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): May 9, 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 May 9, 2022, Praxis Precision Medicines, Inc. (the "Company") announced its financial results for the quarter ended March 31, 2022. 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 May 9, 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.

As previously announced, the Company provided a corporate update on May 9, 2022. As part of the corporate update, the Company presented topline data from Part B of its Phase 2a clinical study of PRAX-944 for the treatment of essential tremor ("ET"). The presentation regarding this data is available in the "Investors + Media" portion of the Company's website at investors.praxismedicines.com and a copy is furnished as Exhibit 99.3 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, Exhibit 99.2 and Exhibit 99.3 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 8.01. Other Events.

On May 9, 2022, the Company announced positive topline results from Part B of its Phase 2a study evaluating the safety and efficacy of PRAX-944 for the treatment of ET. In the study, treatment with PRAX-944 resulted in clinically meaningful improvements in function, which were supported by improvements in tremor amplitude.

In the open-label period through Day 42, patients treated with PRAX-944 demonstrated mean improvement from baseline of 42% in the Modified Activities of Daily Living ("ADL") score (N=11, nominal $p<0.05$). Following randomization, the difference between patients who remained on treatment (N=6) through Day 56 and those randomized to placebo (N=5) was clinically and statistically significant. The Modified ADL is a composite score based on Essential Tremor Rating Assessment Scale ("TETRAS") ADLs with the addition of spiral drawings and handwriting from the TETRAS performance scale.

Part B of the Phase 2a study included both an open-label and randomized withdrawal period. In the open-label period, participants were to be titrated up to a maximum dose of 120 mg over 28 days prior to a stable period at the highest dose reached from Day 29 to Day 42. Participants who remained in the study through Day 42 were then randomized one-to-one to either active drug or placebo from Day 43 to Day 56, with a subsequent safety follow-up visit at Day 70.

PRAX-944 was generally well tolerated in Part B of the Phase 2a study, with no new safety findings. In the study, eight of eleven participants completed the open-label period at the highest dose of 120 mg. Three evaluable participants discontinued during the open-label period due to adverse events ("AE"), including one participant who had a pre-existing medical condition that led to a medical procedure unrelated to study drug. Treatment emergent adverse events were all mild to moderate, with the exception of one severe AE of essential tremor that occurred in a placebo arm patient following withdrawal of PRAX-944.

Following the topline results from this study, the Company intends to update the primary endpoint for the Company's Phase 2b Essential1 Study from safety to efficacy.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release, dated May 9, 2022
99.2	Praxis Precision Medicines, Inc. May 2022 Corporate Presentation
99.3	Praxis Precision Medicines, Inc. PRAX-944 Essential Tremor Phase 2a Topline Results Presentation, dated May 9, 2022
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: May 9, 2022

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

Praxis Precision Medicines Provides Corporate Update and Reports First Quarter 2022 Financial Results

PRAX-944 demonstrated clinically meaningful functional improvement in essential tremor patients in Part B of Phase 2a study

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

Epilepsy Day showcases largest targeted epilepsy portfolio in industry

Cash and investments of $222.5 million as of March 31, 2022 supports runway into 3Q23

BOSTON, May 9, 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 first quarter 2022.

“This is an incredibly exciting time at Praxis, with recent events bringing us closer to our long-term vision,” said Marcio Souza, president and chief executive officer of Praxis. “With positive topline results from our PRAX-944 Phase 2a study in essential tremor, and plans to accelerate development in the ongoing Essential1 study, we will soon have a second late-stage clinical asset along with a deep and innovative early-stage pipeline. We also recently completed our PRAX-114 Aria study, with last patient last visit achieved, and look forward to sharing those topline results in June.”

Recent Business Highlights and Upcoming Milestones:

Psychiatry

- Following the completion of the PRAX-114 Phase 2/3, placebo-controlled Aria Study for monotherapy treatment of Major Depressive Disorder (MDD), Praxis expects to report topline results in June 2022. 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. Following topline results from the Aria Study, the Company intends to engage with the FDA for an end-of-Phase 2 meeting and subsequently initiate a Phase 3, placebo-controlled study in the fourth quarter of 2022.

- The Company anticipates topline results from the PRAX-114 Phase 2, placebo-controlled, dose-ranging Acapella Study for treatment of MDD in the third quarter of 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 expects topline results from the PRAX-114 Phase 2, placebo-controlled study for treatment of post-traumatic stress disorder (PTSD) 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 four weeks in approximately 80 participants with PTSD, using the CAPS-5 total score as the primary endpoint. An 8-week open-label extension period is available for all participants who complete the placebo-controlled portion of the study.

Movement Disorders

- Praxis reported positive topline results from Part B of its Phase 2a study evaluating the safety and efficacy of PRAX-944 for the treatment of essential tremor (ET). In the study, treatment with PRAX-944 resulted in clinically meaningful improvements in function, which were supported by improvements in tremor amplitude.
    - The study included both an open-label and randomized withdrawal period. In the open-label period, participants were to be titrated up to a maximum dose of 120 mg over 28-days prior to a stable period at the highest dose reached from Day 29 to Day 42. Participants who remained in the study through Day 42 were then randomized one-to-one to either active drug or placebo from Day 43 to Day 56, with a subsequent safety follow-up visit at Day 70.

    - In the open-label period through Day 42, patients treated with PRAX-944 demonstrated mean improvement from baseline of 42% in the Modified Activities of Daily Living (ADL) score (N=11, nominal p<0.05). Following randomization, the difference between patients who remained on treatment (N=6) through Day 56 and those randomized to placebo (N=5) was clinically and statistically significant.
    - PRAX-944 was generally well tolerated in the study, with no new safety findings.

- The Company anticipates topline results from the PRAX-944 Phase 2b Essential1 Study for daytime treatment of ET in the second half of 2022. Following the topline results of Part B of the Phase 2a study of PRAX-944 for the treatment of ET, the Company intends to change the primary endpoint of Essential1 from safety to efficacy.

- In April 2022, Praxis presented data from PRAX-944 for ET at the 2022 American Academy of Neurology (AAN) Annual Meeting, including an oral presentation on the translational pharmacology of PRAX-944.

- Praxis initiated a Phase 2, placebo-controlled, crossover study of 10 and 20 mg of PRAX-114 for daytime treatment of ET in the first quarter of 2022 and expects topline results in the second half of 2022.

- In April 2022, the FDA cleared the Investigational New Drug (IND) submission for a Phase 2 study of PRAX-944 for the treatment of Parkinson's disease. Praxis intends to initiate a Phase 2, placebo-controlled trial to evaluate the safety, pharmacokinetics (PK) and efficacy of PRAX-944 as a non-dopaminergic treatment for the motor symptoms of Parkinson's disease in the second half of 2022.

Epilepsy

- In April 2022, Praxis hosted its 2022 Epilepsy Day, which included an overview of the Company's proprietary innovation strategy, updates on its most advanced epilepsy programs and a review of the progress in Praxis' early-stage epilepsy pipeline, including plans to declare antisense oligonucleotide (ASO) candidates for PRAX-080 for PCDH19 and PRAX-090 for SYNGAP1 in 2023.

- Praxis plans to initiate a PRAX-562 Phase 2, placebo-controlled trial for treatment of developmental epileptic encephalopathies (DEEs), including SCN2A-DEE, SCN8A-DEE and Tuberous Sclerosis Complex (TSC) in the second half of 2022.

- Praxis expects to initiate a PRAX-628 Phase 1 study in the fourth quarter of 2022 and subsequently initiate a Phase 2 study in focal epilepsy in 2023.

- In April 2022, Praxis announced that it received an email communication from the FDA that the Company's IND application for the first-in-patient study of PRAX-222, an ASO for the treatment of patients with SCN2A gain-of-function mutations, was placed on clinical hold. The letter detailing the reasons for the hold is expected to be received from the FDA within 30 days of April 28, 2022.

- In April 2022, Praxis entered into a collaboration with the University of Florida Scripps Biomedical Research Institute. As part of the agreement, Praxis will collaborate with Gavin Rumbaugh, Ph.D. and his laboratory, to leverage his phenotypic screening platform to discover and advance a novel small molecule program to treat patients with SYNGAP1.

- As a result of the Company's strategic decision to renew its focus toward epilepsy indications, Praxis has discontinued the planned PRAX-562 Phase 2 trial for treatment of rare adult cephalgias.

