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 13, 2024

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 13, 2024, Praxis Precision Medicines, Inc. (the "Company") announced its financial results for the quarter ended June 30, 2024. A copy of the press release containing these announcements is furnished as Exhibit 99.1 to this Current Report on Form 8-K (the "Current Report").

Item 7.01. Regulation FD Disclosure.

On August 13, 2024, 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.

The information in this Current Report under Items 2.02 and 7.01, including Exhibit 99.1 and Exhibit 99.2 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release, dated August 13, 2024
99.2	Praxis Precision Medicines, Inc. August 2024 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: August 13, 2024

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

Praxis Precision Medicines Provides Corporate Update and Reports Second Quarter 2024 Financial Results

Up to four programs in registrational phase by 2025

Planned interim analysis for ulixacaltamide Essential3 Study 1 to be conducted in Q4 2024

Topline results for Phase 2 EMBOLD study of relutrigine (PRAX-562) in SCN2A and SCN8A developmental and epileptic encephalopathies (DEEs) expected in Q3 2024

PRAX-628 Phase 2/3 POWER1 study to initiate in Q4 2024

Initiation of additional Phase 2 study (RADIANT) for PRAX-628 in focal and generalized epilepsy in 2H 2024, with topline results expected in 1H 2025

Cash and investments of $434 million as of June 30, 2024 maintains runway into 2027

BOSTON, August 13, 2024 — 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 2024.

“In the second quarter we continued to advance our entire portfolio, and we are poised to soon have up to four programs in registrational stage. The Essential3 program continues to progress well, with a pre-planned interim analysis of Study 1 to be conducted later this year. We remain on track for a successful topline readout enabling an NDA filing in 2025,” said Marcio Souza, president and chief executive officer of Praxis. “We look forward to sharing topline results of the EMBOLD study for relutrigine, formerly known as PRAX-562, in SCN2A and 8A patients later this quarter and believe these indications could be the tip of the iceberg for future application of PRAX-562 in other DEEs.”

Mr. Souza added, “we are also excited to build on the encouraging data generated to date with PRAX-628 by executing on the ENERGY program, a comprehensive set of studies, including a new Phase 2 Study (RADIANT), with topline data expected in the first half of 2025 in focal and generalized epilepsy. Additionally, with elsunersen having initiated the first arm of its global confirmatory study in Brazil, we anticipate the rapid advancement of all four clinical programs in our portfolio towards regulatory registrations. Our strong cash position, which fully funds Praxis through several important readouts into 2027, enables this momentum.”

Recent Highlights and Anticipated Milestones:

Cerebrum™ Small Molecule Platform

- **Ulixacaltamide for ET**: Topline results of two studies in the Essential3 Phase 3 program for ulixacaltamide are expected in the second half of 2024 to support a planned New Drug Application (NDA) submission in 2025.
  - Since beginning recruitment in November 2023, there have been over 75,000 pre-screening forms, of which 11,000 referrals meet pre-qualifying eligibility criteria.
  - Praxis to conduct an interim analysis for Study 1 in the Essential3 program in the fourth quarter of 2024. This pre-planned analysis is part of the original Statistical Plan and Protocol for Essential3.
  - Long-term safety study enrollment criteria have been expanded to include patients who participated in previous ET studies, including previous suvecaltamide trials.
- **PRAX-628 for Epilepsy:** Praxis expects to initiate four studies as part of the PRAX-628 ENERGY program, aiming to generate efficacy, safety and pharmacokinetics (PK) data to serve as the basis of regulatory registrations globally.
  - EMPOWER is an observational study in partnership with the Epilepsy Consortium expected to start in the third quarter of 2024, aiming to enroll patients with epilepsy to better characterize seizure burden

- RADIANT is a Phase 2 PK, safety and efficacy study in patients with focal onset seizures (FOS) or generalized epilepsy expected to start in the second half of 2024, with topline results in the first half of 2025
- POWER1 and POWER2 are 12-week Phase 2/3 studies in patients with FOS aiming to show efficacy of PRAX-628. POWER1 is expected to start enrolling patients in the fourth quarter of 2024, with topline results in the second half of 2025. POWER2 is expected to start enrolling patients in the first half of 2025.

- **Relutrigine (PRAX-562) for SCN2A and SCN8A DEEs:** Praxis expects topline results from the Phase 2 EMBOLD study for the treatment of pediatric patients with DEEs in the third quarter of 2024.
  - The EMBOLD study is a Phase 2 study evaluating the safety, tolerability, efficacy (motor seizure frequency) and PK of relutrigine in pediatric patients aged 2 to 18 years with DEEs, followed by an open-label extension.
  - Based on results for the EMBOLD study, Praxis expects to consider a more expansive program of relutrigine in all DEEs with high seizure burden.

Solidus™ Antisense Oligonucleotide (ASO) Platform

- **Elsunersen (PRAX-222) for early-seizure-onset SCN2A Developmental Epilepsies**
  - First arm of the global confirmatory study initiated in Brazil
  - Pivotal phase of the program remains on track, and Praxis plans to advance the program within the US and expand to Europe later in 2024.

Second Quarter 2024 Financial Results:

As of June 30, 2024, Praxis had $433.8 million in cash, cash equivalents, and marketable securities, compared to $81.3 million in cash and cash equivalents as of December 31, 2023. The increase of $352.5 million is primarily due to net proceeds from Praxis' January 2024 and April 2024 follow-on public offerings plus net proceeds from at-the-market sales of common stock, offset by cash used in operating activities.

Praxis recognized $0.4 million in collaboration revenue during the three months ended June 30, 2024, compared to $0.8 million during the three months ended June 30, 2023. The decrease of $0.4 million is associated with a decrease in revenue recorded under the UCB Collaboration Agreement.

Research and development expenses were $27.3 million for the three months ended June 30, 2024, compared to $25.6 million for the three months ended June 30, 2023. The increase in research and development expenses of $1.6 million was primarily attributable to an increase of $8.1 million in Praxis' Cerebrum™ platform and a $1.7 million increase in personnel-related costs, primarily offset by a $8.2 million decrease in costs associated with Praxis' Solidus™ platform. General and administrative expenses were $10.6 million for the three months ended June 30, 2024, compared to $10.1 million for the three months ended June 30, 2023. The increase in general and administrative expenses of approximately $0.5 million was primarily due to increased personnel-related costs.

Praxis reported a net loss of $32.7 million for the three months ended June 30, 2024, including $5.9 million of stock-based compensation expense, compared to $34.3 million for the three months ended June 30, 2023, including $5.8 million of stock-based compensation.

As of June 30, 2024, Praxis had 17.8 million shares of common stock outstanding.

Conference Call

Praxis Precision Medicines will host a conference call and webcast today at 8:00 a.m. ET to review the second quarter 2024 financial results and recent business highlights. Individuals may register for the conference call by clicking the registration link. Once registered, participants will receive dial-in details and a unique PIN which will allow them to access the call. An audio webcast will be accessible through the Investor Relations section of the company's website at www.praxismedicines.com. Following the live webcast, an archived replay will also be available.

