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): August 8, 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 August 8, 2022, Praxis Precision Medicines, Inc. (the "Company") announced its financial results for the quarter ended June 30, 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 August 8, 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 8.01. Other Events.

The Company completed the PRAX-562 Phase 1, two-part, placebo-controlled study evaluating the safety, tolerability, pharmacokinetics and pharmacodynamics of 90 mg of PRAX-562 over 28 days (Part A, N=12) and of 600 mg BID of oxcarbazepine (a sodium channel blocker, or SCB) in combination with 120 mg of PRAX-562 as compared to oxcarbazepine alone in adult healthy volunteers (Part B, N=18). PRAX-562 was well-tolerated as a stand-alone therapy and led to the expected changes in quantitative electroencephalogram ("qEEG") biomarkers; additive effect was shown when combined with oxcarbazepine at supra-therapeutic doses.

PRAX-562 was well-tolerated in Part A of the study, with no clinically significant safety findings. The majority of Treatment Emergent Adverse Events ("TEAEs") were considered mild to moderate in both Part A and Part B of the study.

Part B evaluated the combination of oxcarbazepine and PRAX-562 as compared with oxcarbazepine alone. The co-administration of supra-therapeutic doses of PRAX-562 and oxcarbazepine led to additive sodium blocking effects, providing information about optimal target exposures for concomitant use of PRAX-562 and oxcarbazepine, and additional supportive evidence of PRAX-562 sodium channel blocking effects. Participants in Part B who received PRAX-562 in combination with oxcarbazepine developed TEAEs consistent with sodium channel blocking effects, leading to study withdrawal for five participants. One participant in Part B experienced drug-related Serious Adverse Events ("SAEs") that required hospitalization and resolved that day. No similar SAEs have been previously reported for PRAX-562.

In Part A, dosing with 90 mg of PRAX-562 over 28 days resulted in concentrations that exceeded the EC50 in the maximal electroshock seizure model by 13-fold (based on mean concentration at Day 28), indicating the potential for a wider therapeutic index than other SCBs.

In Part A, statistically significant changes were observed between placebo and 90 mg of PRAX-562 on qEEG and on auditory steady state response, a pharmacosensitive biomarker for assessing neuronal sensory function.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release, dated August 8, 2022
99.2	Praxis Precision Medicines, Inc. August 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.

August 8, 2022

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

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

PRAX-944 Phase 2b Essential1 Study topline results expected in 4Q22; primary endpoint updated to efficacy

PRAX-562 Phase 1 study completed, confirming biomarker change and potential for wide therapeutic window

Cash and investments of $165.4 million as of June 30, 2022 supports runway into 1Q24

BOSTON, August 8, 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 and reported financial results for the second quarter of 2022.

“Through the lens of epilepsy genetics, we have efficiently built a broad portfolio of clinical stage and preclinical CNS programs with uncorrelated risk,” said Marcio Souza, president and chief executive officer of Praxis. “In our clinical stage programs, recent data for PRAX-944 in essential tremor and for PRAX-562 have been encouraging and give us greater confidence as we trend toward key milestones later this year. Reflecting this increased confidence, we updated the primary endpoint in the ongoing Essential1 Study to Modified Activities of Daily Living, the FDA-suggested efficacy endpoint for ET. The results from the PRAX-562 Phase 1 study deepen our conviction that we have a well-tolerated and differentiated sodium channel blocker with potential for a higher therapeutic index than existing therapies.”

Recent Business Highlights and Upcoming Milestones:

Movement Disorders

- In May 2022, 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.
    - During the open-label period of the trial, patients treated with PRAX-944 demonstrated mean improvement from baseline of 42% in the Modified Activities of Daily Living (ADL) score (N=11, nominal $p<0.05$). In the placebo-controlled, randomized withdrawal period of the study, the difference between patients who remained on treatment (N=6) 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 expects topline results from the ongoing PRAX-944 Essential1 Study in the fourth quarter of 2022. Essential1 is a randomized, double-blinded, placebo-controlled, dose-range-finding Phase 2b trial evaluating the efficacy, safety and tolerability of once-daily daytime treatment of 60 mg or 100 mg of PRAX-944 compared to placebo after 56 days, for the treatment of moderate to severe ET. Following the positive topline results of Part B of the Phase 2a study of PRAX-944 for the treatment of ET, the Essential1 study design was revised, including changing the primary endpoint to efficacy from safety. Key study design updates include:
    - The primary endpoint is now the change from baseline to Day 56 on the modified ADL.
    - An extension was added, offering continuation of treatment to those participants randomized to PRAX-944 and new treatment to those randomized to placebo.
    - Approximately 130 participants are now planned to be randomized.

- Praxis plans 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. Topline results are expected in 2023.

- In June 2022, following the PRAX-114 Aria Study results, the Company discontinued the PRAX-114 Phase 2 study for the treatment of ET.

Epilepsy

- Praxis has completed the PRAX-562 Phase 1, two-part, placebo-controlled study evaluating the safety, tolerability, PK and pharmacodynamics of 90 mg of PRAX-562 over 28 days (Part A, N=12) and of 600 mg BID of oxcarbazepine (a sodium channel blocker, or SCB) in combination with 120 mg of PRAX-562 as compared to oxcarbazepine alone in adult healthy volunteers (Part B, N=18). PRAX-562 was well-tolerated as a stand-alone therapy and led to the expected changes in quantitative electroencephalogram (qEEG) biomarkers; additive effect was shown when combined with oxcarbazepine at supra-therapeutic doses. A summary of the findings is included below:
    - PRAX-562 was well-tolerated in Part A of the study, with no clinically significant safety findings. The majority of Treatment Emergent Adverse Events (TEAEs) were considered mild to moderate in both Part A and Part B of the study.
    - Part B evaluated the combination of oxcarbazepine and PRAX-562 as compared with oxcarbazepine alone. The co-administration of supra-therapeutic doses of PRAX-562 and oxcarbazepine led to additive sodium blocking effects, providing information about optimal target exposures for concomitant use of PRAX-562 and oxcarbazepine, and additional supportive evidence of PRAX-562 sodium channel blocking effects. Participants in Part B who received PRAX-562 in combination with oxcarbazepine developed TEAEs consistent with sodium channel blocking effects, leading to study withdrawal for five participants. One participant in Part B experienced drug-related Serious Adverse Events (SAEs) that required hospitalization and resolved that day. No similar SAEs have been previously reported for PRAX-562.
    - In Part A, dosing with 90 mg of PRAX-562 over 28 days resulted in concentrations that exceeded the EC50 in the maximal electroshock seizure (MES) model by 13-fold (based on mean concentration at Day 28), indicating the potential for a wider therapeutic index than other SCBs.
    - In Part A, statistically significant changes were observed between placebo and 90 mg of PRAX-562 on qEEG and on auditory steady state response (ASSR), a pharmacosensitive biomarker for assessing neuronal sensory function.

- Praxis plans to initiate a PRAX-562 Phase 2, placebo-controlled trial for treatment of developmental epileptic encephalopathies (DEEs) in pediatric patients in the second half of 2022, including initial cohorts of patients with SCN2A-DEE and SCN8A-DEE. The Company has completed the juvenile toxicology studies and pediatric formulation development necessary to initiate the study. Topline results are expected in mid-2023.

