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 11, 2023

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 11, 2023, Praxis Precision Medicines, Inc. (the "Company") announced its financial results for the quarter ended March 31, 2023. 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 11, 2023, 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.

On May 11, 2023, the Company announced positive topline results from the PRAX-628 Phase 1 healthy volunteer study evaluating the safety, tolerability and pharmacokinetics ("PK") of single ascending doses ("SAD") and multiple ascending doses ("MAD") of PRAX-628. PRAX-628 is a next-generation, functionally selective small molecule targeting the hyperexcitable state of sodium-channels in the brain. PRAX-628 is currently being developed as a once daily, oral treatment for adult focal onset epilepsy.

In the study, PRAX-628 or placebo was administered to 40 healthy participants (n=30, placebo=10). SAD cohorts evaluated PRAX-628 doses ranging from 5 mg to 45 mg and MAD cohorts evaluated PRAX-628 doses of 20 mg and 30 mg, resulting in concentrations of more than 15-fold the mouse Maximal Electroshock Seizure model EC50. PRAX-628 was generally well-tolerated at all tested doses. PK data demonstrated dose-dependent exposure supporting once-daily dosing without titration to achieve potentially therapeutically effective drug concentration levels. The most common treatment-related adverse events ("AEs") across all cohorts were fatigue, dizziness, somnolence, headache, disturbance in attention and nausea. All AEs were mild, mostly transient and resolved without further intervention, and no AEs led to study drug withdrawal. No serious adverse events, clinically significant ECG findings, vital signs or neurological examination findings were observed.

Additional results from the PRAX-628 Phase 1 study will be presented at an upcoming medical conference. Based on the Phase 1 results and preclinical profile, the Company intends to advance PRAX-628 into a Phase 2 study in focal epilepsy in the fourth quarter of 2023.

Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws, including statements regarding the clinical development of PRAX-628. The forward-looking statements included in this Current Report on Form 8-K are subject to a number of risks, uncertainties and assumptions, including, without limitation, uncertainties inherent in clinical trials, the expected timing of submission for regulatory approval or review by governmental authorities and other risks as described in the Company's Annual Report on Form 10-K for the year ended December 31, 2022 and its other filings with the Securities and Exchange Commission. These statements are based only on facts currently known by the Company and speak only as of the date of this Current Report on Form 8-K. As a result, you are cautioned not to rely on these forward-looking statements and the Company undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future developments or otherwise.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release, dated May 11, 2023
99.2	Praxis Precision Medicines, Inc. May 2023 Corporate Presentation
104	Cover Page Interactive Data File (embedded within the inline XBRL document)

SIGNATURE

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

PRAXIS PRECISION MEDICINES, INC.

Date: May 11, 2023

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

Praxis Precision Medicines Provides Corporate Update and Reports First Quarter 2023 Financial Results

Ulixacaltamide essential tremor End-of-Phase 2 meeting with FDA scheduled for June 2023

PRAX-628 Phase 1 study results support preclinical profile indicating potential for best-in-class-efficacy for focal epilepsy

Cash and investments of $85.8 million as of March 31, 2023 supports runway into 2Q24

BOSTON, May 11, 2023 — 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 first quarter 2023.

"Each of our four clinical-stage programs has made meaningful progress this year and we anticipate additional value inflecting milestones throughout the pipeline in the coming months," said Marcio Souza, president and chief executive officer of Praxis. "We shared positive topline results earlier today from the Phase 1 study of our next-generation, functional-state selective small molecule, PRAX-628, and believe that this program has the potential to change the treatment paradigm for people living with focal epilepsy. We look forward to initiating a PRAX-628 Phase 2 study in focal epilepsy later this year, and also plan to share results from our PRAX-562 and PRAX-222 programs in rare, genetic epilepsies. Finally, we eagerly anticipate the upcoming ulixacaltamide End-of-Phase 2 FDA meeting in June and intend to start a Phase 3 program in essential tremor shortly thereafter."

Recent Business Highlights and Upcoming Milestones:

Cerebrum™ Small Molecule Platform

- Praxis announced topline results from the ulixacaltamide (PRAX-944) Phase 2 Essential1 study for the treatment of moderate to severe essential tremor (ET) in March 2023. An end-of-Phase 2 meeting with the U.S. Food and Drug Administration (FDA) is scheduled for June 2023. Based upon the observed efficacy and safety profile, Praxis intends to initiate the ulixacaltamide Phase 3 program for the treatment of ET in the second half of 2023 following FDA feedback on the clinical registration plan and alignment on the overall development program.

- The Company plans to present additional results from the Essential1 study at upcoming medical conference meetings and company events:
  - Essential1 topline results poster at the World Congress on Parkinson's Disease and Related Disorders 2023 (IAPRD) in Chicago, IL on Monday, May 15, 2023 at 12:15 p.m. CDT
  - Essential1 results presentation and scientific talk at the 2nd International Tremor Conference (ITC) in New York, NY on Thursday, May 18, 2023 at 4:20 p.m. EDT
  - Essential1 results presentation and key opinion leader (KOL) company hosted event (details to follow)

- In May 2023, Praxis announced positive topline results from a Phase 1 healthy volunteer study of PRAX-628 evaluating the safety, tolerability and pharmacokinetics (PK) of PRAX-628 across single and multiple ascending dose cohorts (SAD and MAD). PRAX-628 was generally well-tolerated at all tested doses, including concentrations in the MAD that reached more than 15-fold the mouse Maximal Electroshock Seizure model (MES) EC_{50}, a highly predictive translational model for focal epilepsy. Based on the MES model, the predicted therapeutic range of PRAX-628 is at least 3-fold wider than the current market leader in focal epilepsy, indicating potential for best-in-class efficacy for PRAX-628. The Company intends to initiate a PRAX-628 Phase 2 study for the treatment of focal epilepsy in the fourth quarter of 2023.

- Praxis expects topline results from the PRAX-562 Phase 2 EMBOLD study for the treatment of pediatric patients with developmental and epileptic encephalopathies (DEEs) in the fourth quarter of 2023. The EMBOLD study is a

randomized, double-blind, placebo-controlled Phase 2 clinical trial to evaluate the safety, tolerability, efficacy (motor seizure frequency) and PK of PRAX-562 in pediatric participants aged 2 to 18 years with DEEs, followed by an open-label extension. Approximately 20 participants with SCN2A-DEE or SCN8A-DEE will be enrolled initially.

- In April 2023, Praxis presented the following posters at the 75th Annual American Academy of Neurology (AAN) meeting:
  - PRAX-562-101: A Phase 1 Trial Evaluating the Safety, Tolerability, Pharmacokinetics and Food Effect of PRAX-562 in Healthy Volunteers (Poster Session P8: 9-011)
  - PRAX-562-102: A Phase 1 Trial Evaluating the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of PRAX-562 in Healthy Volunteers (Poster Session P4: 9-011)
  - PRAX-628 is a Novel, Well-tolerated, Activity Dependent Sodium Channel Blocker with Potent Anticonvulsant Activity (Poster Session P4: 9-012)
  - PRAX-628: A Novel Sodium Channel Blocker with Greater Potency and Activity Dependence Compared to Standard of Care (Poster Session P8: 9-012)
  - A Novel Approach to Assess the Impact of Disease in Patients with SCN8A-Related Developmental and Epileptic Encephalopathy (Poster Session P3: 9-008)
  - Disease Impact and Burden in Patients with SCN2A-Related Developmental and Epileptic Encephalopathy (Poster Session P11: 9-011)

Solidus™ Antisense Oligonucleotide (ASO) Platform

- Praxis is conducting the first dose cohort (Part 1) of the PRAX-222 EMBRAVE study for the treatment of pediatric patients with early-onset SCN2A-DEE in the U.S. Following collection of the safety and efficacy data from Part 1 of the EMBRAVE study, the data will be evaluated and submitted to the FDA to support further dose escalation. Part 1 of the EMBRAVE study is a 21-week open label cohort, in which participants will receive PRAX-222 for up to 13 weeks, designed to determine the safety and tolerability of intrathecal delivery of PRAX-222. Topline results are expected in the second half of 2023.

