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): November 9, 2022

PRAXIS PRECISION MEDICINES, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-39620**	**47-5195942**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

Praxis Precision Medicines, Inc.
99 High Street, 30th Floor
Boston, Massachusetts 02110
(Address of principal executive offices, including zip code)

(617) 300-8460
(Registrant's telephone number, including area code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trade Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	**PRAX**	**The Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02. Results of Operations and Financial Condition.

On November 9, 2022, Praxis Precision Medicines, Inc. (the "Company") announced its financial results for the quarter ended September 30, 2022. A copy of the press release is being furnished as Exhibit 99.1 to this Current Report on Form 8-K.

Item 7.01. Regulation FD Disclosure.

On November 9, 2022, the Company updated its corporate presentation for use in meetings with investors, analysts and others. The presentation is available in the "Investors + Media" portion of the Company's website at investors.praxismedicines.com and a copy is furnished as Exhibit 99.2 to this Current Report on Form 8-K.

The information in this Current Report on Form 8-K under Items 2.02 and 7.01, including Exhibit 99.1 and Exhibit 99.2 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release, dated November 9, 2022
99.2	Praxis Precision Medicines, Inc. November 2022 Corporate Presentation
104	Cover Page Interactive Data File (embedded within the inline XBRL document)

SIGNATURE

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

PRAXIS PRECISION MEDICINES, INC.

November 9, 2022

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

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

PRAX-944 Phase 2b Essential1 study topline results for essential tremor expected in 1Q23

PRAX-222 EMBRAVE study for SCN2A-DEE to initiate in 4Q22; topline results for initial dose cohort expected in 2023

PRAX-628 Phase 1 healthy volunteer study to initiate in 4Q22; focal epilepsy study planned for 2023

Cash and investments of $123.7 million as of September 30, 2022 supports runway into 1Q24

BOSTON, November 9, 2022 — Praxis Precision Medicines, Inc. (NASDAQ: PRAX), a clinical-stage biopharmaceutical company translating genetic insights into the development of therapies for central nervous system (CNS) disorders characterized by neuronal excitation-inhibition imbalance, today provided a corporate update and reported financial results for the third quarter of 2022.

“With recent progress in the PRAX-944 Essential1 study, we are positioned to deliver topline results next quarter,” said Marcio Souza, president and chief executive officer of Praxis. “On the heels of the positive topline results from our Phase 2a study in essential tremor, we are encouraged by the profile of PRAX-944 and look forward to sharing these data in the coming months. With first-in-patient studies for our lead epilepsy programs expected to start shortly, as well as a Phase 1 study for our third clinical-stage epilepsy program, PRAX-628, our pipeline continues to advance, setting us up for an exciting year ahead.”

Recent Business Highlights and Upcoming Milestones:

Movement Disorders

- Praxis expects topline results from the ongoing PRAX-944 Essential1 study for the treatment of moderate to severe essential tremor (ET) in the first quarter of 2023. Screening for the Essential1 study will be completed by mid-November 2022. Essential1 is a randomized, double-blind, placebo-controlled, dose-range-finding Phase 2b trial evaluating the efficacy, safety and tolerability of once-daily daytime treatment of 60 mg or 100 mg of PRAX-944 compared to placebo after 56 days. The primary endpoint is change from baseline to day 56 in the modified Activities of Daily Living (mADL[1]) score, the U.S. Food and Drug Administration’s (FDA) suggested efficacy endpoint for ET. Following topline results, Praxis intends to meet with the FDA for an end-of-Phase 2 meeting in the first half of 2023 and initiate its Phase 3 development program for the treatment of ET in mid-2023.
- The Company expects to initiate a randomized, double-blind, placebo-controlled Phase 2 trial to evaluate the efficacy, safety and tolerability of once-daily treatment of up to 100 mg of PRAX-944 as a non-dopaminergic treatment for the motor symptoms of Parkinson’s disease in the first quarter of 2023. Topline results are expected in the second half of 2023. Following the positive topline results of Part B of the Phase 2a study of PRAX-944 for the treatment of ET, the PRAX-944 Parkinson’s disease study design was revised, including changing the primary endpoint to efficacy from safety.
- Praxis presented the following posters at the 2022 International Congress of Parkinson’s Disease and Movement Disorders (MDS) from September 15 – 18, 2022:
    - The Hidden Disease Burden and Treatment Experience of Patients with Essential Tremor: A Retrospective US Claims Analysis (Abstract Number: 968)
    - A Phase 2 Clinical Trial Evaluating the Efficacy, Safety, Tolerability, and Pharmacokinetics of PRAX-944 in Adults with Essential Tremor (Abstract Number: 951)
    - A Phase 2 Randomized, Double-Blind, Placebo-Controlled Trial of PRAX-944 for the Treatment of Essential Tremor (Abstract Number: 950)

[1]mADL is a composite sum of items 1 to 11 of the TETRAS-ADL subscale and items 6 (bilateral) and 7 of the TETRAS-PS; mADL score is calculated as the sum of all 13 items (item 6 of TETRAS-PS x2) and ranges from 0 to 42

- In October 2022, Praxis published the findings from an observational study, “The Hidden Burden of Disease and Treatment Experiences of Patients with Essential Tremor: A Retrospective Claims Data Analysis,” in *Advances in Therapy*[2]. The large claims-based analysis examines US claims data from 2015 to 2019, including diagnosis rates, comorbidities and treatment patterns in patients diagnosed with ET. Study findings highlight the hidden patient impact as well as the urgent unmet need for more treatment options and complexity of ET diagnosis. Key findings from the study include:
    - Approximately 1 million people were diagnosed and sought treatment for ET from 2015 to 2019 and it is estimated that another 1 million remained untreated
    - Propranolol (24%), primidone (20%) and gabapentin (19%) were the most commonly prescribed therapeutics following diagnosis
    - Two in three patients received pharmacological treatment for ET, with 2-year treatment discontinuation rates of approximately 40% (40% for propranolol, 47% for primidone), or about 200,000 patients annually
    - Nearly all patients (96%) had at least one comorbidity; depression and anxiety rates in ET patients were 2 times greater those in the general population aged 65 years and older
    - Confirmed ET diagnosis was established about 1.5 years after the diagnosis of an initial movement disorder

Epilepsy

- Praxis plans to initiate the first dose cohort of the PRAX-222 EMBRAVE study for the treatment of pediatric patients with early-seizure-onset SCN2A developmental and epileptic encephalopathy (DEE) in the U.S. in the fourth quarter of 2022. Following collection of the safety and efficacy data from the initial cohort of patients in the EMBRAVE study, the data will be evaluated and submitted to the FDA to seek authorization for dose escalation. Topline results from the initial dose cohort are expected in 2023.
- In October 2022, Praxis received additional detail from the FDA regarding the clinical hold for its Investigational New Drug (IND) application for PRAX-562 for the treatment of pediatric patients with SCN2A and SCN8A DEEs. Based on the feedback from the FDA, the Company expects that no new preclinical or clinical studies will be required to clear the clinical hold. Praxis is currently engaged with the FDA and expects to initiate a Phase 2, placebo-controlled trial in the first quarter of 2023.
- Praxis expects to initiate a PRAX-628 Phase 1 study in the fourth quarter of 2022 and subsequently initiate a Phase 2 study in focal epilepsy in 2023.

Psychiatry

- Following the completion of the PRAX-114 Phase 2 Acapella Study for the treatment of Major Depressive Disorder in the third quarter of 2022, Praxis does not currently plan to pursue further development of PRAX-114 for psychiatric disorders. The PRAX-114 Phase 2 Acapella study (N=110) was intended to provide additional understanding of the dose range and to evaluate the safety and efficacy of PRAX-114 at doses of 10, 20, 40 and 60 mg. Topline data indicated a linear dose response trend on the primary endpoint of change from baseline in the 17-item Hamilton Depression Rating Scale (HAM-D17) total score at Day 15, but were not statistically significant. In multiple secondary endpoints evaluating 40 mg of PRAX-114 relative to placebo, nominal statistical significance was achieved at Day 4, but not maintained at subsequent timepoints.