- In June 2022, Praxis received an email communication from the FDA regarding the clinical hold for the Company's Investigational New Drug (IND) application for the first-in-patient study of PRAX-222, an antisense oligonucleotide (ASO) for the treatment of patients with SCN2A gain-of-function mutations, which indicated that the IND could be cleared upon submission of additional documentation related to the completed 13-week non-human primate toxicology study supporting the starting dose proposed by the Company. The Company submitted the required data in July 2022 and expects to start its first-in-patient study with PRAX-222 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.

Psychiatry

- In June 2022, Praxis reported that the PRAX-114 Phase 2/3, placebo-controlled Aria Study for monotherapy treatment of Major Depressive Disorder (MDD) did not achieve statistical significance on the primary endpoint or on any secondary endpoints. As a result, the Company closed screening and enrollment in the Phase 2 Acapella Study evaluating the presence of a dose response signal for PRAX-114 in MDD at doses up to 60 mg and intends to read out results from approximately 110 patients in the third quarter of 2022. The Company also

stopped enrollment in the Phase 2 study evaluating PRAX-114 for the treatment of post-traumatic stress disorder.

General Corporate Updates

- In May 2022, Praxis announced the appointment of Jill DeSimone to its board of directors. Most recently, Ms. DeSimone served as president of U.S. Oncology at Merck & Co., Inc. from 2014 to May 2022. During her time at Merck, Ms. DeSimone also temporarily served as interim president of U.S. Pharma to help navigate the business through the COVID-19 pandemic.
- In June 2022, following the Aria Study topline results, Praxis announced a strategic realignment to focus resources on its Movement Disorders and Epilepsy franchises, which resulted in a reduction of the Company's workforce and future operating expenses and extended cash runway into the first quarter of 2024.
- In July 2022, the Company announced that Bernard Ravina, M.D., former chief medical officer of Praxis, transitioned to a part-time role as strategic advisor as of August 1, 2022.

Second Quarter 2022 Financial Results:

As of June 30, 2022, Praxis had $165.4 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 $110.5 million primarily reflects cash used in operations of $111.3 million during the six months ended June 30, 2022. The Company's cash, cash equivalents and marketable securities as of June 30, 2022 are expected to fund operations into the first quarter of 2024.

Research and development expenses were $43.6 million for the three months ended June 30, 2022, compared to $25.7 million for the three months ended June 30, 2021. The increase in research and development expenses of $17.9 million was primarily attributable to $14.1 million in increased expenses related primarily to clinical-related spend for the Company's franchises and $4.0 million in increased personnel-related costs due to increased headcount.

General and administrative expenses were $16.8 million for the three months ended June 30, 2022, compared to $10.8 million for the three months ended June 30, 2021. The increase in general and administrative expenses of $6.0 million was primarily attributable to $3.4 million in increased personnel-related costs due to increased headcount and $2.6 million in increased other general and administrative expenses, none of which were individually material.

Praxis reported a net loss of $60.2 million for the three months ended June 30, 2022, including $7.6 million of stock-based compensation expense, compared to $36.4 million for the three months ended June 30, 2021, including $5.4 million of stock-based compensation expense.

As of June 30, 2022, Praxis had 45.6 million shares of common stock outstanding.

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 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 movement disorders, epilepsy and psychiatric disorders, 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 as described in its Annual Report on Form 10-K for the year ended December 31, 2021, its Quarterly Reports on Form 10-Q 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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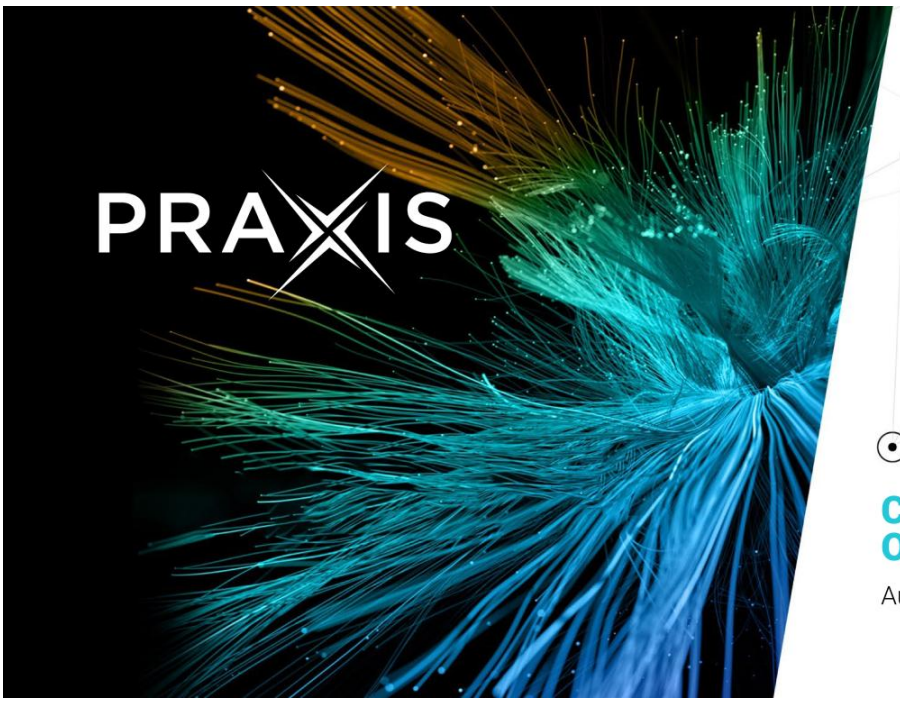
PRAXIS PRECISION MEDICINES, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(Amounts in thousands)
(Unaudited)

	June 30, 2022	December 31, 2021
Assets		
Cash and cash equivalents	$ 56,039	$ 138,704
Marketable securities	109,365	137,207
Prepaid expenses and other current assets	10,176	11,498
Property and equipment, net	1,134	1,213
Operating lease right-of-use assets	3,287	3,653
Other non-current assets	416	472
Total assets	$ 180,417	$ 292,747
Liabilities and stockholders' equity		
Accounts payable	$ 11,821	$ 10,780
Accrued expenses	25,768	26,844
Operating lease liabilities	3,959	4,311
Common stock	5	5
Additional paid-in capital	585,070	567,598
Accumulated other comprehensive loss	(680)	(176)
Accumulated deficit	(445,526)	(316,615)
Total liabilities and stockholders' equity	$ 180,417	$ 292,747

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2022	**2021**	**2022**	**2021**
Operating expenses:				
Research and development	$ 43,620	$ 25,678	$ 96,272	$ 43,607
General and administrative	16,774	10,805	32,971	20,295
Total operating expenses	60,394	36,483	129,243	63,902
Loss from operations	(60,394)	(36,483)	(129,243)	(63,902)
Other income:				
Other income, net	200	82	332	128
Total other income	200	82	332	128
Net loss	$ (60,194)	$ (36,401)	$ (128,911)	$ (63,774)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.32)	$ (0.88)	$ (2.83)	$ (1.59)
Weighted average common shares outstanding, basic and diluted	45,542,600	41,569,782	45,499,131	40,028,807



