
PRAXIS
DARE FOR MORE™
CORPORATE OVERVIEW
April 2024

Forward-looking statements

This presentation may contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial conditions, including but not limited to express or implied statements regarding the current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, 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) the timing of and our ability to obtain and maintain regulatory approval of any of our product candidates, (v) our plans to research, discover and develop additional product candidates, (vi) our ability to enter into collaborations for the development of new product candidates, (vii) our ability to establish manufacturing capabilities, and our collaboration partners' abilities to manufacture our product candidates and scale production, (viii) our ability to meet any specific milestones set forth herein, and (ix) the potential addressable market sizes for product candidates. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements.

For further information regarding the risks, uncertainties and other factors that may cause differences between our expectations and actual results, you should review the "Risk Factors" section of our Annual Report on Form 10-K for the year ended December 31, 2023 to be filed 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.

Four pillars guide how we develop medicines

GENETICS

Focus on therapeutic targets identified through human genetics

TRANSLATIONAL TOOLS

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

EFFICIENT & RIGOROUS

Efficient, rigorous clinical development paths to proof-of-concept in humans applying an agile way of working

PATIENT-GUIDED

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

Praxis is positioned to bring more innovation to patients

4

Assets in clinical trials

>$7B

Commercial opportunity across the portfolio

4

Readouts next eighteen months

2

Discovery platforms to optimize drug development

into

2027

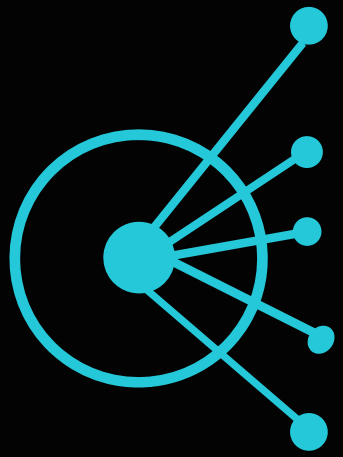
Cash runway

Two platforms to generate optimized therapies for defined patient populations

CEREBRUM™

SMALL MOLECULE PLATFORM

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



Molecule	Indication	Mechanism
ulixacaltamide	Essential Tremor	T-type calcium channel modulator
PRAX-628	Focal Onset Seizures	Sodium channel functional state modulator for broad use
PRAX-562	DEE Epilepsies	Sodium channel functional state modulator for pediatric use
PRAX-020*	KCNT1 Epilepsy	KCNT1 specific inhibitor
PRAX-050	Not disclosed	Not disclosed

SOLIDUS™

ANTISENSE OLIGONUCLEOTIDE (ASO) PLATFORM

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

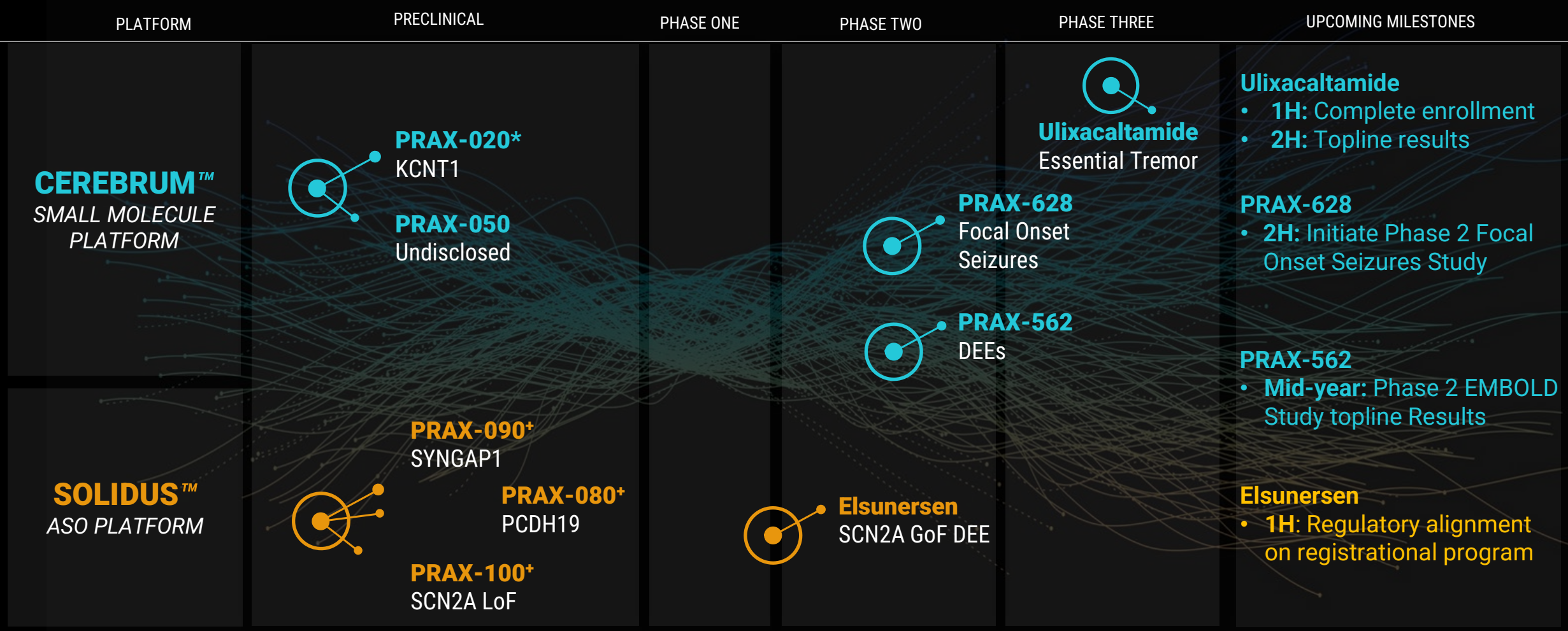
Molecule	Indication	Mechanism
elsunersen	SCN2A GoF	Gapmer ASO
PRAX-080⁺	PCDH19 Mosaic expression	Gapmer ASO
PRAX-090⁺	SYNGAP1 LoF	Splice switching ASO
PRAX-100⁺	SCN2A LoF	Splice switching ASO