Third Quarter 2022 Financial Results:

As of September 30, 2022, Praxis had $123.7 million in cash, cash equivalents and marketable securities, compared to $275.9 million in cash, cash equivalents and marketable securities as of December 31, 2021. This decrease of $152.2 million primarily reflects cash used in operations of $156.2 million during the nine months ended September 30, 2022, partially offset by $4.3 million in net proceeds from at-the-market offerings of shares of the Company's common stock. The Company's cash, cash equivalents and marketable securities as of September 30, 2022 are expected to fund operations into the first quarter of 2024.

[2] 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

Research and development expenses were $30.4 million for the three months ended September 30, 2022, compared to $33.1 million for the three months ended September 30, 2021. The decrease in research and development expenses of $2.7 million was primarily attributable to $6.5 million in decreased clinical-related spend for the Company's Psychiatry franchise, partially offset by $5.2 million in increased expenses for the Company's Movement Disorders and Epilepsy franchises.

General and administrative expenses were $13.9 million for the three months ended September 30, 2022, compared to $11.6 million for the three months ended September 30, 2021. The increase in general and administrative expenses of approximately $2.3 million was primarily due to increased personnel-related costs due to increased headcount.

Praxis reported a net loss of $43.9 million for the three months ended September 30, 2022, including $6.7 million of stock-based compensation expense, compared to $44.7 million for the three months ended September 30, 2021, including $6.5 million of stock-based compensation expense.

As of September 30, 2022, Praxis had 46.9 million shares of common stock outstanding.

About Praxis
Praxis Precision Medicines is a clinical-stage biopharmaceutical company translating genetic insights into the development of therapies for CNS disorders characterized by neuronal excitation-inhibition imbalance. Praxis is applying insights from genetic epilepsies to both rare and more prevalent neurological disorders, using our understanding of shared biological targets and circuits in the brain. Praxis has established a broad portfolio 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 LinkedIn and Twitter.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995 and other federal securities laws, including express or implied statements regarding Praxis' future expectations, plans and prospects, including, without limitation, statements regarding expectations, plans and timing for our clinical data, the anticipated timing of our clinical trials and regulatory filings, the development of our product candidates, including the design of our clinical trials and the treatment potential of our product candidates, and the sufficiency of our cash, cash equivalents and marketable securities, and as well as other statements containing the words “anticipate,” “believe,” “continue,” “could,” “endeavor,” “estimate,” “expect,” “anticipate,” “intend,” “may,” “might,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will” or “would” and similar expressions that constitute forward-looking statements under the Private Securities Litigation Reform Act of 1995.

The express or implied forward-looking statements included in this press release are only predictions and are subject to a number of risks, uncertainties and assumptions, including, without limitation: uncertainties inherent in clinical trials; the expected timing of submissions for regulatory approval or review by governmental authorities; regulatory approvals to conduct trials; risks, uncertainties and assumptions regarding the impact of the continuing COVID-19 pandemic on Praxis' business, operations, strategy, goals and anticipated timelines, Praxis' ongoing and planned preclinical activities, Praxis' ability to initiate, enroll, conduct or complete ongoing and planned clinical trials and Praxis' timelines for regulatory submissions; and other risks concerning Praxis' programs and operations as described in its Quarterly Report on Form 10-Q for the six months ended June 30, 2022 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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617-300-8481

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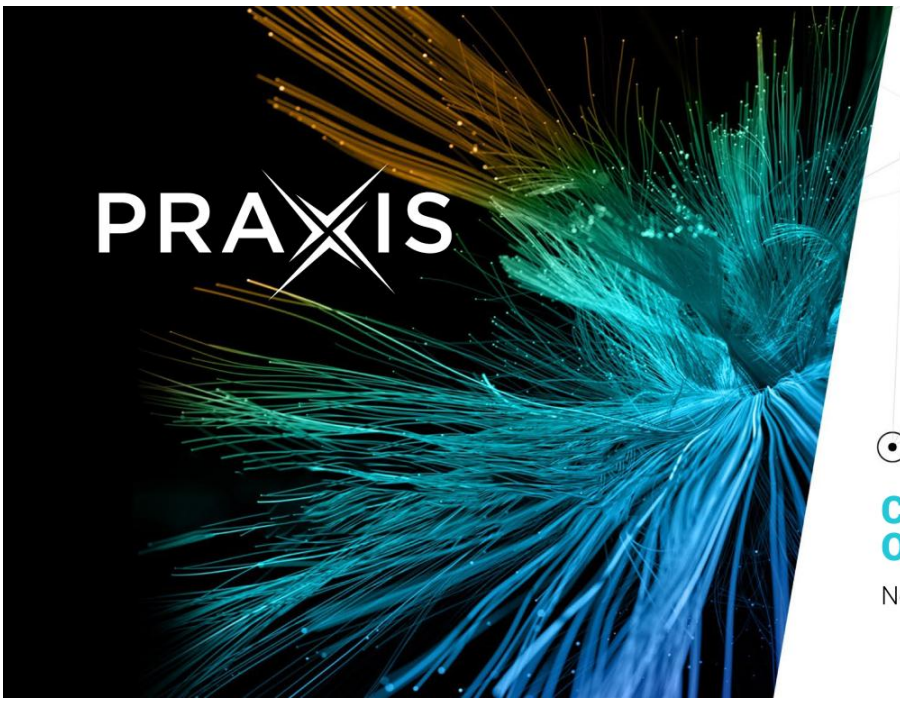
PRAXIS PRECISION MEDICINES, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(Amounts in thousands)
(Unaudited)

	September 30, 2022	December 31, 2021
Assets		
Cash and cash equivalents	$ 62,440	$ 138,704
Marketable securities	61,300	137,207
Prepaid expenses and other current assets	8,572	11,498
Property and equipment, net	1,077	1,213
Operating lease right-of-use assets	3,097	3,653
Other non-current assets	416	472
Total assets	$ 136,902	$ 292,747
Liabilities and stockholders' equity		
Accounts payable	$ 10,122	$ 10,780
Accrued expenses	17,884	26,844
Operating lease liabilities	3,733	4,311
Common stock	5	5
Additional paid-in capital	595,165	567,598
Accumulated other comprehensive loss	(536)	(176)
Accumulated deficit	(489,471)	(316,615)
Total liabilities and stockholders' equity	$ 136,902	$ 292,747

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Operating expenses:				
Research and development	$ 30,439	$ 33,139	$ 126,711	$ 76,746
General and administrative	13,851	11,634	46,822	31,929
Total operating expenses	44,290	44,773	173,533	108,675
Loss from operations	(44,290)	(44,773)	(173,533)	(108,675)
Other income:				
Other income, net	345	73	677	201
Total other income	345	73	677	201
Loss before income taxes	$ (43,945)	$ (44,700)	$ (172,856)	$ (108,474)
Provision for income taxes	—	(5)	—	(5)
Net loss	$ (43,945)	$ (44,705)	$ (172,856)	$ (108,479)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.96)	$ (1.00)	$ (3.79)	$ (2.61)
Weighted average common shares outstanding, basic and diluted	45,774,376	44,714,941	45,591,888	41,608,017



