UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 11, 2021

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.
One Broadway, 16th Floor
Cambridge, Massachusetts 02142
(Address of principal executive offices, including zip code)

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

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

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

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

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

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

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

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

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

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

Emerging growth company ☒

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

Item 2.02. Results of Operations and Financial Condition.

On May 11, 2021, Praxis Precision Medicines, Inc. (the "Company") announced its financial results for the quarter ended March 31, 2021. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

Item 7.01. Regulation FD Disclosure.

On May 11, 2021, the Company updated its corporate presentation for use in meetings with investors, analysts and others. The presentation is available through the Company's website 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 (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 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 May 11, 2021 (furnished herewith).
99.2	Corporate Presentation, dated May 2021 (furnished herewith).

SIGNATURE

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

PRAXIS PRECISION MEDICINES, INC.

Date: May 11, 2021

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

Praxis Precision Medicines Provides Corporate Update and Reports First Quarter 2021 Financial Results

Expands pipeline with new indications for PRAX-114 and PRAX-944

PRAX-114 Phase 2 trial for treatment of post-traumatic stress disorder to initiate in 2H21

PRAX-114 Phase 2 trial for treatment of essential tremor to initiate in 2H21

PRAX-944 Phase 2 trial for treatment of Parkinson's disease to initiate in 1H22

Cash balance of $270.8M as of March 31, 2021 supports cash runway into 4Q22

CAMBRIDGE, Mass., May 11, 2021 — 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 imbalance, today provided a corporate update and reported financial results for the first quarter ended March 31, 2021.

"I'm inspired by our team's continued execution and the progress throughout our pipeline during the first quarter, with key milestones achieved across each of our programs. As the pipeline advances, our conviction in our programs continues to grow," said Marcio Souza, president and chief executive officer of Praxis. "In addition to the ongoing enrollment in our PRAX-114 Phase 2/3 Aria study for monotherapy MDD, we are excited to announce the expansion of PRAX-114 into post-traumatic stress disorder and essential tremor, as well as the expansion of PRAX-944 into Parkinson's disease. These disorders all have significant unmet need, as well as both genetic and mechanistic linkage to the respective targets and programs. We believe that Praxis' foundational approach to identifying targets through human genetics, the extensive use of translational tools to inform development and always keeping patient needs top of mind have been instrumental in developing a deep pipeline of CNS programs with considerable optionality."

Recent Business Highlights and Upcoming Milestones:

Psychiatry

- Praxis plans to initiate a PRAX-114 Phase 2 trial for treatment of post-traumatic stress disorder (PTSD) in the second half of 2021. Topline results are expected in the second half of 2022.
- Praxis expects topline results from the ongoing PRAX-114 Phase 2/3 Aria Study (Study 213) for monotherapy treatment of Major Depressive Disorder (MDD) in the first half of 2022. If positive, the Aria Study is intended to serve as one of two trials required by the U.S. Food and Drug Administration (FDA) to demonstrate clinical efficacy to support registration of PRAX-114 for monotherapy treatment of MDD.
- Praxis plans to initiate a PRAX-114 Phase 2 Study (Study 214) for adjunctive treatment of MDD in the third quarter of 2021. Topline results from Study 214 are expected in the first half of 2022.
    - Study 214 is designed to include patients with moderate to severe MDD (HAM-D>23) with insufficient response to standard of care antidepressant treatment in the current episode and will evaluate efficacy and safety of PRAX-114 at doses of 10mg, 20mg, 40mg and 60mg.
    - Study 214 will provide controlled data to support advancing a Phase 3 adjunctive MDD trial and will increase the understanding of the dose range for expected Phase 3 monotherapy and adjunctive treatment trials.
- Praxis has completed the Part A (N=33) and Part C (N=13) MDD cohorts of the PRAX-114 Phase 2a trial for treatment of patients with MDD and perimenopausal depression (PMD). Praxis expects to announce topline results from the ongoing Part B cohort for treatment of patients with PMD in the second half of 2021.

- Across both MDD cohorts (N=46), PRAX-114 led to a rapid and marked improvement in the HAM-D score of participants, with mean improvements of 16.4 points, or 65%, at Day 15 for monotherapy treatment (N=11) and 12.7 points, or 51%, at Day 15 for adjunctive treatment (N=35).
- Anxiety symptoms, as assessed by the HAM-A, demonstrated an improvement of 11 points, or 50%, at Day 15 across both MDD cohorts.
- Insomnia symptoms, as assessed by the total of 3 HAM-D insomnia items, demonstrated an improvement of 3.1 points, or 76%, at Day 15 across both MDD cohorts.
- PRAX-114 demonstrated a generally well-tolerated safety profile throughout the 14-day treatment period in Part A and the 28-day treatment period in Part C. Treatment emergent adverse events were generally mild to moderate. Rates of somnolence, which is characterized by sleepiness or drowsiness, increased with exposure, demonstrating a pharmacological effect which was substantially mitigated by dosing at night versus daytime dosing.

- In May 2021, Praxis published a white paper, "*Best Practices in Clinical Trials of Antidepressants: Overcoming Challenges to Optimize Success*," highlighting essential learnings and best practices to improve the chances of success in MDD clinical trials through appropriate study design and conduct.
- Preclinical and clinical data for PRAX-114 was presented at the Society of Biological Psychiatry Meeting (SOBP) from April 29 - May 1, 2021. One abstract included preclinical data demonstrating PRAX-114's extrasynaptic GABAA receptor preference, robust β-EEG link to preclinical anxiety and depression models, and wide therapeutic window with exposures associated with efficacy separating from those associated with sedation by 11-fold. A second abstract included clinical data demonstrating that PRAX-114's robust CNS pharmacodynamic effect and translational β-EEG and tolerability data generated in preclinical experiments was replicated in a clinical study in healthy participants.

Movement Disorders

- Praxis expects to initiate a PRAX-114 Phase 2 trial for treatment of essential tremor (ET) in the second half of 2021. Topline results are expected in the second half of 2022.
- Praxis expects to initiate a PRAX-944 Phase 2 trial for treatment of Parkinson’s disease in the first half of 2022.
- Praxis is currently in the second of two cohorts in its PRAX-944 Phase 2a trial for ET, assessing up to twelve patients titrated up to 120 mg/day of PRAX-944. Preliminary topline open-label safety, tolerability and efficacy data is expected in mid-2021.
- To inform dose selection for PRAX-944 for tremor studies, population PK-PD analyses were performed to predict the effect of PRAX-944 exposure on selected EEG endpoints including the sigma band absolute power during non-rapid eye movement (NREM) sleep, which is believed to be a relevant biomarker for the T-type calcium channel in the thalamus, a key part of the tremor network. PRAX-944 had a significant pharmacodynamic (PD) effect on sigma band EEG power during NREM sleep across the 5 to 120 mg dose range evaluated. The results of the analysis suggest that doses as low as 5 mg/day may show effect while doses of up to ~120 mg/day may drive additional PD effect relative to the doses explored in ET patients to date (up to 40mg/day).
- Praxis plans to initiate a Phase 2 randomized, double-blind, placebo-controlled trial of PRAX-944 for treatment of ET in the fourth quarter of 2021. In addition, a Phase 1 study to explore faster titration schemes for PRAX-944 for treatment of ET is expected to initiate in mid-2021.
- Praxis recently interacted with the FDA to discuss the development of PRAX-944 for treatment of ET and received feedback pertaining to clinical endpoints necessary to support PRAX-944's potential approval. The FDA

indicated that primary clinical endpoints to support approval for treatment of ET should adequately measure clinically meaningful benefit for patients such as assessment of activities of daily living or performance-based functional tests.