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

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

PRAXIS

Four clinical stage assets and multitude of early-stage programs

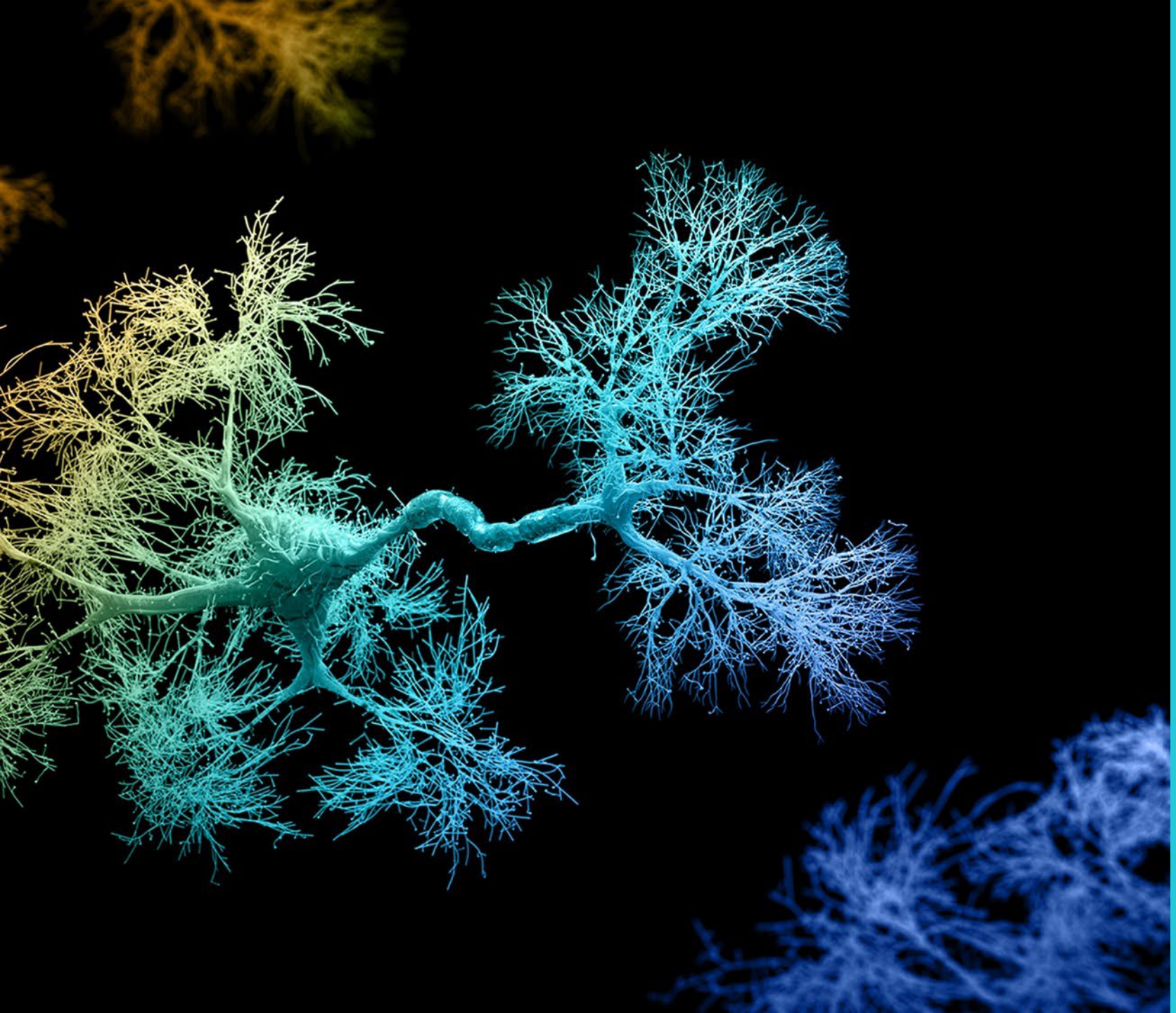


*PRAX-020 (KCNT1) is a research collaboration with UCB

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

CEREBRUM™

SMALL MOLECULE PLATFORM



Ulixacaltamide

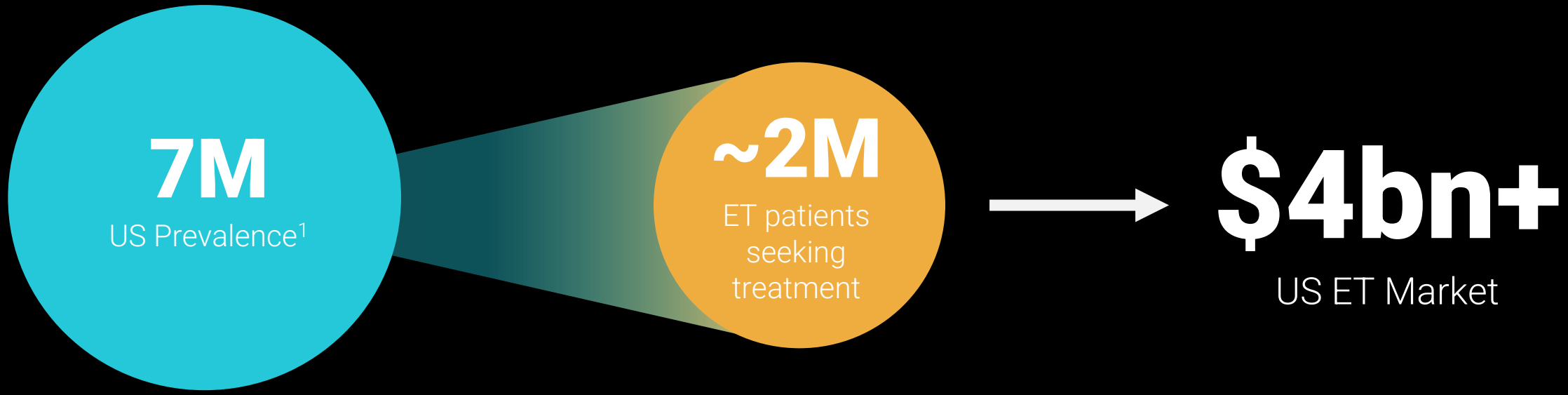
Milestones

1H 2024: Enrollment complete

2H 2024: Topline results

2025: File NDA

Essential tremor market is significantly underserved and ready for disruption



- Essential Tremor (ET) is the most prevalent movement disorder
- People with ET experience significant disruption of their daily activities
- Hallmark feature of ET is action tremor that primarily affects the hands[2,3]
- Almost all ET patients suffer from at least one comorbid condition (e.g., depression, anxiety, sleep disorders, cognitive dysfunction)[4]

Vast majority of the patients are left without any treatment option

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

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

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

11 items from the well-established TETRAS ADL scale

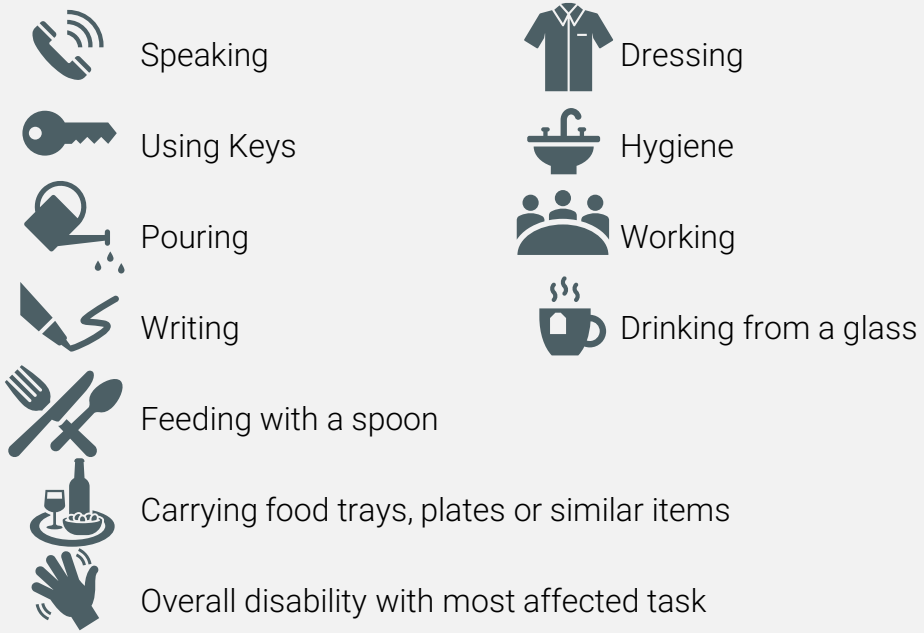
Each item is individually scored, up to a total of 33

0 = Slightly abnormal. Tremor is present but does not interfere with __.

1 = Mildly abnormal. Spills a little.

2 = Moderately abnormal. Spills a lot or changes strategy to complete task.

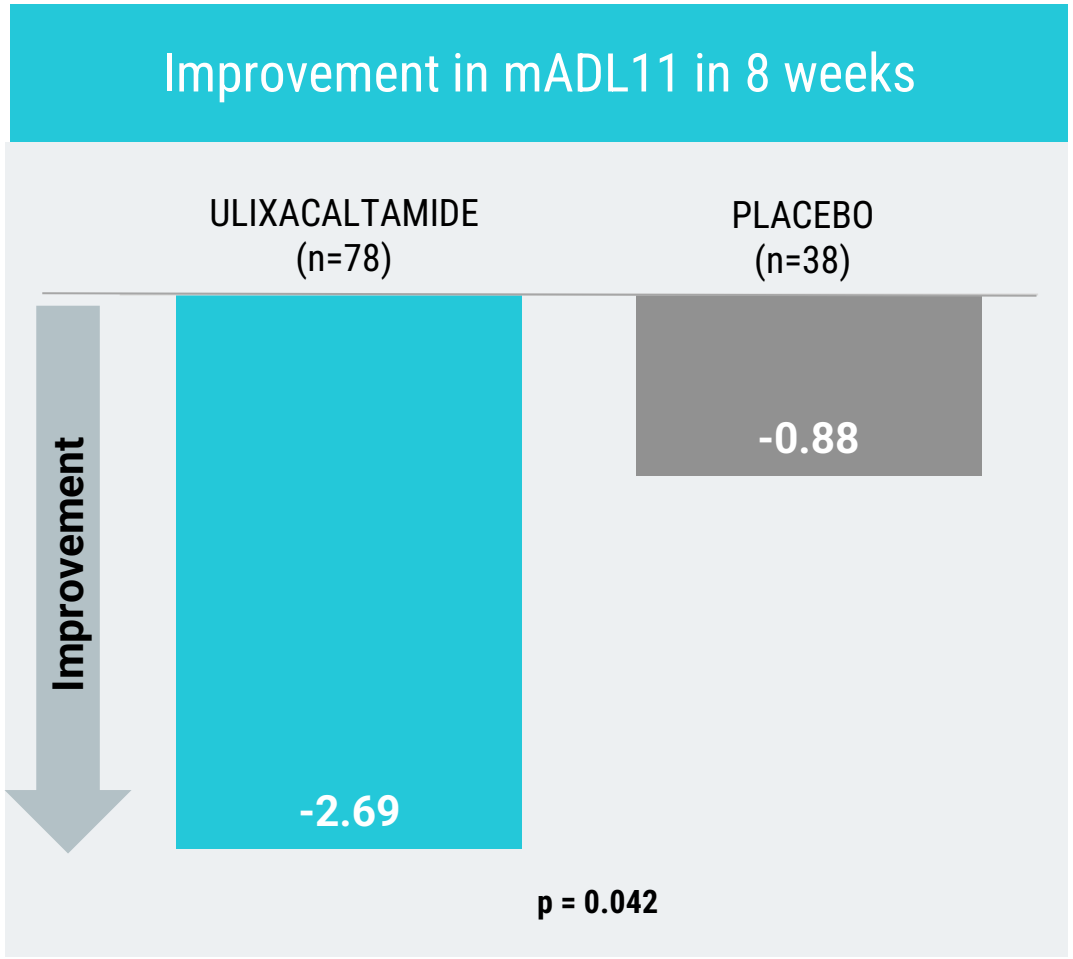
3 = Severely abnormal. Cannot drink from a glass or uses straw or sippy cup.