CORPORATE OVERVIEW

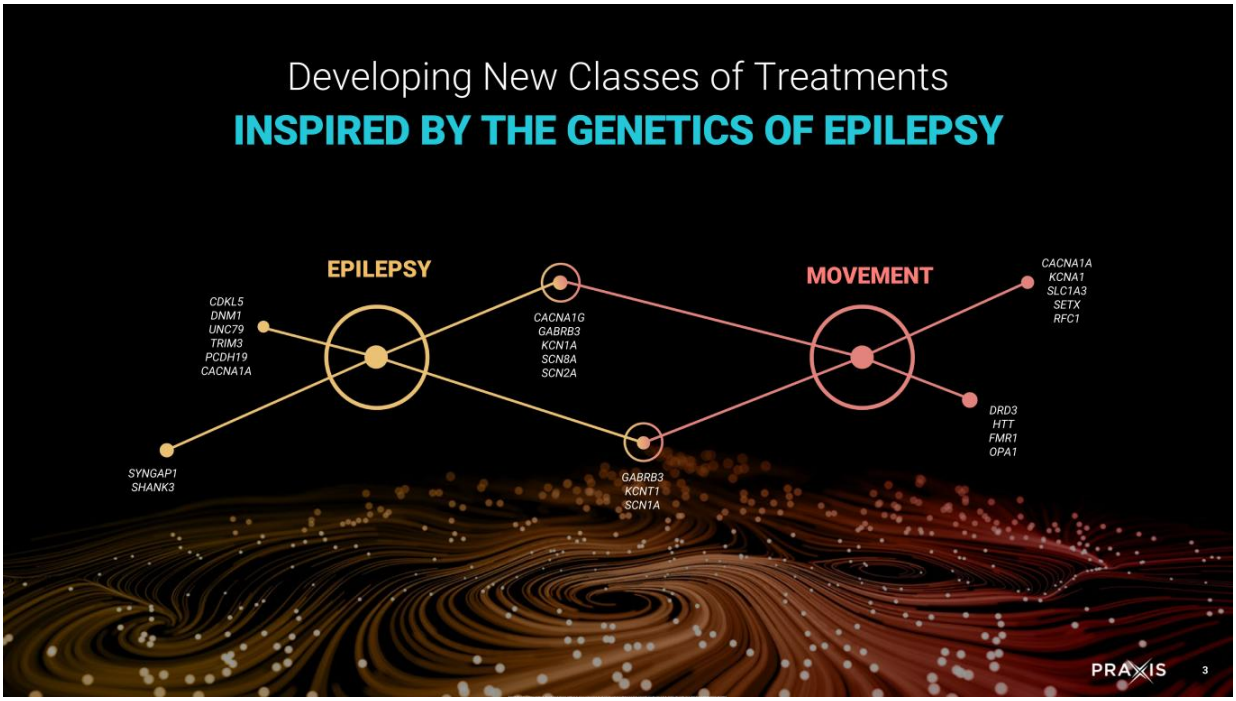
November 2022

Forward-looking statements

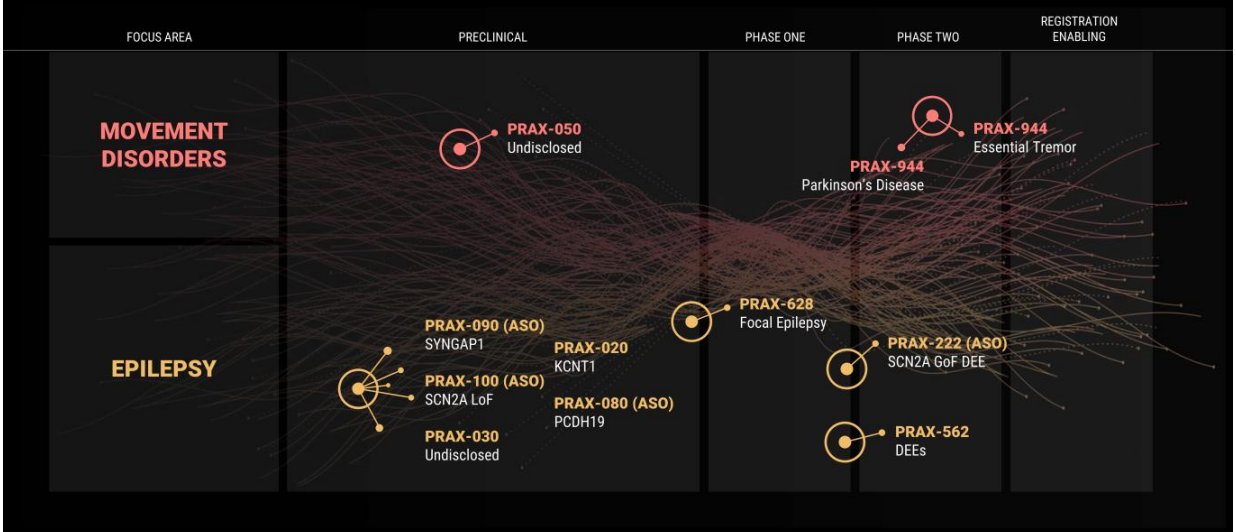
This presentation may contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial conditions, including but not limited to express or implied statements regarding the current beliefs, expectations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

For further information regarding the risks, uncertainties and other factors that may cause differences between our expectations and actual results, you should review the "Risk Factors" section of our Quarterly Report on Form 10-Q filed for the quarter ended June 30, 2022 and other filings with the Securities and Exchange Commission.

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


Developing New Classes of Treatments
INSPIRED BY THE GENETICS OF EPILEPSY
EPILEPSY
MOVEMENT
CDKL5
DNM1
UNC79
TRIM3
PCDH19
CACNA1A
SYNGAP1
SHANK3
CACNA1G
GABRB3
KCN1A
SCN8A
SCN2A
GABRB3
KCNT1
SCN1A
CACNA1A
KCNA1
SLC1A3
SETX
RFC1
DRD3
HTT
FMR1
OPA1
PRAXIS
3

Targeting movement disorders & epilepsies connected by neuronal imbalance



SCN2A-LOF, SYNGAP1 & PCDH19 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