Rare Disease

- Praxis has completed the single ascending dose (SAD) and the multiple ascending dose (MAD) cohorts in its Phase 1 trial of PRAX-562 in healthy volunteers up to the highest planned dose. The highest planned dose in the MAD cohort was well tolerated with concentrations that exceed EC_{75} in the MES mouse model, a model with demonstrated predictive validity. Praxis will be escalating the dose further to explore tolerability at higher dose levels. Safety, tolerability and PK data from the ongoing Phase 1 trial of PRAX-562 is expected in mid-2021.

- Praxis expects to initiate an exploratory Phase 2 trial of PRAX-562 in the second half of 2021 for treatment of patients with rare adult cephalgias, including a cohort of participants with Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing (SUNCT) and Short-lasting Unilateral Neuralgiform headache with Autonomic symptoms (SUNA), and a cohort of participants with Trigeminal Neuralgia (TN).

- Praxis plans to initiate a Phase 2 trial of PRAX-562 for treatment of developmental epileptic encephalopathies (DEEs), including SCN8A-DEE and SCN2A-DEE, in the first half of 2022.

- In April 2021, Praxis announced that the FDA granted orphan drug designation to PRAX-562 for treatment of SCN8A-DEE and for treatment of SCN2A-DEE. Data from preclinical studies demonstrated that PRAX-562 dose-dependently inhibits seizures in SCN8A and SCN2A animal models, completely extinguishing seizures at the highest dose level tested in each model.

- Praxis plans to complete the ongoing IND-enabling toxicology study by the end of 2021 for its lead antisense oligonucleotide (ASO) candidate, PRAX-222, and to initiate a Phase 1/2 trial of PRAX-222 for treatment of SCN2A-DEE in the first half of 2022. PRAX-222 is a precision medicine candidate designed to down-regulate SCN2A mRNA in epilepsy patients with SCN2A gain-of-function mutations.

General Corporate Updates

- In April 2021, Praxis announced the appointment of Jeffrey Chodakewitz, M.D., to its board of directors. Dr. Chodakewitz has more than 30 years of management experience in the biopharmaceutical industry. Most recently he served as the chief medical officer and executive vice president, global medicines development & medical affairs at Vertex Pharmaceuticals.

- In April 2021, Praxis announced the appointment of Merit Cudkowicz, M.D., to its board of directors. Dr. Cudkowicz is the chief of neurology at Mass General Hospital, director of the Sean M. Healey & AMG Center for ALS, and director and the Julieanne Dorn professor of neurology at Harvard Medical School. She has brought innovations to accelerate the development of treatments for people with neurological disorders such as ALS, including a leadership role in the first antisense oligonucleotide treatment for a neurological disorder.

First Quarter 2021 Financial Results:

As of March 31, 2021, Praxis had $270.8 million in cash, cash equivalents and marketable securities, compared to $296.6 million in cash and cash equivalents as of December 31, 2020. This decrease of $25.8 million primarily reflects cash used in operations. The company's cash, cash equivalents and marketable securities as of March 31, 2021 are expected to fund operations into the fourth quarter of 2022.

Research and development expenses were $17.9 million for the first quarter of 2021, compared to $6.9 million for the first quarter of 2020. The increase in R&D expenses of $11.0 million was primarily attributable to $4.5 million in increased personnel-related costs due to increased headcount, $2.7 million in increased expenses related to our

discovery-stage programs, $1.8 million in increased expenses related to our PRAX-562 program, $1.3 million in increased expenses related to our PRAX-114 program and $0.6 million in increased expenses related to our PRAX-944 program.

General and administrative expenses were $9.5 million for the first quarter of 2021, compared to $1.6 million for the first quarter of 2020. The increase in general and administrative expenses of $7.9 million was primarily attributable to $3.8 million in increased personnel-related costs due to increased headcount, $2.3 million in increased professional fees and $1.8 million increase in other general and administrative expenses, including $1.1 million in increased insurance and other costs related to becoming a public company.

Praxis reported net loss of $27.4 million for the first quarter of 2021, including $4.7 million of stock-based compensation expense, compared to $8.3 million for the first quarter of 2020, including $0.1 million of stock-based compensation expense.

As of March 31, 2021, Praxis had 38.6 million shares of common stock outstanding.

About Praxis
Praxis Precision Medicines is a clinical-stage biopharmaceutical company translating genetic insights into the development of therapies for central nervous system disorders (CNS) characterized by neuronal imbalance. Praxis is applying insights from genetic epilepsies to broader neurological and psychiatric disorders, using our understanding of shared biological targets and circuits in the brain. Praxis has established a broad portfolio, including multiple disclosed programs across CNS disorders including depression, epilepsy, movement disorders and pain syndromes, with three clinical-stage product candidates. For more information, please visit https://praxismedicines.com/ and follow us on LinkedIn and Twitter.

Forward-Looking Statements
This press release may contain 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 and plans for presenting pre-clinical and clinical data, projections regarding future revenues and financing performance, our long-term growth, cash, cash equivalents and marketable securities, the anticipated timing of our clinical trials and regulatory filings, the development of our product candidates and advancement of our preclinical programs, the timing, progress and success of our collaborations, 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 and in the availability and timing of data from ongoing clinical trials; whether interim results from a clinical trial will be predictive of the final results of the trial; whether results from preclinical studies or earlier clinical studies will be predictive of the results of future trials; the expected timing of submissions for regulatory approval or review by governmental authorities; regulatory approvals to conduct trials or to market products; whether Praxis' cash resources will be sufficient to fund Praxis' foreseeable and unforeseeable operating expenses and capital expenditure requirements; 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, Praxis' timelines for regulatory submissions and Praxis' financial position; and other risks concerning Praxis' programs and operations are described in additional detail in its Annual Report on Form 10-K for the year ended December 31, 2020 and other subsequent filings made with the Securities and Exchange Commission from time to time. Although Praxis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Praxis. As a result, you are cautioned not to rely on these forward-looking statements. Any forward-looking statement made in this press release speaks only as of the date on which it is made. Praxis undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future developments or otherwise.

