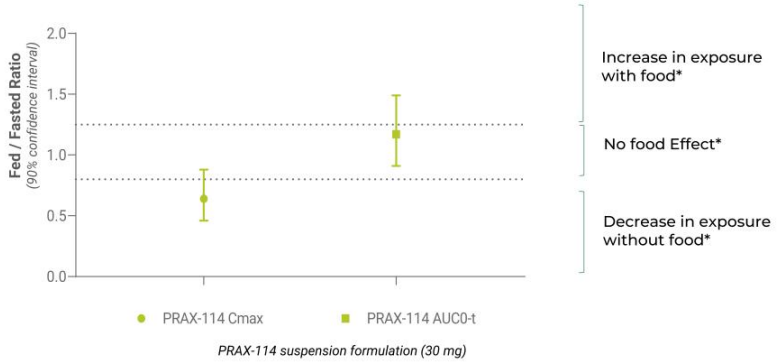
No MTD identified up to 80mg

Tolerability profile maintained throughout dose escalation

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

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

Effect of high-fat meal on pharmacokinetics



PRAX-114 suspension formulation (30 mg)

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

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

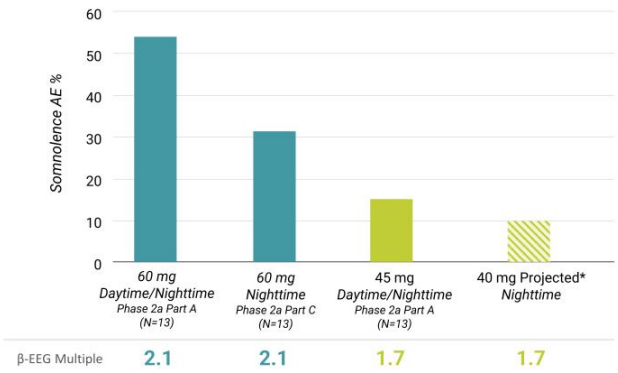
Visit	HAM-A *Anxiety Rating Scale* Mean (SD) N=52	HAM-D *Insomnia Item Total (max score of 6)* Mean (SD) N=52
Day 1 (BL)	22.4 (4.16)	4.2 (1.3)
Day 8 (CFB)	-12.4 (7.55)	-2.8 (1.9)
Day 15 (CFB)	-11.6 (6.67)	-3.1 (1.7)

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



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

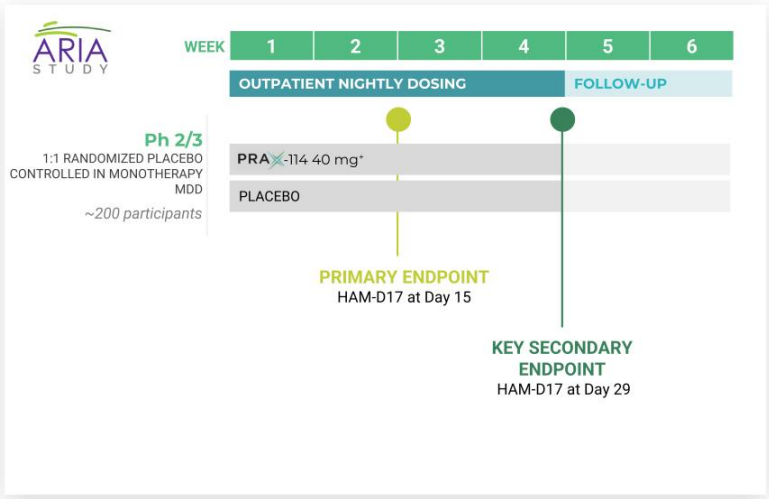
*Estimated somnolence rate for PRAX-114 40 mg tablet is derived by combining somnolence AE data from all 45 mg nighttime dosing cohorts. This estimate does not reflect data from any patients dosed at the 40 mg level and there is no guarantee that actual data for patients dosed at the 40 mg level will reflect such estimates.
**Modified Observer's Assessment of Alertness/Sedation Scale (MOAA/S) was administered during the inpatient phase of Part A of the Phase 2a to assess potential for daytime somnolence; one participant in PMD cohort of Phase 2a study discontinued treatment due to AEs of moderate daytime sedation and mild feeling abnormal