- Improvement based on regaining function
- Each point reduction provides benefit to a patient
- ADL assessment performed by a physician
- Aligned as primary endpoint for Essential3 studies with FDA

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

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



Validated the clinical hypothesis

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

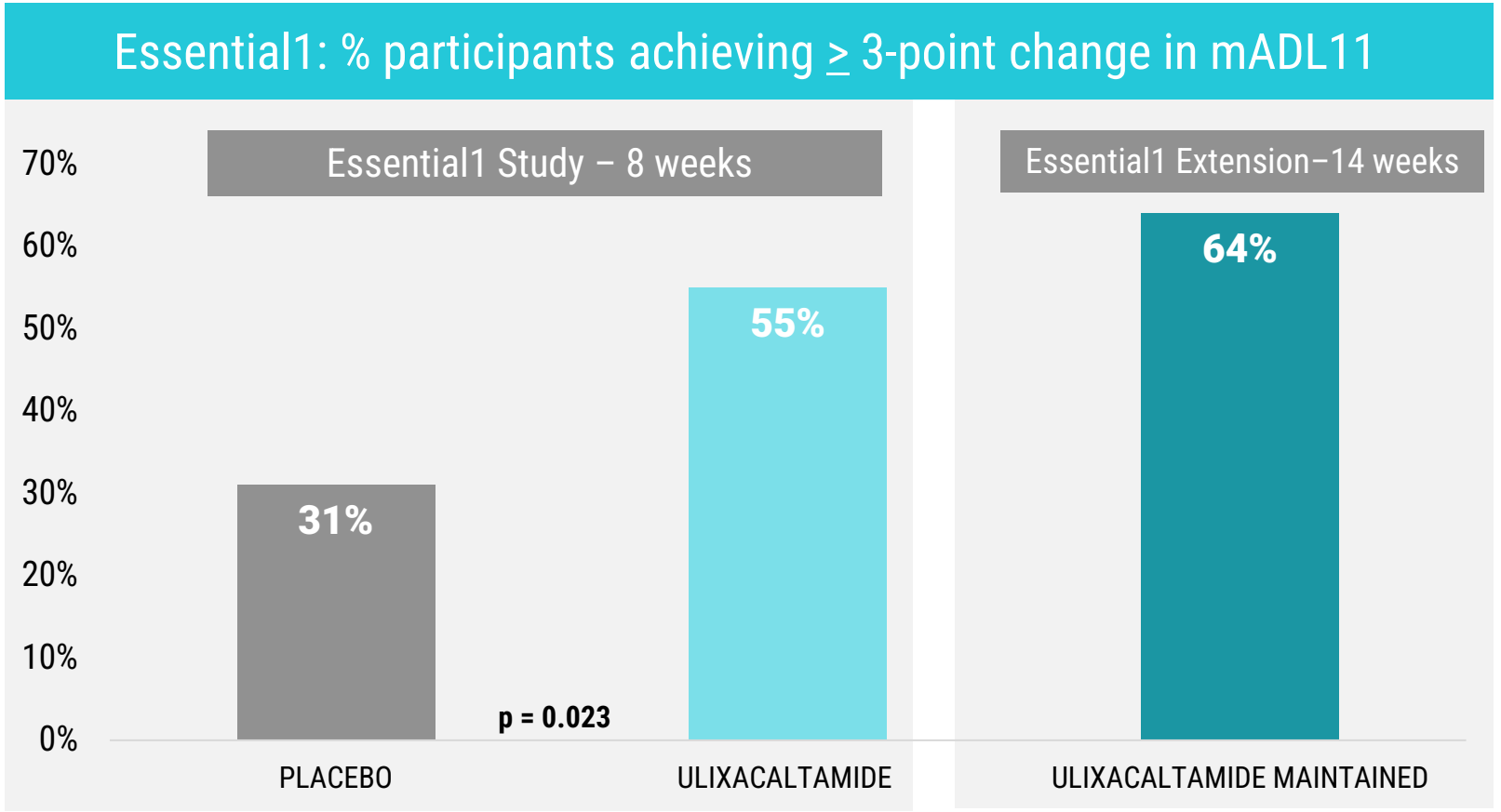
Sets up a clear path to registration

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

Results from Essential1 study, p value is nominal

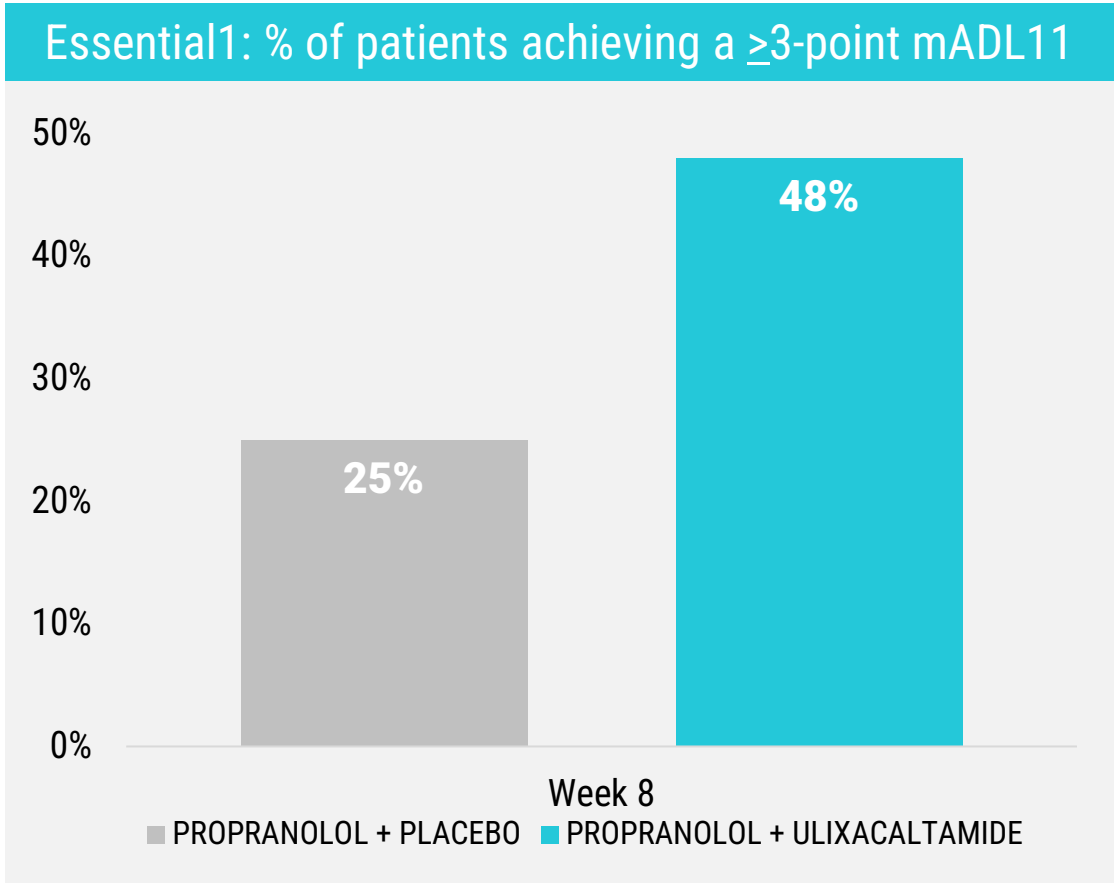
Majority of patients achieved at least a 3-point change in mADL11 at 8 weeks

Durable response in extension study patients who continued through 14 weeks



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

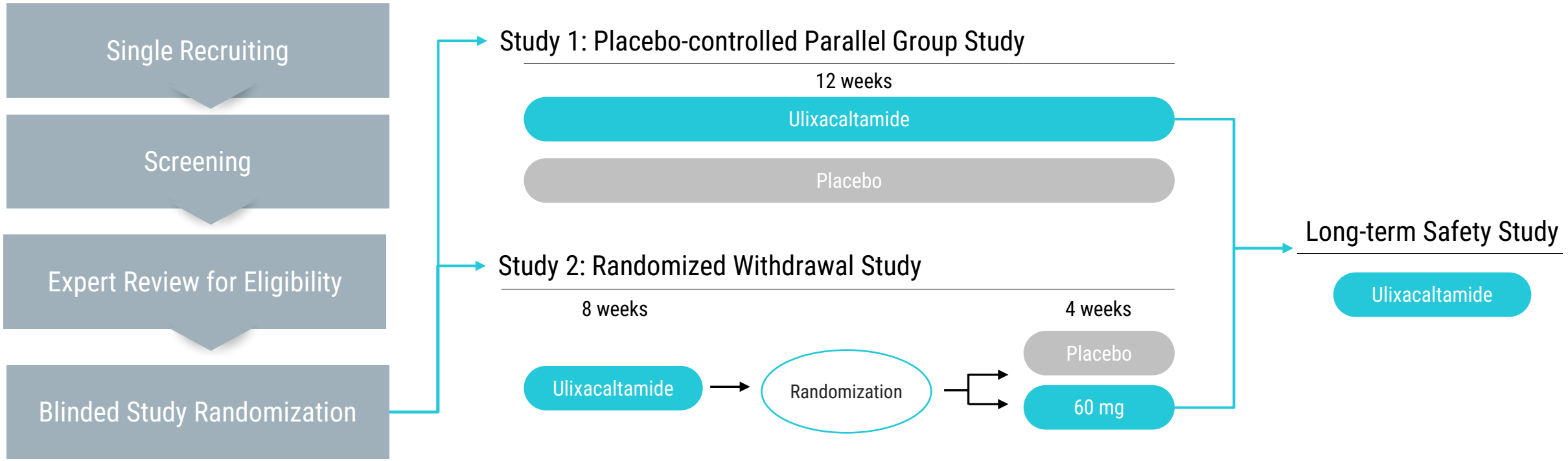
Adding ulixacaltamide benefited more patients on propranolol with ≥ 3-point improvement