First Quarter 2022 Financial Results:

As of March 31, 2022, Praxis had $222.5 million in cash, cash equivalents and marketable securities, compared to $275.9 million in cash, cash equivalents and marketable securities as of December 31, 2021. This decrease of $53.4 million primarily reflects cash used in operations of $54.1 million during the three months ended March 31, 2022. The Company's cash, cash equivalents and marketable securities as of March 31, 2022 are expected to fund operations into the third quarter of 2023.

Research and development expenses were $52.7 million for the three months ended March 31, 2022, compared to $17.9 million for the three months ended March 31, 2021. The increase in research and development expenses of $34.7 million was primarily attributable to $28.1 million in increased expenses related primarily to clinical-related spend for the Company's franchises, $4.6 million in increased personnel-related costs due to increased headcount and $1.5 million in increased expenses for other exploratory CNS indications.

General and administrative expenses were $16.2 million for the three months ended March 31, 2022, compared to $9.5 million for the three months ended March 31, 2021. The increase in general and administrative expenses of $6.7 million was primarily attributable to $5.0 million in increased personnel-related costs due to increased headcount, $1.3 million in increased professional fees and a $0.4 million increase in other general and administrative expenses.

Praxis reported a net loss of $68.7 million for the three months ended March 31, 2022, including $7.9 million of stock-based compensation expense, compared to $27.4 million for the three months ended March 31, 2021, including $4.7 million of stock-based compensation expense.

As of March 31, 2022, Praxis had 45.5 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 first quarter 2022 via a conference call and webcast today, May 9, 2022, at 4:30 p.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 7849239. 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 and epilepsy, 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, its Quarterly Reports on Form 10-Qand 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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619-849-5388

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

	March 31, 2022	December 31, 2021
Assets		
Cash and cash equivalents	$ 77,854	$ 138,704
Marketable securities	144,662	137,207
Prepaid expenses and other current assets	11,957	11,498
Property and equipment, net	1,142	1,213
Operating lease right-of-use assets	3,473	3,653
Other non-current assets	416	472
Total assets	$ 239,504	$ 292,747
Liabilities and stockholders' equity		
Accounts payable	$ 13,269	$ 10,780
Accrued expenses	30,929	26,844
Operating lease liabilities	4,284	4,311
Common stock	5	5
Additional paid-in capital	576,955	567,598
Accumulated other comprehensive loss	(606)	(176)
Accumulated deficit	(385,332)	(316,615)
Total liabilities and stockholders' equity	$ 239,504	$ 292,747

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

	Three Months Ended March 31,	
	2022	2021
Operating expenses:		
Research and development	$ 52,652	$ 17,929
General and administrative	16,197	9,490
Total operating expenses	68,849	27,419
Loss from operations	(68,849)	(27,419)
Other income:		
Other income, net	132	46
Total other income	132	46
Net loss	$ (68,717)	$ (27,373)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.51)	$ (0.71)
Weighted average common shares outstanding, basic and diluted	45,455,179	38,470,710

CORPORATE OVERVIEW

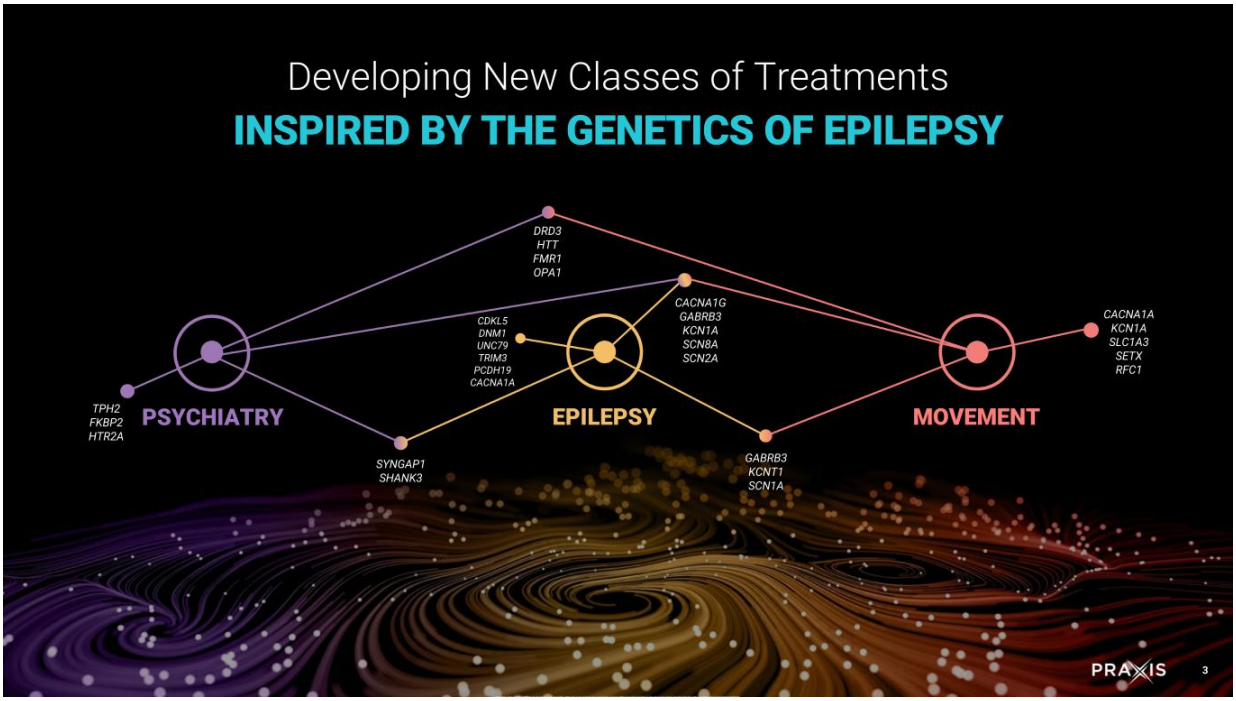
May 2022

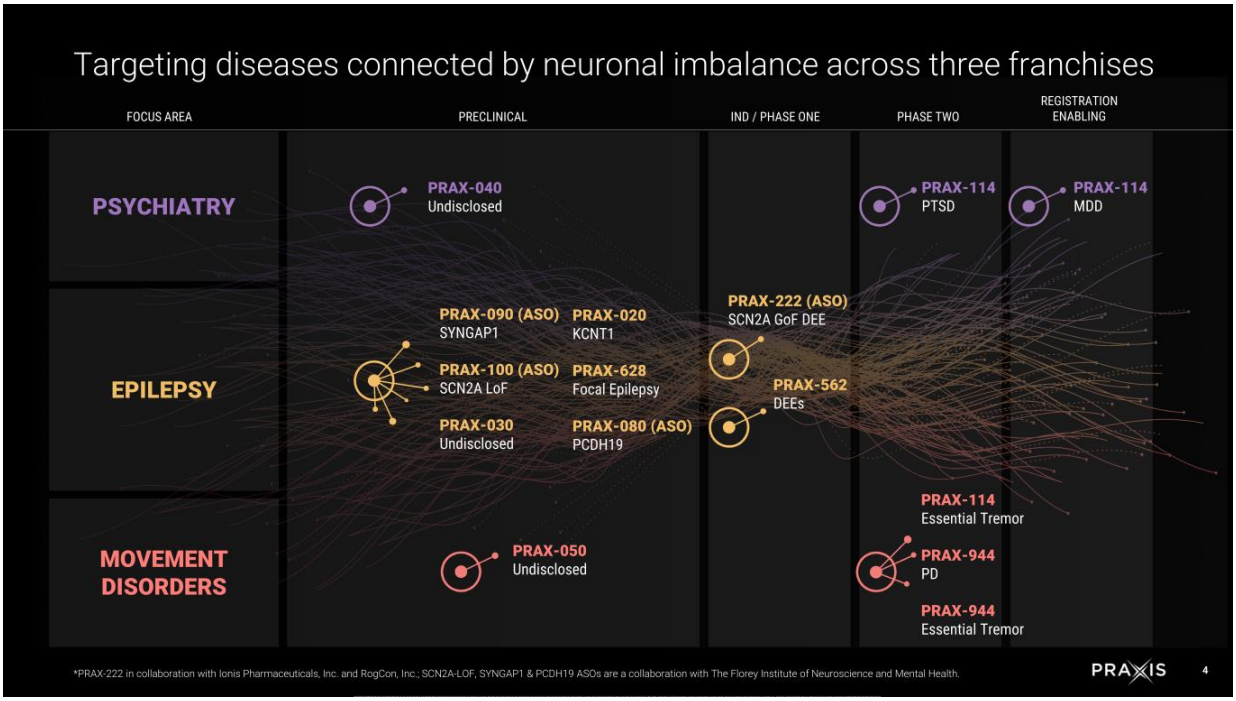
Forward-looking statements

This presentation may contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial conditions, including but not limited to express or implied statements regarding the current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our preclinical and clinical results and other future conditions. Any forward-looking statements in this presentation are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, risks relating to: (i) the success and timing of our ongoing clinical trials, (ii) the success and timing of our product development activities and initiating clinical trials, (iii) the success and timing of our collaboration partners' product development activities, (iv) our ability to obtain and maintain regulatory approval of any of our product candidates, (v) our plans to research, discover and develop additional product candidates, (vi) our ability to enter into collaborations for the development of new product candidates, (vii) our ability to establish manufacturing capabilities, and our and our collaboration partners' abilities to manufacture our product candidates and scale production, (viii) our ability to meet any specific milestones set forth herein, and (ix) uncertainties and assumptions regarding the impact of the COVID-19 pandemic on our business, operations, clinical trials, supply chain, strategy, goals and anticipated timelines. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements.