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

	March 31, 2021	December 31, 2020
Assets		
Cash and cash equivalents	$ 131,152	$ 296,608
Marketable securities	139,659	—
Prepaid expenses and other current assets	7,753	5,718
Property and equipment, net	109	82
Operating lease right-of-use assets	571	754
Other non-current assets	9	15
Total assets	$ 279,253	$ 303,177
Liabilities and stockholders' equity		
Accounts payable	$ 5,774	$ 4,088
Accrued expenses	7,386	10,869
Operating lease liabilities	578	763
Common stock	4	4
Additional paid-in capital	442,524	437,007
Accumulated other comprehensive loss	(86)	—
Accumulated deficit	(176,927)	(149,554)
Total liabilities and stockholders' equity	$ 279,253	$ 303,177

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

	Three Months Ended March 31,	
	2021	**2020**
Operating expenses:		
Research and development	$ 17,929	$ 6,868
General and administrative	9,490	1,601
Total operating expenses	27,419	8,469
Loss from operations	(27,419)	(8,469)
Other income:		
Interest income, net	46	128
Total other income	46	128
Loss before benefit from income taxes	(27,373)	(8,341)
Benefit from income taxes	—	11
Net loss	$ (27,373)	$ (8,330)
Accretion and cumulative dividends on redeemable convertible preferred stock	—	(2,064)
Gain on repurchase of redeemable convertible preferred stock	—	493
Net loss attributable to common stockholders	$ (27,373)	$ (9,901)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.71)	$ (6.08)
Weighted average common shares outstanding, basic and diluted	38,470,710	1,629,340


PRAXIS
CORPORATE
OVERVIEW
May 2021
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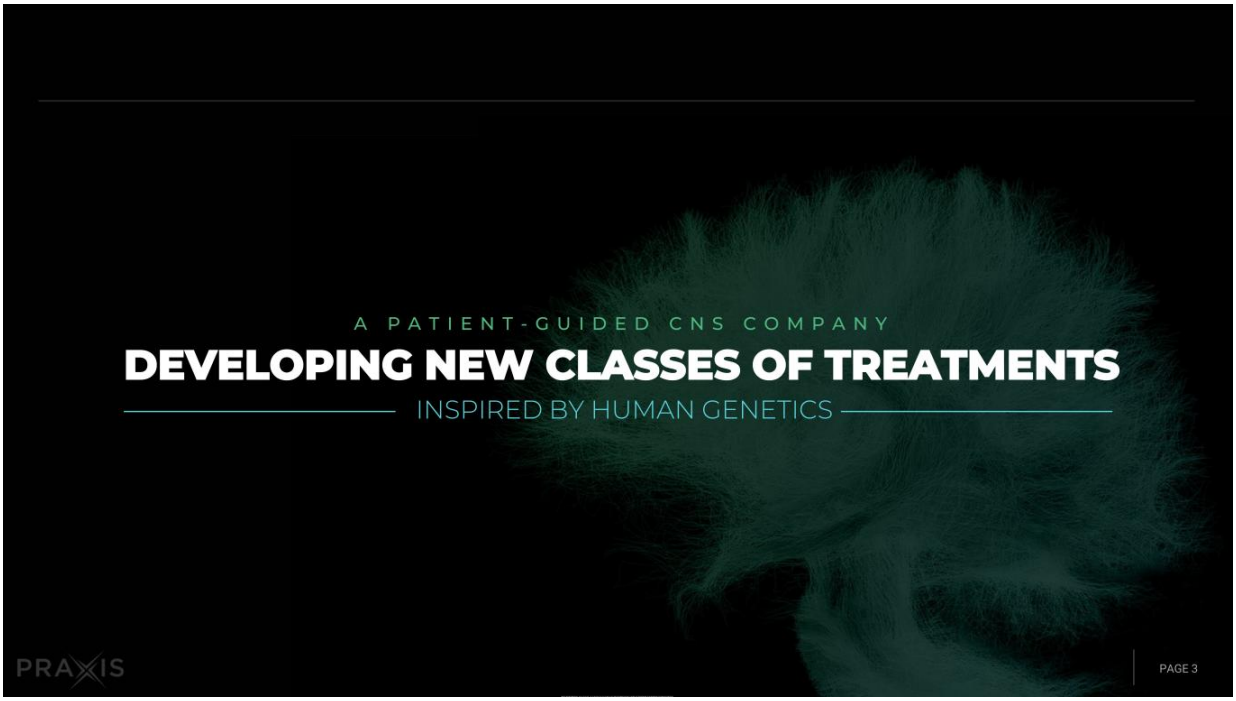
Forward-looking statements

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

For further information regarding the risks, uncertainties and other factors that may cause differences between Praxis' expectations and actual results, you should review the "Risk Factors" section of our Annual Report on Form 10-K filed for the period ended December 31, 2020 and subsequent 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 Praxis believes 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.


