

Corporate Presentation

August 2026



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,” “will,” “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 focal onset seizures, primary generalized tonic-clonic seizures, and bipolar mania, including the initiation, timing, progress and results of the ongoing and planned clinical trials; expectations for the efficacy, tolerability, and commercial potential of RAP-219; the potential multi-billion dollar market opportunity for RAP-219 in focal onset seizures, if approved; expectations for the development of a long-acting injectable formulation of RAP-219; the prioritization of the Company’s $\alpha 6\beta 4$ program, including the development candidate’s potential in chronic pain and migraine and the Company’s IND-enabling activities; the deferral of further investment in the RAP-219 diabetic peripheral neuropathic pain program; the potential of Rapport’s RAP technology platform; and expectations for Rapport’s uses of capital, including its cash runway into the second half of 2029. 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.

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 Ceesay^a
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
25+ 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 zseventybio
Bristol Myers Squibb



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

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Paul Silva
Director
Former Chief Accounting Officer, Vertex Pharmaceuticals

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

Small molecule precision medicines for patients with neurological and psychiatric disorders

Strong Foundation and Differentiated Precision Approach

Company builders with industry-proven leadership

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

Distinct profile with transformative potential across neurological and psychiatric disorders



Robust Clinical and Discovery Pipeline

Potential **first-in-class programs** targeting receptor associated proteins (RAPs)

Clinical stage lead program with pipeline-in-a-product potential

Medicinal chemistry-enabled **discovery portfolio** unlocks regenerative pipeline

Global IP portfolio with worldwide rights



RAP-219: Pipeline-in-a-Product with Near-Term Catalysts Ahead

Novel forebrain restricted TARPγ8 AMPAR modulator

Robust Phase 2a clinical data in **drug-resistant focal onset seizures (FOS)**; Phase 3 program initiated in Q2 2026

Expanding epilepsy portfolio to **primary generalized tonic-clonic seizures (PGTCS)**

Bipolar mania Phase 2 topline results expected in October 2026



Well Financed to Address Large Market Opportunity

Strong financial position with **\$436.1 million** as of June 30, 2026^a

Capitalized to complete Phase 3 program in FOS allowing RAP-219 to address a market size of ~\$15B

Cash runway expected to fund operations into 2H 2029



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

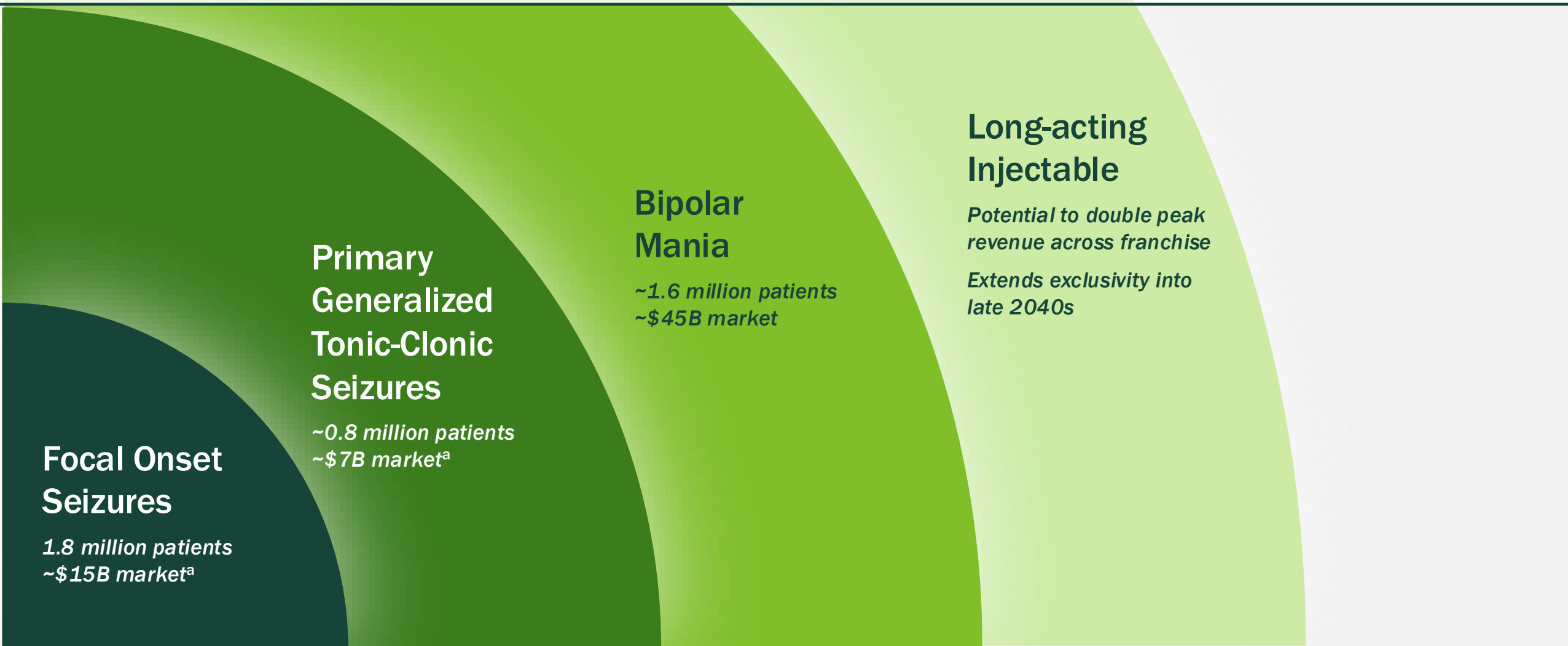
The Potential of RAPs

- ✓ 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

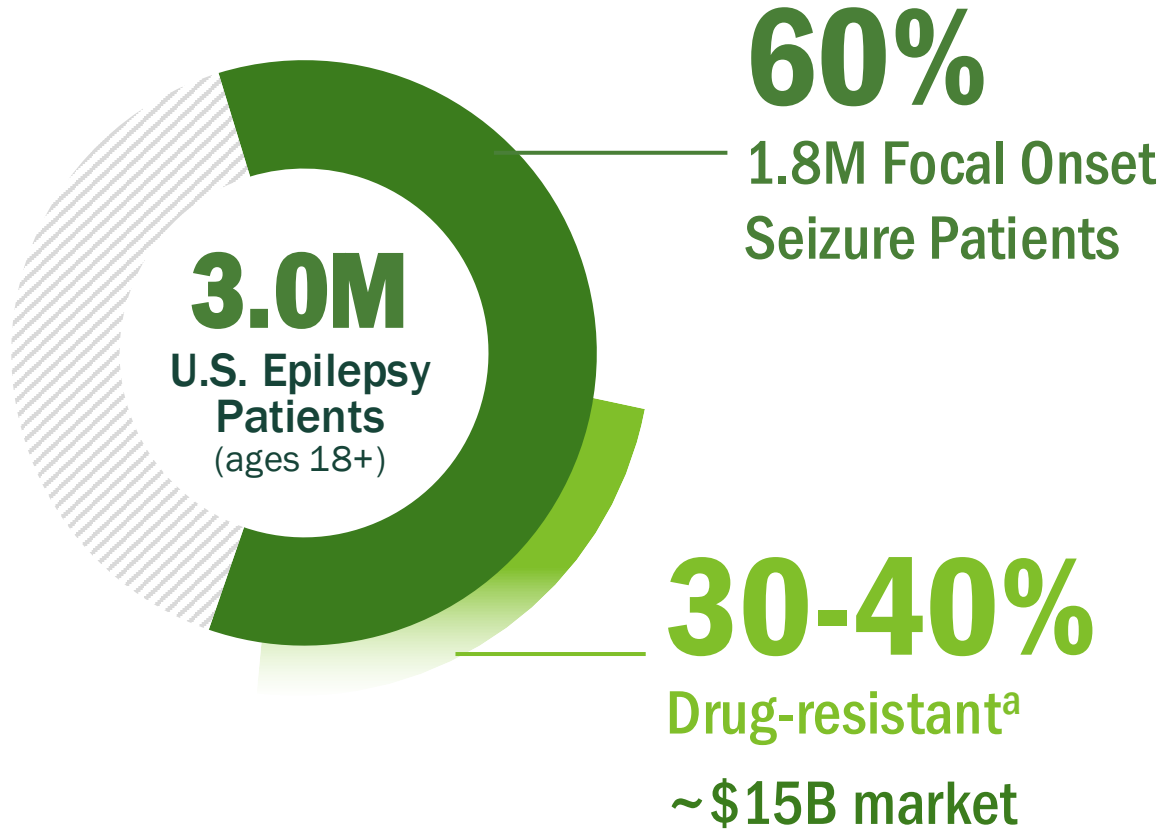
Precision neuroscience pipeline with opportunity to address large market opportunities

Program	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Next Expected Milestone
RAP-219 TARPy8 AMPA	Focal Onset Seizures					Phase 3 Initiated 2Q 2026
	Primary Generalized Tonic-Clonic Seizures					Phase 3 Initiation 1H 2027
	Bipolar Mania					Topline Results October 2026
	Long-Acting Injectable					Phase 1 Topline Results (PK) 2027
nAChR	RAP-641 ($\alpha 6\beta 4$) Chronic Pain & Migraine					Phase 1 Trial Initiation
	$\alpha 9\alpha 10$ Hearing/Vestibular Disorders					Development Candidate Nomination

RAP-219 pipeline-in-a-product supports long term growth runway



Unmet need in epilepsy highlights limitations of current antiseizure medications



Limitations of Antiseizure Medications (ASMs)