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

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

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



ESSENTIAL 3
AN AT-HOME RESEARCH STUDY

Essential3 Program is well powered

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

ESSENTIAL 3
AN AT-HOME RESEARCH STUDY

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

Path to success

De-risked

Trial design based on key learnings from Essential1

Regulatory alignment based on successful End-of-Phase 2 meeting

Efficient

Focused execution

Single protocol: Optimized screening, enrollment, analysis

Streamlined Design

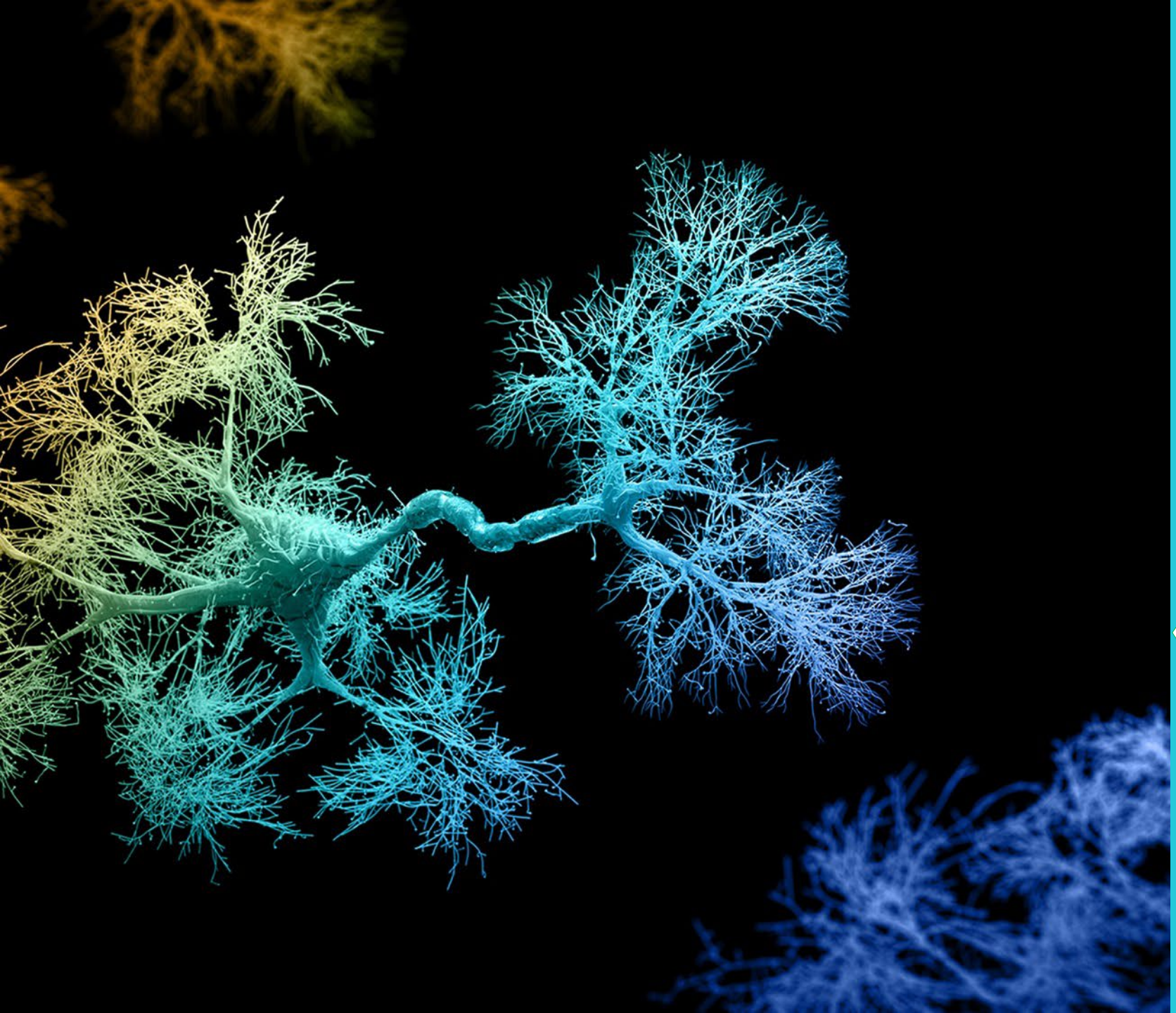
Decentralized study to expand reach and reduce study burden to participants

Patient-driven Approach

mADL11 as a clinically meaningful primary endpoint

NDA Readiness

Clear path to filing in 2025



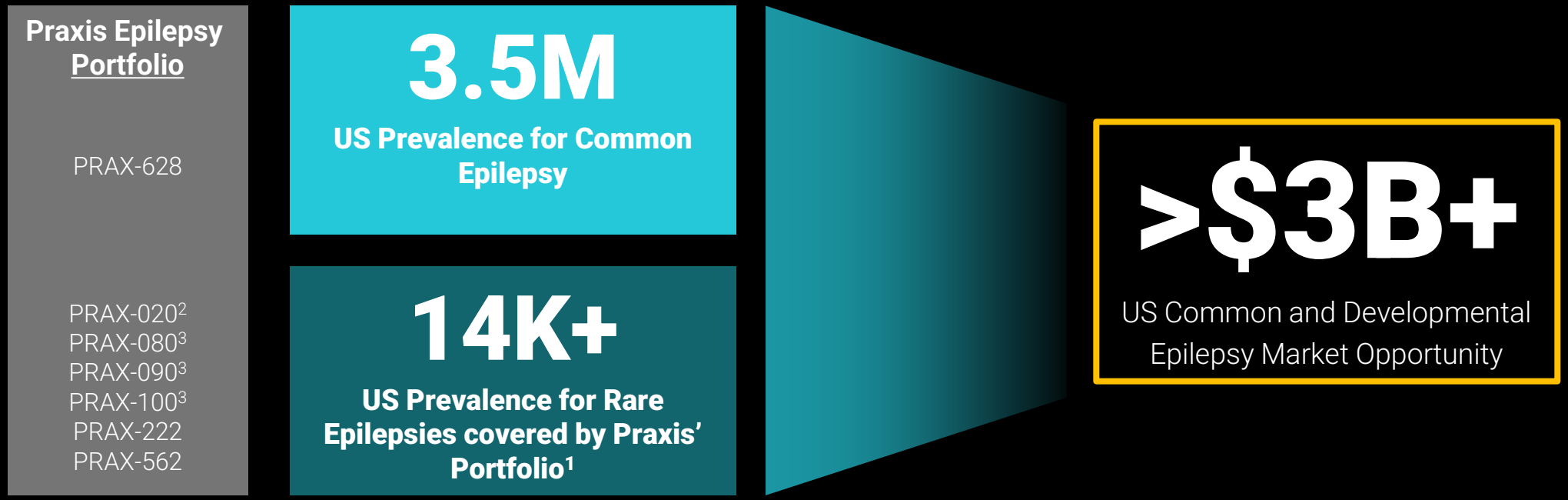
PRAX-628

Milestones

✓ 1Q 2024: Topline results of Phase 2a PPR

2H 2024: Initiate Phase 2b in Focal Onset Seizures

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



[1] SCN2A Gof, SCN2A LoF, SYNGAP1, PCDH19, SCN8A, KCNT1 developmental epilepsies
[2] PRAX-020 (KCNT1) is a research collaboration with UCB
[3] PRAX-080 (PCDH19), PRAX-090 (SYNGAP1) & PRAX-100 (SCN2A-LoF) ASOs are a collaboration with The Florey Institute of Neuroscience and Mental Health

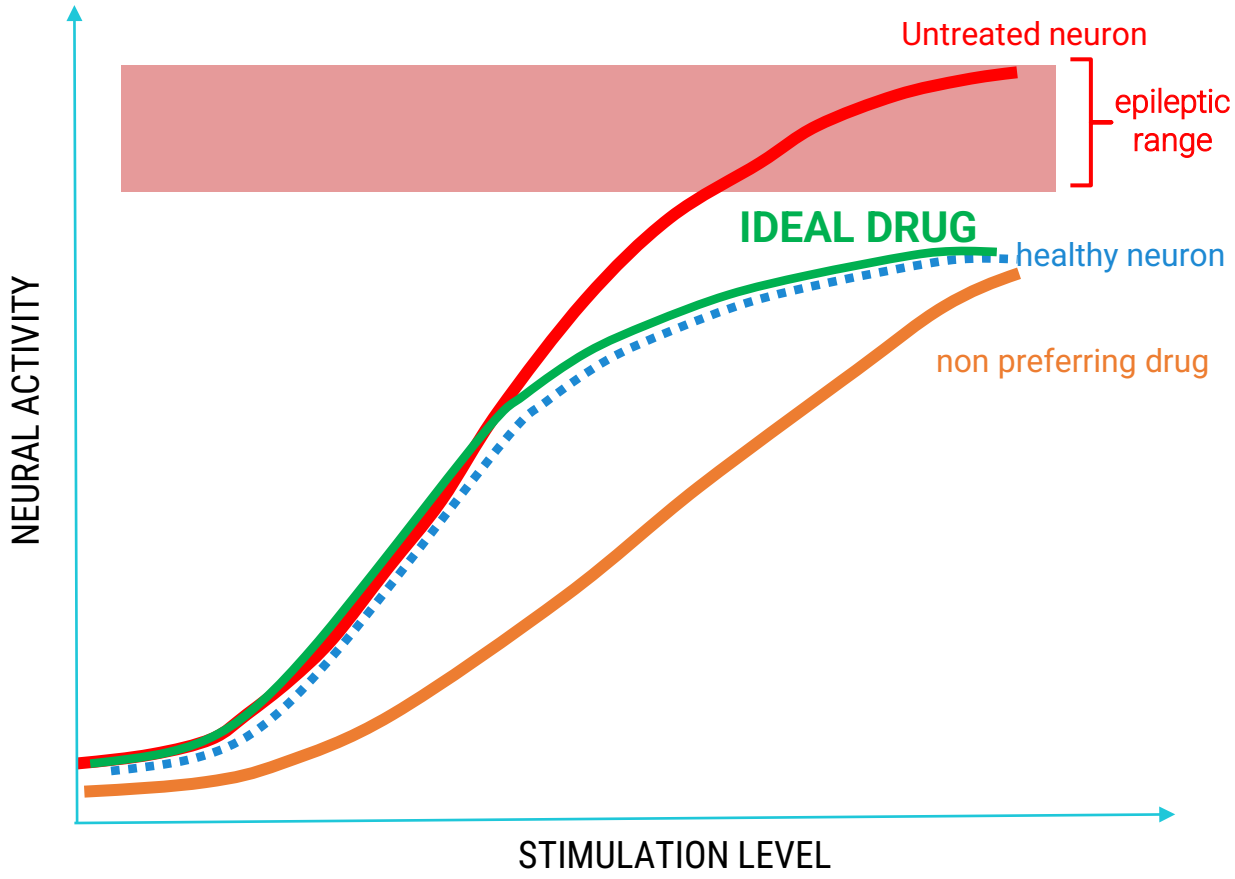
PRAX-628: Precision medicine therapeutic for Focal Onset Seizures