About Ulixacaltamide

Ulixacaltamide is a differentiated and highly selective small molecule inhibitor of T-type calcium channels designed to block abnormal neuronal burst firing in the Cerebello-Thalamo-Cortical (CTC) circuit correlated with tremor activity. Ulixacaltamide, the most advanced program within Praxis' Cerebrum™ small molecule platform, is currently in late-stage development for the treatment of essential tremor, www.praxisessentialtremor.com.

About PRAX-628

PRAX-628 is a next-generation, functionally selective small molecule targeting the hyperexcitable state of sodium-channels in the brain that is currently being developed as a once daily, oral treatment for adult focal onset epilepsy. Preclinical data demonstrates PRAX-628 is differentiated from standard of care, with the potential to be best-in-class for focal epilepsy. In vitro, PRAX-628 has demonstrated superior selectivity for disease-state Na_V channel hyperexcitability. In vivo studies of PRAX-628 have demonstrated unprecedented potency in the maximal electroshock seizure (MES) model, a highly predictive translational model for efficacy in focal epilepsy. Data from the PRAX-628-101 study demonstrated that PRAX-628 can be safely dosed in healthy subjects to greater than 15 times the predicted human equivalent of the rodent MES EC50.

About Elsunersen (PRAX-222)

Elsunersen is an antisense oligonucleotide (ASO) designed to selectively decrease SCN2A gene expression, directly targeting the underlying cause of early-seizure-onset SCN2A-DEE to treat seizures and other symptoms in patients with gain-of-function SCN2A mutations. In vitro studies of elsunersen have demonstrated reduction in both SCN2A gene expression and protein levels. In vivo, elsunersen has demonstrated significant, dose-dependent reduction in seizures, improvement in behavioral and locomotor activity and increased survival in SCN2A mouse models, with potential to be the first disease-modifying treatment for SCN2A-DEE. Elsunersen has received Orphan Drug Designation (ODD) and Rare Pediatric Disease Designation (RPD) from the FDA, and ODD and PRIME designations from the European Medicines Agency (EMA) for the treatment of SCN2A-DEE. The Elsunersen program is ongoing under a collaboration with Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), and RogCon, Inc. To learn more about the EMBRAVE study, please visit https://www.embravestudy.com/.

About Relutrigine (PRAX-562)

Relutrigine is a first-in-class small molecule in development for the treatment of developmental and epileptic encephalopathy (DEE) as a preferential inhibitor of persistent sodium current, shown to be a key driver of seizure symptoms in early onset SCN2A-DEE and SCN8A-DEE. Relutrigine's mechanism of sodium channel blocking is consistent with superior selectivity for disease state sodium channel (NaV) channel hyperexcitability. In vivo studies of relutrigine have demonstrated dose-dependent inhibition of seizures up to complete control of seizure activity in SCN2A, SCN8A and other DEE mouse models. Relutrigine has been generally well-tolerated in three Phase 1 studies and has demonstrated biomarker changes indicative of NaV channel blocking effects. Relutrigine has received ODD and RPD from the FDA, and ODD from the European Medicines Agency for the treatment of SCN2A-DEE and SCN8A-DEE. To learn more about the EMBOLD study, please visit https://www.emboldstudy.org/.

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/X.

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, the development of our product candidates, the anticipated timing of regulatory submissions and interactions and our projected cash runway, 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; preliminary analyses from ongoing studies differing materially from final data from preclinical studies and completed clinical trials; the expected timing of clinical trials, data readouts and the results thereof, and submissions for regulatory approval or review by governmental authorities; regulatory approvals to conduct trials; and other risks concerning Praxis’ programs and operations as described in its Annual Report on Form 10-K for the year ended December 31, 2023 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.

Investor Contact:
Praxis Precision Medicines
investors@praxismedicines.com
857-702-9452

Media Contact:
Dan Ferry
Life Science Advisors
Daniel@lifesciadvisors.com
617-430-7576

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

	June 30, 2024	December 31, 2023
Assets		
Cash and cash equivalents	$ 145,143	$ 81,300
Marketable securities	288,688	—
Prepaid expenses and other current assets	4,837	3,580
Property and equipment, net	369	588
Operating lease right-of-use assets	1,610	2,064
Other non-current assets	416	416
Total assets	$ 441,063	$ 87,948
Liabilities and stockholders' equity		
Accounts payable	$ 8,195	$ 5,815
Accrued expenses	10,058	7,416
Operating lease liabilities	1,946	2,495
Deferred revenue	1,764	2,553
Common stock	14	13
Additional paid-in capital	1,145,308	723,577
Accumulated other comprehensive loss	(71)	—
Accumulated deficit	(726,151)	(653,921)
Total liabilities and stockholders' equity	$ 441,063	$ 87,948

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,	
	2024	**2023**	**2024**	**2023**
Collaboration revenue	$ 357	$ 781	$ 788	$ 1,464
Operating expenses:				
Research and development	27,260	25,614	54,244	51,118
General and administrative	10,585	10,127	25,918	23,397
Total operating expenses	37,845	35,741	80,162	74,515
Loss from operations	(37,488)	(34,960)	(79,374)	(73,051)
Other income:				
Other income, net	4,811	648	7,144	1,284
Total other income	4,811	648	7,144	1,284
Net loss	$ (32,677)	$ (34,312)	$ (72,230)	$ (71,767)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.74)	$ (7.38)	$ (4.41)	$ (17.51)
Weighted average common shares outstanding, basic and diluted	18,824,479	4,649,371	16,364,421	4,097,833

