R&D Portfolio Overview

October 2, 2023

Forward-looking statements

This presentation may contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial conditions, including but not limited to express or implied statements regarding the current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our preclinical and clinical results and other future conditions. Any forward-looking statements in this presentation are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, risks relating to: (i) reported interim data from ongoing studies and trials differing materially from final data from preclinical studies and completed clinical trials; (ii) the success and timing of our ongoing clinical trials, (iii) the success and timing of our product development activities and initiating clinical trials, (iv) the success and timing of our collaboration partners' product development activities, (v) the timing of and our ability to obtain and maintain regulatory approval of any of our product candidates, (vi) our plans to research, discover and develop additional product candidates, (vii) our ability to enter into collaborations for the development of new product candidates, (viii) our ability to establish manufacturing capabilities, and our collaboration partners' abilities to manufacture our product candidates and scale production, (ix) our ability to meet any specific milestones set forth herein, and (x) 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, 2022, our Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission.

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

Overview

INTRODUCTION
Marcio Souza, *President & CEO*

ULIXACALTAMIDE
Alex La Croix, *Program Lead*

MOVEMENT DISORDER KOL
Professor Alberto Espay, MD

KOL DISCUSSION
Rich Able, PhD,
VP Global Medical Affairs

Q&A AND BREAK

EPILEPSY OVERVIEW
Steve Petrou, PhD,
Chief Scientific Officer

PRAX-628
Karl Hansen, PhD
Chief Technical Operations Officer

EPILEPSY KOL
Professor Jacquie French, MD

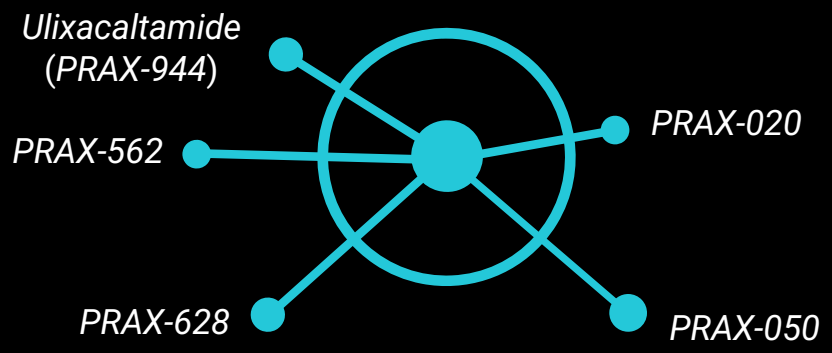
Q&A AND CONCLUSION

Developing Treatments Inspired by the Genetics of Epilepsy

ENABLED BY TWO PLATFORMS

CEREBRUM™

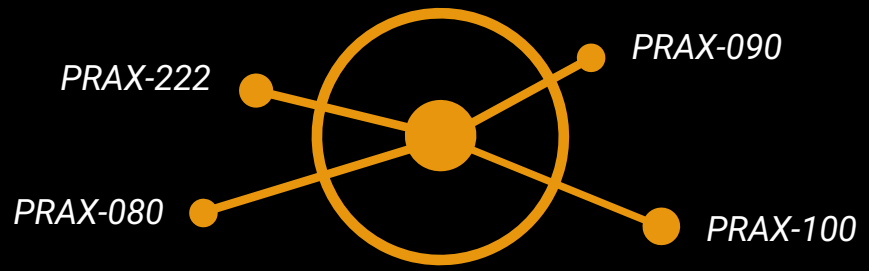
SMALL MOLECULE PLATFORM



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

SOLIDUS™

ANTISENSE OLIGONUCLEOTIDE (ASO) PLATFORM



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

Targeting movement disorders & epilepsies connected by neuronal imbalance

Today's Focus

PLATFORM	PRECLINICAL	PHASE ONE	PHASE TWO	REGISTRATION ENABLING
CEREBRUM™ *SMALL MOLECULE PLATFORM*	**PRAX-020*** KCNT1 **PRAX-050** Undisclosed		**Ulixacaltamide** Essential Tremor **PRAX-628** Focal Epilepsy **PRAX-562** DEEs	
SOLIDUS™ *ASO PLATFORM*	**PRAX-090⁺** SYNGAP1 **PRAX-100⁺** SCN2A LoF **PRAX-080⁺** PCDH19		**PRAX-222** SCN2A GoF DEE	

*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

Our Four Pillars

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

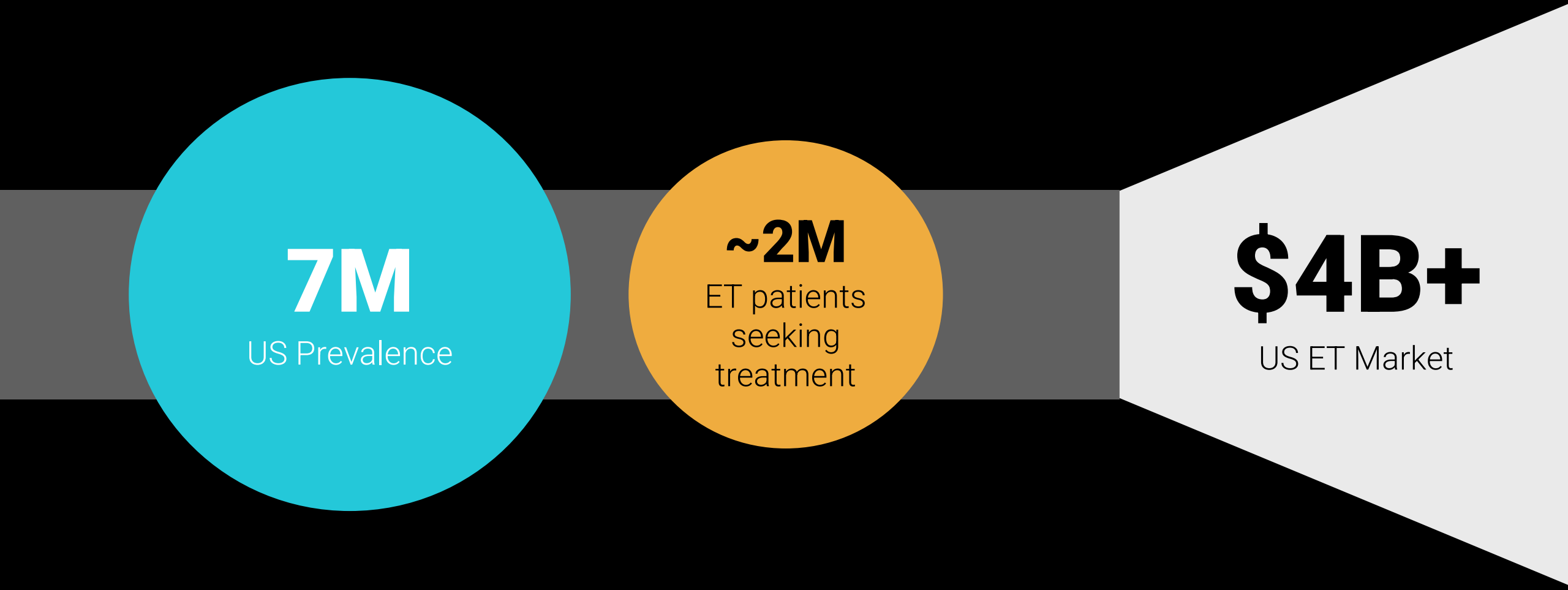
EFFICIENT & RIGOROUS

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

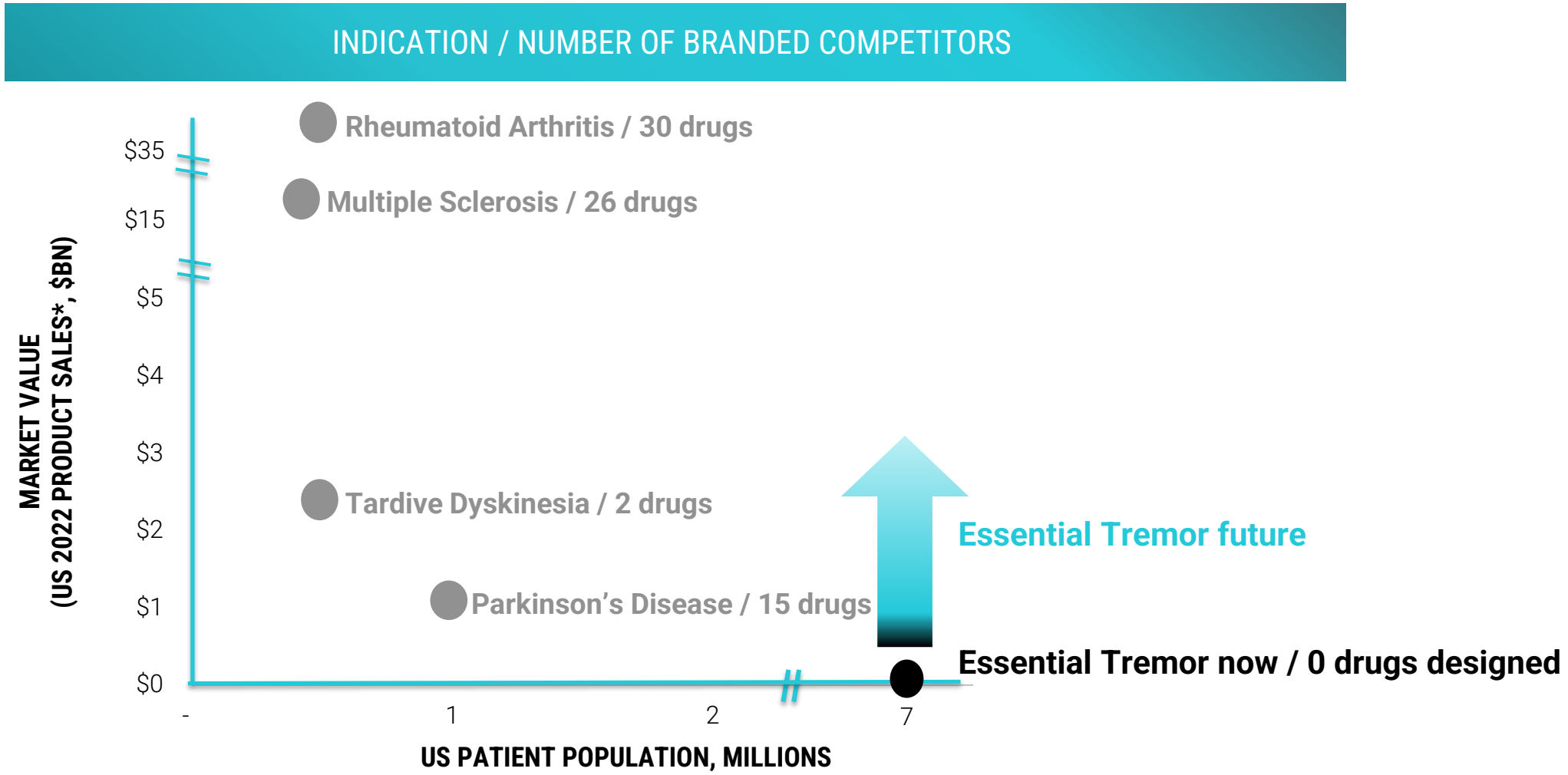
PATIENT-GUIDED

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

Essential tremor market is significantly underserved and ready for disruption

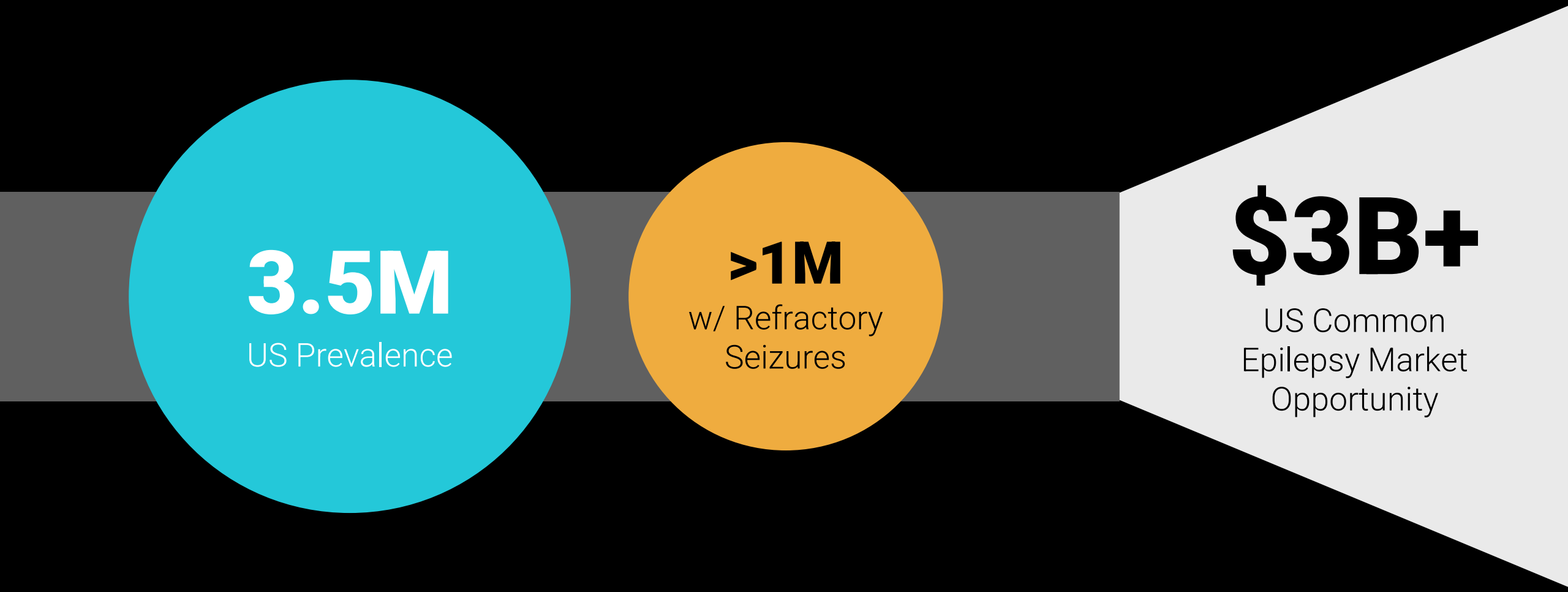


Essential tremor has large market potential and limited competition compared with other diseases

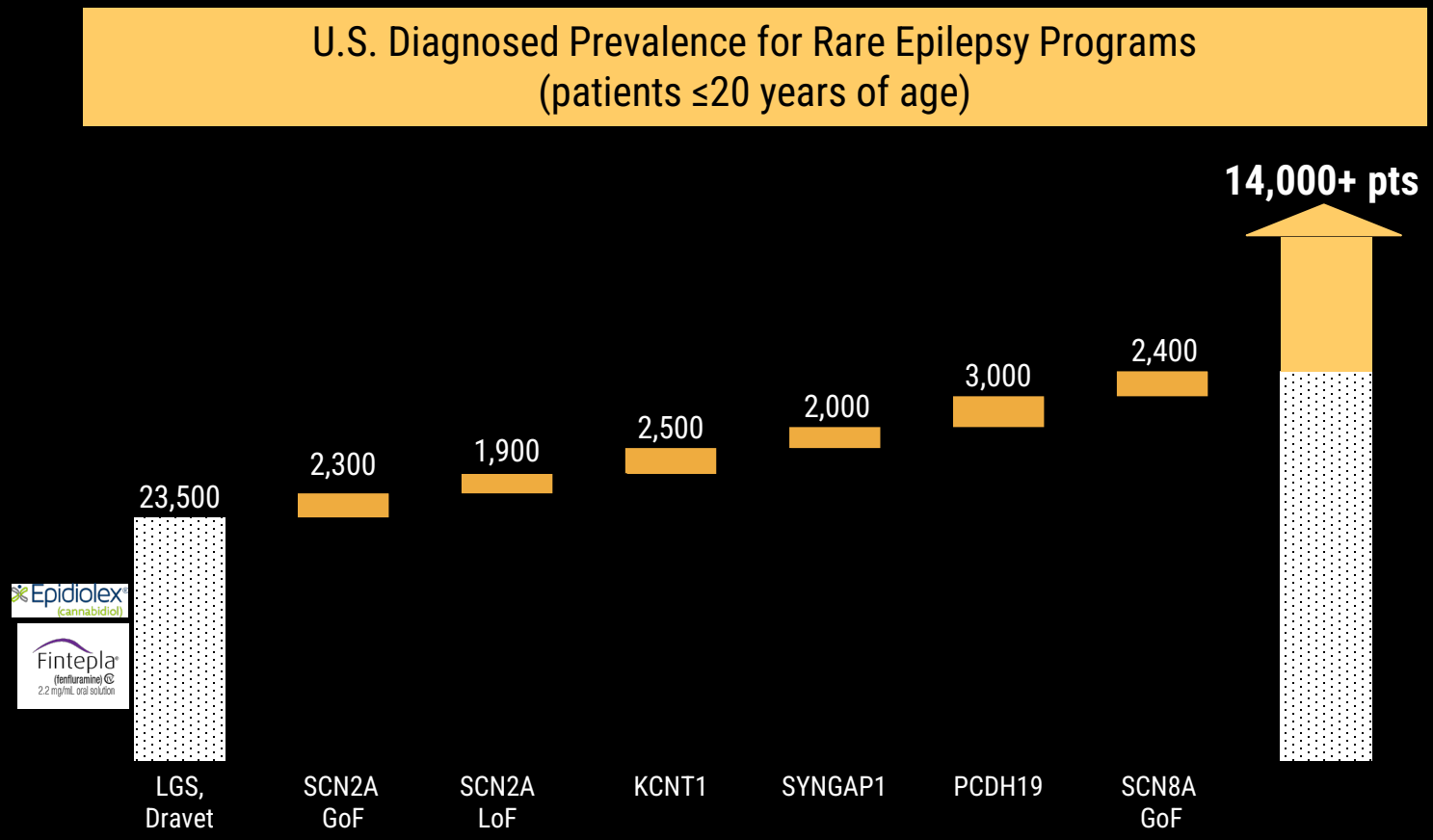


Source: Evaluate Pharma US Sales by Product, (#) number of drugs with branded revenue report by company
*US products sales are not indication specific