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

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/

PRAX-114 monotherapy MDD Phase 2/3 Aria Study topline data expected 2Q 2022*



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

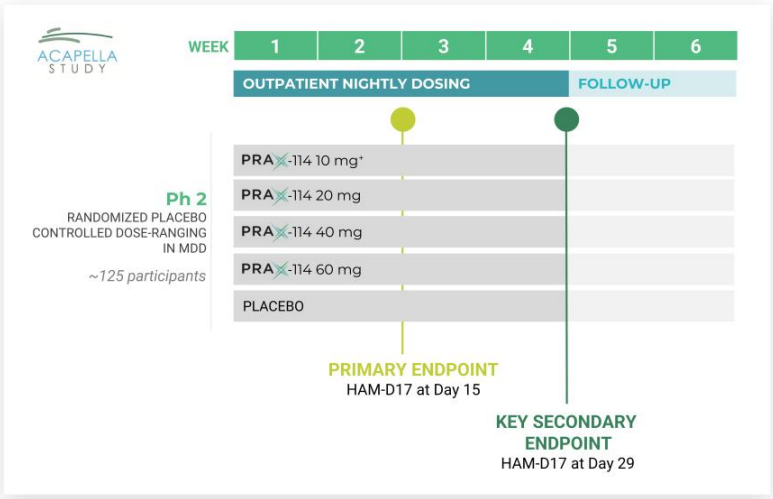
KEY EXCLUSION CRITERIA

Treatment-resistant depression
Current antidepressant treatment

PRAXIS

* Topline results expected in June 2022
*PRAX-114 administered in tablet formulation
clinicaltrials.gov/ct2/show/NCT04832425; https://theariastudy.com/

PRAX-114 MDD Phase 2 Acapella Study topline data expected mid-year 2022



PHASE 2

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

KEY INCLUSION CRITERIA

Ages 18-65
HAM-D17 ≥ 20
At least one prior episode of MDD

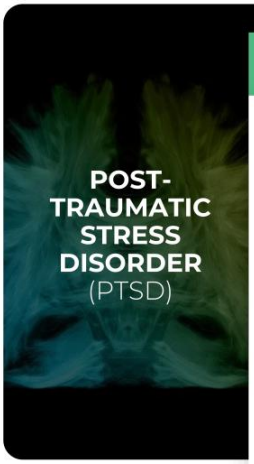
KEY EXCLUSION CRITERIA

Treatment-resistant depression

PRAXIS

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

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



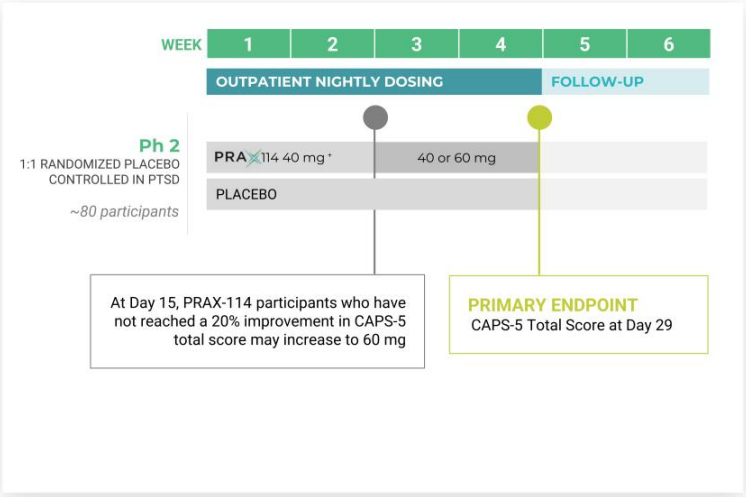
Dysfunction of GABA pathway is associated with chronic stress and symptoms of PTSD

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

Dosing has started in PRAX-114 PTSD Phase 2 study



TOPLINE DATA EXPECTED 2H22

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

KEY INCLUSION CRITERIA

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

*PRAX-114 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

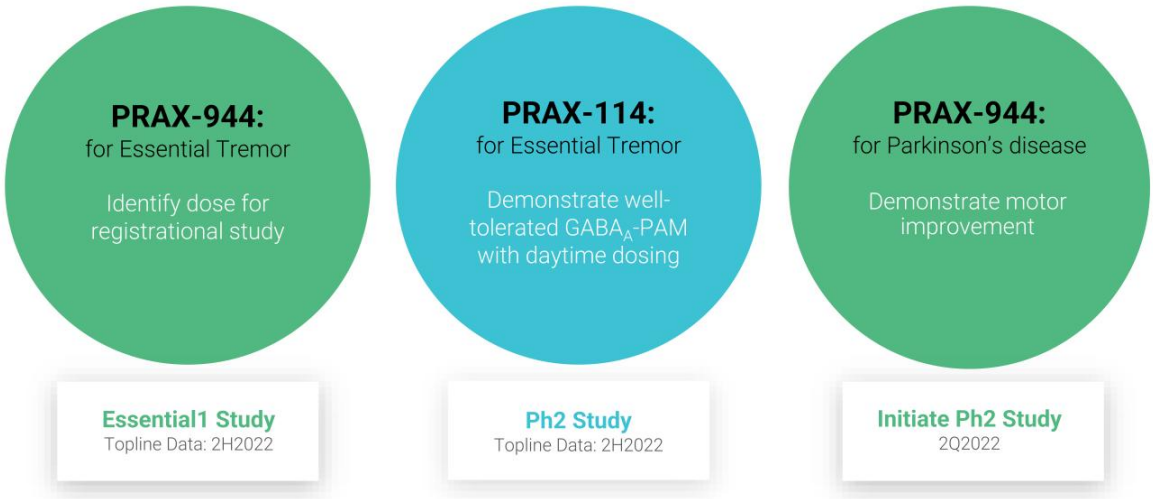
2Q 2022
Initiate PRAX-944 Ph 2 PD Trial

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

2H 2022
PRAX-114 Ph 2 ET Topline

PRAXIS

Movement Disorder franchise focus for 2022



Essential1 Study
Topline Data: 2H2022

Ph2 Study
Topline Data: 2H2022

Initiate Ph2 Study
2Q2022

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]

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.