Limited Efficacy: Despite over 30 FDA approved ASMs, 30-40% of patients are still drug-resistant^a

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

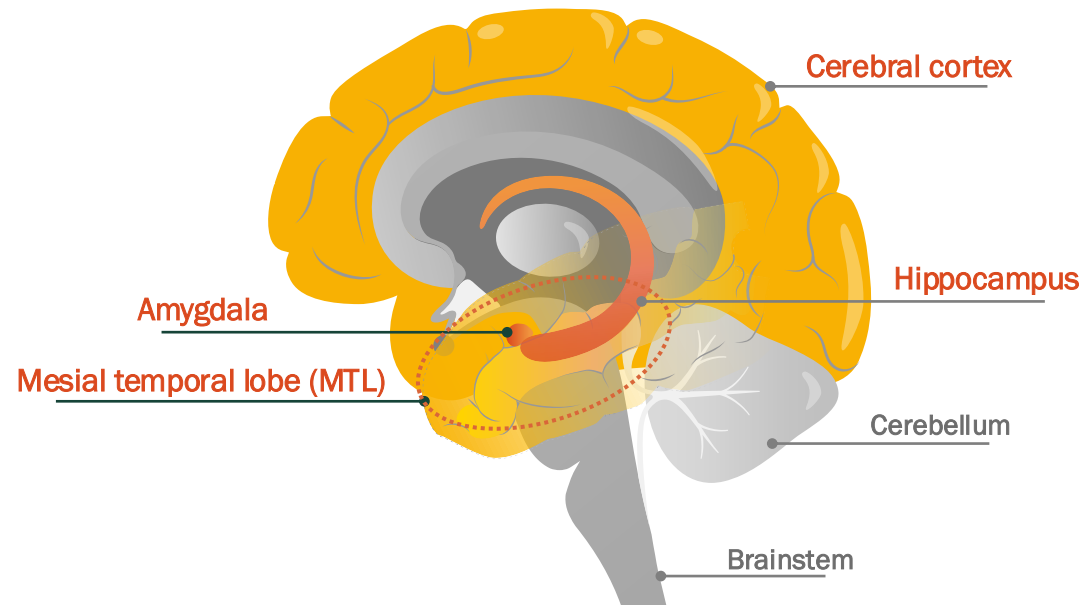
Potential for Serious Adverse Events: Such as severe cutaneous reactions, serious hematological disorders, and hepatic failure

Risk of Breakthrough Seizures: Missing doses of medicines with short half-lives create potential for breakthrough seizures¹

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

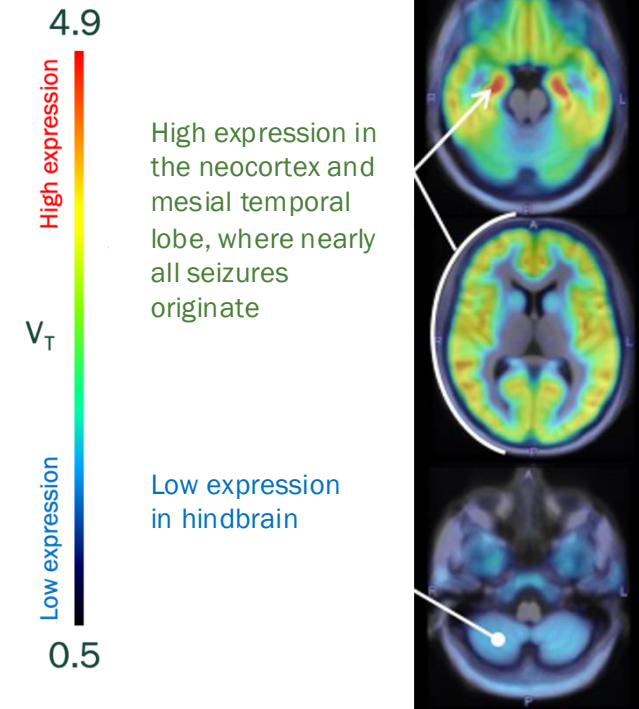
RAP-219 target, TARP γ 8, is selectively expressed in brain regions where focal onset seizures originate

Focal Onset Seizure Origination and Propagation



MTL and cerebral cortex are the key brain areas associated with focal onset seizures

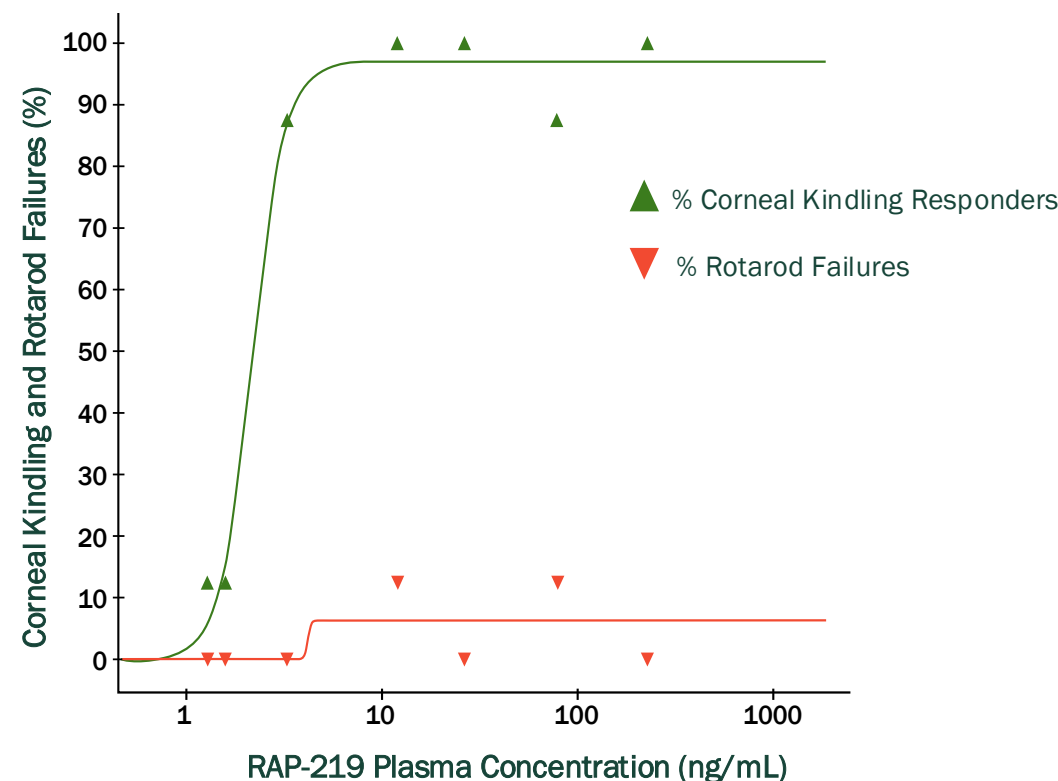
TARP γ 8 Clinical PET



PET results confirm TARP γ 8 is highly expressed in the MTL and neocortex

Robust activity of RAP-219 across a broad array of seizure models established our early confidence