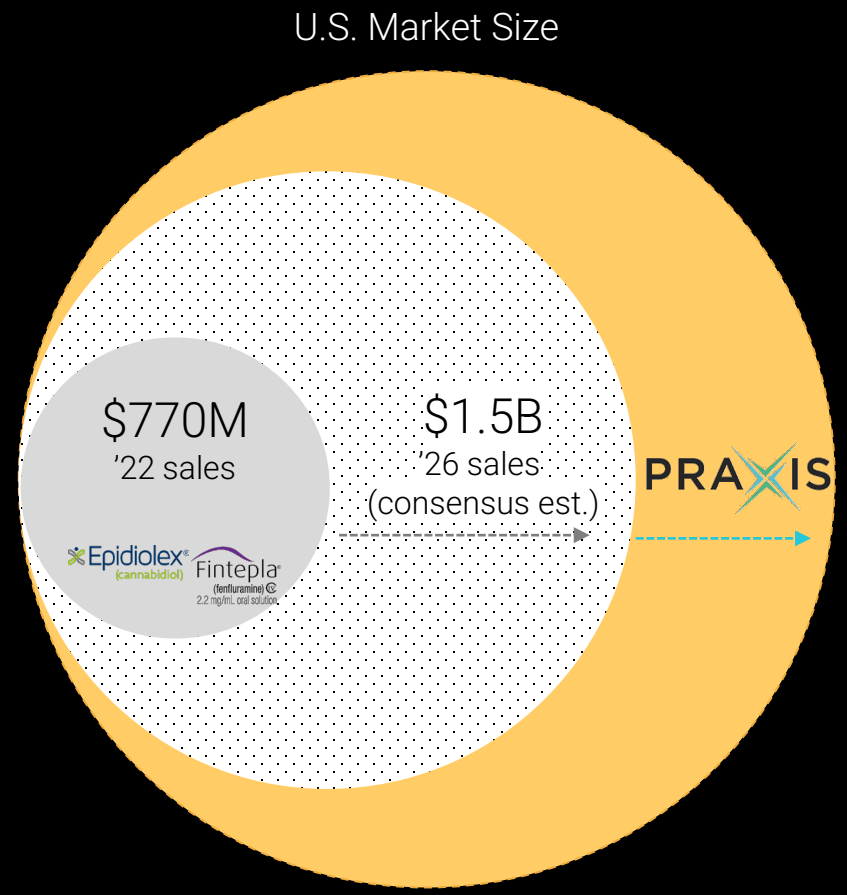
We aim to address unmet need in the $3B+ US common epilepsy market



Delivering first and best-in-class precision medicines for 14,000+ rare epilepsy patients



First- and best-in-class PRAX precision medicines



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

PRAX-222 *(elsunersen)* Update

Revolution in ASO for Epilepsy

Patients with SCN2A-DEE have a debilitating and ultimately fatal trajectory

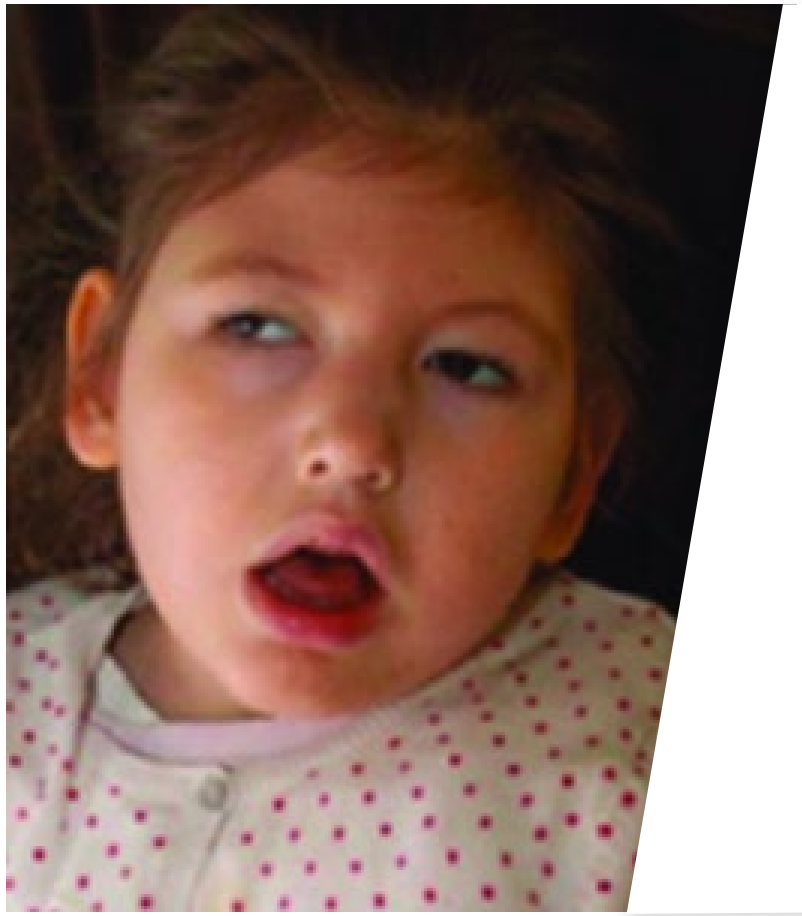
Significant seizure burden at or around birth

Refractory epilepsy and developmental arrest

Significant risk of SUDEP

Early mortality

We have a mission to disrupt the trajectory of SCN2A-DEE…



ONE PATIENT AT A TIME!

https://onlinelibrary.wiley.com/doi/full/10.1111/epi.12554

PRAXIS

We have a mission to disrupt the trajectory of SCN2A-DEE…

Very first patient to receive PRAX-222

A preterm newborn presenting with Status Epilepticus at birth

- Pre-natal exome sequencing SCN2A c.3986C>A p.(Ala1329Asp)
- Medical team requested emergency access to PRAX-222 after exhausting standard options

We have a mission to disrupt the trajectory of SCN2A-DEE…

Very first patient to receive PRAX-222

PRAX-222 initiated when patient was 13 weeks old;
poor prognosis due to continuous Status Epilepticus

After 1 dose

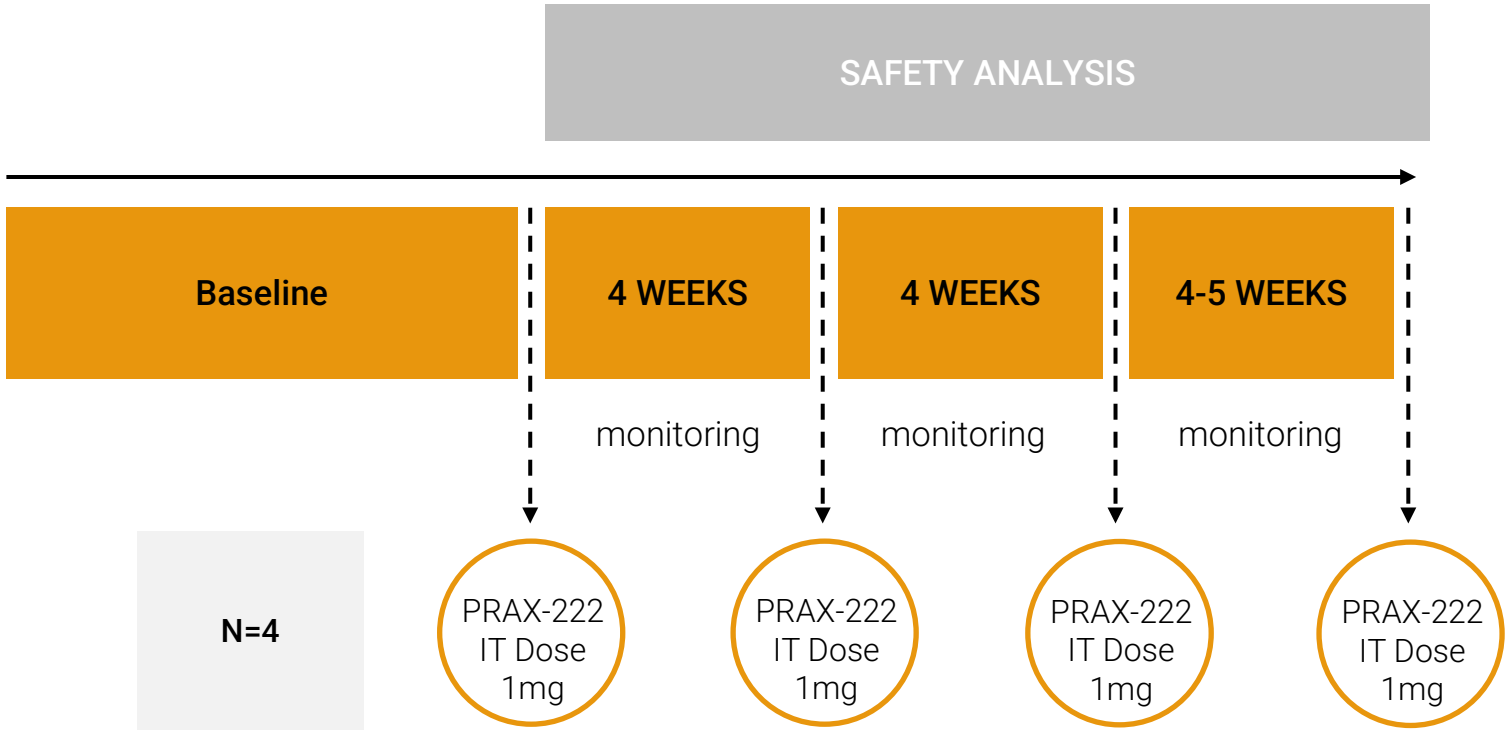
- PRAX-222 was well-tolerated
- Status epilepticus interrupted intermittently

After 7 doses

- PRAX-222 was well-tolerated
- No severe or serious adverse events
- Status epilepticus ceased
- Reduction in seizure frequency
- Breastfeeding
- Clinically stable

PRAX-222 EMBRAVE Part 1 design

EMBRAVE

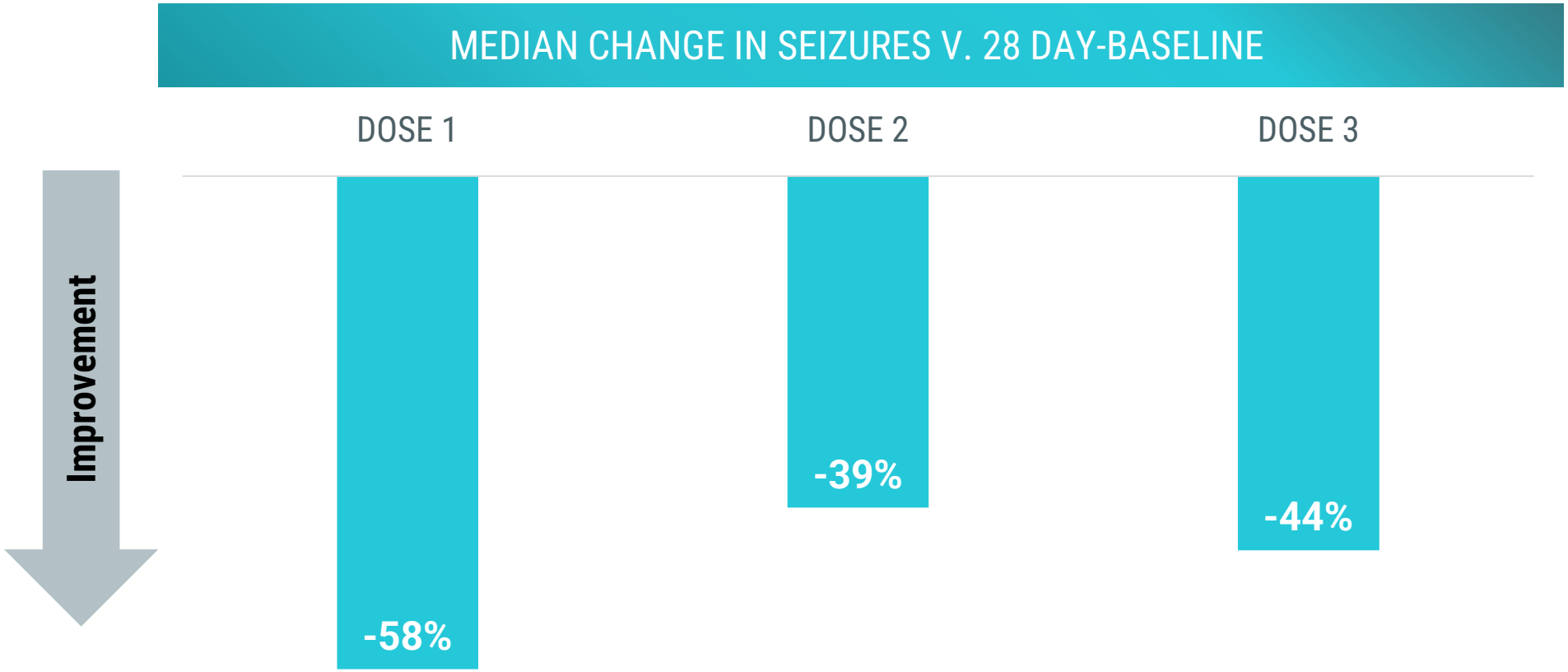


GOAL:
Assess preliminary safety of PRAX-222

21-week study

Unprecedented efficacy after 1 dose of PRAX-222
Preliminary results of 3 monthly doses

EMBRAVE

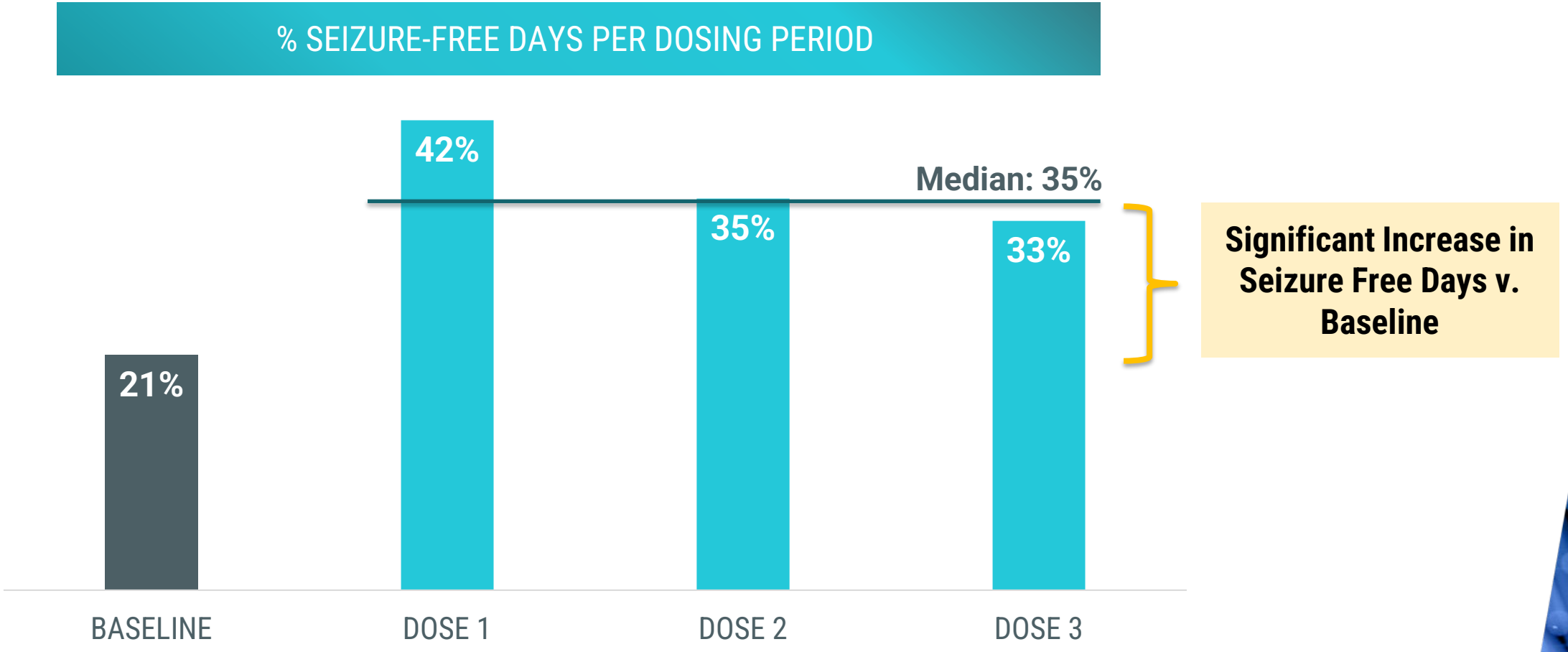


44% Median Seizure Reduction Across 3 Doses (range 27%-80%)

Data through September 26 2023

Unprecedented increase in seizure-free days
Improvements observed after one dose

EMBRAVE



Data through September 26, 2023; calculated as number of seizures over number of days between dose, per patient

PRAXIS

PRAX-222 Safety profile supports program advancing

EMBRAVE

- As of cutoff, 4 patients evaluable through three doses each, 1 received 7 doses
- Safety inclusive of 4 patients receiving 3 doses, 2 patients receiving 4 doses
  - No TEAEs or SAEs considered related to study drug
  - All TEAEs recovered/resolved
  - DMC provided opinion to continue dosing without modifications