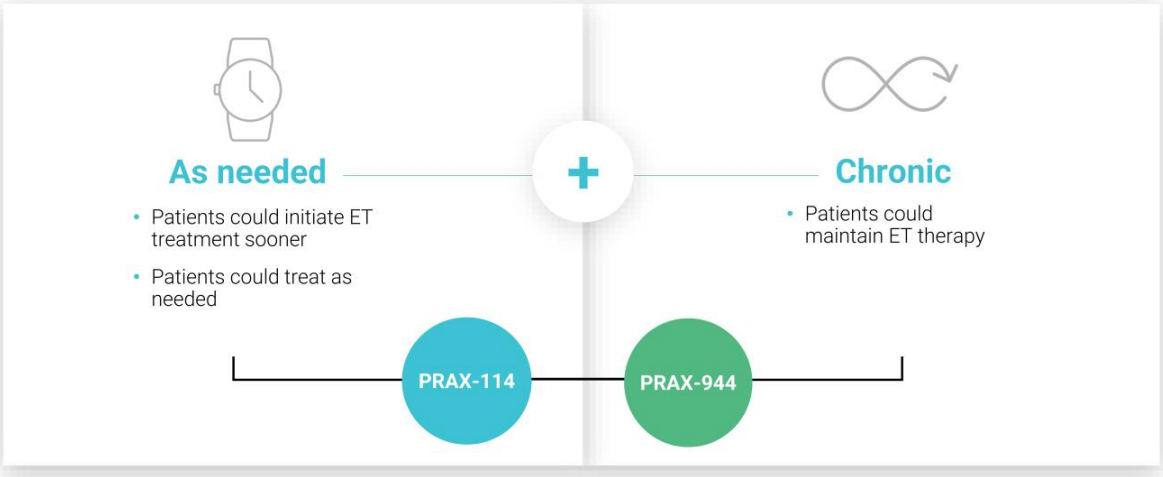
ET burden of disease extends beyond the tremor

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.

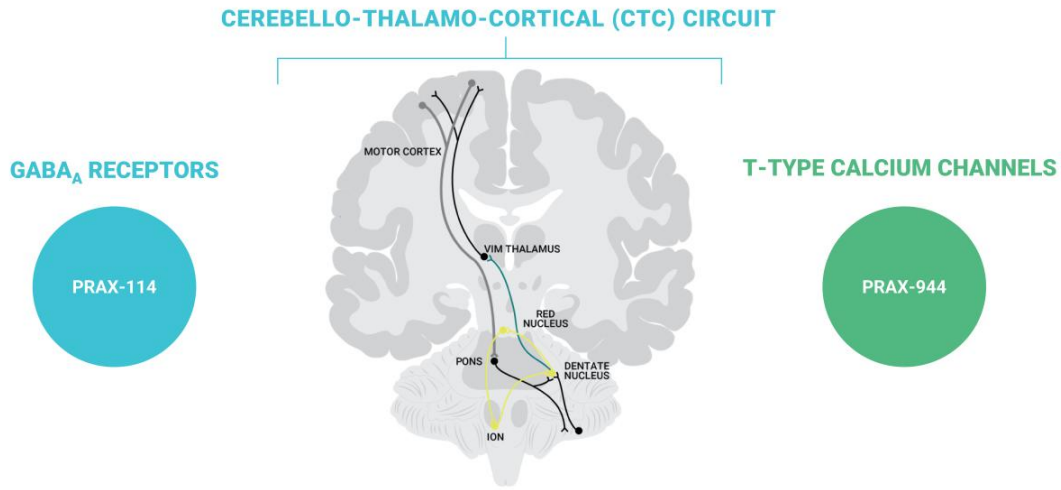
Our focus is on elevating the standard of care to capture the $4B+ US ET market

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

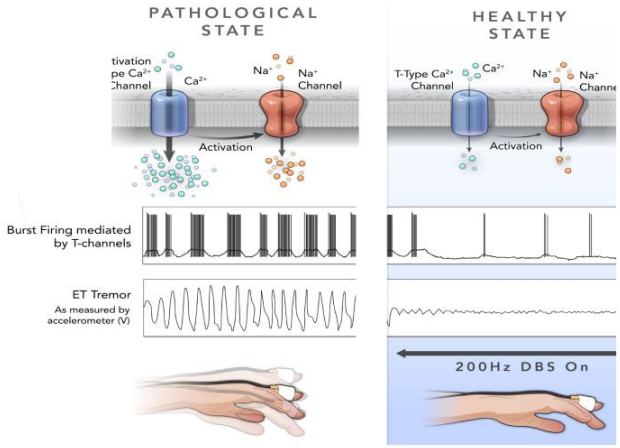
Praxis treatments could allow patients to fit the right therapy to their needs to realize improved outcomes