Corneal Kindling Responders and Rotarod Failures in Mice



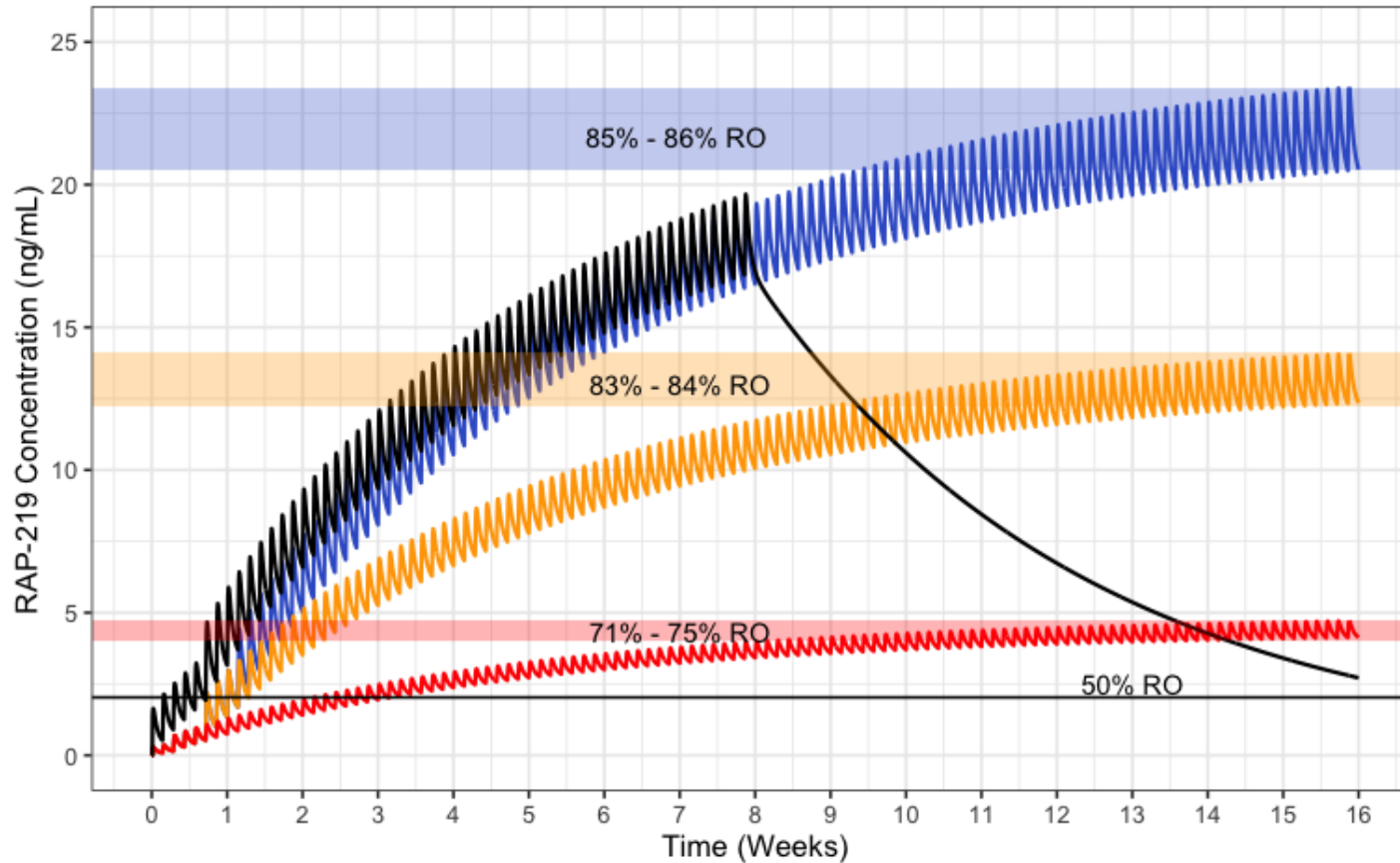
Epilepsy Model^a

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

Robust, dose-dependent seizure protection observed in gold-standard preclinical model

Robust activity observed across a broad array of preclinical focal and generalized seizure models

RAP-219 dose-exposure-receptor occupancy (RO) relationship



- Preclinical models demonstrated maximal seizure protection at >50% RO (**black horizontal line**)
- All Phase 3 FOS trial doses achieve target RO

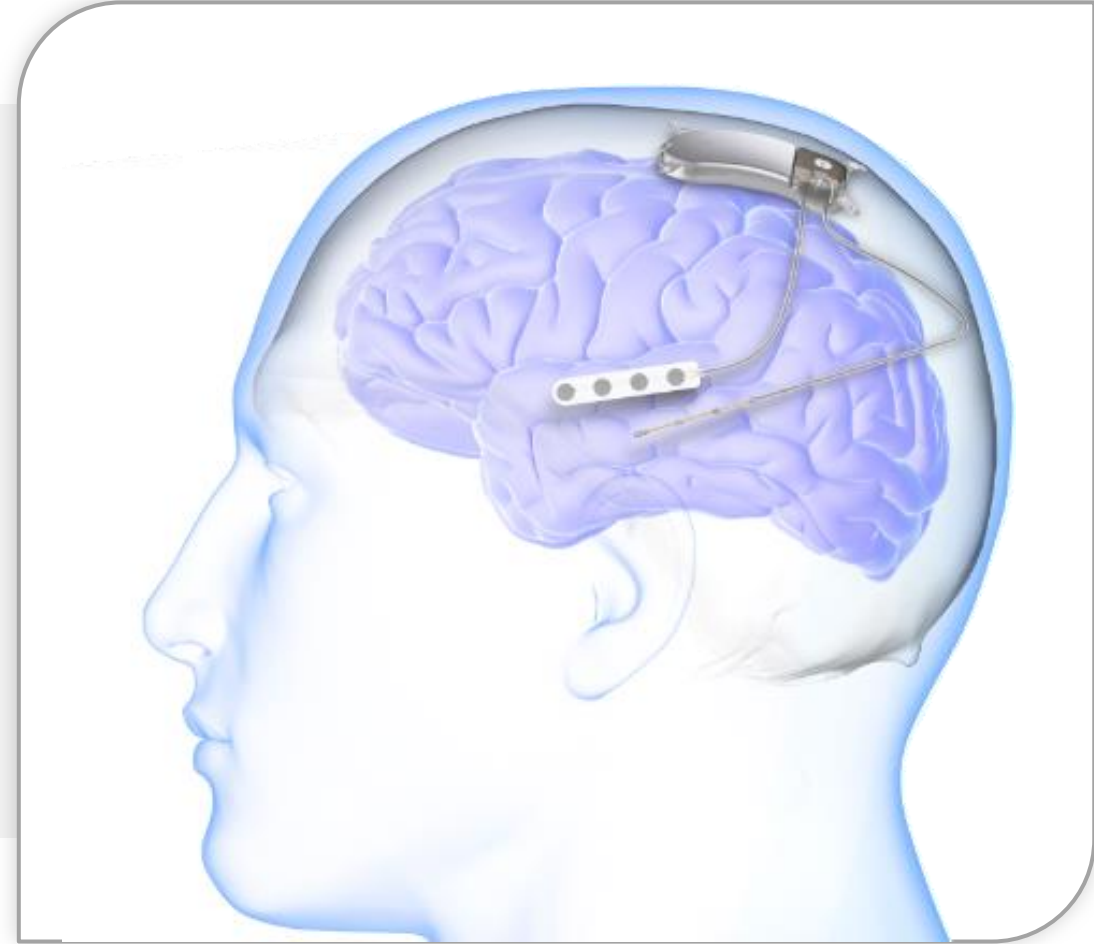
■ Ph3 high dose (1.25mg)
■ Ph3 mid dose (0.75mg)
■ Ph3 low dose (0.25mg)
■ Ph2 dose (1.25mg)

RAP-219 in Focal Onset Seizures

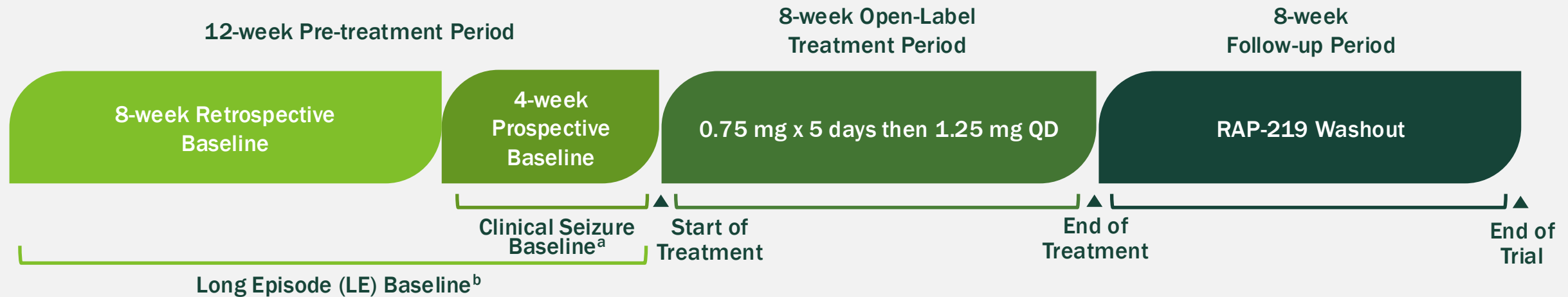
Phase 2a proof-of-concept trial in FOS patients with an objective electrographic biomarker for clinical seizure reduction

Neuropace RNS System®

- FDA-approved device for patients with drug-resistant focal onset seizures
- 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
- ASMs resulting in a $\geq 30\%$ reduction in LEs were associated with a $\geq 50\%$ reduction in clinical seizures