Data through September 26 2023

PRAX-222 – Delivering on early safety and efficacy

Next Steps

Complete data collection for all patients

Compile package and meet with FDA

Initiate global pivotal phase in 2024

What to expect from Praxis through 1H 2024

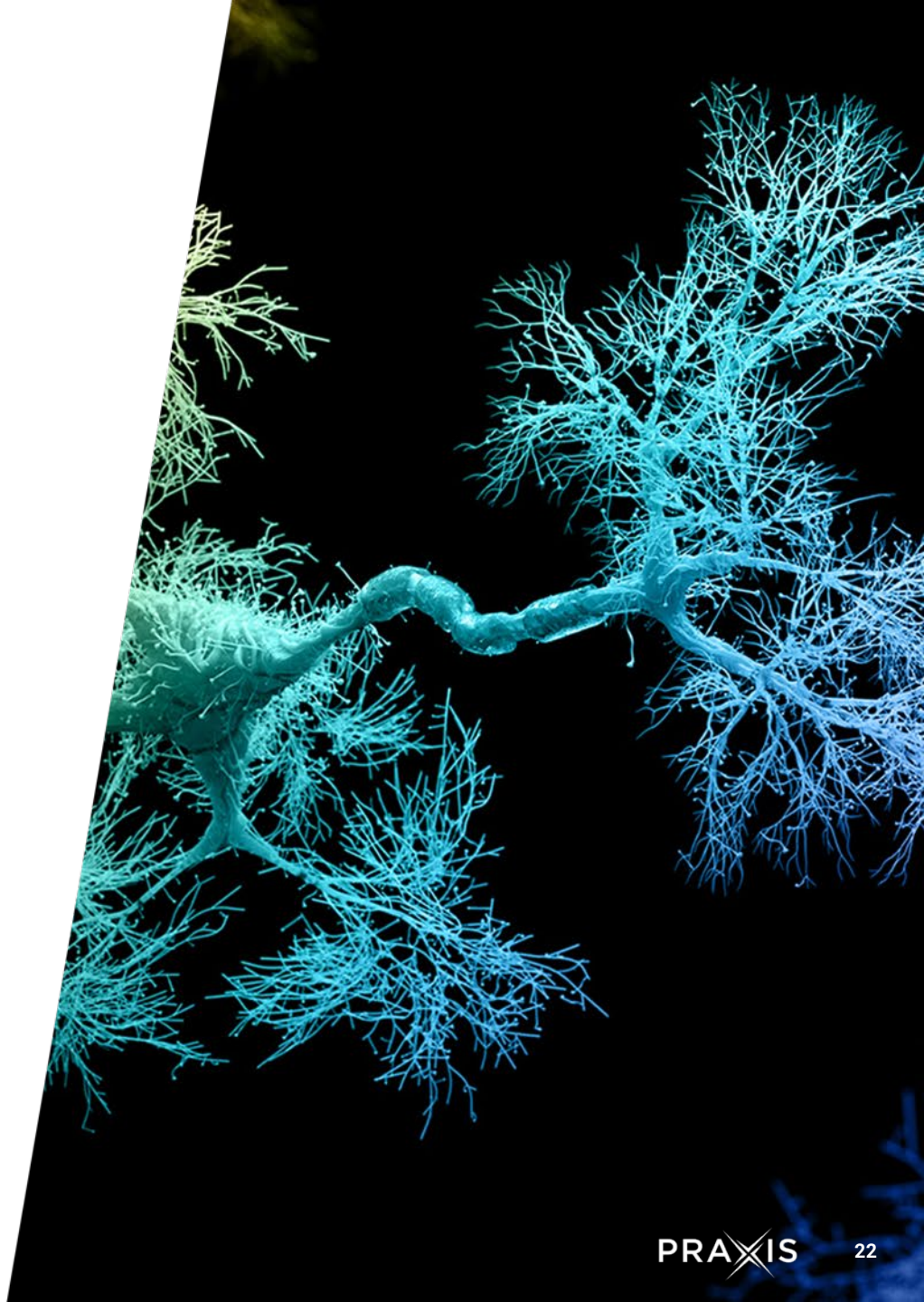
PLATFORM	1Q23	2Q23	3Q23	4Q23	1H 24
CEREBRUM™ *SMALL MOLECULE PLATFORM*	**Ulixacaltamide Ph 2b Essential1 Study Topline Results** Essential Tremor	**Ulixacaltamide End-of-Ph 2 FDA Meeting** Essential Tremor **PRAX-628 Ph 1 Topline Results**		**Ulixacaltamide Ph 3 Initiation** Essential Tremor **PRAX-628 Phase 2 PPR study Topline Results** Focal Epilepsy	**Ulixacaltamide Phase 3 Complete Enrollment** Essential Tremor **Initiate PRAX-628 Focal Epilepsy Phase 2 Study** Focal Epilepsy **PRAX-562 Ph 2 EMBOLD Study Topline Results** DEEs
SOLIDUS™ *ASO PLATFORM*				**PRAX-222 EMBRAVE Study First Dose Cohort (Part 1) Topline Safety Results** SCN2A GoF DEE	**PRAX-222 Cohort Extension** SCN2A GoF DEE

Ulixacaltamide (PRAX-944)

Essential Tremor

- Clinical insights from Essential1 (PRAX-944-222)
- Phase 3 Development Plan

Alex La Croix
Movement Disorders Program Lead



There is a clear need for a safe, tolerable and effective treatment in Essential Tremor

Essential Tremor (ET) is the most common movement disorder

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

Action tremors significantly disrupt daily living for people with ET

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

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

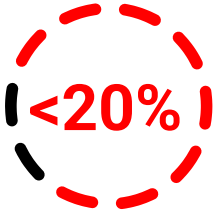
SOURCE: 1. GHOSH (2016) (P.231, C.1, PH.1, L.1-2), 2. Elble RJ. Curr Neurol Neurosci Rep. 2013 Jun;13(6):353. 3. Putzke JD, et al. J Neurol Neurosurg Psychiatry. 2006 Nov;77(11):1235-7.
4. Vetterick, C., Lyons, K.E., Matthews, L.G. et al. The Hidden Burden of Disease and Treatment Experiences of Patients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

The only approved medication is not widely used by patients

<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

>½



Of those who start propranolol
<20% still receive propranolol after 2 years

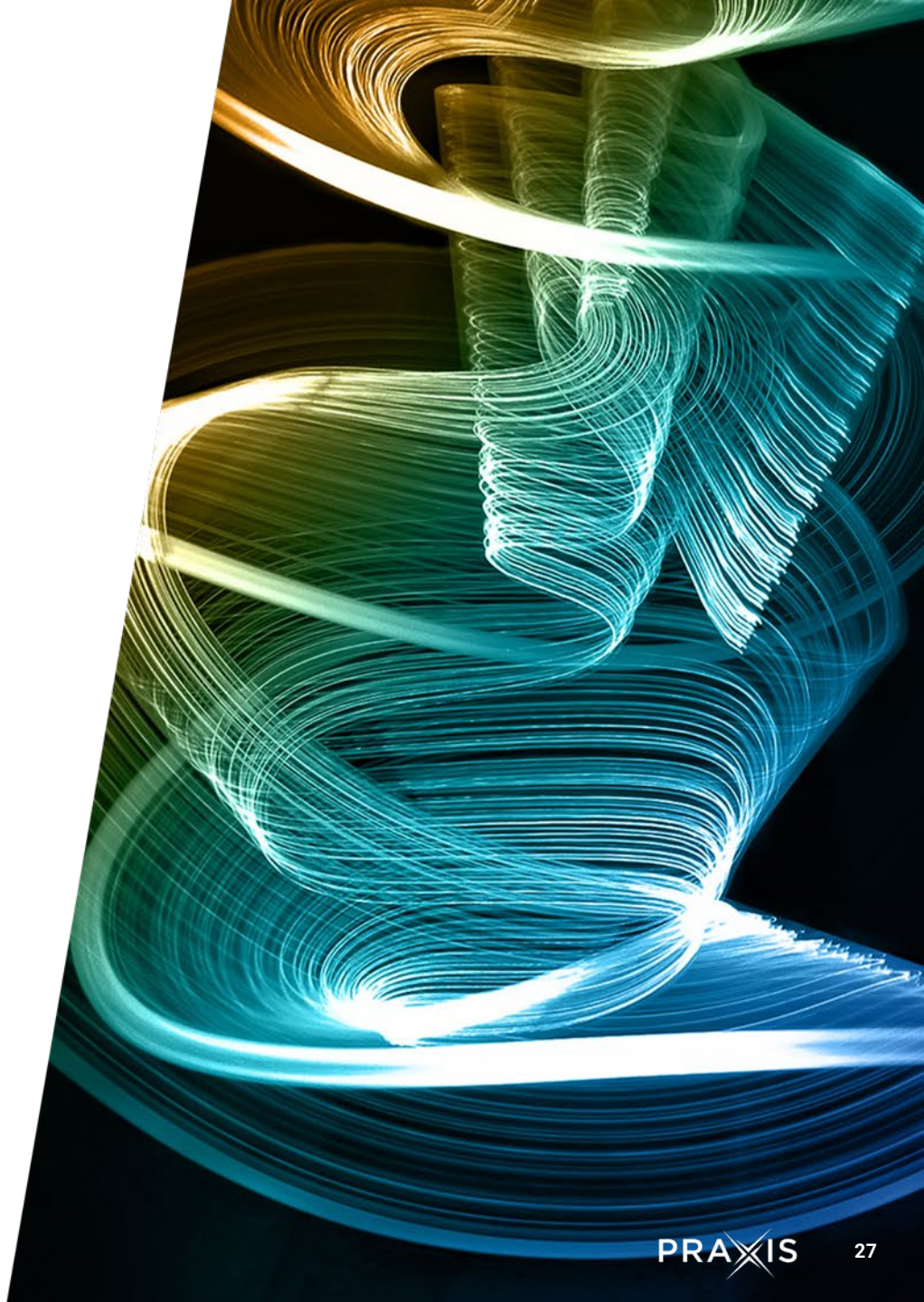
SOURCE: Vetterick, C., Lyons, K.E., Matthews, L.G. et al. The Hidden Burden of Disease and Treatment Experiences of Patients with Essential Tremor: A Retrospective Claims Data Analysis. Adv Ther (2022). https://doi.org/10.1007/s12325-022-02318-8

PRAXIS

Ulixacaltamide: Revolutionizing the treatment of essential tremor

First-in-Class mechanism	• First drug specifically designed for ET patients
Differentiated profile	• Easy titration and simple once-daily dosing • Continued improvement observed with longer duration on treatment • Improvement in functioning without the common side effects associated with current treatments • Low discontinuation
Broad Use	• 18+ years of age and all types of patients, including those with intention tremor • Benefit with or without propranolol

Using Essential1 to drive innovation in our Phase 3 strategy



Essential1 as the foundation for our Phase 3 program

TESTING A CLINICAL HYPOTHESIS

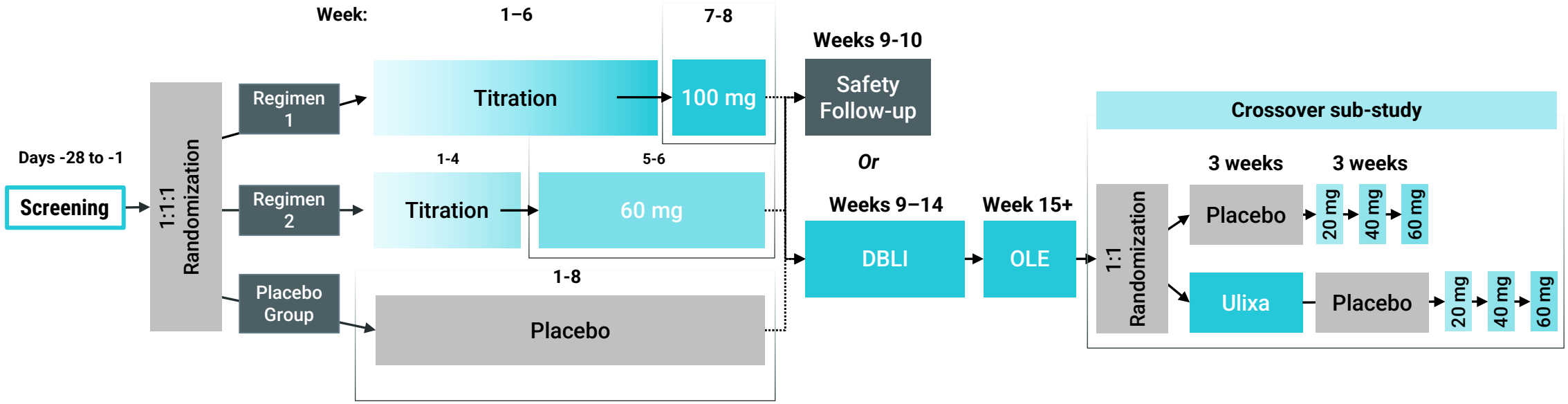
- Strong efficacy signal with robust endpoint (mADL11)
  - Early clinical benefit in Week 8 results
  - Long-term, durable benefit
- Well-tolerated with a differentiated safety profile
- Tested Phase 3 design concepts

INNOVATION IN REGISTRATION STUDY DESIGN

- Agreement with FDA on dose and primary endpoint
- Study design structured around the patient
- Robust recruitment strategy

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

ESSENTIAL1 DESIGN



ADL = activities of daily living, DBLI – double blind lead-in, OLE = open label extension

ClinicalTrials.gov NCT05021991

Compelling data demonstrates clinical effect of ulixacaltamide on functional improvement in mADL11

Modified ADL11 items

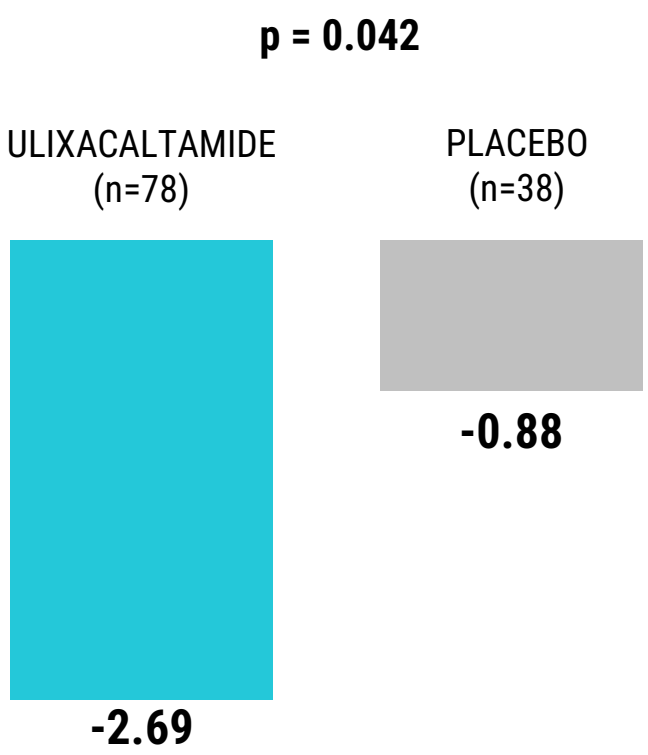
1. Speaking
2. Feeding with a spoon
3. Drinking from a glass
4. Hygiene
5. Dressing
6. Pouring
7. Carrying food trays, plates or similar items
8. Using keys
9. Writing
10. Working
11. Overall disability with most affected task

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 33

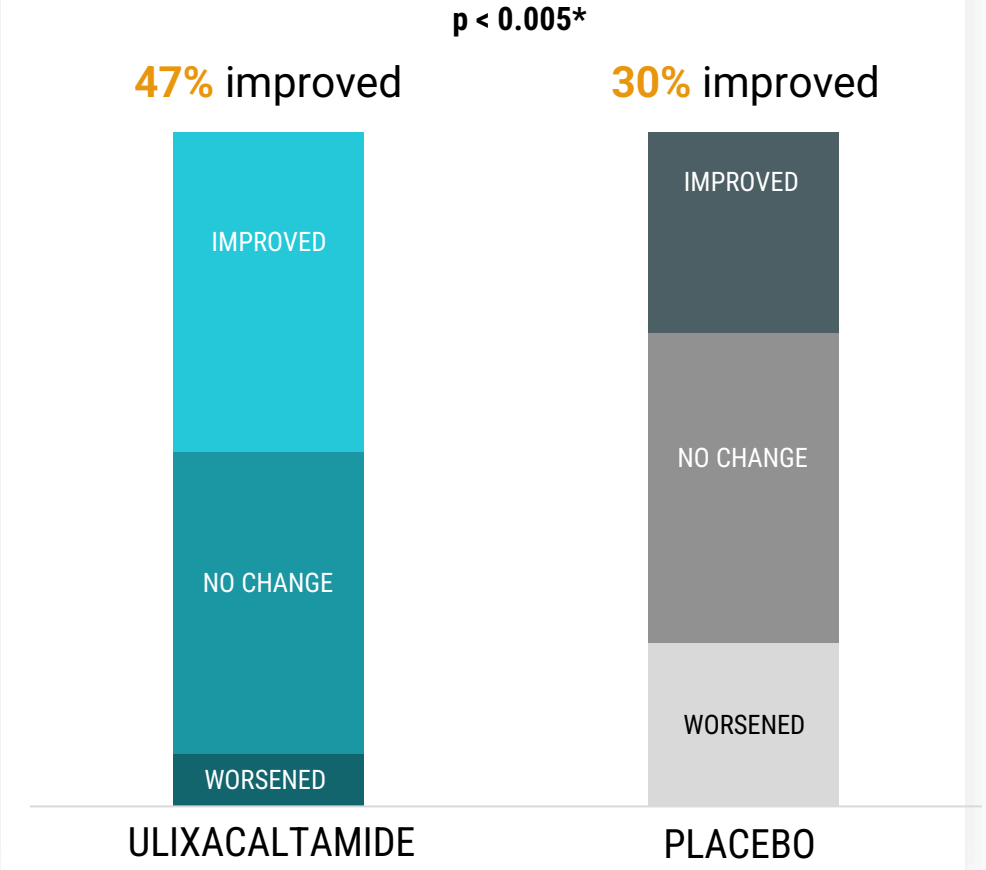
Improvement in mADL11 in 8 weeks - Essential1 Study



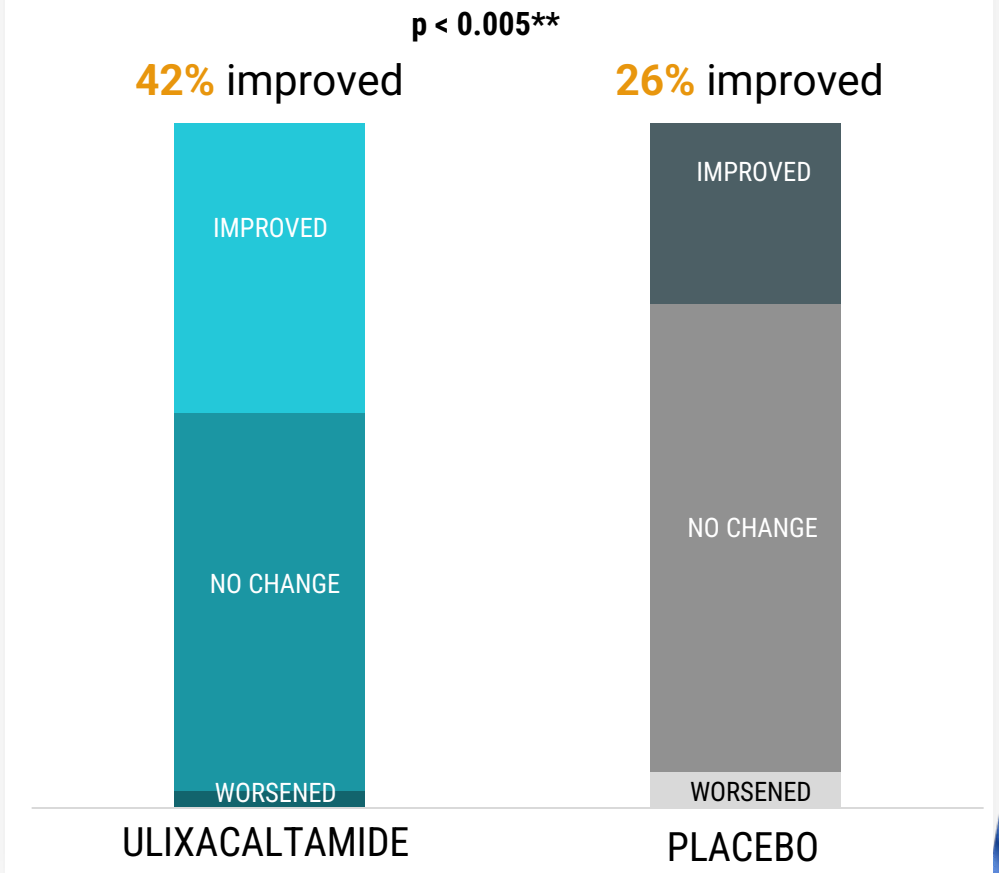
[1] Results from Essential1 study. mITT: Modified Intention to Treat population, p values are nominal