First Quarter 2023 Financial Results:

As of March 31, 2023, Praxis had $85.8 million in cash, cash equivalents and marketable securities, which is expected to fund operations into the second quarter of 2024.

Praxis recognized $0.7 million in collaboration revenue during the three months ended March 31, 2023 related to its Option and License Agreement with UCB.

Research and development expenses were $25.5 million for the three months ended March 31, 2023, compared to $52.7 million for the three months ended March 31, 2022. The decrease in research and development expenses of $27.1 million was primarily attributable to $25.3 million in decreased expenses related to the Company's Cerebrum™ and Solidus™ platforms and a $3.0 million decrease in personnel-related expenses.

General and administrative expenses were $13.3 million for the three months ended March 31, 2023, compared to $16.2 million for the three months ended March 31, 2022. The decrease in general and administrative expenses of approximately $2.9 million was primarily due to a decrease in consulting and insurance-related costs as well as a decrease in personnel-related expenses.

Praxis reported a net loss of $37.5 million for the three months ended March 31, 2023, including $7.6 million of stock-based compensation expense, compared to $68.7 million for the three months ended March 31, 2022, including $7.9 million of stock-based compensation expense.

As of March 31, 2023, Praxis had 58.0 million shares of common stock outstanding.

About Praxis

Praxis Precision Medicines is a clinical-stage biopharmaceutical company translating insights from genetic epilepsies into the development of therapies for CNS disorders characterized by neuronal excitation-inhibition imbalance. Praxis is applying genetic insights to the discovery and development of therapies for rare and more prevalent neurological

disorders through our proprietary small molecule platform, Cerebrum™, and antisense oligonucleotide (ASO) platform, Solidus™, using our understanding of shared biological targets and circuits in the brain. Praxis has established a diversified, multimodal CNS portfolio including multiple programs across movement disorders and epilepsy, with four clinical-stage product candidates. For more information, please visit www.praxismedicines.com and follow us on Facebook, 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 the anticipated timing of our clinical trials and the development of our product candidates, 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; Praxis' ability to continue as a going concern; and other risks concerning Praxis' programs and operations as described in its Annual Report on Form 10-K for the year ended December 31, 2022, 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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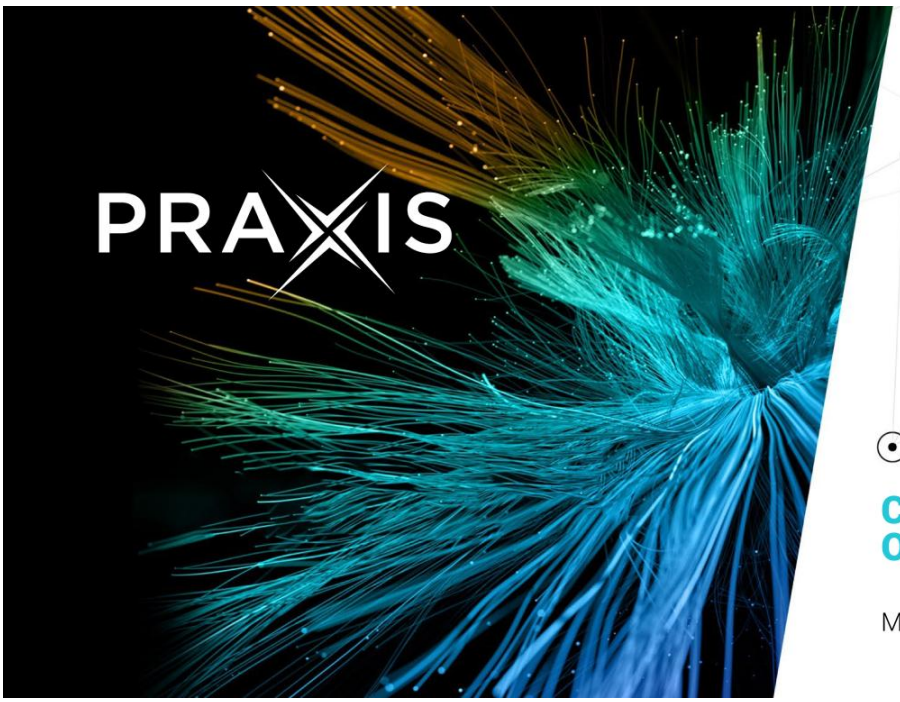
PRAXIS PRECISION MEDICINES, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(Amounts in thousands)
(Unaudited)

	March 31, 2023	December 31, 2022
Assets		
Cash and cash equivalents	$ 80,839	$ 61,615
Marketable securities	4,983	38,874
Prepaid expenses and other current assets	8,580	10,351
Property and equipment, net	865	971
Operating lease right-of-use assets	2,700	2,901
Other non-current assets	416	416
Total assets	$ 98,383	$ 115,128
Liabilities and stockholders' equity		
Accounts payable	$ 16,986	$ 14,672
Accrued expenses	9,352	15,850
Operating lease liabilities	3,260	3,500
Deferred revenue	4,317	5,000
Common stock	6	5
Additional paid-in capital	632,580	606,918
Accumulated other comprehensive loss	(19)	(173)
Accumulated deficit	(568,099)	(530,644)
Total liabilities and stockholders' equity	$ 98,383	$ 115,128

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

	Three Months Ended March 31,	
	2023	**2022**
Collaboration revenue	$ 683	$ —
Operating expenses:		
Research and development	25,504	52,652
General and administrative	13,270	16,197
Total operating expenses	38,774	68,849
Loss from operations	(38,091)	(68,849)
Other income:		
Other income, net	636	132
Total other income	636	132
Net loss	$ (37,455)	$ (68,717)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.71)	$ (1.51)
Weighted average common shares outstanding, basic and diluted	53,102,907	45,455,179



CORPORATE OVERVIEW

May 2023

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, and (viii) our ability to meet any specific milestones set forth herein. 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 for the year ended December 31, 2022, 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 Treatments Inspired By The Genetics of Epilepsy

ENABLED BY TWO PLATFORMS

CEREBRUM™

SMALL MOLECULE PLATFORM

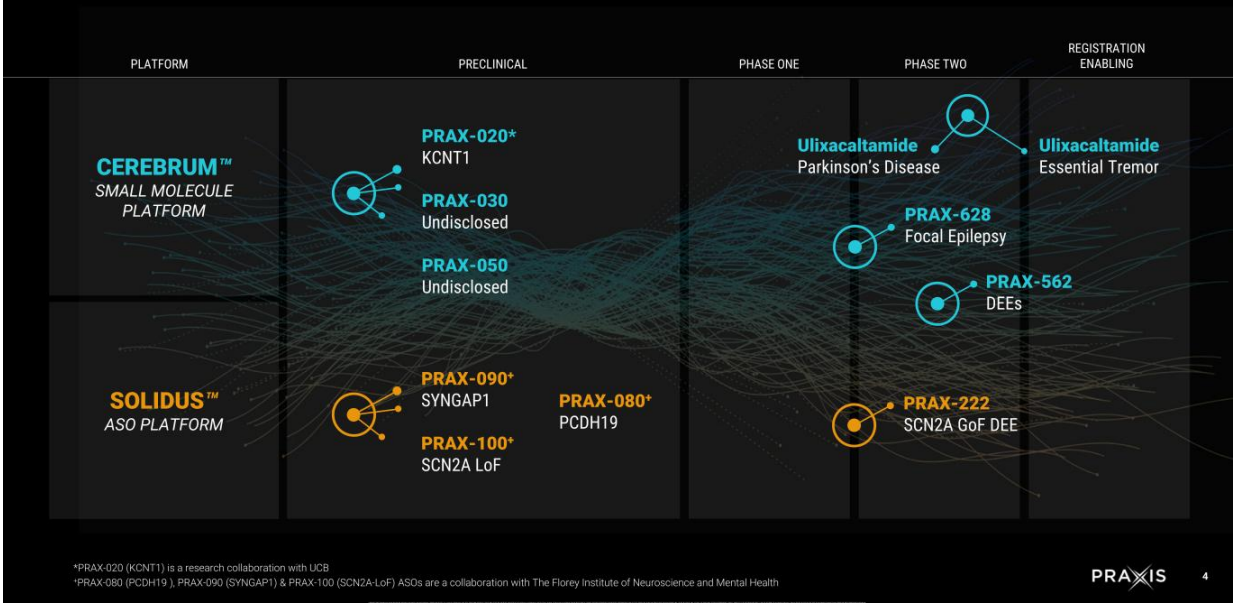
Cerebrum™ utilizes deep understanding of neuronal excitability and neuronal networks and applies a series of computational and experimental tools to develop orally available precision therapies