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

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.


Developing New Classes of Treatments
INSPIRED BY THE GENETICS OF EPILEPSY
DRD3
HTT
FMR1
OPA1
CACNA1G
GABRB3
KCN1A
SCN8A
SCN2A
CDKL5
DNM1
UNC79
TRIM3
PCDH19
CACNA1A
CACNA1A
KCN1A
SLC1A3
SETX
RFC1
TPH2
FKBP2
HTR2A
PSYCHIATRY
EPILEPSY
MOVEMENT
SYNGAP1
SHANK3
GABRB3
KCNT1
SCN1A
PRAXIS
3


Targeting diseases connected by neuronal imbalance across three franchises
FOCUS AREA
PRECLINICAL
IND / PHASE ONE
PHASE TWO
REGISTRATION ENABLING
PSYCHIATRY
EPILEPSY
MOVEMENT DISORDERS
PRAX-040
Undisclosed
PRAX-114
PTSD
PRAX-114
MDD
PRAX-090 (ASO)
SYNGAP1
PRAX-020
KCNT1
PRAX-100 (ASO)
SCN2A LoF
PRAX-628
Focal Epilepsy
PRAX-030
Undisclosed
PRAX-080 (ASO)
PCDH19
PRAX-222 (ASO)
SCN2A GoF DEE
PRAX-562
DEEs
PRAX-114
Essential Tremor
PRAX-944
PD
PRAX-944
Essential Tremor
PRAX-050
Undisclosed
*PRAX-222 in collaboration with Ionis Pharmaceuticals, Inc. and RogCon, Inc.; SCN2A-LOF, SYNGAP1 & PCDH19 ASOs are a collaboration with The Florey Institute of Neuroscience and Mental Health.
PRAXIS
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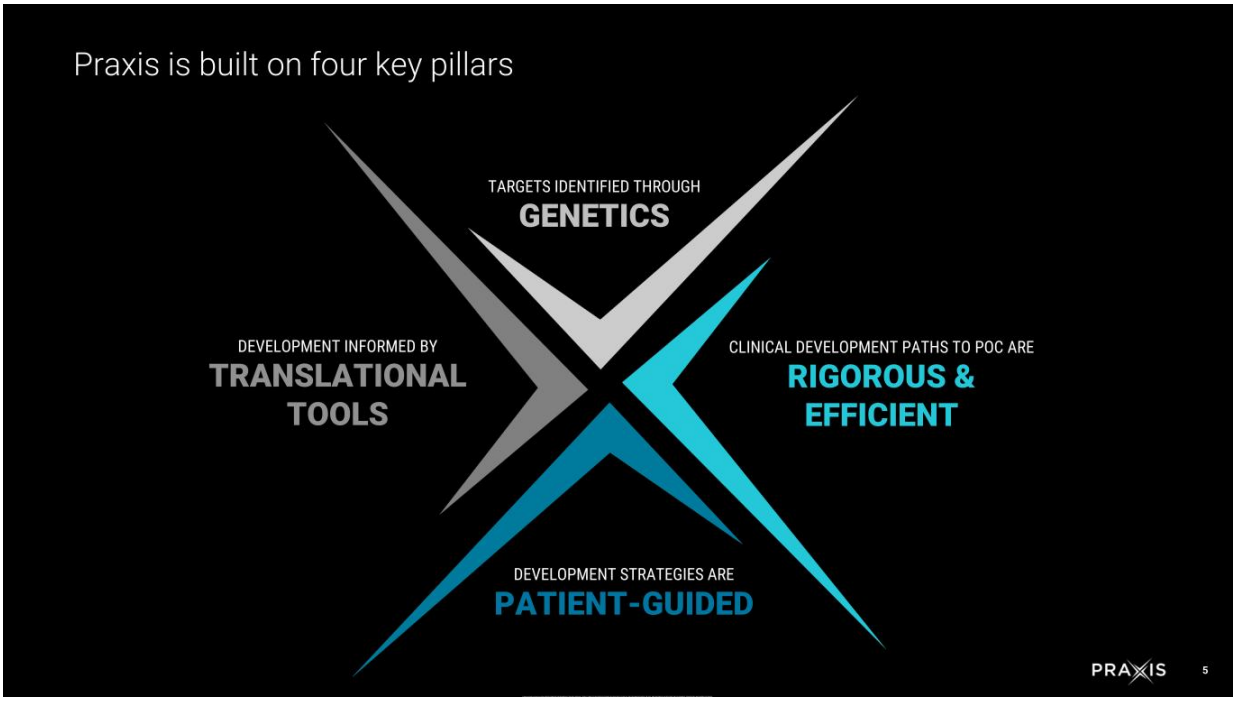
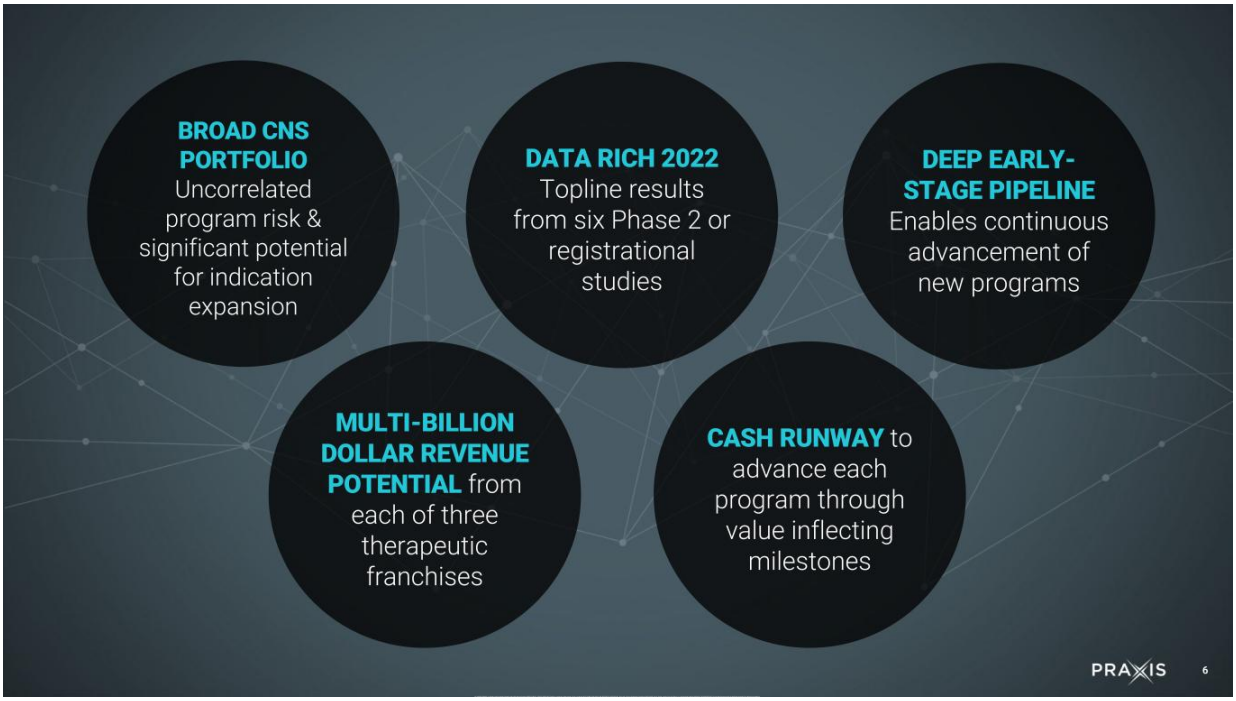