Patients and investigators reported higher overall improvement with ulixacaltamide compared to placebo

PGI-C - mITT



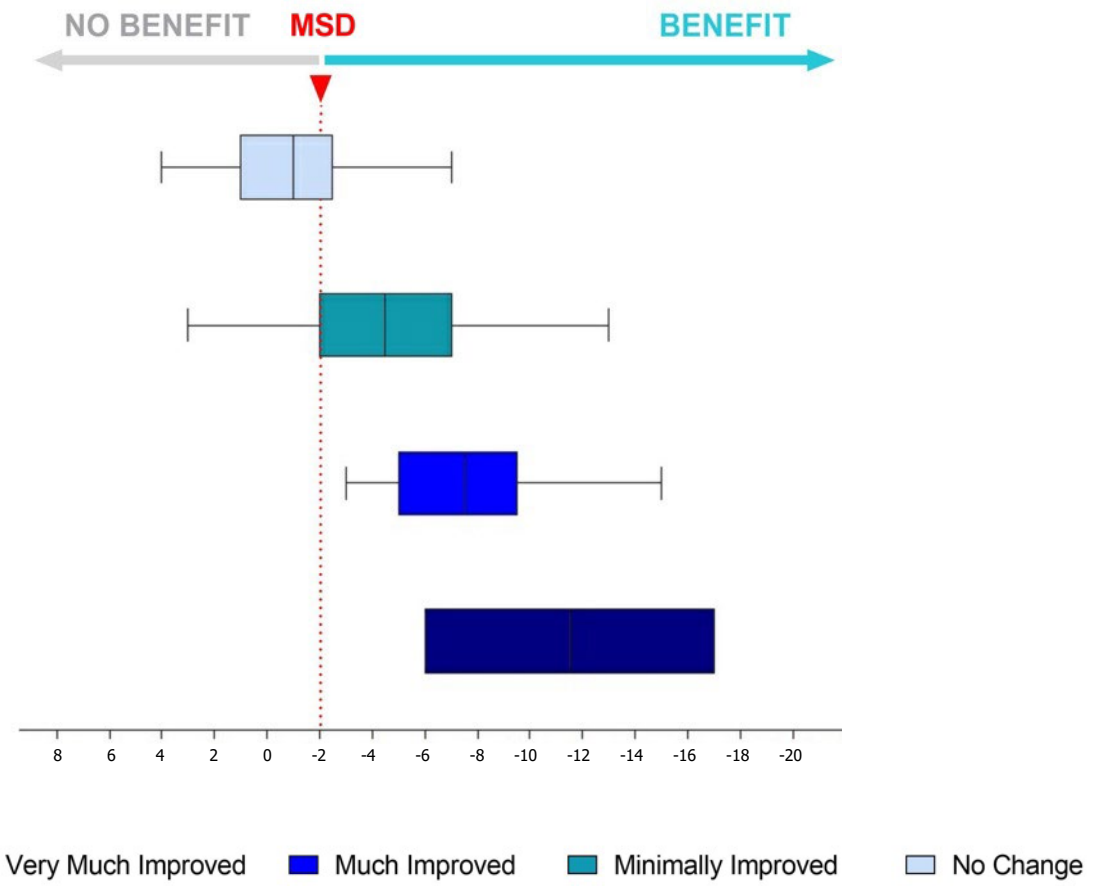
CGI-S - mITT



Results from Essential1 study;; CGI-S= clinical global impression improvement scale; PGI-C = patient global impression of change , all p-values are nominal
*RANK ANALYSIS
**RANK ANCOVA

Using Essential1 to define clinical meaningfulness in essential tremor

ESSENTIAL1 ANCHOR-BASED ASSESSMENT PGI-C:mADL11



Patient-Focused Drug Development: Incorporating Clinical Outcome Assessments Into Endpoints For Regulatory Decision-Making

Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

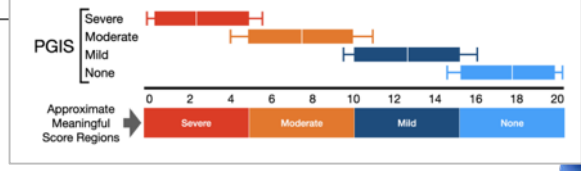
Comments and suggestions regarding this draft document should be submitted within ___ days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Office of Communications, Division of Drug Information at druginfo@fda.hhs.gov, 855-543-3784, or 301-796-3400 or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010 or (CDRH) Patient Science and Engagement Program at CDRH-PRO@fda.hhs.gov, 301-796-6715.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

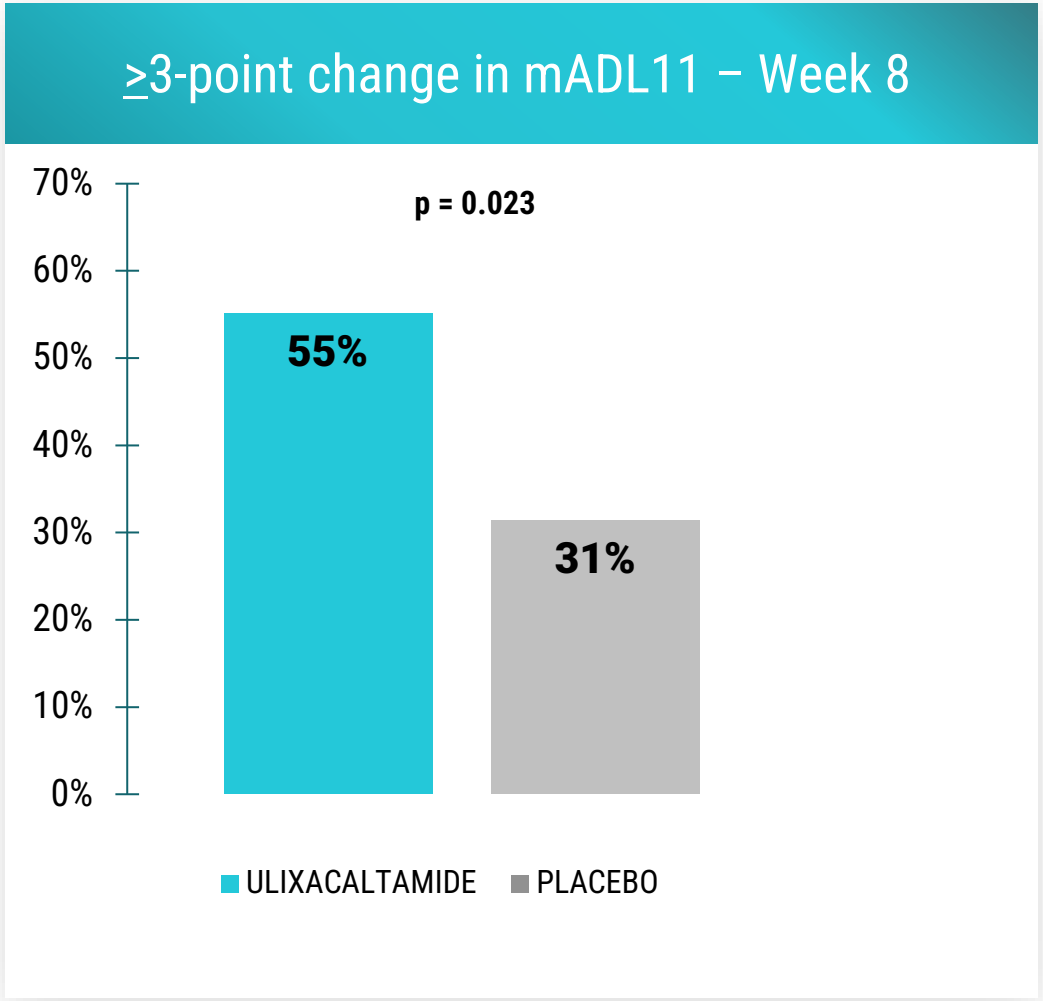
April 2023
Procedural

Figure 1. Example of Approach for Interpreting COA Scores in Terms of Meaningful Score Regions Corresponding to Patient Global Impression of Severity (PGIS).



MSD=Meaningful Score Difference

Clear response achieved in ulixacaltamide treated patients at Week 8

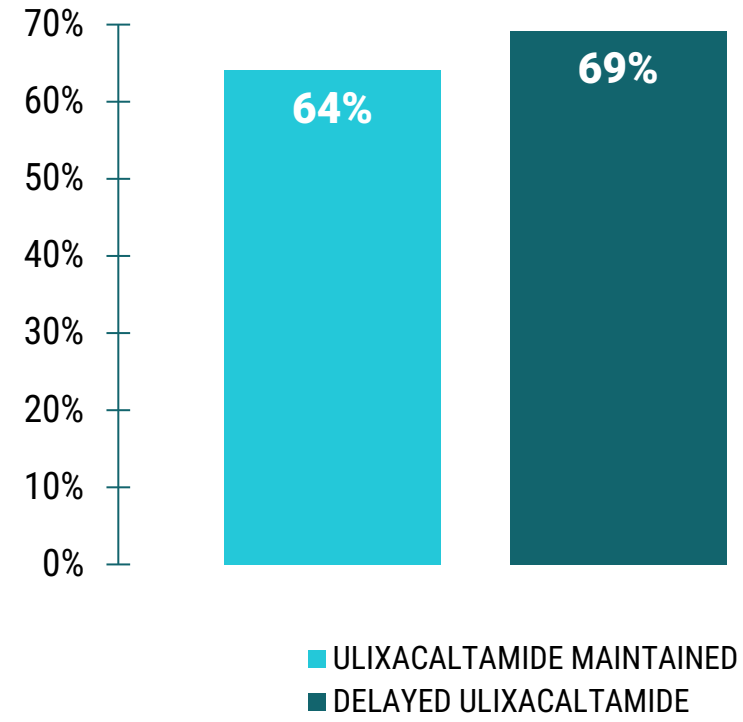


- Statistically-significant difference between ulixacaltamide and placebo groups

Results from Essential1 study

Robust response to ulixacaltamide treatment through Week 14

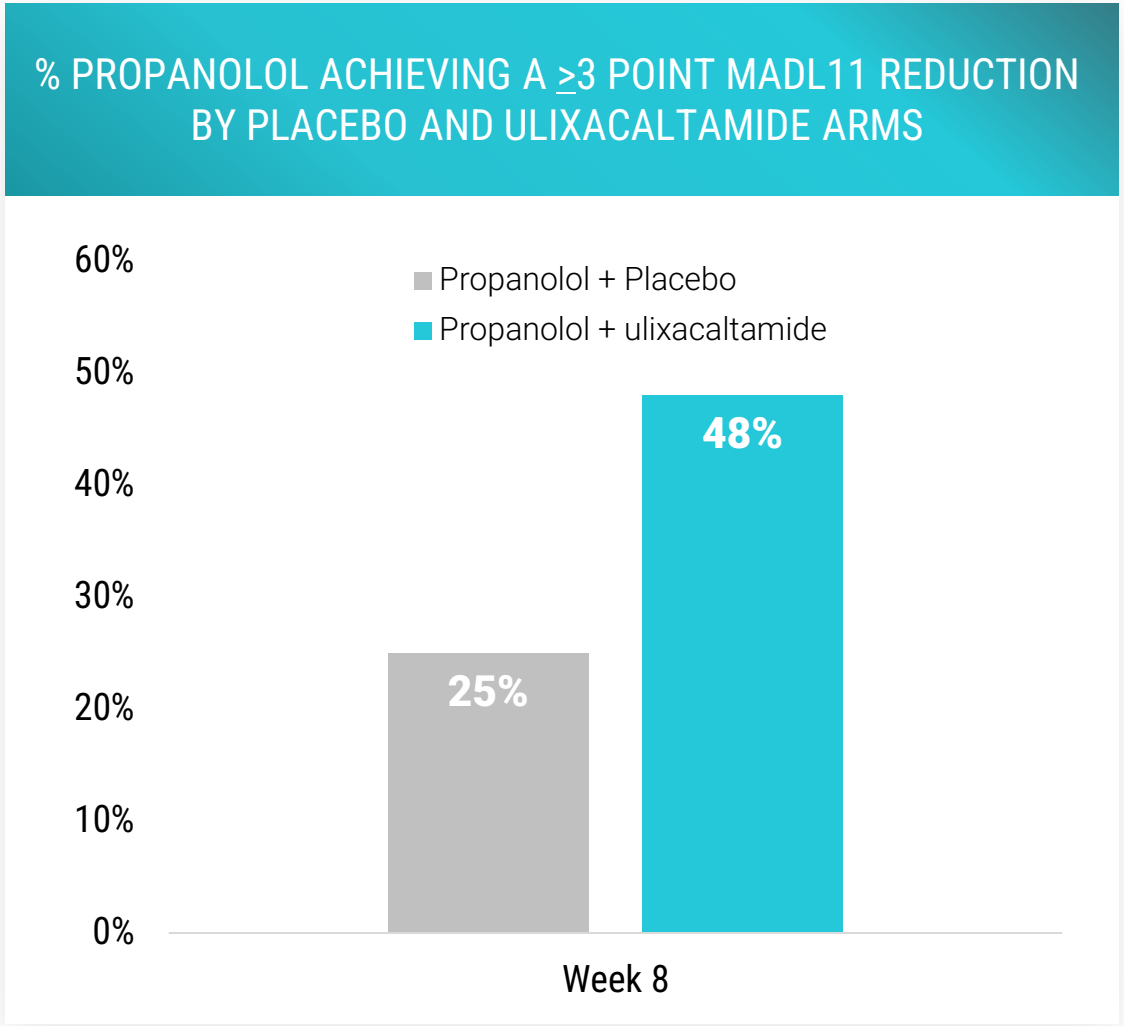
≥3-point change in mADL11 – Week 14



- Durable response in patients who continued on ulixacaltamide after Week 8
- Strong response from placebo patients who transitioned to ulixacaltamide after Week 8