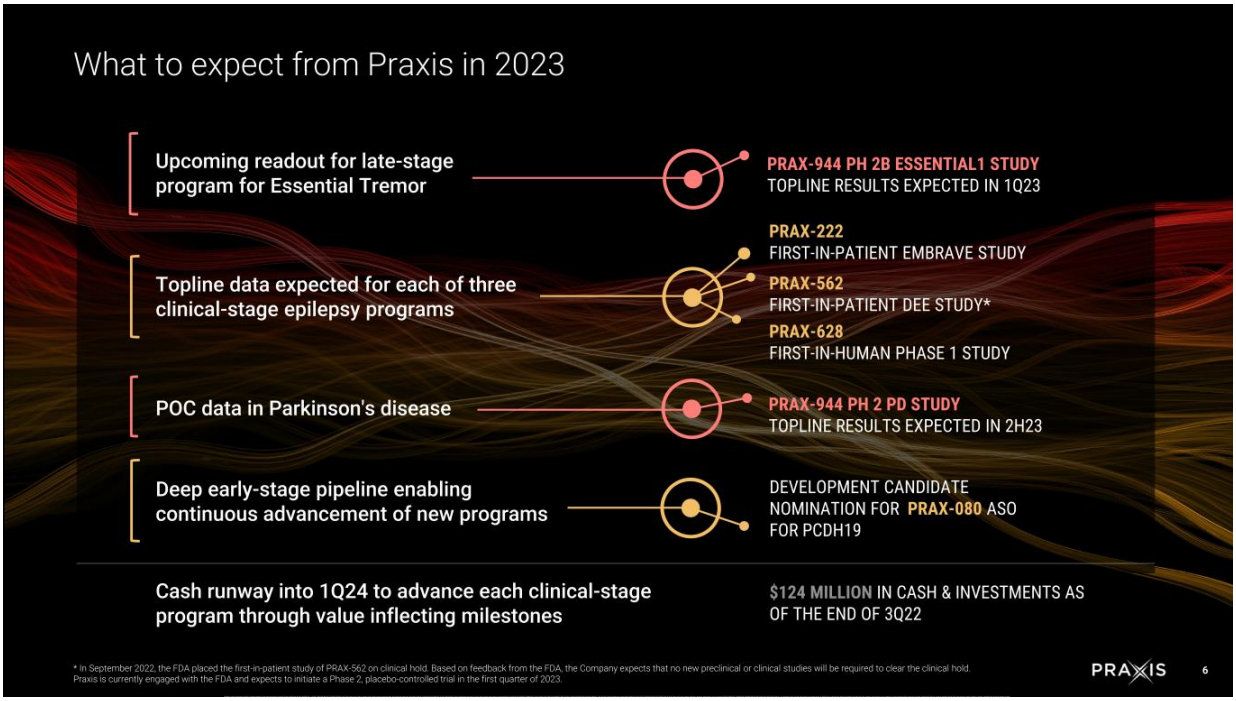
EFFICIENT & RIGOROUS

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

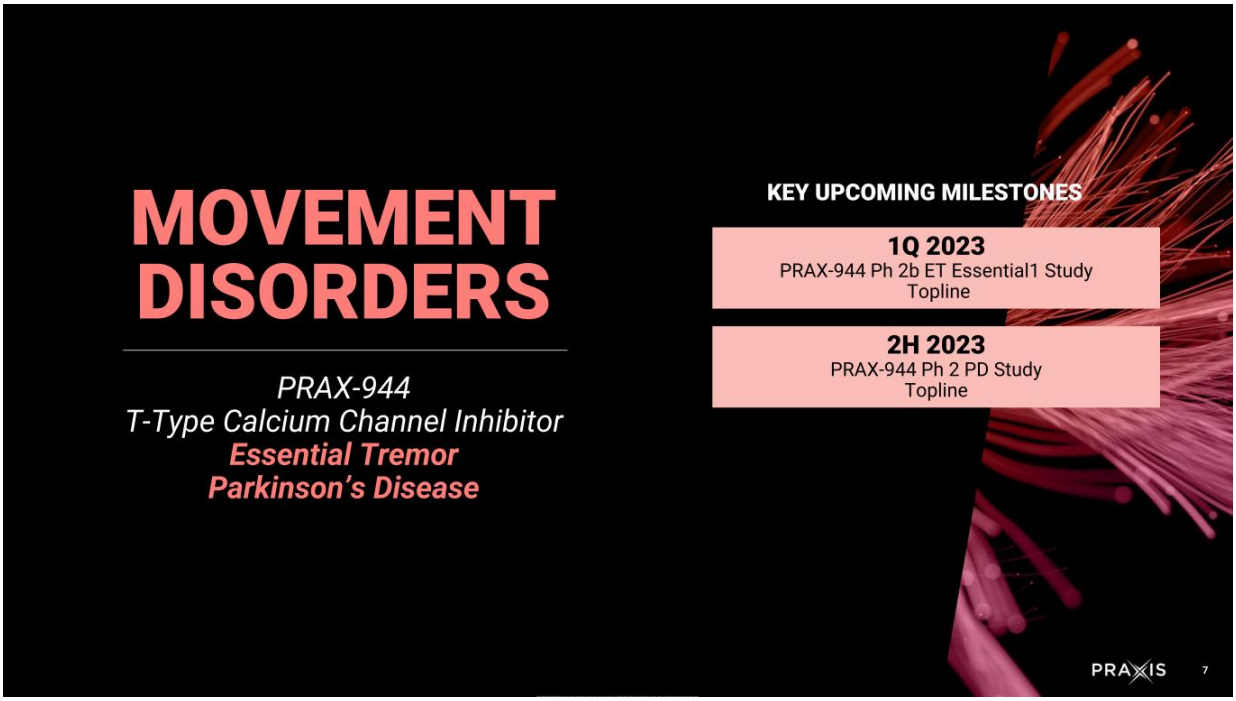
PATIENT-GUIDED

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

What to expect from Praxis in 2023



* In September 2022, the FDA placed the first-in-patient study of PRAX-562 on clinical hold. Based on feedback from the FDA, the Company expects that no new preclinical or clinical studies will be required to clear the clinical hold. Praxis is currently engaged with the FDA and expects to initiate a Phase 2, placebo-controlled trial in the first quarter of 2023.


MOVEMENT DISORDERS
PRAX-944
T-Type Calcium Channel Inhibitor
Essential Tremor
Parkinson's Disease
KEY UPCOMING MILESTONES
1Q 2023
PRAX-944 Ph 2b ET Essential1 Study Topline
2H 2023
PRAX-944 Ph 2 PD Study Topline
PRAXIS
7

Essential tremor 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

PRAXIS

PRAX-944 is a differentiated, selective T-type calcium channel blocker in development for ET and Parkinson's disease

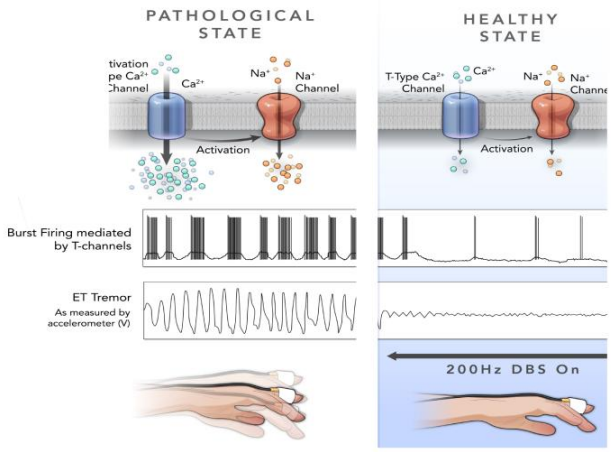
Highly selective for T-type calcium channels

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

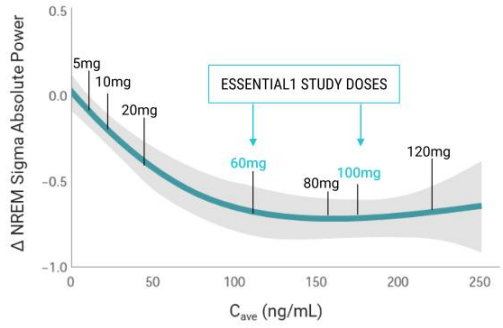
Burst firing in the CTC circuit correlated with tremor in patients with ET and PD

Deep Brain Stimulation reduces burst firing and tremor

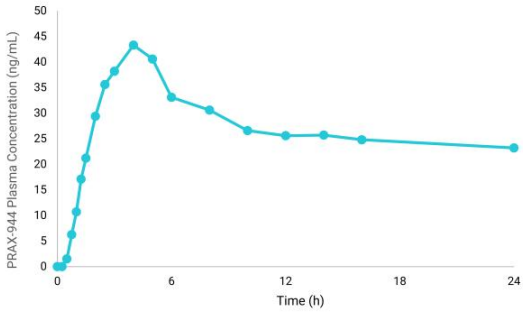
Source: Based on Milosevic 2018 figured on actual ET patient intraoperative real-time single-unit recordings of action potentials of individual neurons

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

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



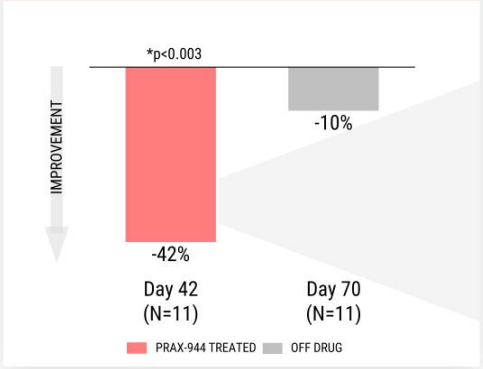
SUSTAINED EXPOSURE WITH BLUNTED CMAX



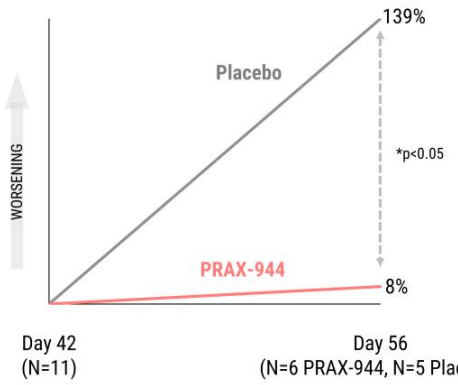
Source: Praxis Data on file

Marked functional benefit observed in PRAX-944 treated patients in Ph 2a study; withdrawal of PRAX-944 results in regression to baseline severity