Differentiated Profile

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

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

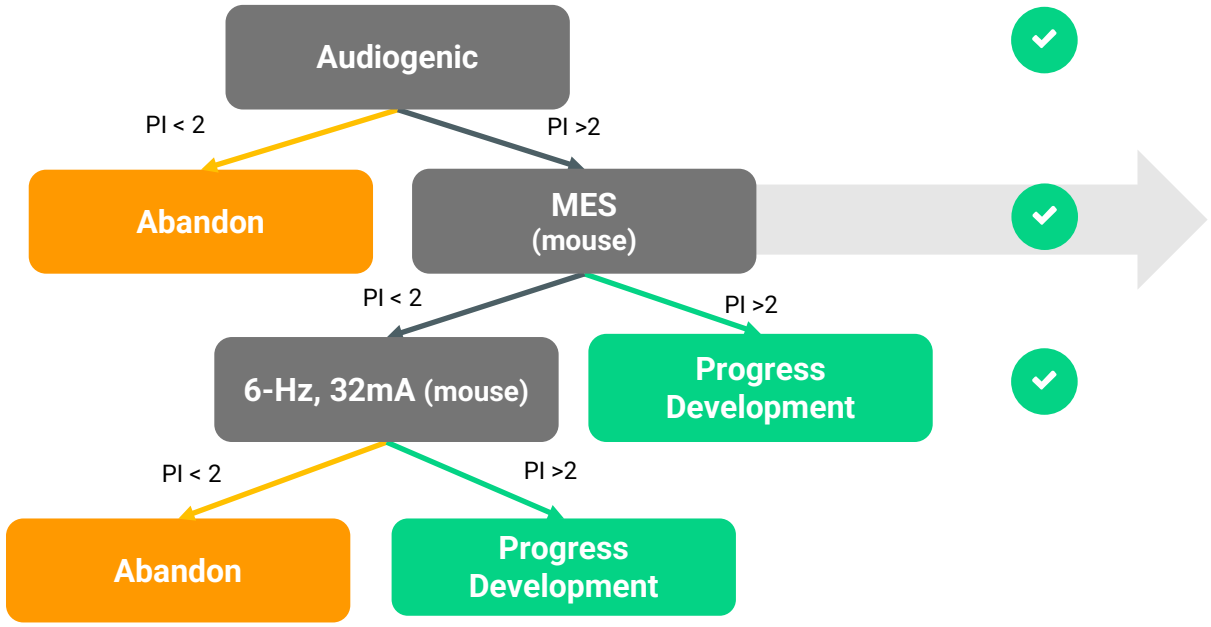
Goal: Preferential action against neuronal hyperexcitability



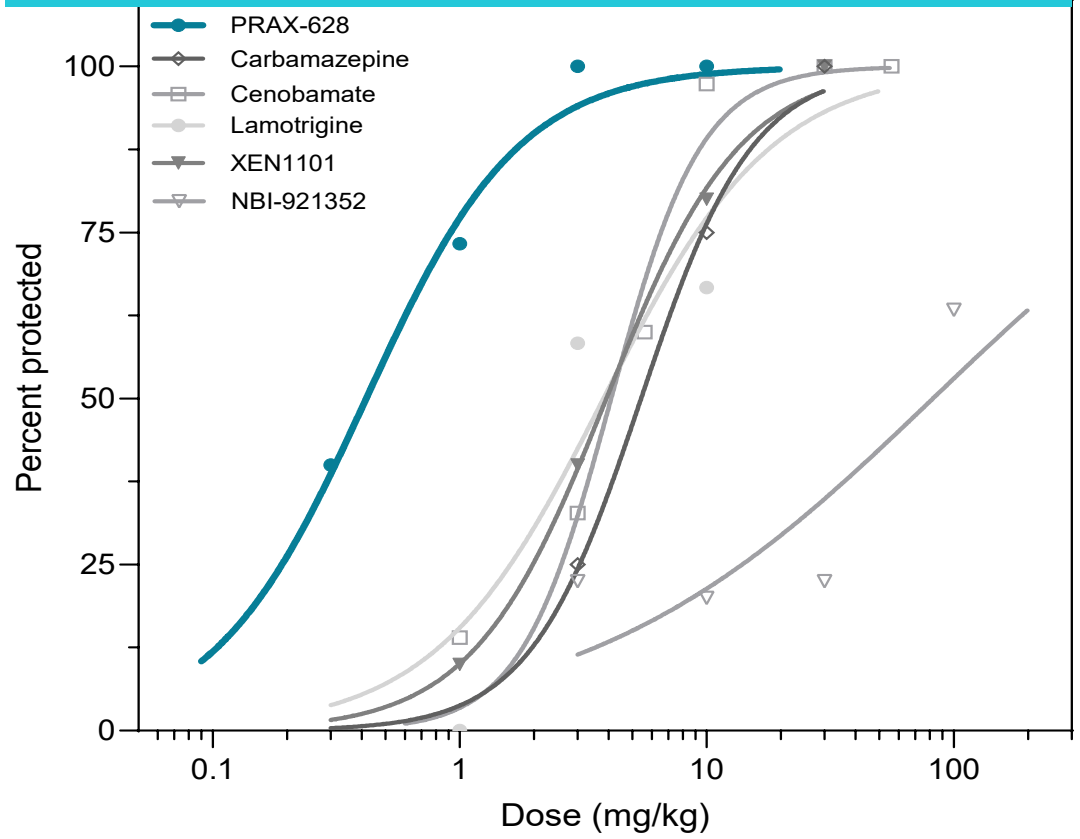
PRAX-628 shows a differentiated pre-clinical profile

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

PRAX-628 Results[2]



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



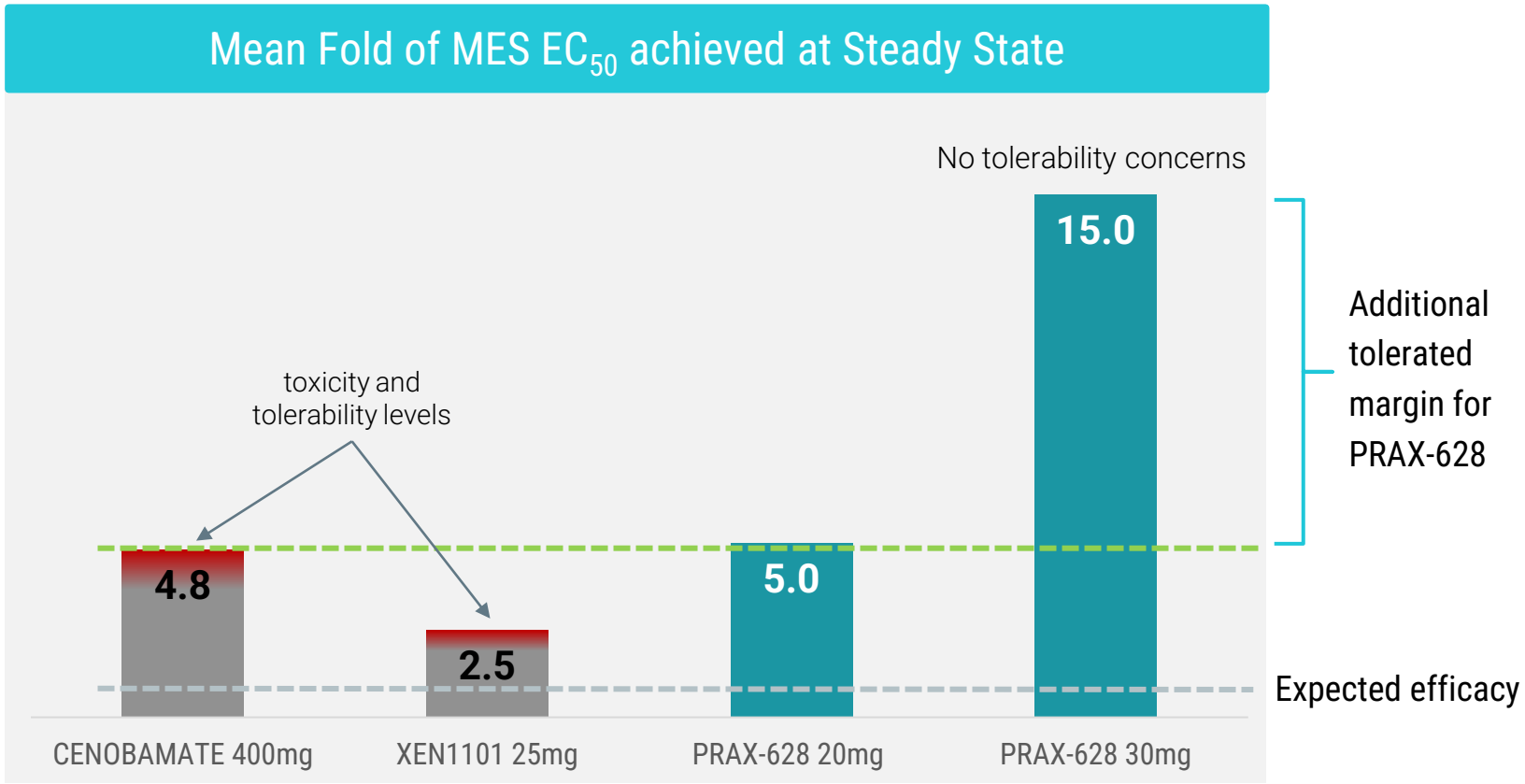
Protective index (PI) measured as tolerability / efficacy (TD50 / ED50); MES = maximal electroshock seizure

1. https://praxismedicines.com/wp-content/uploads/2023/12/Anderson_AES2023_Predictive-Validity_Poster_Final.pdf; 2. Praxis data on file

3. https://praxismedicines.com/wp-content/uploads/2023/12/Kahlig_AES2023_628-In-Vivo_Poster_Final.pdf