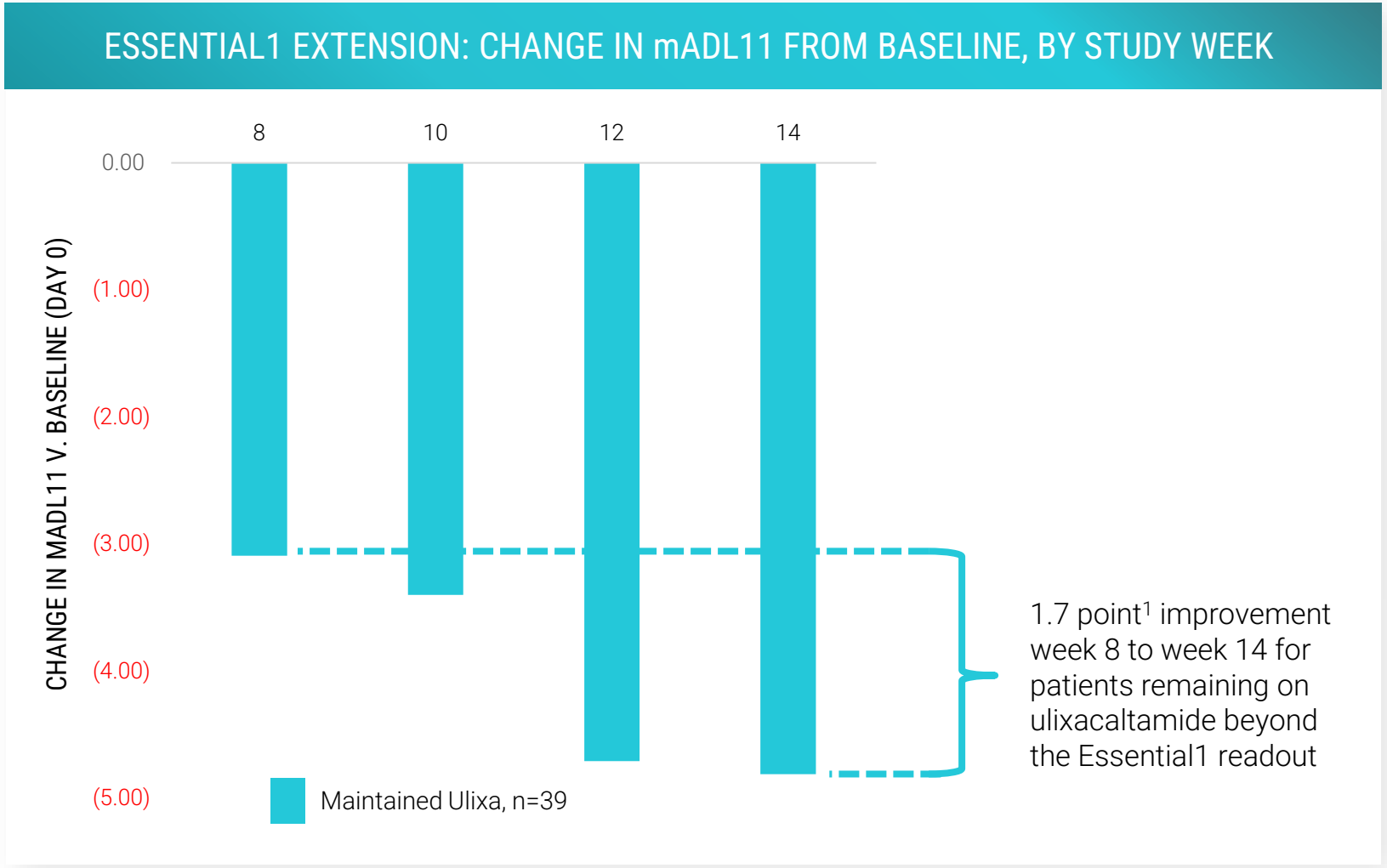
Results from Essential1 study

Benefit of ulixacaltamide is independent of propranolol use



Results from Essential1 study

Ulixacaltamide treated subjects continue to benefit after 14 weeks on treatment



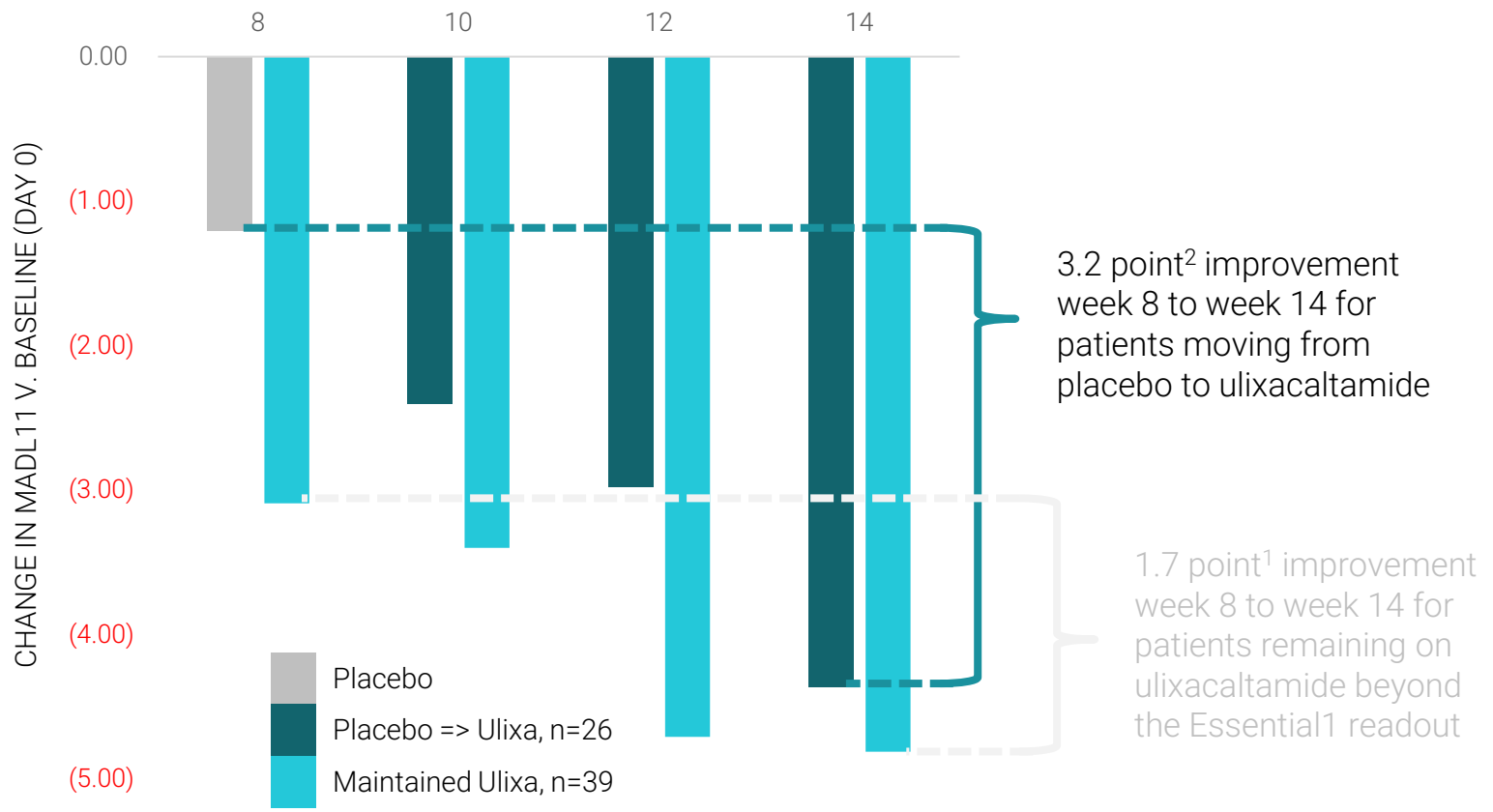
- Patients on drug from Day 1 continue to show durable effect through 14 weeks

[1]Results from Essential1 study; Improvement in the mADL11 of 1.7 points from 3.09 at Week 8 (95% CI: 0.98, 5.2) to 4.81 (95% CI: 2.38, 7.23) after 14 weeks of treatment

PRAXIS

Transition of subjects from placebo to ulixacaltamide confirms treatment benefit

ESSENTIAL1 EXTENSION: CHANGE IN mADL11 FROM BASELINE, BY STUDY WEEK



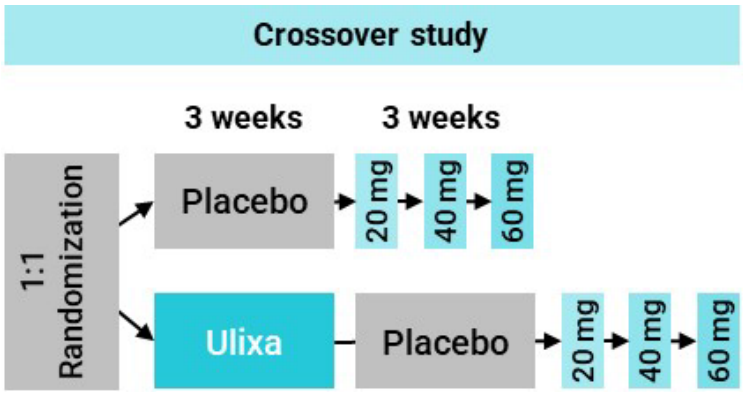
- Placebo patients switched to ulixacaltamide after Week 8 experience similar benefit through Week 14 as compared to benefit seen in the drug arm during the first 8 weeks of Essential1

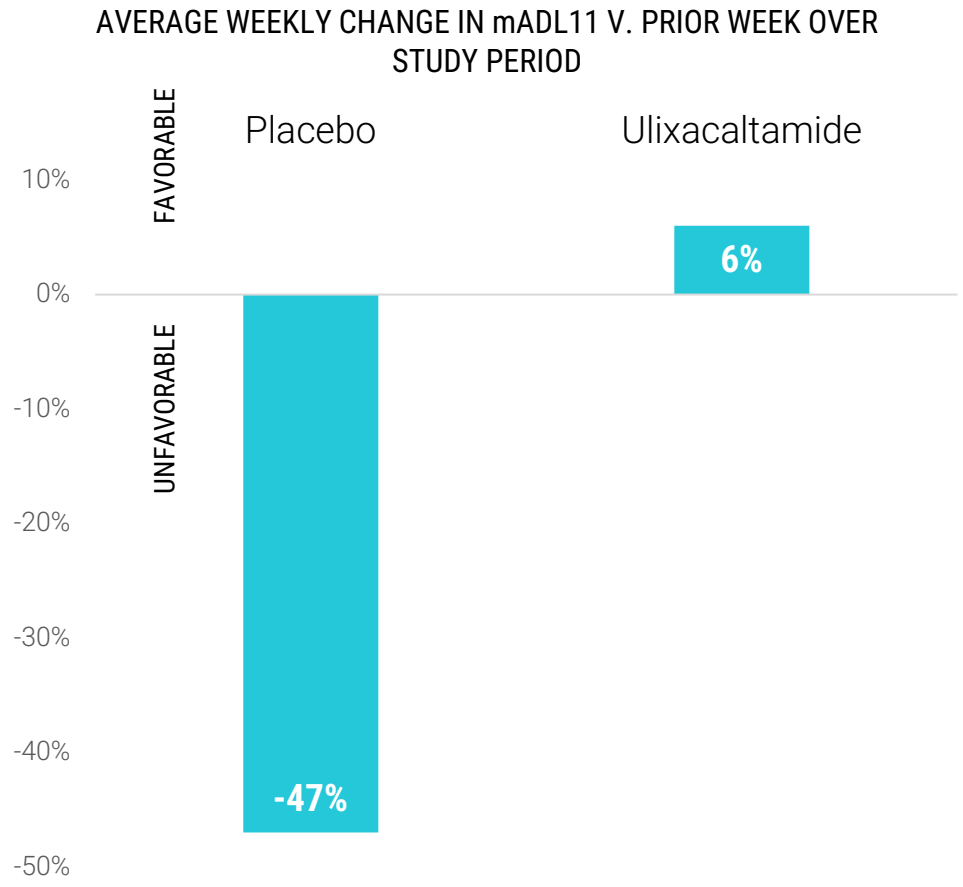
[1]Improvement in the mADL11 of 1.7 points from 3.09 at Week 8 (95% CI: 0.98, 5.2) to 4.81 (95% CI: 2.38, 7.23) after 14 weeks of treatment
[2]Improvement in mADL11 of 3.2 points, from 1.21 at Week 8 (95% CI: -1.04, 3.46) to 4.36 (95% CI: 1.68, 7.05)

PRAXIS

Essential1 randomized withdrawal approach confirms effect of ulixacaltamide

ESSENTIAL1 SUB-STUDY

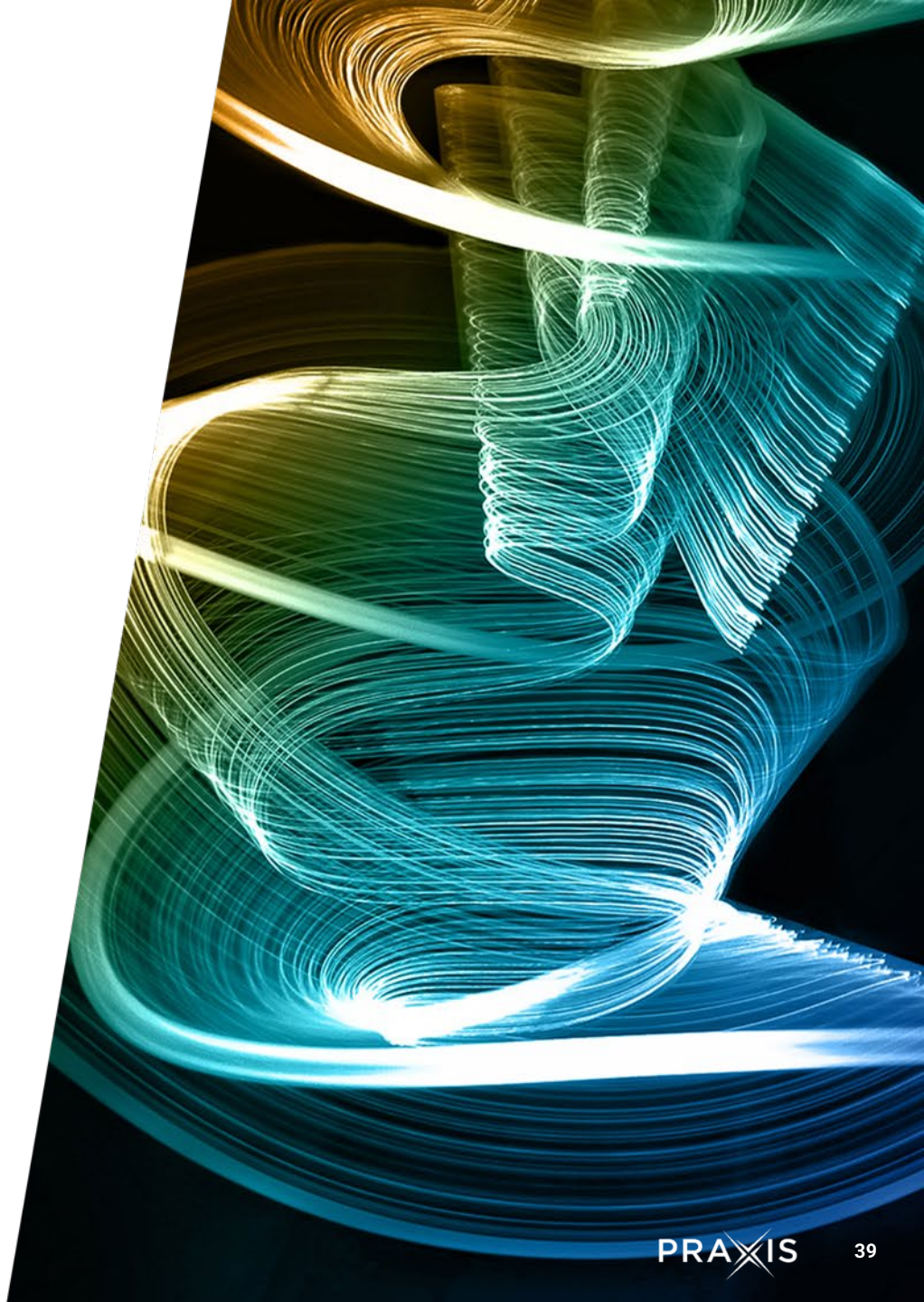




Sub-study design summary: Patients were re-randomized in a blinded-fashion to either receive placebo or continue to receive ulixacaltamide. Twenty-one patients who completed assessments at Week 14 of the OLE were eligible to participate in the blinded sub-study. Patients were evaluated weekly over a total of 6 weeks, with 11 patients assigned to ulixacaltamide and 10 to placebo for the initial 3-week period, crossing over to either placebo or ulixacaltamide for an additional 3-week period. Blinded rescue was triggered for patients on placebo if loss in the mADL11 exceeded 2 points at any timepoint.

*Mean change in effect of the mADL11

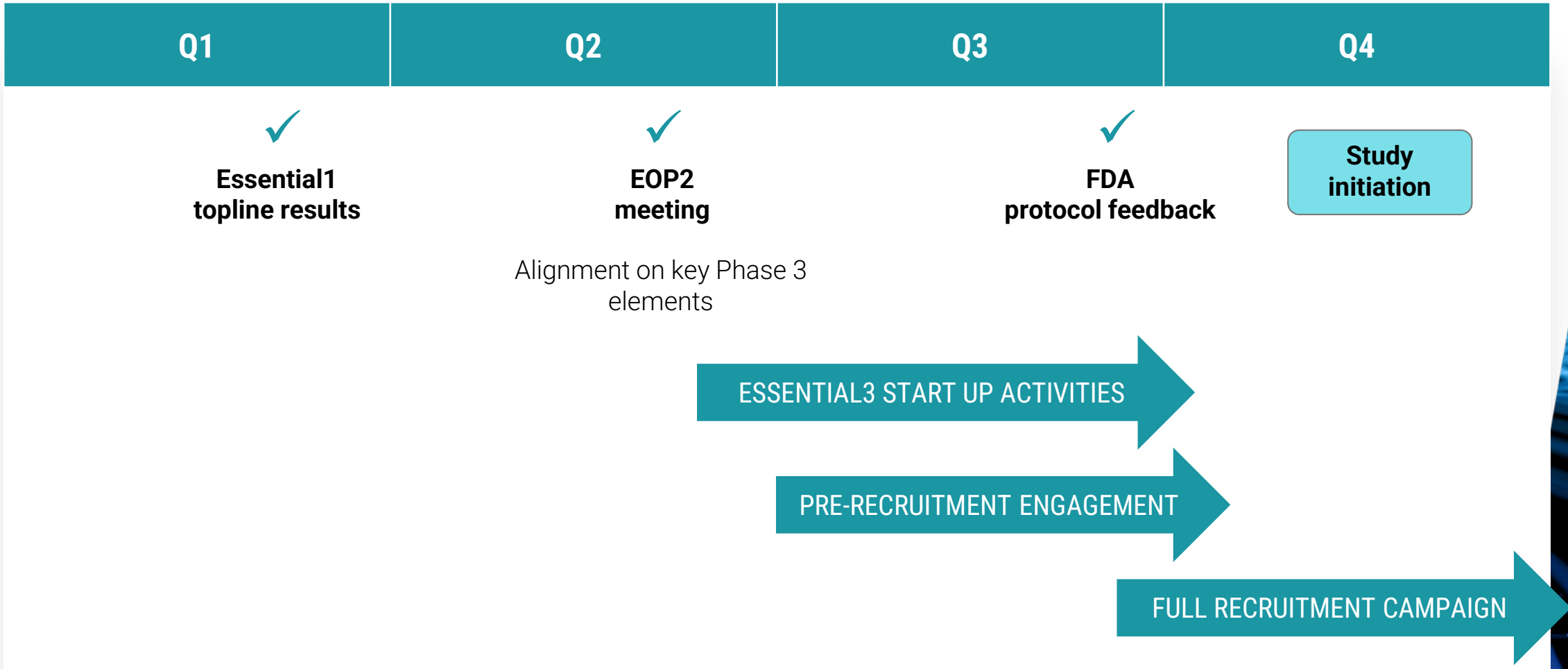
Design and execution of our Phase 3 strategy



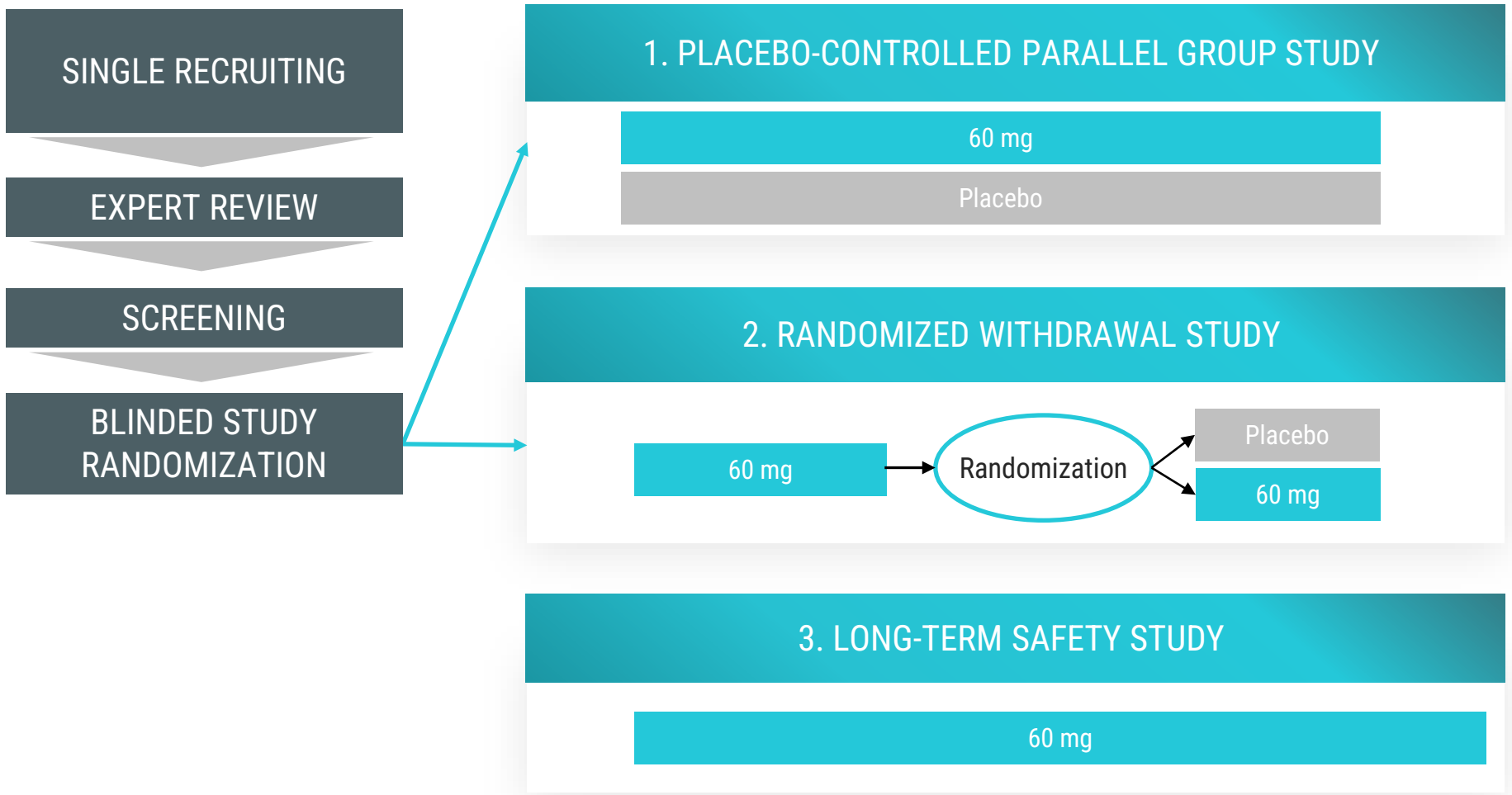
Essential1 as the foundation for our Phase 3 program