Tackling Movement Disorders through two mechanisms of action



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

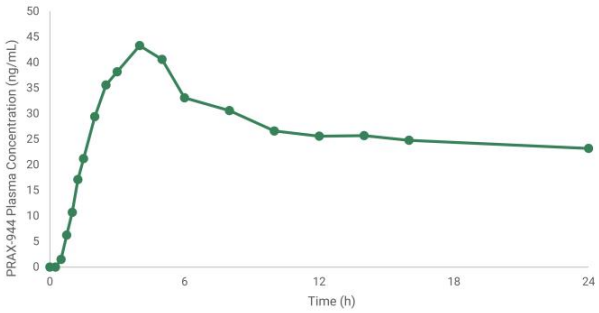
Burst firing in the CTC circuit correlated with tremor in patients with ET and PD

Deep Brain Stimulation reduces burst firing and tremor

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

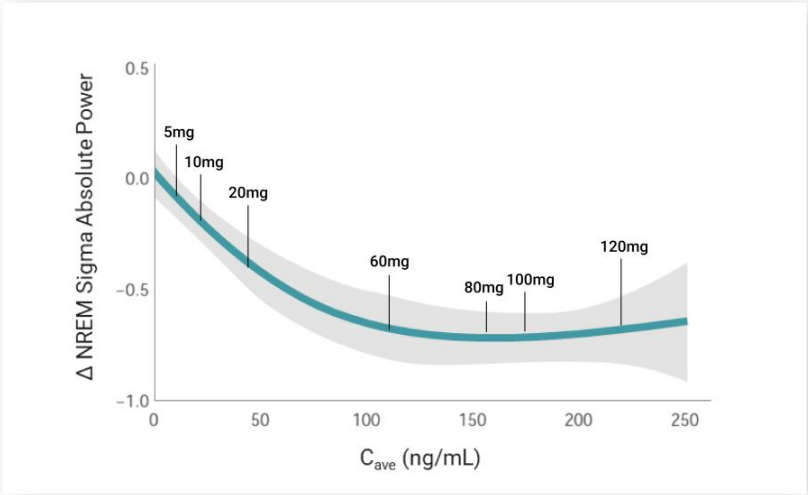
MR formulation is well-tolerated

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

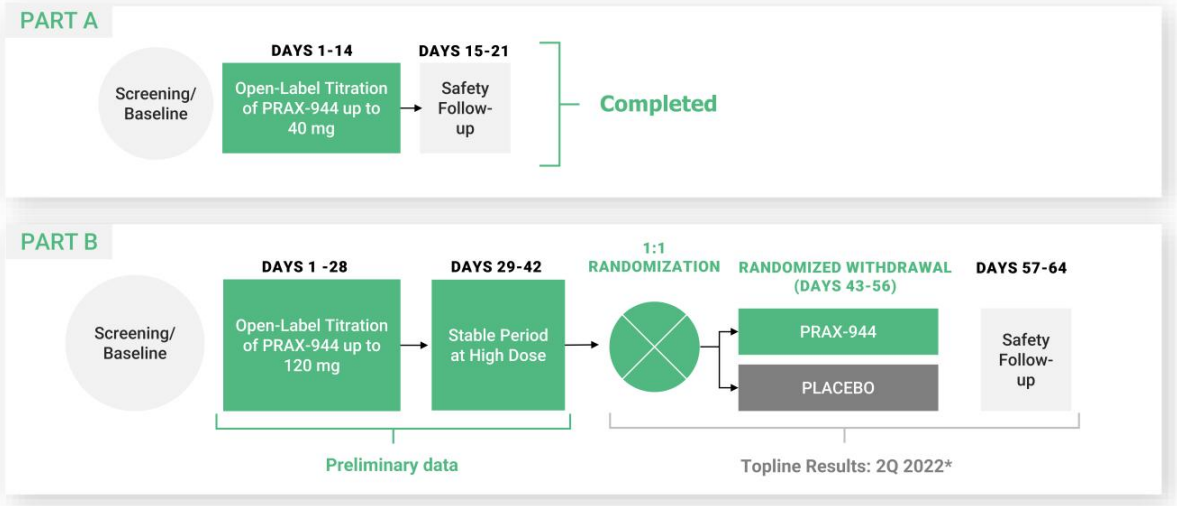


KEY TAKEAWAYS

- 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

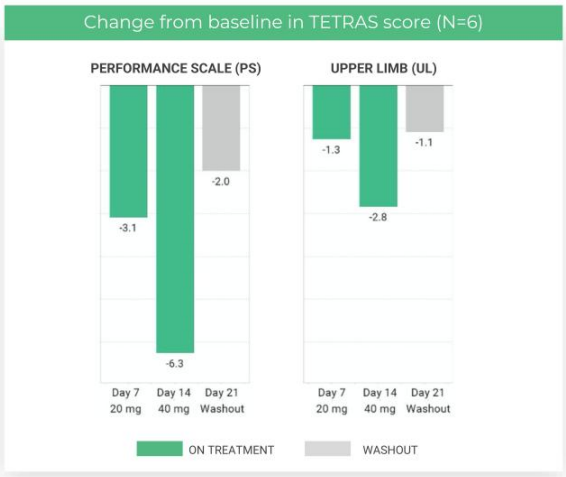
SOURCE: PRAXIS STUDY-944-105; PRAXIS DATA ON FILE