Ability to significantly exceed therapeutic concentrations while well tolerated

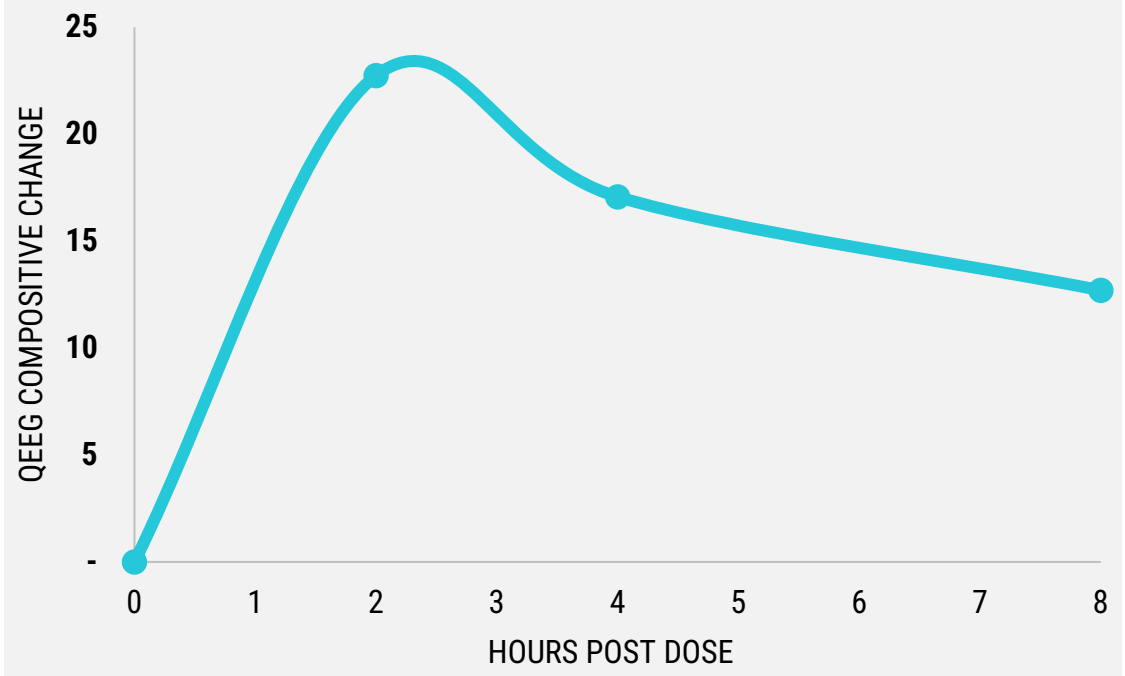
PRAX-628 has unprecedented margins over best-in-class ASMs based on MES efficacy and clinical tolerability in humans



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

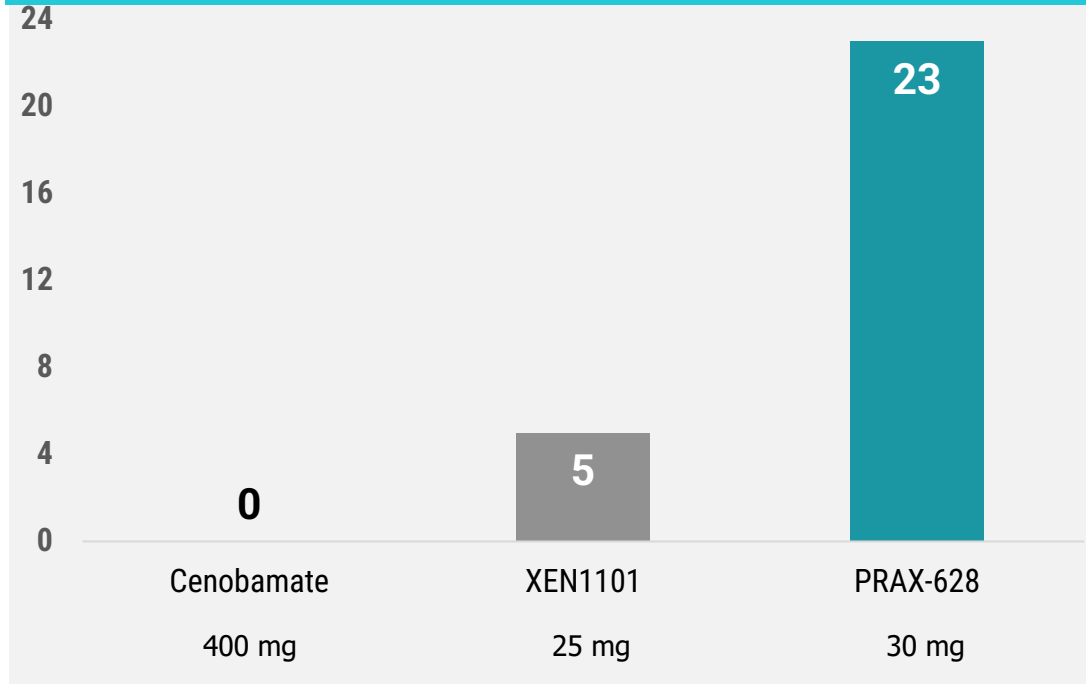
Phase 1 study demonstrated brain activity and rapid achievement of therapeutic concentrations

PRAX-628 composite qEEG change



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

Hours of day 1 drug coverage



- PRAX-628 achieves nearly complete coverage on Day 1

The Phase 2 PRAX-628 Photo Paroxysmal Response (PPR) study demonstrated proof of concept, and de-risks advancing to efficacy studies in Focal Onset Seizures

Study Design

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

Study Results

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

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

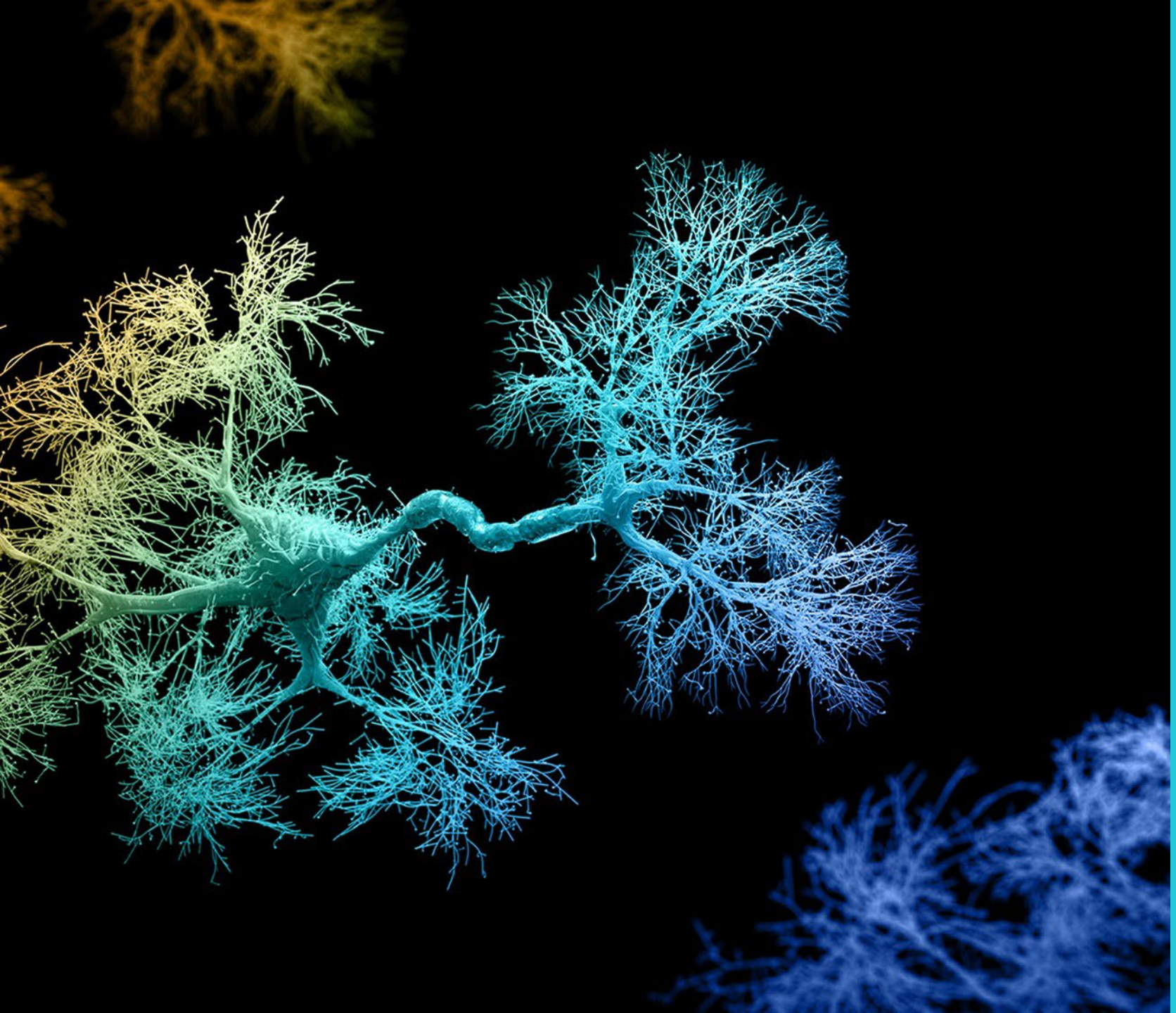
PRAX-628 has presented an ideal precision ASM profile

Ideal Treatment

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

Initiate two (2H 2024, 1H 2025) registration enabling trials in Focal Onset Seizures