- Established reliable endpoint in mADL11
- Observed clinical meaningful results over time
- De-risked key elements of registration strategy

Moving towards Essential3 initiation



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



Powering the parallel design and randomized withdrawal studies

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	
Secondary endpoints	○ TETRAS-ADL ○ CGI-S ○ PGI-S/C ○ Other endpoints	

Decentralized design maximizes quality and control

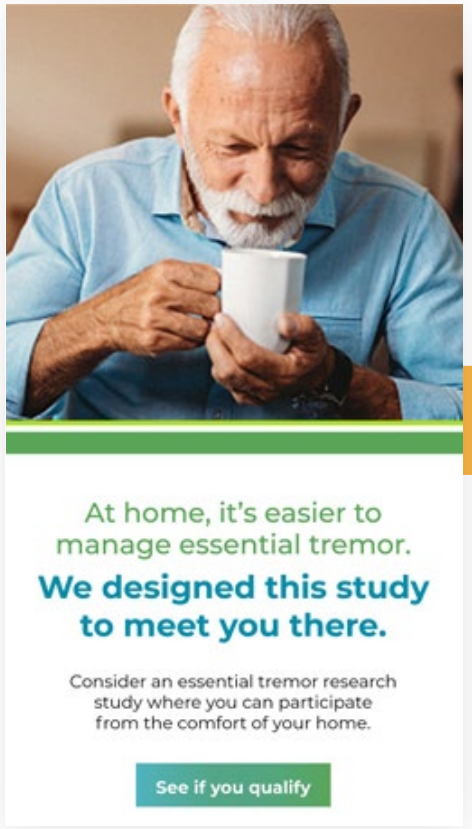
Structured video neurologic exam to confirm ET diagnosis and review by consistent eligibility review committee

Assessment done in the patient's home

Real-time data capture and quality check

Dedicated nationwide investigators → consistency in assessments and outcomes

Streamlining recruitment and enrollment de-risks execution



Two studies under single protocol with uniform inclusion/ exclusion criteria

Blinded study randomization

Stratification within studies to maintain balance of key variables

Unprecedented engagement and interest in Essential3

~600

patients already engaged since September in anticipation of E3

Engagement campaign expanding in October to achieve full enrollment in 1H 2024

Path to success with ulixacaltamide

AGILE WAY OF WORKING

Focused execution

SINGLE PROTOCOL

Optimized screening, enrollment, analysis

STREAMLINED DESIGN

Decentralized study to expand reach and reduce study burden

PATIENT-DRIVEN APPROACH

mADL11 as a clinically meaningful primary endpoint

NDA READINESS

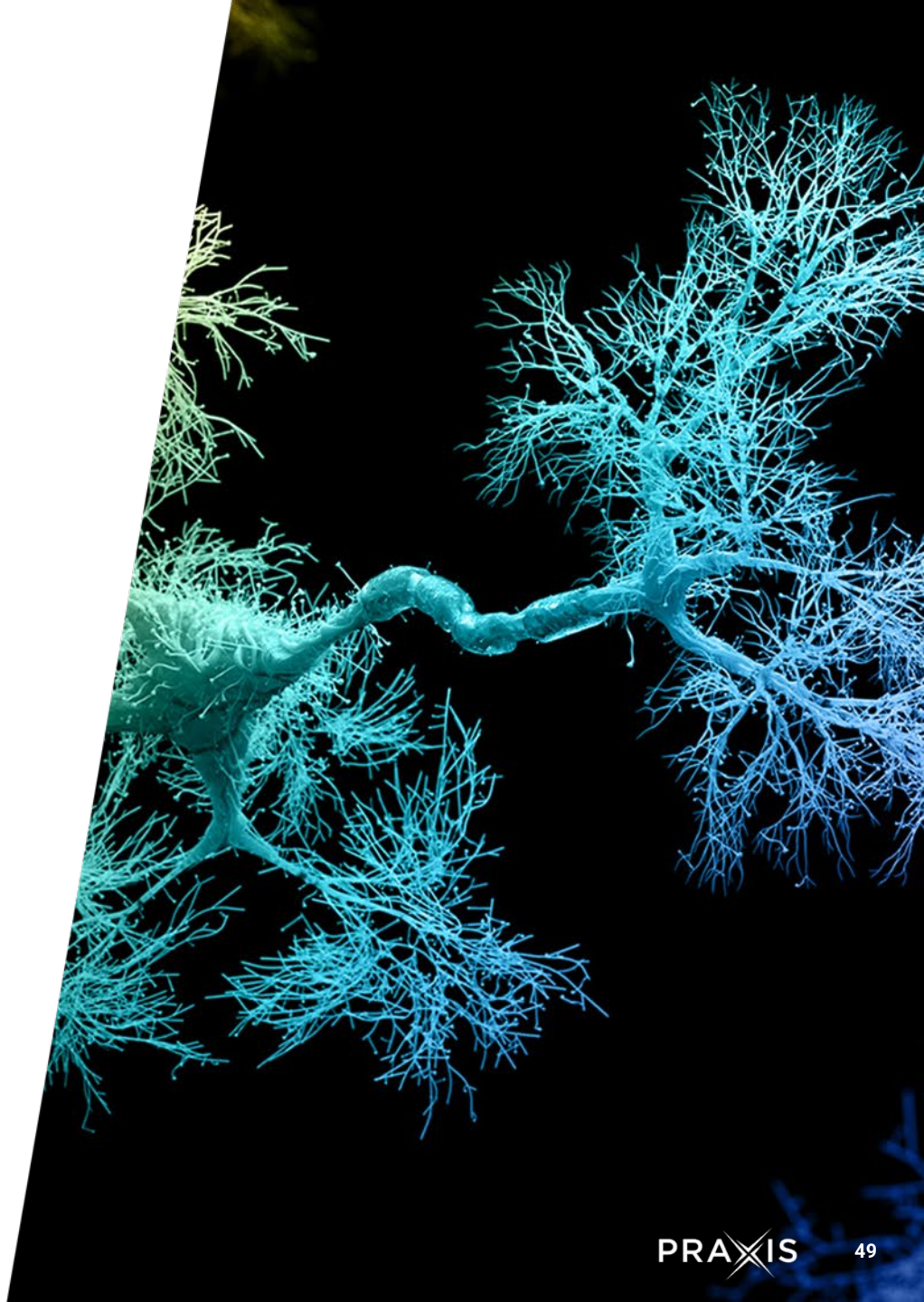
Clear path to filing in 2025

Epilepsy Portfolio

Developing Precision Therapies in Epilepsy

Steve Petrou, PhD.

Chief Scientific Officer



Utilizing our pillars to develop precision therapies in Epilepsy

	Development Pillar	Manifestation in Epilepsy	Clinical Program
	GENETICS	Impacting rare and common disorders	Reversing genetic etiology => 222 (ASO)
	TRANSLATIONAL TOOLS	Clinical and preclinical data guiding development	
	EFFICIENT & RIGOROUS	Innovation and efficiency in trial design and execution	Genetically validated targets and disease specific pharmacology => 628 (Small Molecule)
	PATIENT-GUIDED	Understand disease mechanisms and patient clinical needs to urgently deliver precision therapies	

SOLIDUS™

ASO PLATFORM

Tackling Developmental and Epileptic Encephalopathies

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
- The patient, carer and societal burden is immense, with urgent needs that can be met by Praxis's precision medicine approach

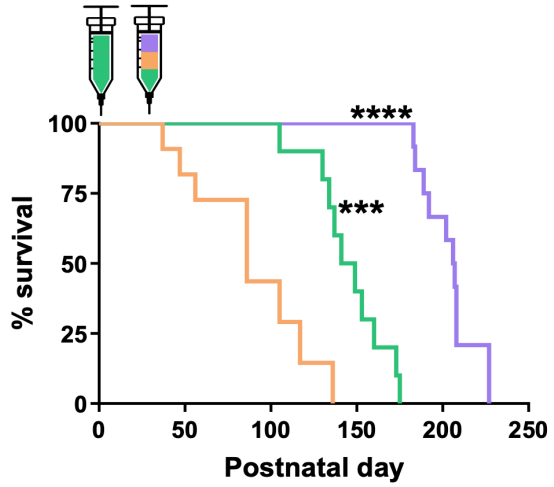
RESEARCH APPROACH

- 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

*Epidemiology of Developmental and Epileptic Encephalopathy and of Intellectual Disability and Epilepsy in Children. PMID: 36581463
**Genes4Epilepsy: An epilepsy gene resource. Epilepsia Volume 64, Issue 5 p. 1368-1375
github.com/bahlolab/genes4epilepsy

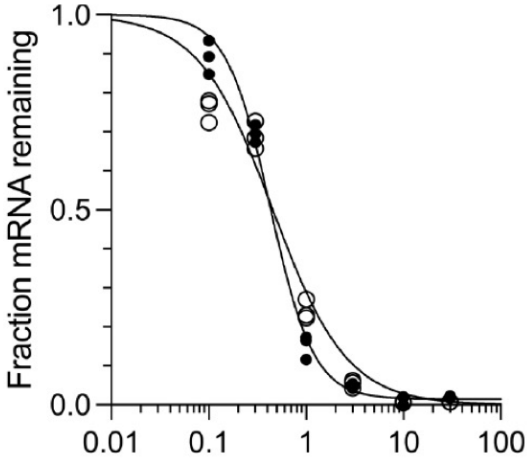
PRAXIS preclinical evidence for efficacy in SCN2A-DEE GoF and PCDH19-GCE mosaicism

PRAX-222 pre-clinical Proof of Concept



- Gapmer ASO that binds *SCN2A* mRNA and tags it for degradation by RNAaseH
- Rescue of phenotype seen across multiple domains 2-4 weeks after single ICV dose in mouse model
  - Neuronal excitability restored to WT control
  - Complete abolition of seizures
  - Treated mice behavior across motor, psychosocial and cognitive domains identical to WT control

PRAX-080



- PCDH19-Girls Clustering Epilepsy is a severe DEE affecting females and mosaic males
- PRAX-080 is a PCDH19 gapmer ASO program designed to completely ablate expression of WT and MT forms to remove mosaic expression
- Potent, selective, well tolerated gapmer ASOs have been identified and program is poised to advance in the future.

Praxis data on file

CEREBRUM™

SMALL MOLECULE PLATFORM

PRAX-628 is poised to address the Focal Epilepsy Market

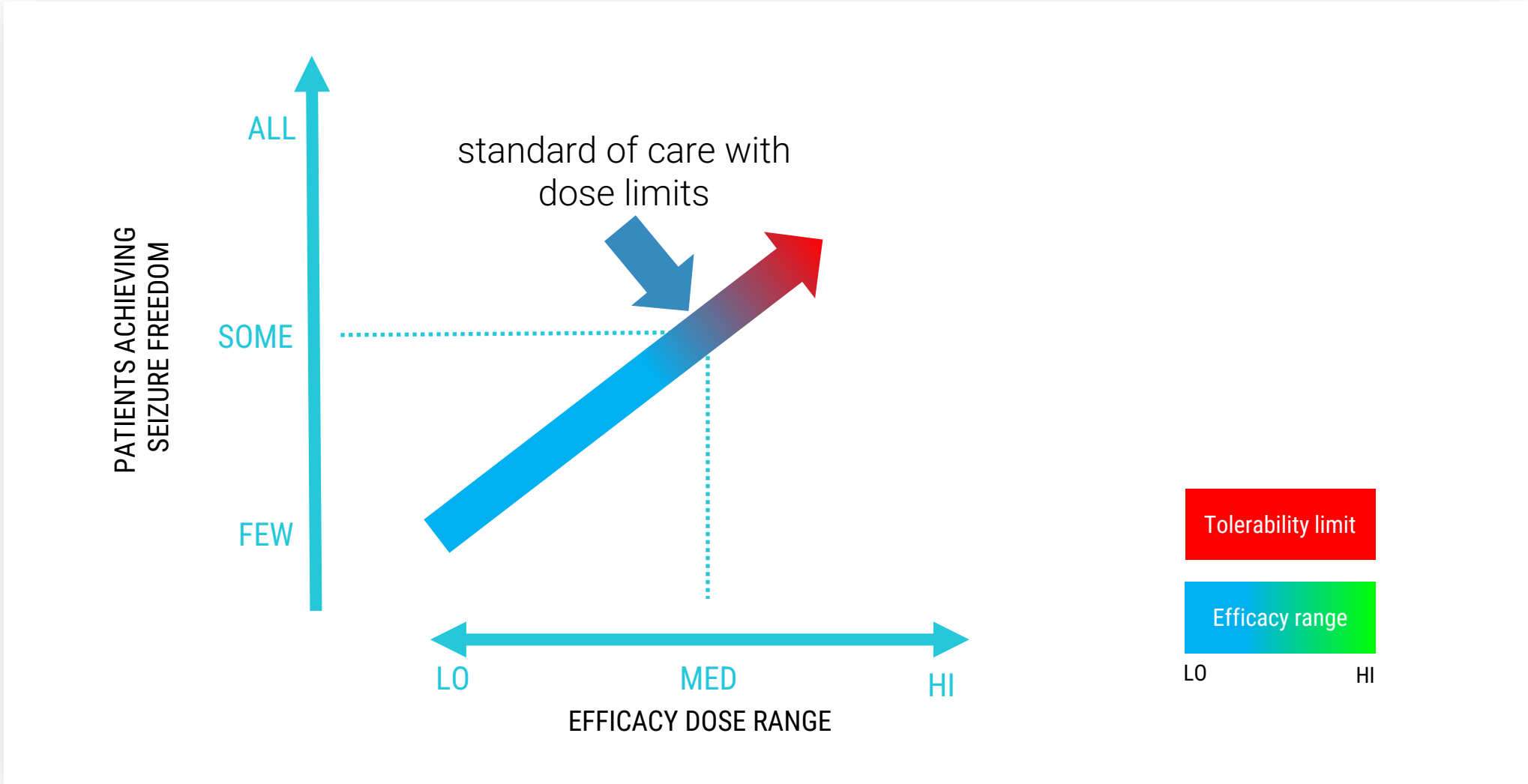
Limitation of the current treatments

- Complex dosing
- Long time to wait for efficacy
- On-target and off target side effects
- Efficacy capped by tolerability

CURRENT ASMs PRE-DATE EPILEPSY PRECISION MEDICINE

	Drug	First reported
Lamictal®	Lamotrigine	1981
Keppra®	Levetiracetam	1985
Lyrica®	Pregabalin	1993
Vimpat®	Lacosamide	1996
Fycompa®	Perampanel	2001
Aptiom®	Eslicarazepine	1986
Briviact®	Brivaracetam	2001
Xcopri®	Cenobamate	2006
	XEN1101	2010
	PRAX-628	12/2019

Can a better side effect profile lead to better efficacy?



