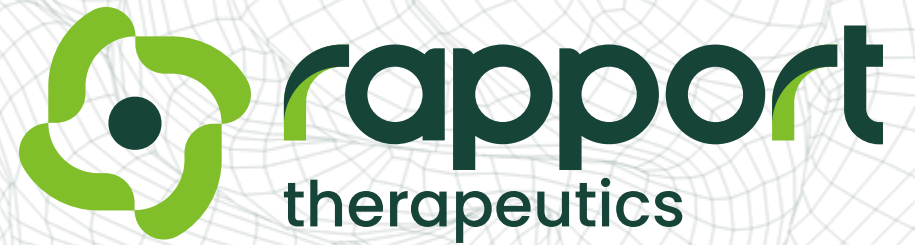


Corporate overview

November 2024



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 drug-resistant focal epilepsy, peripheral neuropathic pain and bipolar disorder, including the initiation, timing, progress and results of our ongoing and planned clinical trials; the Company’s ability to resolve a clinical hold with the FDA; the potential activity and tolerability of RAP-219; the potential of Rapport’s RAP technology platform; the ongoing and planned development of RAP-199 and Rapport’s discovery-stage programs; 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 Registration Statement on Form S-1, 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 (the SEC). 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.

Leadership with track record of innovation and expertise

Management Team



David Bredt, 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



Brad Galer, M.D.
Chief Medical Officer
 20+ years biopharma development experience; Former CMO, Zogenix
 ZOGENIX NUVO
 endo



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



Kathy Wilkinson
Chief People Officer
 15+ years of human resources experience in biotech
 bluebirdbio 2seventybio
 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.
Board Chair
 Partner, Third Rock Ventures

James Healy, M.D., Ph.D.
Director
 Managing Partner, Sofinnova Investments

Reid Huber, Ph.D.
Director
 Partner, Third Rock Ventures; CEO, Merida Biosciences

John Maraganore, Ph.D.
Director
 Former Founding CEO, Alnylam

Robert Perez
Director
 Operating Partner, General Atlantic
 Former CEO, Cubist Pharmaceuticals
 Founder and Chairman, Life Science Cares

Paul Silva
Director
 Former Chief Accounting Officer, Vertex Pharmaceuticals

Raymond Sanchez, M.D.
Director
 Senior Advisor, Bain Life Sciences; Former CMO, Cerevel Therapeutics


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



¹Employee director

Ushering in a new era of precision neuroscience

Vision: To become a leader in precision neuroscience through the discovery and development of transformational small molecule medicines for patients suffering from central nervous system (CNS) disorders



Potential for differentiated approach to generate precision small molecule medicines

Road-tested capability of identifying **key mediators of receptor function**

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

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



Accomplished scientific innovators & company builders

Pioneering discovery team

Company builders with industry-proven leadership



Robust clinical & discovery pipeline

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

RAP-219 clinical program
Non-sedative forebrain restricted TARP γ 8 AMPAR¹ modulator – significant opportunity in initial indication in focal epilepsy

Discovery programs
Medicinal chemistry-enabled portfolio with potential in additional indications



Well financed

\$100M Series A announced 2022

\$150M Series B announced 2023

\$174M IPO² completed 2024

Funding through end of 2026, including multiple RAP-219 clinical proof-of-concept (PoC) trials

We believe the current state and limitations of neuromedicine compels the creation of Rapport

RAPs are components of the broader neuronal receptor complexes and play critical roles in regulating receptor assembly and function

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 serve as unique binding sites targetable by novel pharmacophores designed for increased selectivity
- ✓ RAP targeting can provide tissue / neuroanatomical specificity
- ✓ RAPs enable differentiated pharmacology and potentially provide optimal 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

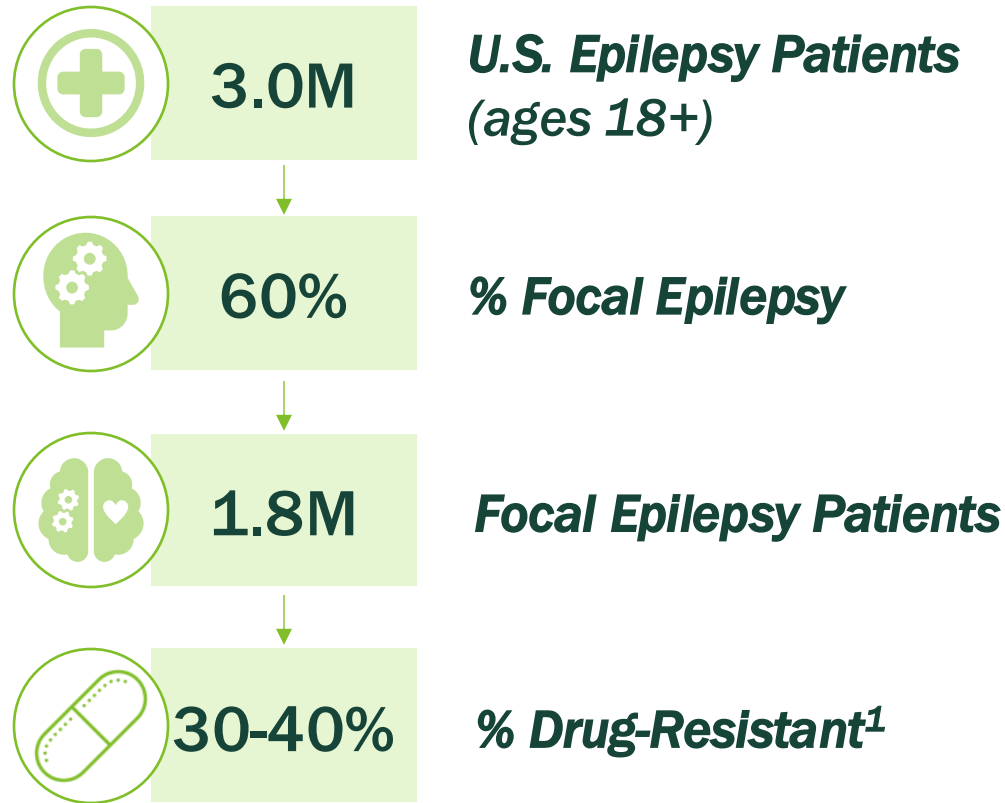
Advancing our precision neuroscience pipeline to potentially address large market opportunities

Category	Program	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Next Expected Milestone
TARPy8 AMPAR Programs	RAP-219 <i>Focal Epilepsy</i>	▶					Topline Results Mid-2025
	RAP-219 <i>Peripheral Neuropathic Pain*</i>	▶					Trial Initiation*
	RAP-219 <i>Bipolar Disorder</i>	▶					Trial Initiation 2025
nAChR Discovery Programs	α 6 <i>Chronic Pain</i>	▶					Nominate Development Candidate
	α 9 α 10 <i>Hearing Disorders</i>	▶					Nominate Development Candidate

Strong intellectual property with worldwide rights to all programs

Focal epilepsy is a large market with high unmet need

Key highlights of U.S. focal epilepsy market



Limitations of current therapies

- ✗ **Limited Efficacy:** Despite over >20 FDA approved anti-seizure medications (ASMs), 30-40% of patients are 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
- ✗ **Complicated Administration:** Long titration, drug-drug interactions, and lab monitoring

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

Expanding the potential of RAP-219

Focal epilepsy

U.S. patients: 1.8 million¹

Peripheral neuropathic pain

U.S. patients: ~5.6 million²

Bipolar disorder

U.S. patients: ~7 million³

TARPy8 is a preclinically and clinically validated target for epilepsy, which RAP-219 is designed to selectively target

Strong mechanistic data in both peripheral neuropathic pain and bipolar disorder,
and compelling preclinical data in peripheral neuropathic pain

Once daily (QD) dosing | No evidence of sedation or motoric impairment | No observed drug-drug interactions (DDI)