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



PRAX-562

Milestones

Mid-2024: Topline results in Phase 2 EMBOLD Study

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

PRAX-562

SCN2A, SCN8A

FORMULATED FOR PEDIATRIC USE

SMALL MOLECULE

FUNCTIONAL STATE MODULATOR

Superior selectivity for disease-state Na_V channel hyperexcitability

Unprecedented therapeutic window with potential for superior safety and efficacy

Convenient auto-titration regimen with stable PK

PRAX-562 Phase 1 summary

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

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

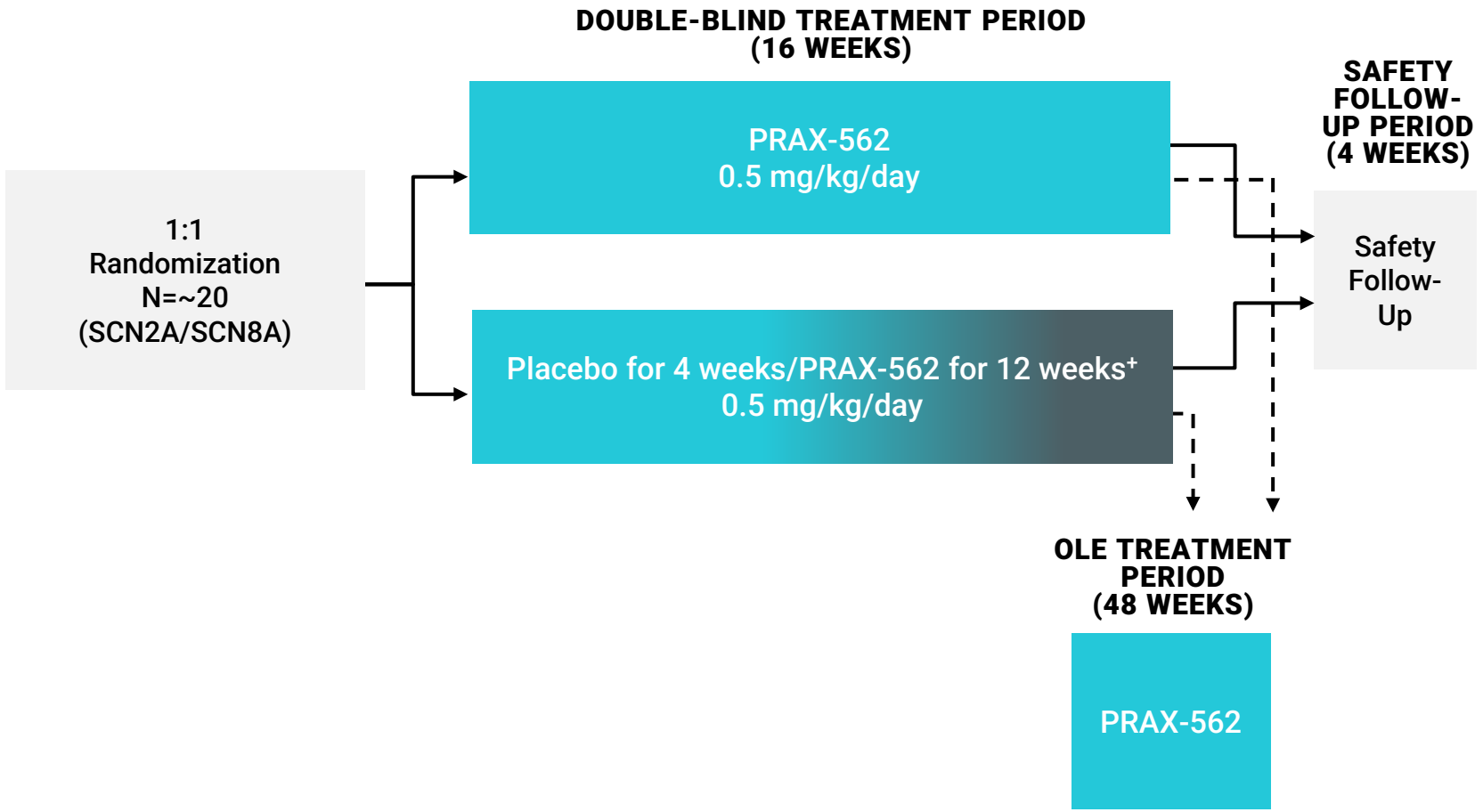
No MTD at exposures multiple fold above therapeutic range indicates potential for superior therapeutic index

Significant changes observed between placebo and PRAX-562 on qEEG biomarkers

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

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

PRAX-562 Phase 2 EMBOLD study topline data expected in mid-2024



PRIMARY ENDPOINT:

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

KEY SECONDARY:

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

EMBOLD

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

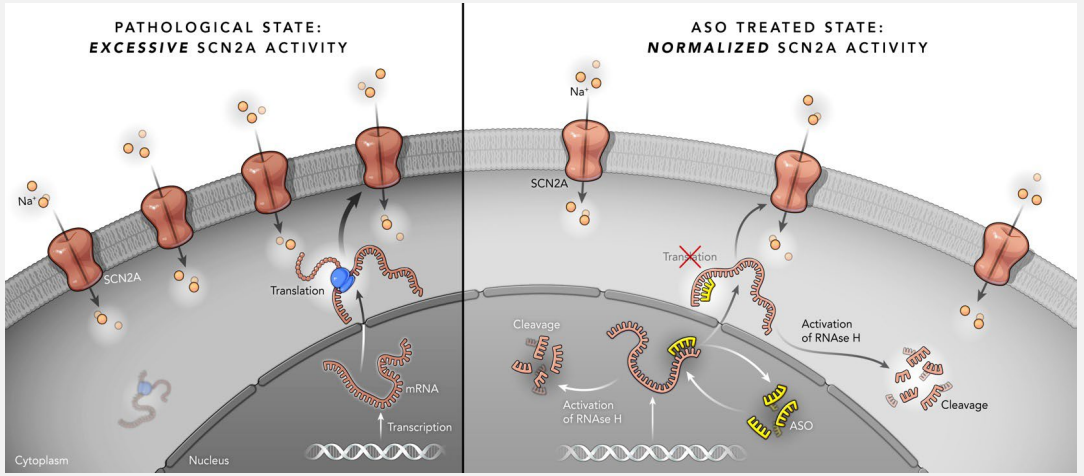
Elsunersen (PRAX-222)

SOLIDUS™ ASO PLATFORM

Elsunersen specifically designed for SCN2A GoF patients

DISEASE OVERVIEW

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



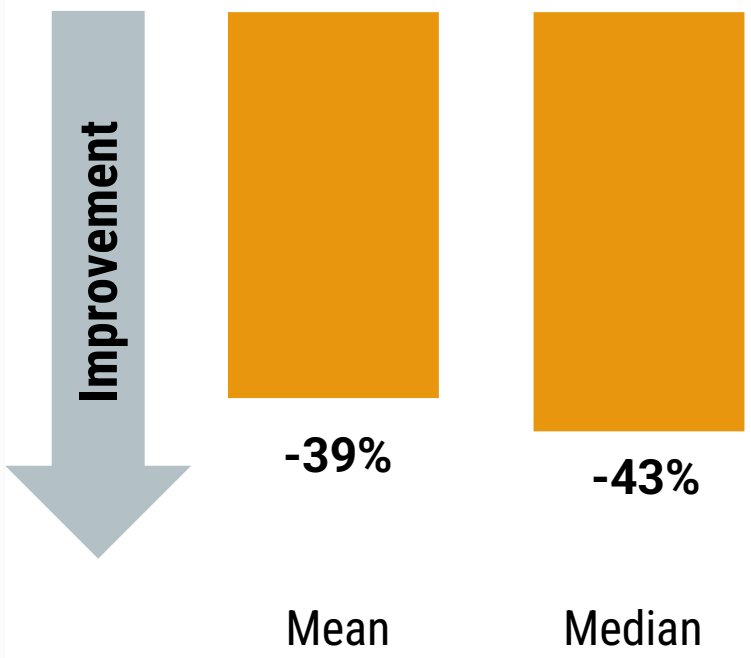
RESEARCH APPROACH

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

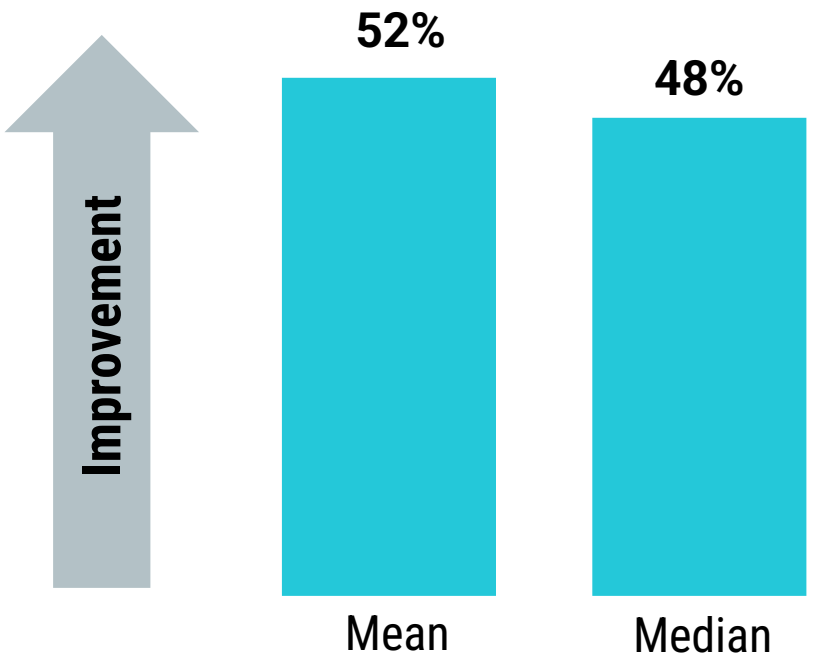
Significant reduction in seizures observed for SCN2A patients

EMBRAVE

Overall % reduction in seizures from 28-day baseline (n=4)