CORPORATE OVERVIEW

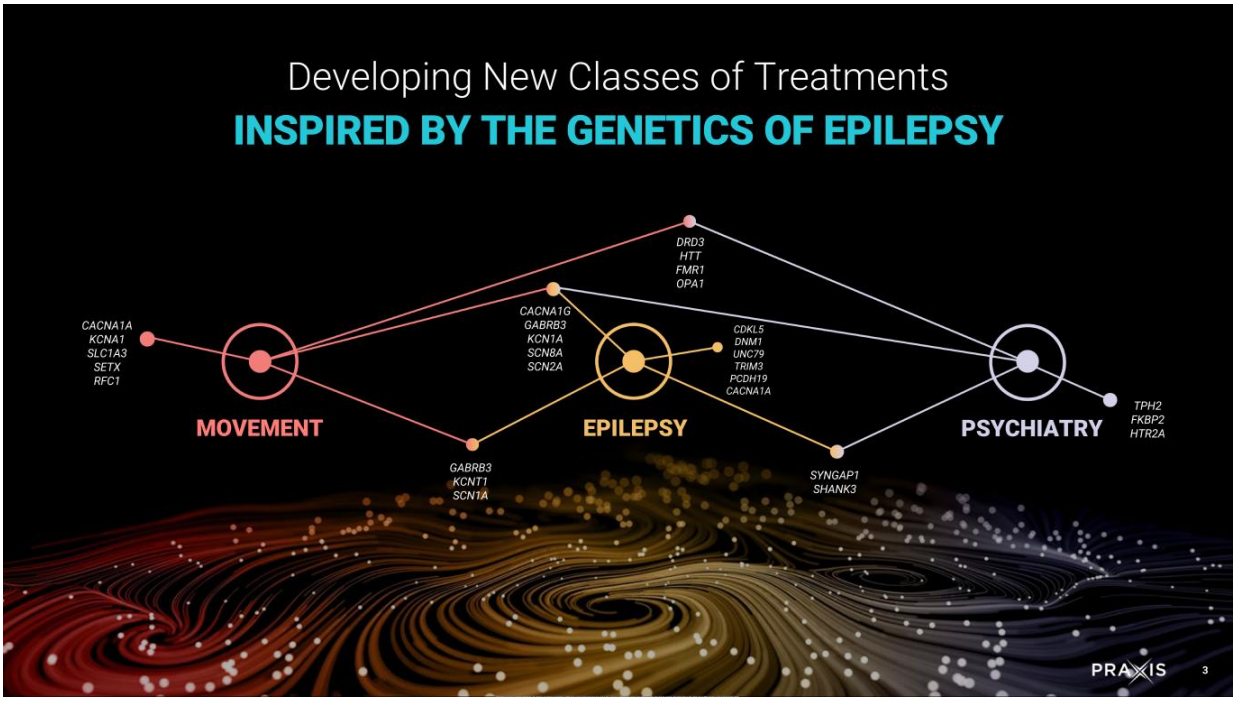
August 2022

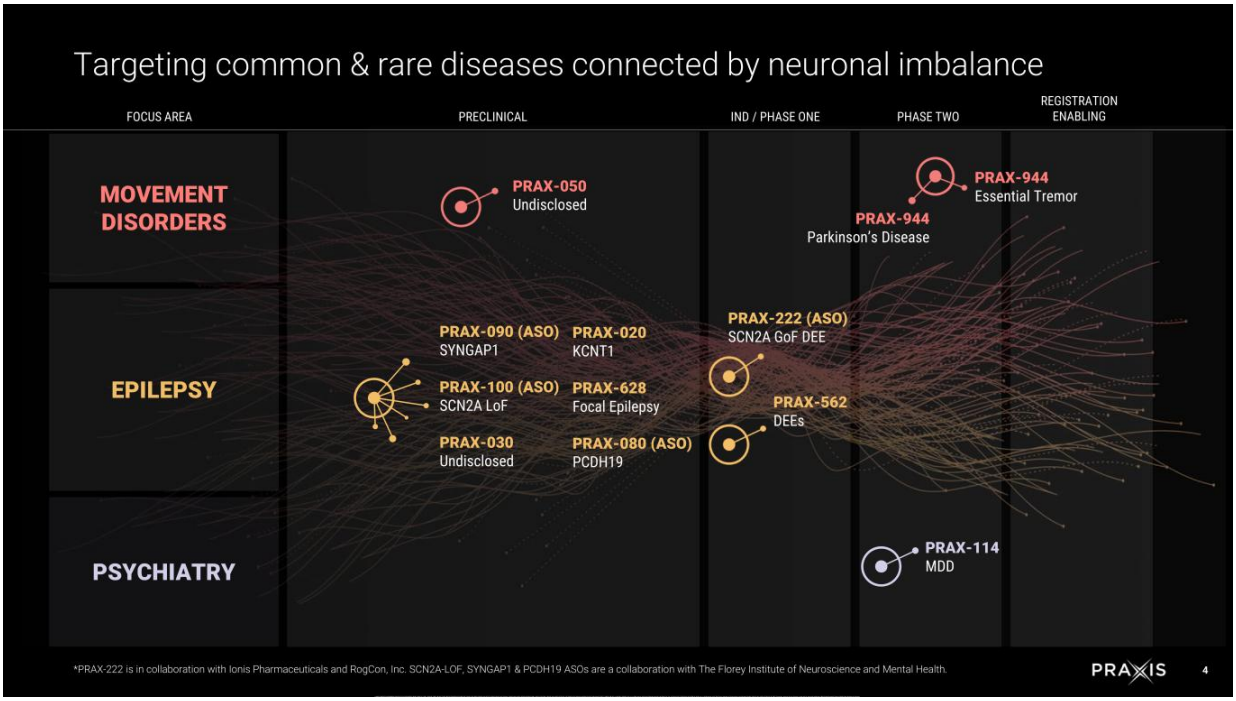
Forward-looking statements

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
CACNA1A
KCNA1
SLC1A3
SETX
RFC1
MOVEMENT
DRD3
HTT
FMR1
OPA1
CACNA1G
GABRB3
KCN1A
SCN8A
SCN2A
CDKL5
DNM1
UNC79
TRIM3
PCDH19
CACNA1A
EPILEPSY
PSYCHIATRY
TPH2
FKBP2
HTR2A
GABRB3
KCNT1
SCN1A
SYNGAP1
SHANK3
PRAXIS
3