Evaluating long acting injectable (LAI)

Potency and metabolic profile positions RAP-219 as the first potential ASM in a depot formulation,
which enables appealing administration alternative

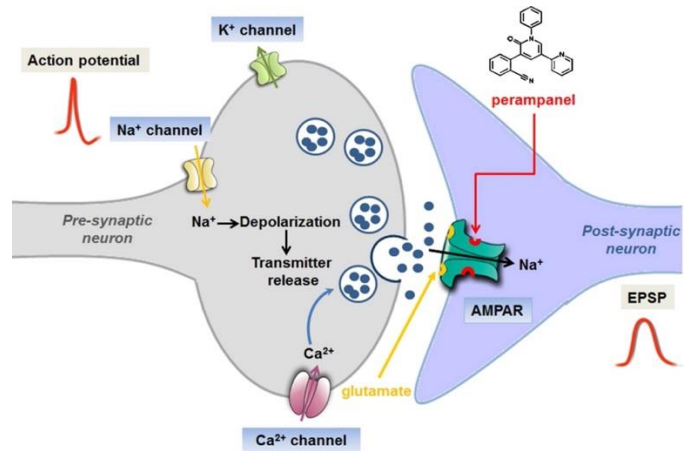
Opportunity for improving patient adherence

RAP-219 overview

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- C. Phase 2a proof-of-concept trial in focal epilepsy
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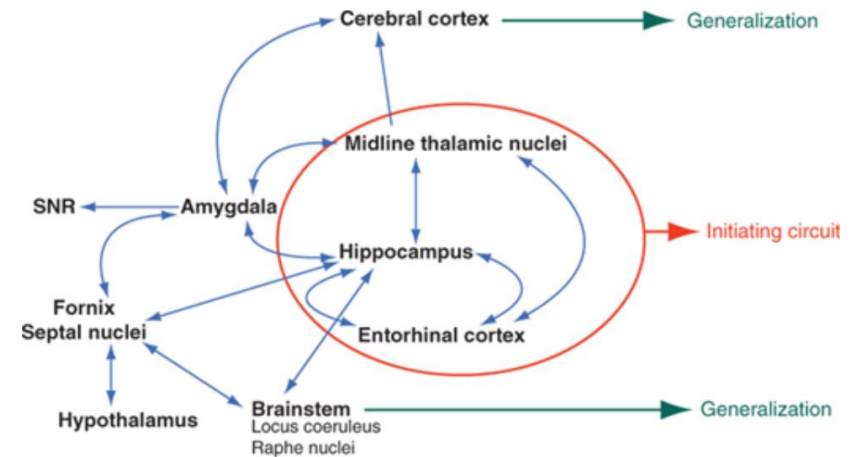
AMPA inhibition is a clinically validated approach for epilepsy

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

Hippocampus and cortex are important sites of focal onset seizure origination



ISBN 978-0-07-129621-6

- Hippocampus is a common seizure initiation site, with approximately 50% of all seizures originating in or around this area
- Cerebral cortex, which expresses abundant TARP γ 8, is another common site of FOS initiation, originating up to 50% of all seizures
- Seizures originating in the cerebral cortex often spread into and are propagated by the hippocampus

Molecular science of transmembrane AMPA regulatory proteins (TARPs)

TARPs: Auxiliary subunits that associate with AMPA receptors in the brain
Crucial for regulating the trafficking, subcellular localization and gating of AMPA receptors

- TARPs display distinct regional expression profiles, offering opportunity for precision neuromedicine targets
- TARP γ 8 is most enriched in the hippocampus and present in other forebrain structures

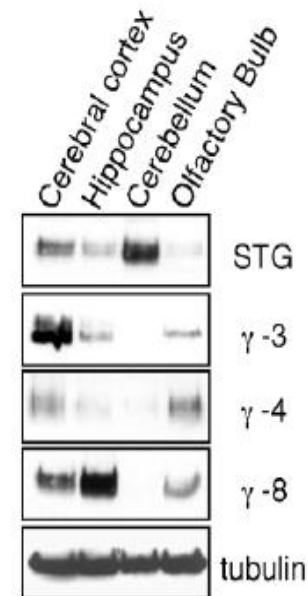
Cryogenic electron microscopy of
GluA1/2 + TARP γ 8 complex



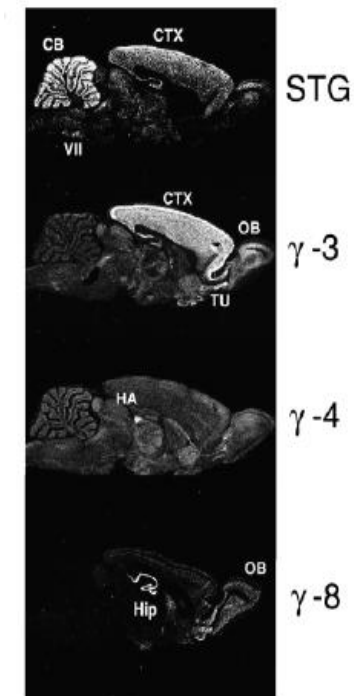
GluA1
GluA2
TARP γ 8

NatComm 2022 13:734

TARPs in rat brain



JCB 2003 161:805

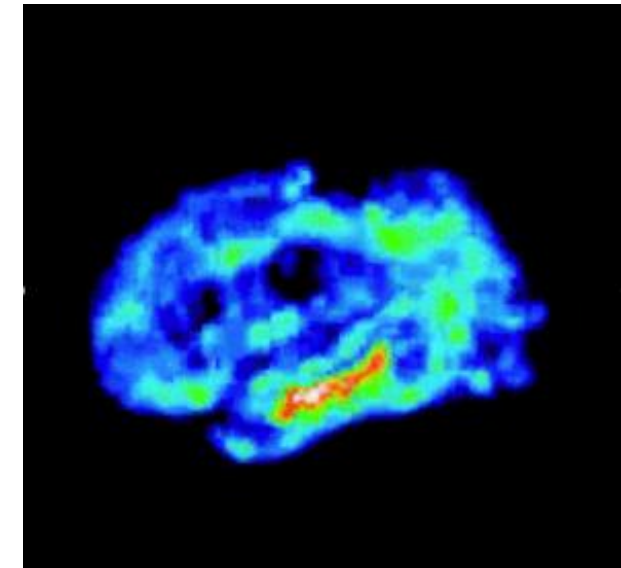


Observed to be highly potent and selective TARP γ 8 AMPAR NAM

RAP-219 potency and selectivity

TARP γ 8-containing AMPA receptors (IC ₅₀)	~100 pM
vs. AMPA receptors (GluA1) lacking TARPs	>100,000x
vs. AMPA receptors containing other TARPs (γ 2, γ 3, γ 4, γ 7)	>4,000x
vs. NMDA receptors (2A, 2B, 2D)	>500,000x
vs. GPCRs/ion channels/enzymes (panel of 52)	>10,000x
vs. kinases (panel of 373)	>100,000x