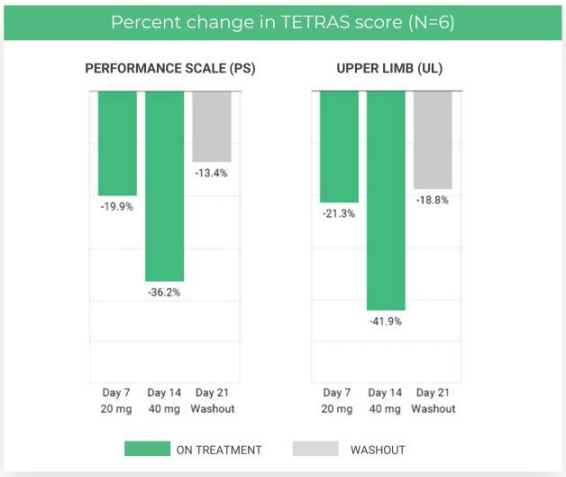
Enrollment completed in PRAX-944 Phase 2a ET study



CLINICALTRIALS.GOV/CT2/SHOW/NCT05021978
*Topline results expected in May 2022

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

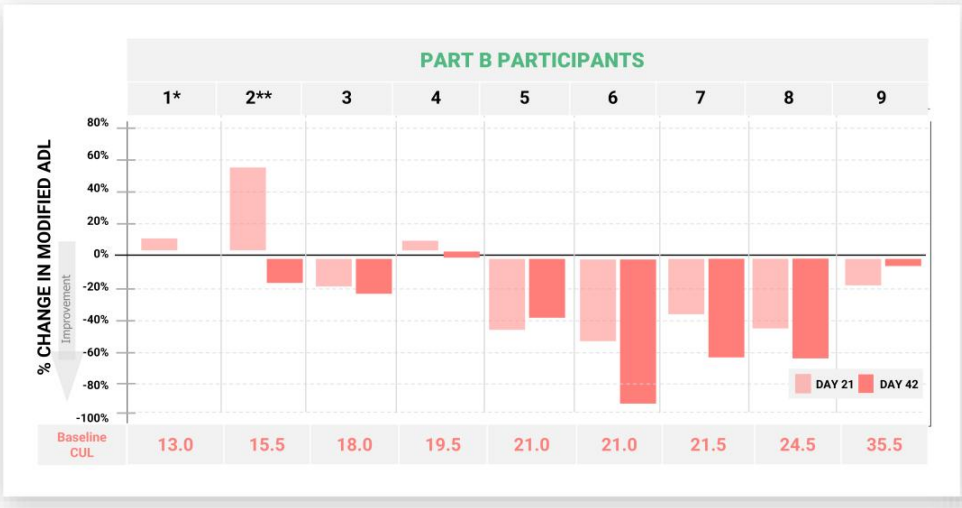




Preliminary Part B data: TETRAS Combined Upper Limb (CUL) and TETRAS Activities of Daily Living (ADL)

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 at 40mg due to an AE, 2 participants at same site discontinued at 20 mg, but had protocol violations related to eligibility, 1 participant discontinued at 20mg due to an AE

Preliminary Part B data: modified ADL by baseline CUL score



Modified ADL as suggested by FDA:

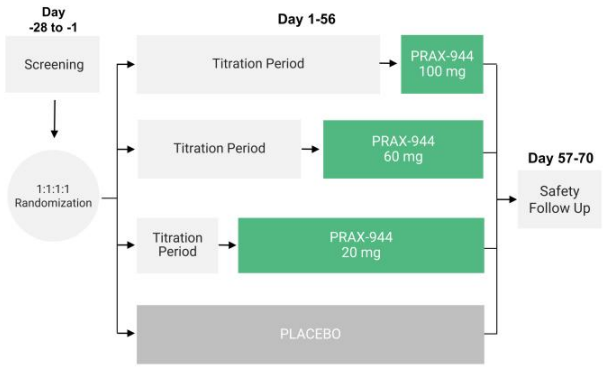
- Score of 1 re-coded as 0; highest score of 3
- Exclude social impact
- Include: handwriting and spirals

PRAXIS

PRELIMINARY DATA AS OF 10-DEC-2021 CUTOFF; ONGOING CLINICALTRIALS.GOV/CT2/SHOW/NCT05021978; *PART B PATIENT 1 DISCONTINUED AFTER DAY 21 ASSESSMENT; **PART B PATIENT 2 DAY 42 – MODIFIED ADL INCLUDED MISSING DATA FOR ONE ITEM; % CHANGE CALCULATED BASED ON IMPUTED WORST SCORE

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 for treatment of adults with ET