SOLIDUS™

ANTISENSE OLIGONUCLEOTIDE (ASO) PLATFORM

Solidus™ is an efficient, targeted precision medicine discovery and development engine for ASOs anchored on proprietary, computational methodology

Targeting movement disorders & epilepsies connected by neuronal imbalance



*PRAX-020 (KCNT1) is a research collaboration with UCB
+PRAX-080 (PCDH19), PRAX-090 (SYNGAP1) & PRAX-100 (SCN2A-LoF) ASOs are a collaboration with The Florey Institute of Neuroscience and Mental Health

Leveraging genetics to efficiently translate insights into therapies

GENETICS

Focus on therapeutic targets identified through human genetics

TRANSLATIONAL TOOLS

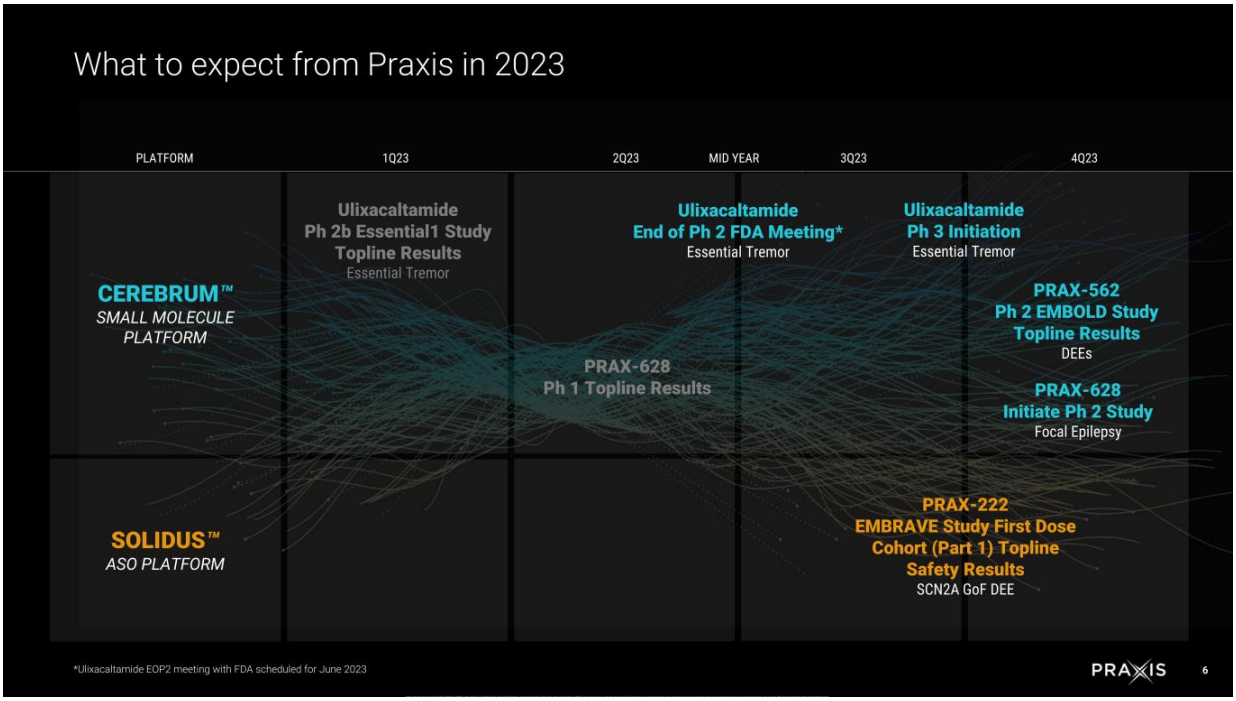
Translational tools validate potential of target and product candidate and can provide early proof of biology

EFFICIENT & RIGOROUS

Efficient, rigorous clinical development paths to proof-of-concept in humans

PATIENT-GUIDED

Patient-guided development strategies to deliver on what patients actually need


What to expect from Praxis in 2023
PLATFORM
1Q23
2Q23
MID YEAR
3Q23
4Q23
CEREBRUM™
SMALL MOLECULE PLATFORM
Ulixacaltamide
Ph 2b Essential1 Study
Topline Results
Essential Tremor
Ulixacaltamide
End of Ph 2 FDA Meeting*
Essential Tremor
Ulixacaltamide
Ph 3 Initiation
Essential Tremor
PRAX-562
Ph 2 EMBOLD Study
Topline Results
DEEs
PRAX-628
Ph 1 Topline Results
PRAX-628
Initiate Ph 2 Study
Focal Epilepsy
SOLIDUS™
ASO PLATFORM
PRAX-222
EMBRAVE Study First Dose
Cohort (Part 1) Topline
Safety Results
SCN2A GoF DEE
*Ulixacaltamide EOP2 meeting with FDA scheduled for June 2023
PRAXIS
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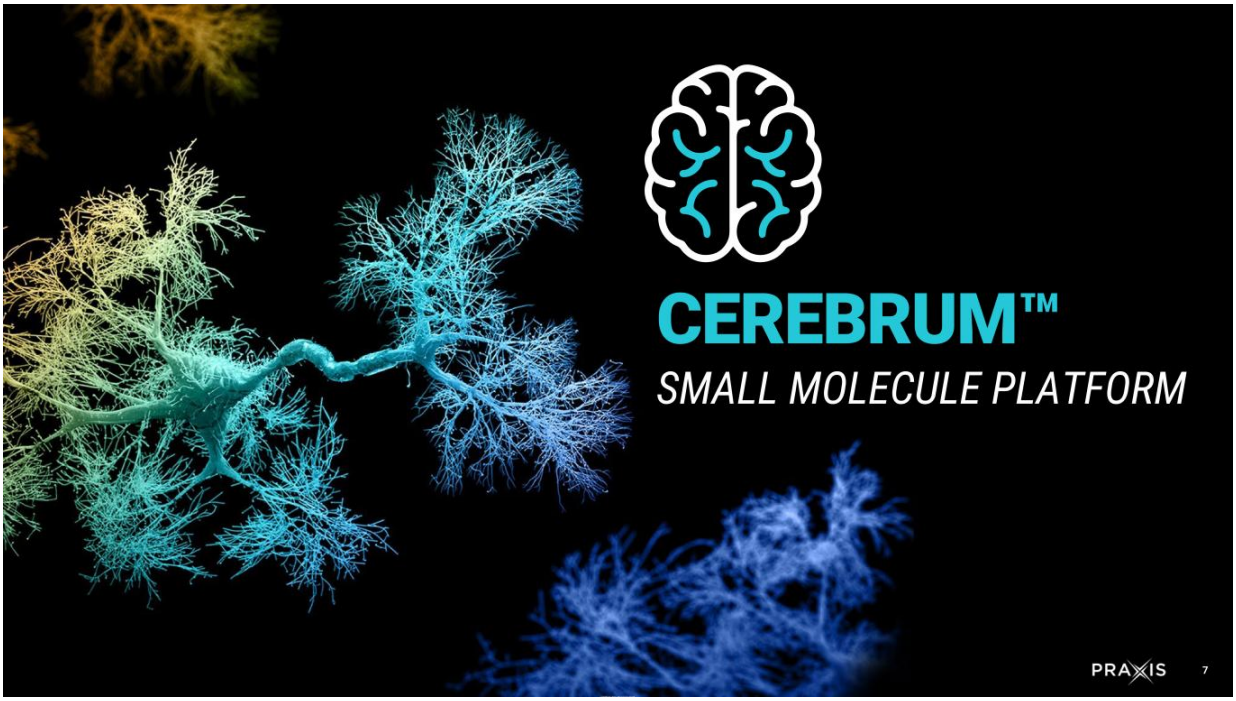
CEREBRUM™
SMALL MOLECULE PLATFORM
PRAXIS
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Ulixacaltamide (PRAX-944)