Targeting common & rare diseases connected by neuronal imbalance
FOCUS AREA
PRECLINICAL
IND / PHASE ONE
PHASE TWO
REGISTRATION ENABLING
MOVEMENT DISORDERS
EPILEPSY
PSYCHIATRY
PRAX-050
Undisclosed
PRAX-944
Essential Tremor
PRAX-944
Parkinson's Disease
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
MDD
*PRAX-222 is in collaboration with Ionis Pharmaceuticals 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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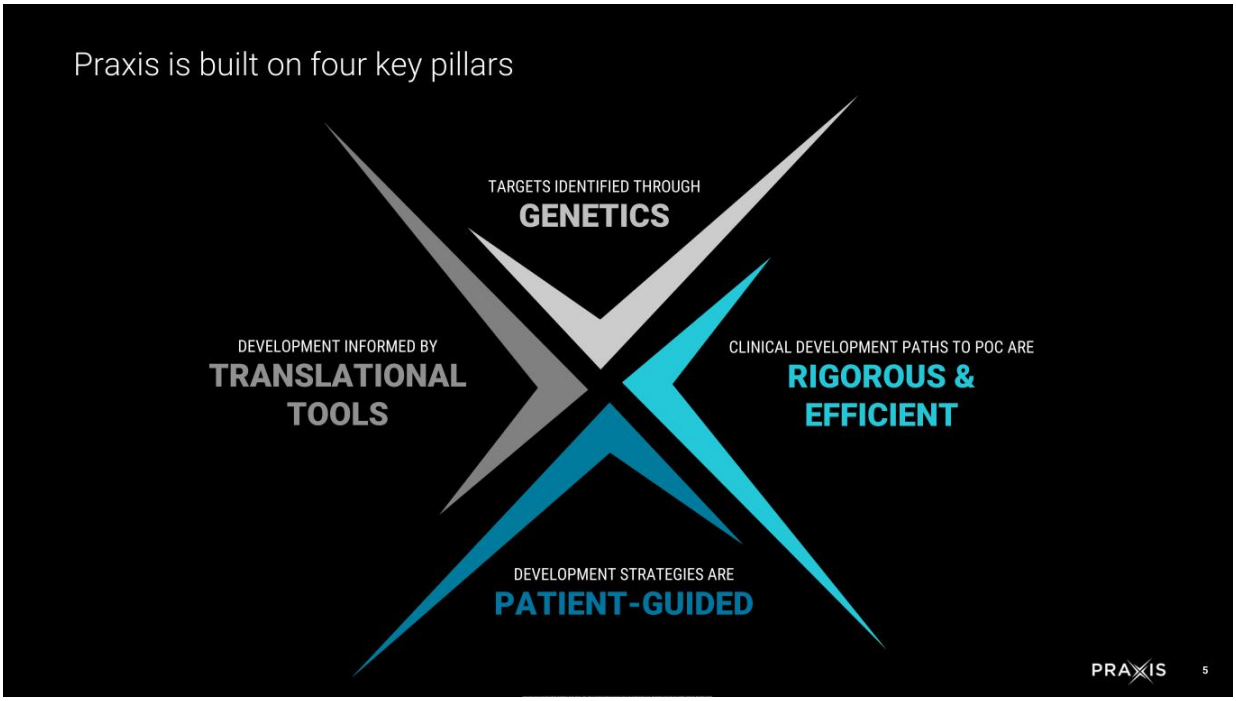
Praxis is built on four key pillars
TARGETS IDENTIFIED THROUGH
GENETICS
DEVELOPMENT INFORMED BY
TRANSLATIONAL TOOLS
CLINICAL DEVELOPMENT PATHS TO POC ARE
RIGOROUS & EFFICIENT
DEVELOPMENT STRATEGIES ARE
PATIENT-GUIDED
PRAXIS
5


BROAD CNS PORTFOLIO
Uncorrelated program risk & significant potential for indication expansion
DATA RICH 2022
Topline results from four Phase 2 or registrational studies
DEEP EARLY-STAGE PIPELINE
Enables continuous advancement of new programs
MULTI-BILLION DOLLAR REVENUE POTENTIAL from each of two key therapeutic franchises
CASH RUNWAY into 1Q24 to advance each program through value inflecting milestones
PRAXIS
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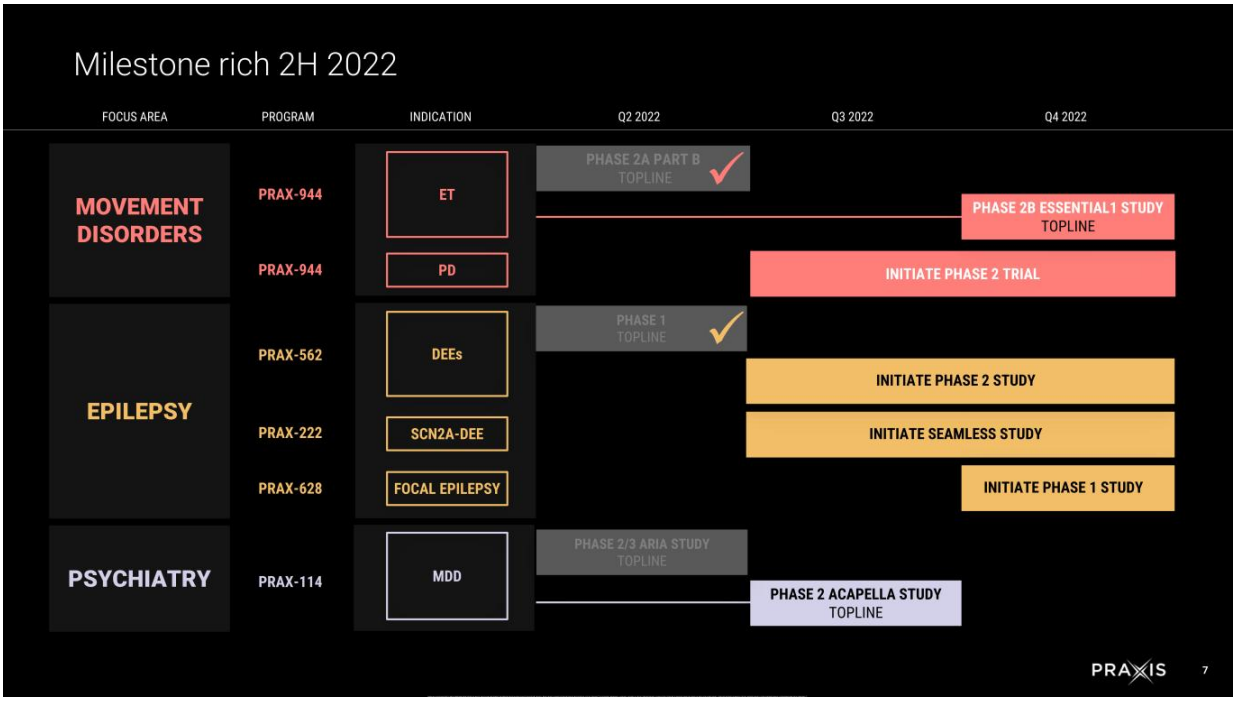
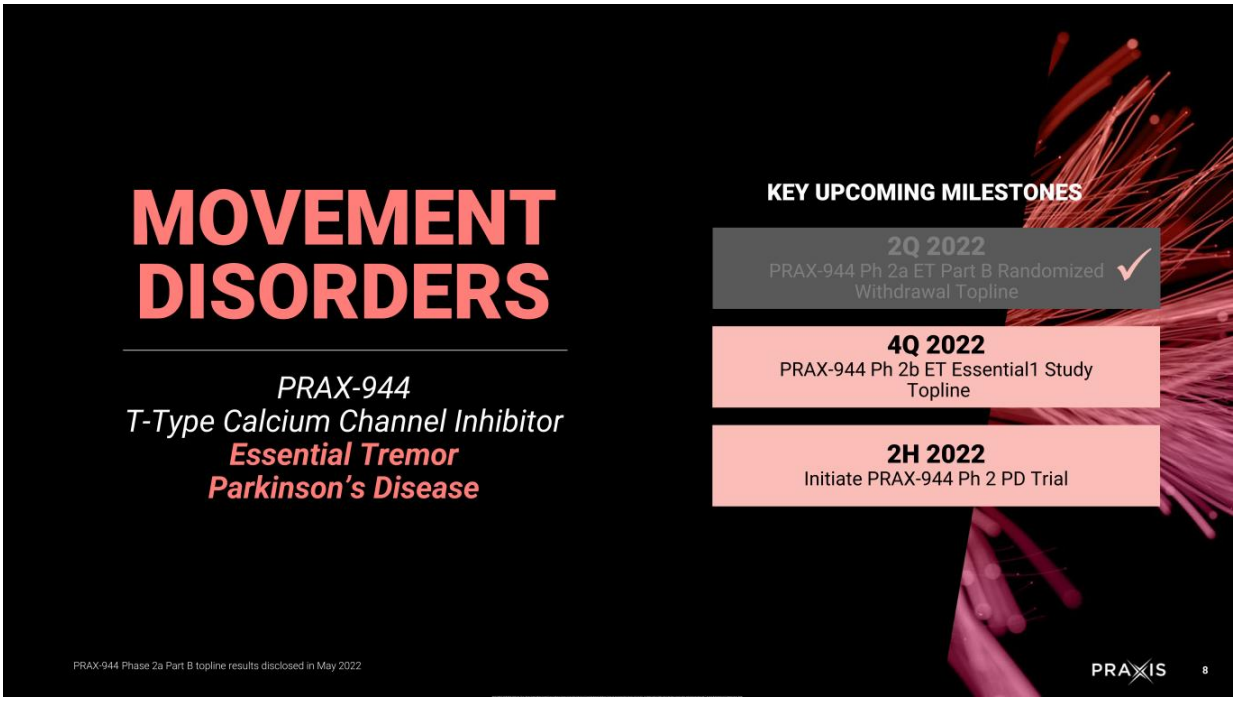