A PATIENT-GUIDED CNS COMPANY
DEVELOPING NEW CLASSES OF TREATMENTS
INSPIRED BY HUMAN GENETICS
PRAXIS
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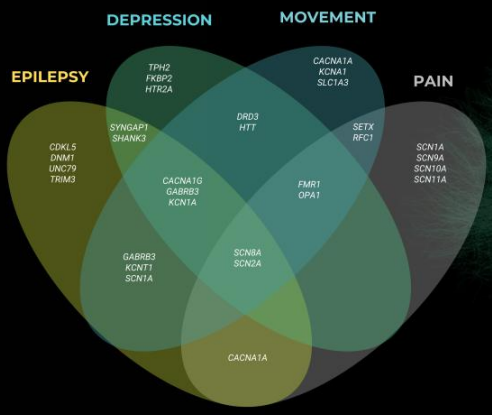
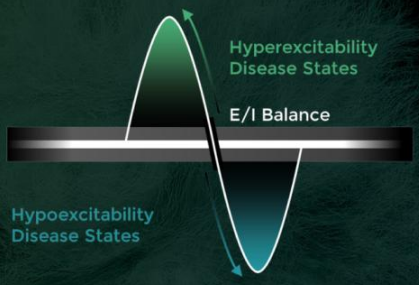
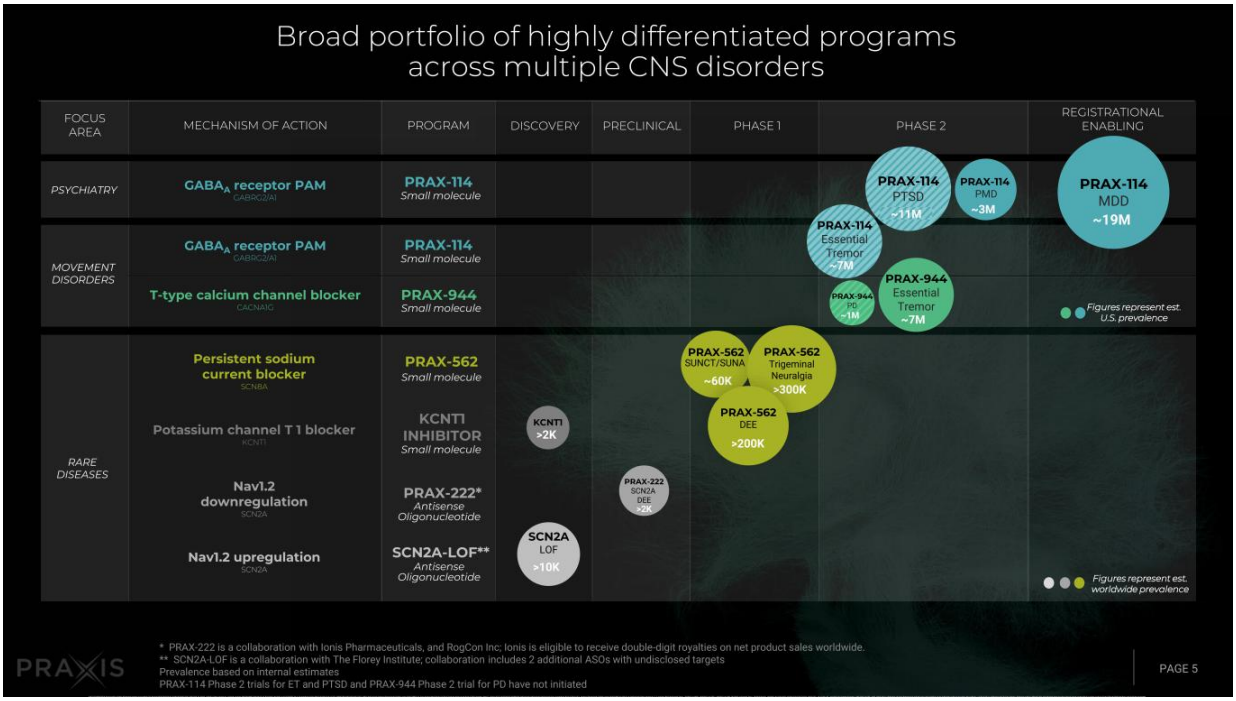
The biology of epilepsy offers insights into brain function for CNS disorders

Targets Elucidated By Genetics



Targeting Common & Rare Diseases Connected By Neuronal Imbalance





* PRAX-222 is a collaboration with Ionis Pharmaceuticals, and RogCon Inc; Ionis is eligible to receive double-digit royalties on net product sales worldwide.
** SCN2A-LOF is a collaboration with The Florey Institute; collaboration includes 2 additional ASOs with undisclosed targets
Prevalence based on internal estimates
PRAX-114 Phase 2 trials for ET and PTSD and PRAX-944 Phase 2 trial for PD have not initiated

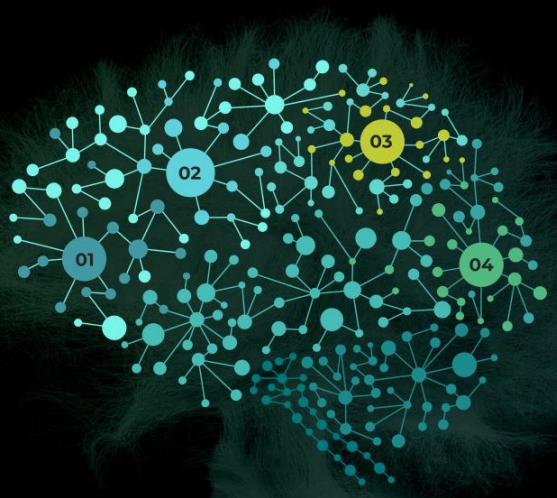
Leveraging genetics to efficiently translate insights into therapies

01 **Targets identified through genetics**

02 **Translational tools to inform development**

03 **Efficient, rigorous clinical development paths to PoC**

04 **Patient-guided development strategies**



Substantial potential for value creation across the portfolio

MULTIPLE POTENTIAL VALUE-CREATING MILESTONES
EXPECTED WITHIN THE NEXT 12+ MONTHS

MID 2021	2H 2021	1H 2022	2H 2022
PRAX-114 Initiate Phase 2 Adjunctive MDD Trial	**PRAX-114** Phase 2a PMD Topline	**PRAX-114** Phase 2/3 Monotherapy MDD Aria Study Topline	**PRAX-114** Phase 2 PTSD Topline
PRAX-944 Phase 2a ET Topline	**PRAX-944** Initiate Phase 2 Randomized Controlled ET Trial	**PRAX-114** Phase 2 Adjunctive MDD Topline	**PRAX-114** Phase 2 ET Topline
PRAX-562 Phase 1 Safety, Tolerability & PK	**PRAX-114** Initiate Phase 2 PTSD Trial	**PRAX-944** Initiate Phase 2 PD Trial	**PRAX-944** Phase 2 Randomized Controlled ET Topline
	PRAX-114 Initiate Phase 2 ET Trial	**PRAX-562** Initiate Phase 2 DEE Trial	
	PRAX-562 Initiate Phase 2 Adult Cephalgia Trial	**PRAX-222** Initiate Phase 1/2 SCN2A-DEE Trial	
	PRAX-222 Complete IND-enabling Toxicology Studies for PRAX-222		
	KCNT1 INHIBITOR Nominate Development Candidate for KCNT1		

PRAXIS


PRAX-114
GABA$_A$ Receptor PAM
PSYCHIATRY & MOVEMENT DISORDERS
Depression
Post-traumatic Stress Disorder
Essential Tremor
UPCOMING MILESTONES
MID 2021
Initiate Ph 2 Adjunctive MDD Trial
2H 2021
Ph 2a PMD Topline
2H 2021
Initiate Ph 2 PTSD Trial
2H 2021
Initiate Ph 2 ET Trial
1H 2022
Ph 2/3 Monotherapy MDD Aria Study Topline
1H 2022
Ph 2 Adjunctive MDD Topline
2H 2022
Ph 2 PTSD Topline
2H 2022
Ph 2 ET Topline
PRAXIS
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Major depressive disorder is a growing and debilitating disorder with substantial unmet need despite numerous treatment options

~19 million Americans and an estimated 300 million people worldwide affected by MDD