Phase 2a trial in drug-resistant focal onset seizure patients



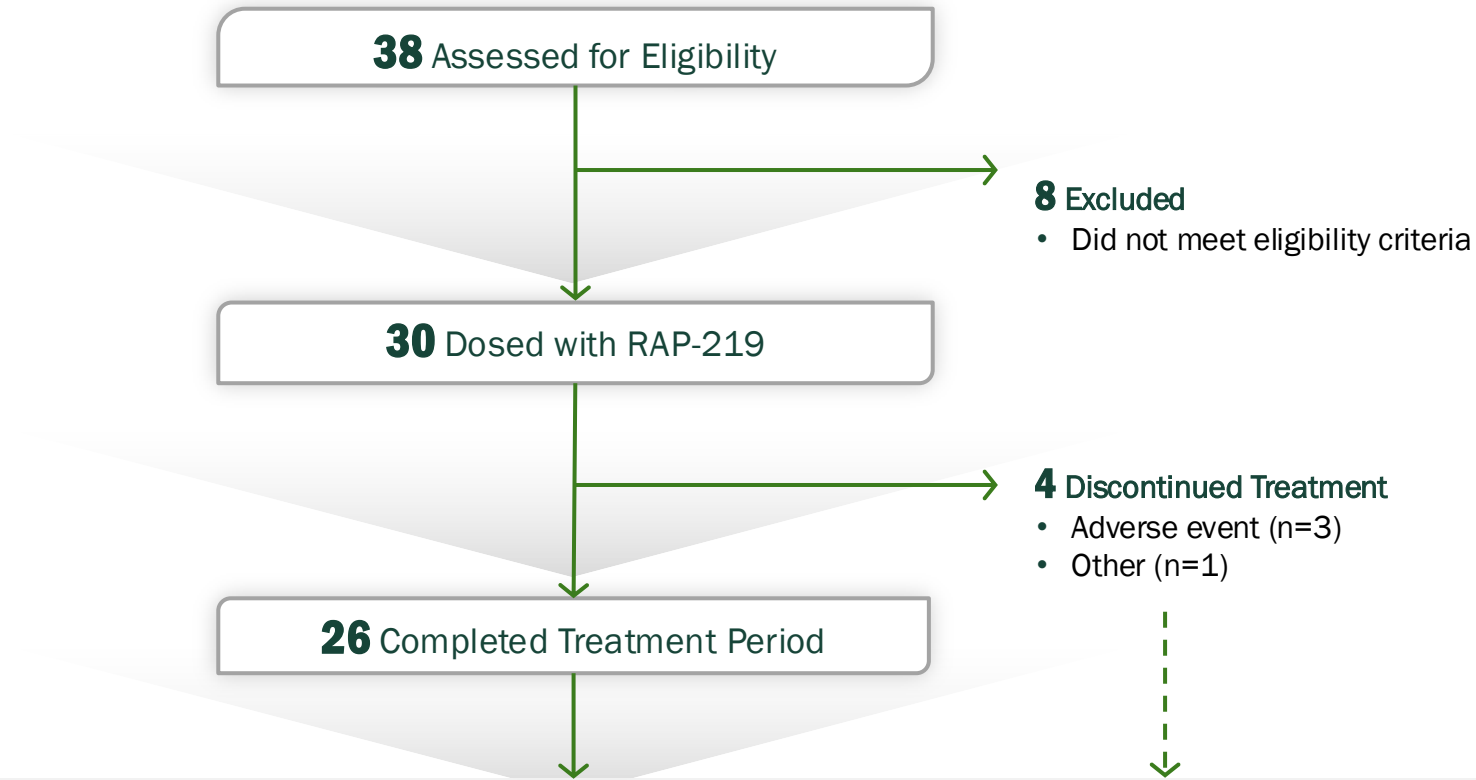
Key Entry Criteria

1. Drug-resistant focal onset seizures
2. RNS[®] probe implanted in seizure onset zone within mesial temporal lobe (MTL) ≥ 15 months before screening
3. Stable RNS System settings and other 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 LEs and electrographic seizures

Key Endpoints

- **LE reduction** (power determinations based on this outcome measure)
 - Proportion of patients with $\geq 30\%$ reduction compared with LE baseline
 - Median percent change from LE baseline
- **Clinical seizure reduction**
 - Proportion of patients with $\geq 50\%$ reduction compared with pre-treatment baseline; proportion of patients who achieved seizure freedom
 - Median percent change from baseline

Patient disposition and analysis populations



Analysis Populations

- Safety population (N=30)
- mITT population for LE efficacy (N=27)
 - Safety population minus 2 patients with <3 weeks of treatment and 1 patient with RNS setting change
- mITT-CS population for clinical seizure efficacy (N=25)
 - mITT population minus 2 patients who did not have clinical seizures during prospective baseline
- Completed follow-up (N=29)

mITT: patients with ≥ 3 weeks of treatment, $\geq 70\%$ adherence, and no RNS system detection or stimulation setting changes. mITT-CS: patients in the mITT with ≥ 1 CS during the prospective baseline. CS – clinical seizure; LE – long episode; mITT – modified intent-to-treat; RNS – responsive neurostimulator.

Patient demographic and baseline characteristics

Highly drug-resistant FOS patients are representative of those in registrational trials

Safety Population	N=30
Age, years, mean (SD)	40.1 (10.4)
Age at first seizure, years, mean (SD)	15.8 (9.3)
Sex, male, n (%)	18 (60)
Years since RNS implantation, median (range)	4.6 (2–11)
No. of concomitant ASMs	
Median (range)	3 (1–4)
1, n (%) 2, n (%) 3, n (%) 4, n (%)	2 (7) 7 (23) 18 (60) 3 (10)
Most frequent concomitant ASMs [†] , n (%)	
Lamotrigine	15 (50)
Levetiracetam	12 (40)
Cenobamate	11 (37)
Zonisamide	9 (30)
Clobazam	7 (23)
Lacosamide	7 (23)

[†]Maintenance ASMs in ≥20% of patients at baseline.

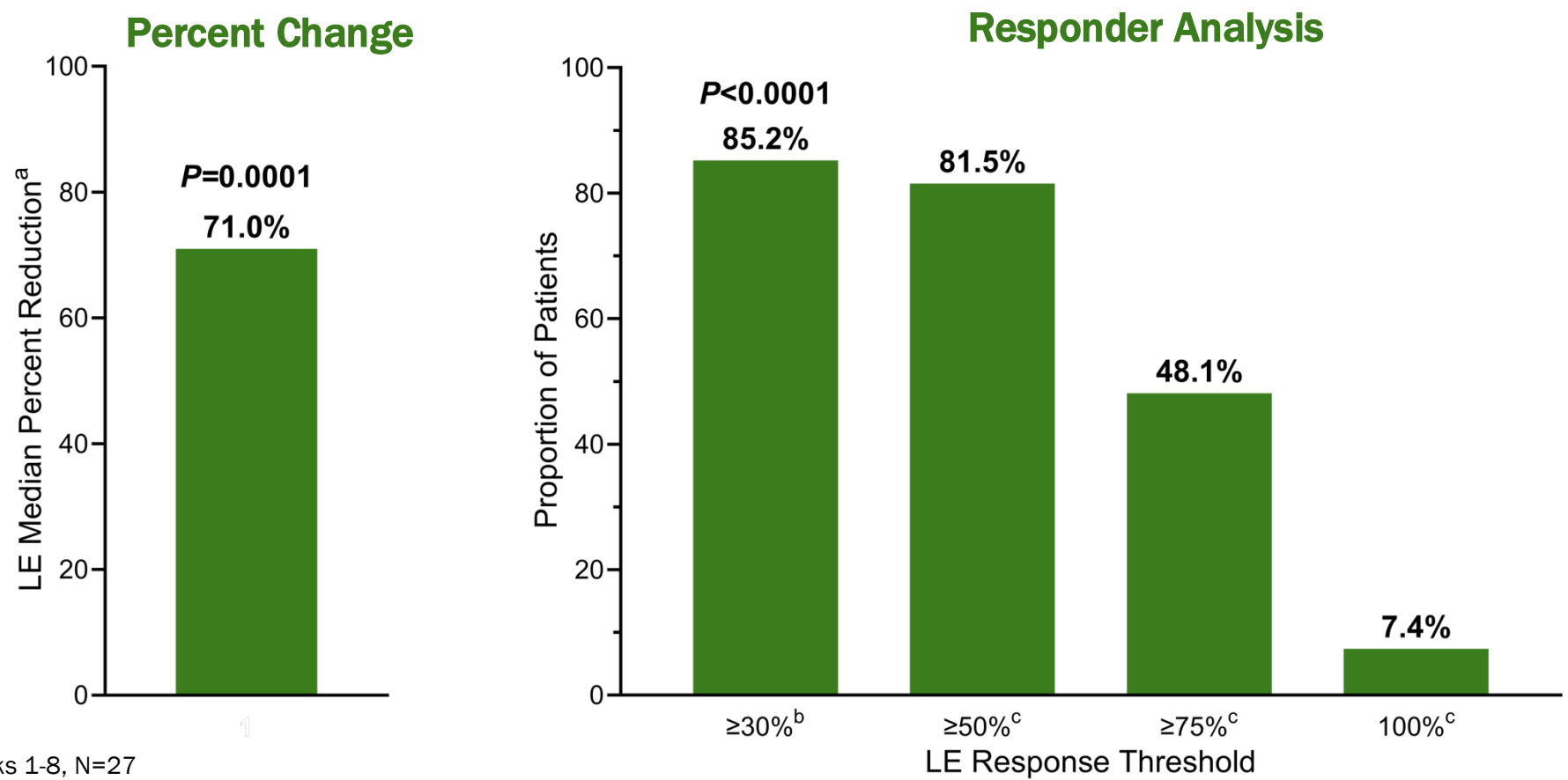
ASM – antiseizure medication; FOS – focal onset seizures; MTL – mesial temporal lobe; RNS – responsive neurostimulator; SD – standard deviation.

FOS efficacy analyses

- Efficacy analyses for 8-week treatment period:
- mITT population (N=27) for long episodes
 - mITT-CS population (N=25) for clinical seizures

Primary endpoints achieved with high statistical significance

71% reduction in long episodes (LEs); 85.2% responder rate (≥30% LE reduction)