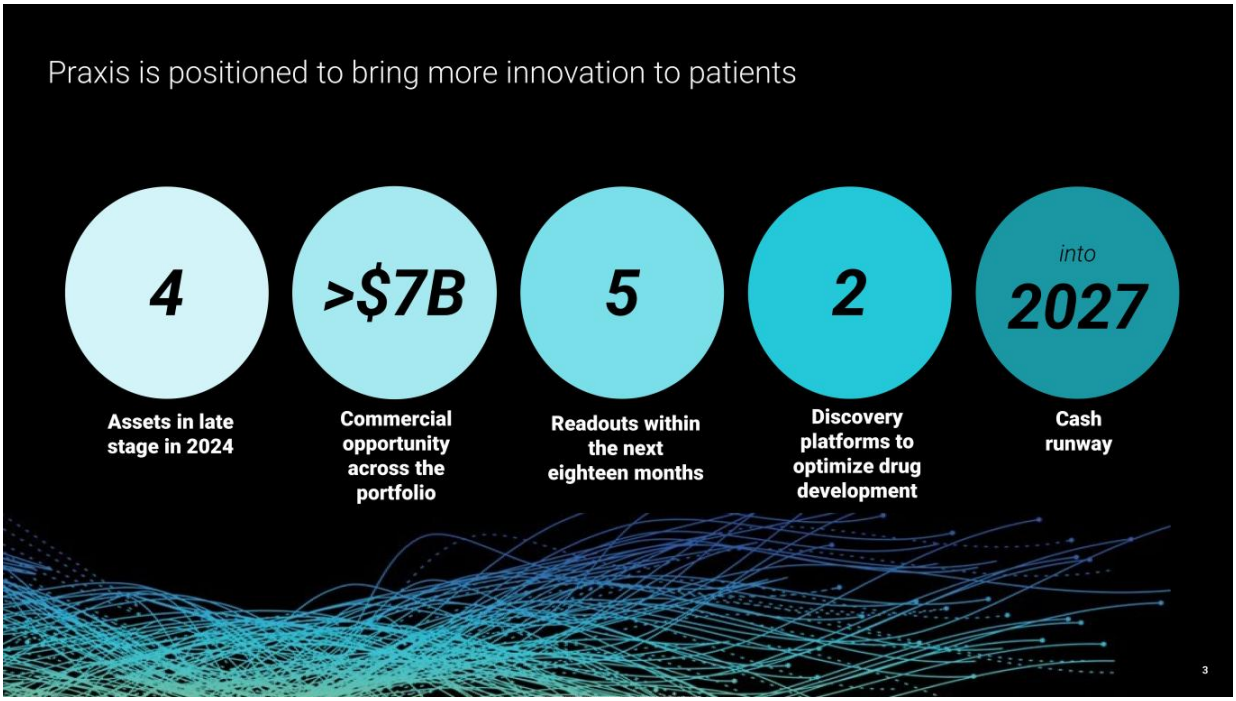

PRAXIS
DARE FOR MORE®
CORPORATE OVERVIEW
August 2024

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, statements regarding the estimated market for our product candidates, if approved, our development plans, our preclinical and clinical results and other future conditions, including our cash runway, and the safety, efficacy, and regulatory and clinical design or progress, potential regulatory submissions, approvals and timing thereof of any of our product candidates. 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) the timing of and 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 collaboration partners' abilities to manufacture our product candidates and scale production, (viii) our ability to meet any specific milestones set forth herein, and (ix) the potential addressable market sizes for product candidates. 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, 2023 filed with the Securities and Exchange Commission ("SEC") and our other filings with the SEC.

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.


Praxis is positioned to bring more innovation to patients
4
Assets in late stage in 2024
>$7B
Commercial opportunity across the portfolio
5
Readouts within the next eighteen months
2
Discovery platforms to optimize drug development
into
2027
Cash runway
3

Four pillars guide how we develop medicines

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 applying an agile way of working

PATIENT-GUIDED

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

Two platforms to generate optimized therapies for defined patient populations

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

Molecule	Indication	Mechanism
ulixacaltamide	Essential Tremor	T-type calcium channel modulator
PRAX-628	Focal Onset Seizures & Generalized Epilepsy	Sodium channel functional state modulator for broad use
relutrigine	DEE Epilepsies	Sodium channel functional state modulator for pediatric use
PRAX-020*	KCNT1 Epilepsy	KCNT1 specific inhibitor
PRAX-050	Not disclosed	Not disclosed

SOLIDUS™

ANTISENSE OLIGONUCLEOTIDE (ASO) PLATFORM

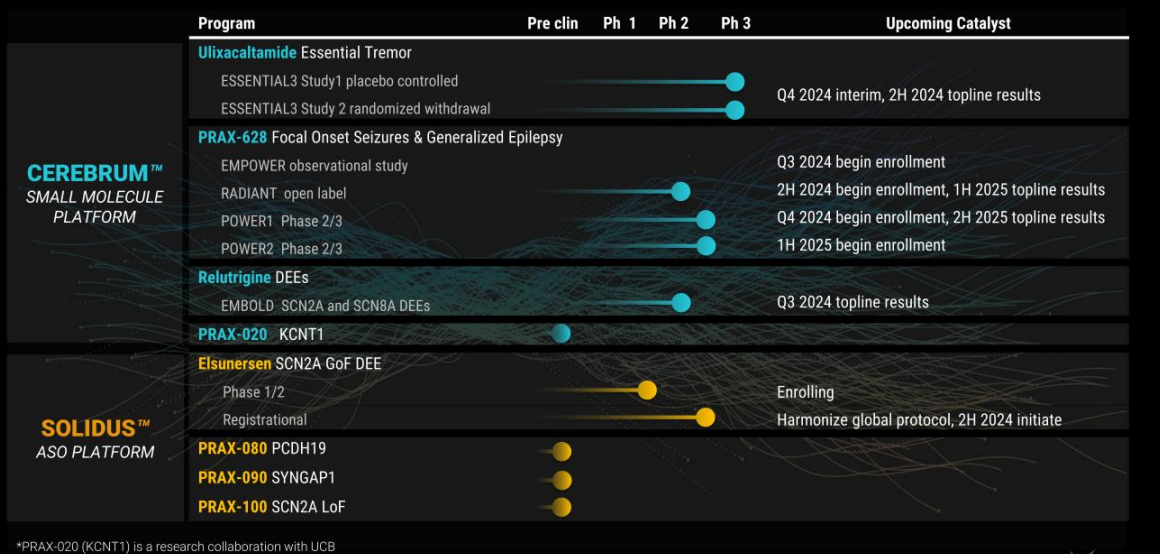
Solidus™ is an efficient, targeted precision medicine discovery and development engine for ASOs anchored on proprietary, computational methodology

Molecule	Indication	Mechanism
elsunersen	SCN2A GoF	Gapmer ASO
PRAX-080**†	PCDH19 Mosaic expression	Gapmer ASO
PRAX-090**†	SYNGAP1 LoF	Splice switching ASO
PRAX-100**†	SCN2A LoF	Splice switching ASO