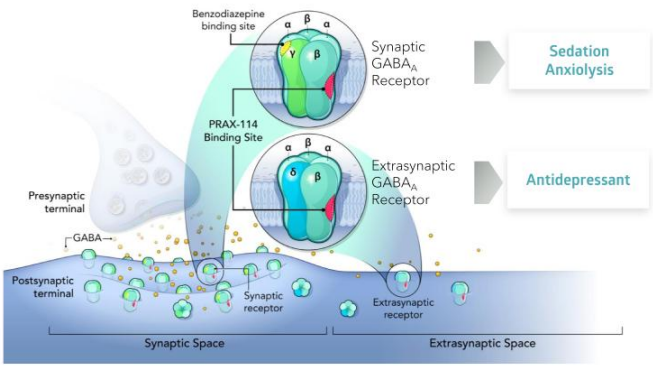
Slow onset of action for existing treatment options

Low response rate

Limiting safety profile can lead to discontinuation of treatment

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

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



GABA: Gamma-aminobutyric acid; $GABA_A$ PAMs: $GABA_A$ receptor positive allosteric modulators

PRAX-114 shows 10.5-Fold greater potentiation of extrasynaptic than synaptic $GABA_A$ receptors

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

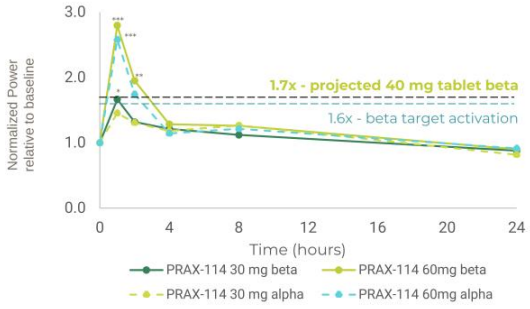
$\alpha_4\beta_3\delta$: extrasynaptic $GABA_A$ receptor **$\alpha1\beta_2\gamma_2$:** synaptic $GABA_A$ receptor

* Equivalent of full activation by GABA

Source: PRAXIS data

Extrasynaptic $GABA_A$ preference allows PRAX-114 the potential to achieve high-levels of GABAergic activation with improved tolerability

PRAX-114 shows robust qEEG signal and target activation



N= 7-9 human subjects per dose, PRAX-114 only p compared to placebo control, *p < 0.05, ** p < 0.01, *** p < 0.001

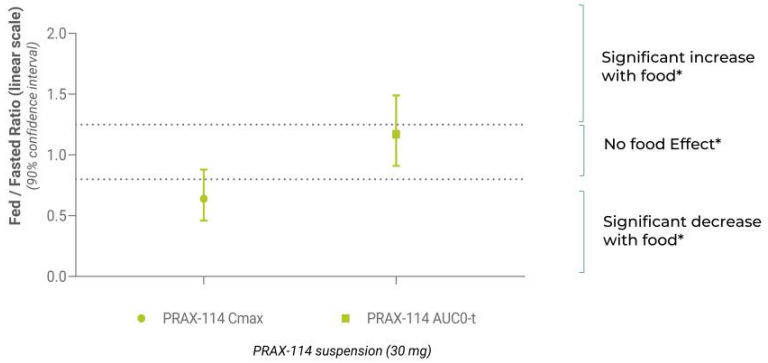
No MTD identified up to 80mg

Tolerability profile maintained throughout dose escalation

Exposure-dependent rates of somnolence resolved 1 to 3 hours post-dosing, consistent with peak concentrations

PRAX-114 can be dosed at bedtime with or without food

Effect of high-fat meal on pharmacokinetics



PRAX-114 suspension (30 mg)

*Definition of food effect from FDA guidance - Assessing the Effects of Food on Drugs in INDs and NDAs

PRAX-114 phase 2a: rapid and marked improvement in depression scores

Phase 2a MDD combined* HAM-D monotherapy & adjunctive results

Visit	HAM-D *Monotherapy* Mean (SD) N=11	HAM-D *Adjunctive* Mean (SD) N=35
Day 1 (BL)	25.2 (1.94)	24.7 (2.94)
Day 8 (CFB)	-17.5 (4.95)	-13.5 (7.99)
Day 15 (CFB)	-16.4 (5.75)	-12.7 (6.88)

Phase 2a MDD combined* HAM-A anxiety and HAM-D insomnia item results

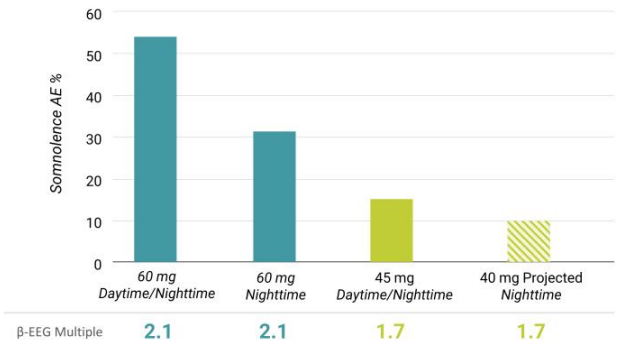
Visit	HAM-A *Anxiety Rating Scale* Mean (SD) N=46	HAM-D *Insomnia Item Total (max score of 6)* Mean (SD) N=46
Day 1 (BL)	22.0 (4.08)	4.1 (1.4)
Day 8 (CFB)	-12.0 (7.53)	-2.8 (1.9)
Day 15 (CFB)	-11.1 (6.66)	-3.1 (1.67)

PRAXIS

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

Low rates of somnolence with PRAX-114 at targeted exposure level

Estimated somnolence rate of approximately 10% for 40 mg tablet (1.7x beta power) administered at nighttime

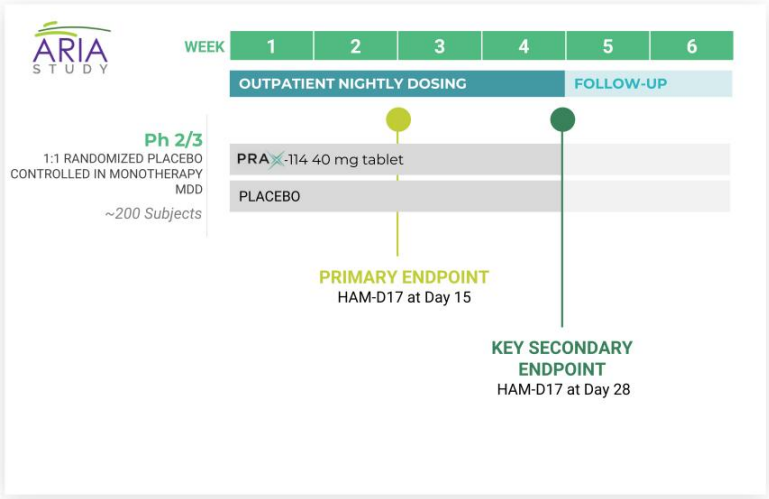


β-EEG Multiple	2.1	2.1	1.7	1.7

No evidence of decreased alertness in the morning after administration of PRAX-114 in Phase 2a trial*