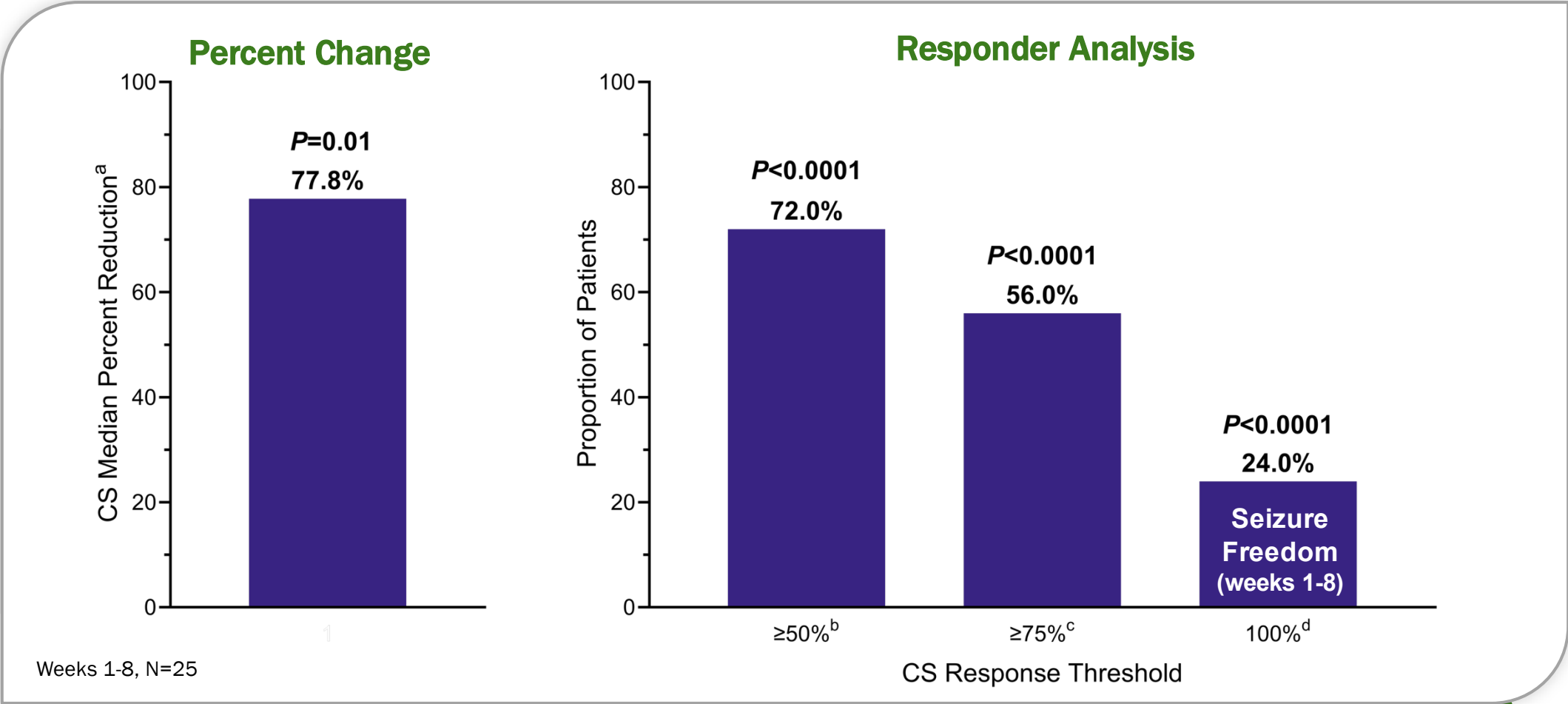
48 LEs at baseline (median, per 28 days); 92% electrographic seizure / LE concordance^d



^a Median percent change statistical comparison used the Wilcoxon signed rank test to determine if the % change in LE was greater than 0%. ^b Responder analysis statistical comparison was based on a one-sample exact test to determine whether the proportion of responders is >10%. ^c Statistical comparisons were not made for other cut points. 95% confidence intervals for responder analysis– Clopper-Pearson exact binomial: ≥50%, (61.9, 93.7); ≥75%, (28.7, 68.1); 100%, (0.9, 24.3). ^d Concordance at baseline was determined by an independent epileptologist reviewer.

Clinical seizure secondary endpoints achieved with statistical significance

77.8% clinical seizure reduction; 72% achieved clinically meaningful response ($\geq 50\%$ reduction)

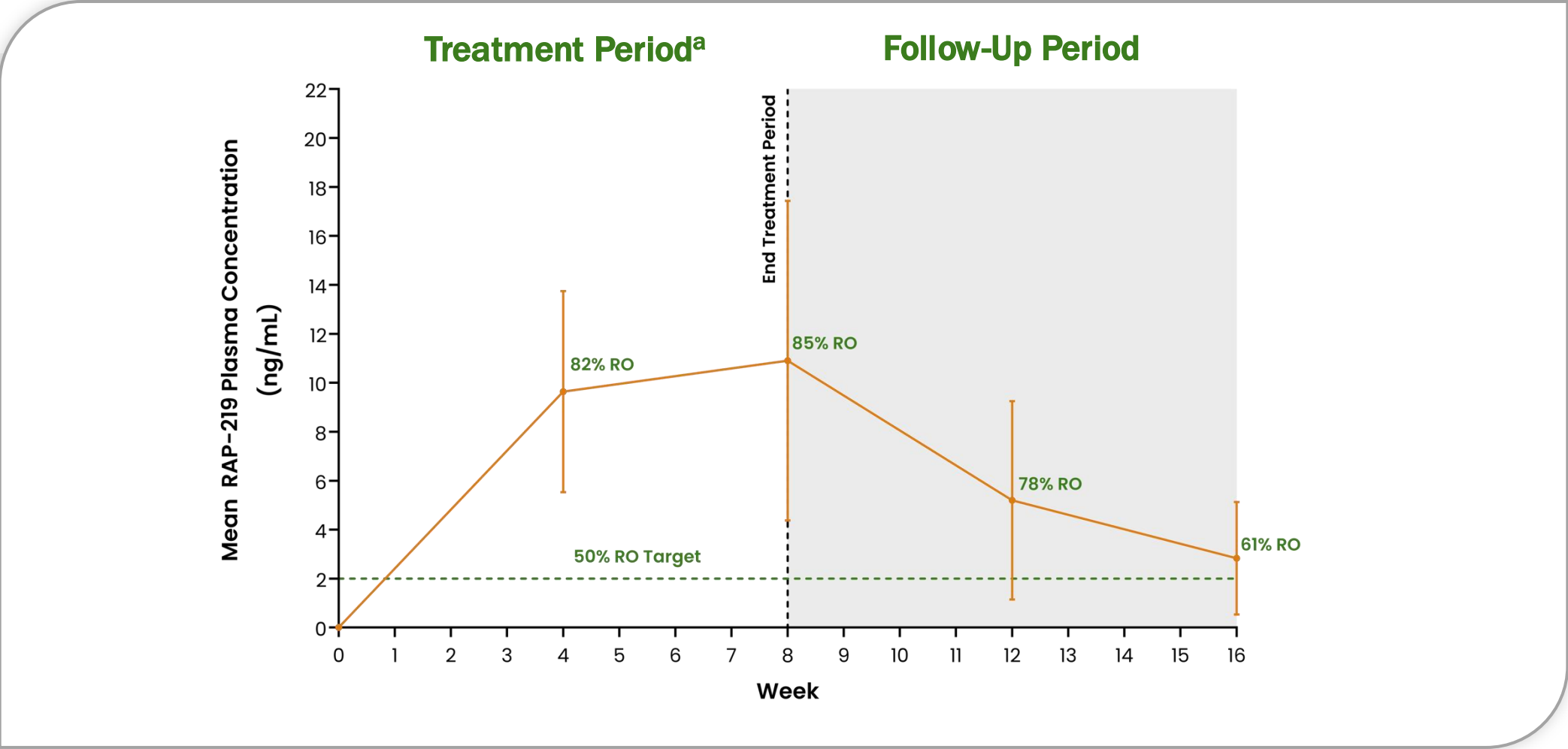


10 clinical seizures at baseline (median, per 28 days)

^a Statistical comparison for median percent change used the Wilcoxon signed-rank test to determine if the median % reduction from baseline in CS was greater than 20%. Responder analysis statistical comparison is based on a one sample exact test to determine whether the proportion of responders is, (b) $>20\%$; (c) $>7\%$; (d) $>1.5\%$ for the 50% responder, 75% responder, and seizure freedom groups, respectively. CS – clinical seizures.

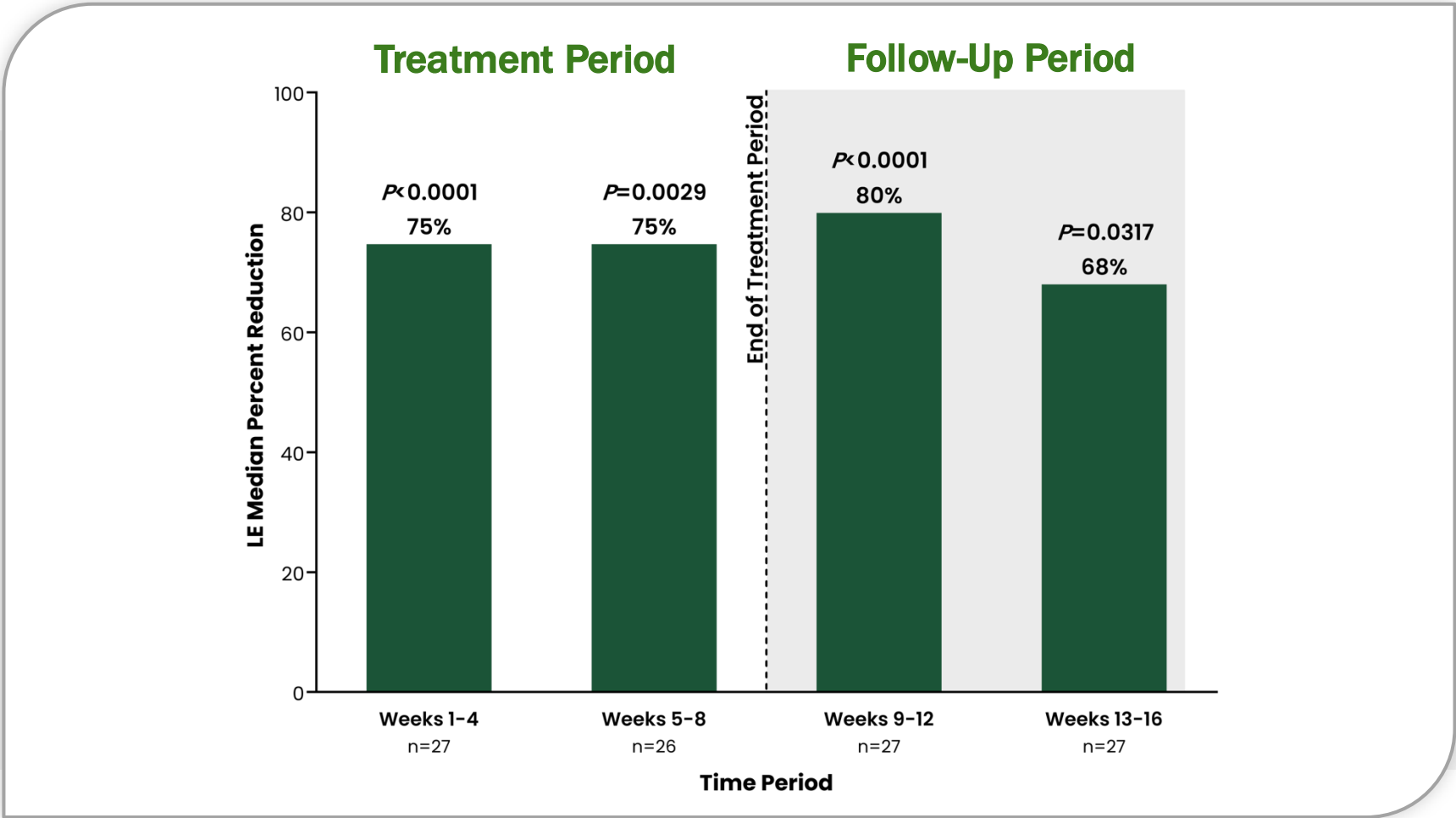
Observed RAP-219 mean plasma concentrations