Praxis is built on four key pillars
TARGETS IDENTIFIED THROUGH
GENETICS
DEVELOPMENT INFORMED BY
TRANSLATIONAL TOOLS
CLINICAL DEVELOPMENT PATHS TO POC ARE
RIGOROUS & EFFICIENT
DEVELOPMENT STRATEGIES ARE
PATIENT-GUIDED
PRAXIS
5


BROAD CNS PORTFOLIO
Uncorrelated program risk & significant potential for indication expansion
DATA RICH 2022
Topline results from six Phase 2 or registrational studies
DEEP EARLY-STAGE PIPELINE
Enables continuous advancement of new programs
MULTI-BILLION DOLLAR REVENUE POTENTIAL from each of three therapeutic franchises
CASH RUNWAY to advance each program through value inflecting milestones
PRAXIS
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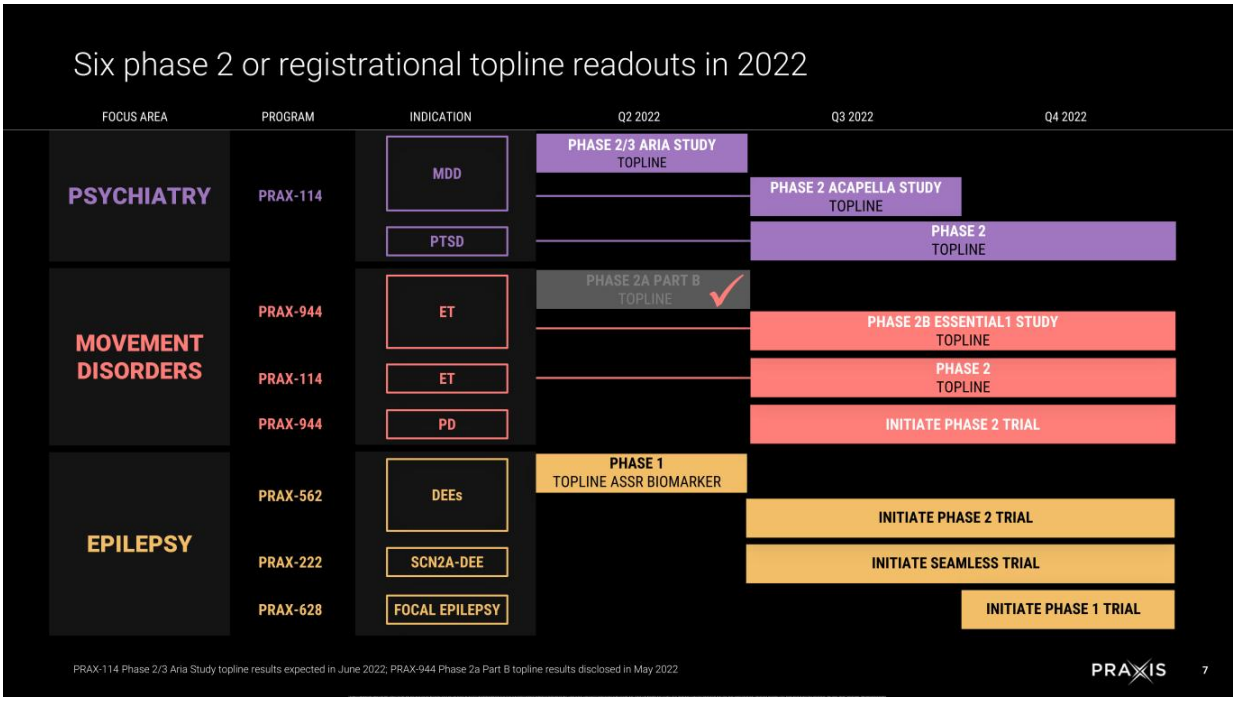
Six phase 2 or registrational topline readouts in 2022
FOCUS AREA
PROGRAM
INDICATION
Q2 2022
Q3 2022
Q4 2022
PSYCHIATRY
PRAX-114
MDD
PHASE 2/3 ARIA STUDY TOPLINE
PHASE 2 ACAPELLA STUDY TOPLINE
PTSD
PHASE 2 TOPLINE
MOVEMENT DISORDERS
PRAX-944
ET
PHASE 2A PART B TOPLINE
PHASE 2B ESSENTIAL1 STUDY TOPLINE
PRAX-114
ET
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
PRAX-628
FOCAL EPILEPSY
INITIATE PHASE 1 TRIAL
PRAX-114 Phase 2/3 Aria Study topline results expected in June 2022; PRAX-944 Phase 2a Part B topline results disclosed in May 2022
PRAXIS
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PSYCHIATRY
PRAX-114
GABA$_A$ Receptor PAM
Depression
Post-traumatic Stress Disorder
KEY UPCOMING MILESTONES
JUNE 2022
Ph 2/3 Monotherapy MDD Aria Study Topline
3Q 2022
Ph 2 MDD Dose-Ranging Acapella Study Topline
2H 2022
Ph 2 PTSD Topline
PRAXIS
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PRAX-114 is a novel $GABA_A$-PAM ideally suited to address the unmet needs of patients living with major depressive disorder

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

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

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

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

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

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

* Equivalent of full activation by GABA
Source: PRAXIS data

Source: Praxis Data on file

NO MTD IDENTIFIED up to 80 mg

TOLERABILITY PROFILE maintained throughout dose escalation

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

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

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

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

EFFICACY MAINTAINED WHILE ON TREATMENT

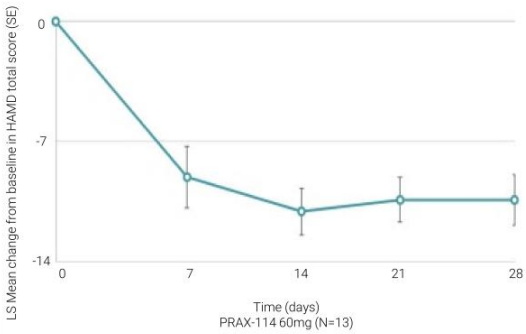
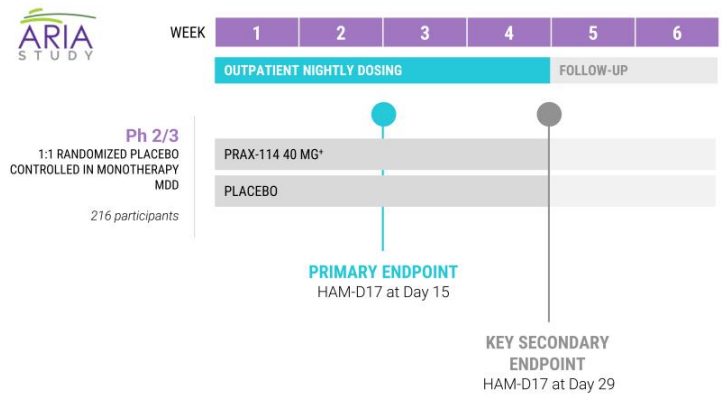


Figure 10. Reduction of HAM-D total score observed in MDD patients treated with PRAX-114 for 28 days in Part C.

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

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



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

KEY ASSUMPTION
80% powered for 0.4 effect size

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

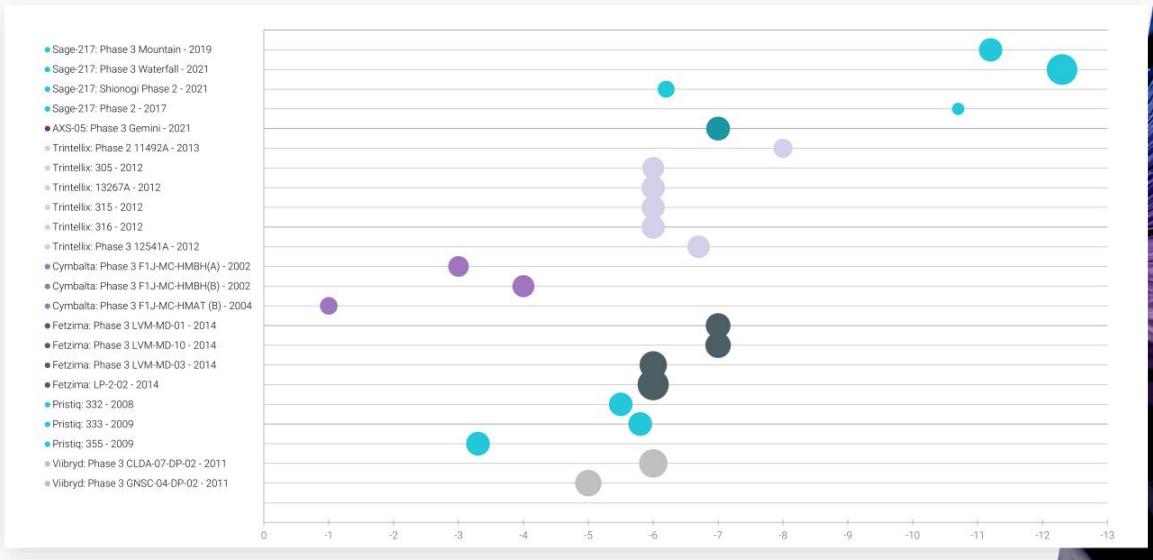
PRAX-114 clinical program leverages best practices in conduct of MDD trials