TARP γ 8 clinical PET in human



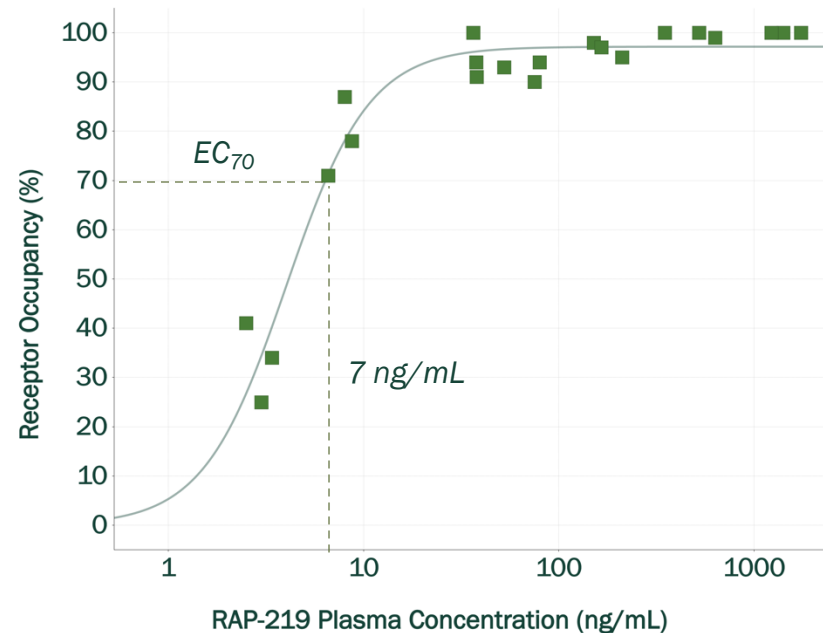
ACNP 2018 27.6: 536

Selective for hippocampus and other forebrain structures

Minimal or no expression in the cerebellum and brainstem

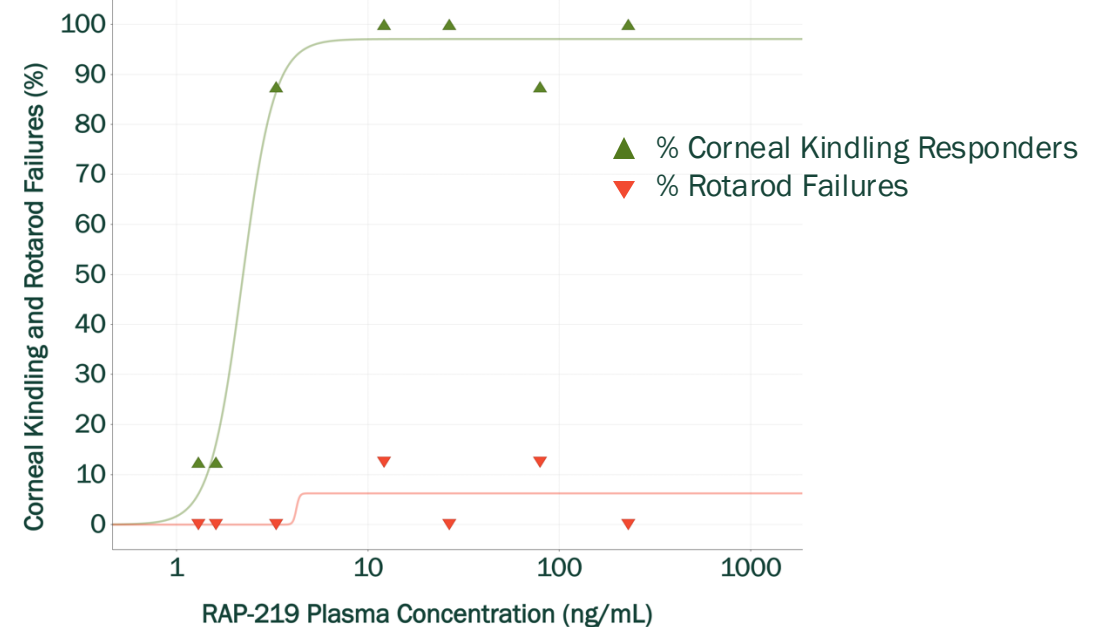
Differentiated precision preclinical profile of RAP-219

Receptor occupancy (%) in rats



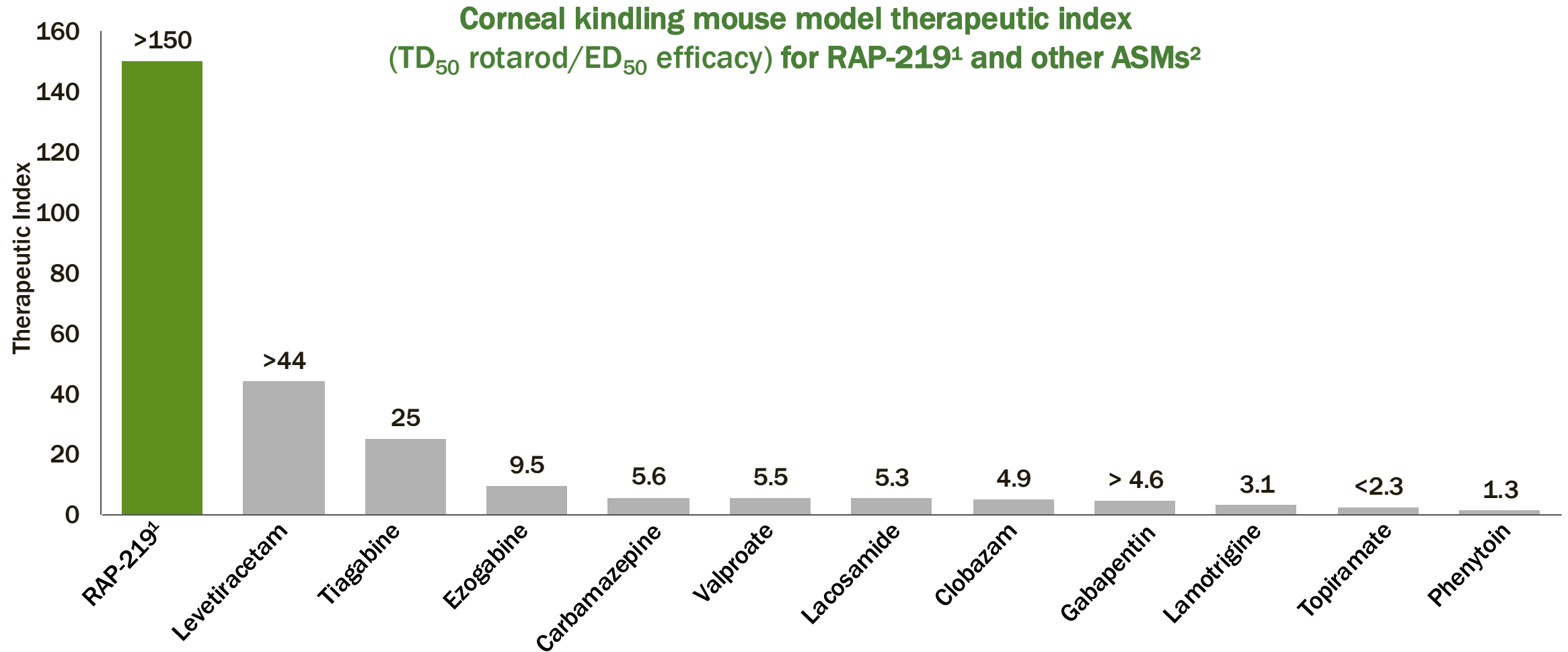
- Oral administration of RAP-219 (0.001-10 mg/kg)
- Plasma EC_{70} 's of 7 ng/mL in rats (shown above) and plasma EC_{70} 's of 3 ng/mL in mice

