

Investor & Analyst Day

June 2, 2025



Disclaimer

This presentation contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, each as amended. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, but are not limited to, express or implied statements regarding: the clinical development of RAP-219 for the treatment of refractory focal epilepsy, bipolar mania and diabetic peripheral neuropathic pain, including the initiation, timing, progress and results of our ongoing and planned clinical trials; expectations for the activity, tolerability, and commercial potential of RAP-219; the potential of Rapport's RAP technology platform; and expectations for Rapport's uses of capital, expenses and financial results, including its cash runway through the end of 2026.

Forward-looking statements are based on management's current expectations and are subject to risks and uncertainties that could negatively affect Rapport's business, operating results, financial condition and stock value. Factors that could cause actual results to differ materially from those currently anticipated include: risks relating to the company's research and development activities; Rapport's ability to execute on its strategy including obtaining the requisite regulatory approvals on the expected timeline, if at all; uncertainties relating to preclinical and clinical development activities; the company's dependence on third parties to conduct clinical trials, manufacture its product candidates and develop and commercialize its product candidates, if approved; Rapport's ability to attract, integrate and retain key personnel; risks related to the company's financial condition and need for substantial additional funds in order to complete development activities and commercialize a product candidate, if approved; risks related to regulatory developments and approval processes of the U.S. Food and Drug Administration and comparable foreign regulatory authorities; risks related to establishing and maintaining Rapport's intellectual property protections; and risks related to the competitive landscape for Rapport's product candidates; as well as other risks described in “Risk Factors,” in the company's Annual Report on Form 10-K and most recent Quarterly Report on Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in Rapport's subsequent filings with the Securities and Exchange Commission. Any forward-looking statements represent Rapport's views only as of today and should not be relied upon as representing its views as of any subsequent date. Rapport expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in its expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law, and claims the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

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- 03** **RAP-219: Phase 1 Data | RAP-219: Phase 2a Focal Epilepsy Trial Overview**
Jeff Sevigny, M.D., Chief Medical Officer
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Jacqueline French, M.D., Professor of Neurology, NYU Langone | Jeff Sevigny, M.D.
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William Motley, M.D., RAP-219 Program Leader
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Leadership with track record of innovation and expertise

Management Team



David Brett, M.D., Ph.D.
Founder, Chief Scientific Officer
20 years neuroscience drug discovery experience; Former Global Head of Neuroscience Discovery, Janssen Global Services
Johnson&Johnson *Lilly*



Abe Ceesay¹
Chief Executive Officer
15+ years commercial and executive leadership experience; Former President, Cerevel Therapeutics
cerevel *Ironwood* *genzyme*
TIBURIO *scPharmaceuticals*



Cheryl Gault
Chief Operating Officer
20+ years corporate strategy and corporate development experience
cyclerion *Ironwood* *genzyme*



Troy Ignelzi
Chief Financial Officer
20+ years financial leadership experience in biotech and pharma sectors
KARUNA THERAPEUTICS *scPharmaceuticals*
Lilly *CINCOR* *ESPERION*



Jeff Seigny, M.D.
Chief Medical Officer
15+ years translational and clinical drug development
Lilly *Prevail* *Biogen*
NOVARTIS *MERCK*



Kathy Wilkinson
Chief People Officer
15+ years of human resources experience in biotech
bluebirdbio *seventybio*
Bristol Myers Squibb



Swamy Yeleswaram, Ph.D.
Chief Development Officer
25+ years drug discovery experience; Founding scientist of Incyte
Incyte *Bristol Myers Squibb*

Board of Directors

Steve Paul, M.D.
Founder and Board Chair
Partner, Third Rock Ventures

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Former Founding CEO, Alnylam

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Senior Advisor, Bain Life Sciences; Former CMO, Cerevel Therapeutics

Paul Silva
Director
Former Chief Accounting Officer, Vertex Pharmaceuticals

Wendy Young, Ph.D.
Director
Former Head of Small Molecule Drug Discovery, Genentech

¹ Employee director.

Small molecule precision medicines for patients with neurological and psychiatric disorders

Strong Foundation & Differentiated Precision Approach

Company builders with industry-proven leadership

Differentiated pharmacology we believe promotes **high selectivity and specificity**

Potential to transform the treatment of neurological and psychiatric disorders with **differentiated profile**



Robust Clinical & Discovery Pipeline

Potential **first-in-class programs** leveraging receptor associated protein (RAP) science

RAP-219 forebrain restricted TARP γ 8 AMPAR modulator – significant opportunity in initial indication in focal epilepsy

Medicinal chemistry-enabled **discovery portfolio** with potential in additional indications



RAP-219: Pipeline-in-a-Product with Multiple Catalysts

Topline Phase 2a Results in **refractory focal epilepsy** expected in Q3 25

Initiate Phase 2a in **bipolar mania** in Q3 25 with topline results in 1H 27

Finalizing plans for Phase 2a in **diabetic peripheral neuropathic pain**



Well Financed

\$285.4 million as of March 31, 2025¹

Cash runway expected to fund operations **through end of 2026**



Advancing precision therapeutics aimed at solving long-standing challenges in neuromedicine

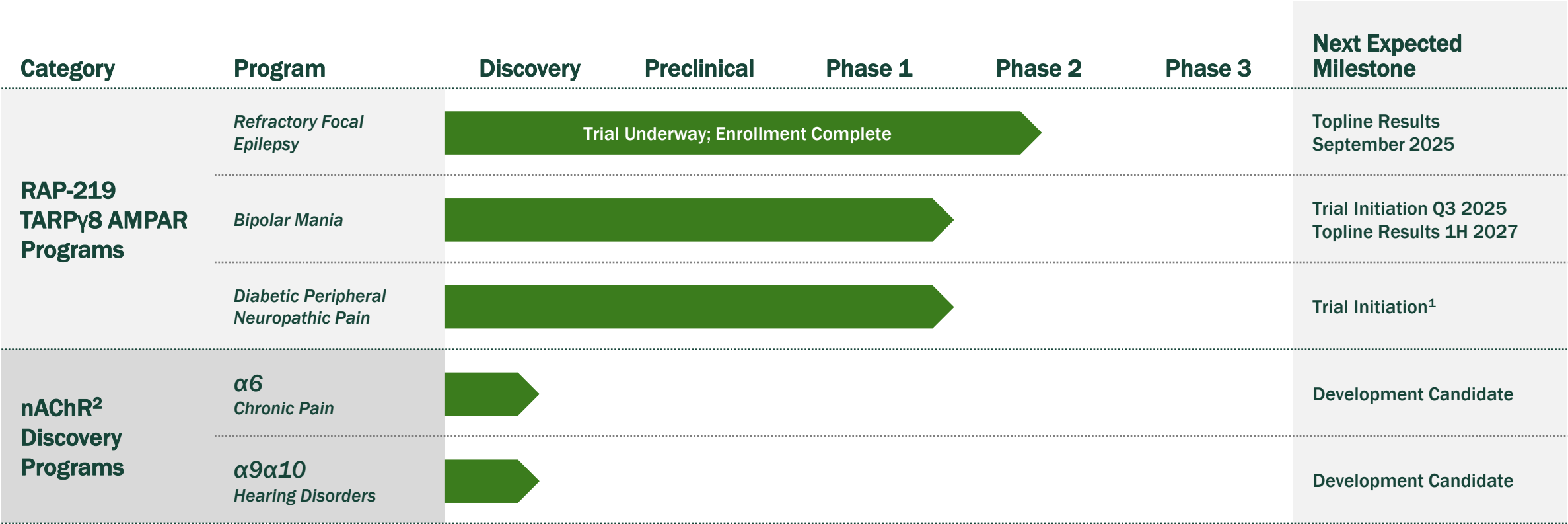
Conventional CNS drug discovery

- ✗ Drugs interact with receptors that are ubiquitous in the brain and body
- ✗ Drugs not designed with precision for disease-specific neuroanatomic sites / receptors
- ✗ Drug interactions and adverse events lead to noncompliance and discontinuation
- ✗ Drug discovery with conventional approaches (lacking RAPs) can miss high potential, previously unexplored targets

The potential of RAPs

- ✓ RAPs are components of the broader neuronal receptor complexes and play critical roles in regulating receptor assembly and function
- ✓ RAPs serve as unique binding sites targetable by novel pharmacophores designed for increased selectivity, providing neuroanatomical specificity
- ✓ RAPs can enable differentiated pharmacology and potentially provide favorable efficacy, safety, and administration profiles
- ✓ RAPs can “unlock” drug targets previously inaccessible to study in vitro, allowing for potentially first-in-class drug discovery programs

Precision neuroscience pipeline with opportunity to address large market opportunities



Strong intellectual property with worldwide rights to all programs

Note: We have conducted four Phase 1 trials supportive of multiple RAP-219 indications.
¹ IND is currently on clinical hold with the FDA; ² nicotinic acetylcholine receptor.