KEY OPERATIONAL CONTROLS

RIGOROUS PATIENT SELECTION	• Enrollment of patients with at least one prior episode of MDD (associated with a lower placebo response rate) [1] • Two-level subject & data quality procedure using the SAFER independent clinical interview to confirm eligibility [2]
HIGH QUALITY SITE SELECTION	• Enrollment of sites with a known track-record of high-quality data generation • Experienced raters, adequate resources, low frequency of operational issues and proven performance in running studies successfully during the pandemic
OPTIMIZED TRIAL DESIGN & EXECUTION	• Integration of a placebo control reminder script for patients at every visit • Inclusion of the AiCure smartphone-based adherence monitoring system with structured site intervention [3]

1: Sonawalla SB, Rosenbaum JF. Placebo response in depression. Dialogues Clin Neurosci. Mar 2002;4(1):105-13.
2: Freeman MP, Pooley J, Flynn MJ, et al. Guarding the Gate: Remote Structured Assessments to Enhance Enrollment Precision in Depression Trials. J Clin Psychopharmacol. Apr 2017;37(2):176-181. doi:10.1097/JCP.0000000000000669
3: https://aicure.com/

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



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

PRAXIS

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

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

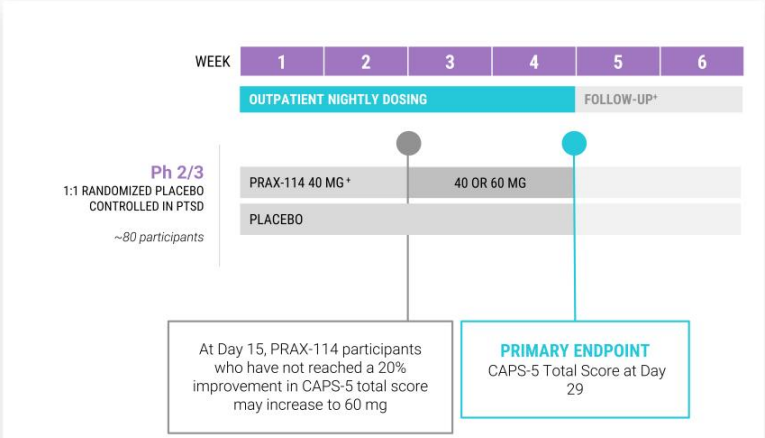
POST-TRAUMATIC STRESS DISORDER (PTSD)

11M

ADULT PTSD
ESTIMATED US PREVALENCE

1. **Post-traumatic Stress Disorder** is a debilitating psychiatric disorder that leads to social, occupational and interpersonal dysfunction
2. **Profound unmet need**, meaningful link to PRAX-114 MOA, and complementarity to MDD program

PRAX-114 PTSD Phase 2 topline data expected 2H22



At Day 15, PRAX-114 participants who have not reached a 20% improvement in CAPS-5 total score may increase to 60 mg

PRIMARY ENDPOINT
CAPS-5 Total Score at Day 29

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

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

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

MOVEMENT DISORDERS

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

PRAX-114
$GABA_A$ Receptor PAM
Essential Tremor

KEY UPCOMING MILESTONES

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

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

2H 2022
PRAX-114 Ph 2 ET Topline

2H 2022
Initiate PRAX-944 Ph 2 PD Trial

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

Daring for more for people living with essential tremor

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

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

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

Source: Primary market research and praxis internal modeling and projections
1. Claims analysis indicates that 50% of diagnosed patients are on treatment; 2. Based on minimum of range for net price estimates from praxis covering analysts as of 16-december-2021- $3.6k

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

As needed

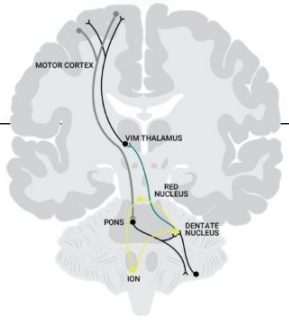
- Patients could initiate ET treatment sooner
- Patients could treat as needed

Chronic

- Patients could maintain ET therapy

PRAX-114

$GABA_A$ RECEPTORS



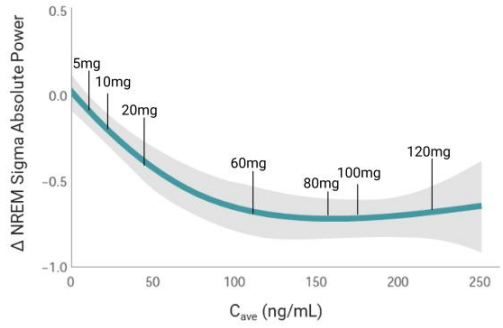
PRAX-944

T-TYPE CALCIUM CHANNELS

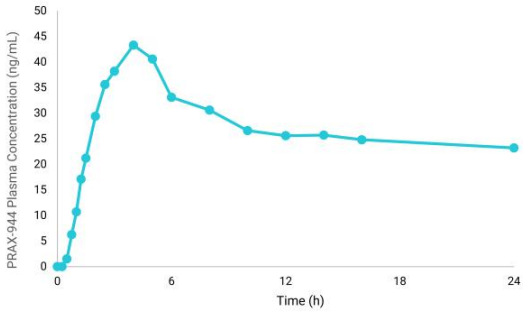
CEREBELLO-THALAMO-CORTICAL (CTC) CIRCUIT

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

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



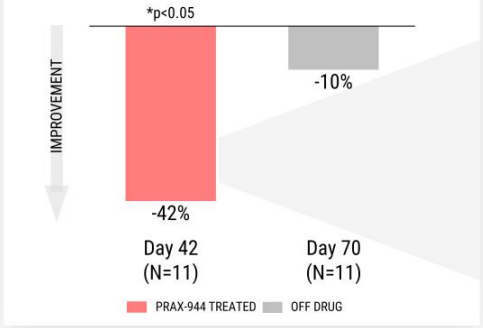
SUSTAINED EXPOSURE WITH BLUNTED MR CMAX



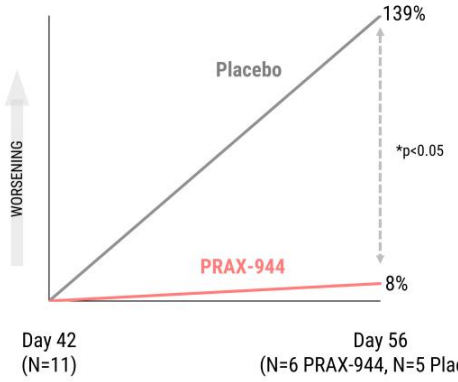
Source: Praxis Data on file

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

MODIFIED ADLs IN OPEN LABEL
MEAN % CHANGE FROM BASELINE



MODIFIED ADLs IN RANDOMIZED WITHDRAWAL
MEAN % CHANGE FROM DAY 42



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

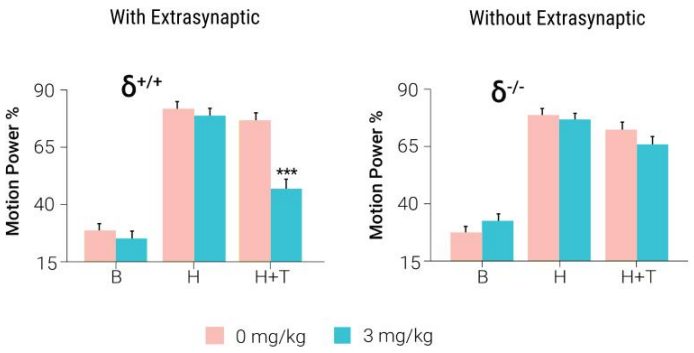
PRAX-944 was generally well tolerated in Part B of Phase 2a study