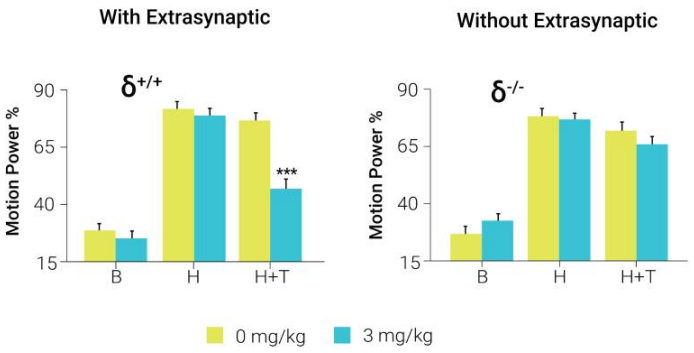
KEY INCLUSION CRITERIA

Ages 18 or older

Diagnosis of ET for at least 3 years

TETRAS UL score ≥10

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



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

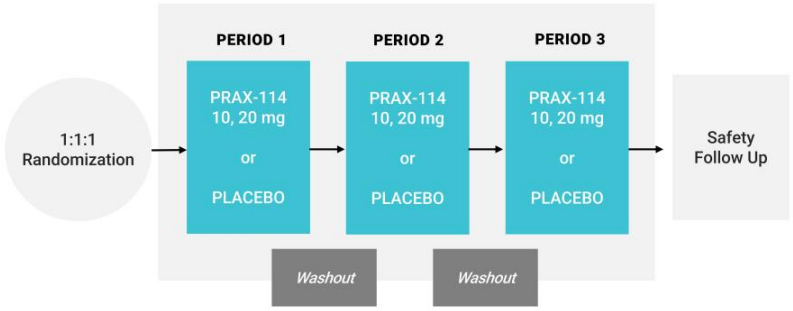
Potentiation		Fold Potentiation
$\alpha_4\beta_3\delta$ %*	$\alpha_1\beta_2\gamma_2$ %	$\alpha_4\beta_3\delta$/ $\alpha_1\beta_2\gamma_2$
300%	29%	10.5

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



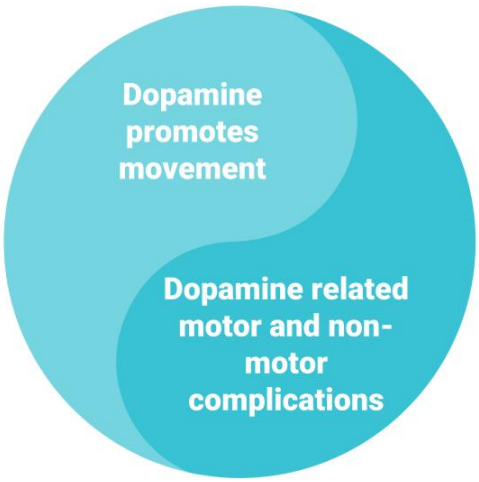
KEY QUESTION:

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

TOPLINE DATA:

2H2022

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



Why Parkinson's disease matters?

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

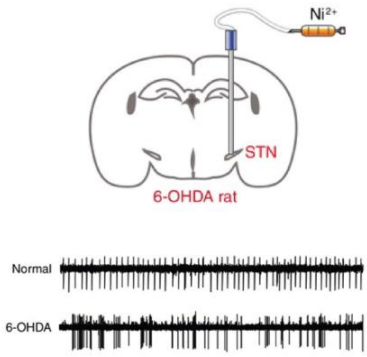
Incidence is age related. Average age of onset is early 60s. High risk in men.

Progressive disability motor and non-motor symptoms

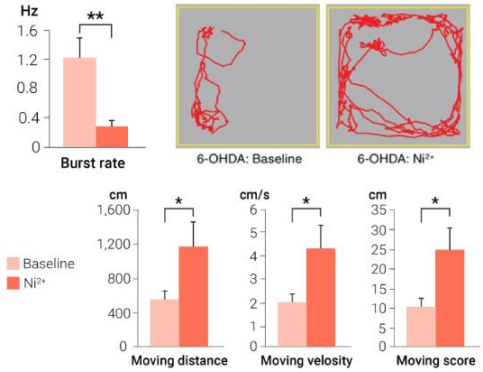
1. HTTPS://WWW.PARKINSON.ORG/UNDERSTANDING-PARKINSONS/STATISTICS 2. GLOBAL DATA REPORT: PARKINSON'S DISEASE - GLOBAL DRUG FORECAST AND MARKET ANALYSIS TO 2029, APRIL 2021 3.CLAIMS ANALYSIS; SECONDARY RESEARCH