RAP-219 enables “pipeline-in-a-product” opportunity

~1.8M

Focal epilepsy in U.S. patients¹

~7.2M

Bipolar disorder in U.S. patients²

~5.6M

Peripheral neuropathic pain
in U.S. patients³



TARPy8 is a preclinically
and clinically validated
target for epilepsy



Once daily (QD) dosing
Differentiated tolerability profile
No observed drug-drug
interactions (DDI)

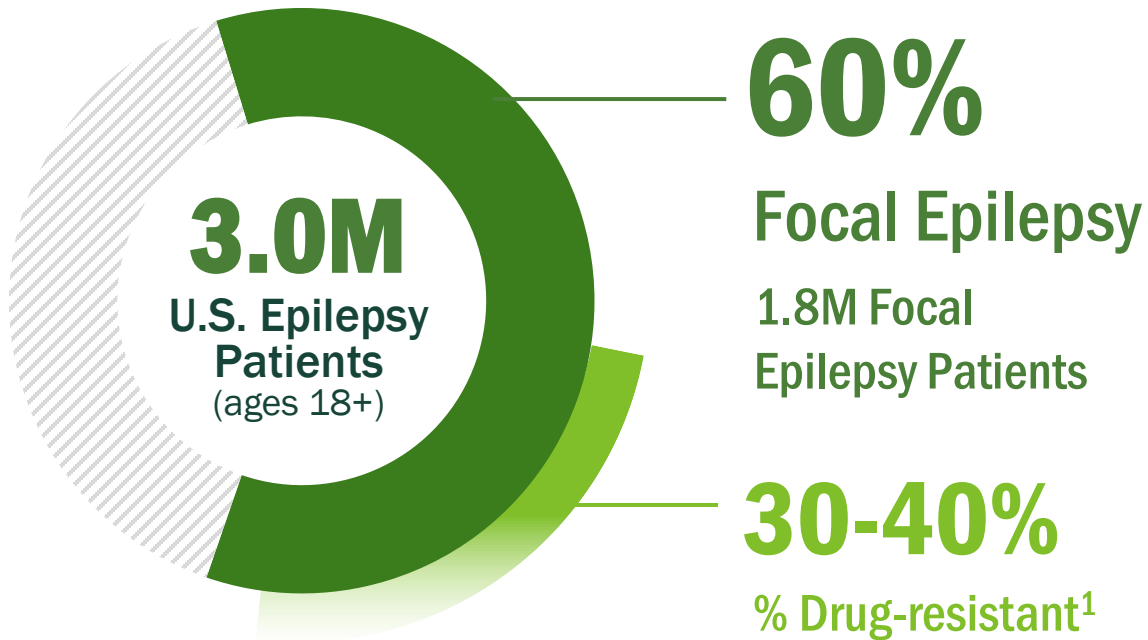


Compelling data supporting
potential in bipolar disorder and
peripheral neuropathic pain



Potency data and metabolic
profile support RAP-219's
development as a long acting
injectable, which could improve
compliance and outcomes

Unmet need in epilepsy highlights limitations of current antiseizure medications



Limitations of antiseizure medications (ASMs)

Limited Efficacy: Despite over 20 FDA approved ASMs, 30-40% of patients are still drug-resistant¹

Tolerability Issues: Especially CNS side-effects, such as sedation, ataxia, and cognitive problems

Potential for Serious Adverse Events: Such as severe cutaneous reactions, serious hematological disorders, and hepatic failure

Risk of Breakthrough Seizures: Missing doses of seizure medicine is the most common cause of breakthrough seizures due to the short half-life of many antiseizure medications²

Complicated Administration: Long titration, drug-drug interactions, and lab monitoring

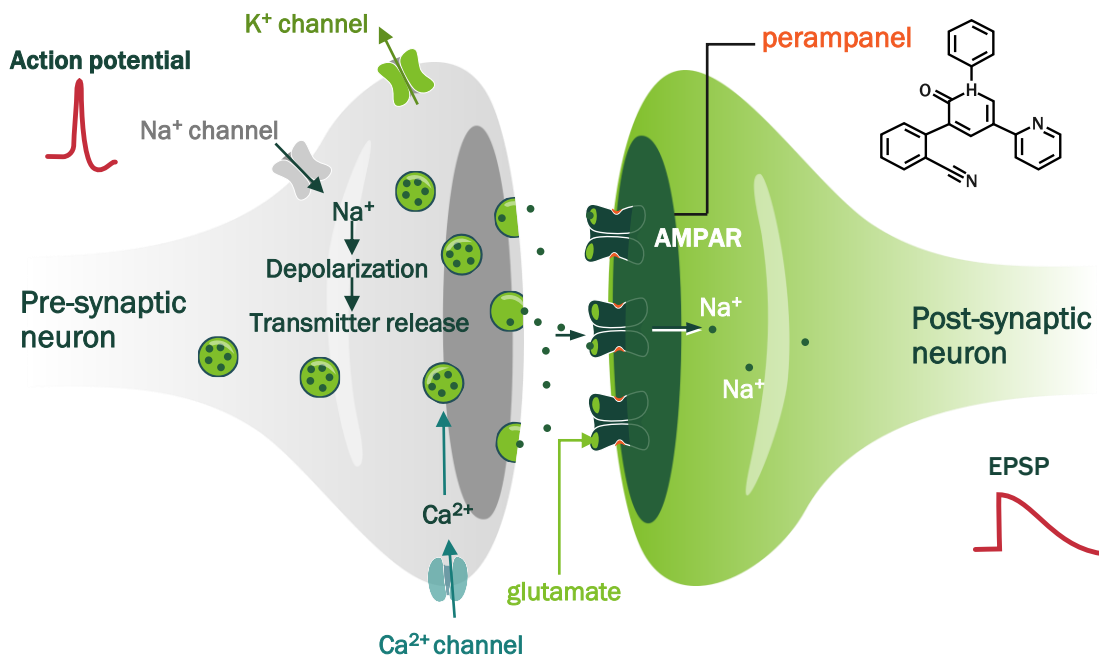
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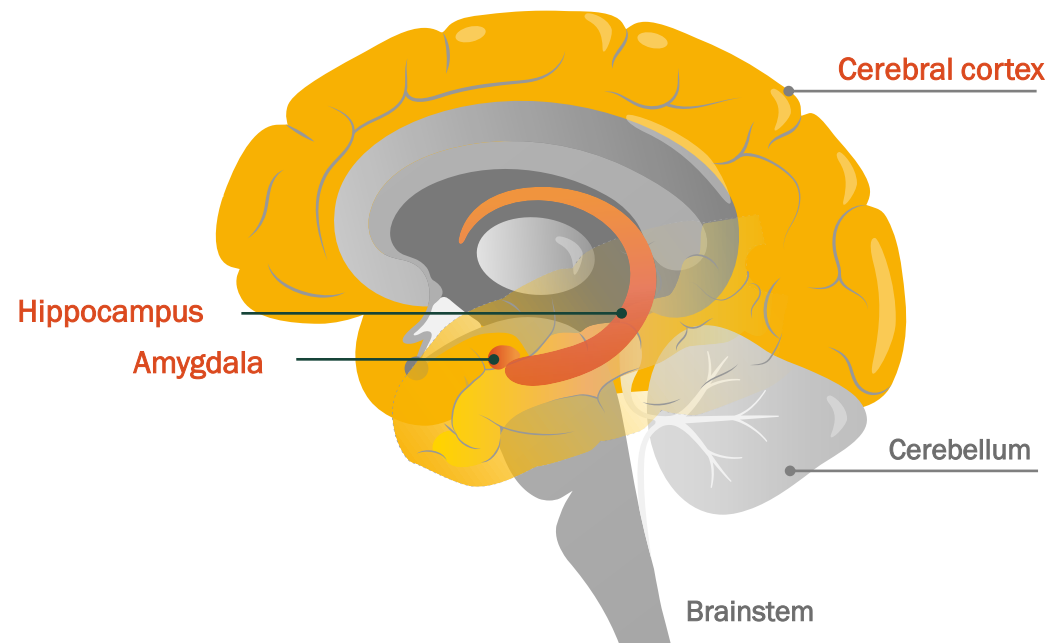
AMPA inhibition is a clinically validated approach for epilepsy

AMPA receptors (AMPA) in epilepsy



- AMPA type glutamate receptors at excitatory synapses can mediate seizure initiation and spread
- AMPAR target is clinically validated - perampanel (FYCOMPA®) is an FDA/EMA approved pan-AMPA antagonist for the treatment of focal onset and generalized seizures

Mesial temporal lobe and cerebral cortex are the key brain areas associated with focal onset seizures



- ~50% of all focal onset seizures originate in the mesial temporal lobe (MTL), which includes the hippocampus and amygdala
- Most of the remaining 50% originate in the cerebral cortex and spread into the mesial temporal structures
- Focal onset seizures do not originate in hindbrain structures

RAP-219 target/TARPy8 is selectively expressed in brain regions associated with focal onset seizures

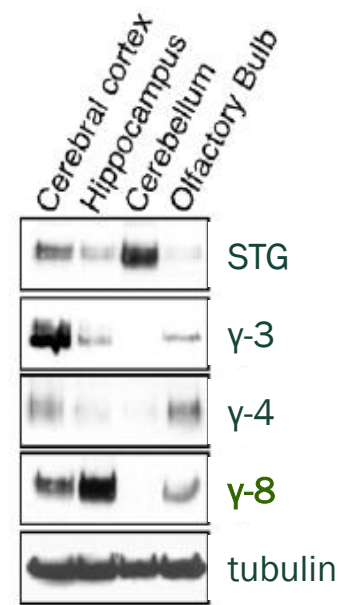
TARPs regulate the trafficking, subcellular localization and gating of AMPA receptors

Cryogenic electron microscopy of GluA1/2 + TARPy8 complex



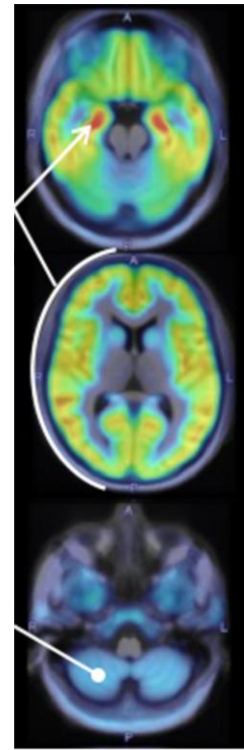
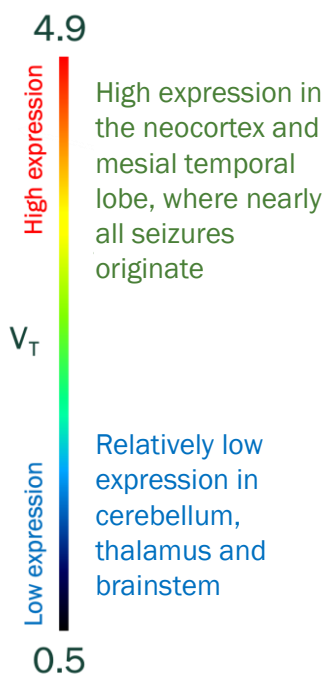
NatComm 2022 13:734