Essential Tremor and Parkinson's Disease

KEY UPCOMING MILESTONES

June 2023
ET End-of-Phase 2 FDA Meeting

2H 2023
ET Phase 3 Initiation

Essential Tremor (ET) is the most common movement disorder…

Up to 7 million people in the United States may have ET[1]

Action tremors significantly disrupt daily living for people with ET

Hallmark feature is action tremor that primarily affects the hands[2,3]

Almost all ET patients suffer from at least one comorbid condition (e.g. depression, anxiety, sleep disorders, cognitive dysfunction)[4]

SOURCE: 1. GHOSH (2016) (P.231, C.1, PH.1, L.1-2), 2. Elble RJ. Curr Neurol Neurosci Rep. 2013 Jun;13(6):353. 3. Putzke JD, et al. J Neurol Neurosurg Psychiatry. 2006 Nov;77(11):1235-7.
4. Vetterick, C., Lyons, K.E., Matthews, L.G. et al. The Hidden Burden of Disease and Treatment Experiences of Patients with Essential Tremor: A Retrospective Claims Data Analysis. Adv Ther (2022). https://doi.org/10.1007/s12325-022-02318-8

…but ET often remains undiagnosed, misdiagnosed, undertreated and untreated

Approximately 1 million people are diagnosed with ET and on treatment, while another 1 million patients are estimated to remain untreated

Of patients who seek treatment, ~40% discontinue within 2 years, or 200,000 patients annually

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

Many ET patients are frequently misdiagnosed, leading to ET diagnosis about 1.5 years after an initial movement disorder diagnosis

SOURCE: Vetterick, C., Lyons, K.E., Matthews, L.G. et al. The Hidden Burden of Disease and Treatment Experiences of Patients with Essential Tremor: A Retrospective Claims Data Analysis. Adv Ther (2022). https://doi.org/10.1007/s12325-022-02318-8

Ulixacaltamide is a differentiated, selective T-type calcium channel blocker in development for ET and Parkinson's disease

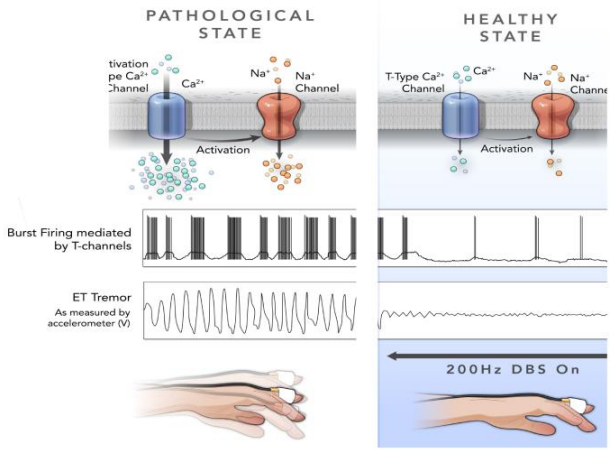
Highly selective for T-type calcium channels

Highly potent across all three T-type isoforms

Potential for effectiveness across range of neuronal activity levels

Source: Praxis Data on file, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9310641/

T-Type calcium channels are gatekeepers of neuronal firing patterns in the Cerebello-Thalamo-Cortical (CTC) circuit



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

TTCC drive burst firing in the CTC circuit

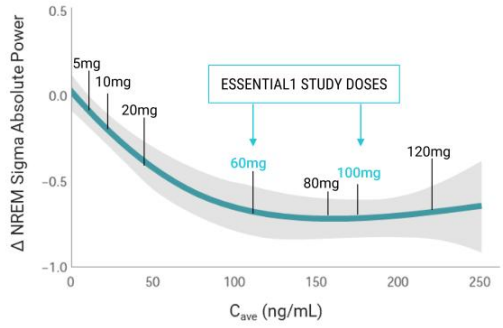
Burst firing in the CTC circuit correlated with tremor in patients with ET and PD

Deep Brain Stimulation reduces burst firing and tremor

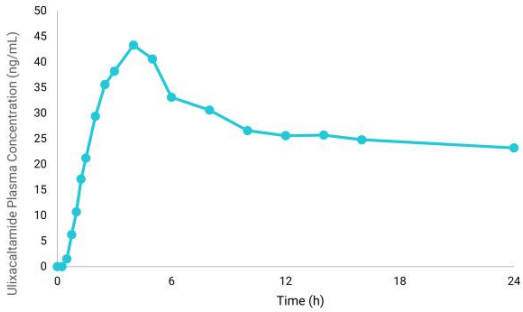
Source: Based on Milosevic 2018 figured on actual ET patient intraoperative real-time single-unit recordings of action potentials of individual neurons

Ulixacaltamide's wide dosing range and modified release formulation may support tolerability & efficacy profile

PREDICTABLE PK, FLEXIBILITY IN TITRATION & WIDE DOSING RANGE UP TO ~100 MG CONFIRMED IN ESSENTIAL1



SUSTAINED EXPOSURE WITH BLUNTED C_{MAX}



Source: Praxis Data on file

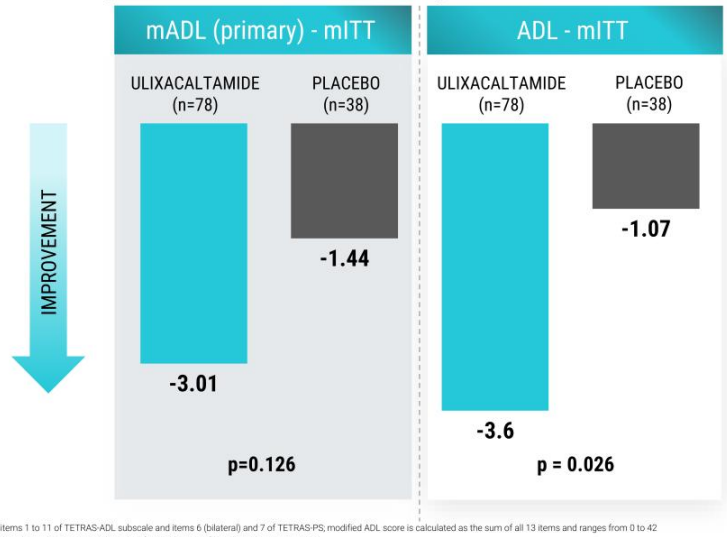
Breaking ground with Essential1 - path forward toward registration

ESSENTIAL1 ENABLES PROGRESS

- Clinically meaningful effect observed in functional outcomes
- Improvement or stabilization in all TETRAS ADL* measurements
- Therapeutic drug levels achieved, suggesting individualized exposure response curve consistent with translational data
- Well tolerated safety profile, no new safety signals identified
- TETRAS performance subscale not a reliable measure for clinical studies
- Opportunity to further control for potential confounding factors in subsequent clinical trials, including ET patients with intention tremor

clinicaltrials.gov/ct2/show/NCT05021991
*https://www.jneurology.com/articles/the-essential-tremor-rating-assessment-scale-neuromed-1-1038.pdf

Essential1 topline results show mADL* and ADL improvement over placebo at Day 56 in Phase 2b ET study