Corneal kindling responders and rotarod failures in mice



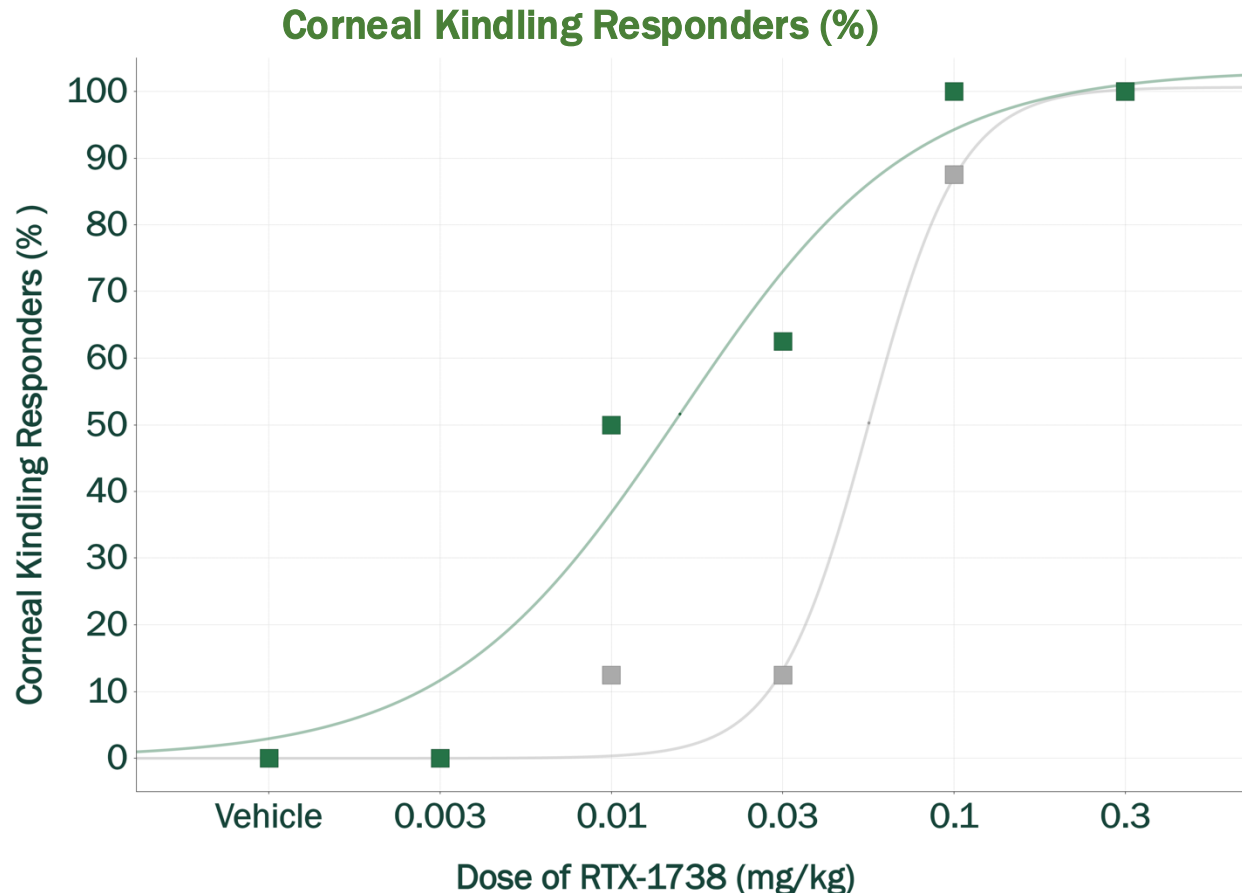
- Valid model in focal epilepsy
- Oral administration of RAP-219 resulted in significant seizure reduction in kindled mice at low plasma levels (<7 ng/mL) corresponding to a projected 50-70% receptor occupancy
- No motoric impairments observed at highest doses tested

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



TARP γ 8 NAM effectiveness persists with repeat dosing

Antiseizure activity maintained after prolonged exposure



- Efficacy in corneal kindling used to evaluate RTX-1738 (an analog of RAP-219)
- RTX-1738 (3 mg/kg) tested following either single day or seven consecutive days of oral administration
- Antiseizure activity was maintained or became more potent after 7-day dosing

- Single oral administration, tested 2 hours post dose
- Seven-day oral administration, tested 2 hours after last dose

TARPy8 AMPAR NAMs active in preclinical epilepsy models

Preclinical epilepsy models are highly translatable, with probabilities of clinical success up to 70%, according to epileptologist Jackie French

Model	
Corneal Kindling – mouse*	✓
PTZ – mouse*	✓
Rotarod*	✓
Amygdala kindling – mouse	✓
Hippocampal kindling – mouse	✓
6Hz stimulation – mouse	✓
Frings audiogenic seizure – mouse	✓
GAERS absence epilepsy – rat	✓

- Robust efficacy across a broad array of preclinical focal and generalized seizure models
- Potent activity in kindling model has been observed to predict efficacy in focal epilepsy
- Activity not seen in maximal electroshock (MES) model, consistent with performance of levetiracetam and some other effective ASMs

"Chronic seizure models [like corneal kindling] offer the most etiologically relevant platform on which to accurately replicate clinical epilepsy and are thus deserving of more use earlier in ASD identification."

– Barker-Haliski, Expert Opinion on Drug Discovery

RAP-219 overview

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RAP-219 Phase 1 SAD/MAD trials

In Phase 1, RAP-219 was generally well tolerated

- No serious adverse events were reported
- No clinically meaningful abnormal changes in labs, ECGs, or vital signs

Single-ascending-dose (SAD) trial

- Treatment related TEAEs were generally consistent with the effects seen in non-clinical toxicology studies
 - All treatment related TEAEs were Grade 1 or Grade 2
 - At the highest doses of 2 mg and 3 mg, CNS pharmacology was observed to be generally consistent with non-clinical studies

Multiple-ascending-dose (MAD) trial

- No treatment related TEAEs above Grade 1 were reported
 - No AE dose response relationship
 - Highest dose evaluated (Cohort 5: 0.75 mg x 5 days, then 1.25 mg x 23 days) had no treatment related TEAEs
 - The MAD trial indicated exposures up to 3-fold higher than those achieved in the SAD trial, exceeding projected target RO

RAP-219 first-in-human Phase 1 trials

Single ascending dose (SAD) trial: RAP-219-101

Part 1

- Randomized, double-blind, placebo-controlled single ascending dose trial
- 5 cohorts, N=8 per cohort (6 active & 2 placebo)
- 0.25 mg to 3 mg doses

Part 2

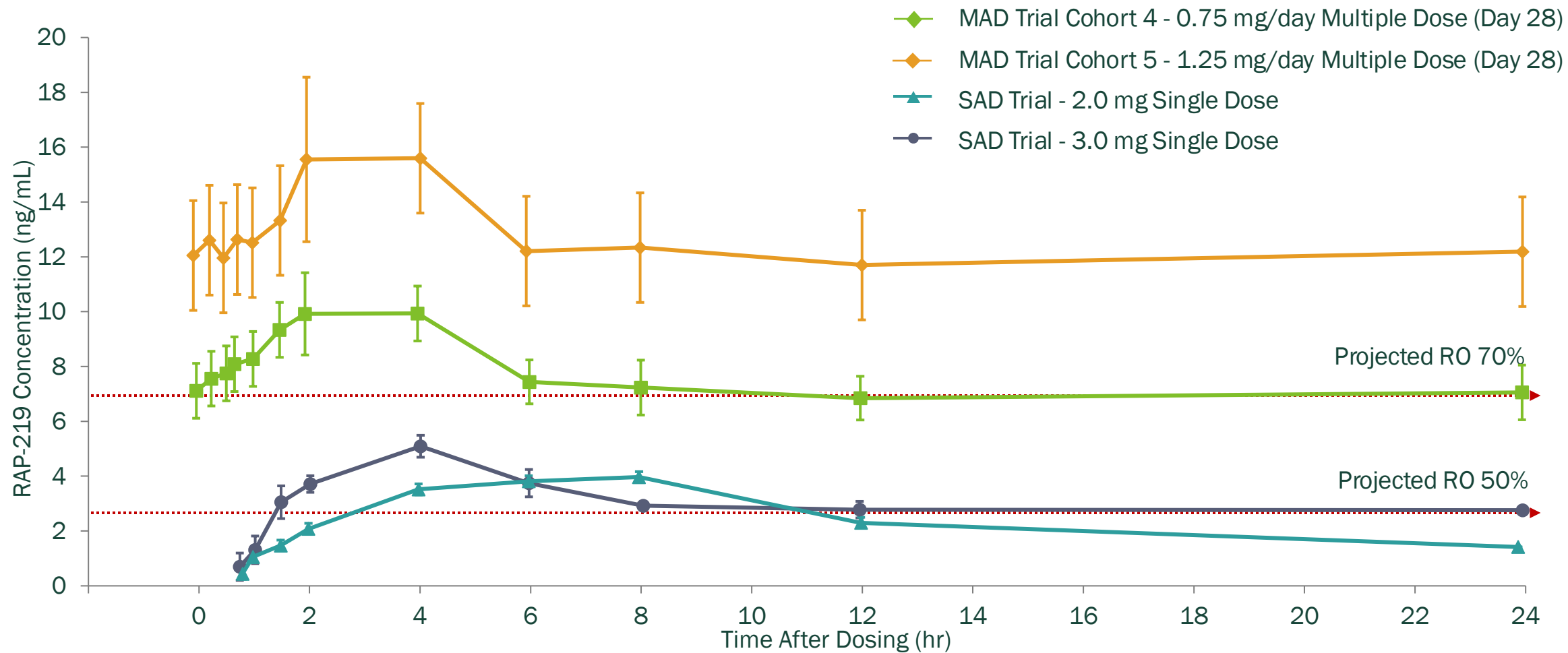
- Open label food effect study, 1 mg with food, N=6