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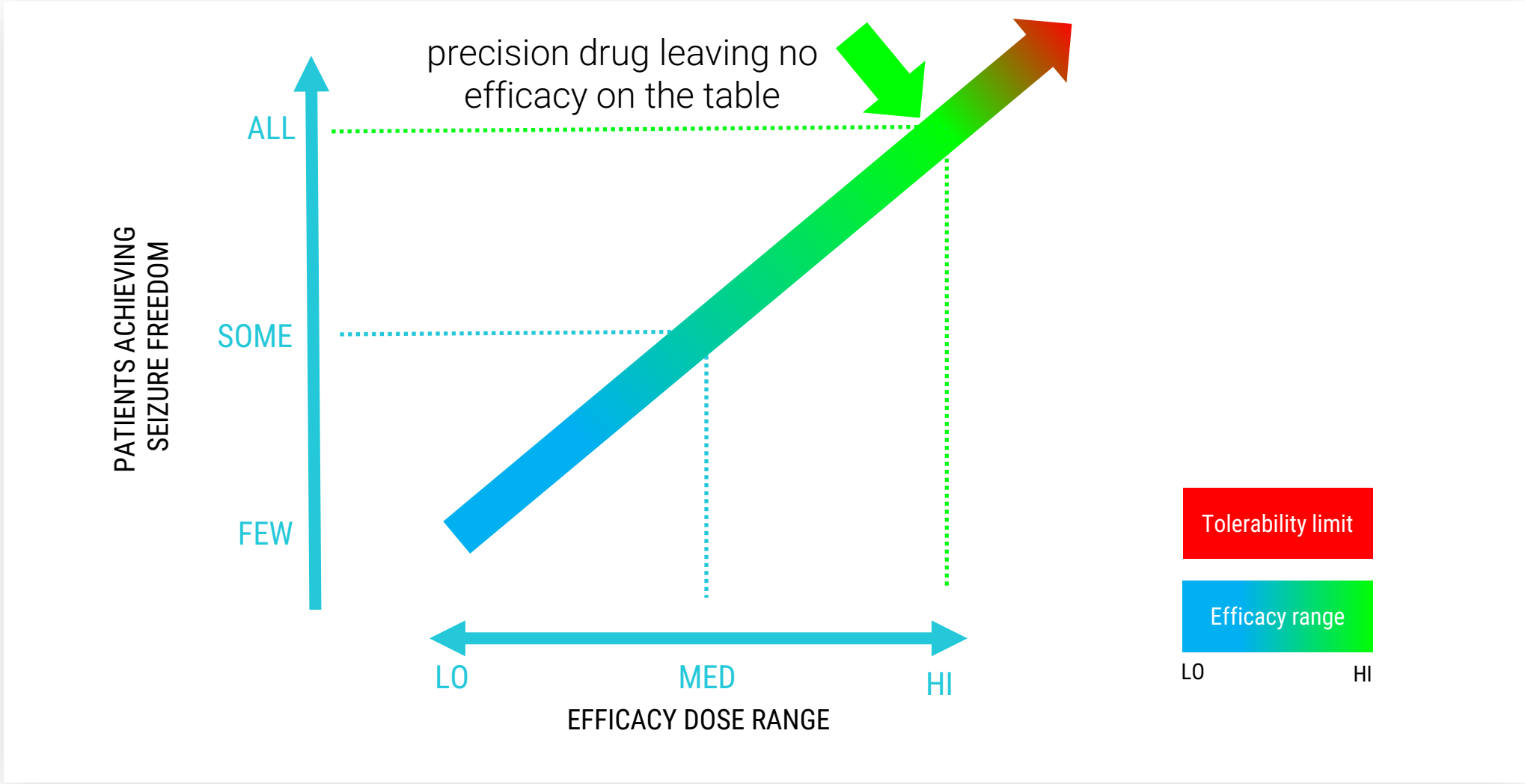
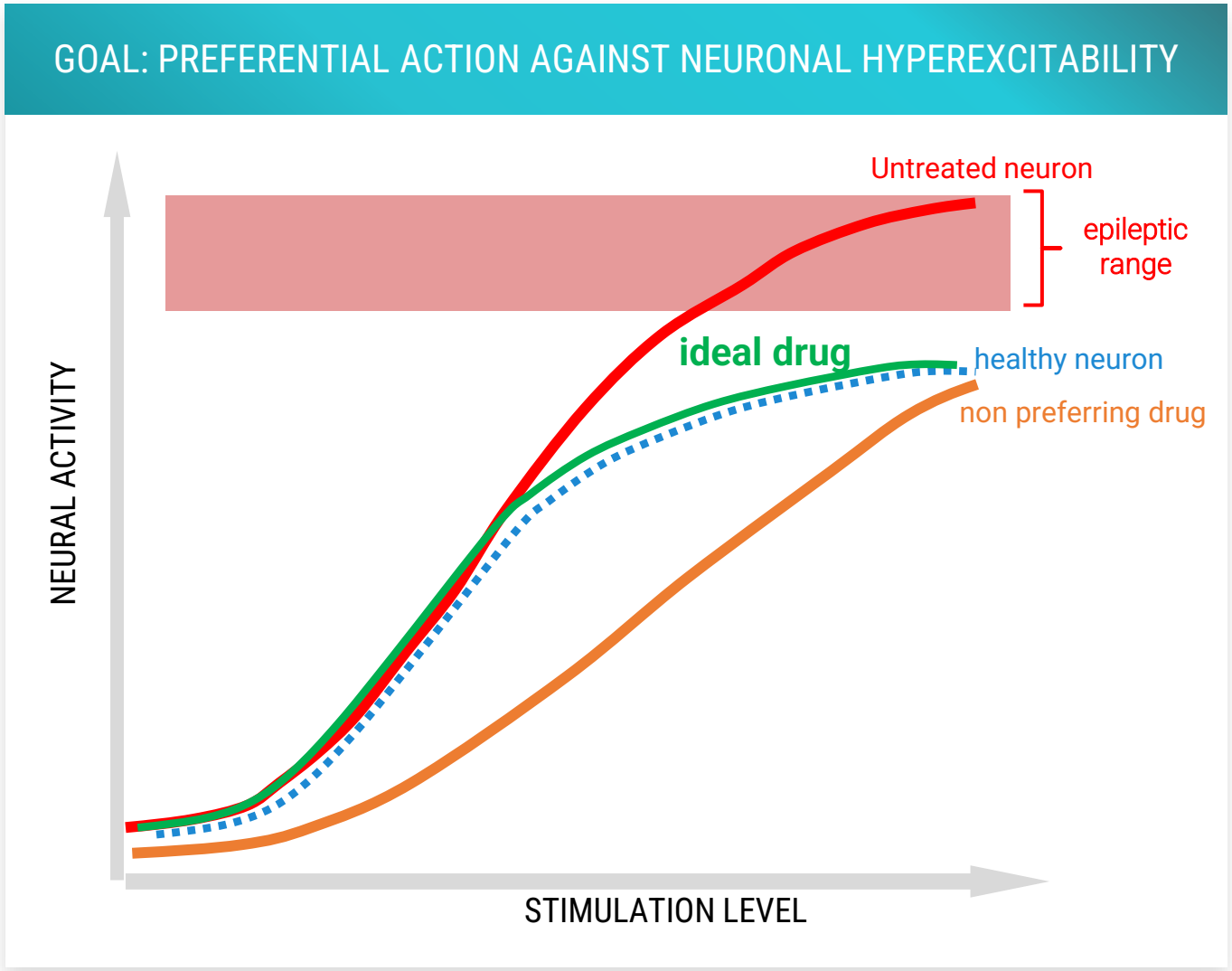


Ideal profile by precision sodium channel modulation



Actual profile of precision sodium channel modulation (PRAX-628)

BIOPHYSICAL "LEVERS" TO ACHIEVE PREFERENTIAL ACTION:

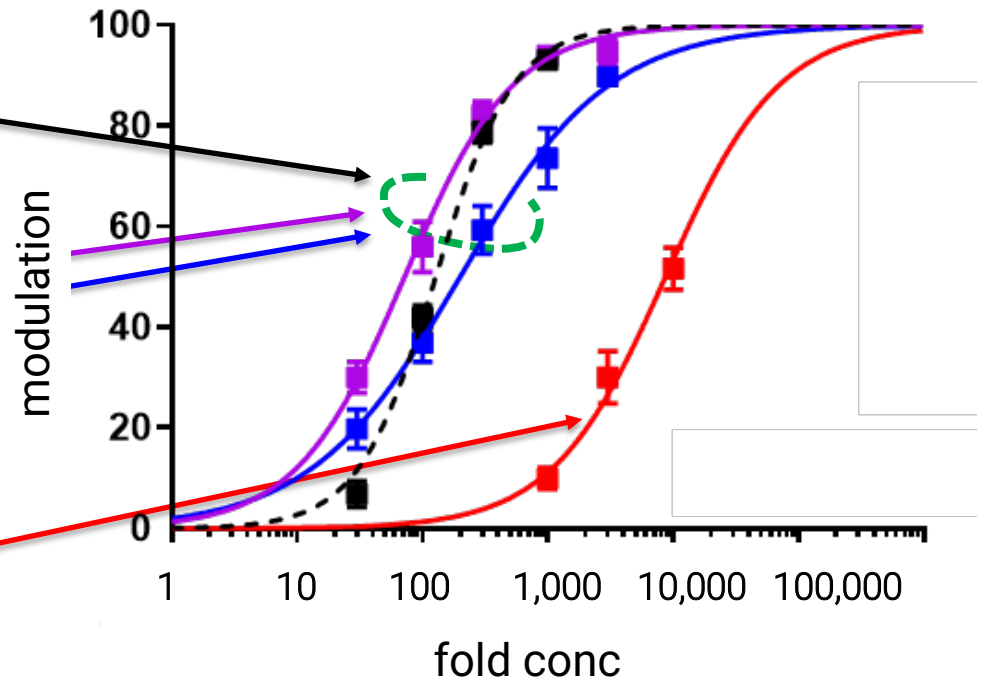
A. Reduce pro-excitatory channel function
   - Inhibit pathological persistent current

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

C. Maintain channel availability during low activity
   - Minimize block against steady state peak current

D. Kinetics of drug binding and unbinding
   - Bind fast, unbind slow

ACTION AGAINST HUMAN BRAIN SODIUM CHANNEL



PRAX-628

Praxis data on file

Actual profile of precision sodium channel modulation (PRAX-628)

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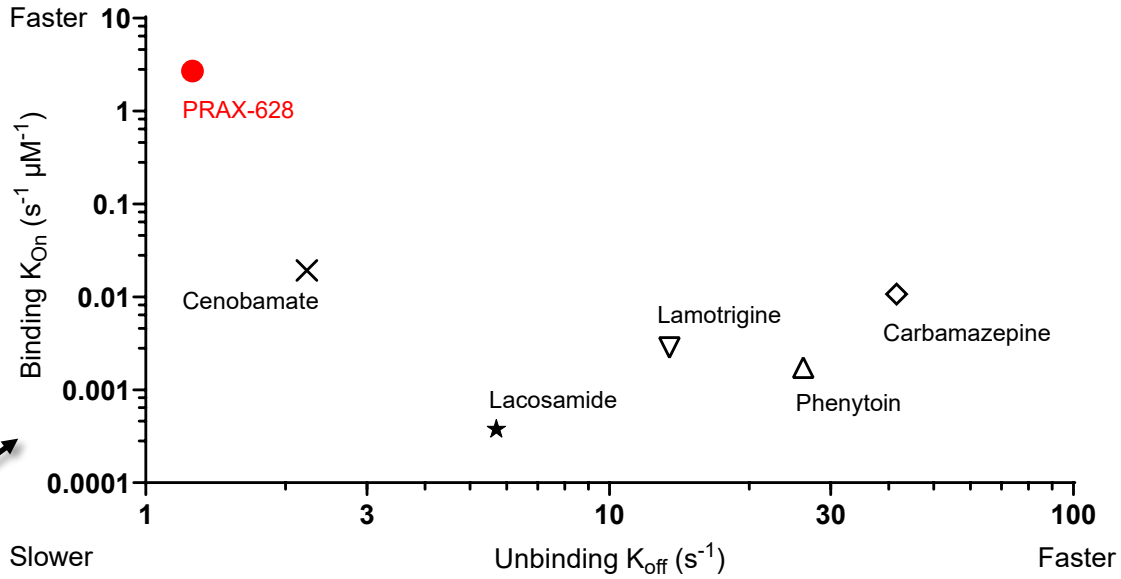
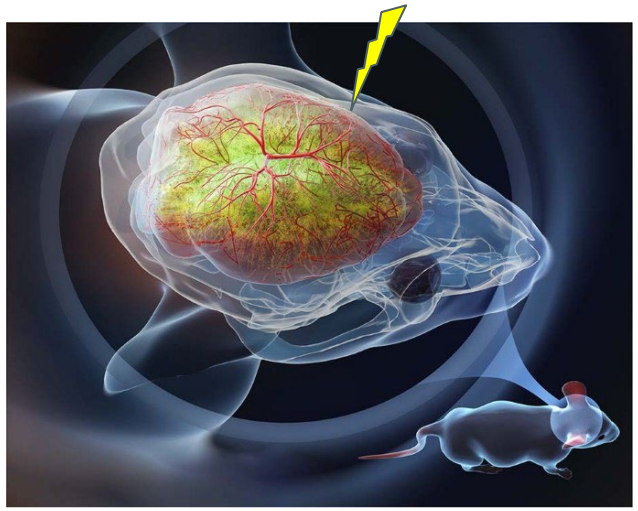
   - Bind fast, unbind slow

DIFFERENTIATED BINDING PROFILE FAVOURING PREFERENTIAL ACTION



Praxis data on file

MES is a rapidly deployed and efficient pre-clinical assay that predicts clinical exposure and efficacy in Focal Onset Seizures (FOS)

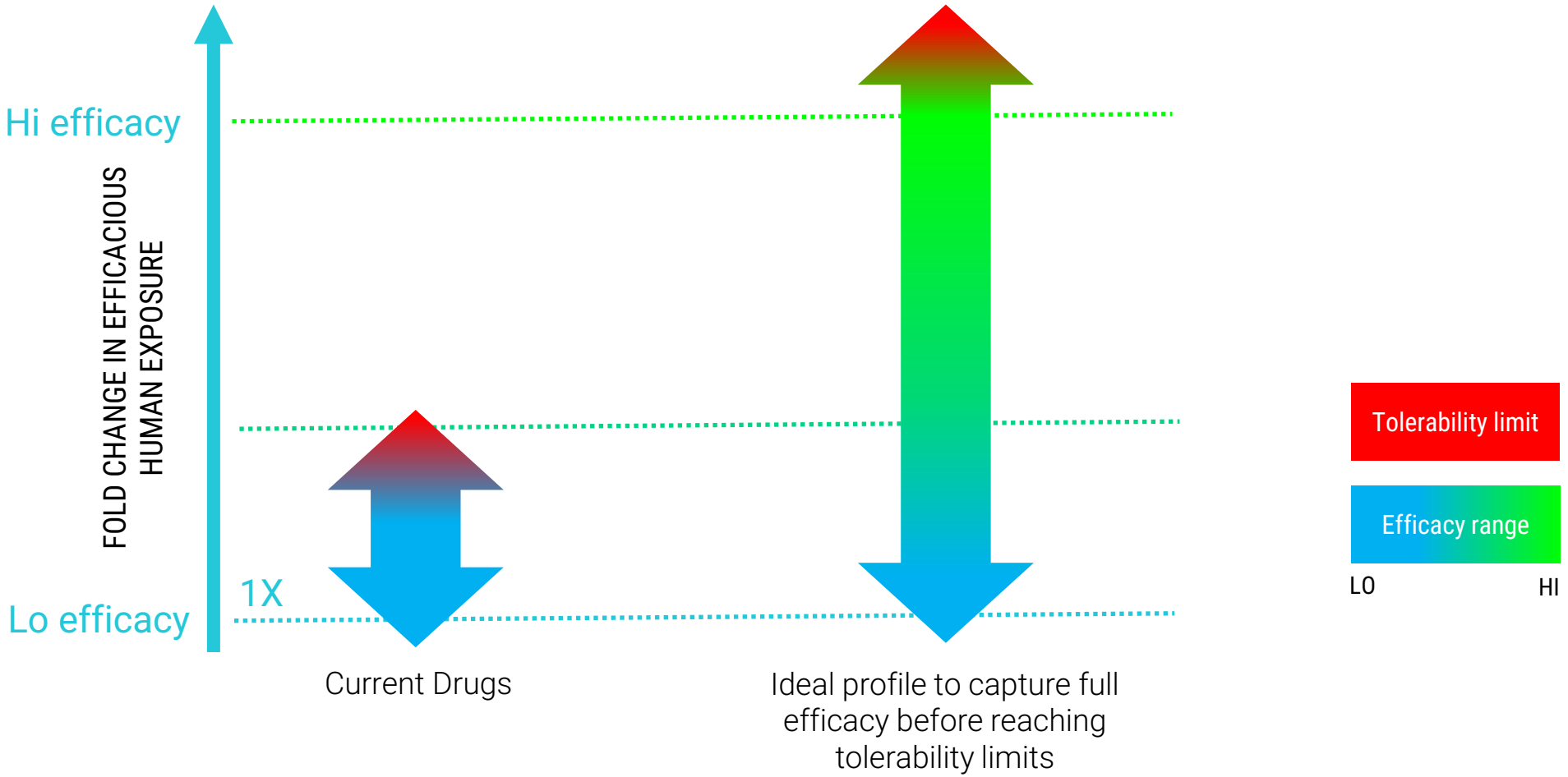


"Maximal electroshock seizure (MES) is an experimental paradigm that induces synchronous neural discharges in the brain through artificial current input (Kamei et al., 1978), and is used to induce acute epileptic behaviors (Fischer & Muller, 1988)" *

- Drugs that work in MES work in FOS
- Efficacious exposures in MES models correspond to efficacious exposures in human FOS

* PMID: 31011134

Combining MES and human safety studies for predictive translation

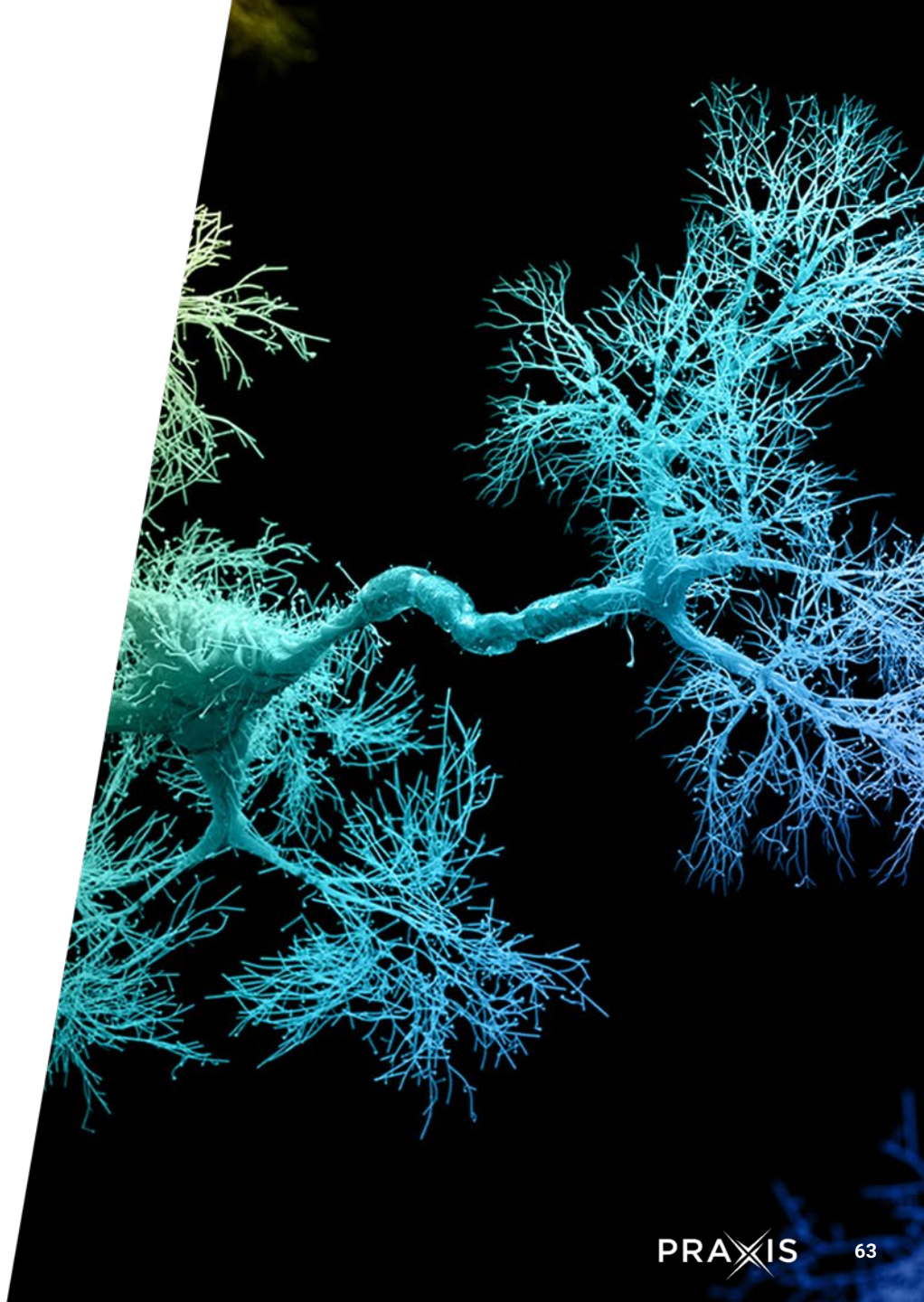


PRAX-628 Clinical Update

Karl Hansen, PhD.

Chief Technical Operations Officer

PRAX-628 Program Lead



What would the profile of a precision ASM be?