SAFETY SUMMARY

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

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

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



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

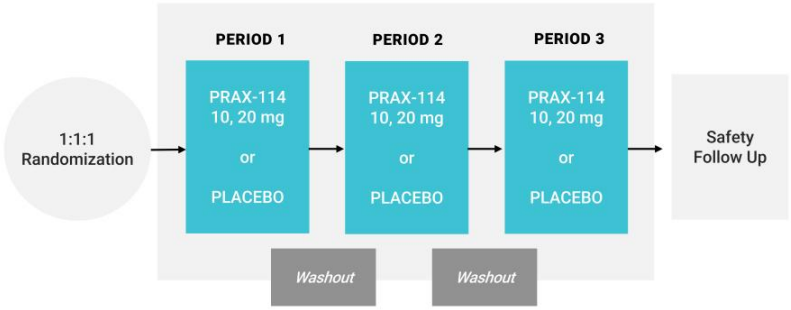
POTENTIATION		FOLD POTENTIATION
$\alpha_4\beta_3\delta$ %*	$\alpha_1\beta_2\gamma_2$ %	$\alpha_4\beta_3\delta$/ $\alpha_1\beta_2\gamma_2$
300%	29%	10.5

$A_1\beta_3\delta$: extrasynaptic $gaba_A$ receptor; $\alpha1\beta_2\gamma_2$: synaptic $gaba_A$ receptor; * equivalent of full gaba activation
Source: Praxis Data on file

PRAXIS

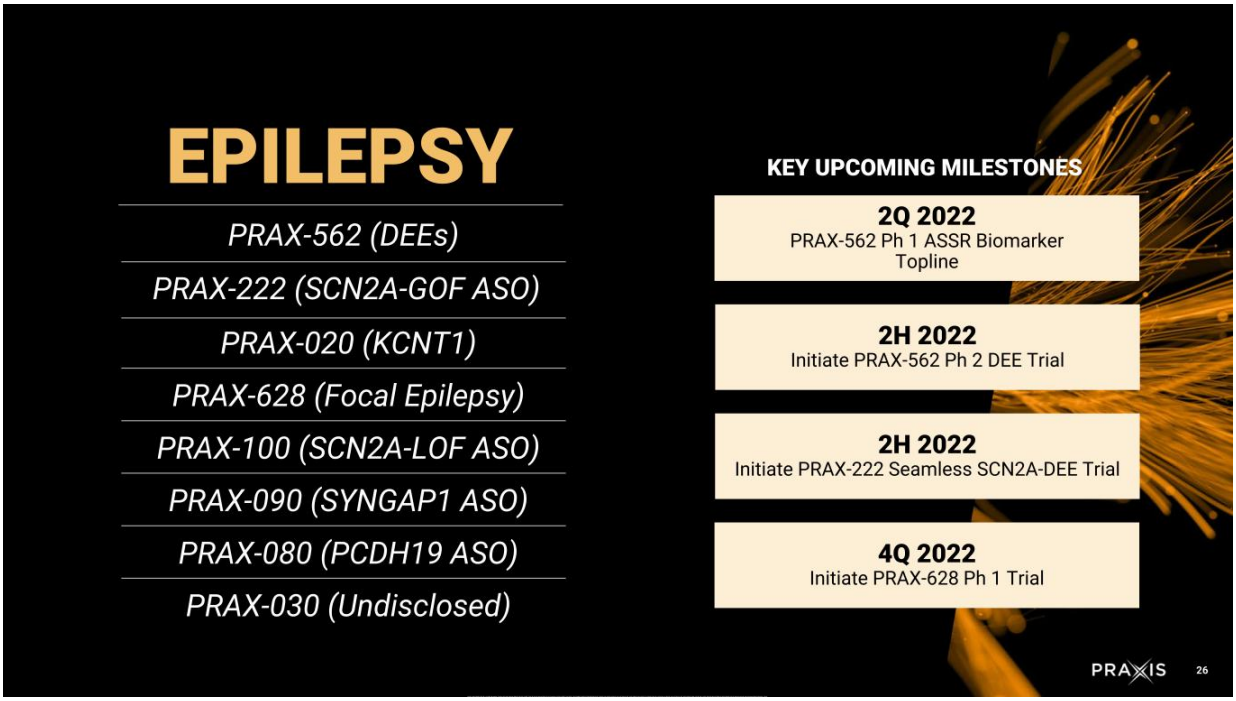
PRAX-114 ET Phase 2 study designed to evaluate safety, tolerability, PK and efficacy of daytime dosing

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



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

TOPLINE DATA:
2H2022


EPILEPSY
PRAX-562 (DEEs)
PRAX-222 (SCN2A-GOF ASO)
PRAX-020 (KCNT1)
PRAX-628 (Focal Epilepsy)
PRAX-100 (SCN2A-LOF ASO)
PRAX-090 (SYNGAP1 ASO)
PRAX-080 (PCDH19 ASO)
PRAX-030 (Undisclosed)
KEY UPCOMING MILESTONES
2Q 2022
PRAX-562 Ph 1 ASSR Biomarker Topline
2H 2022
Initiate PRAX-562 Ph 2 DEE Trial
2H 2022
Initiate PRAX-222 Seamless SCN2A-DEE Trial
4Q 2022
Initiate PRAX-628 Ph 1 Trial
PRAXIS
26

TARGETS IDENTIFIED THROUGH GENETICS

Three key imperatives guide our epilepsy portfolio build

Focus on nodes of pathophysiological convergence informed by genetics

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

Focus directly on underlying genetic defects in rare epilepsy

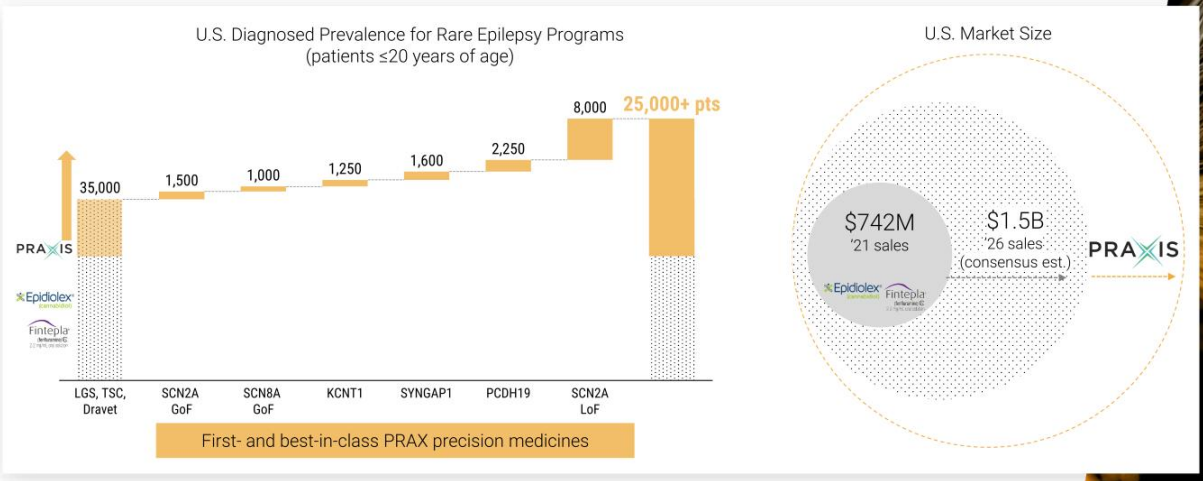
- **PRAX-222*** *ASO*
- **KCNT1 INHIB.** *SMALL MOLECULE*
- **PCDH19*** *ASO*
- **SYNGAP1*** *ASO*
- **SCN2A-LOF *** *ASO*
- **PRAXIS-030** *SMALL MOLECULE*