Multiple ascending dose (MAD) trial: RAP-219-102

- Randomized, double-blind, placebo-controlled multiple ascending dose trial
- 5 cohorts, N=8 per cohort (6 active & 2 placebo)
- 0.25 mg QD to 1.25 mg QD
- 2 weeks (Cohorts 1 & 2) or 4 weeks (Cohorts 3-5) of QD dosing

RAP-219 SAD vs. MAD exposures

MAD trial achieved 3-fold higher C_{max} than SAD trial



RAP-219 MAD trial results

At highest dose, no TEAEs above Grade 1 and no treatment-related TEAEs

Treatment Emergent Adverse Events (TEAEs) in Phase 1 RAP-219-102 (MAD) Trial by Cohort and Pooled Placebo	Pooled Placebo (N=10)	Cohort 1 (0.25 mg × 2 weeks) (N=6)	Cohort 2 (0.25 mg × 1 week; 0.5 mg × 1 week) (N=6)	Cohort 3 (0.5 mg × 4 weeks) (N=6)	Cohort 4 (0.75 mg × 4 weeks) (N=6)	Cohort 5 (0.75 mg x 5 days; 1.25 mg x 23 days) (N=6)
Any TEAEs	4 (40.0%)	5 (83.3%)	6 (100%)	3 (50.0%)	5 (83.3%)	2 (33.3%)
Grade 1 (Mild) Related ¹	2 (20.0%)	3 (50.0%)	3 (50.0%)	2 (33.3%)	0	0
Grade 2 (Moderate) Related ¹	0	0	0	0	0	0
Grade 1 (Mild) Unrelated	2 (20.0%)	2 (33.3%)	4 (66.7%)	2 (33.3%)	4 (66.7%)	2 (33.3%)
Grade 2 (Moderate) Unrelated	0	3 (50.0%)	3 (50.0%)	0	2 (33.3%)	0
Grade 3 (Severe)	0	0	0	0	0	0
Grade 4 (Potentially Life Threatening)	0	0	0	0	0	0
Grade 5 (Death Related to AE)	0	0	0	0	0	0

Dose for Phase 2a focal epilepsy trial

Potentially optimal target profile emerging for RAP-219 in focal epilepsy

Ideal Product Profile	RAP-219 Emerging Profile
Reduces seizures potently without evidence of sedation	<ul style="list-style-type: none">• At low dose, reduced seizures in validated preclinical epilepsy models
Displays no dose limiting toxicities	<ul style="list-style-type: none">• Highest dose evaluated in IND-enabling studies were considered to be generally well tolerated
Potential for reduced drug-drug interactions	<ul style="list-style-type: none">• Low DDI potential as RAP-219 not observed to interact with CYP enzymes• Well suited for polypharmacy as no dose adjustments anticipated when combined with other ASMs
Generally well tolerated	<ul style="list-style-type: none">• Achieved exposures exceeding projected target RO• No SAEs and no abnormal laboratory or ECGs reported• No treatment related TEAEs above Grade 1 reported in the MAD trial
Potential for greater therapeutic index	<ul style="list-style-type: none">• RAP-219 exposure achieved with planned Phase 2a dose exceeded targeted therapeutic levels with no apparent treatment related AEs
Convenient administration	<ul style="list-style-type: none">• QD dosing• Single step-up dosing

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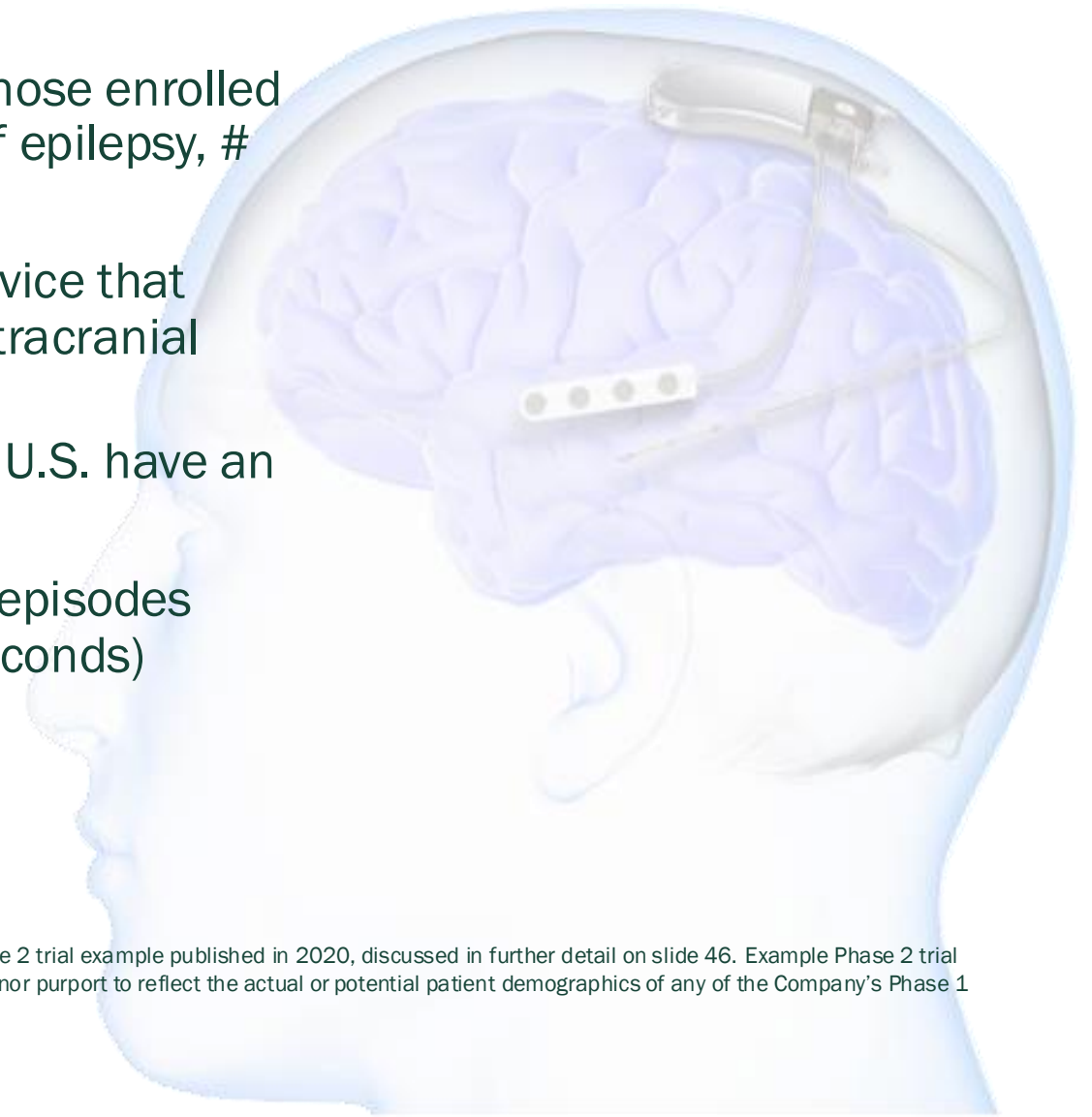
Phase 2a proof-of-concept trial in focal epilepsy