Milestone rich 2H 2022
FOCUS AREA
PROGRAM
INDICATION
Q2 2022
Q3 2022
Q4 2022
MOVEMENT DISORDERS
PRAX-944
ET
PHASE 2A PART B TOPLINE
PHASE 2B ESSENTIAL1 STUDY TOPLINE
PRAX-944
PD
INITIATE PHASE 2 TRIAL
EPILEPSY
PRAX-562
DEEs
PHASE 1 TOPLINE
INITIATE PHASE 2 STUDY
PRAX-222
SCN2A-DEE
INITIATE SEAMLESS STUDY
PRAX-628
FOCAL EPILEPSY
INITIATE PHASE 1 STUDY
PSYCHIATRY
PRAX-114
MDD
PHASE 2/3 ARIA STUDY TOPLINE
PHASE 2 ACAPELLA STUDY TOPLINE
PRAXIS
7


MOVEMENT DISORDERS
PRAX-944
T-Type Calcium Channel Inhibitor
Essential Tremor
Parkinson's Disease
KEY UPCOMING MILESTONES
2Q 2022
PRAX-944 Ph 2a ET Part B Randomized Withdrawal Topline
4Q 2022
PRAX-944 Ph 2b ET Essential1 Study Topline
2H 2022
Initiate PRAX-944 Ph 2 PD Trial
PRAX-944 Phase 2a Part B topline results disclosed in May 2022
PRAXIS
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At Praxis, we DARE for MORE for people living with essential tremor

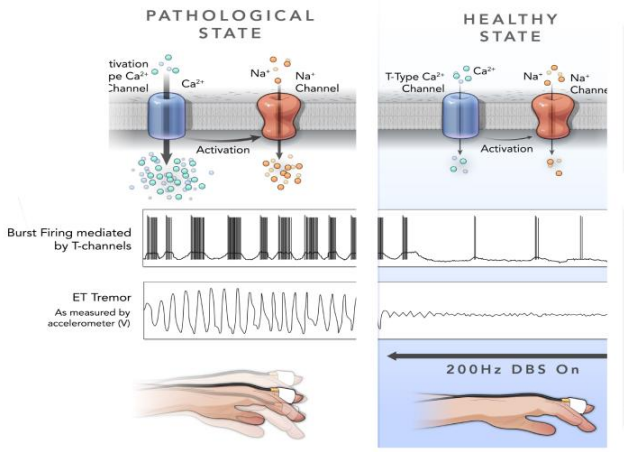
0 medications developed specifically for ET & only 1 medication approved for ET >50 years ago

~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

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 figured on actual ET patient intraoperative real-time single-unit recordings of action potentials of individual neurons

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

Highly selective for T-type calcium channels

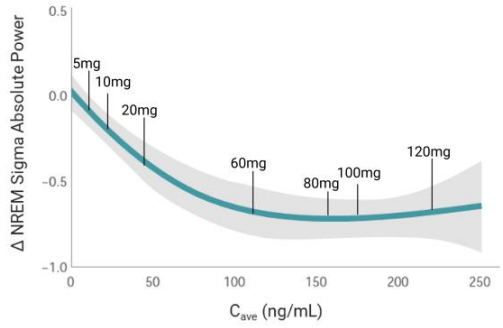
Highly potent across all three T-type isoforms

Potential for effectiveness across range of neuronal activity levels

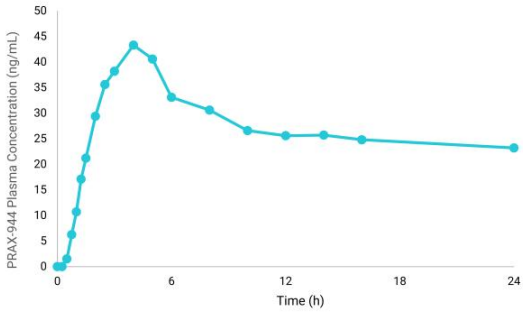
Source: Praxis Data on file

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

PREDICTABLE PK, WIDE DOSING RANGE UP TO ~100 MG & FLEXIBILITY IN TITRATION



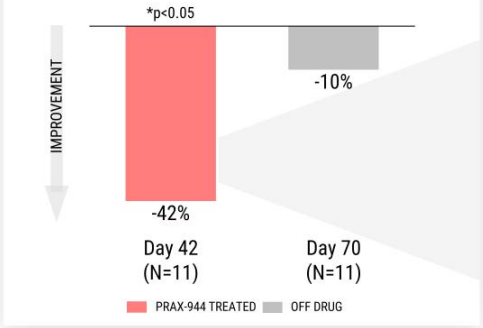
SUSTAINED EXPOSURE WITH BLUNTED MR CMAX



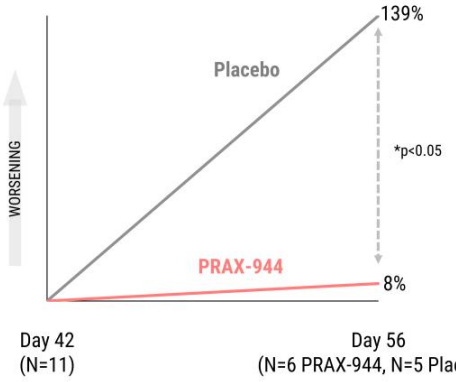
Source: Praxis Data on file

Marked functional benefit observed in patients treated with PRAX-944, while withdrawal of PRAX-944 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