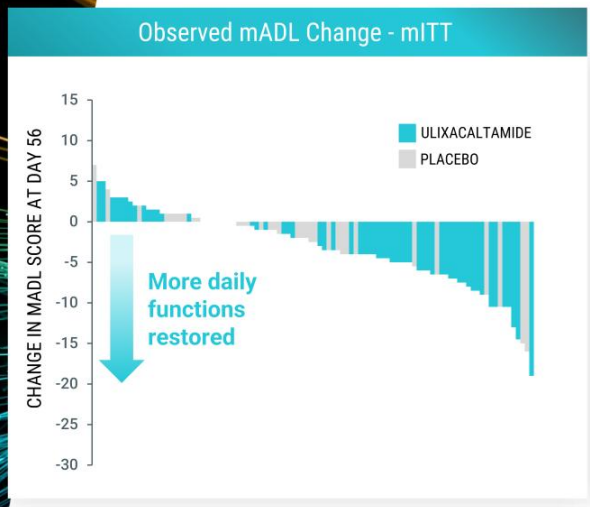


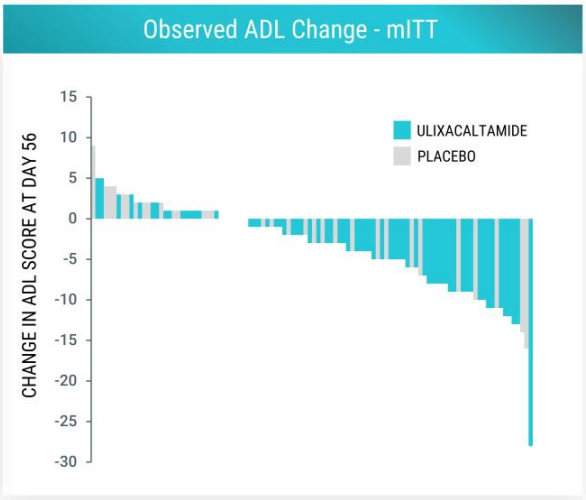
No dose related difference in efficacy between 60 mg and 100 mg groups

*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
MMRM, Adjusted by baseline value, propranolol use and familial history of ET, all p values are nominal
mITT ANALYSIS: Defined as all patients enrolled under Version 4 of Protocol (or enrolled in prior version and eligible for V4), who were randomized to treatment, and received 1 dose of study drug [n=116]; excluded from mITT analysis are 16 patients enrolled under earlier protocol version that did not meet Version 4 inclusion/exclusion criteria and dose levels

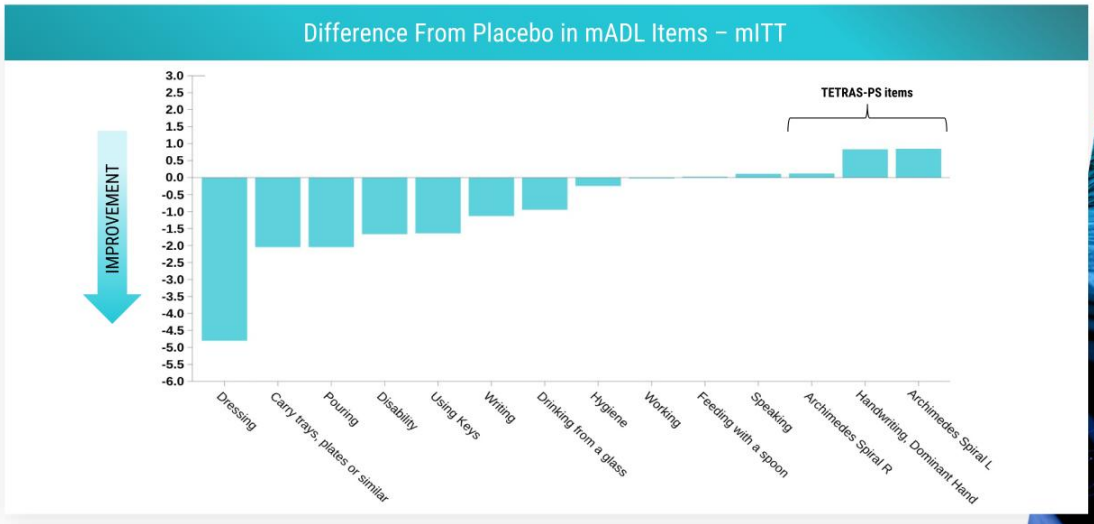
PRAXIS

More patients taking ulixacaltamide showed improvements in ADL scores compared to patients on placebo in Essential1 study





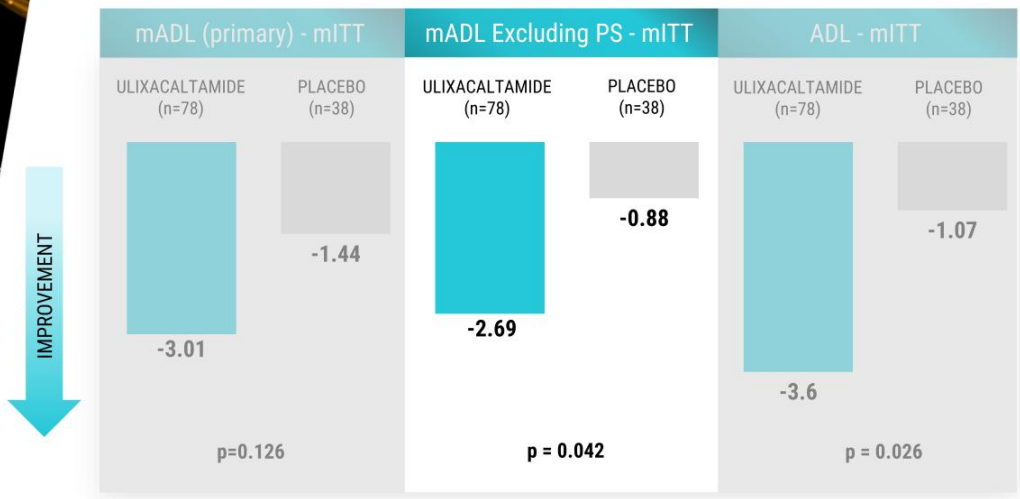
Ulixacaltamide demonstrated consistent effect relative to placebo across ADL scored items in Essential1 study



Fold-change difference between placebo and ulixacaltamide at Day 56 for mADL individual Item scores adjusted by placebo MMRM, Adjusted by baseline value, propranolol use, and familial history of ET

PRAXIS

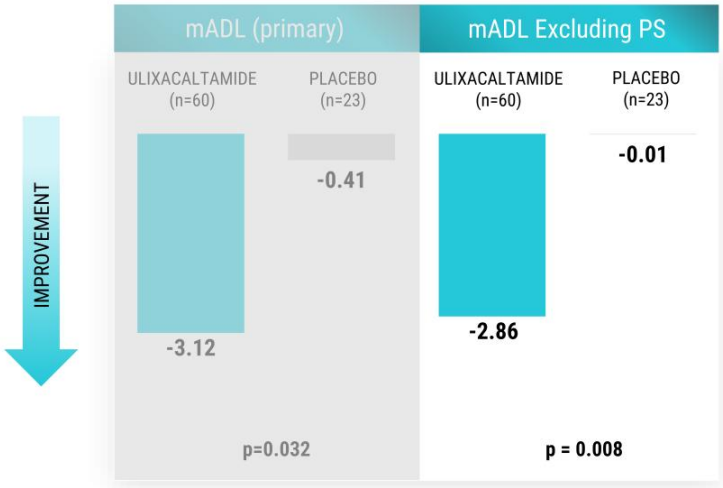
Ulixacaltamide demonstrated improvement over placebo in the mADL excluding PS at Day 56 in Essential1 study



MMRM, Adjusted by baseline value, propranolol use and familial history of ET, all p values are nominal

mADL and mADL excluding PS improvement over placebo at Day 56

mITT Excluding ET Patients with Intention Tremor



We intend to control for the presence of ET participants with intention tremor in future trials

MMRM, Adjusted by baseline value, propranolol use and familial history of ET, all p values are nominal

Breaking ground with Essential1 – next steps toward registration

ESSENTIAL1 ENABLES PROGRESS

- Clinically meaningful effect observed in functional outcomes
- Improvement or stabilization in all TETRAS ADL measurements
- Therapeutic drug levels achieved, suggesting individualized exposure response curve consistent with translational data
- Well tolerated safety profile, no new safety signals identified
- TETRAS performance subscale not a reliable measure for clinical studies
- Opportunity to further control for potential confounding factors in subsequent clinical trials, including ET patients with intention tremor