Key design considerations for an ideal trial

- Same population to be used in registrational trials – refractory FOS patients
- Informs dose selection and effect size
- Utilizes a recognized seizure biomarker demonstrated to predict clinical response
- Enables rapid progression into registrational trials

Focal epilepsy patients with a responsive neurostimulation (RNS) system

- RNS system patients had similar demographics to those enrolled in a third-party registrational FOS study¹ (duration of epilepsy, # of seizures, # of ASMs)
- The RNS system is an FDA-approved implantable device that continually monitors and records seizure activity (intracranial EEG, or iEEG data) in patients with FOS
 - >5,000 refractory focal epilepsy patients in the U.S. have an implanted RNS device²
- RNS detects³ a biomarker of clinical seizures - long episodes (LEs) exceeding a specified duration (typically 30 seconds)



Long episodes – a biomarker-based endpoint demonstrated to predict clinical response

Change in seizure activity recorded through intracranial EEG (iEEG) predicted ASM clinical response

Received: 15 July 2019 | Revised: 14 November 2019 | Accepted: 21 November 2019
DOI: 10.1111/epi.16412

FULL-LENGTH ORIGINAL RESEARCH

Epilepsia

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

Imran H. Quraishi¹ | Michael R. Mercier¹ | Tara L. Skarpaas² | Lawrence J. Hirsch¹

“In addition to providing a shorter lag time than diaries or other patient reports, it could be argued that long episodes are an even better therapeutic target than reported clinical seizures.”

Researcher in the single-center cohort, long episodes, but not episode starts, had a significantly greater reduction in the first week for clinically efficacious compared to ineffective medications. In this cohort, having no long episodes in the first week was highly predictive of ASD efficacy. In the multicenter cohort, both long episodes and episode starts had a significantly greater reduction for effective medications starting in the first 1-2 weeks. In this larger dataset, a $\geq 50\%$ decrease in episode starts was 90% specific for efficacy with a positive predictive value (PPV) of 67%, and a $\geq 84\%$ decrease in long episodes was 80% specific with a PPV of 48%. Conversely, a $< 25\%$ decrease in long episodes (including any increase) or a $< 20\%$ decrease in episode starts had a predictive value for inefficacy of $> 80\%$.

Significance: In RNS System patients with stable detection settings, when new ASDs are started, detection rates within the first 1-2 weeks may provide an early, objective indication of efficacy. These data could be used to identify responses to medication



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

Tara L. Skarpaas^{*,*}, Thomas K. Tcheng[†], Martha J. Morrell^{‡,§}

“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.”

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, depending on a patient's seizure frequency, it may take months to detect a response, and this process must be repeated with each dose adjustment. A physiological biomarker that provides a rapid assessment of a medication's effect on cortical excitability could quickly and objectively establish whether a given medication and dose are likely to be clinically effective. Chronic

electrocorticographic (ECoG) sensing and recording devices could provide such information.

Pathologically increased cortical excitability is a hallmark of epilepsy [6,7], and AEDs measurably decrease cortical excitability. For instance, Badawy et al. [8] demonstrated that AED induced changes in transcranial magnetic stimulation-evoked measures of cortical excitability could predict seizure-freedom. This was observed regardless of the AED used. Further, Meisel et al. [9] demonstrated that the effect of AEDs could be quantified in a graded manner using intrinsic measures of cortical excitability recorded during intracranial monitoring. However, neither evoked nor intrinsic measures of cortical excitability have been available outside of the clinic or hospital.

The aim of this retrospective study was to explore whether chronic ambulatory ECoG data recorded by a closed-loop neurostimulation system (the RNS[®] System, NeuroPace Inc.) could reveal potential biomarkers

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E-mail addresses: tskarpaas@neuropace.com, (T.L. Skarpaas),
tcheng@neuropace.com, (T.K. Tcheng), mmorrell@neuropace.com, (M.J. Morrell).

- 30-40% reduction in LEs within 1-4 weeks of new ASM was associated with a $\geq 50\%$ seizure reduction¹
- No decrease in LEs predicts ASM will not be clinically efficacious

RAP-219 Phase 2a PoC trial in focal epilepsy

Principal Investigator:

Jacqueline French, M.D.
Professor, Neurology, NYU Grossman School of
Medicine

Trial Goal:

Evaluate efficacy of RAP-219 using LE
biomarker

Design Overview:

- Signal detection trial in adult drug-resistant focal epilepsy patients with implanted RNS systems
- Multi-center open-label trial to enroll approximately 20 patients
- MAD Cohort 5 dose: 0.75 mg/day for 5 days followed by 1.25 mg/day

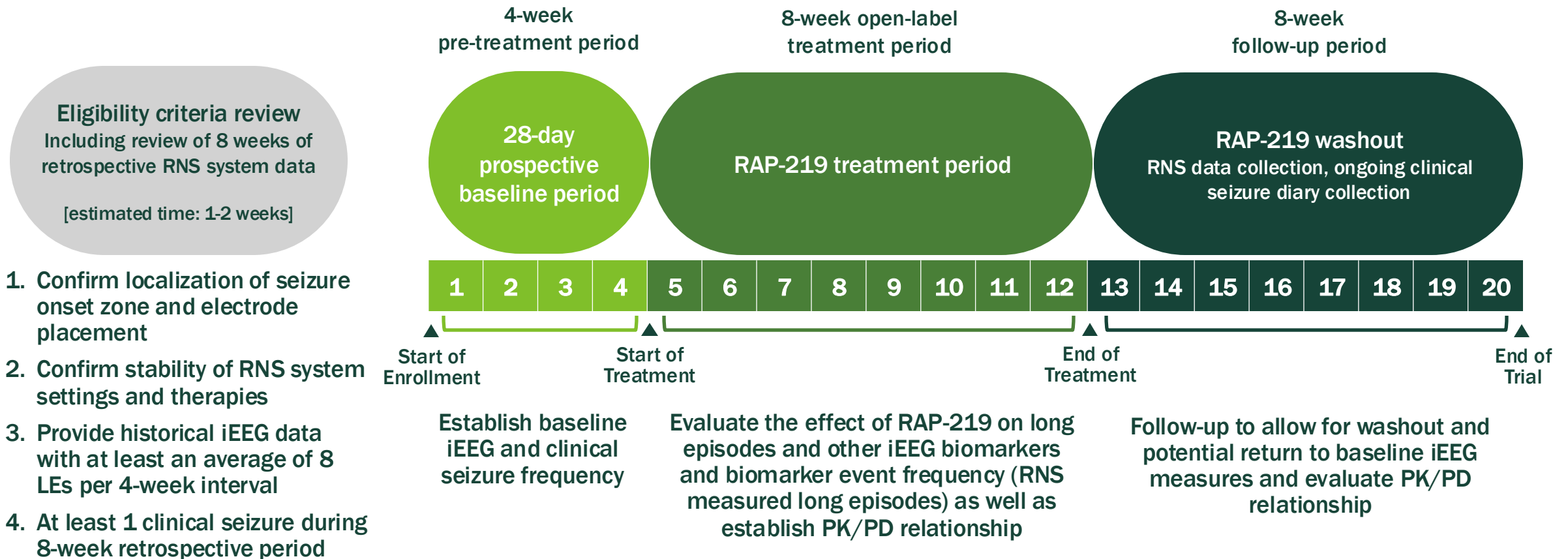
Key endpoints:

- Change in LE frequency on treatment compared to baseline
- LE frequency responder analysis (% of patients that demonstrate $\geq 30\%$ reduction in LEs)
- Change in estimated EES, clinical seizure frequency, and additional iEEG biomarkers
- Clinically meaningful improvements in global ratings (PGIC/CGIC)

Phase 2a trial ongoing; topline results expected in mid-2025

RAP-219 Phase 2a PoC trial schema in focal epilepsy

Trial schema



Focal epilepsy PoC model comparison

Ideal Model	RNS	Photosensitivity (PPR)	Transcranial Magnetic Stimulation (TMS)
Uses focal epilepsy patient population	✓ Yes	✗ No	✗ No
Recognized seizure biomarker	✓ Long episode reduction shown to predict clinical seizure reduction	✗ Generalized photoparoxysmal EEG responses	✗ TMS-evoked EEG potentials (TEPs)
Obtains data on effect size	✓ Measures drug effect on FOS biomarker of focal onset seizure	? Measures evoked generalized epileptiform discharges	? Measures provoked cortical hyperexcitability in normal healthy volunteers
Informs dose selection for registrational trials	✓ PK/PD data will allow direct measure of degree of efficacy at different exposure levels	? Indirect dose response readout for non-FOS seizure	? Indirect dose response readout of cortical hyperexcitability in HNV
Enables rapid progression into registrational trial	✓ Expect translatable data that can inform dose and effect size for future registrational trials	? Does not provide dosing or effect size for FOS registration trials	? Does not provide dosing or effect size for FOS registration trials

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Chronic peripheral neuropathic pain

Strong mechanistic and compelling preclinical data for RAP-219

Peripheral neuropathic pain

- Diagnosed prevalence of ~5.6 million¹ in the U.S.
- Conditions include painful diabetic neuropathy, postherpetic neuralgia, trigeminal neuralgia, and idiopathic sensory polyneuropathy
- Caused by injury or dysfunction of peripheral nerves → CNS maladaptive changes
- Significant unmet need for new drugs with:
 - Novel MOA
 - Once per day dosing
 - Improved tolerability
 - Minimal or no drug-drug interactions
 - No abuse or cardiovascular liabilities

Rationale for RAP-219

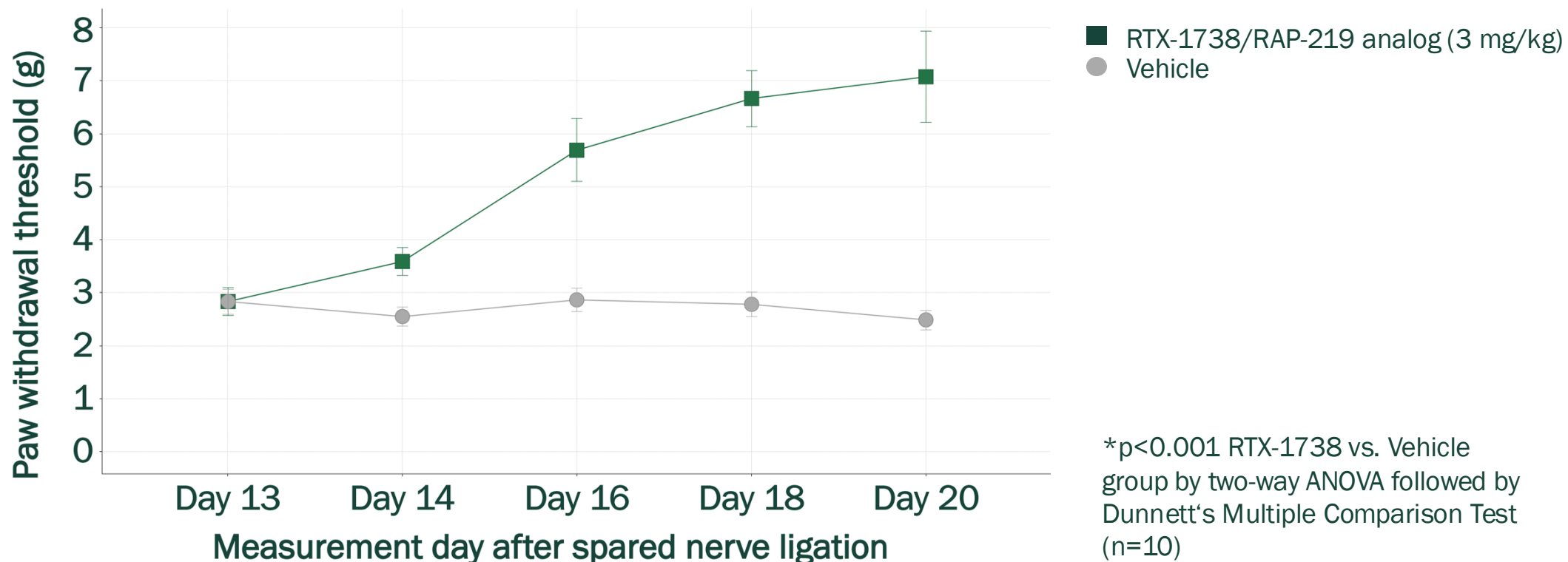
- TRPV8 is expressed in areas of the CNS associated with pain
 - Spinal cord dorsal horn, where the sensation of pain (nociception) enters the CNS
 - The anterior cingulate cortex, where the affective or emotional aspects of pain resides
- Positive results observed in multiple animal models of pain, including neuropathic pain

Preclinical evidence supporting RAP-219 in chronic pain

Study of RTX-1738, TARP γ 8 NAM (RAP-219 analog)

RTX-1738 attenuates tactile allodynia in spinal nerve ligation (SNL) rat model

Starting on Day 16 (third day of dosing) and continuing through Day 20, paw withdrawal thresholds were elevated, reflecting decreased pain behavior



Bipolar disorder acute mania

Strong mechanistic data for RAP-219

Bipolar disorder

- Affects 2.8 percent of the adult population in the US (approximately 7 million adults)
- Extreme shifts in mood – “manic-depressive”
- Manic episodes characterized by feelings of over-excitement, irritability, impulsivity, grandiose beliefs and racing thoughts
- Typically treated with antipsychotic medications as either monotherapy or in combination therapy with mood stabilizers
- Drug treatments often poorly tolerated with safety risks

Rationale for RAP-219

- Bipolar disorder is associated with hyperactivity in the hippocampus, where TARPy8 is enriched
- Bipolar risk alleles overrepresented in genes encoding synaptic signaling proteins with high specificity of expression in neurons of the prefrontal cortex and hippocampus
- Other ASMs (such as valproate, lamotrigine, and carbamazepine) are FDA approved to treat bipolar disorder
- The corneal kindling model of epilepsy is believed by some experts to be predictive of bipolar treatments

Phase 2a trial in bipolar disorder patients with acute mania expected to be initiated in 2025

Ongoing research of RAP-219 to inform future development

MAD 2 and PET studies to evaluate dose escalation pace and receptor occupancy

RAP-219-104 (MAD Trial 2)

- Objective: Assess dosing regimens that may enable reaching therapeutic exposures quicker
- Double-blind, placebo controlled
- Two cohorts with option to add up to three additional
- Expected to be completed in Q4 2024

Positron Emission Tomography (PET) Trial

- Objective: Confirm brain target receptor occupancy and brain region specificity across a range of RAP-219 dosing and exposure levels
- Up to four cohorts
- Expected to be completed in 1H 2025