22-day half-life resulted in concentrations above target 50% RO throughout follow-up



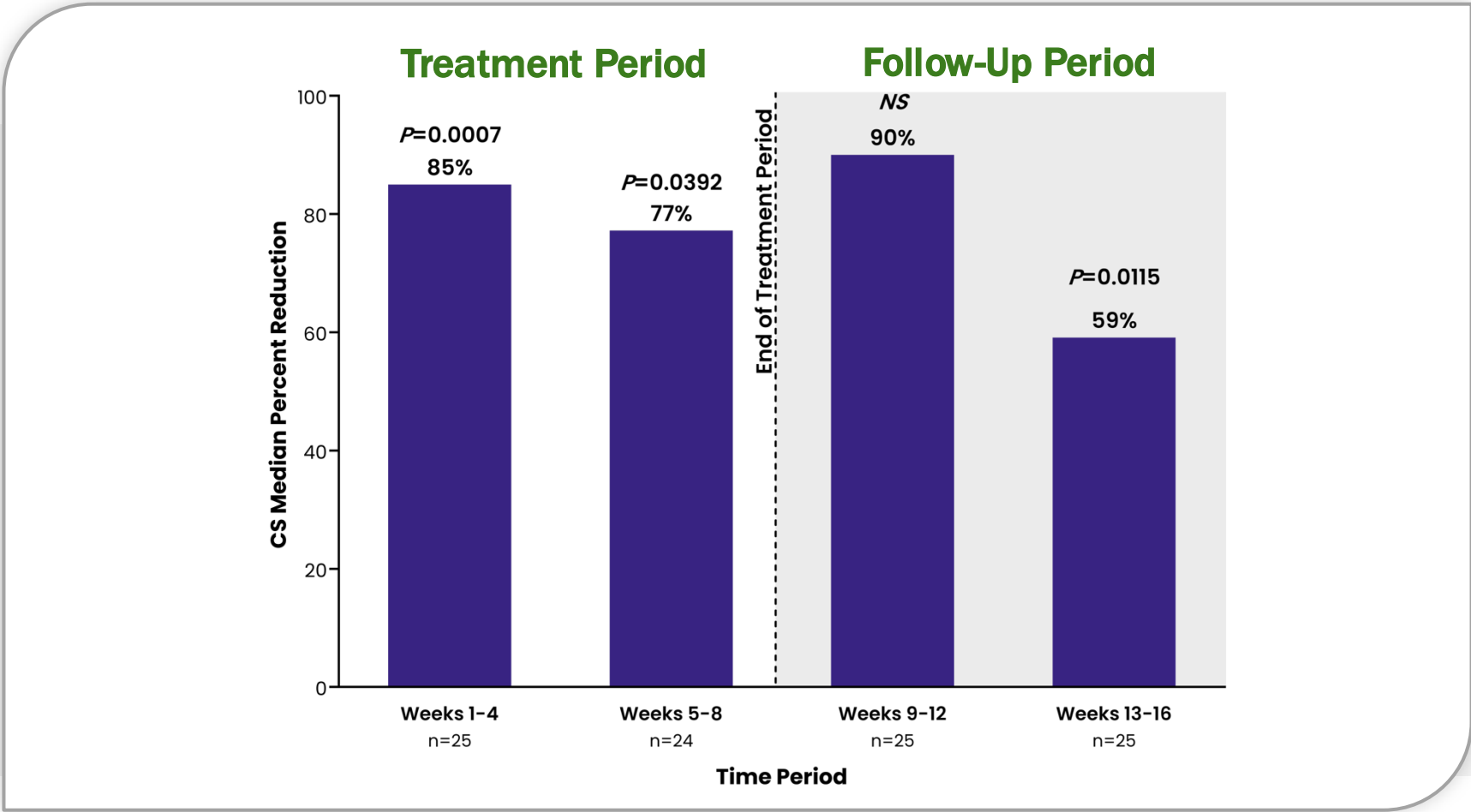
Effect of RAP-219 on long episodes in follow-up period

Significant and durable LE reduction, consistent with sustained RAP-219 exposures



Effect of RAP-219 on clinical seizures in follow-up period

Clinically meaningful reduction in clinical seizures throughout treatment and follow-up



Sustained treatment effect of RAP-219 over 16 weeks, consistent with RAP-219’s long half-life and sustained exposures

	Treatment Period Weeks 1-8	Weeks 1-12 (Treatment Period Weeks 1-8 and Follow-up Period Weeks 9-12)	Weeks 1-16 (Treatment Period Weeks 1-8 and Follow-up Period Weeks 9-16)
Long Episodes Median Percent Reduction	71% (n=27, p=0.0001)	71% (n=27, p<0.0001)	69% (n=27, p=0.001)
Clinical Seizures Median Percent Reduction	78% (n=25, p=0.01)	75% (n=25; p=0.0068)	68% (n=25, p=0.0072)
100% Responders (Clinical Seizure Freedom)	24% (n=25, p<0.0001)	20% (n=25, p<0.0001)	12% (n=25, p<0.0001)

RAP-219 was generally well tolerated

10% discontinuation rate due to TEAEs

Safety Population	Treatment Period Weeks 1–8 (N=30)	Follow-Up Period Weeks 9–16 (N=30)
Any TEAE, n (%)	25 (83.3)	10 (33.3)
TEAE related to study drug	23 (76.7)	2 (6.7)
TEAEs by maximum grade (n)		
Grade 1 TEAE (mild)	15 (50.0)	7 (23.3)
Grade 2 TEAE (moderate)	10 (33.3)	0
Grade 3 TEAE (severe)	0	3 (10.0)*
TEAEs reported overall, in ≥10% of patients, n (%)		
Dizziness	8 (26.7)	0
Headache	6 (20.0)	0
Fatigue	4 (13.3)	0
Fall	3 (10.0)	1 (3.3)
Nausea	3 (10.0)	0
Somnolence	3 (10.0)	0
Memory impairment	2 (6.7)	1 (3.3)

TEAE Summary

- For AEs starting during the treatment period, 50% of patients experienced an AE of maximum grade mild; 33% experienced an AE of maximum grade moderate
- No falls were considered related to RAP-219; reports of memory impairment occurred in patients with baseline memory impairment
- 3 patients experienced SAEs; all deemed by investigator to be unrelated to RAP-219
- In the treatment period, 3 (10%) patients discontinued RAP-219 due to TEAEs: Grade 1 worsening of preexisting memory impairment, Grade 1 panic attack, Grade 2 worsening of preexisting anxiety
- No clinically meaningful laboratory, vital signs, or ECG abnormalities

Emerging best-in-class profile potential for RAP-219 in FOS, with commercial opportunity with >\$2 billion in US, if approved

Potential for Best-in-Class Efficacy



Phase 2a results demonstrated statistically significant reductions in long episodes and clinical seizures

Generally Well Tolerated



All TEAEs were mild or moderate
10% discontinuation rate

Ease of Use



Once daily dosing, rational polypharmacy potential, low risk of drug-drug interactions (DDIs), and long half-life

Long-Acting Injectable (LAI)



Developing first ever LAI for epilepsy patients, providing IP extension leading to potential commercial upside

Strong interest from both epileptologists and neurologists†

- Highly favorable HCP reception to RAP-219 profile
- The magnitude of seizure reduction (78%) and seizure freedom at 8 weeks (24%) repeatedly cited as meaningful and key differentiators
- Stated desire for early-line use

“

This is very good; seizure reduction at week eight is 78%, which is very encouraging. Looking in a little more detail, greater than 75% seizure reduction at week eight was achieved in 56% of patients, that is encouraging.”