NEXT STEPS

- End of Phase 2 meeting with the FDA scheduled for June 2023

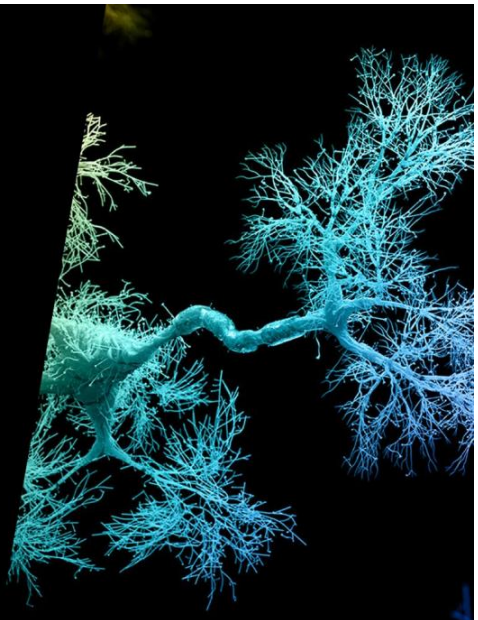
- Preliminary elements of Phase 3 program planned to start in 2H23:
  - Parallel design with 60 mg and placebo treatment arms
  - Primary endpoint of mADL excluding PS
  - 6-week treatment duration

PRAX-562

SCN2A, SCN8A & OTHER DEEs

KEY UPCOMING MILESTONES

4Q 2023
Ph 2 EMBOLD Study Topline Results



Preclinical and emerging clinical data demonstrate PRAX-562 has the potential to be a first- and best- in-class Na_V blocker for DEEs

PRAX-562

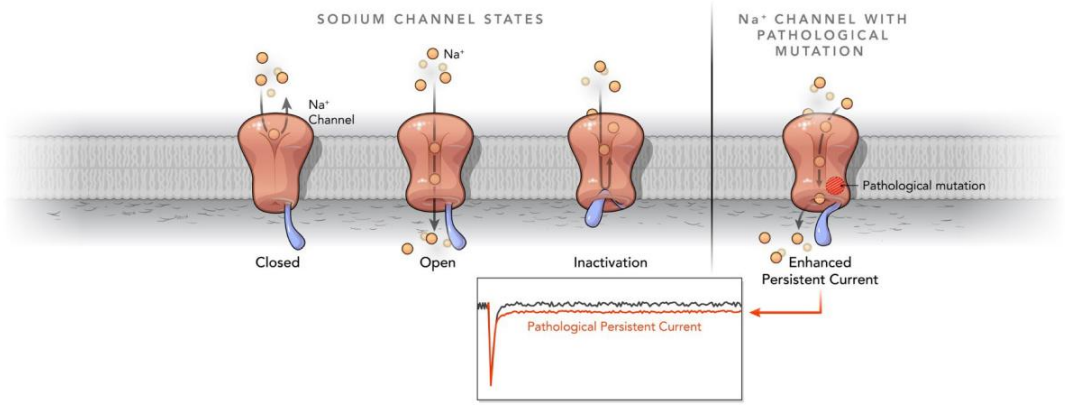
SCN2A, SCN8A
+ OTHER DEEs

PAN-NA_V BLOCKER

SMALL MOLECULE

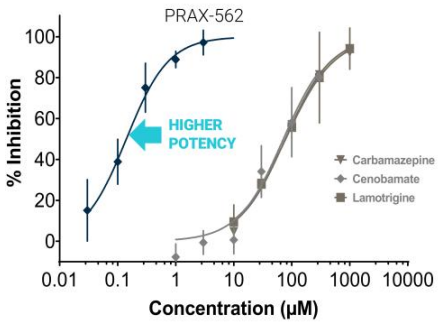
- Superior selectivity for disease-state Na_V channel hyperexcitability
- Unprecedented therapeutic window with potential for superior safety and efficacy
- Convenient auto-titration regimen with stable PK

Persistent sodium current (I_{Na}) is a critical driver of pathological hyperexcitability in CNS disorders



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

% INHIBITION OF $hNa_v1.6$ PERSISTENT I_{Na}

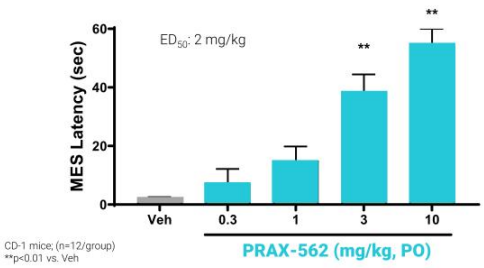


COMPARISON OF POTENCY AND SELECTIVITY

	Persistent I_{Na} IC50 (nM)	Ratio of persistent to peak inhibition
PRAX-562	**141**	**60** ← MORE 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

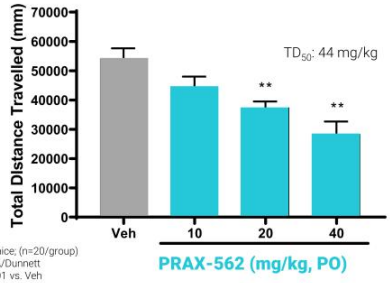
Our mechanistic hypothesis translates to a wide therapeutic index in vivo for PRAX-562

MES EFFICACY



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

sLMA TOLERABILITY



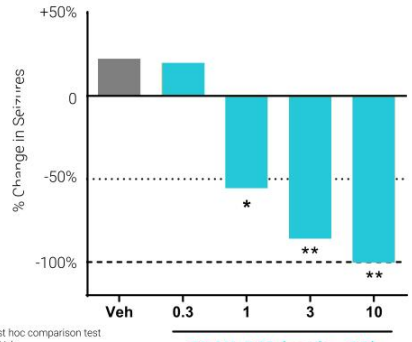
CD-1 mice; (n=20/group)
ANOVA/Dunnett
**p<0.01 vs. Veh

Molecule	Plasma Therapeutic Index
PRAX-562	17.2x

Therapeutic Index (TI) = TC50 / EC50

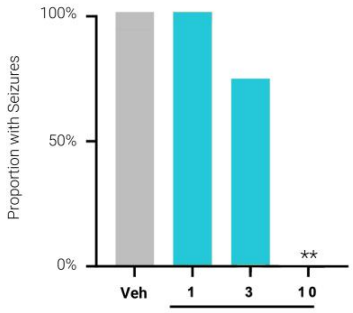
PRAX-562 completely inhibits seizures in SCN2A and SCN8A GoF mutation mouse models

IN VIVO POC IN SCN2A SPONTANEOUS 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_3 = 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 summary

PRAX-562 has been generally well tolerated in over 130 healthy volunteers

No MTD at exposures multiple fold above therapeutic range indicates potential for superior therapeutic index

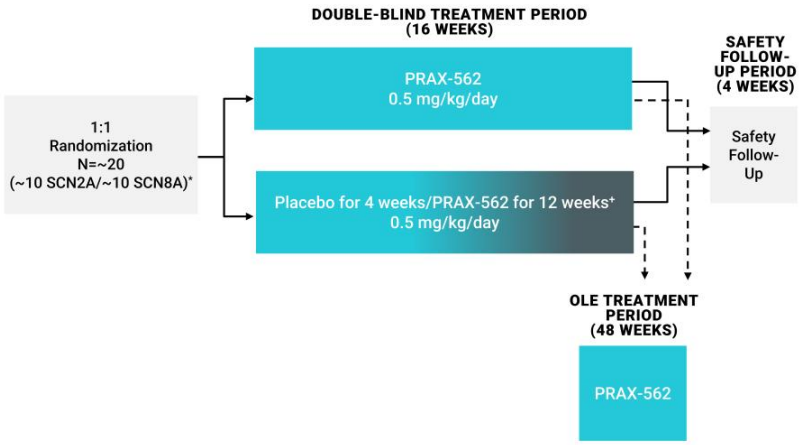
All TEAEs mild to moderate as stand-alone therapy*, with headache & dizziness most common TEAEs

Significant changes observed between placebo and 90 mg of PRAX-562 on qEEG and on ASSR biomarkers