*PRAX-020 (KCNT1) is a research collaboration with UCB

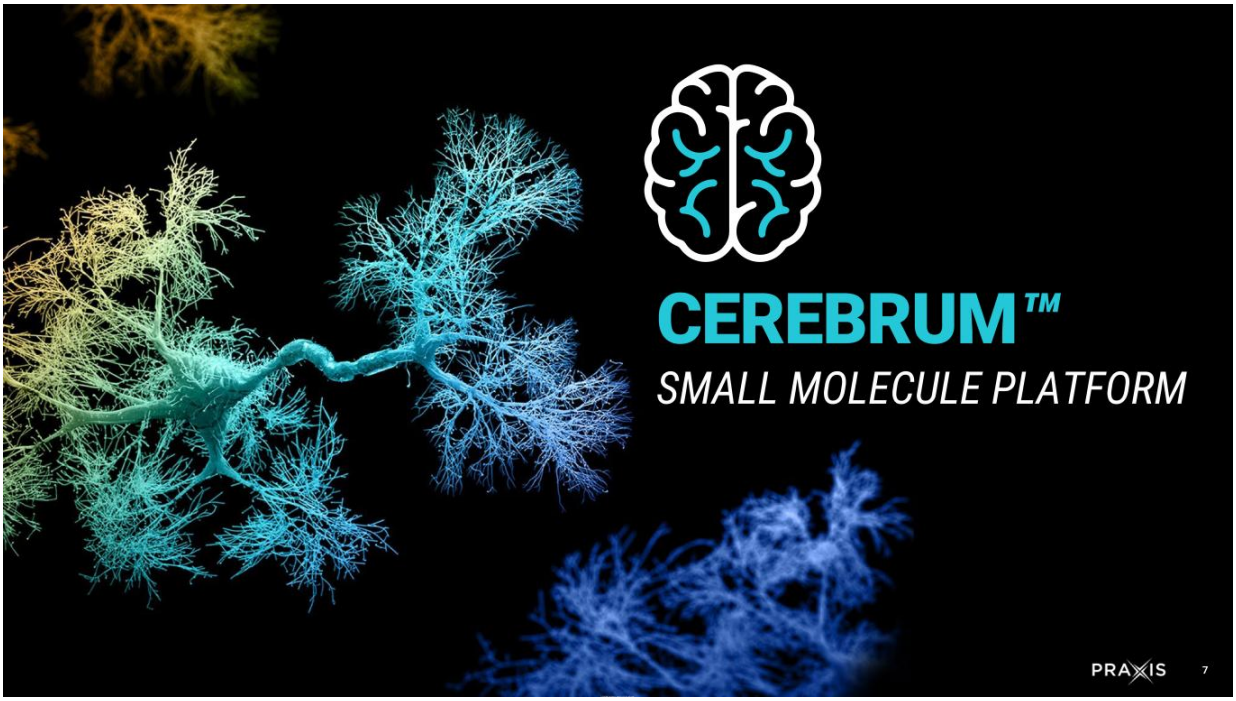
†PRAX-080 (PCDH19), PRAX-090 (SYNGAP1) & PRAX-100 (SCN2A-LoF) ASOs are a collaboration with The Florey Institute of Neuroscience and Mental Health

Four clinical stage assets and multitude of early-stage programs



*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


CEREBRUM™
SMALL MOLECULE PLATFORM
PRAXIS
7

Ulixacaltamide

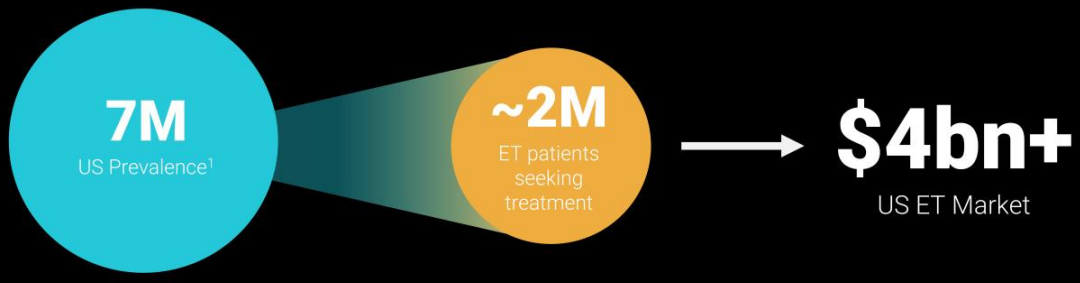
Milestones

Q4 2024: Interim analysis of Essential3 Study 1

2H 2024: Topline results for Essential 3

2025: NDA filling

Essential tremor market is significantly underserved and ready for disruption



- Essential Tremor (ET) is the most prevalent movement disorder
- People with ET experience significant disturbance of their daily activities
- Hallmark feature of ET 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]

Vast majority of patients are left without any treatment option

- <30% of patients are eligible to receive propranolol due to other medications/health conditions
- Of those who start propranolol >50% discontinue after only 1 month
- Of those who start propranolol <20% still receive propranolol after 2 years

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

Modified Activities of Daily Living 11 (mADL11) as Primary Endpoint

11 items from the well-established TETRAS ADL scale

Each item is individually scored, up to a total of 33

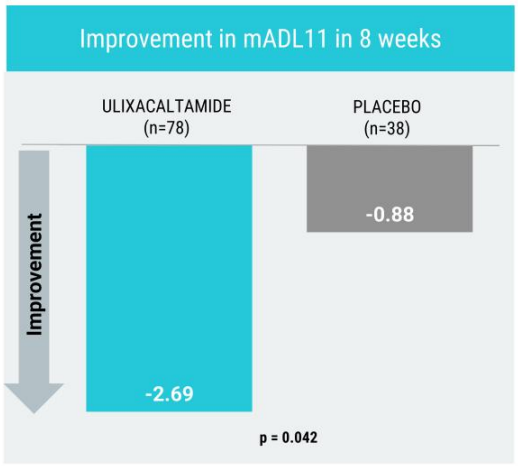
0 = Slightly abnormal. Tremor is present but does not interfere with __.
1 = Mildly abnormal. Spills a little.
2 = Moderately abnormal. Spills a lot or changes strategy to complete task.
3 = Severely abnormal. Cannot drink from a glass or uses straw or sippy cup.

Each point reduction provides benefit to a patient

- Improvement based on regaining function
- ADL assessment performed by a physician
- Aligned with FDA as primary endpoint for Essential3 studies

TETRAS = TRG Essential Tremor Rating Assessment Scale; ADL = Activities of Daily Living

Essential1 Phase 2b study set foundation for the Essential3 Phase 3 program



Validated the clinical hypothesis

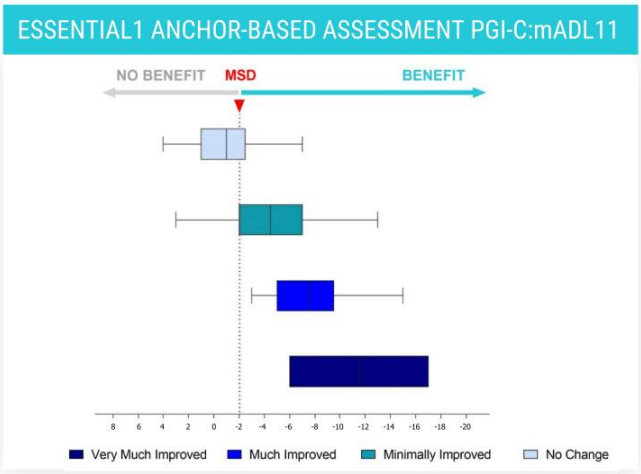
- Strong efficacy signal with robust endpoint (mADL11)
  - Early clinical benefit in 8-Week Study
  - Long-term, durable benefit
- Well-tolerated with a differentiated safety profile
- Tested Phase 3 design concepts

Sets up a clear path to registration

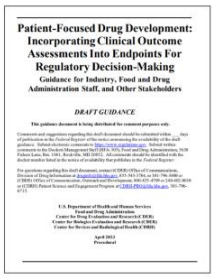
- Alignment with FDA on dose and primary endpoint
- Phase 3 program design structured around patient needs
- Robust recruitment strategy