*The Modified Observer's Assessment of Alertness/Sedation Scale (MOAA/S) was administered during the inpatient phase of Part A of the Phase 2a to assess the potential for daytime somnolence

PRAX-114 monotherapy MDD Aria Study topline data expected 1H 2022



PHASE 2/3

First of two registrational trials for monotherapy MDD

KEY INCLUSION CRITERIA

Ages 18-65
HAM-D17 ≥ 23
At least one prior episode of MDD

KEY EXCLUSION CRITERIA

Treatment-resistant depression
Current antidepressant treatment

PRAX-114 has broad potential in psychiatry and movement disorders

Dysfunction of GABA pathway is associated with chronic stress and symptoms of PTSD

11M
ADULT PTSD ESTIMATED US PREVALENCE

Post-traumatic Stress Disorder is a debilitating psychiatric disorder that leads to social, occupational and interpersonal dysfunction

Profound unmet need, meaningful link to PRAX-114 MOA, and complementarity to MDD program

Extrasynaptic $GABA_A$ receptors are associated with anti-tremor activity in ET

7M
ESSENTIAL TREMOR ESTIMATED US PREVALENCE

$GABA_A$ PAM neuroactive steroids are **clinically validated** for the treatment of **essential tremor**

PRAX-114 extrasynaptic $GABA_A$ preference has demonstrated a **wide therapeutic window and well-tolerated safety profile** relative to other $GABA_A$ PAMs in the class

Reducing **daytime, action-based tremors** without significant somnolence could provide meaningful impact to quality of life for people living with ET

Potential **complementarity with PRAX-944** for essential tremor


PRAX-944
T-Type calcium channel inhibitor
MOVEMENT DISORDERS
Essential Tremor
Parkinson's Disease
UPCOMING MILESTONES
Mid 2021
Ph2a ET Topline
2H 2021
Initiate Ph2 Randomized Controlled ET Trial
1H 2022
Initiate Ph2 PD Trial
2H 202
Ph2 Randomized Controlled ET Topline
PRAXIS
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PRAX-944 is a selective T-type calcium channel inhibitor for the treatment of Essential Tremor

ET is the most common movement disorder

Characterized by involuntary progressive tremor especially in the hands

Tremor markedly impairs activities of daily living (ADL), including eating, dressing, and speaking

Normal | Parkinson's disease | Essential tremor

Up to 7 million patients in the U.S.

1-2% of the world population lives with essential tremor

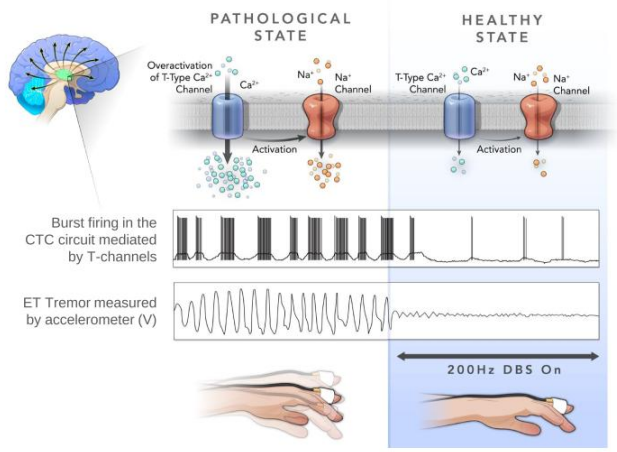
80% estimated discontinuation rate for available therapies due to limited efficacy and poor tolerability

Last option is invasive brain surgery

Source: Louis 2014; Diaz & Louis 2010; Praxis ET Claims Analysis; Uptodate.com; Annals of Indian Academy of Neurology

Large body of clinical, preclinical and human genetic evidence supporting key role of T-type calcium channels in ET

T-Type calcium channels are gatekeepers of neuronal firing patterns



T-type calcium channels drive burst firing in the cerebello-thalamo-cortical (CTC) circuit

Mutations in T-type calcium channels are genetically linked to early onset familial ET

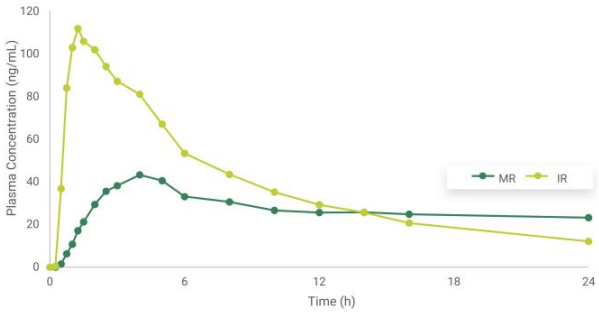
Abnormal neuron burst firing in the CTC circuit correlated with tremor activity in ET patients

Deep Brain Stimulation (DBS) leads to near complete silencing of bursting firing and significant tremor reduction

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

PRAX-944 is designed to enable once daily dosing and a well-tolerated safety profile

Sustained exposure with blunted MR Cmax allows for potential of sustained efficacy and improved tolerability



Mean PRAX-944 Concentration-Time Profiles after single 20 mg Modified Release (MR) and Immediate release (IR) oral doses

MR formulation is well-tolerated

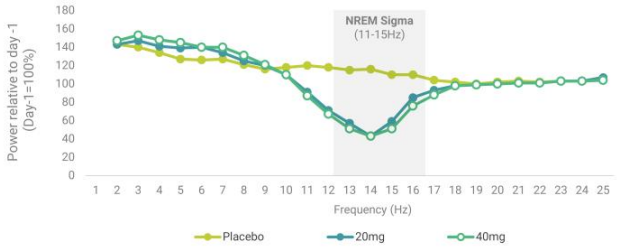
Titration and fit for purpose formulation are key to tolerability profile

No MTD identified up to 120 mg per day

Majority of AEs have been mild, transient and resolved without intervention

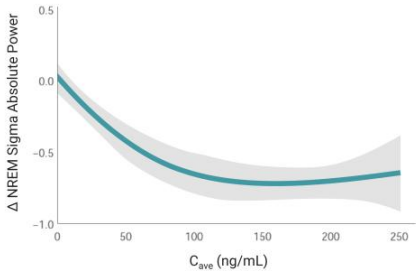
PK-PD analysis suggests that doses of PRAX-944 of up to ~120 mg/day may drive additional pharmacodynamic effect

Robust pharmacodynamic EEG effects in humans



- NREM sigma EEG biomarker is relevant to T-type calcium channel inhibitor mechanism
- Clinically, PRAX-944 demonstrated robust reduction in NREM sigma at 20mg and 40mg

PRAX-944 shows significant pharmacodynamic effect on sigma band EEG power during NREM sleep*