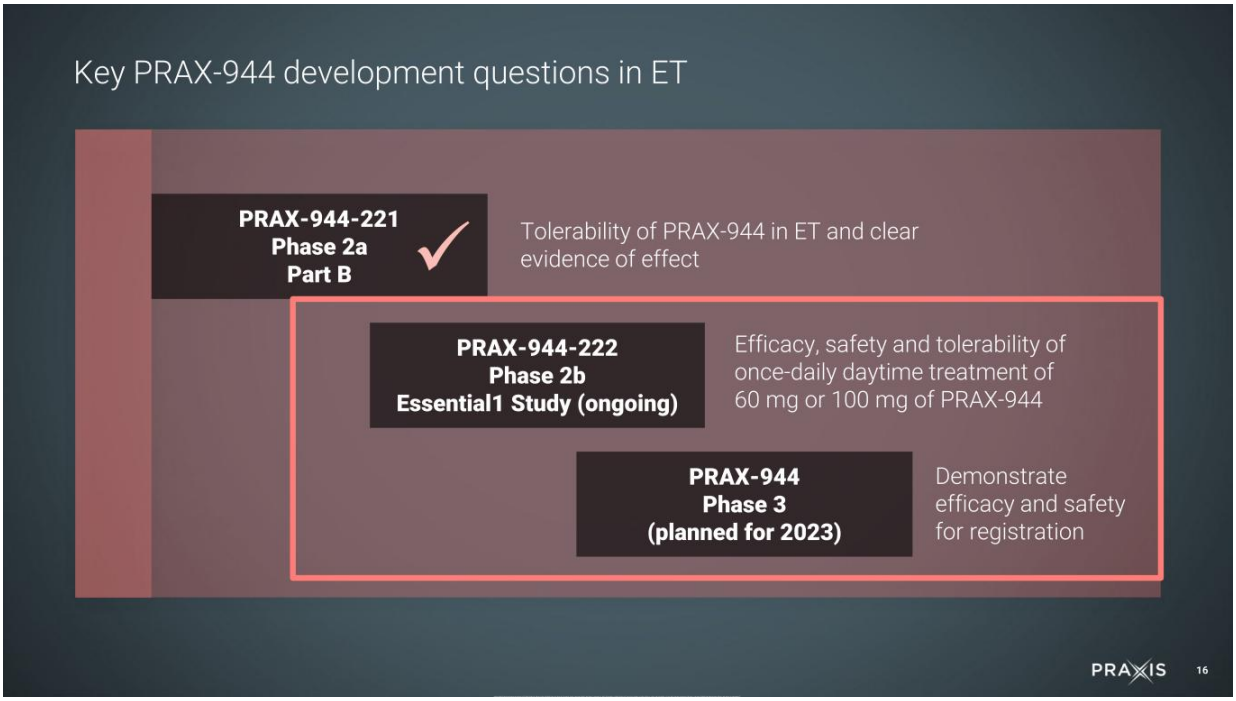
*Nominal p-value based on ANCOVA
Source: Praxis Data on file from Part B of Phase 2a study

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

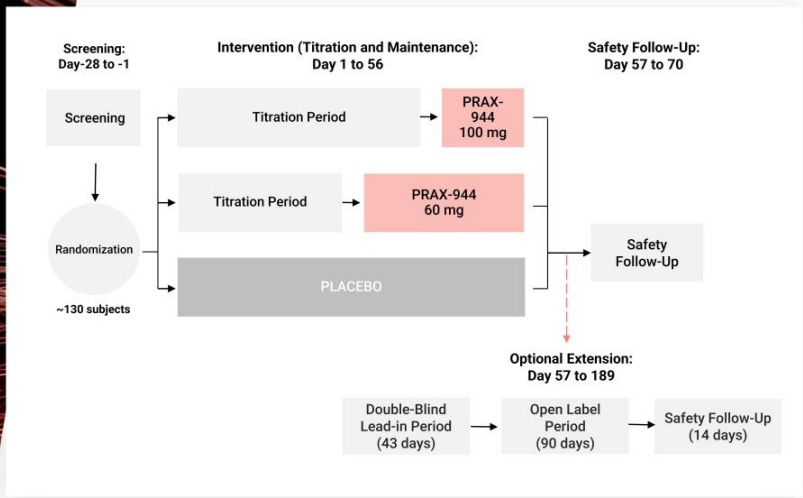
SAFETY SUMMARY

- 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


Key PRAX-944 development questions in ET
PRAX-944-221
Phase 2a
Part B
Tolerability of PRAX-944 in ET and clear evidence of effect
PRAX-944-222
Phase 2b
Essential1 Study (ongoing)
Efficacy, safety and tolerability of once-daily daytime treatment of 60 mg or 100 mg of PRAX-944
PRAX-944
Phase 3
(planned for 2023)
Demonstrate efficacy and safety for registration
PRAXIS
16

PRAX-944 Phase 2b Essential1 study topline results expected 4Q22



PRIMARY ENDPOINT:

Change from baseline to Day 56 on the Modified ADL*, functionally relevant & FDA-suggested endpoint

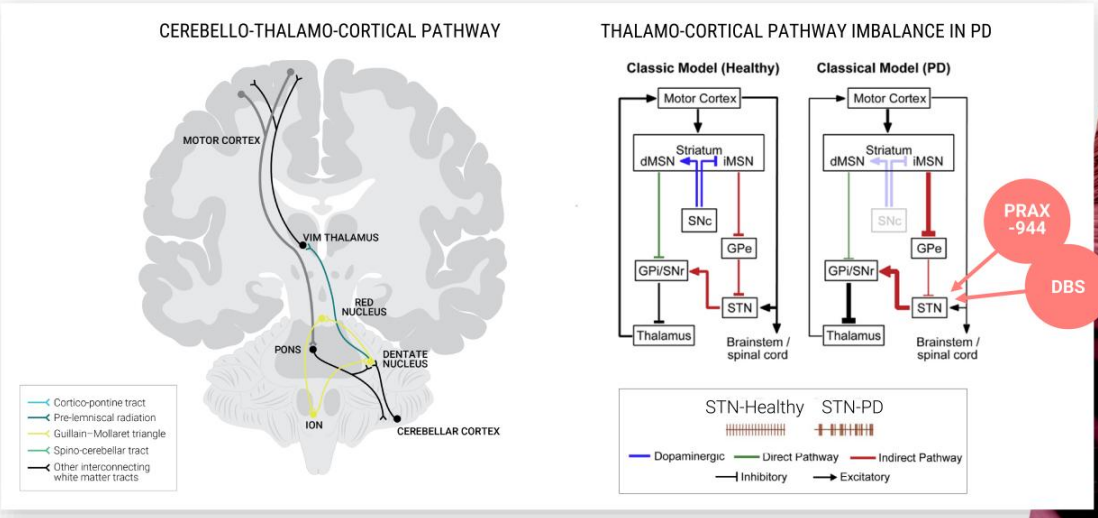
MODIFIED ADL:

TETRAS-ADL less social impact with addition of TETRAS-PS handwriting & spirals

Score of 1 re-coded as 0; highest score of 3 per item

*Composite sum of items 1 to 11 of TETRAS-ADL subscale and items 6 (bilateral) and 7 of TETRAS-PS; modified ADL score is calculated as the sum of all 13 items and ranges from 0 to 42
clinicaltrials.gov/ct2/show/NCT05021991

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

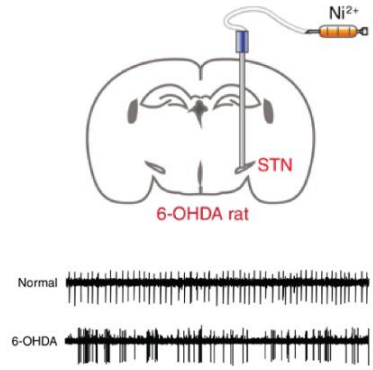


Mcgregor mm, nelson ab. Neuron. 2019. Doi:10.1016/j.Neuron.2019.03.004
Tai c-h et al. J clin invest. 2011. Doi:10.1172/jci46482

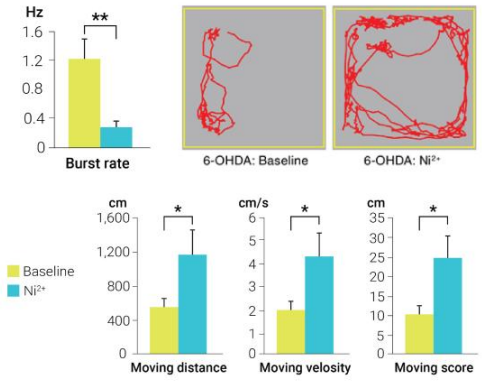
PRAXIS

Blocking T-type calcium channels with Ni^{2+} improves motor function in burst firing model of movement deficit in Parkinson's disease

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

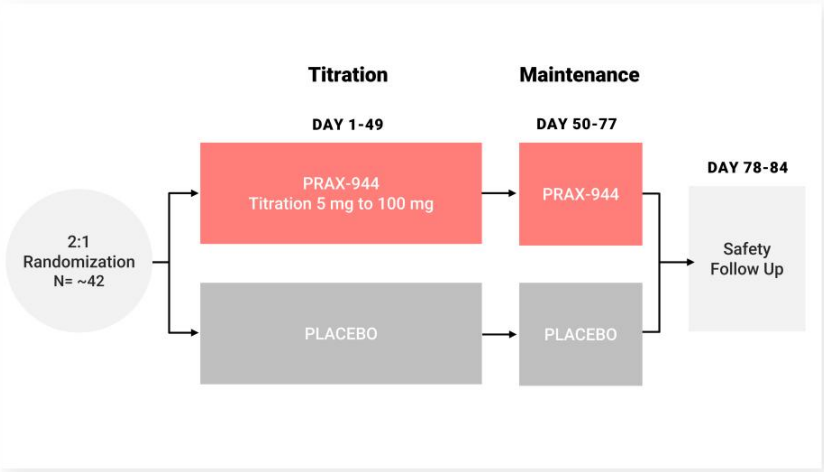


BLOCK OF BURST FIRING IMPROVES MOVEMENT IN 6-OHDA PARKINSON'S MODEL



Pan et al (2016) j clin invest doi: 10.1172/jci88170

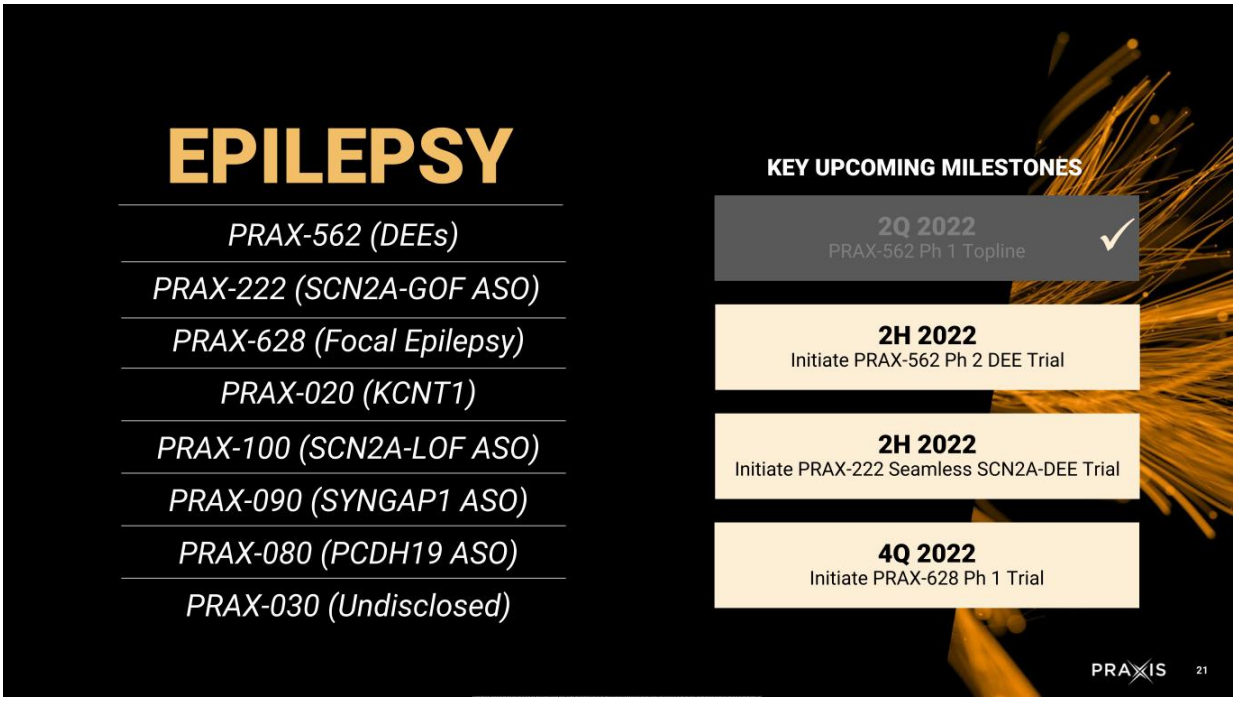
PRAX-944 Phase 2 Parkinson's disease study expected to initiate 2H22



CLINICAL MEASUREMENTS:

Motor function

KEY QUESTION:
Does PRAX-944 demonstrate motor improvement in patients?