Results from Essential1 study, p value is nominal

Using Essential1 to define clinical meaningfulness in essential tremor



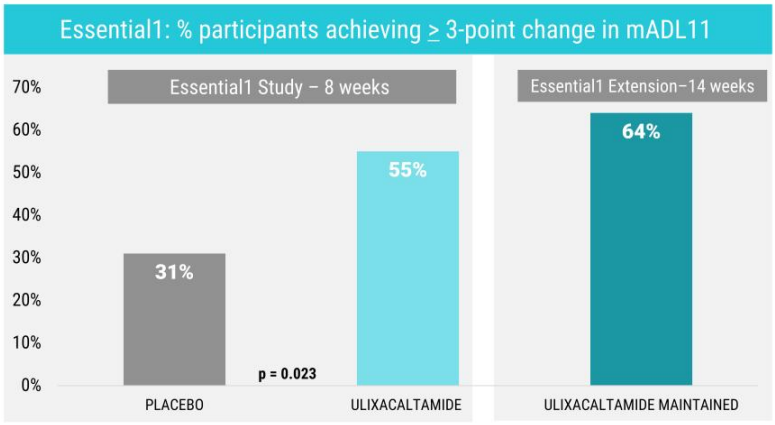
- Patient response on mADL11 endpoint was well-correlated to PGI-C response
- Aligned with recently issued guidance from Clinical Outcomes Assessment for novel endpoints


Patient-Focused Drug Development: Incorporating Clinical Outcome Assessments Into Endpoints For Regulatory Decision-Making
Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders
DRAFT GUIDANCE
This guidance document is being distributed for comment purposes only.

MSD=Meaningful Score Difference, PGI-C = Patient Global Impression of Change

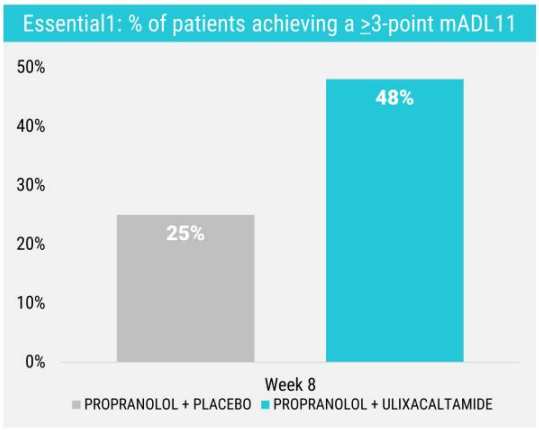
Majority of patients achieved at least a 3-point change in mADL11 at 8 weeks

Durable response in extension study patients who continued through 14 weeks



Results from Essential1 study measuring participants achieving meaningful change at 8 and 14 weeks based on ≥3-point improvement from baseline
https://praxismedicines.com/wp-content/uploads/2023/09/Giroux_MDS2023_E1_MSD_SUBMIT.pdf

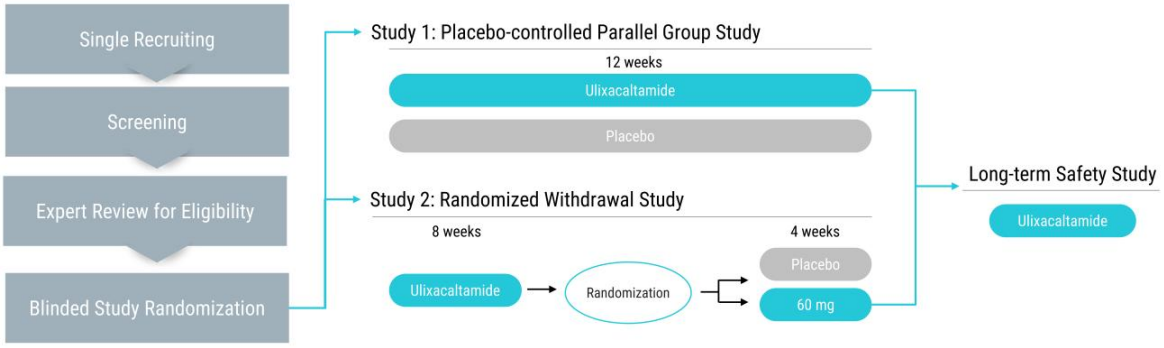
Adding ulixacaltamide benefited more patients on propranolol with ≥ 3-point improvement



Among patients who could tolerate propranolol, adding ulixacaltamide led to ~2-fold increase in the proportion achieving at least a 3-point improvement in mADL11

Results from Essential1 study showing % of participants on stable propranolol dose achieving meaningful change at 8 weeks based on a meaningful score difference of ≥3 points

Essential3: An innovative Phase 3 program that optimizes all aspects of study conduct



ESSENTIAL 3
AN AT-HOME RESEARCH STUDY

Essential3 Program is well powered

Study	Study 1 – Parallel Design	Study 2 – Randomized Withdrawal
Participants	400	200
Primary endpoint and power	mADL11 Change from Baseline to Week 12 between ulixacaltamide and placebo **90% power to detect difference**	Difference in maintenance of response rate during the 4-week RW period between ulixacaltamide and placebo **90% power to detect difference**
Stratification	Intention tremor status, family history, and propranolol use	
Main Secondary endpoints	○ TETRAS-ADL ○ CGI ○ PGI	

ESSENTIAL 3
AN AT-HOME RESEARCH STUDY

CGI = Clinical Global Impression (Severity); PGI = Patient Global Impression (Severity and Change)

Path to success

De-risked
Trial design based on key learnings from Essential1
Regulatory alignment based on successful End-of-Phase 2 meeting

Efficient
Focused execution
Single protocol: Optimized screening, enrollment, analysis

Interim Analysis
Increases optionality, including potential for sample size re-estimation

Streamlined Design
Decentralized study to expand reach and reduce study burden to participants

Patient-driven Approach
mADL11 as a clinically meaningful primary endpoint

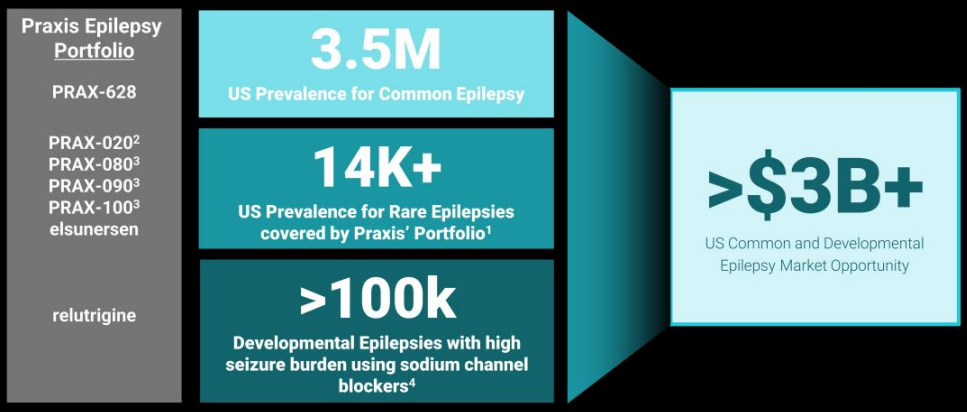
NDA Readiness
Clear path to filing in 2025