MODIFIED ADLs IN OPEN LABEL
MEAN % CHANGE FROM BASELINE

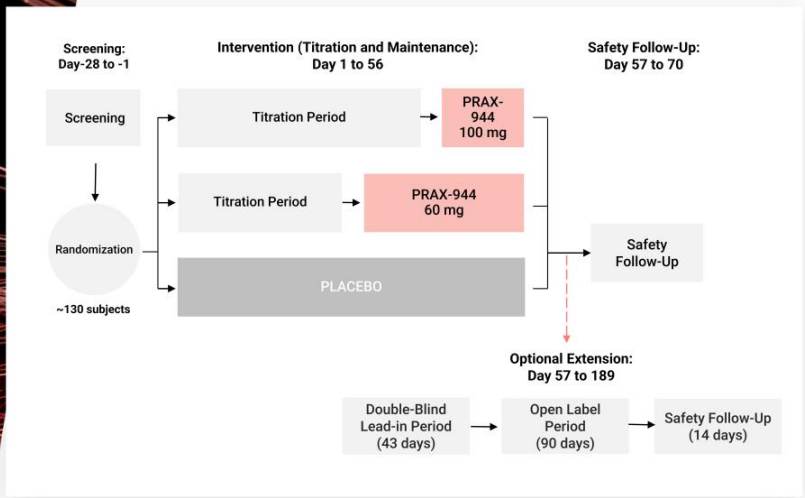


MODIFIED ADLs IN RANDOMIZED WITHDRAWAL
MEAN % CHANGE FROM DAY 42



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

PRAX-944 Phase 2b Essential1 study topline results expected 1Q23



PRIMARY ENDPOINT:

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

STUDY POWERING:

33 evaluable participants per regimen provides 80% power to detect 0.6 effect size between pooled PRAX-944 and placebo groups, or placebo adjusted difference of 3.6 pts in mADL at Day 56 (SD=6)

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

Modified ADLs: A modified measure of TETRAS activities of daily living (ADLs) that is functionally relevant and FDA recommended

TETRAS ADL measures observed:

1. Speaking
2. Feeding with a spoon
3. Drinking from a glass
4. Hygiene
5. Dressing
6. Pouring
7. Carrying food trays, plates or similar items
8. Using keys
9. Writing
10. Working
11. Overall disability with most affected task
12. Social Impact

Each measure is individually scored from 0-4:

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

TOTAL SCORE OF UP TO 48

Modified ADL measures observed:

1. Speaking
2. Feeding with a spoon
3. Drinking from a glass
4. Hygiene
5. Dressing
6. Pouring
7. Carrying food trays, plates or similar items
8. Using keys
9. Writing
10. Working
11. Overall disability with most affected task
12. Handwriting
13. Spirals (x2)
14. ~~Social impact~~

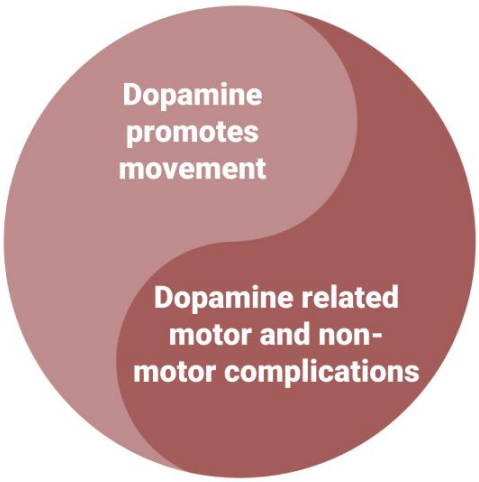
Each measure is individually scored from 0-3:

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.

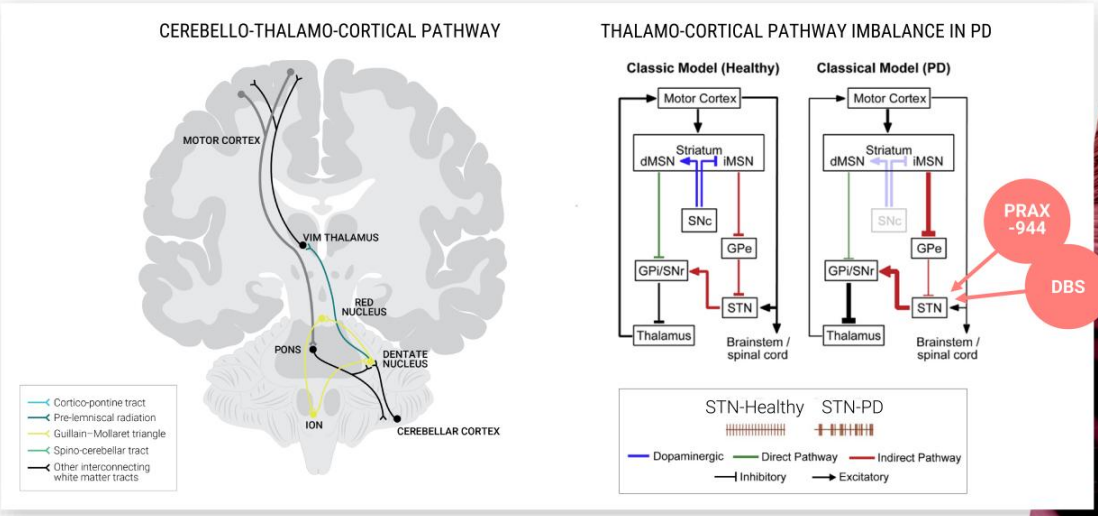
TOTAL SCORE OF UP TO 42

PRAXIS

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



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

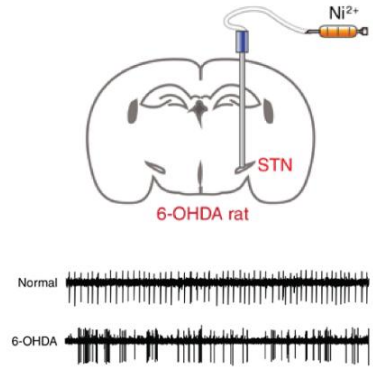


Mcgregor mm, nelson ab. Neuron. 2019. Doi:10.1016/j.Neuron.2019.03.004
Tai c-h et al. J clin invest. 2011. Doi:10.1172/jci46482