Source: Praxis data on file; https://investors.praxismedicines.com/news-releases/news-release-details/praxis-precision-medicines-provides-corporate-update-and-5

* Co-administration of supra-therapeutic doses of PRAX-562 and oxcarbazepine led to additive sodium blocking effects, including resulting in SAEs

PRAX-562 Phase 2 EMBOLD Study topline data expected 4Q23



PRIMARY ENDPOINT:

Incidence and severity of treatment-emergent adverse events (TEAEs)

KEY SECONDARY:

Change from baseline in monthly (28 day) motor seizure frequency

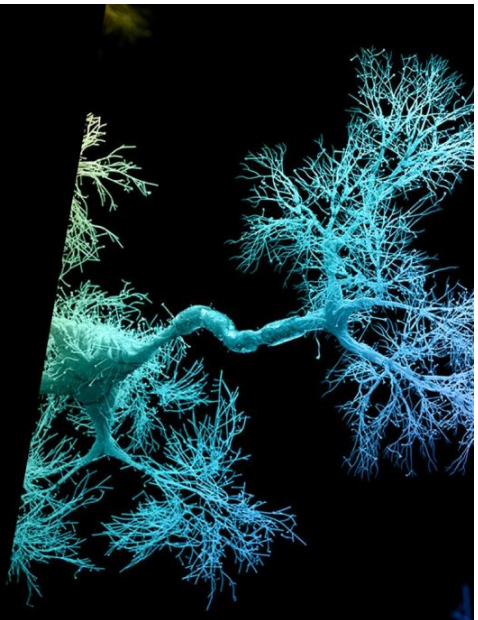
* Two distinct cohorts in early-onset SCN2A-DEE and SCN8A-DEE patients
+ Participants receive either 0.5 mg/kg/day PRAX-562 QD for 16 weeks or 0.5 mg/kg/day PRAX-562 QD for 12 weeks & matching placebo QD for 4 weeks. Participants in the PRAX-562/placebo arm will receive placebo for 4 consecutive weeks during the 16-week treatment period, with timing of placebo administration blinded for both participants and investigator. Dose adjustment is permitted to a max of 1.0 mg/kg/day and a min of 0.25 mg/kg/day.

PRAX-628

Focal Epilepsy

KEY UPCOMING MILESTONES

4Q 2023
Initiate Focal Epilepsy Study



Focal epilepsy affects ~2 million people in the US alone

Defined as epilepsy that originates in one side or area of the brain and affects one side of the body

Most common type of epilepsy in adults and children - occurs in 60% of epilepsy cases

~ 50% have family history but genetics is not well understood

Most common age of onset is in the first year of life and in the 6th and 7th decade

Preclinical and Phase 1 data demonstrate potential of PRAX-628 as best-in-class treatment for focal epilepsy

PRAX-628

FOCAL EPILEPSY

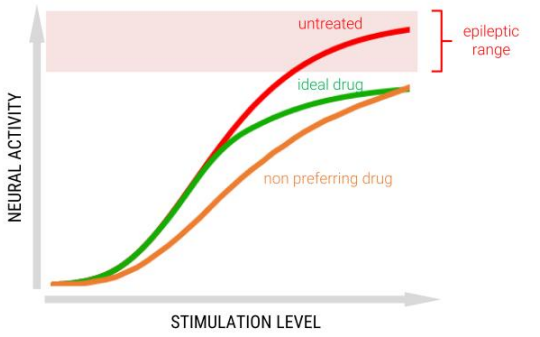
FUNCTIONALLY SELECTIVE

SMALL MOLECULE

- Superior selectivity for functional-state Na_V channel hyperexcitability
- Unprecedented therapeutic window could translate to superior safety and efficacy
- Favorable safety and tolerability profile across broad concentration range in healthy volunteers

Restoring physiological neural activity by precisely modulating biophysics

PREFERENTIAL ACTION AGAINST HYPEREXCITABILITY



BIOPHYSICAL "LEVERS" TO ACHIEVE PREFERENTIAL ACTION

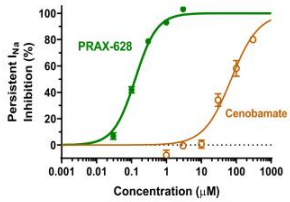
A. Reduce pro-excitatory channel function
   - Inhibit persistent current

B. Dynamic block of channels during high activity
   - Inhibit voltage dependent current
   - Inhibit use dependent current

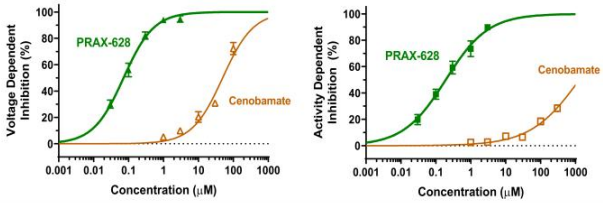
C. Maintain channel availability during low activity
   - Reduce potency against steady state peak current

PRAX-628 delivers improved potency and separation to tonic (toxic) inhibition

A. REDUCE PRO-EXCITATORY CHANNEL FUNCTION



B. DYNAMIC BLOCK OF CHANNELS DURING HIGH ACTIVITY



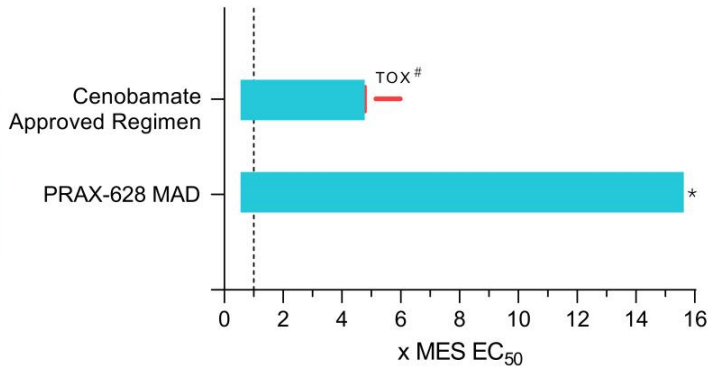
C. MAINTAIN CHANNEL AVAILABILITY DURING LOW ACTIVITY BY SPARING TONIC BLOCK INHIBITION

RATIO TO TONIC BLOCK (TOXIC ACTIVITY)

	PRAX-628	CENOBAMATE
Persistent I_{Na}	68	24
Voltage Dependent	121	35
Activity Dependent	44	1.3

Source: Praxis data on file

PRAX-628 was generally well-tolerated in humans at concentrations that provide a wider potential therapeutic range compared to Cenobamate



	Human Equivalent of Mouse MES EC_{50}, ng/mL
Cenobamate	9,600
PRAX-628	24

C_{max}: > 46,100 ng/mL, 400 mg C_{max} (Vernillet et al 2020)
* No limit due to toxicity was identified for PRAX-628 to date
x MES EC_{50} = multiple of predicted human EC_{50} based on the rodent MES model