Western blot



JCB 2003 161:805

TARPy8 clinical PET



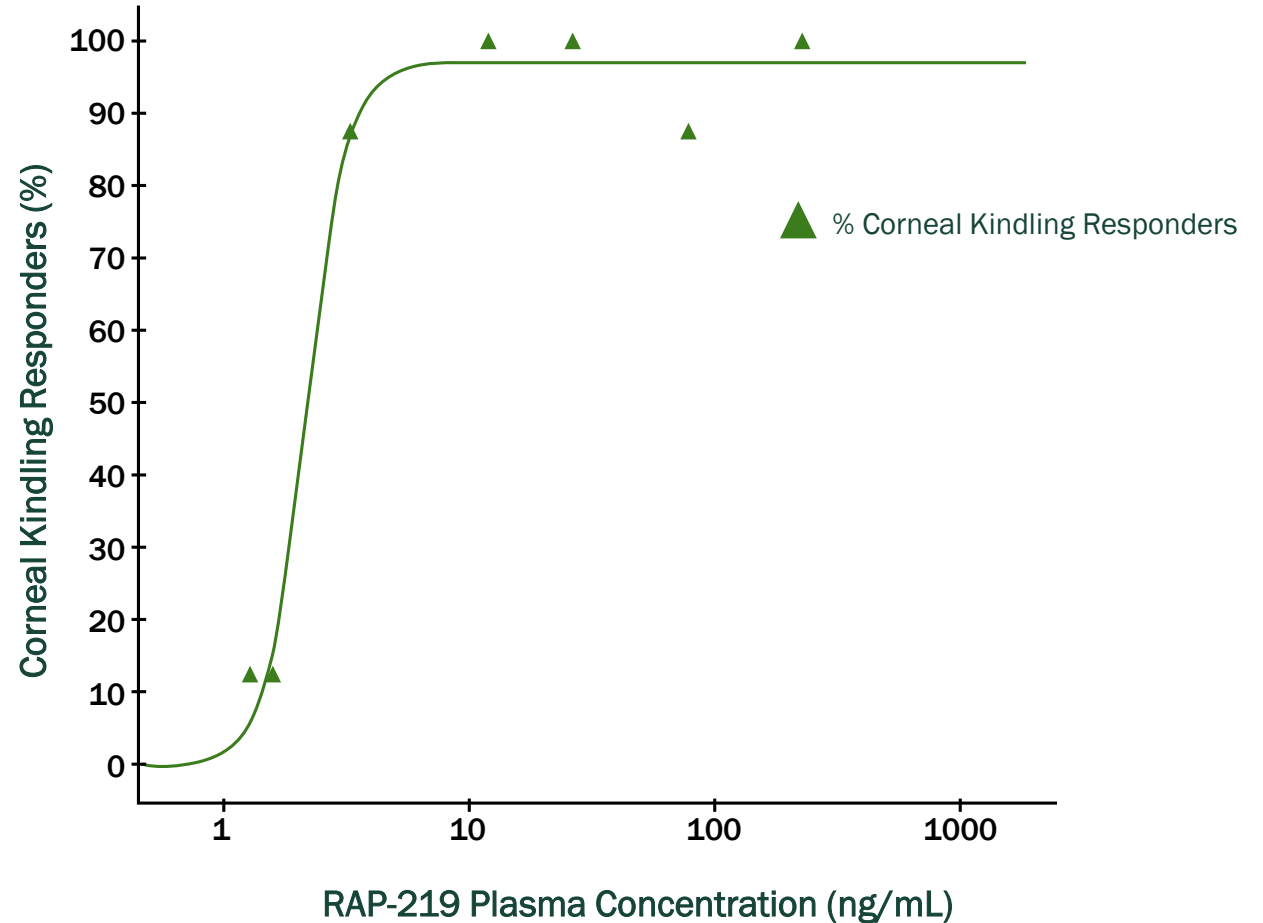
RAP-219 possesses potentially optimal drug properties for an ASM

Potency at TARP γ 8	✓	IC ₅₀ ~ 100 pM
Selectivity vs. other TARPs, NMDAR	✓	>4,000X target affinity
Selectivity vs. CEREP and kinase panels	✓	>10,000X target affinity
PK	✓	Orally bioavailable %F = 80-100
Brain penetration	✓	Brain/plasma ~70%
DDI/CYP inhibition/CYP induction	✓	>10,000 X target affinity. Not CYP substrate
Solubility/permeability	✓	BCS Class I
Target receptor occupancy	✓	50% RO at <50 μ g/kg oral dose in rodent
Preclinical safety	✓	NOAEL in top dose of IND enabling studies
Non-sedating	✓	No effects at exposures 1000X EC ₅₀

Robust dose-dependent seizure protection observed in the gold standard pre-clinical model for refractory focal epilepsy

Corneal Kindling Responders in Mice

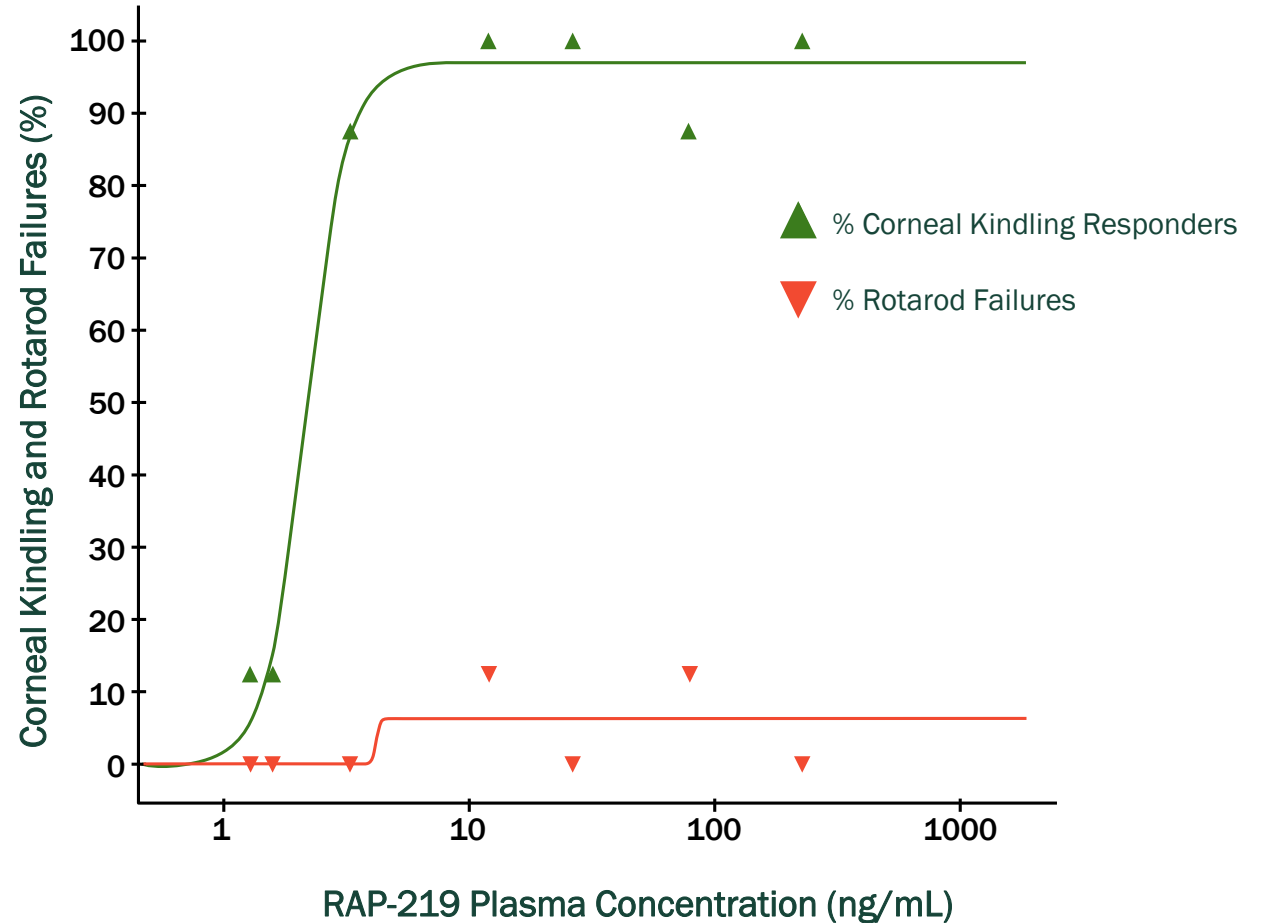
Robust, dose-dependent seizure protection observed at 50-70% receptor occupancy