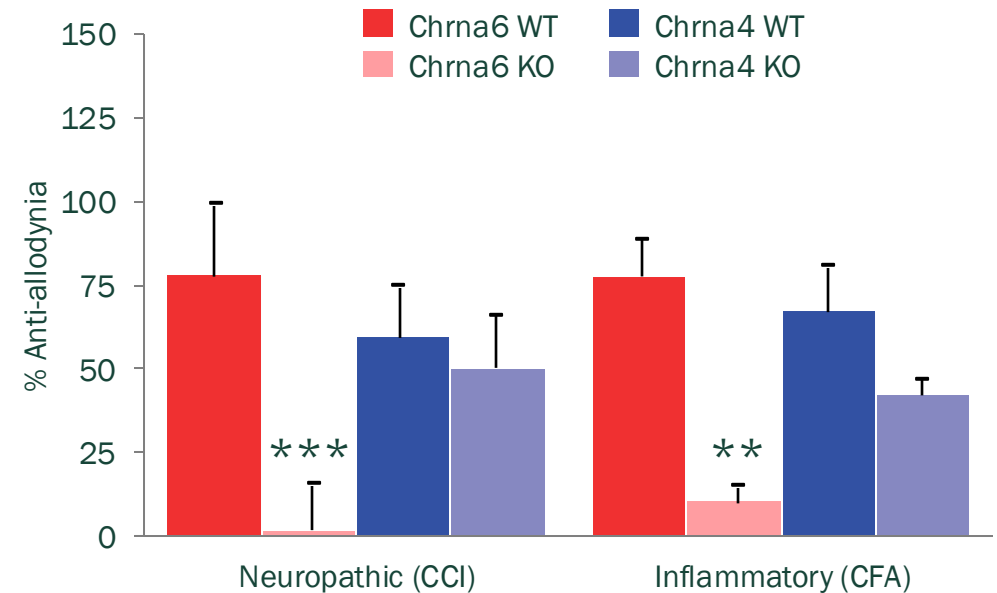
MAD 2 and PET trial topline results expected in Q1 2025

nAChR discovery programs

α 6 nAChR program

Preclinically-validated approach to neuropathic pain

- nAChR agonists have been observed to be efficacious in third-party preclinical and clinical neuropathic pain studies; preclinical evidence in acute, inflammatory, and neuropathic pain
- Abbott's pan-nAChR agonist demonstrated significant improvements in patients with diabetic neuropathic pain, but up to 66% of patients withdrew from the trial due to AEs such as nausea, dizziness, vomiting, abnormal dreams, and asthenia
- Evidence shows that α 6 is a potential target for chronic pain

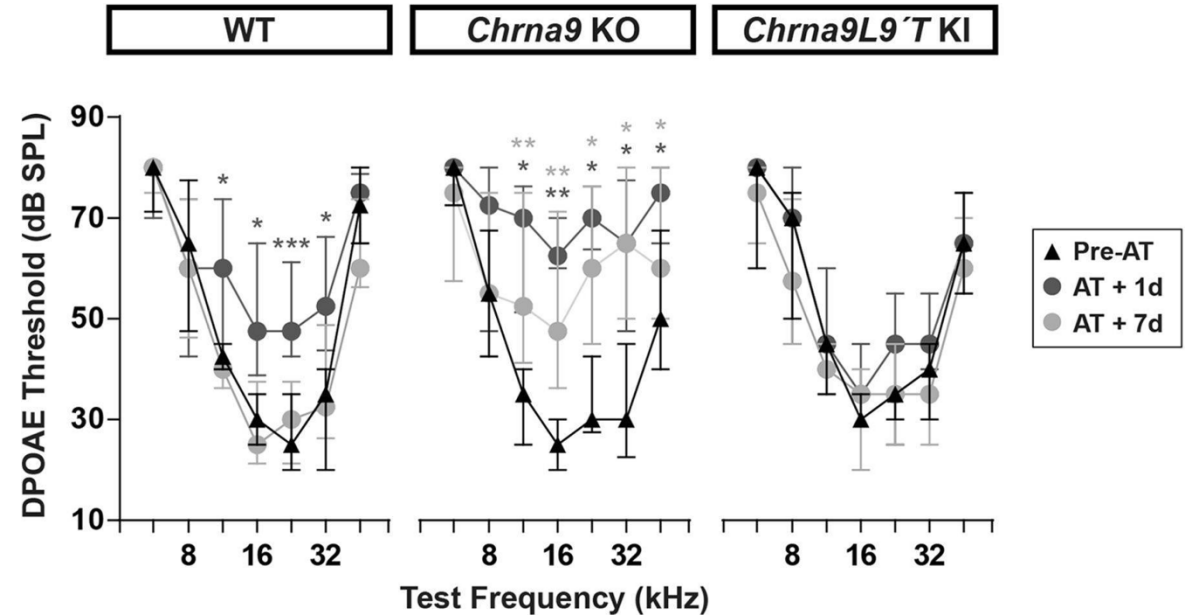


Genetic knockout (KO) mice demonstrate requirement of α 6- but not α 4-containing nicotinic receptors for anti-allodynia mediated by intrathecal nicotine administration

$\alpha 9\alpha 10$ nAChR program

Potential for first-in-class approach to hearing disorders

- Potential for $\alpha 9\alpha 10$ nAChRs in hearing disorders demonstrated in preclinical studies
- Engagement of $\alpha 9\alpha 10$ has been observed to mitigate hearing loss in preclinical models
- Our RAP platform technology enabled Rapport to identify potentially first-in-class orally-delivered agonists that are selective for $\alpha 9\alpha 10$ nAChRs



- (Left) Auditory brainstem responses (ABRs) are elevated at 1 day but not at 7 days following acoustic trauma (AT).
- (Middle) $\alpha 9$ KO elevates ABR thresholds at 1 and 7 days after acoustic trauma.
- (Right) $\alpha 9$ gain of function knock-in (L9'T KI) completely prevents acoustic trauma hearing deficits.

Cash runway and anticipated catalysts

Trial	Next Expected Milestone
RAP-219 Multiple Ascending Dose (MAD) 2 trial	Expected to be completed Q4 2024; topline results Q1 2025
RAP-219 Human Positron Emission Tomography (PET) trial	Topline results Q1 2025
RAP-219 Phase 2a proof-of-concept trial focal epilepsy	Topline results mid-2025
RAP-219 Phase 2a proof-of-concept trial peripheral neuropathic pain	Trial initiation*
RAP-219 Phase 2a proof-of-concept trial bipolar disorder	Trial initiation 2025

Cash balance of \$320.7mm¹ (as of 9/30/24) supports Rapport through end of 2026

Rapport Therapeutics: Charting new paths in neuroscience with groundbreaking precision design

Experienced leadership

Proven track record of building companies, novel therapies, and development platforms

Proprietary program

Pioneered discoveries of receptor associated proteins (RAPs); IP expiration in 2036 + potential PTE

Neuroanatomical specificity

Technology designed to create precisely targeted neuromedicines, potentially overcoming limitations of conventional treatments

Lead asset in clinical development for treatment of focal epilepsy

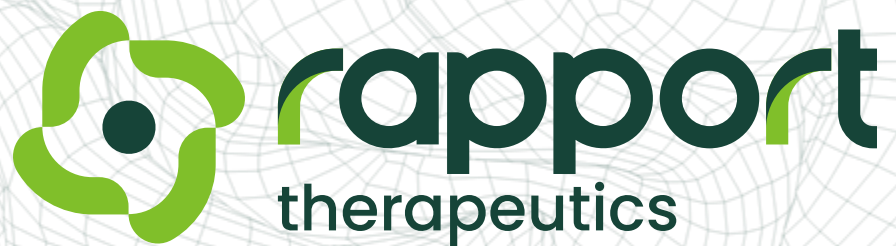
Data support initiating Phase 2a proof-of-concept trial for RAP-219

Therapeutic potential across multiple indications

Significant markets, including epilepsy, peripheral neuropathic pain, and bipolar disorder

Steady cadence of milestones anticipated

Robust clinical and discovery pipeline with multiple anticipated upcoming milestones



Thank you