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

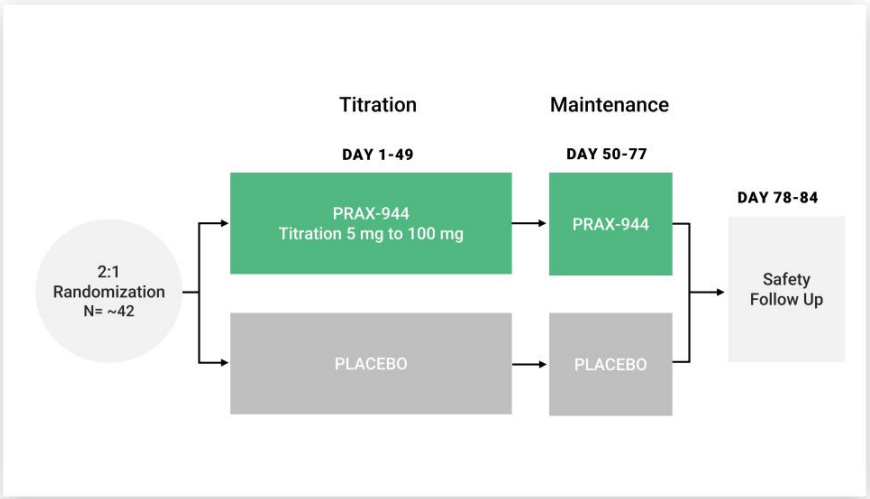
BURST FIRING IN STN OF 6-OHDA PARKINSON'S MODEL



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



PRAX-944 study to evaluate motor function in Parkinson's disease patients expected to initiate in 2Q22



CLINICAL MEASUREMENTS:

Motor function

KEY QUESTION:

Does PRAX-944 demonstrate motor improvement in patients?

EPILEPSY

PRAX-562

PRAX-222 ASO

PRAX-020

PRAX-628

SCN2A-LOF ASO

SYNGAP1 ASO

PCDH19 ASO

KEY UPCOMING MILESTONES

2Q 2022
PRAX-562 Ph 1 ASSR Biomarker Topline

2Q 2022
Initiate PRAX-562 Ph 2 DEE Trial

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

PRAXIS

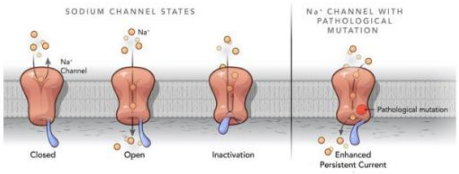
PRAX-562: Block of persistent sodium current can reduce neuronal hyperexcitability and impact multiple disease states

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

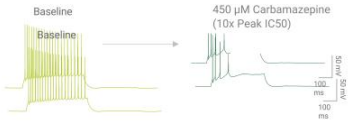
- Standard sodium channel blockers are an important class of medicines in neurology and psychiatry, broadly used in epilepsy, pain, migraine and bipolar disorder
- All standard NaV blockers target peak sodium current
- In general, efficacy is limited by side effects

Depakote, Tegretol-XR, Lidoderm, Oxtellar XR, Dilantin, EXPAREL, Lamictal

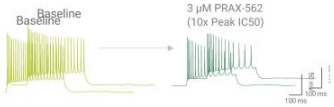
Modulation of persistent sodium current reduces hyperexcitability without disrupting AP



Carbamazepine Representative AP Traces

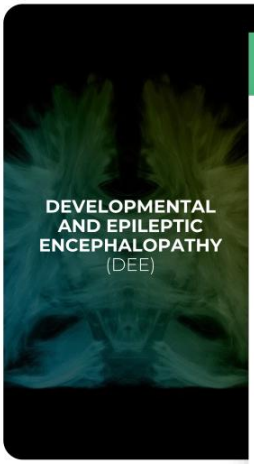


PRAX-562 Representative AP Traces



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

PRAX-562 has broad potential in rare CNS conditions such as DEEs



DEE is a group of monogenic disorders with severe seizure, developmental delay & high mortality rate

200K+
CHILDREN WITH DEEs WORLDWIDE

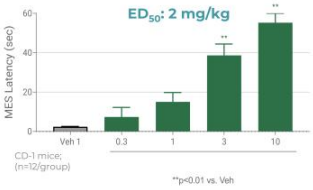
~40% Caused by a single gene mutation

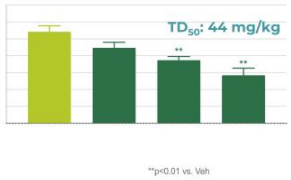
1. A pathologic feature of many DEEs is **the dysregulated neuronal activity** leading to hyperexcitability and seizure
2. This phenomenon is **observed in pediatric epilepsies with an identified genetic cause**, such as SCN8A, SCN2A and others

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

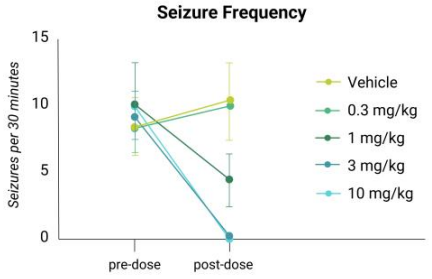
Molecule	Brain Therapeutic Index
PRAX-562	**16.4x**
Carbamazepine	5.9x
Lamotrigine	4.6x