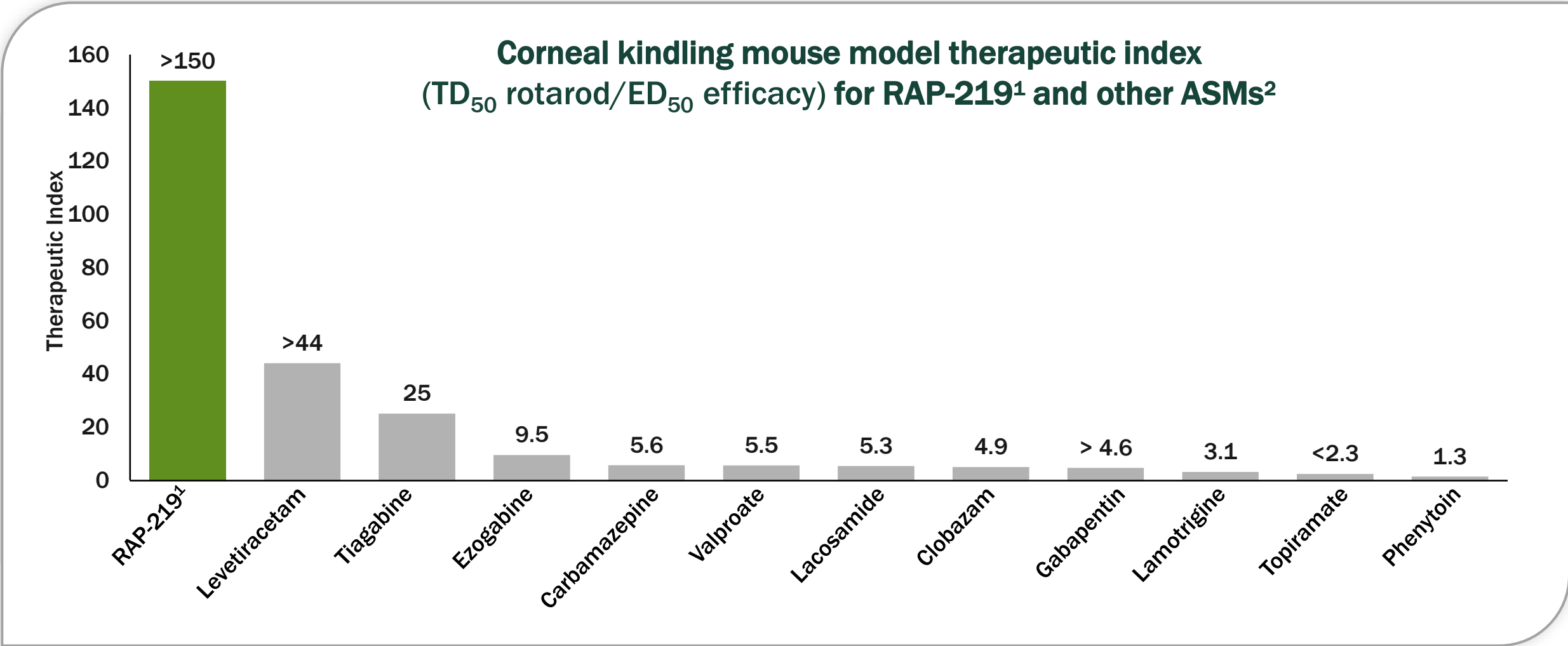
Highly potent with no rotarod failures observed at highest exposure

Corneal Kindling Responders and Rotarod Failures in Mice

The Rotarod Performance Test is considered a gold standard assay for assessing motor coordination and detecting common ASM side effects like sedation, somnolence, and ataxia



RAP-219 precision has the potential to significantly improve the therapeutic index



TARPy8 AMPAR NAMs active across a range of preclinical epilepsy models

Model

Corneal kindling – mouse*



PTZ – mouse*



Rotarod*



Amygdala kindling – mouse



Hippocampal kindling – mouse



6Hz stimulation – mouse



Frings audiogenic seizure – mouse



GAERS absence epilepsy – rat



Chronic seizure models [like corneal kindling] offer the most etiologically relevant platform on which to accurately replicate clinical epilepsy”

Barker-Haliski, Expert Opinion on Drug Discovery

- Preclinical epilepsy models are highly translatable, with **probabilities of clinical success up to 70%**, according to epileptologist Jacqueline French, MD
- **Robust efficacy** across a broad array of preclinical focal and generalized seizure models
 - Activity not seen in maximal electroshock (MES) model, consistent with performance of levetiracetam and some other effective ASMs
- Potent activity in **kindling model** has been observed to **predict efficacy** in focal epilepsy

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Phase 1 development: 100 healthy volunteers exposed to RAP-219

Single dose up to 3 mg and multiple doses up to 1.75 mg

01 SAD-101

8/cohort
(6 active: 2 placebo)

N=36*

3.0 mg

2.0 mg

1.0 mg

Food Effect

0.5 mg

0.25 mg

02 MAD-102

8/cohort
(6 active: 2 placebo)

N=30*

0.75 mg x 5d →
1.25 mg x 23d

0.75 mg x 28d

0.5 mg x 28d

0.25 mg x 7d →
0.5 mg x 7d

0.25 mg x 14d

03 PET-103

N=16*

0.25 mg x 7d →
0.5 mg x 7d

0.25 mg x 14d

0.75 mg x 5d →
1.25 mg x 9d

04 MAD-104

8/cohort
(6 active: 2 placebo)

N=18*

0.5 mg x 2d →
1.0 mg x 2d →
1.75 mg x 24d

0.75 mg x 2d →
1.25 mg x 2d →
1.75 mg x 4d

0.75 mg x 3d →
1.25 mg x 3d →
1.75 mg x 2d

Safety and tolerability of RAP-219 in Phase 1 multiple dose studies

Favorable profile in healthy volunteers

TEAEs (≥ 5% participants)	Total (N=64)		Placebo (N=16)
	n (%)	n grade 1/2	n (%)
Headache	12 (18.75%)	9/3	0
Dry mouth	5 (7.81%)	4/1	0
Brain fog	5 (7.81%)	5/0	1 (6.25%)
Fatigue	5 (7.81%)	5/0	0
Sinus tachycardia	4 (6.25%)	4/0	0
Insomnia	4 (6.25%)	4/0	0
Decreased appetite	4 (6.25%)	4/0	1 (6.25%)
Diarrhea	4 (6.25%)	4/0	0
Vision blurred	4 (6.25%)	3/1	0
Medical device site reaction	3 (4.69%)	0/3	1 (6.25%)
Constipation	3 (4.69%)	3/0	1 (6.25%)
Disturbance in attention	3 (4.69%)	3/0	0
Catheter site hematoma	3 (4.69%)	2/1	0
Back pain	3 (4.69%)	3/0	0
Abnormal dreams	3 (4.69%)	3/0	0
Bowel movement irregularity	3 (4.69%)	2/1	0

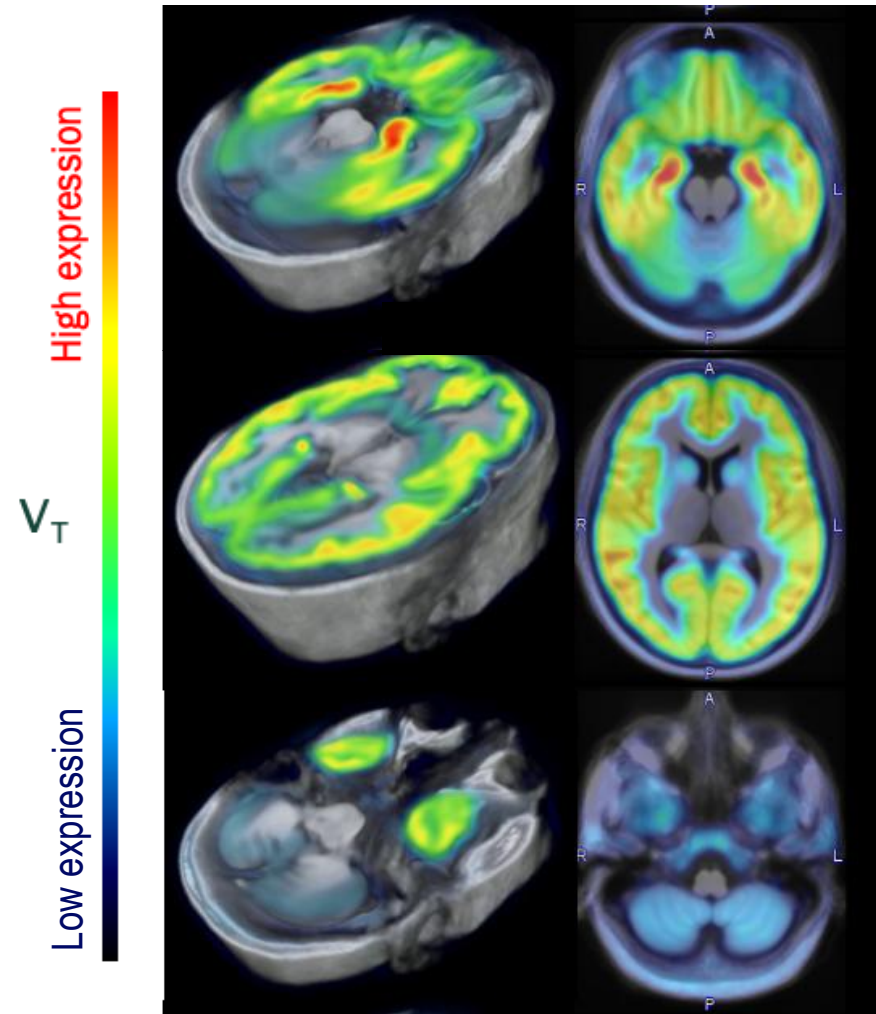
TEAE SUMMARY

- All Grade 1 or 2
- Tended to occur early in treatment and resolve without further action
- No SAEs or clinically significant laboratory, vital signs, or ECG abnormalities
- 3 discontinuations

RAP-219 human PET study

TARPy8 highly expressed in neocortex and mesial temporal lobe

High expression of TARPy8 in the neocortex and mesial temporal lobe (including hippocampus and amygdala), where nearly all focal onset seizures originate and relatively low expression in cerebellum, thalamus, and brainstem supports a potentially favorable and differentiated benefit/risk profile