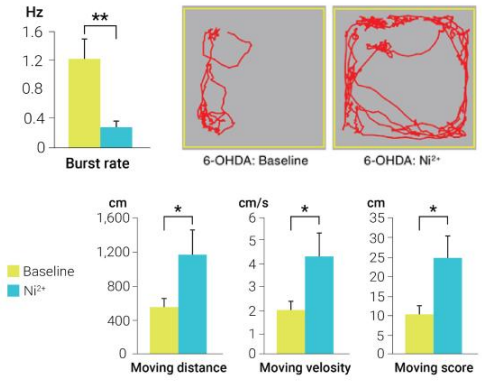
PRAXIS

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

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

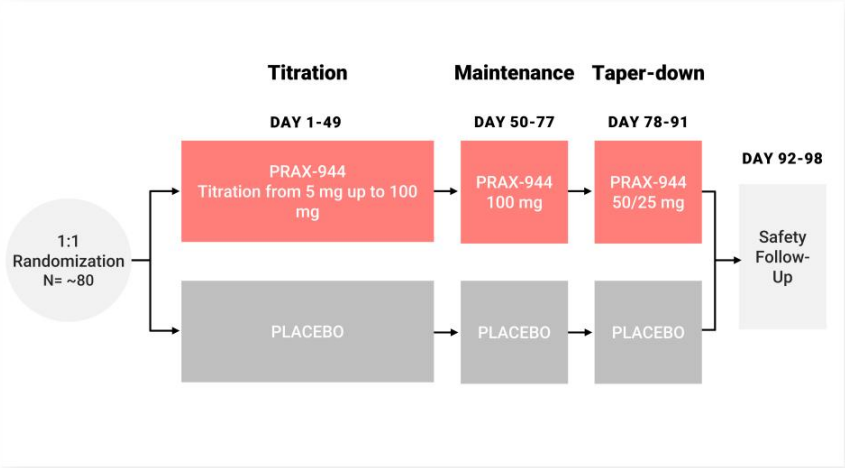


BLOCK OF BURST FIRING IMPROVES MOVEMENT IN 6-OHDA PARKINSON'S MODEL



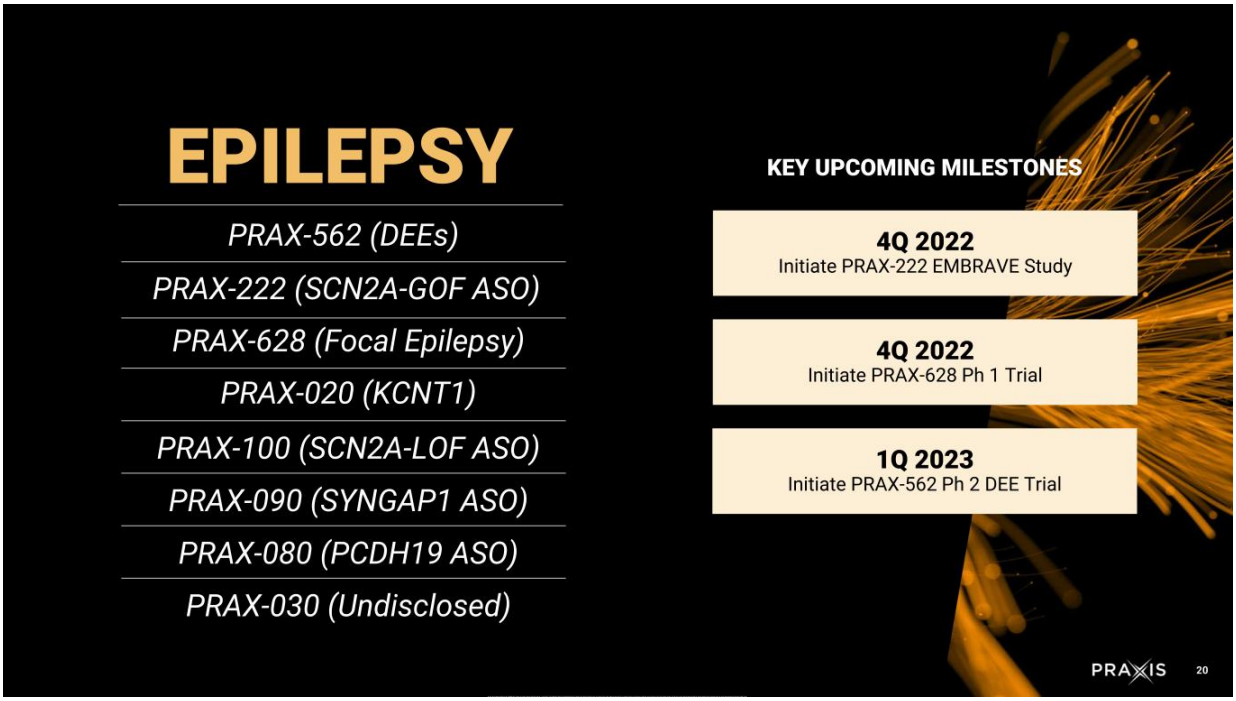
Pan et al (2016) j clin invest doi: 10.1172/jci88170

PRAX-944 Phase 2 Parkinson's disease study topline data expected 2H23

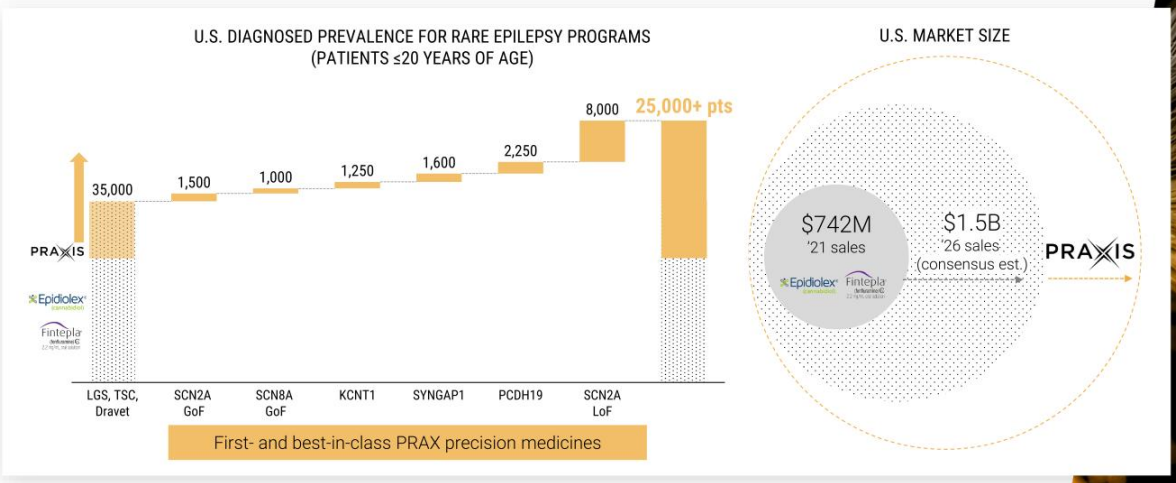


PRIMARY ENDPOINT:

Change from baseline to Day 77 in the International Parkinson and Movement Disorder Society (MDS) Unified Parkinson's Disease Rating Scale (UPDRS) Part III (motor examination) score in the OFF state


EPILEPSY
PRAX-562 (DEEs)
PRAX-222 (SCN2A-GOF ASO)
PRAX-628 (Focal Epilepsy)
PRAX-020 (KCNT1)
PRAX-100 (SCN2A-LOF ASO)
PRAX-090 (SYNGAP1 ASO)
PRAX-080 (PCDH19 ASO)
PRAX-030 (Undisclosed)
KEY UPCOMING MILESTONES
4Q 2022
Initiate PRAX-222 EMBRAVE Study
4Q 2022
Initiate PRAX-628 Ph 1 Trial
1Q 2023
Initiate PRAX-562 Ph 2 DEE Trial
PRAXIS
20

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



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

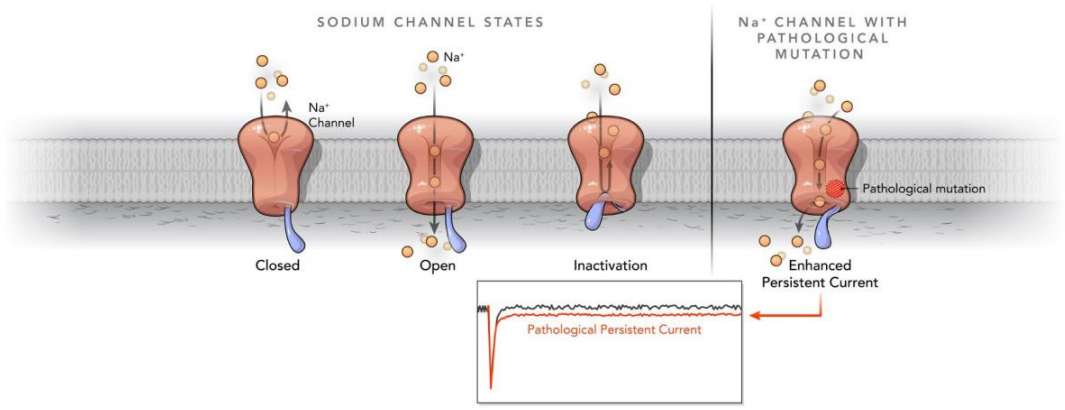
Preclinical and emerging clinical data demonstrate PRAX-562 will be a first- and best-in-class NaV blocker for DEEs