Focus on implicated genes in common diseases

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

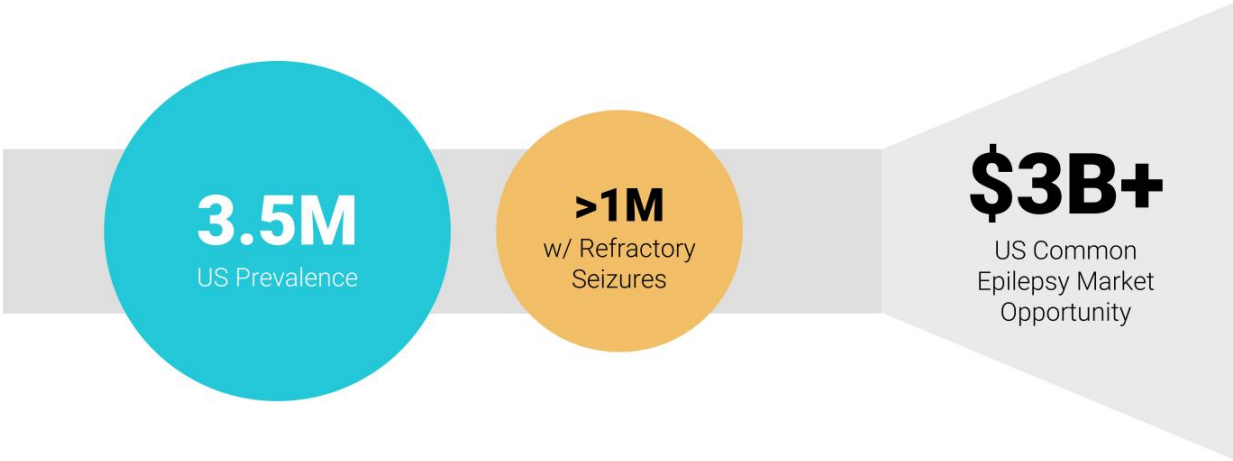
*PRAX-222 in collaboration with Ionis Pharmaceuticals, Inc. and RogCon, Inc.. PCDH19 (PRAX-080), SYNGAP1(PRAX-090), SCN2A-LOF(PRAX-100) ASOs are a collaboration with The Florey Institute of Neuroscience and Mental Health.

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



LGS: Lennox-Gastaut Syndrome; TSC: Tuberous Sclerosis Complex
Source: Ambit Genetic Testing and Claims Data Analysis; EvaluatePharma; Sanders S. J. *et al. Trends Neurosci.* (2018); Wolff M. *et al* Brain (2017);

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



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

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

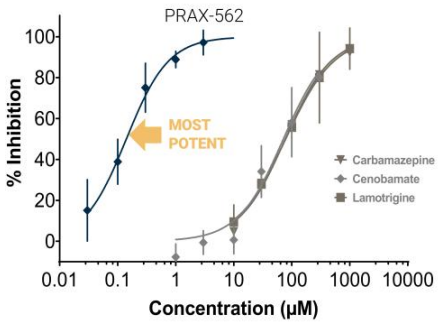
PRAX-562

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

- Superior selectivity for disease-state Na_V channel hyperexcitability
- Unprecedented therapeutic window translating to superior safety and efficacy
- Convenient auto-titration regimen with stable PK

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

% INHIBITION OF $hNa_V1.6$ PERSISTENT I_{Na} (SAME DATA AS ON PRIOR SLIDE)



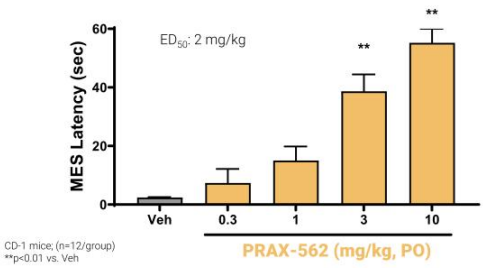
COMPARISON OF POTENCY AND SELECTIVITY

	Persistent I_{Na} IC50 (nM)	Ratio of persistent to peak inhibition	
PRAX-562	**141**	**60**	MOST SELECTIVE
Carbamazepine	77,520	30	
Cenobamate	73,263	23	
Lidocaine	68,230	19	
Lamotrigine	78,530	16	
Vixotrigene (BIIB074)	3,676	14	
Lacosamide	833,100	n/a*	
Valproic Acid	<10% @ 1 mM	No inhibition	

*solubility concerns

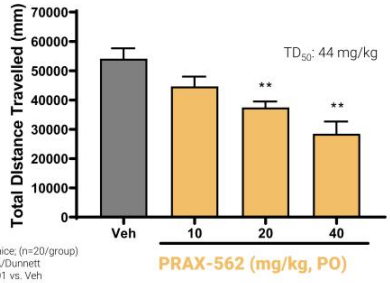
Our mechanistic hypothesis translates to a wide therapeutic index in vivo

MES EFFICACY



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

sLMA TOLERABILITY



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

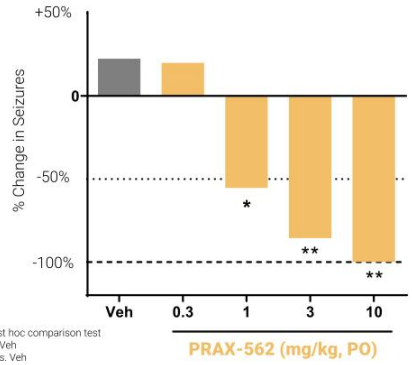
Molecule	Plasma Therapeutic Index
PRAX-562	17.2x

Therapeutic Index (TI) = TC50 / EC50

PRAXIS

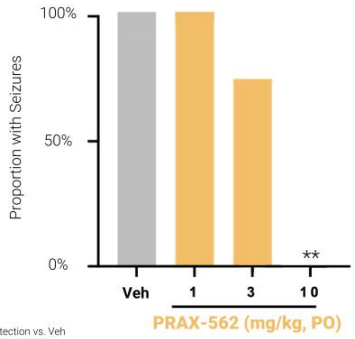
PRAX-562 completely blocks seizures in SCN2A and SCN8A GoF mutation mouse models

IN VIVO POC IN SCN2A SPONTAEOUS SEIZURES[1]



Sidack's post hoc comparison test
*p<0.05 vs. Veh
**p<0.001 vs. Veh

IN VIVO POC IN SCN8A AUDIOGENIC EVOKED SEIZURES[2]



**Significant protection vs. Veh
χ^2_2 = 16.0, Fisher's p = 0.0002

[1] PRAX-562 inhibition of spontaneous seizures in Q54 GoF mice.
[2] PRAX-562 inhibition of audiogenic seizures in N1768D D/+ mice

Three epilepsy drugs in clinic by end of 2022

PRAX-222
(SCN2A)

Initiate Seamless Study: 2H2022*

PRAX-562
(SCN2A, SCN8A, TSC)

Initiate Phase 2 Study: 2H22

PRAX-628
(FOCAL EPILEPSY)

Initiate Phase 1 Study: 4Q22

PRAX-222 and PRAX-562 received Orphan Drug Designations for severe pediatric epilepsy indications from the FDA and EMA, and Rare Pediatric Disease designation from the FDA

*In April 2022, the FDA placed the first-in-patient study of PRAX-222 on clinical hold. The letter detailing the reasons for the hold is expected to be received from the FDA within 30 days of April 28, 2022.

PRAXIS


PRAXIS
DARE for MORE™

PRAX-944
ESSENTIAL TREMOR

Phase 2a Part B Topline Results

May 9, 2022

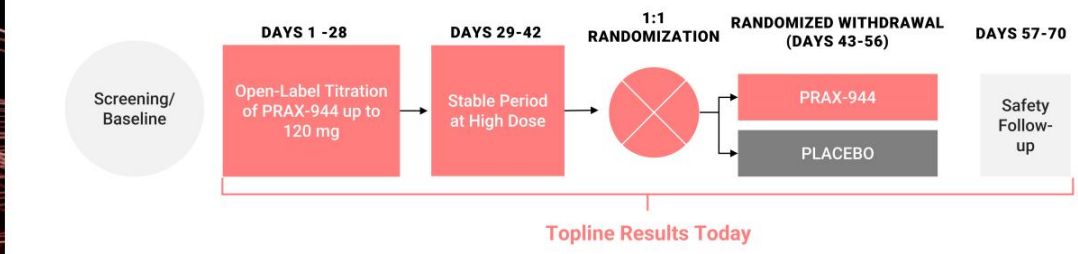
Forward-looking statements

This presentation may contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial conditions, including but not limited to express or implied statements regarding the current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our preclinical and clinical results and other future conditions. Words such as, but not limited to, "believe," "expect," "anticipate," "estimate," "intend," "plan," "would," "should" and "could," and similar expressions or words, identify forward-looking statements. Any forward-looking statements in this presentation are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, risks relating to: (i) the success and timing of our ongoing clinical trials, (ii) the success and timing of our product development activities and initiating clinical trials, (iii) the success and timing of our collaboration partners' ongoing and planned clinical trials, (iv) our ability to obtain and maintain regulatory approval of any of our product candidates, (v) our plans to research, discover and develop additional product candidates, (vi) our ability to enter into collaborations for the development of new product candidates, (vii) our ability to establish manufacturing capabilities, and our and our collaboration partners' abilities to manufacture our product candidates and scale production, (viii) our ability to meet any specific milestones set forth herein, and (ix) uncertainties and assumptions regarding the impact of the COVID-19 pandemic on our business, operations, clinical trials, supply chain, strategy, goals and anticipated timelines. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements.