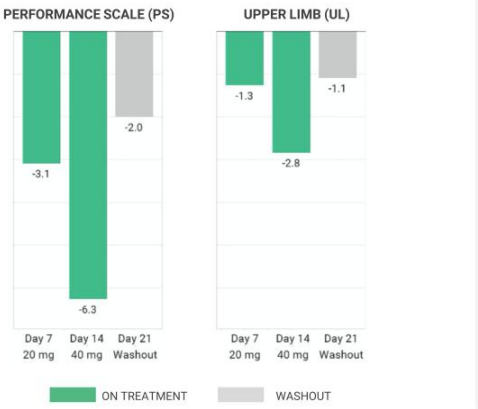


- Effect observed over wide, well-tolerated dose range from 5 mg to 120 mg
- Dose/concentration response effect justifies assessing dose levels up to 120 mg

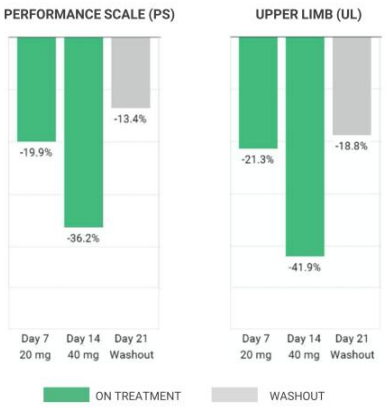
*C_{avg} shows average concentration over 24-hour dose interval at dose range of 5 – 120 mg/day

PRAX-944 phase 2a ET Part A data shows dose dependent reduction in tremor amplitude

Change from baseline in TETRAS score (N=6)

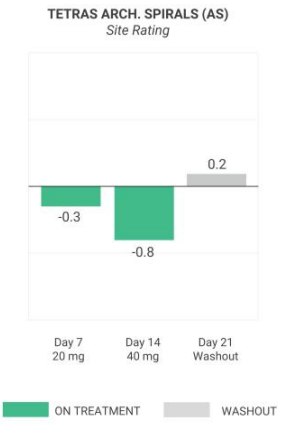


Percent change in tremor amplitude (N=6)

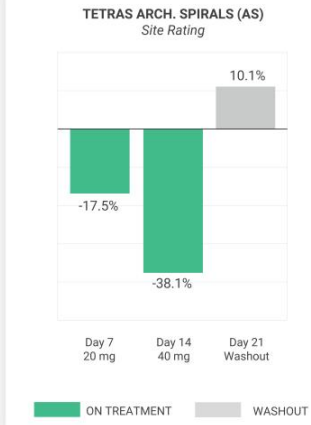


PRAX-944 phase 2a ET Part A Archimedes spiral data indicates functional improvement

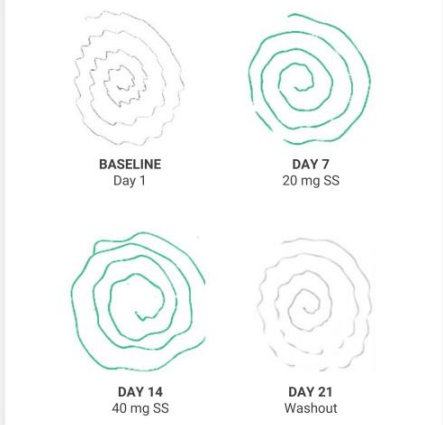
Change from baseline in TETRAS score (N=6)



Percent change in tremor amplitude (N=6)

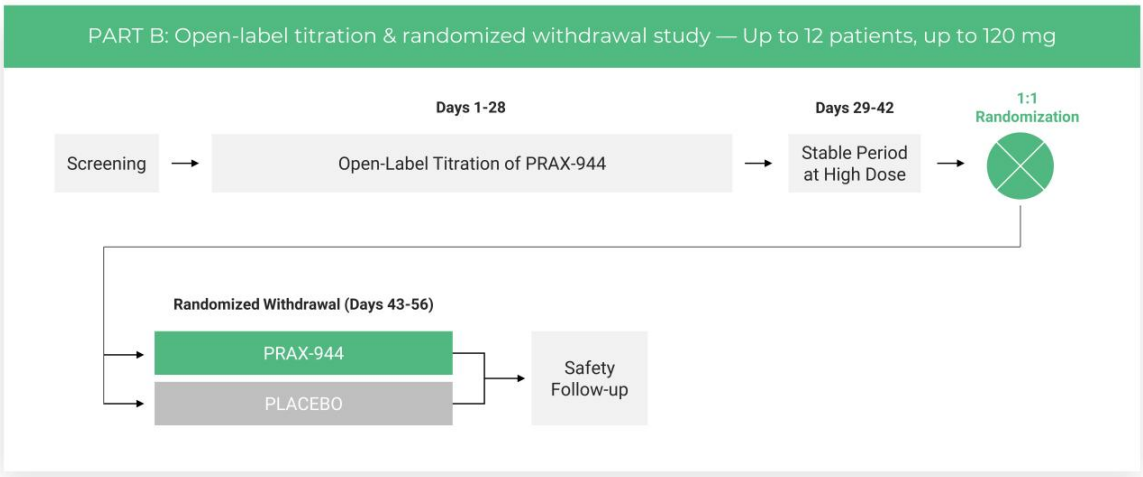


PRAX-944 Archimedes spiral*



*PRAX-944 phase 2a Part A participant dominant hand Archimedes spirals

PRAX-944 phase 2a ET Part B clinical trial design




PRAX-562
Persistent Sodium Channel Blocker
RARE DISEASES
Adult Cephalgias
Pediatric Epilepsies (DEEs)
UPCOMING MILESTONES
Mid 2021
Ph 1 Safety, Tolerability & PK
2H 2021
Initiate Ph 2 Adult Cephalgia Trial
1H 2022
Initiate Ph 2 DEE Trial
PRAXIS
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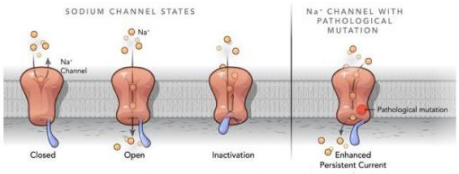
Block of persistent sodium current can reduce neuronal hyperexcitability and impact multiple disease states

Standard sodium channel blockers target peak sodium current and disrupt AP, leading to side effects

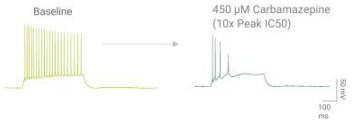
- Standard sodium channel blockers are an important class of medicines in neurology and psychiatry, broadly used in epilepsy, pain, migraine, and bipolar disorder
- All standard NaV blockers target peak sodium current
- In general, efficacy is limited by side effects