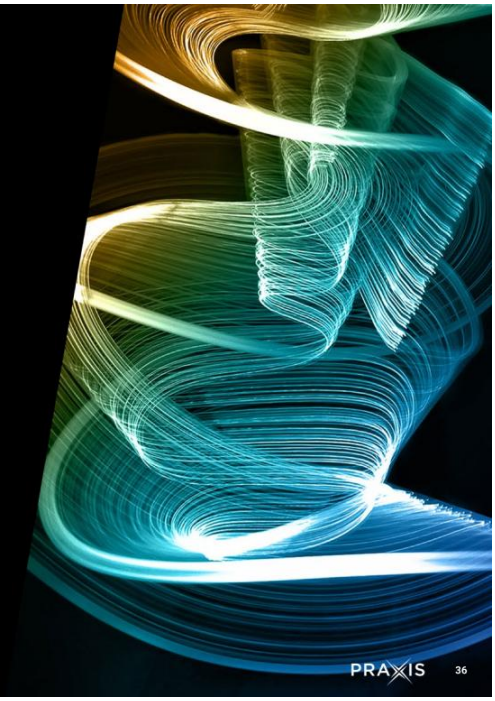

SOLIDUS™
ASO PLATFORM
PRAXIS
35

PRAX-222

SCN2A-GoF ASO

KEY UPCOMING MILESTONES

2H 2023
EMBRAVE Study First Dose Cohort (Part 1)
Topline Safety Results



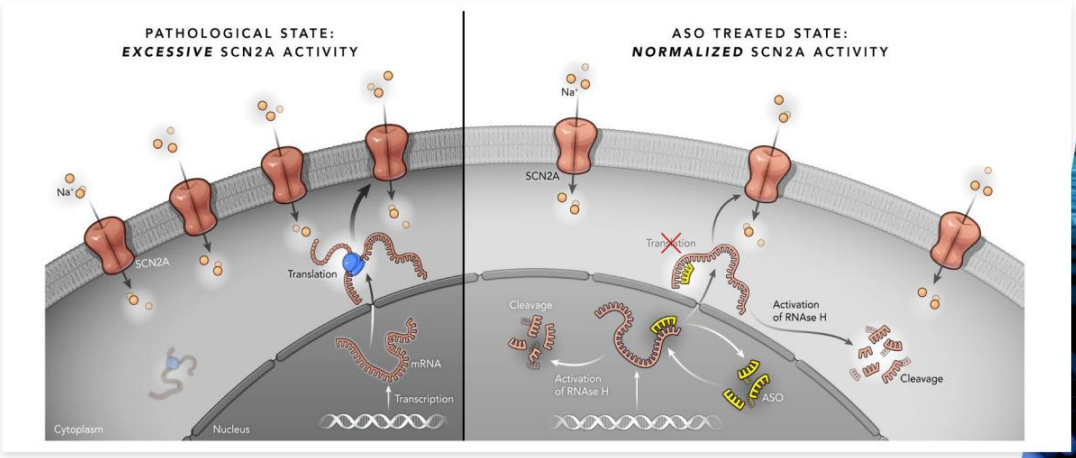
Preclinical data suggest PRAX-222 has potential to be disease-modifying for early onset SCN2A gain-of-function DEE

PRAX-222

INTRATHECALLY-ADMINISTERED ASO for SCN2A GoF DEE

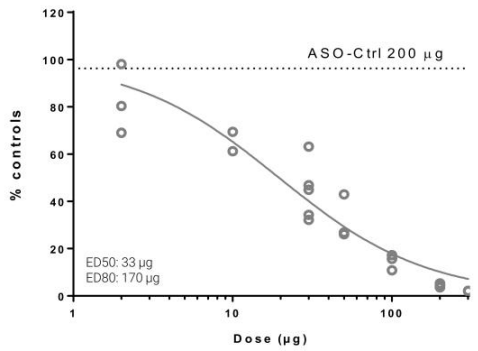
- Dose-dependent reduction in interictal spikes, seizures and increased survival
- Improvement in behavioral and locomotor activity
- Survival benefit extended with repeat dosing

PRAX-222 is an ASO designed to down-regulate SCN2A expression in patients with gain-of-function mutation

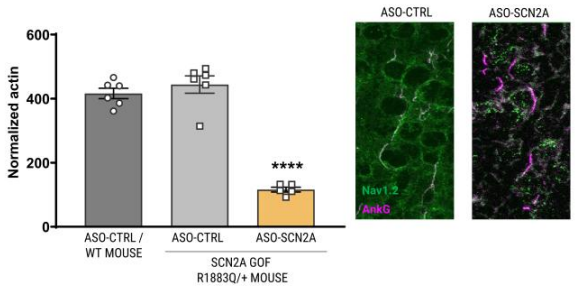


In vitro, PRAX-222 down-regulates both mRNA and protein

SCN2A mRNA KNOCKDOWN



SCN2A PROTEIN KNOCKDOWN

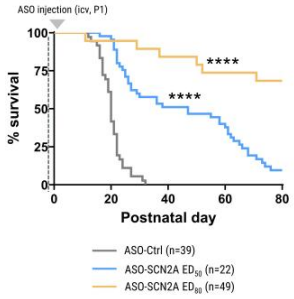


ASOs were administered at P30 and brains were collected 14 days post-ICV for qPCR analysis

PRAX-222 increases survival in SCN2A GoF mice

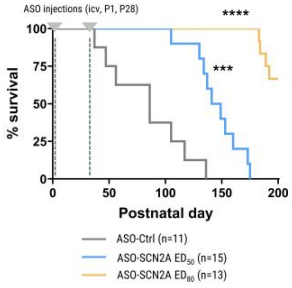
SCN2A ASO INCREASES SURVIVAL WITH A SINGLE DOSE INJECTION

SCN2A GOF model



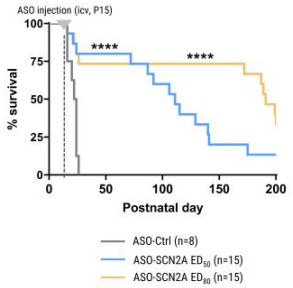
RE-DOSING SIGNIFICANTLY EXTENDS SURVIVAL

SCN2A GOF model



ADMINISTRATION POST-DISEASE ONSET ALSO EXTENDS SURVIVAL

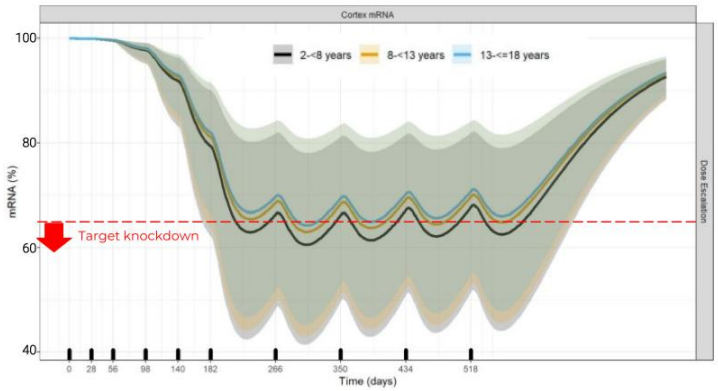
SCN2A GOF model



***p<0.001
****p<0.0001
All experiments conducted with SCN2A R1882Q mouse model

PRAXIS

PRAX-222 PK/PD modeling informs starting dose and proposed escalation based on level of knockdown anticipated to achieve clinical benefit and tolerability



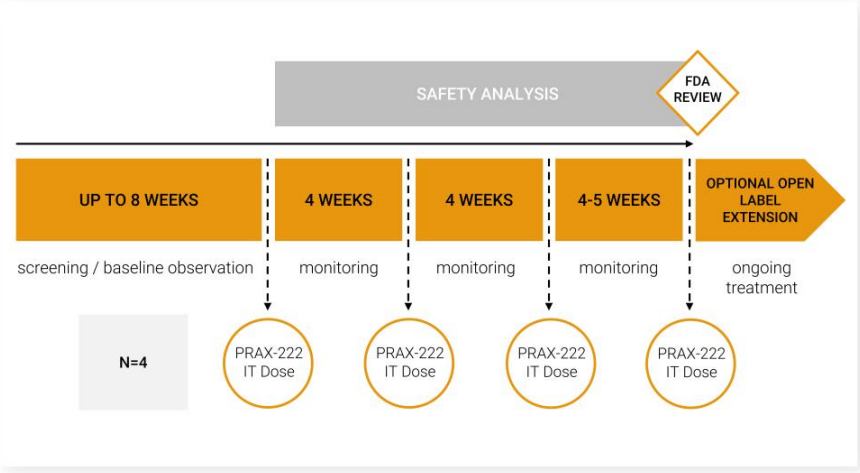
Median and 95% prediction interval illustrated

Simulated mRNA knockdown in human cortex in pediatric patients

Achieves distribution in key areas of brain based on NHP data

Source: Praxis data on file.

PRAX-222 EMBRAVE study initial dose cohort (Part 1) results expected 2H23



GOAL:
Assess preliminary safety of PRAX-222

21-week study

Open label design


PRAXIS
DARE FOR MORE™