EPILEPSY
PRAX-562 (DEEs)
PRAX-222 (SCN2A-GOF ASO)
PRAX-628 (Focal Epilepsy)
PRAX-020 (KCNT1)
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 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
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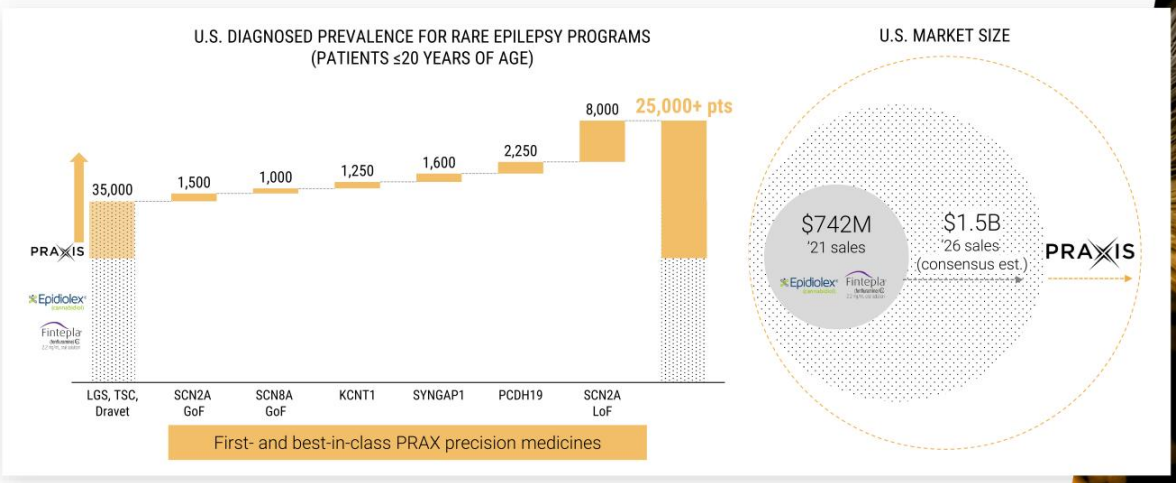
Three key imperatives guide our epilepsy portfolio build

TARGETS IDENTIFIED THROUGH GENETICS

FOCUS ON NODES OF PATHOPHYSIOLOGICAL CONVERGENCE INFORMED BY GENETICS	FOCUS DIRECTLY ON UNDERLYING GENETIC DEFECTS IN RARE EPILEPSY	FOCUS ON IMPLICATED GENES IN COMMON DISEASES
PRAX-562 *SMALL MOLECULE*	**PRAX-222*** *ASO*	**PRAX-944** *SMALL MOLECULE*
PRAX-628 *SMALL MOLECULE*	**KCNT1 INHIB.** *SMALL MOLECULE*	**PRAX-114** *SMALL MOLECULE*
	PCDH19* *ASO*	**TARGET ID BY POLYGENIC RISK VARIANTS** *SMALL MOLECULE*
	SYNGAP1* *ASO*	
	SCN2A-LOF * *ASO*	
	PRAXIS-030 *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);

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

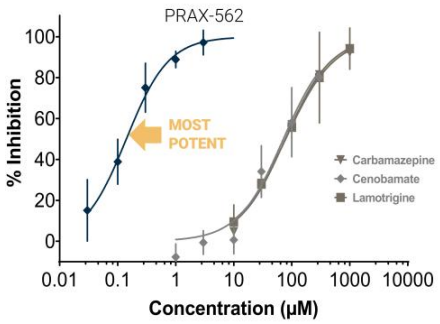
PRAX-562

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

- Superior selectivity for disease-state Na_V channel hyperexcitability
- Unprecedented therapeutic window with potential for 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}



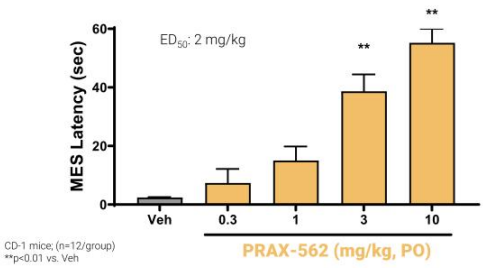
COMPARISON OF POTENCY AND SELECTIVITY

	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

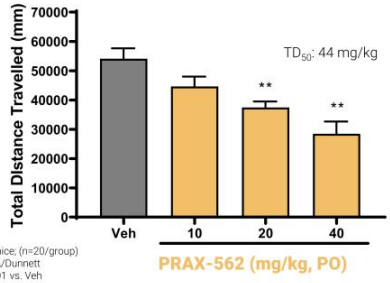
Our mechanistic hypothesis translates to a wide therapeutic index in vivo

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

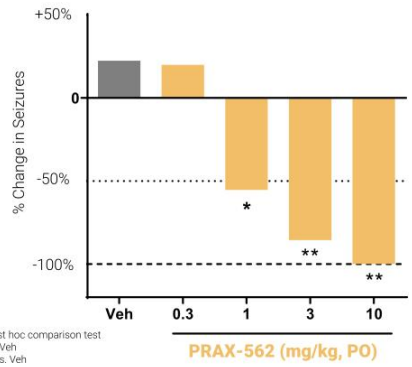
Molecule	Plasma Therapeutic Index
PRAX-562	17.2x

Therapeutic Index (TI) = TC50 / EC50

PRAXIS

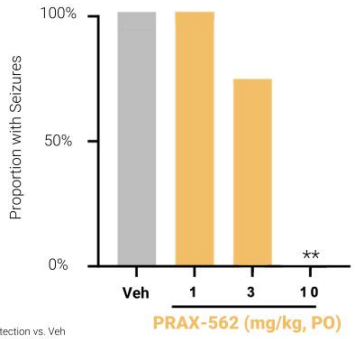
PRAX-562 completely blocks seizures in SCN2A and SCN8A GoF mutation mouse models

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

PRAX-562 Phase 1 study summary

Two-part , placebo-controlled study evaluating safety, tolerability, PK & PD of 90 mg of PRAX-562 over 28 days (Part A, N=12) and of 600 mg BID of oxcarbazepine in combination with 120 mg of PRAX-562 as compared to oxcarbazepine alone in adult healthy volunteers (Part B, N=18)

- PRAX-562 was well-tolerated in Part A of the study, with no clinically significant safety findings. The majority of TEAEs were considered mild to moderate in both Part A and Part B of the study.
- Co-administration of supra-therapeutic doses of PRAX-562 and oxcarbazepine led to additive sodium blocking effects, providing information about optimal target exposures for concomitant use of PRAX-562 and oxcarbazepine, and additional supportive evidence of PRAX-562 sodium channel blocking effects. Participants in Part B who received PRAX-562 in combination with oxcarbazepine developed TEAEs consistent with sodium channel blocking effects, leading to study withdrawal for five participants. One participant in Part B experienced drug-related SAEs that required hospitalization and resolved that day. No similar SAEs have been previously reported for PRAX-562.
- In Part A, dosing with 90 mg of PRAX-562 over 28 days resulted in concentrations that exceeded the EC50 in the MES model by 13-fold (based on mean concentration at Day 28), indicating the potential for a wider therapeutic index than other SCBs.
- In Part A, statistically significant changes were observed between placebo and 90 mg of PRAX-562 on qEEG and on ASSR, a pharmacosensitive biomarker for assessing neuronal sensory function.

Source: Praxis Data on file

Three epilepsy drugs in clinic by end of 2022

PRAX-222	PRAX-562	PRAX-628
(SCN2A)	*(SCN2A, SCN8A, TSC)*	*(FOCAL EPILEPSY)*
Initiate Seamless Study: 2H22*	**Initiate Phase 2 Study: 2H22**	**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


PRAXIS
DARE for MORE™