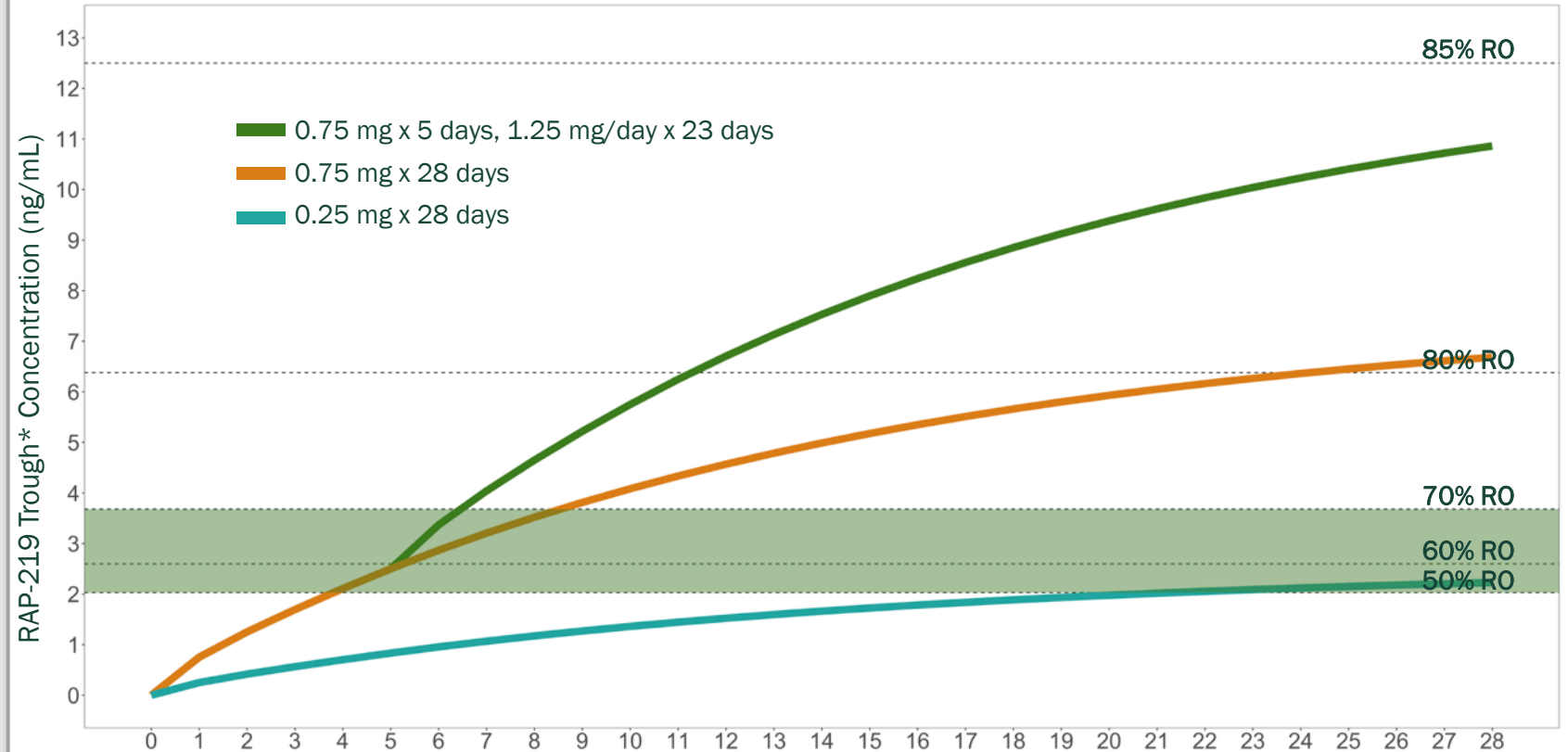


RAP-219 dose-exposure-RO relationship

Human PET RO data support lower dose levels, potentially increasing dose flexibility

- Preclinical models demonstrated maximal seizure protection at 50-70% RO (**green band**)
- Human target RO (50-70%) achieved at doses/exposures lower than predicted from animal models (as low as 0.25 mg), and lower than the dose being used in Phase 2a FOS trial, potentially affording greater flexibility in dose selection
- Phase 2a dose (**green line**) achieves target RO within 5 days and > 80% RO by day 28

Simulated RO based on Phase 1 PK and PET RO data



*Trough values calculated based on non-parametric superposition using data from the 101 and 102 studies

RAP-219 summary

Phase 1 results provide strong support for further development of RAP-219

Generally well tolerated

- No SAEs; relatively low incidence of TEAEs; none greater than Grade 2
- Consistent with target biology, no sedation observed

Precision targeting of areas where focal onset seizures originate

- PET results confirm TARPγ8 expressed in neocortex and mesial temporal lobe with relatively low expression in cerebellum, thalamus, and brainstem

Doses as low as 0.25 mg predicted to achieve clinically efficacious exposures, based on human dose-exposure-RO PET results

- May afford flexibility in dosing to optimize tolerability and potential benefit

Excellent pharmaceutical properties supporting development

- Once-a-day dosing; minimal or no DDIs; no CYP interactions observed

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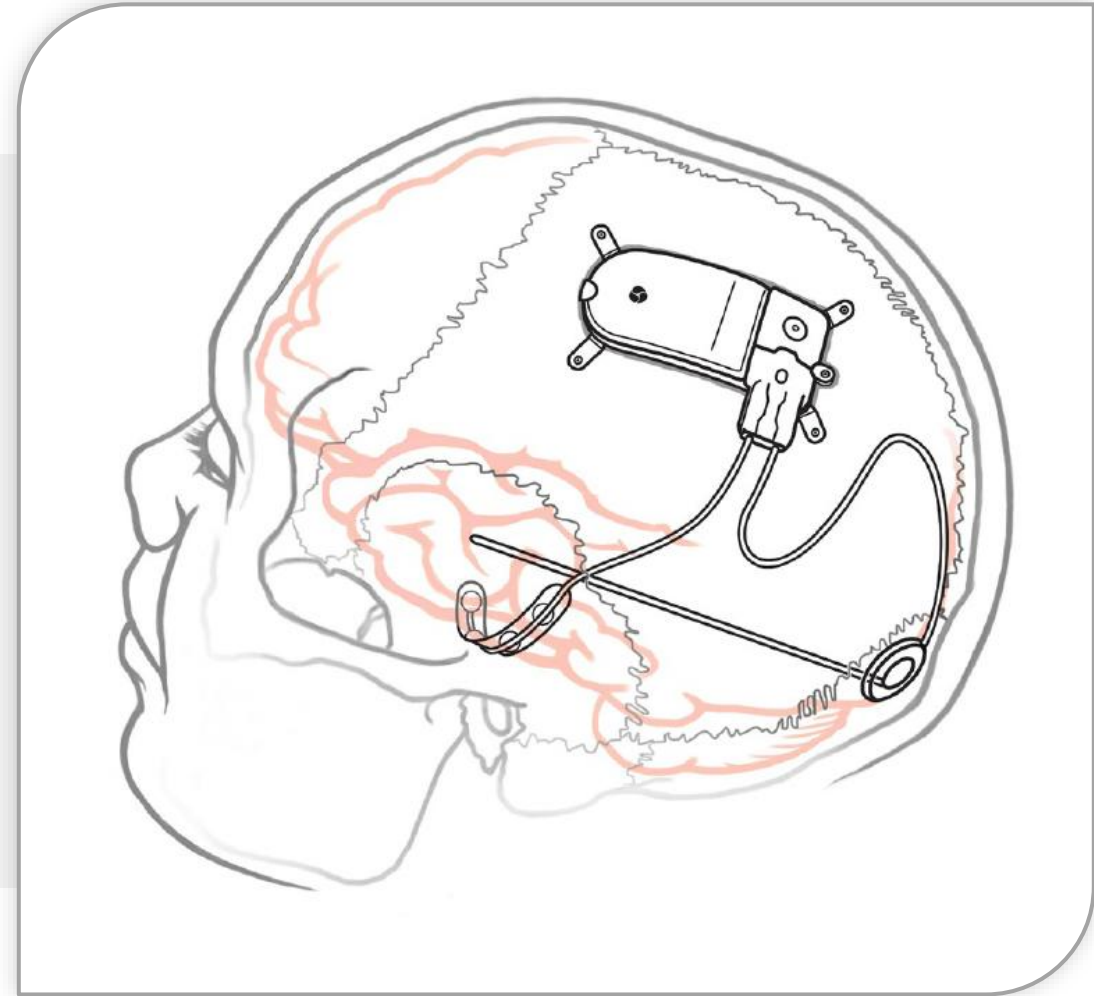


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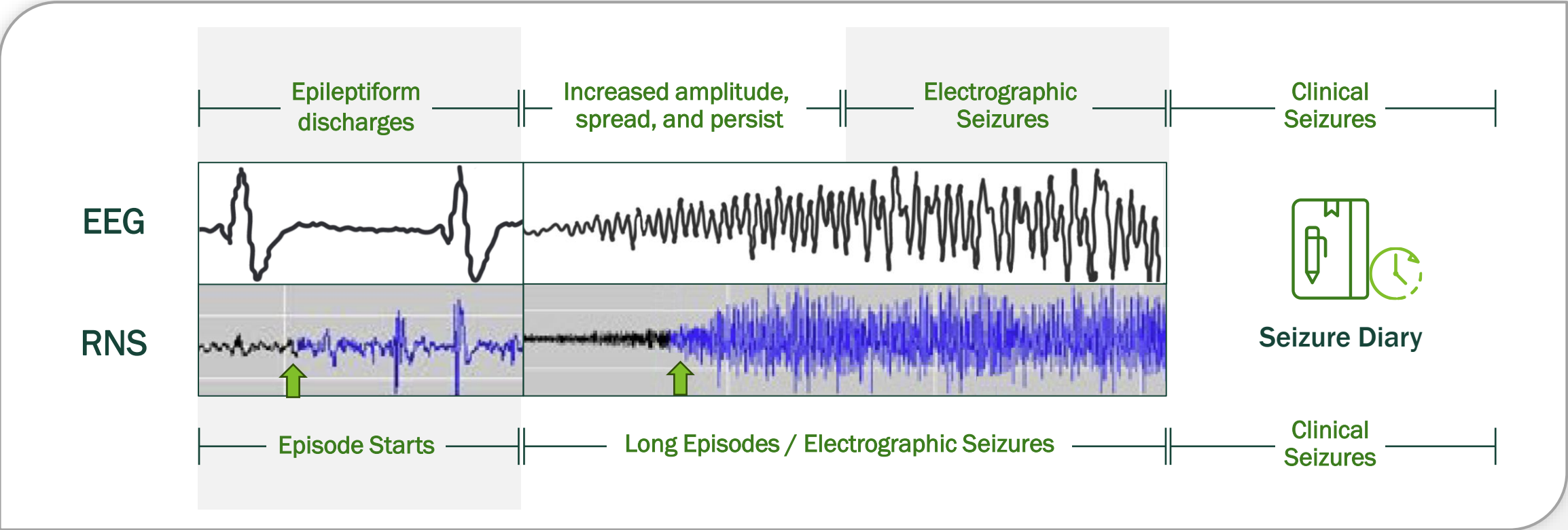
Phase 2a proof-of-concept trial in FOS patients with implanted RNS system