PRAX-628

Milestones

Q3 2024: Begin enrolling EMPOWER observational study
2H 2024: Begin enrolling RADIANT open label study
Q4 2024: Begin enrolling POWER1 registrational study
1H 2025: Begin enrolling POWER2 registrational study
1H 2025: Topline results for RADIANT
2H 2025: Topline results for POWER1

The Praxis epilepsy portfolio targets significant unmet need in both the common and rare epilepsy markets



[1] SCN2A Gof, SCN2A LoF, SYNGAP1, PCDH19, SCN8A, KCNT1
[2] PRAX-020 (KCNT1) is a research collaboration with UCB
[3] PRAX-080 (PCDH19), PRAX-090 (SYNGAP1) & PRAX-100 (SCN2A-LoF) ASOs are a collaboration with The Florey Institute of Neuroscience and Mental Health
[4] Poke G, Stanley J, Scheffer IE, Sadleir LG. Epidemiology of Developmental and Epileptic Encephalopathy and of Intellectual Disability and Epilepsy in Children

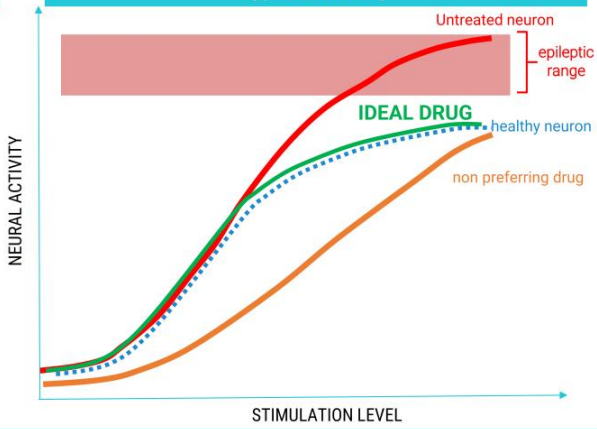
PRAX-628: Precision medicine therapeutic for focal onset seizures and generalized epilepsy

Differentiated Profile

Next generation, functionally selective small molecule targeting the hyperexcitable states of sodium channels in the brain, with the potential to address limitations of current treatments

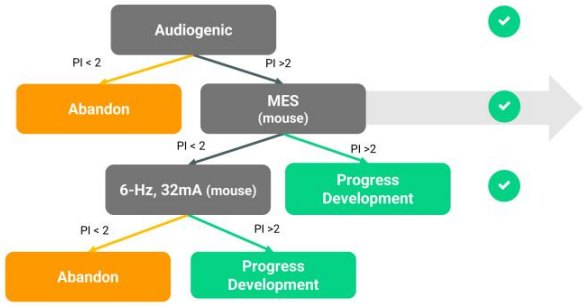
- Ideal safety/tolerability profile
- Achieves brain penetration
- Rapidly achieves therapeutic concentrations without titration
- Favorable half-life and PK profile
- Optimized efficacy

Goal: Preferential action against neuronal hyperexcitability



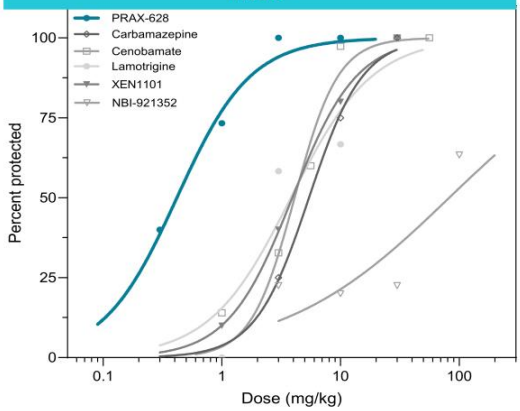
PRAX-628 shows a differentiated pre-clinical profile

Preclinical decision tree optimized for focal seizure drug discovery[1]



PRAX-628 Results[2]

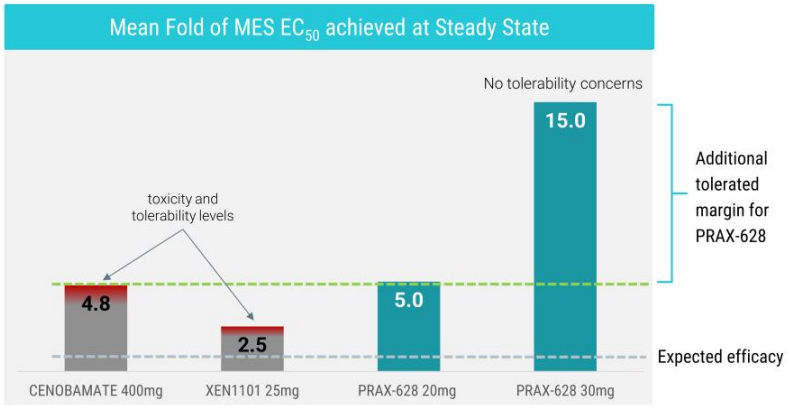
PRAX-628 has differentiated potency in the MES model[3]



Protective index (PI) measured as tolerability / efficacy (TD50 / ED50); MES = maximal electroshock seizure
1. https://praxismedicines.com/wp-content/uploads/2023/12/Anderson_AES2023_Predictive-Validity_Poster_Final.pdf; 2. Praxis data on file
3. https://praxismedicines.com/wp-content/uploads/2023/12/Kahlig_AES2023_628-In-Vivo_Poster_Final.pdf

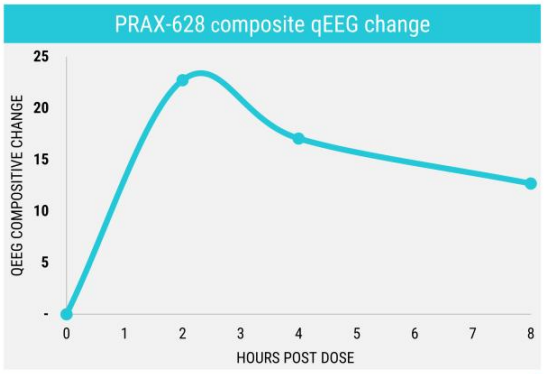
Ability to significantly exceed therapeutic concentrations while well tolerated

PRAX-628 has unprecedented margins over best-in-class ASMs based on MES efficacy and clinical tolerability in humans