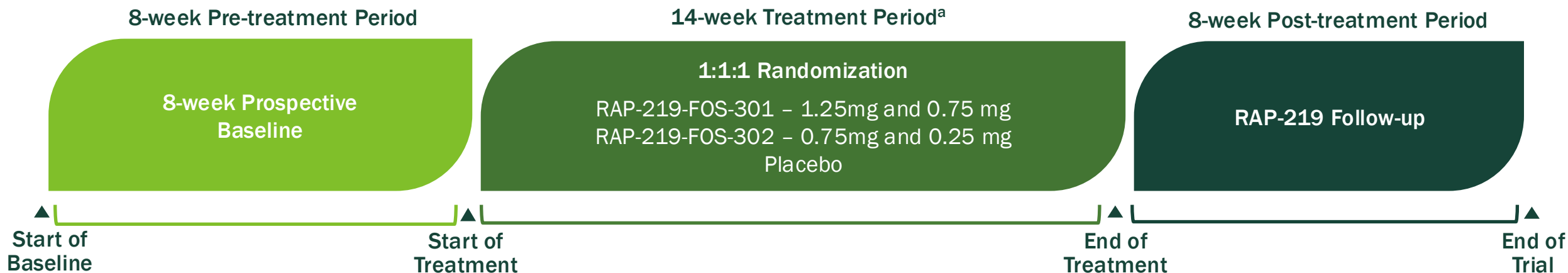
– US epileptologist

Phase 2a data support advancement into Phase 3 FOS registrational trials

- ✓ Topline results reported September 2025; additional analyses presented at Annual Epilepsy Society (AES) meeting
- ✓ Successfully completed end-of-Phase 2 (EOP2) FDA meeting in December 2025
- ✓ Initiated open-label, long-term safety trial

- ➡ Initiated Phase 3 FOS program in 2Q 2026
 - Two global, multi-center, placebo-controlled clinical trials
 - Traditional clinical seizure primary endpoint, measured by seizure diary
- ➡ Community enthusiasm provides tailwinds for trial
 - Strength of Phase 2a data
 - Novel mechanism
 - Ease-of-use and no reported DDI
- ➡ Historically high probability of success in Phase 3 for FOS following robust Phase 2 outcomes
- ➡ Progressing registrational/NDA-enabling activities

RAP-219 Phase 3 clinical trials in FOS



Population

- Drug-resistant FOS
- N = ~320 in each trial

Dosing Levels, Duration of Treatment and Follow-up

- Evaluating 3 doses, representing RO from 50-85%
- 12-week maintenance treatment period following titration
- 8-week follow-up period (or rollover to open-label extension)

Open-label Extension (OLE)

- Patients enrolling in OLE long-term safety trial will stay on drug and not enter follow-up

Primary Endpoint (US-FDA)

- Percent change from baseline in clinical seizure frequency as measured by clinical seizure diaries, RAP-219 vs placebo

Key Secondary Endpoints

- Responder rate, RAP-219 vs placebo (≥50% reduction in seizures from baseline) (EMA primary endpoint)
- Longest seizure-free period, RAP-219 vs placebo

Safety Monitoring

- TEAEs collected from consent to last visit

Expanding RAP-219 into Primary Generalized Tonic-Clonic Seizures (PGTCS)

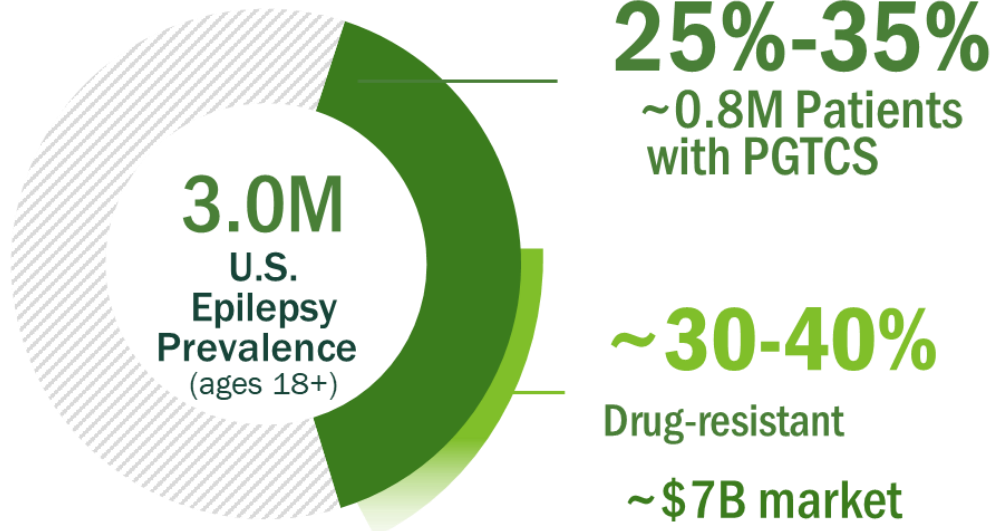
Opportunity for highly differentiated PGTCS treatment

Today's Standard of Care

Few treatment options with limited efficacy: ~6 drugs approved for PGTCS; 30-40% drug-resistance

Potential for SAEs: liver failure, SJS, DRESS, QT prolongation

Mortality risk: uncontrolled PGTCS increase SUDEP risk



Potential for RAP-219

Robust clinical data in FOS: 78% clinical seizure reduction

Generally well tolerated: with 10% discontinuation rate

Easy to administer: with once daily dosing; low risk of drug-drug interactions

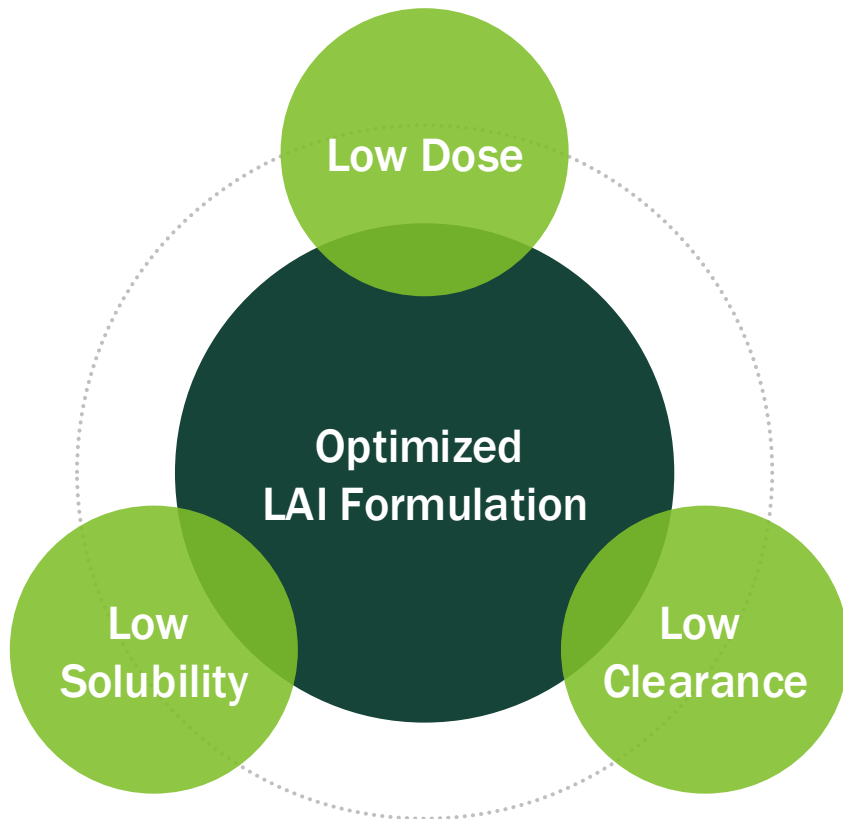
Long half-life and potential long-acting injectable: may reduce breakthrough seizure risk

Planning single, multi-center, placebo-controlled Phase 3 registrational trial

RAP-219 Life Cycle Extension through Long-acting Injectable

RAP-219 properties are ideal for long-acting injectable (LAI) formulation

Factors Driving Long-Acting Injectable Suitability



RAP-219 LAI Formulation in Development for Once-Monthly Subcutaneous Administration

- ✓ Candidate formulation achieved all phase-appropriate TPP attributes
- ✓ LAI provisional patent filed
- ➔ IND-enabling activities underway to support Phase 1 clinical trial in healthy volunteers

“

I think that it will be used, and if it works like the [RAP-219 target product profile] says, that's going to be a great advance for patients with epilepsy.”