Limitation of the current treatments:

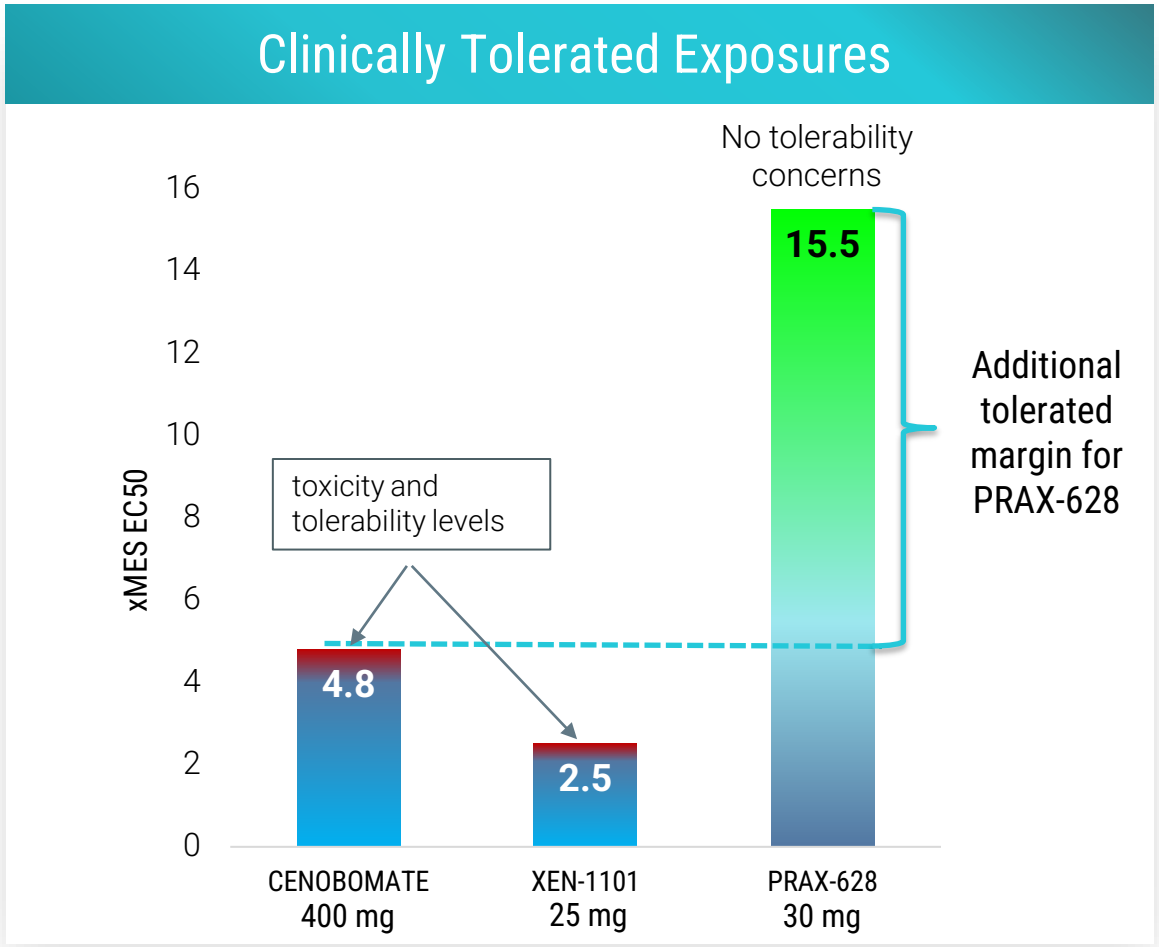
- On-target and off-target side effects
- Efficacy capped by tolerability
- Complex dosing
- Long time to wait for efficacy

Ideal Treatment

- ❑ Tolerable safety profile
- ❑ Reaches the brain
- ❑ Rapidly achieves therapeutic concentrations without titration
- ❑ Continuous coverage at higher therapeutic levels
- ❑ Ability to provide maximum efficacy

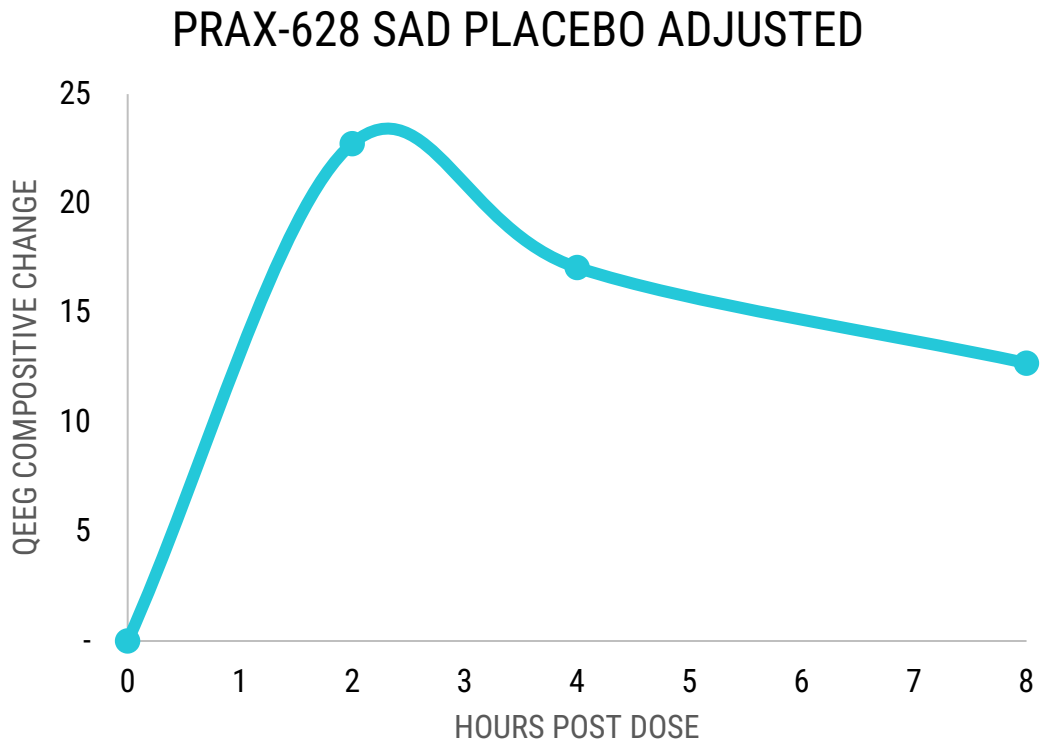
PRAX-628 has completed a Phase 1 SAD / MAD study which shows it is on track to be the first Precision ASM for Focal Epilepsy

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 C_{max}: >46,100 ng/mL, 400 mg C_{max} (Vernillet et al 2020), XEN1101 C_{max}: >107 ng/mL (Phase 1 data)
x MES EC_{50} = multiple of predicted human EC_{50} based on the rodent MES model

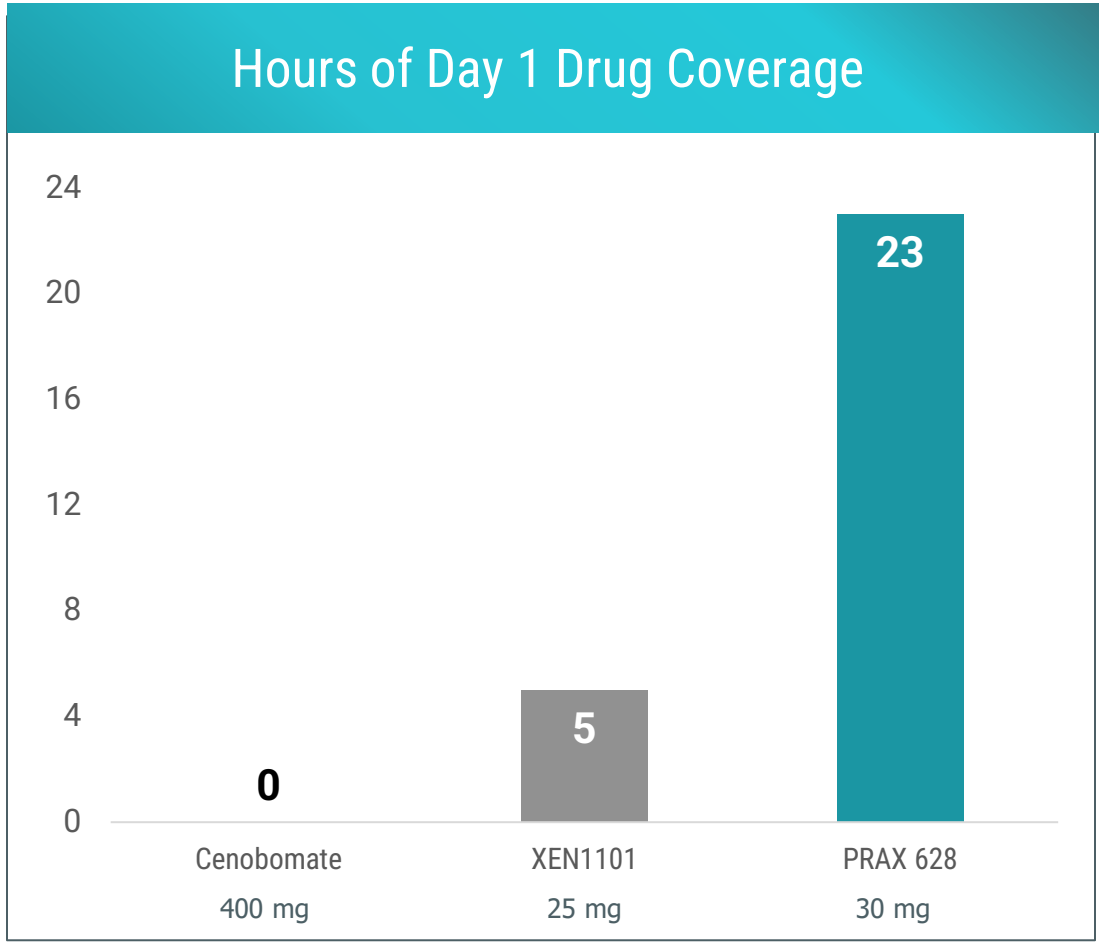
Composite qEEG shows clear brain activity across all doses within hours of administration



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

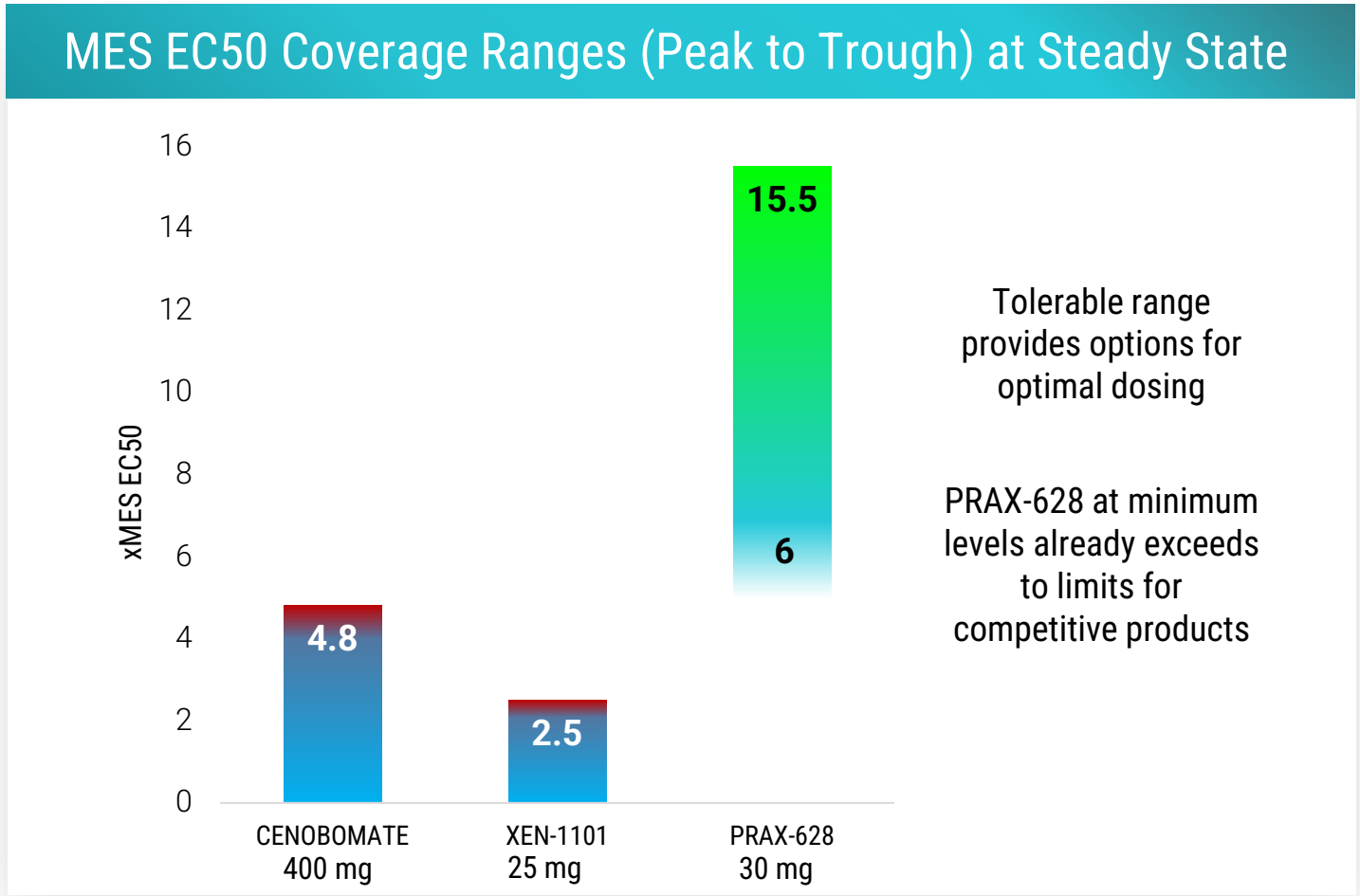
Source: Praxis data on file, Ph1 study.

PRAX-628 achieves nearly complete coverage on Day 1



Estimated based on SAD Food effect data, Praxis data on file (Ph1 study)

PRAX-628 maintains higher active MES EC50 multiples at steady state



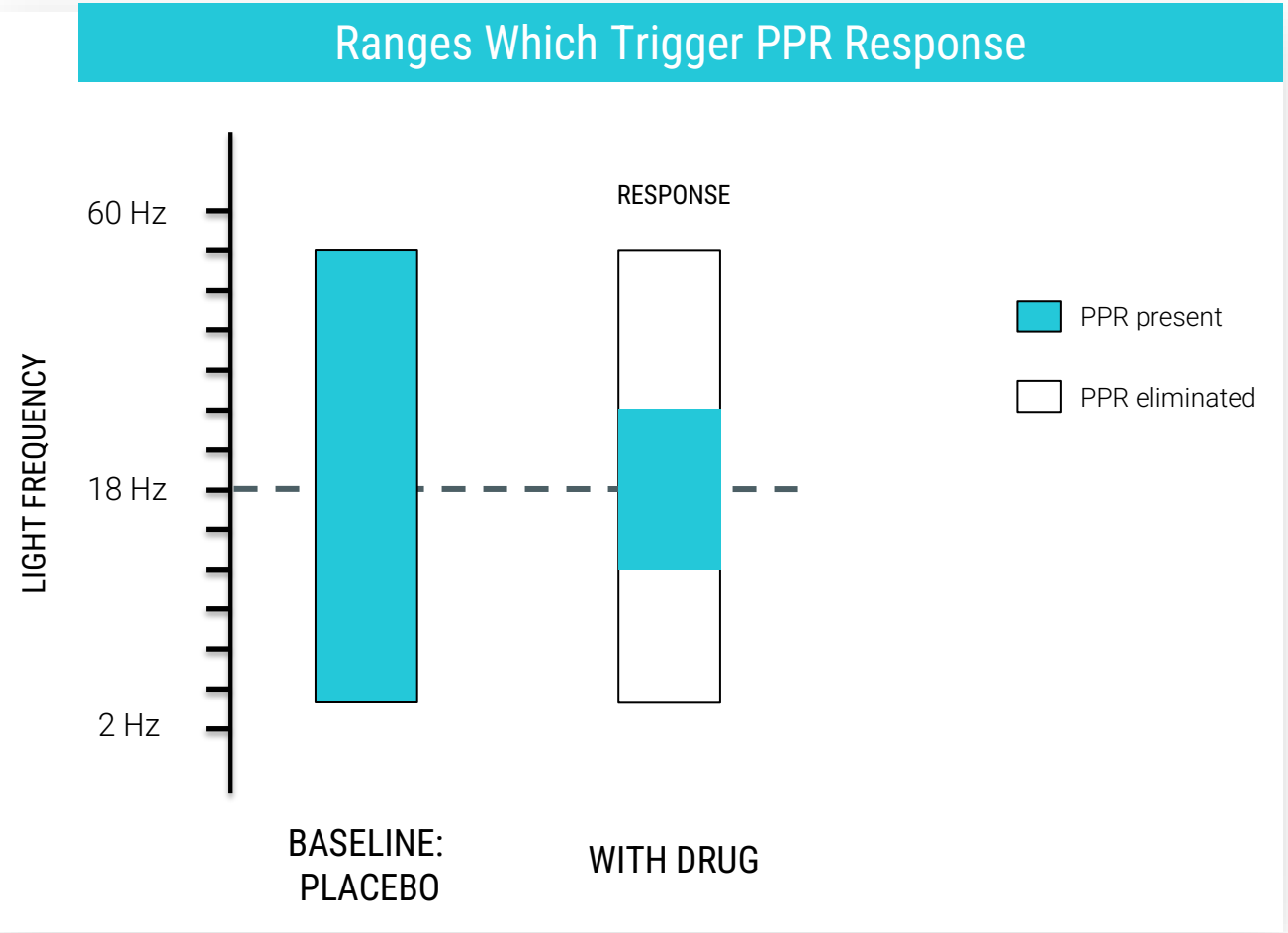
Estimated based on SAD Food effect data, Praxis data on file (Ph1 study)

PRAX-628 has presented an ideal precision ASM profile through Phase 1

Ideal Treatment

- ☑ Tolerable safety profile
- ☑ Continuous coverage at higher therapeutic levels
- ☑ Reaches the brain
- ☑ Rapidly achieves therapeutic concentrations
- ☑ Ability to provide maximum efficacy

The Phase 2 PRAX-628 PPR study will provide insight into efficacy and inform dose selection for pivotal studies



- The PPR Photosensitivity Model has been used to assess many AEDs[1]
- Reduction of PPR photosensitivity range by drug versus PBO correlates to drug efficacy in a small sample size

[1] Source: First Pub: C.D. Binnie Electroencephalography and clinical neurophysiology A, 1986, 63, 35-41; LEV paper: DGA Kasteleijn-Nolst Trenité Epilepsy Research 25(1996) 225-230; DGA Kasteleijn-Nolst Trenité Neurology 93(6) 2019 e559-e567 cenobamate paper


PRAXIS
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