PRAX-562

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

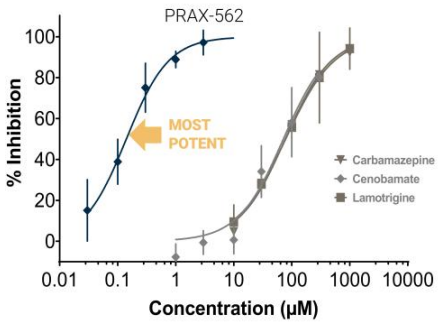
- Superior selectivity for disease-state Na_V channel hyperexcitability
- Unprecedented therapeutic window with potential for superior safety and efficacy
- Convenient auto-titration regimen with stable PK

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



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

% INHIBITION OF $hNa_V1.6$ PERSISTENT I_{Na}



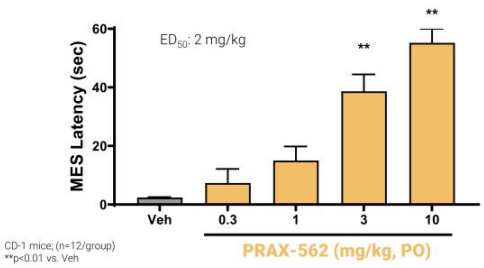
COMPARISON OF POTENCY AND SELECTIVITY

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

*solubility concerns

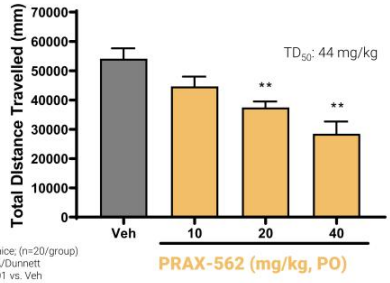
Our mechanistic hypothesis translates to a wide therapeutic index in vivo

MES EFFICACY



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

sLMA TOLERABILITY



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

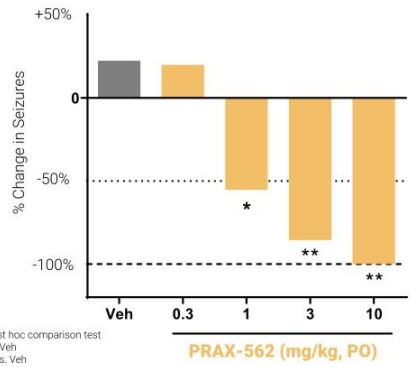
Molecule	Plasma Therapeutic Index
PRAX-562	17.2x

Therapeutic Index (TI) = TC50 / EC50

PRAXIS

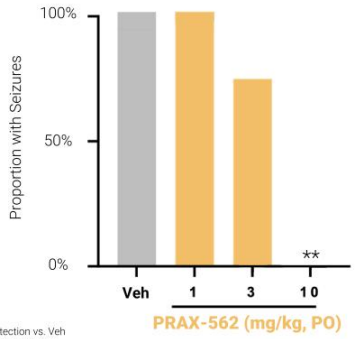
PRAX-562 completely blocks seizures in SCN2A and SCN8A GoF mutation mouse models

IN VIVO POC IN SCN2A 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_2 = 16.0, Fisher's p = 0.0002

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

PRAX-562 Phase 1 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

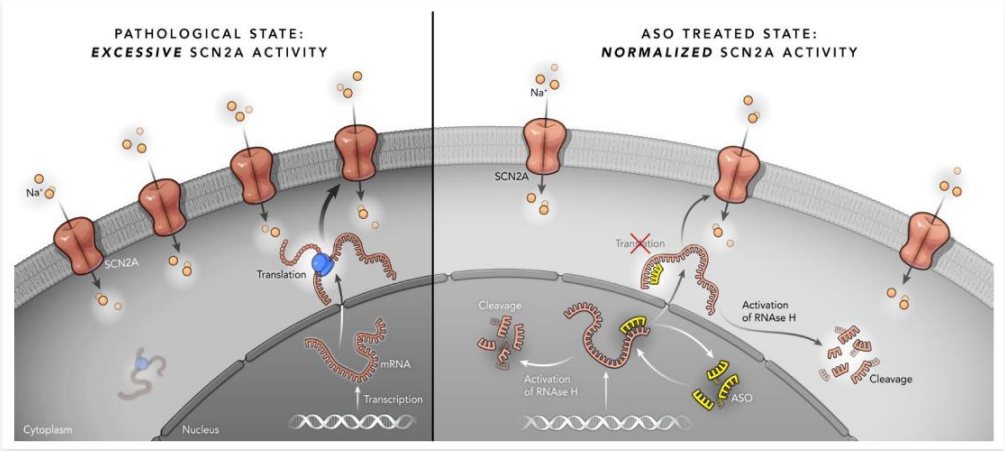
Preclinical data suggest PRAX-222 has potential to be disease-modifying for early onset SCN2A gain-of-function DEE

PRAX-222

INTRATHECALLY-ADMINISTERED ASO for SCN2A GOF DEE

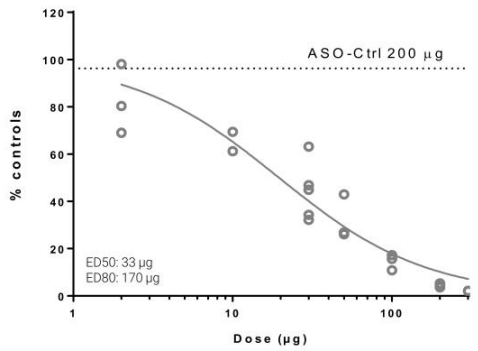
- Dose-dependent reduction in interictal spikes, seizures and increased survival
- Improvement in behavioral and locomotor activity in animal models
- Survival benefit extended with repeat dosing

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

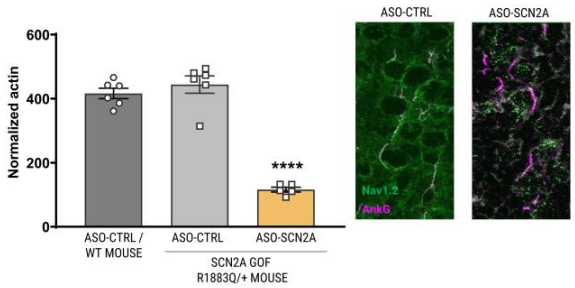


In vitro, PRAX-222 down-regulates both mRNA and protein

SCN2A mRNA KNOCKDOWN



SCN2A PROTEIN KNOCKDOWN

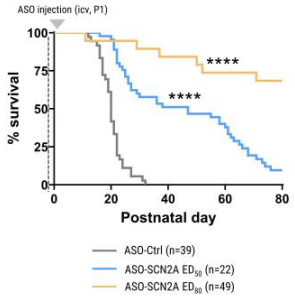


ASOs were administered at P30 and brains were collected 14 days post-ICV for qPCR analysis

PRAX-222 increases survival in SCN2A GoF mice

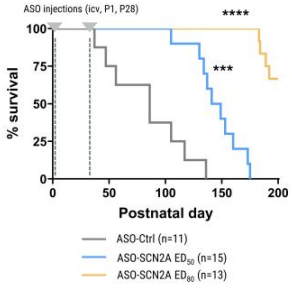
SCN2A ASO INCREASES SURVIVAL WITH A SINGLE DOSE INJECTION

SCN2A GOF model



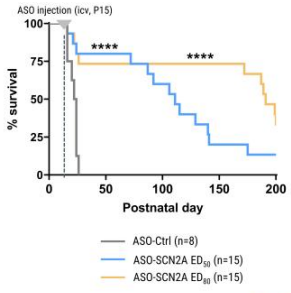
RE-DOSING SIGNIFICANTLY EXTENDS SURVIVAL