Neuropace RNS System®

- Two probes implanted into regions of the brain known to have epileptiform activity
- Probes **continuously detect and record epileptiform activity**, including **long episodes (LEs)** & stimulate the region to attenuate seizure activity
- FDA-approved device for patients with refractory FOS
- Approx. 6,500 RNS-treated patients in the U.S.¹



Progression of epileptiform activity to clinical seizures



RNS measures and stores episode starts and long episodes in real time, all the time

RNS system provides objective measure of epileptiform activity and early signal of clinical response to ASMs

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Clinical and electrocorticographic response to antiepileptic drugs in patients treated with responsive stimulation

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ABSTRACT

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Keywords:
Closed-loop
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Neurostimulation
Partial seizures
Medically intractable epilepsy
Antiepileptic drug

Objective: The objective of this study was to explore whether chronic electrocorticographic (ECoG) data recorded by a responsive neurostimulation system could be used to assess clinical responses to antiepileptic drugs (AEDs). **Methods:** Antiepileptic drugs initiated and maintained for ≥3 months by patients with responsive stimulation (RNS) System were identified. Such “AED Starts” that produced reported clinical seizure frequency were categorized as clinically responsive. **Results:** Electrographic features recorded by the RNS System 3 months before the AED Start, first month after the AED Start, and 3 months after the AED Start were compared. The most commonly added medications were clobazam (n = 31), and pregabalin (n = 25). Across all four medication groups, AED Starts that qualified as clinically beneficial were higher than for lacosamide (18.8%) and pregabalin (12%). Across all medication groups, the clinically beneficial AED Starts were in the detection of epileptiform activity (p < 0.001) at 1 (n = 31) and 3 months (n = 25). AED Starts that were not beneficial at 1 (n = 71) and 3 months (n = 59) were held constant, the clinically beneficial AED Starts were in the detection of epileptiform activity (p < 0.001) at 1 (n = 32) and 3 months (n = 35) (p < 0.001) at 1 (n = 59) or 3 months (n = 60) for AED Starts that were not beneficial. **Conclusions:** Significant quantitative changes in ECoG data were observed, the results suggest that quantitative assessment of whether a patient may have a favorable clinical response to a new AED. © 2018 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND 4.0 International license.

1. Introduction

Establishing whether an antiepileptic drug (AED) is effective for an individual patient with epilepsy generally relies on patient self-reported seizures over time. However, patient and caregiver seizure reports may be inaccurate [1–5]. Also, dependence on a patient's seizure history may be problematic [6,7]. Pathologically increased neuronal excitability, which is the underlying mechanism of epilepsy [6,7], and AEDs, in turn, reduce neuronal excitability [8]. In a recent study, Badawy et al. [9] found that in patients with responsive stimulation (RNS) System, the RNS System provided an objective measure of epileptiform activity and early signal of clinical response to ASMs. The RNS System provides an objective measure of epileptiform activity and early signal of clinical response to ASMs. The RNS System provides an objective measure of epileptiform activity and early signal of clinical response to ASMs.

“Changes in long episode rates had the strongest correlation with changes in clinical seizure rates. These data suggest that these measures may provide an objective assessment of cortical excitability and response to AEDs.”

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DOI: 10.1111/epi.16412

Epilepsia

FULL-LENGTH ORIGINAL RESEARCH

Early detection rate changes from a brain-responsive neurostimulation system predict efficacy of newly added antiseizure drugs

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Abstract
Objective: Brain-responsive neurostimulation (RNS System, NeuroPace) is used to treat medically refractory focal epilepsy and also provides long-term ambulatory neurophysiologic data. We sought to determine whether these data could predict the clinical response to antiseizure drugs (ASDs). **Methods:** First, newly added medications were identified in RNS System patients followed at a single epilepsy center. Daily detection rates including “episode starts” (predominantly interictal activity) and “long episodes” (often electrographic seizures) were compared before and after ASD initiation. Efficacy was determined from documentation of clinical improvement and medication retention. Next, the analysis was repeated on an independent sample of patients from a multicenter long-term treatment trial, using an efficacy measure of ≥50% reduction in diary-recorded seizure frequency after 3 months. **Results:** In the single center cohort, there was a significantly greater reduction in the seizure frequency in patients who received efficacious medications. In this cohort, highly predictive of ASD efficacy, episode starts had a significantly greater reduction in the first 1–2 weeks. In this larger multicenter cohort, there was a significantly greater reduction in the seizure frequency in patients who received efficacious medications. In this cohort, highly predictive of ASD efficacy, episode starts had a significantly greater reduction in the first 1–2 weeks. In this larger multicenter cohort, there was a significantly greater reduction in the seizure frequency in patients who received efficacious medications. In this cohort, highly predictive of ASD efficacy, episode starts had a significantly greater reduction in the first 1–2 weeks.

“It could be argued that long episodes are an even better therapeutic target than reported clinical seizures.”

 **rapport**
therapeutics

Epilepsy & Behavior. 2018; 83: 192-200; Epilepsia. 2020; 61:138-148.

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Well-established relationship between long episode and clinical seizure responder rates

- Skarpaas (2018)¹: significant correlation exists between reduction in long episodes and clinical seizure frequency
- Quraishi (2020)²: ASMs resulting in a $\geq 20\%$ decrease in long episodes were clinical efficacious ($\geq 50\%$ reduction in seizures)
- Gammaitoni (2024)³: ASMs resulting in a $\geq 30\%$ reduction in LEs were associated with a $\geq 50\%$ reduction in clinical seizures

Optimal Cut Point for Reduction in Long Episode Frequency to Predict Meaningful Change in Clinical Seizure Frequency

Poster #1.494

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*Report Therapeutics, Inc., Boston, MA, USA; NeuroRace, Inc., Mountain View, CA, USA; *New York University Comprehensive Epilepsy Center, New York, NY, USA; *New York University Grossman School of Medicine, NYU Langone Health, New York, NY, USA; *Freeman School of Medicine of the University of Pennsylvania, Philadelphia, PA, USA

Background

Novel proof-of-concept (POC) designs utilizing validated biomarkers with positive predictive utility of antiepileptic medication (AEM) treatment effects are needed that:

- Provide interim patient numbers with the ability to predict success of Phase 3 studies to models that closely represent clinical seizure (CS) activity
- Are not reliant on patient diaries, which have been shown to under- and over-report seizures*

The responsive neurostimulator (RNS) system, NeuroCyber™, continuously senses electrocorticographic (EEG) activity and responds to electrographic seizure onset with bursts of electrical stimulation. The RNS system also continuously detects long episodes (LEs) (≥1 sec of sustained electrographic activity (frequency >30 Hz) that represent electrographic seizures and provide an ongoing neurocybernetic CS counter†. A change of at least 30% in LE frequency following a novel AEM trial has been reported to correlate with change in CS frequency†.

Objectives

Using data from an open-label, long-term treatment study of the RNS system and an anchor-based approach based on change in pre-assessed CS frequency.

Examine the relationship between change in LE frequency and change in CS frequency.

Define the cut point for LE frequency reduction that correlates with a clinically meaningful improvement in CS frequency (RNS system).

Methods

Retrospective data, including LE and CS frequency, were obtained from a long-term treatment study of the RNS system†.

Data inclusion criteria were based on inclusion criteria utilized for the RNS Phase 3a study of RNS-209.

References

- French JA, et al. *Epilepsia* 2010;51:2239-44.
- French JA, et al. *Epilepsia* 2010;51:2239-44.
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- French JA, et al. *Epilepsia* 2010;51:2239-44.

- Data from patients who met the following criteria were obtained for the 3 weeks prior to ("pre-start baseline") and 3 weeks following ("post-start period") AEM start.
- Received 1 dose of a new AEM
- No changes to the RNS system settings during the pre-start baseline and post-start period.
- ≥18 hrs per 28 days during the pre-start baseline.
- Data available for both LE and CS frequency during the pre-start baseline and post-start period.

Outcomes

Relationships between the percentage change in LE frequency and percentage change in CS frequency.

- Median change (%) in LE frequency and in CS frequency per 28 days
- Post-start period vs pre-start baseline
- LE frequency recorded by the RNS system (LE criteria: individually predefined by epileptologist, AEM data during assessment period)
- CS frequency recorded in daily seizure diaries

- Change (%) in LE and CS frequency from baseline to each assessment period
- CS frequency per 28 days from baseline to assessment by CS responder subgroup

- Patients with <25%, 25 to <50%, 50% to <75%, and 75% to 100% reduction in frequency from baseline
- Reduction (%) in LE and CS frequency with ≥50% LE reduction

Receiver operating characteristic (ROC) of the LE reduction threshold to predict clinically meaningful (≥50%) or profound reduction (≥75%) in CS when sensitivity is approximately equal to specificity.

CS frequency ratio defined as: 100% = 100% reduction from baseline in CS frequency or 75% or 100% reduction on the dependent variable

Results

Data from 40 patients who initiated olanzapine (CS: n=30, 75%), levetiracetam (CS: n=10, 25%) or topiramate (CS: n=0, 0%) were included in the analysis (Table 1). An RNS system electrode was implanted in the medial temporal lobe of 70% of patients included in the analysis.

Table 1. Demographics and Baseline Characteristics

Parameter (n=40)	CS (n=30)	LEV (n=10)	TPM (n=0)	Overall (n=40)
Female (n=24)	15 (50%)	9 (90%)	0 (0%)	24 (60%)
Age at AEM start (years, mean±SD)	34.3±12.1	34.4±12.1	34.4±12.1	34.4±12.1
Median (range) baseline LE frequency (per 28 days)	4 (2-15)	1 (0-20)	0 (0-0)	4 (2-15)
Median (range) baseline CS frequency (per 28 days)	5 (1-15)	2 (0-5)	0 (0-0)	5 (1-15)
Median (range) baseline LE frequency (per 28 days)	5 (1-15)	2 (0-5)	0 (0-0)	5 (1-15)

Overall, 40 patients experienced a median -27.8% change in LE frequency and median -47.8% change in CS frequency.