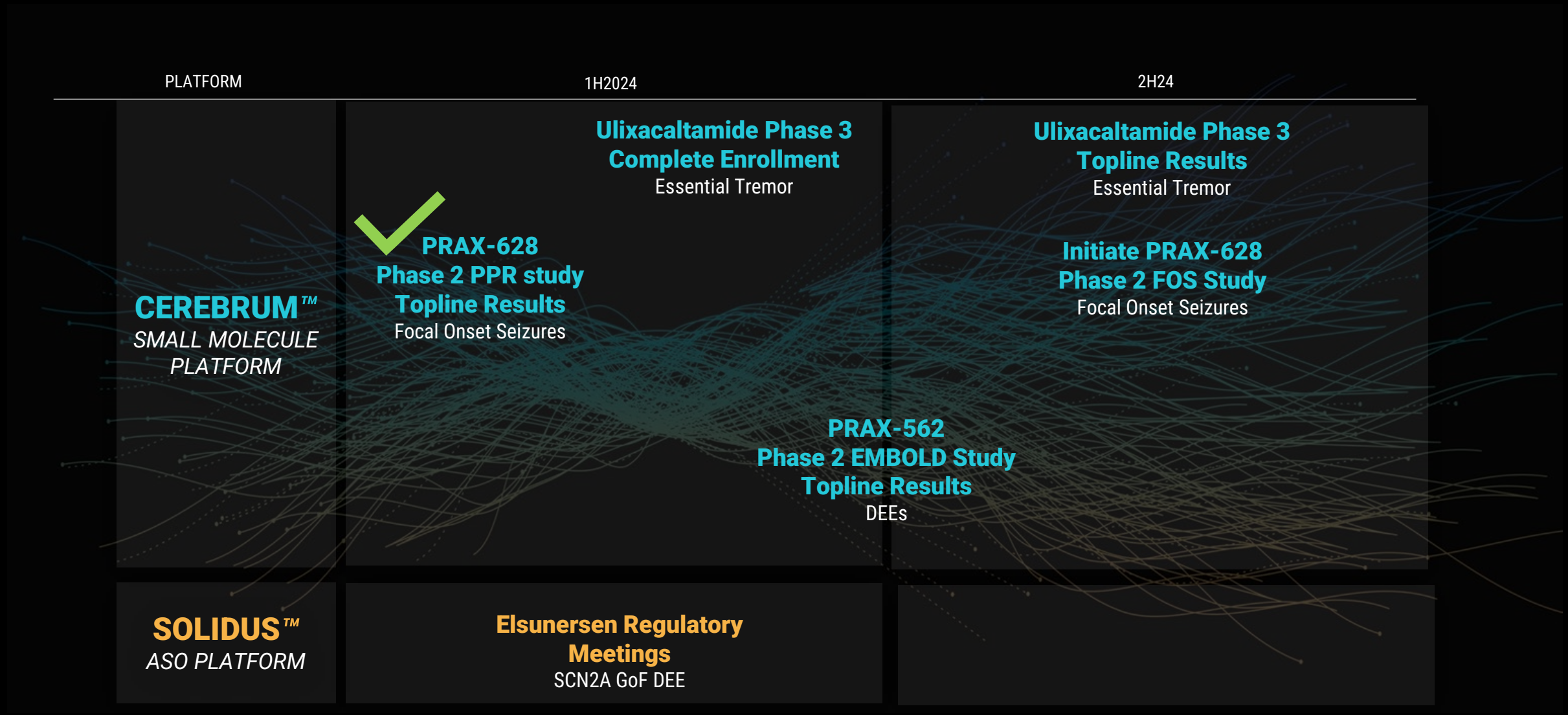
Overall relative % increase in seizure-free days from 28-day baseline (n=4)

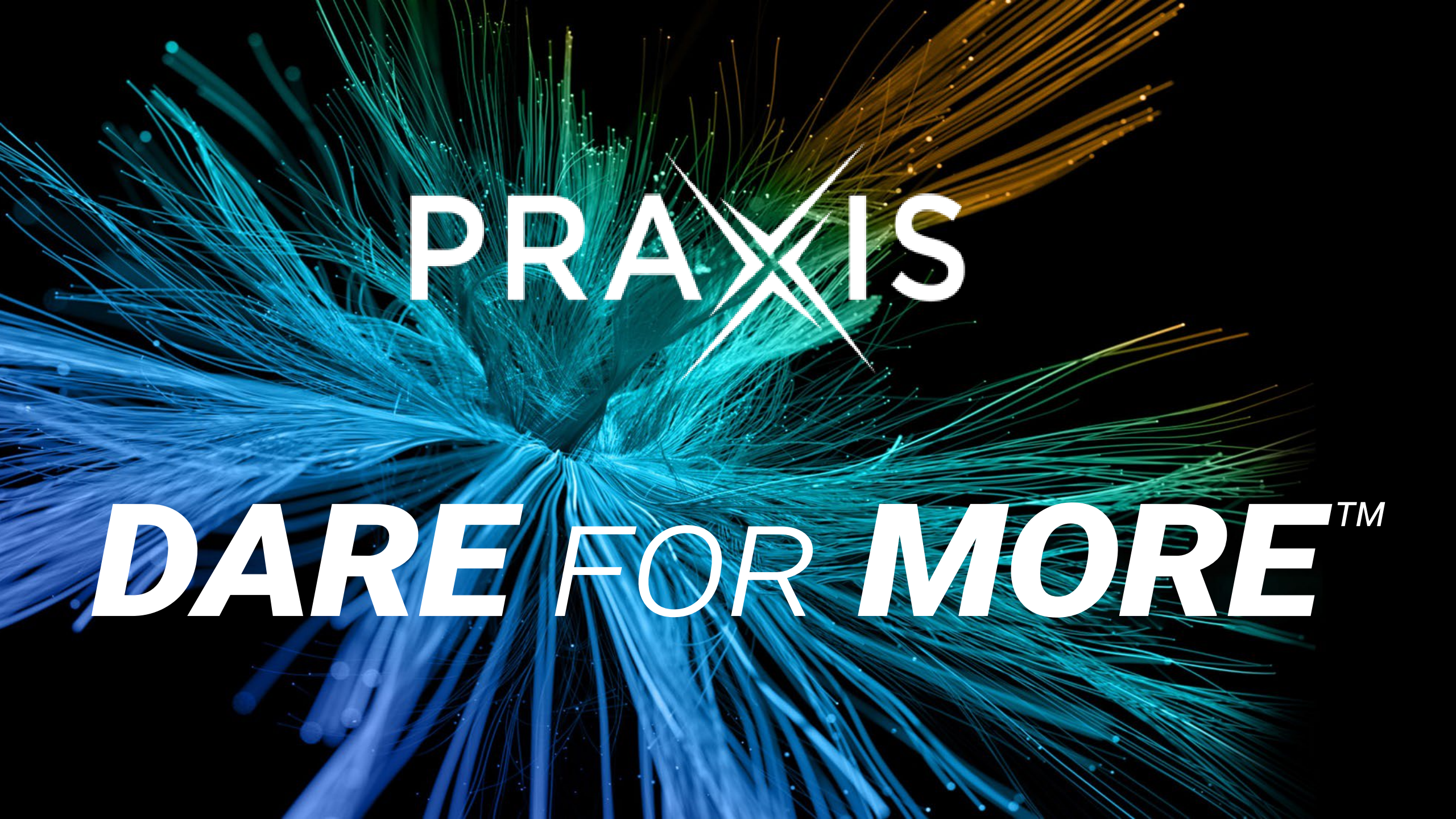


- No TEAEs or SAEs considered related to study drug
- All TEAEs recovered/resolved

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

What to expect from Praxis during 2024

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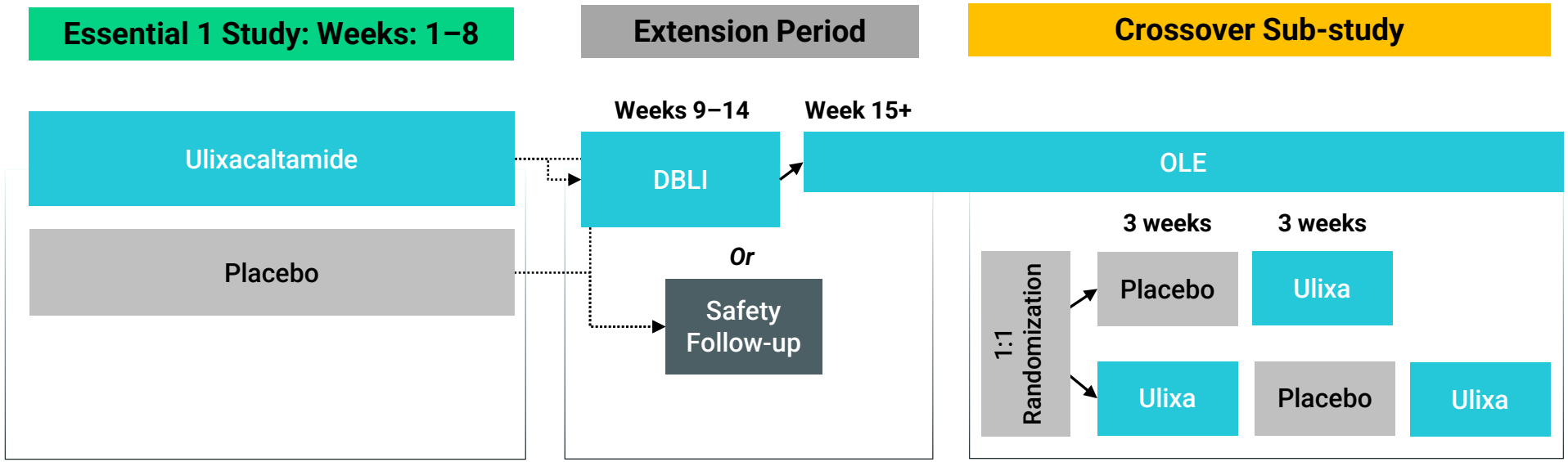
Appendix

Essential1 Phase 2b study evaluating the efficacy and safety of ulixacaltamide for essential tremor

ESSENTIAL1 DESIGN



DBLI = double blind lead-in, OLE = open label extension
ClinicalTrials.gov NCT05021991