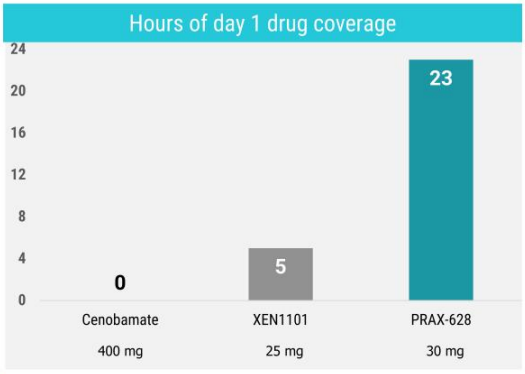


Source: Praxis data on file (Ph1 study), Cenobamate Cmax: >46,100 ng/mL, 400 mg Cmax (Vernillet et al 2020), XEN1101 Cmax: >107 ng/mL (Phase 1 data)
x MES EC50 = multiple of predicted human EC50 based on the rodent MES model; IEC2023_628-SAD-MAD

Phase 1 study demonstrated brain activity and rapid achievement of therapeutic concentrations



- Composite endpoint from qEEG showed separation of drug versus placebo in the SAD and MAD cohorts
- Difference between PRAX-628 and placebo significant for all doses at first point measured
- Effect consistent with known PK profile



- PRAX-628 achieves nearly complete coverage on Day 1

The Phase 2 PRAX-628 Photo Paroxysmal Response (PPR) study demonstrated proof of concept; de-risks advancing to studies in focal and generalized epilepsy

Study Results

- 100% response in treated patients
- PRAX-628 achieved between 3-13x multiples of MES EC_{50} exposure
- Safety was consistent with prior dose escalation study and AEs were mild

- Patients must demonstrate PPR response during screening and baseline to be evaluable
- Response Assessment
  - **Partial:** Reduction, other than to zero, in the number of generalized PPR events at any assessment period vs baseline
  - **Complete:** Reduction to zero in the number of generalized PPR events at any assessment period vs baseline
- Safety monitored and PK samples collected during observation period

Dose	Categorical Response	Response Rate
15 mg	None	0% (0/5)
	Partial	20% (1/5)
	Complete	80% (4/5)
45 mg	None	0% (0/3)
	Complete	100% (3/3)
Evaluable Response		**100% (8/8)**

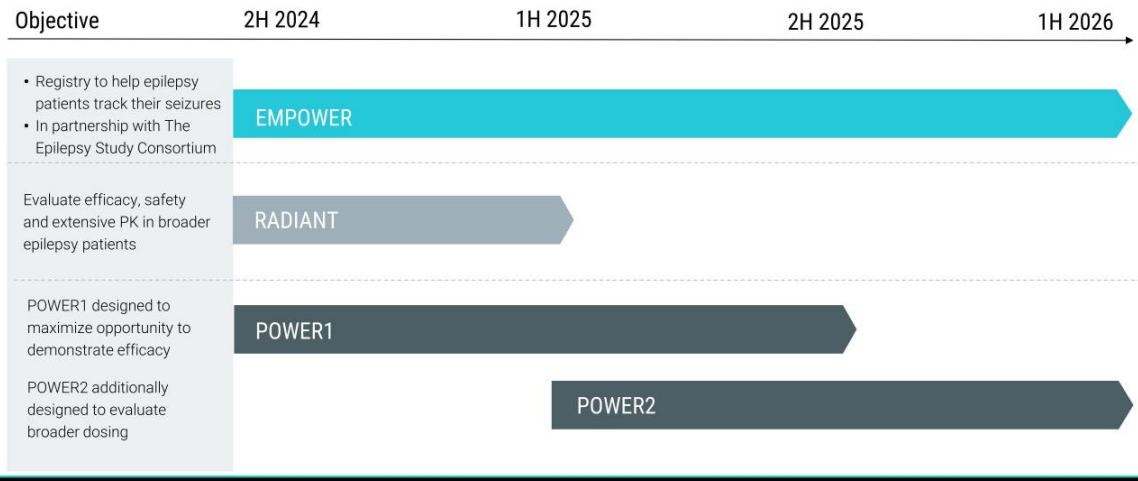
PRAX-628 presents an ideal precision ASM profile

- Significantly more potent than competitive molecules in highly translatable pre-clinical models
- Rapidly achieves therapeutic concentrations after once-daily dose
- Ability to significantly exceed therapeutic concentrations while well tolerated
- Proof of concept achieved in epilepsy patients

Initiate three efficacy trials in the ENERGY program

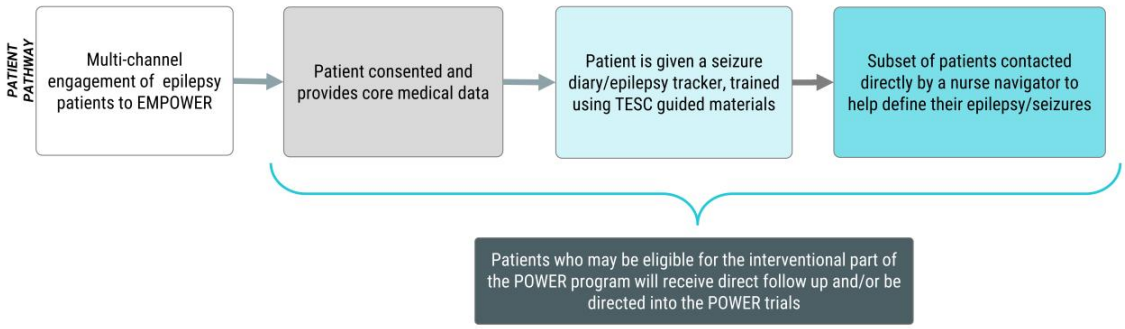
https://praxismedicines.com/wp-content/uploads/2023/12/Kahlig_AES2023_628-In-Vivo_Poster_Final.pdf
https://praxismedicines.com/wp-content/uploads/2023/09/IEC2023_628-SAD-MAD.pdf

PRAX-628 ENERGY program to demonstrate efficacy and bring an improved therapy to focal and generalized epilepsy patients

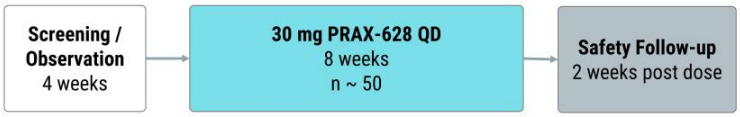


EMPOWER Observational Study to better understand patient journey

In partnership with The Epilepsy Study Consortium (TESC)



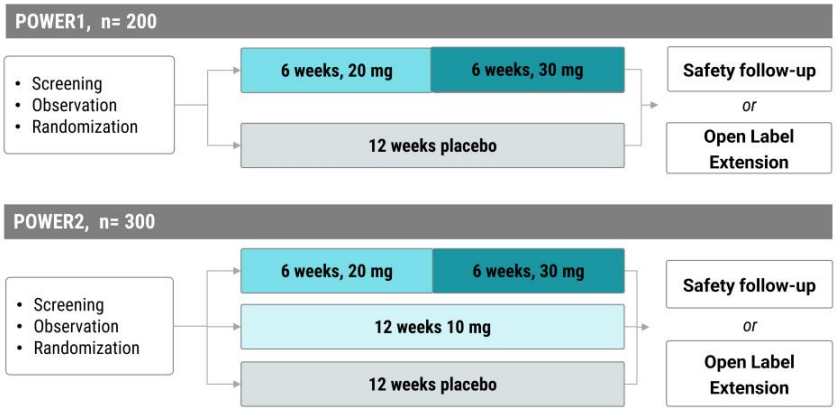
RADIANT Phase 2 open label study to evaluate safety and efficacy in focal onset or generalized epileptic seizures