Depakote divalproex sodium
Tegretol-XR carbamazepine extended-release tablets
Lidoderm lidocaine patch 5%
Oxtellar XR
Dilantin extended phenytoin sodium capsules, USP
EXPAREL
Lamictal

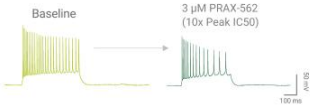
Modulation of persistent sodium current reduces hyperexcitability without disrupting AP



Carbamazepine Representative AP Traces



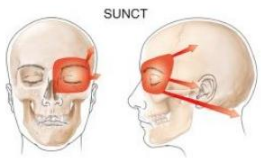
PRAX-562 Representative AP Traces



Source: Schachter et al. antiseizure drugs UptoDate 2020, Praxis data

PRAX-562 has broad potential in rare CNS conditions

SUNCT, SUNA & TN are devastating headache disorders with limited treatment options



SUNCT and SUNA Cephalgias are devastating primary headaches highly responsive to IV sodium channel blockers

Trigeminal Neuralgia is characterized by intense, stabbing, electric-shock pain typically in the lower face and jaw, usually on one side of the face

DEE is a group of monogenic disorders with severe seizure, developmental delay & high mortality rate

Caused by a single gene mutation

200k+
CHILDREN WITH DEEs WORLDWIDE

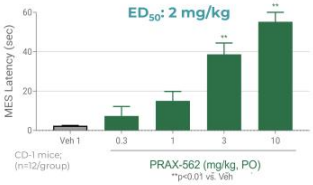
A pathologic feature of many DEEs is the dysregulated neuronal activity leading to hyperexcitability and seizure

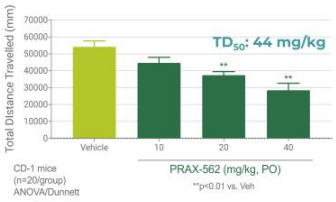
This phenomenon is observed in pediatric epilepsies with an identified genetic cause, such as SCN8A, SCN2A and others

Source: Eltze et al. 2013 ; Howell et al 2018

PRAX-562 mediated persistent current block protects mice from seizure with a wide therapeutic window *in-vivo*

PRAX-562 shows robust anti-seizure activity without impairment of locomotor activity





PRAX-562 showed significantly improved TI as compared to currently prescribed sodium channel blockers

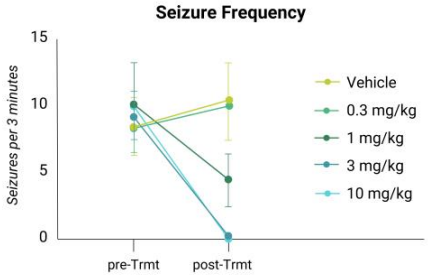
Molecule	Brain Therapeutic Index
PRAX-562	**16.4x**
Carbamazepine	5.9x
Lamotrigine	4.6x

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

PRAX-562 had an increased ratio between drug levels that demonstrated preclinical anti-seizure activity versus those that caused toxicity

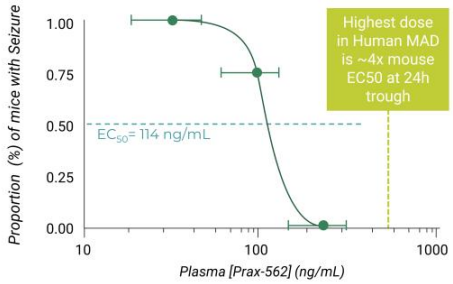
Treatment with PRAX-562 has shown significant reduction of seizures in genetic pediatric epilepsy animal models

PRAX-562 elicited dose-dependent prevention of seizures in SCN2A* mouse model



Baseline seizure frequency was measured for 30 minutes prior to treatment (Pre) and then again 30 minutes after treatment (Post). Symbols represent mean ± SEM, n=6-10 per symbol.

PRAX-562 elicited dose-dependent prevention of seizures in SCN8A* mouse model



PRAX-562 inhibition of audiogenic seizures in D/+ mice

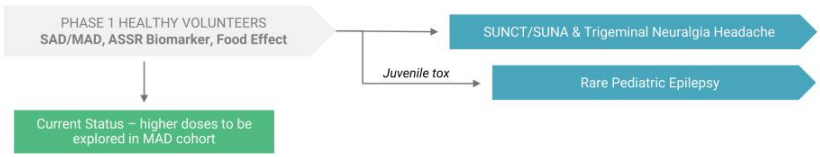
*FDA granted orphan drug and rare pediatric designation for PRAX-562 for treatment of SCN2A-DEE and SCN8A-DEE

PRAX-562 development strategy in headache and pediatric epilepsies

OBJECTIVE

Identify PoC and safety in SUNCT/SUNA & Trigeminal Neuralgia headaches while continuing efforts to expand to rare pediatric epilepsies

Clinical Strategy



HEALTHY VOLUNTEER PHASE 1 SAD/MAD, ASSR, AND FOOD EFFECT

Study Design	▪ Randomized, placebo controlled
Patient Population	▪ ♀ or ♂ 18-55 years of age ▪ Healthy Volunteers
Study Objectives	▪ 1°: Safety and tolerability of single and multiple ascending doses of PRAX-562 in healthy volunteers ▪ 2°: Pharmacokinetics of single and multiple ascending doses of PRAX-562 in healthy volunteers ▪ Exploratory: EEG Auditory Steady-State Response (ASSR)

Substantial potential for value creation across the portfolio

MULTIPLE POTENTIAL VALUE-CREATING MILESTONES
EXPECTED WITHIN THE NEXT 12+ MONTHS

MID 2021	2H 2021	1H 2022	2H 2022
PRAX-114 Initiate Phase 2 Adjunctive MDD Trial	**PRAX-114** Phase 2a PMD Topline	**PRAX-114** Phase 2/3 Monotherapy MDD Aria Study Topline	**PRAX-114** Phase 2 PTSD Topline
PRAX-944 Phase 2a ET Topline	**PRAX-944** Initiate Phase 2 Randomized Controlled ET Trial	**PRAX-114** Phase 2 Adjunctive MDD Topline	**PRAX-114** Phase 2 ET Topline
PRAX-562 Phase 1 Safety, Tolerability & PK	**PRAX-114** Initiate Phase 2 PTSD Trial	**PRAX-944** Initiate Phase 2 PD Trial	**PRAX-944** Phase 2 Randomized Controlled ET Topline
	PRAX-114 Initiate Phase 2 ET Trial	**PRAX-562** Initiate Phase 2 DEE Trial	
	PRAX-562 Initiate Phase 2 Adult Cephalgia Trial	**PRAX-222** Initiate Phase 1/2 SCN2A-DEE Trial	
	PRAX-222 Complete IND-enabling Toxicology Studies for PRAX-222		
	KCNT1 INHIBITOR Nominate Development Candidate for KCNT1		