SCN2A GOF model



ADMINISTRATION POST-DISEASE ONSET ALSO EXTENDS SURVIVAL

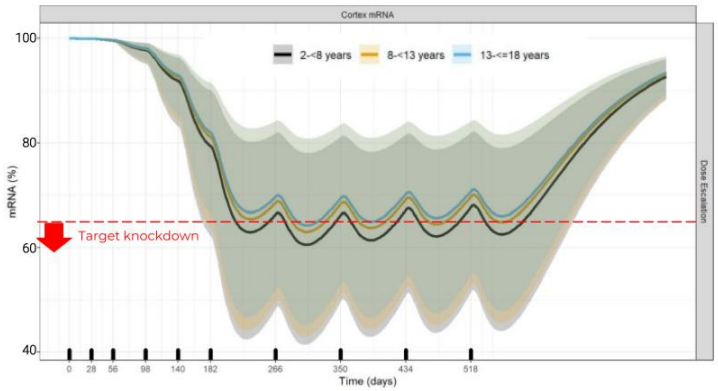
SCN2A GOF model



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

PRAXIS

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



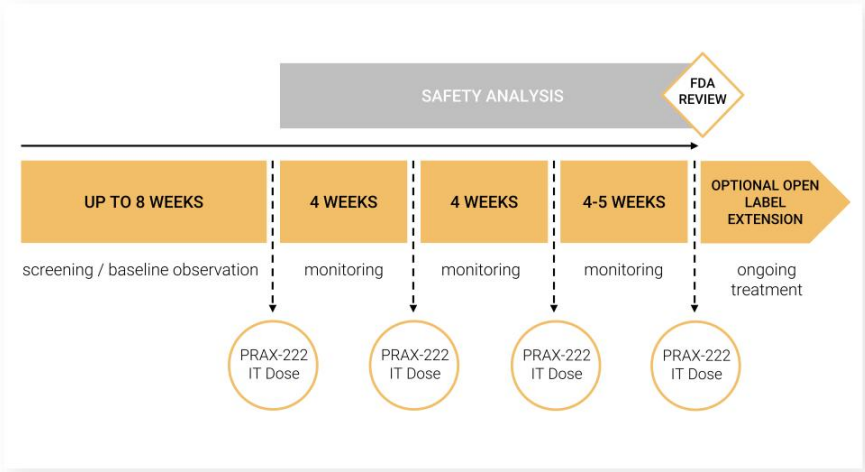
Median and 95% prediction interval illustrated

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



GOAL:
Assess preliminary safety of PRAX-222

21-week study

Open label design

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 data demonstrates PRAX-628 will be a best-in-class NaV blocker for focal epilepsy

PRAX-628

FOCAL EPILEPSY

PAN-NA_V
ACTIVITY DEPENDENT
BLOCKER

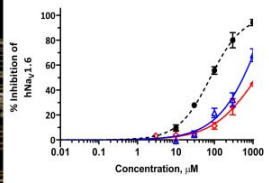
SMALL MOLECULE

- Superior selectivity for disease-state Na_V channel hyperexcitability
- Unprecedented therapeutic window translating to superior safety and efficacy
- PK differentiated for broad epilepsy population

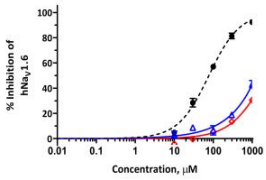
Our internal discovery effort focused on developing a Na_V blocker with high disease state dependence and wide therapeutic index

LOW DISEASE-STATE DEPENDENCE THIN THERAPEUTIC INDEX

LAMOTRIGINE



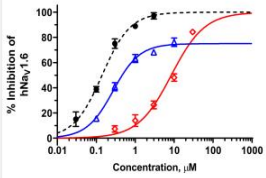
CARBAMAZEPINE



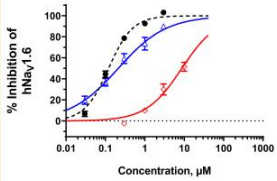
"Na_V Fingerprint"
Persistent I_{Na} Inhibition
Peak I_{Na}, UDV-10Hz (Disease-State Dependence) Inhibition
Peak I_{Na}, Tonic Block Inhibition

HIGH DISEASE-STATE DEPENDENCE WIDE THERAPEUTIC INDEX

PRAX-562

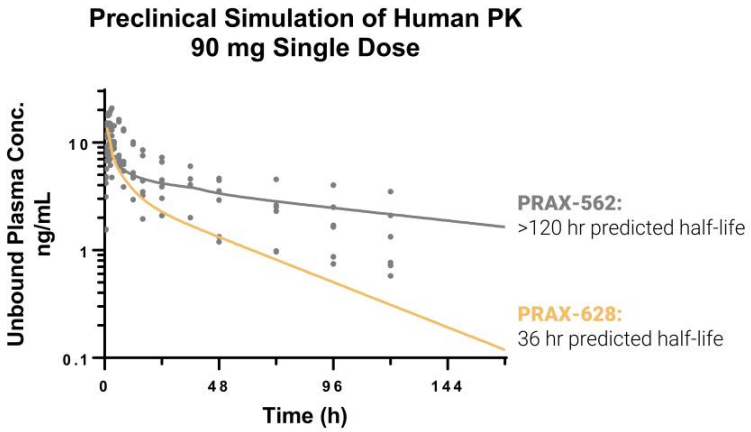


PRAX-628



Source: Praxis data on file

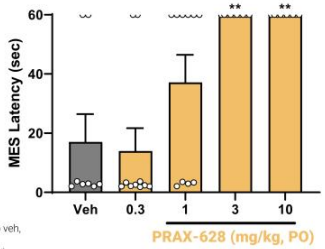
PRAX-628 has unique pharmacological properties that enable acute dosing in a broader patient population



Modeling 90mg, single dose of PRAX-628 or PRAX-562. Preclinical simulation recapitulates PRAX-562 clinical data.

PRAX-628 protects mice from seizures with a wide therapeutic window

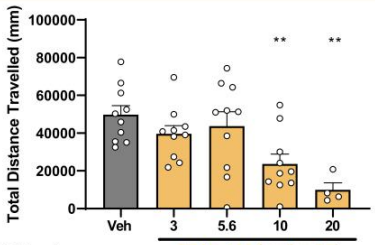
MES EFFICACY



CD-1 mice; (n=8/group veh, n=10 PRAX)
ANOVA/Dunnett (PRAX)
**p<0.01 vs. Veh

ED_{50}: 0.67 mg/kg

sLMA TOLERABILITY



CD-1 mice; (n=10/group)
ANOVA/Dunnett
**p<0.01 vs. Veh

TD_{50}: 10.3 mg/kg

Molecule	Plasma Therapeutic Index
PRAX-628	16.7x

Therapeutic Index (TI) = TC_{50} / EC_{50}

Three epilepsy drugs expected in clinic by first quarter 2023

PRAX-222	PRAX-628	PRAX-562
(SCN2A)	*(FOCAL EPILEPSY)*	*(SCN2A, SCN8A)*
Initiate EMBRAVE Study: 4Q22⁺	**Initiate Phase 1 Study: 4Q22**	**Initiate Phase 2 Study: 1Q23***

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

* Initial dose cohort; following collection of safety and efficacy data from first cohort, the data will be evaluated and submitted to the FDA to seek authorization for further dose escalation
⁺ In September 2022, the FDA placed the first-in-patient study of PRAX-562 on clinical hold


PRAXIS
DARE FOR MORE™