- Measuring seizure frequency, seizure freedom, safety and pharmacokinetics
- Will allow the evaluation of PRAX-628 in a broader population, including generalized epilepsy
- Initiate in 2H 2024 with topline results in 1H 2025

QD = Once daily

Proposed study designs for POWER1 and POWER2



- POWER1 to initiate Q4 2024 with topline readout 2H 2025
- POWER2 to initiate in 1H 2025

Relutrigine (PRAX-562)

Milestones

Q3 2024: Topline results in Phase 2 EMBOLD Study

Preclinical and emerging clinical data demonstrate relutrigine has the potential to be a first- and best-in-class small molecule for DEEs

RELUTRIGINE

SCN2A, SCN8A

FORMULATED FOR PEDIATRIC USE

SMALL MOLECULE

FUNCTIONAL STATE MODULATOR

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

Relutrigine Phase 1 summary

Relutrigine has been generally well tolerated in over 130 healthy volunteers

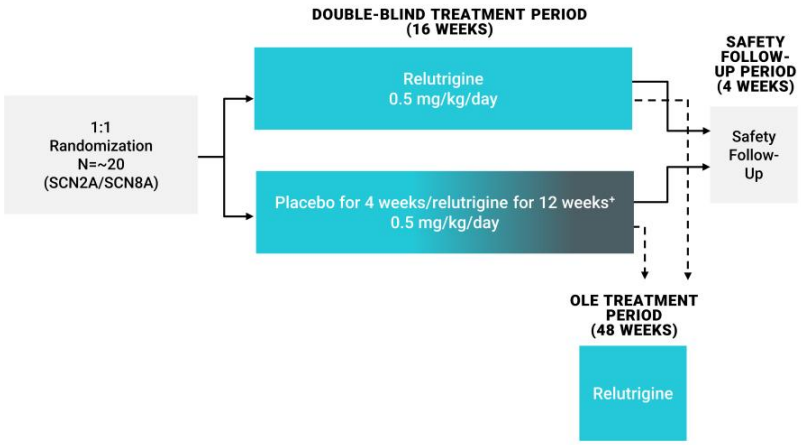
All TEAEs mild to moderate as stand-alone therapy*, with headache & dizziness most common TEAEs

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

Significant changes observed between placebo and relutrigine on qEEG 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 relutrigine and oxcarbazepine led to additive sodium blocking effects, including resulting in SAEs

Relutrigine Phase 2 EMBOLD study topline data expected in Q3 2024



PRIMARY ENDPOINT:

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

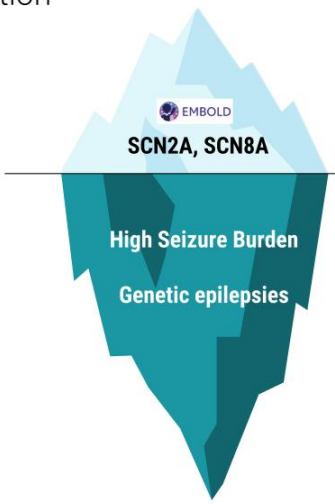
KEY SECONDARY:

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

EMBOLD

+ Participants receive either 0.5 mg/kg/day relutrigine QD for 16 weeks or 0.5 mg/kg/day relutrigine QD for 12 weeks & matching placebo QD for 4 weeks. Participants in the relutrigine/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.

EMBOLD is the tip of the iceberg for the potential of relutrigine in broader DEE population



EMBOLD study

Potential future development

Many DEEs already use sodium channel blockers

Broad applicability for relutrigine in genetic driver with high seizure burden

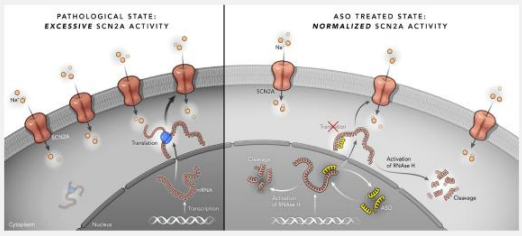
>100k patients


Elsunersen (PRAX-222)
SOLIDUS™ ASO PLATFORM
PRAXIS
35

Elsunersen specifically designed for SCN2A GoF patients

DISEASE OVERVIEW

- Epilepsy and developmental impairment before the age of 16 years occurs in 1 in 340 children
- The majority of these cases result from sporadic de novo genetic variation
- In both de novo and familial forms of epilepsy some 900 genes have been identified
- Many of these genes also represent opportunities for intervention in other neurological disorders
- Patients with SCN2A-DEE have a debilitating and ultimately fatal trajectory
- Affects approximately 1,500 patients in the US

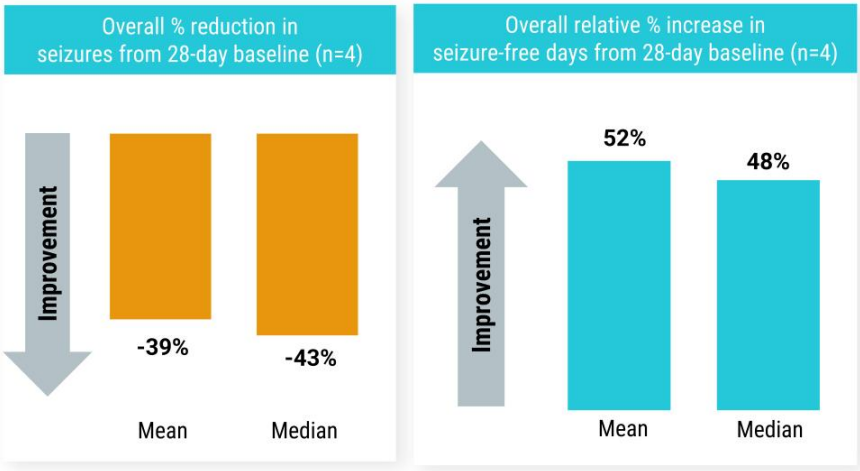


RESEARCH APPROACH

Modifying gene expression to address both gain and loss of function disorders is achieved through various ASO modalities to either silence harmful genes or enhance expression of reduced function or missing genes

Significant reduction in seizures observed for SCN2A patients

EMBRAVE



- No TEAEs or SAEs considered related to study drug
- All TEAEs recovered/resolved

Data from Part 1 of EMBRAVE Study, https://praxismedicines.com/wp-content/uploads/2023/12/Frizzo_AES2023_EMBRAVE_Poster_Final.pdf


PRAXIS
DARE FOR MORE®