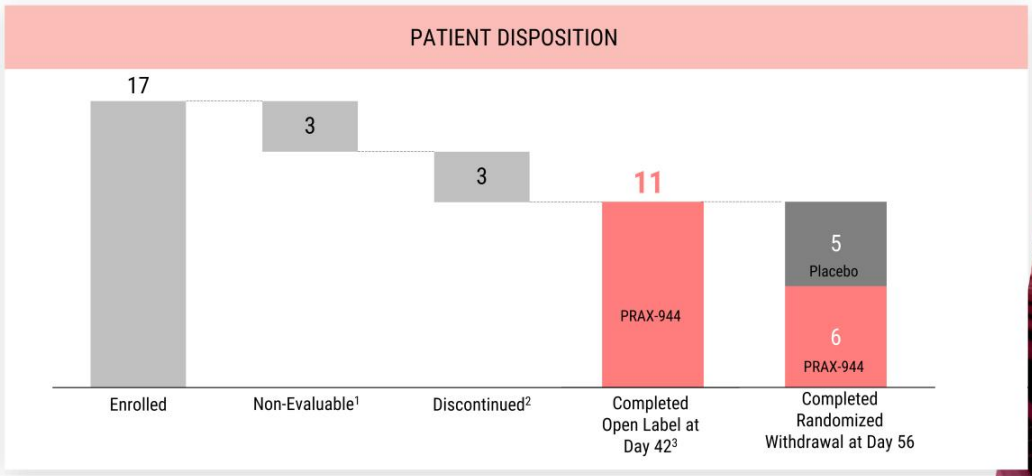
For further information regarding the risks, uncertainties and other factors that may cause differences between Praxis' expectations and actual results, you should review the "Risk Factors" section of our Annual Report on Form 10-K filed for the period ended December 31, 2021, our Quarterly Reports on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

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

PRAX-944 Phase 2a Part B open-label and randomized withdrawal study design



PRAX-944 Phase 2a Part B patient disposition



[1] Site suspended due to protocol violations, no evaluable data for three patients after Day 1; See Slide 10 for safety data
[2] Three patients discontinued at the 40mg (escalation), 60mg (escalation), and 40mg (down-titration) dose level
[3] Three patients down titrated to 20mg, 60mg, 100mg dose level
Source: Praxis Data on file

PRAXIS

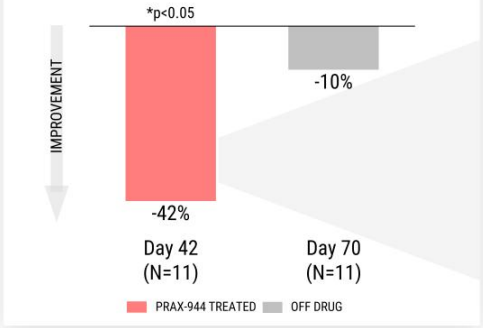
PRAX-944 Phase 2a Part B participants representative of broad essential tremor population

BASELINE DEMOGRAPHICS	EVALUABLE PARTICIPANTS[1] (N=14)	COMPLETED (N=11)
Age, mean (range)	59 (26-76)	62 (43-76)
Gender (Male/Female) (n, %)	11/3 (79%/21%)	8/3 (73%/27%)
# previously on ET medication (n, %)	9 (64%)	6 (55%)
# currently on ET medication (n, %)	3 (21%)	2 (18%)
Family History – First-degree relative with ET (n, %)	8 (57%)	5 (45%)
ET worsened over past 3 years (n, %)	12 (86%)	9 (82%)
TETRAS Modified ADL, mean (SD)	16.6 (4.2)	16.9 (4.3)
Kinesia ONE, mean (SD)	9.9 (4.1)	11.2 (3.6)

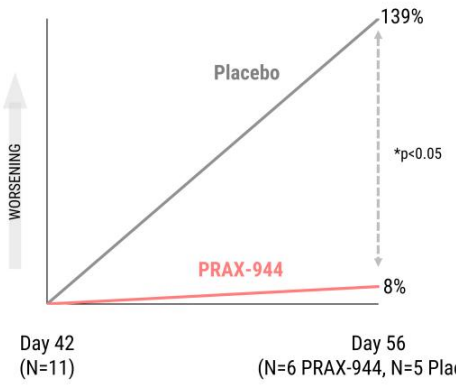
[1] Excludes the three non-evaluable patients from site suspended due to protocol violations
Source: Praxis Data on file

Marked functional benefit observed on treatment, with withdrawal resulting in regression to baseline severity

MODIFIED ADLs IN OPEN LABEL
MEAN % CHANGE FROM BASELINE



MODIFIED ADLs IN RANDOMIZED WITHDRAWAL
MEAN % CHANGE FROM DAY 42

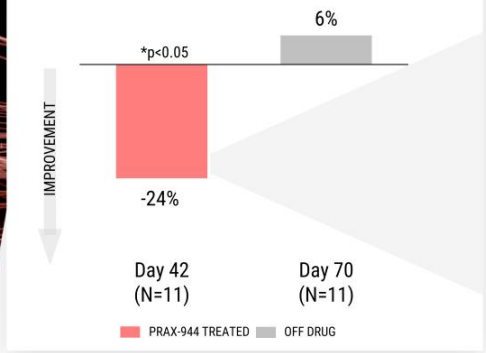


*Nominal p-value based on ANCOVA
Source: Praxis Data on file

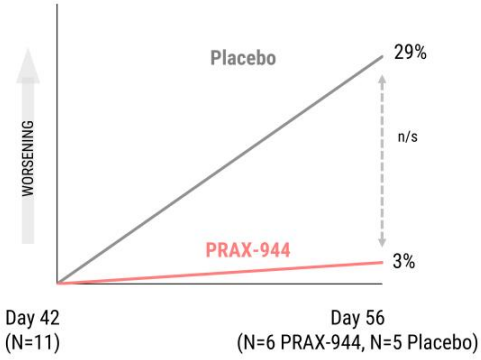
PRAXIS

Functional benefit with PRAX-944 supported by tremor analysis

KINESIA ONE IN OPEN LABEL
MEAN % CHANGE FROM BASELINE



KINESIA ONE IN RANDOMIZED WITHDRAWAL
MEAN % CHANGE FROM DAY 42



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

Impact of PRAX-944 on ability to draw

EXAMPLE OF SPIRAL TASK FROM PART B PATIENT

Day 1
Baseline

Day 42
On PRAX-944

Day 56
Blinded Off Drug

PRAX-944 was generally well tolerated with no new safety findings

SAFETY SUMMARY

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

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

PRAX-944 Phase 2a Part B - TEAE summary

TREATMENT-EMERGENT ADVERSE EVENTS (TEAEs) IN >1 PARTICIPANT

PREFERRED TERM	PART B[1] (N=14)
Constipation	6
Dizziness	4
Fatigue	3
Cognitive Disorder	2
Headache	2
Insomnia	2
Paraesthesia	2

[1] Excludes the three non-evaluable patients from site suspended due to protocol violations; One severe AE of essential tremor reported while on placebo following withdrawal of PRAX-944; all other AEs mild to moderate

Source: Praxis Data on file

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

TEAEs LEADING TO DOSE DOWN-TITRATION*

PREFERRED TERM	PART B (N=14)
Dizziness postural	1
Paraesthesia	1
Somnolence	1

TEAEs LEADING TO STUDY DRUG DISCONTINUATION

PREFERRED TERM	PART B[4] (N=14)
Confusional state/disturbance in attention[1]	1
Cyst[2]	1
Hypotension/gait disturbance/ muscle fatigue/speech disorder[3]	1

*Protocol permitted patients to dose titrate down once during Part B
[1] Participant also down-titrated prior to discontinuation
[2] Participant had a pre-existing condition which was unrelated to study drug and required a medical procedure
[3] Same participant
[4] Suspended site had 3 participants discontinue with AEs of: dizziness, cognitive disorder (2), hallucinations
Source: Praxis Data on file

Six phase 2 or registrational topline readouts in 2022