Change in LE Frequency by CS Responder Group

A linear correlation between change in LE frequency and CS responder group (patients with <25%, 25 to <50%, 50% to <75%, and 75% to 100% reduction from baseline) was observed (Figure 1).

Figure 1. Percentage of Frequency Reduction by CS Responder Group

ROC Analysis

A 100% reduction in LE frequency was identified as the optimal cut point that correlated with a clinically meaningful reduction (≥50% reduction from baseline) in CS (AUC=0.75) (Figure 2A, Table 2).

A 100% reduction in LE frequency was identified as the cut point for profound change (≥75% reduction from baseline) in CS (AUC=0.75) (Figure 2B).

Figure 2. LE Frequency Percentage Reduction Cut Point for A. 100% and B. 75% CS Frequency Reduction

Table 2. Clinical Seizure Reduction and Correlated LE Frequency Reduction

CS Frequency Reduction (%)	AUC	Reduction Cut Point (LE Frequency %)	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)
<25%	0.75	25.6	54.3	84.7	64.4
25-49%	0.75	25.6	54.3	84.7	64.4
50-74%	0.75	25.6	54.3	84.7	64.4
75-100%	0.75	25.6	54.3	84.7	64.4

*Negative predictive value of the cut point for the correlation between CS and LE frequency reduction was 100%.

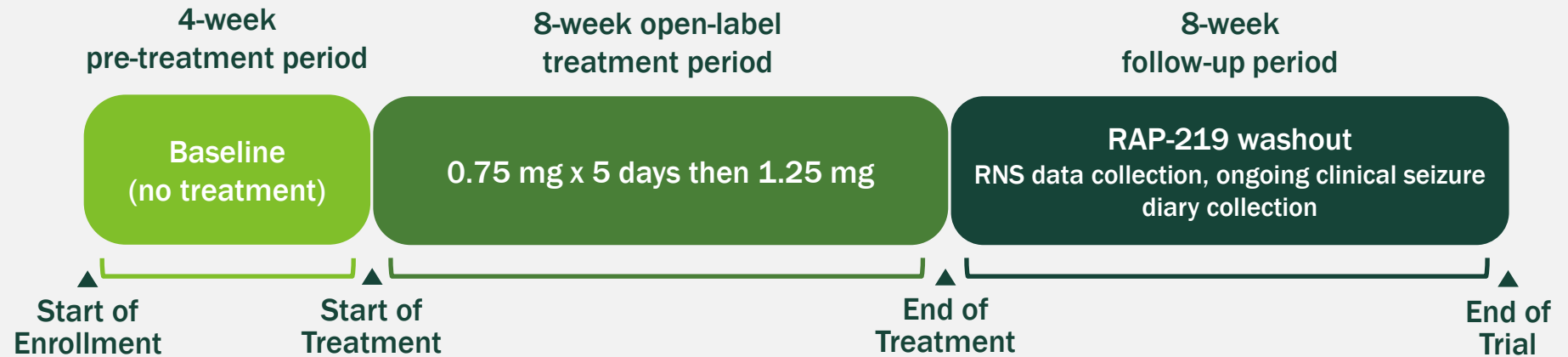
Outcomes in Patients with at Least a 30% LE Reduction

Phase 2a proof-of-concept trial in focal epilepsy patients

KOL-guided, innovative study using validated biomarker of clinical seizures

Key Entry Criteria

1. Medically refractory focal epilepsy
2. RNS probe implanted in seizure onset zone within MTL ≥ 15 months before screening
3. Stable RNS System settings and therapies
4. ≥ 16 LEs during 8-week retrospective review period
5. ≥ 1 clinical seizure reported during 8-week retrospective review period
6. $> 50\%$ concordance between long episodes and electrographic seizures



Key Endpoints

- Long episode reduction
 - **proportion** of patients with $\geq 30\%$ reduction compared with baseline*
 - median percent change from baseline
- Clinical seizure reduction
 - **proportion** of patients with $\geq 50\%$ reduction compared with pre-treatment baseline
 - median percent change from baseline
- Percent change in estimated electrographic seizure frequency and additional iEEG biomarkers

Preliminary baseline characteristics of Phase 2a trial patients

Seizure frequency consistent with patients enrolled in registrational FOS trials

Baseline Characteristics from First 14 Patients Enrolled	Median (range)		Median (1 st to 4 th quartile range)
Age	37 (20-61)	CS frequency per 28 days in 4-week prospective baseline	10 (4.25-18.25)
Sex (n)	7F/7M	LE frequency per 28 days in 12-week baseline	51 (21-194)
Age at first seizure	19 (0.5-31)	Concordance between LEs and electrographic seizures (rated by an independent reviewer)	92% (71-96)
Years since RNS implantation	4.4 (1.4-10.2)	Concomitant antiseizure medications	3

Agenda



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Abe Ceesay, Chief Executive Officer
- 02** **RAP-219: Program Overview**
David Brett, M.D., Ph.D., Founder, Chief Scientific Officer
- 03** **RAP-219: Phase 1 Data | RAP-219: Phase 2a Focal Epilepsy Trial Overview**
Jeff Sevigny, M.D., Chief Medical Officer
- 04** **Fireside Chat: KOL Perspective**
Jacqueline French, M.D., Professor of Neurology, NYU Langone | Jeff Sevigny, M.D.
- 05** **RAP-219: Phase 2a FOS Trial: Framing Future Data**
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- 06** **Financial Update**
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- 07** **Questions and Answers**
- 08** **Closing Remarks**
Abe Ceesay

Fireside Chat: KOL Perspective



Jacqueline French, M.D.
Professor of Neurology, NYU Langone



Jeff Sevigny, M.D.
Chief Medical Officer

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RAP-219 Phase 2a trial in patients with focal epilepsy

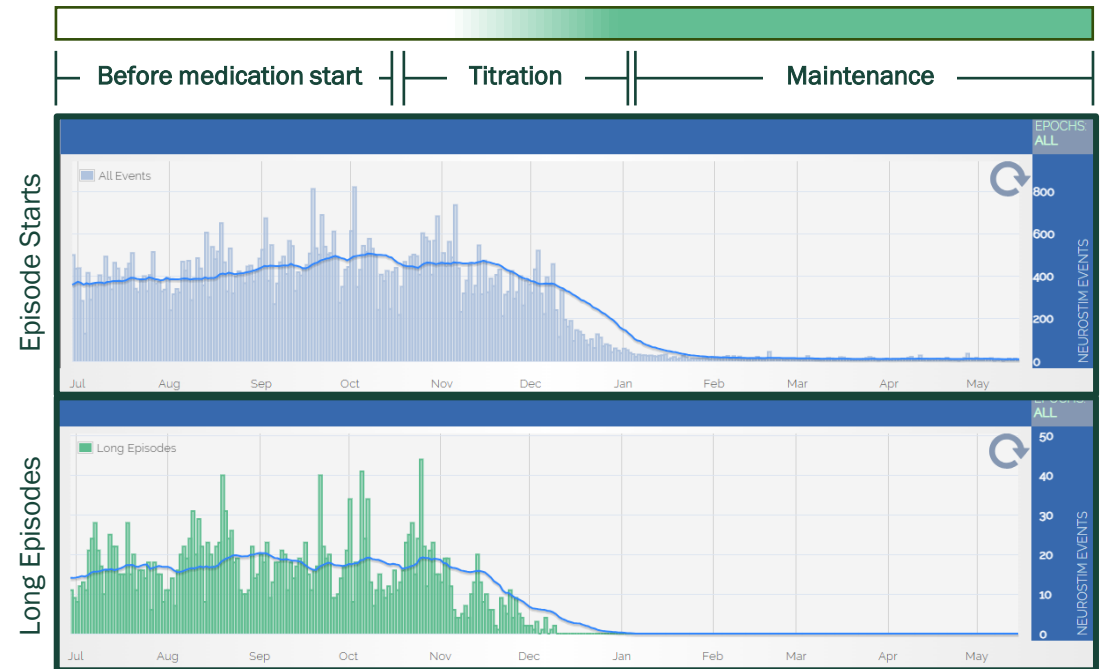
Goal:

Generate data from ≥ 20 participants showing convincing reductions in long episodes and clinical seizures to support advancement to registrational studies

RNS electrographic biomarker data is a highly objective complement to clinical seizure diary data

- Each patient serves as case study with 12 weeks of baseline data, detailed pharmacodynamic measures of onset of effect, and depth of response
- Depth of response and responder proportion can offer strong evidence of activity to support advancement to registrational trials
- As noted earlier, responder is defined by a $\geq 30\%$ reduction in LE seizure frequency, consistent with a clinically meaningful effect