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

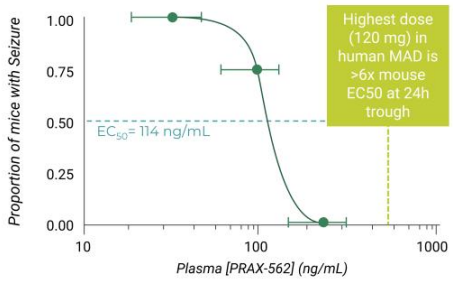
Treatment with PRAX-562 has shown significant reduction of seizures in genetic pediatric epilepsy animal models

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



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

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

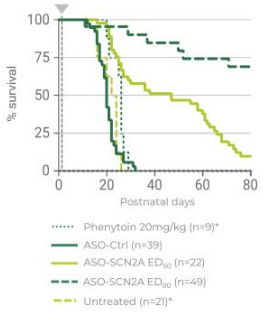
PRAX-222 is expected to initiate seamless trial for SCN2A-DEE in 2Q22

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

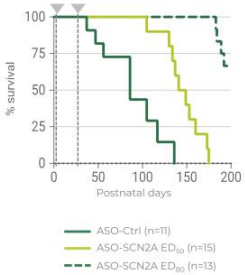
Increased Survival with Single ASO Dose at PN Day 1

ASO injection (icv)



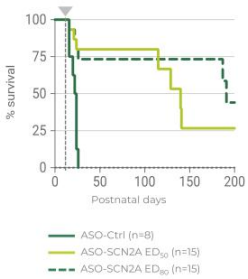
Redosing Significantly Extends Survival

ASO injections (icv)



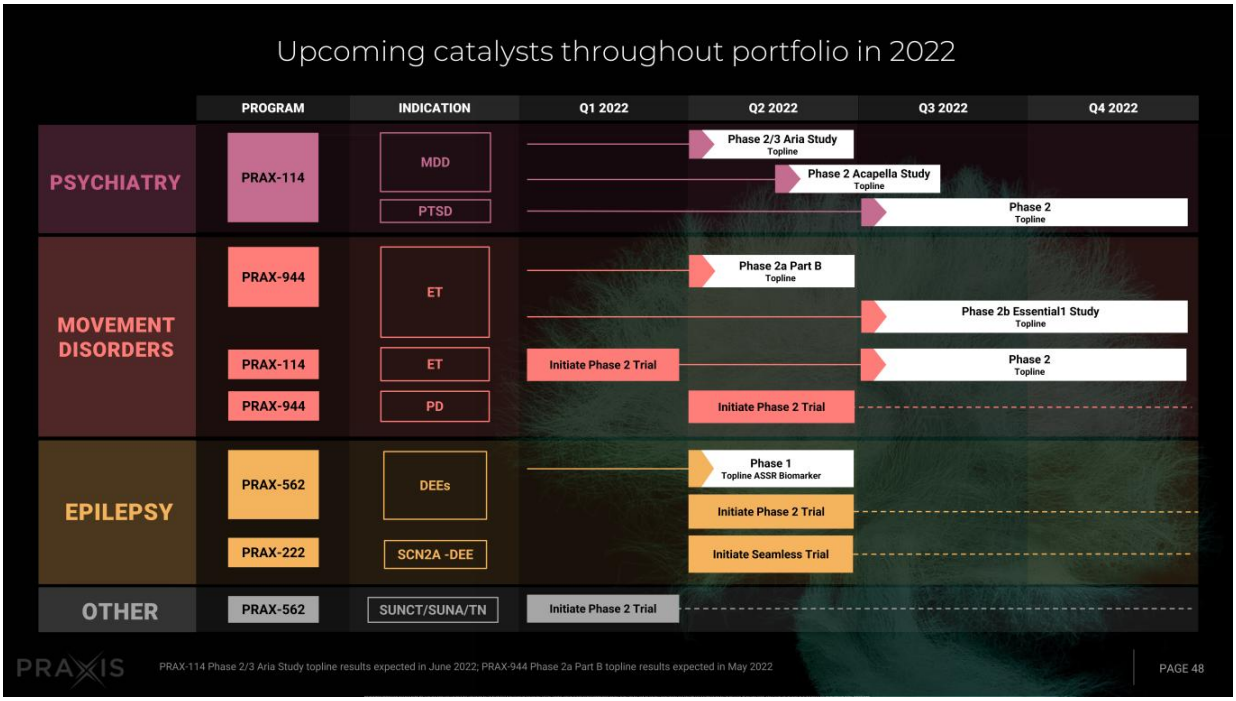
Administration Post-Disease Onset Also Extends Survival

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
Topline
Phase 2b Essential1 Study
Topline
PRAX-114
ET
Initiate Phase 2 Trial
Phase 2
Topline
PRAX-944
PD
Initiate Phase 2 Trial
EPILEPSY
PRAX-562
DEEs
Phase 1
Topline ASSR Biomarker
Initiate Phase 2 Trial
PRAX-222
SCN2A -DEE
Initiate Seamless Trial
OTHER
PRAX-562
SUNCT/SUNA/TN
Initiate Phase 2 Trial
PRAXIS
PRAX-114 Phase 2/3 Aria Study topline results expected in June 2022; PRAX-944 Phase 2a Part B topline results expected in May 2022
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