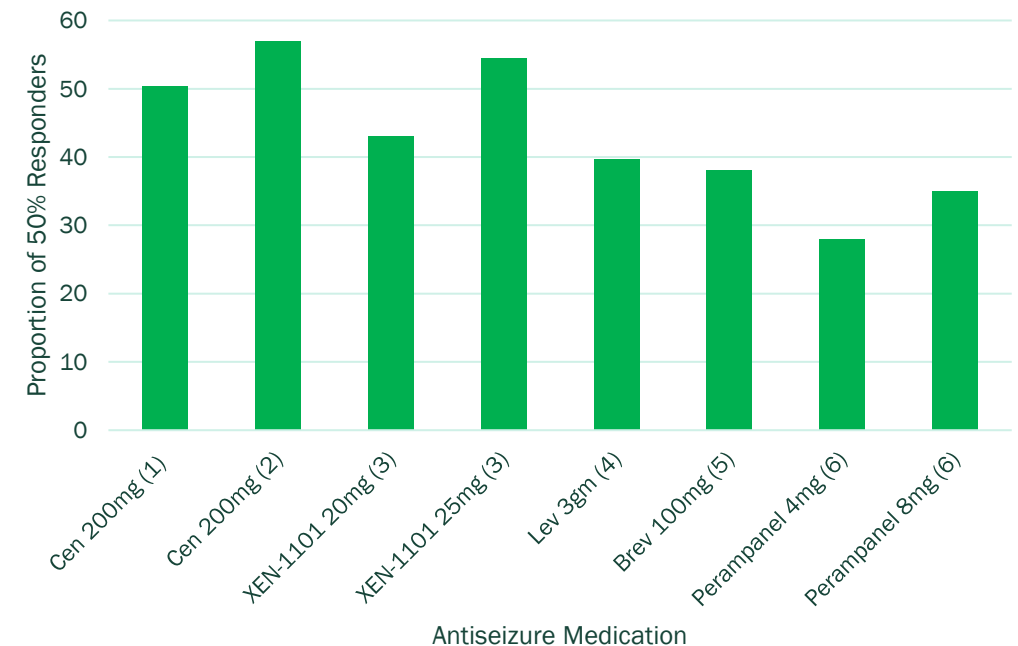
Example highly effective medication starts of a *marketed ASM**



Responder rates in registrational trials of approved and pipeline ASMs

- ~25-55% of patients achieve a clinically meaningful $\geq 50\%$ clinical seizure reduction in registrational trials for approved therapies
- Responder rates in this range result in statistically significant placebo-adjusted median percent changes
- **Target responder rate set at $\geq 40\%$ to align with clinical relevance and support advancement to pivotal trials**

Non-Placebo Adjusted Proportion of 50% CS Responders in Registrational Trials of Approved and Pipeline Programs



Key endpoints and anticipated topline data

		Outcome
Topline Data	Long Episode Primary Endpoint Analysis	LE frequency reduction responder analysis (% of patients that demonstrate $\geq 30\%$ reduction in LEs compared with baseline)* Median percent change in LE frequency on treatment compared with baseline
	Clinical Seizure Key Secondary Endpoint Analysis	Proportion of patients achieving $\geq 50\%$ reduction in clinical seizures compared with baseline Median percent change in clinical seizure frequency compared with baseline
	TEAE Incidence and Grade	

*Power determinations were based on this outcome measure.

Targets for anticipated topline data

		Outcome	RAP-219 Target
Topline Data	Long Episode Primary Endpoint Analysis	LE frequency reduction responder analysis (% of patients that demonstrate ≥30% reduction in LEs compared with baseline)*	≥40%
		Median percent change in LE frequency on treatment compared with baseline	~30%
	Clinical Seizure Key Secondary Endpoint Analysis	Proportion of patients achieving ≥50% reduction in clinical seizures compared with baseline	≥40%
		Median percent change in clinical seizure frequency compared with baseline	~50%
	TEAE Incidence and Grade		

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Pipeline targets large market opportunities

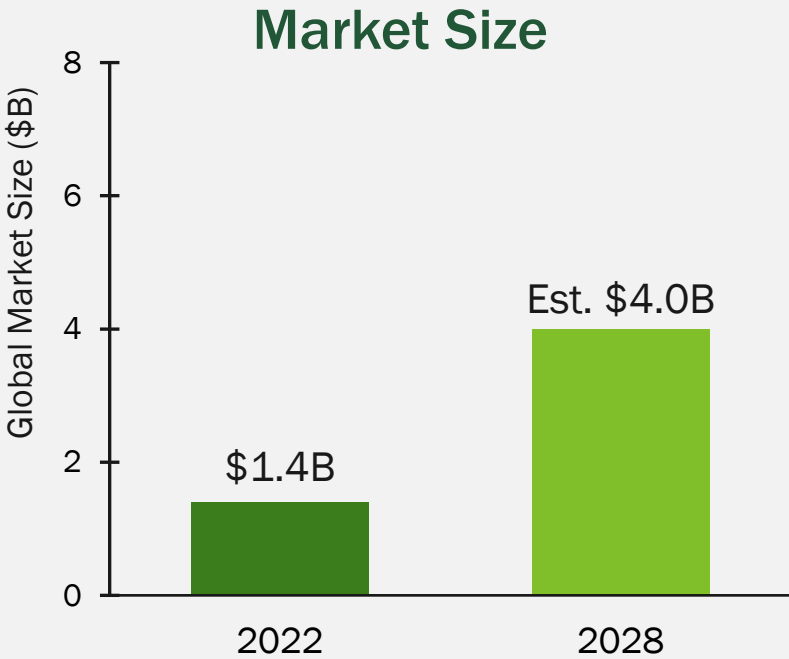
~1.8M

Focal epilepsy in U.S. patients¹



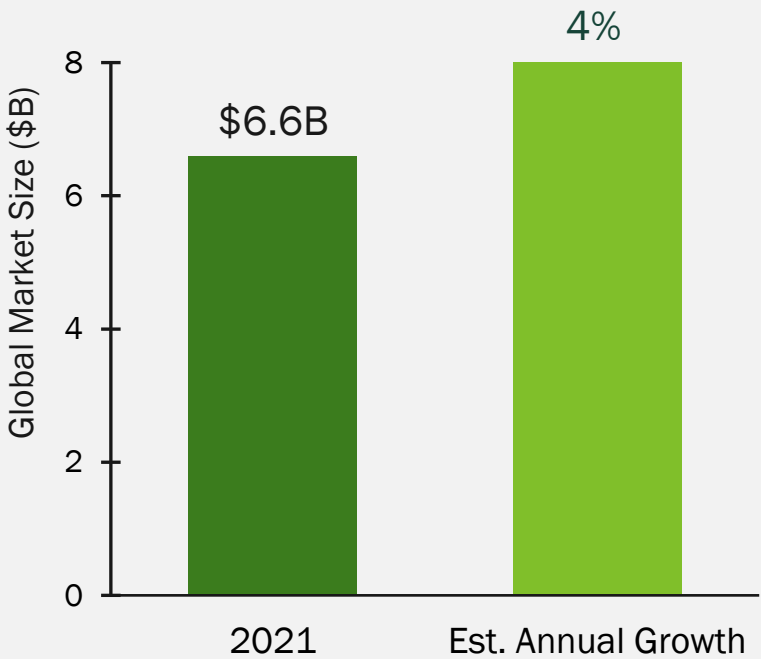
~7.2M

Bipolar disorder in U.S. patients²

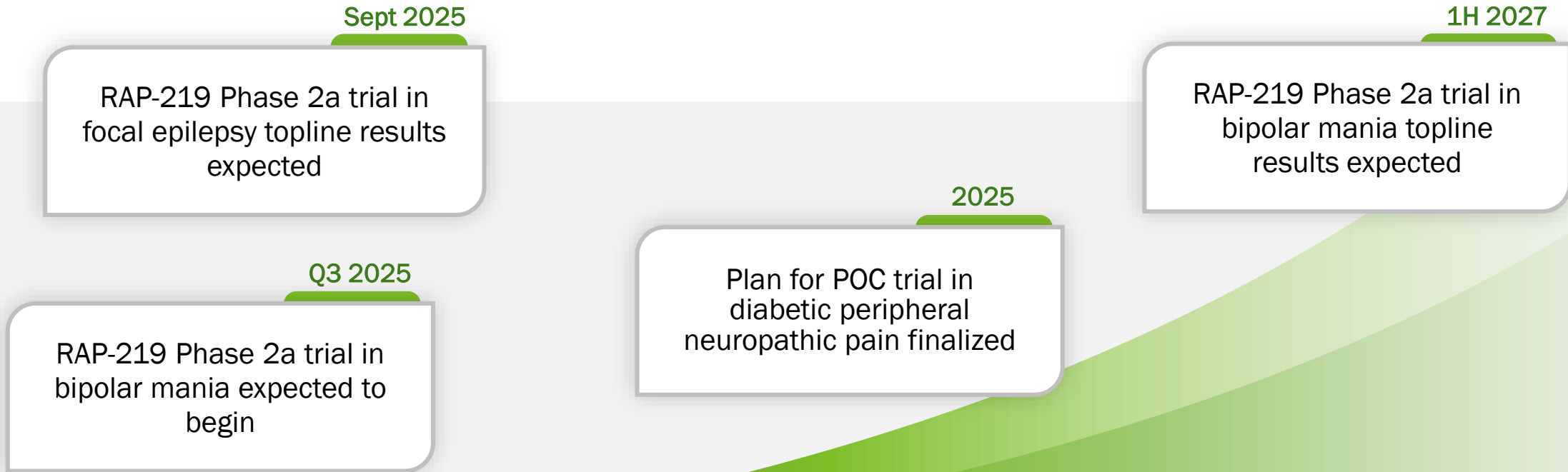


~5.6M

Peripheral neuropathic pain in U.S. patients³



Cash runway and anticipated catalysts



Cash balance of \$285.4mm¹ (as of 3/31/25) supports Rapport through end of 2026

Questions & Answers



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Rapport Therapeutics: investment summary



RAP-219 precision designed to maximize efficacy while avoiding typical ASM adverse events

- Highly expressed in forebrain regions associated with seizures and minimal expression in hindbrain areas potentially associated with AEs



Phase 2a FOS trial design improves probability of success for future pivotal trials

- Objective and translatable biomarker used as more reliable measure than patient-reported diaries
- Trial patients are representative of registration and commercial target patient population
- Majority of epilepsy opinion leaders believe design is superior to other proof-of-concept designs¹



Validated across preclinical and Phase 1 studies

- Efficacy in highly predictive seizure models
- Potential to significantly improve therapeutic index
- Generally well tolerated across four Phase 1 trials with 100 subjects dosed (no TEAEs above Grade 2)



Differentiated profile promotes broad potential use

- QD dosing and rapid achievement of target RO associated with maximal seizure protection
- Minimal drug-drug interactions and not observed to interact with CYP enzymes
- Long half life minimizes daily drug fluctuations and may reduce risk of breakthrough seizures
- Potency and physicochemical properties enable potential as first long-acting injectable ASM

Thank you