– US Neurologist[†]

LAI commercial opportunity adds value to RAP-219

High interest in an LAI from HCPs and patients, seeing significant value add to SoC



Franchise Benefits

RAP-219 Lifecycle Opportunity

Lifecycle opportunity for RAP-219; expected to extend exclusivity into late 2040s creating durable revenue

Unique dosage form value

- Potential for first LAI in epilepsy
- No branded LAI in bipolar beyond 2026 offering ability to be only branded LAI agent in bipolar disorder; limited options vs other psychiatric diseases

Increase branded share

Patients early in treatment journey may prefer LAI option and HCPs indicate strong receptivity to utilizing RAP-219 early in treatment paradigm as well as enthusiasm for the LAI formulation

Next-Generation Formulations

Potential to develop multiple generations of LAI products with varying administration frequency



Desired Clinical Benefits

Focal onset epilepsy

Protect against breakthrough seizures, improve QoL and ensure high-risk populations (e.g. patients with cognitive impairment) are protected against poor adherence due to memory issues

Bipolar disorder

- Reduce mood episode frequency, relapse rate
- Decrease ER visits and inpatient admissions
- Subcutaneous formulation may increase adoption

Indication agnostic benefits

- Increase compliance & adherence in diseases with high risks of morbidity and mortality associated with missed doses
- 'Safety net' – LAIs can remain in the blood for weeks, maybe months, allowing peace-of-mind compared to oral drugs which carry greater risk of missed doses
- Improve patient experience by decreasing pill burden

The LAI formulation could meaningfully expand RAP-219 market share, improve medication adherence, and potentially double peak franchise revenue

RAP-219 in Bipolar Mania

Bipolar mania is characterized by episodes involving marked mood changes and increased energy

A single weeklong manic episode—or one requiring hospitalization—meets diagnostic criteria; disorder is considered lifelong, with most patients experiencing multiple episodes throughout life

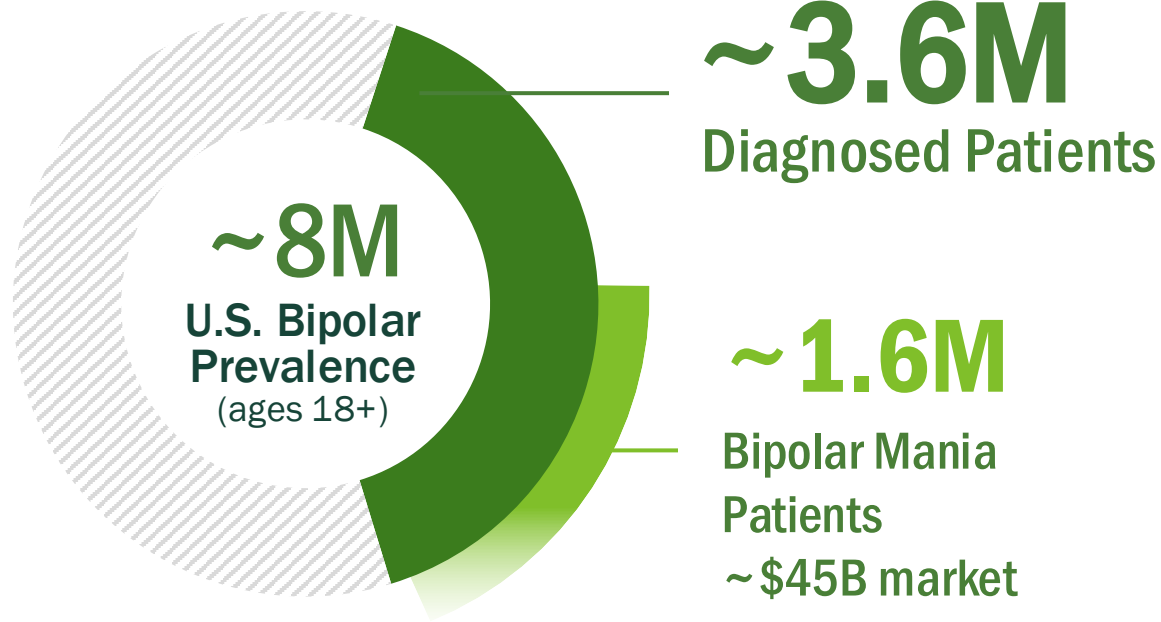
Bipolar disorder confers a **high lifetime suicide risk** of 10-20%; 5 times greater in males

Patients also have **higher risk of premature mortality** as they are prone to coronary heart disease, chronic obstructive pulmonary disease, diabetes mellitus, and influenza or pneumonia

Common Manic Episode Symptoms

- ✓ Inflated self-esteem or grandiosity
- ✓ Decrease need for sleep
- ✓ More talkative
- ✓ Flight of ideas or racing thoughts
- ✓ Distractibility
- ✓ Increase in goal-directed actions
- ✓ Excessive involvement in risk taking activities

Bipolar mania is a common psychiatric disease with significant need for well-tolerated, effective treatments



Limitations of Standard of Care

Tolerability issues: metabolic and neurological side effects including weight gain and cognitive impairment often lead to early discontinuation of medication

Limited efficacy: need for drugs with placebo-adjusted ≥ 4 Young Mania Rating Scale (YMRS) reduction

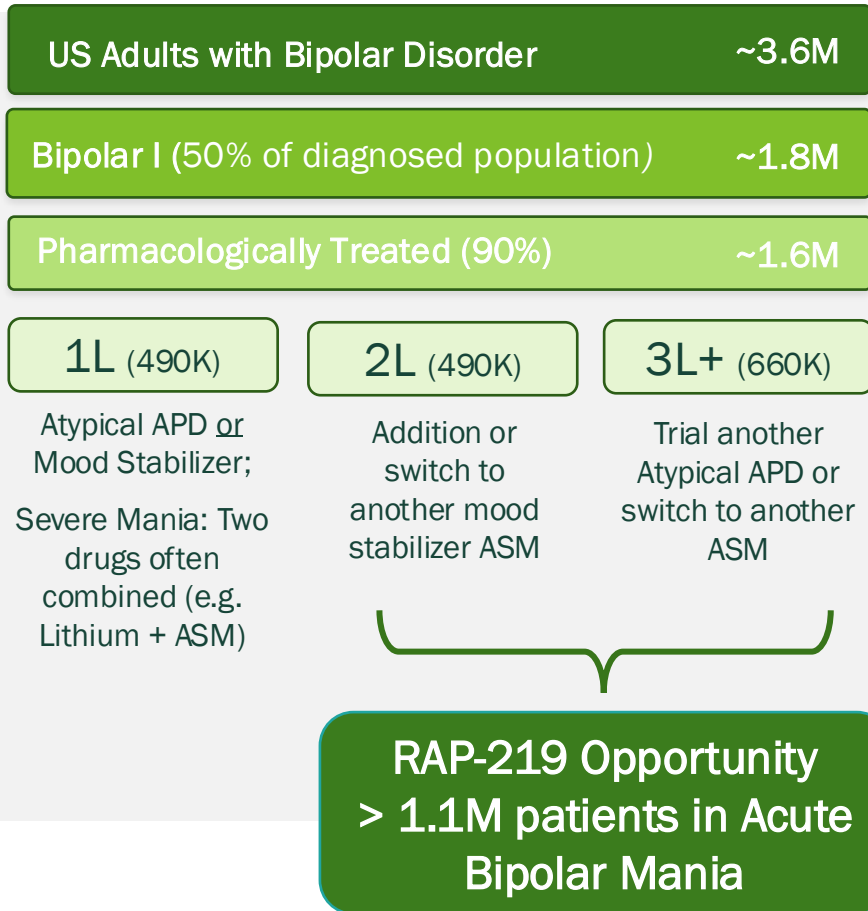
Potential for serious adverse events: antipsychotics associated with extensive warnings and precautions—boxed and non-boxed—and confer risk of drug-drug interactions

Low adherence: medication intolerance leads to poor compliance with medication and high risk of relapse

~50% of bipolar patients are treated with ASMs in combination with lithium at first-line or used second-line

RAP-219 in bipolar mania has the potential to create significant value for patients

Bipolar Mania Patient Flow



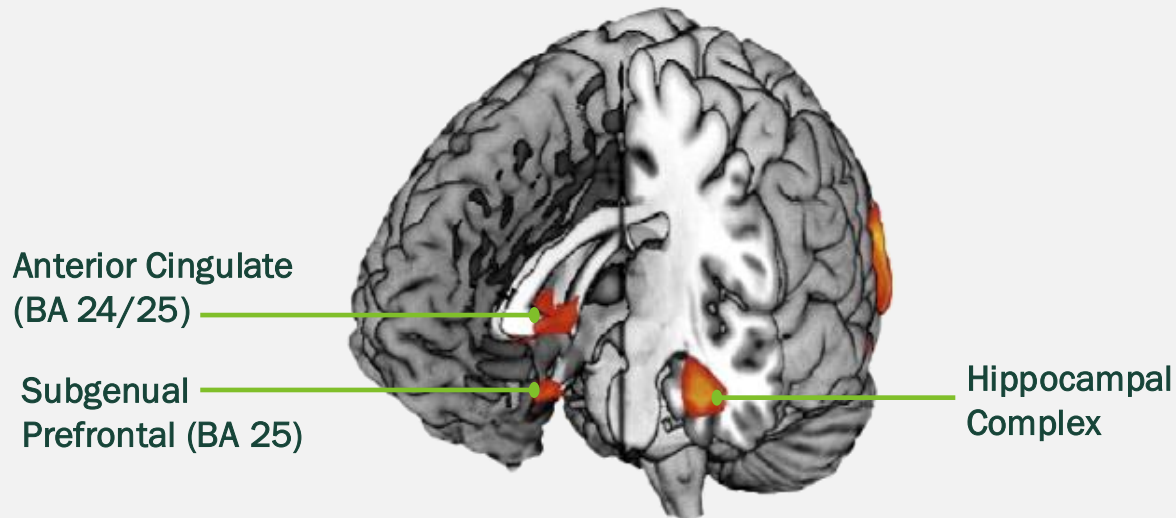
Potential for RAP-219

- Strong HCP preference for RAP-219 early due to limitations of existing drugs
 - Poor control of manic episodes
 - Low adherence due to side effects for dopaminergic atypical antipsychotics & ASMs (e.g. weight gain, metabolic changes, extrapyramidal symptoms, sedation/somnolence)
- Novel mechanism of action positions RAP-219 for early use where ASMs are part of the standard-of-care, and for patients that do not tolerate medications with a dopaminergic mechanism
- Limited potential for drug-drug interactions positions RAP-219 well for concomitant use with the existing treatment paradigm which is common across lines of therapy:
 - 2L: >60% of patients on polypharmacy
 - 3L+: >90% of patients on polypharmacy

RAP-219 circuit-selective approach to bipolar mania

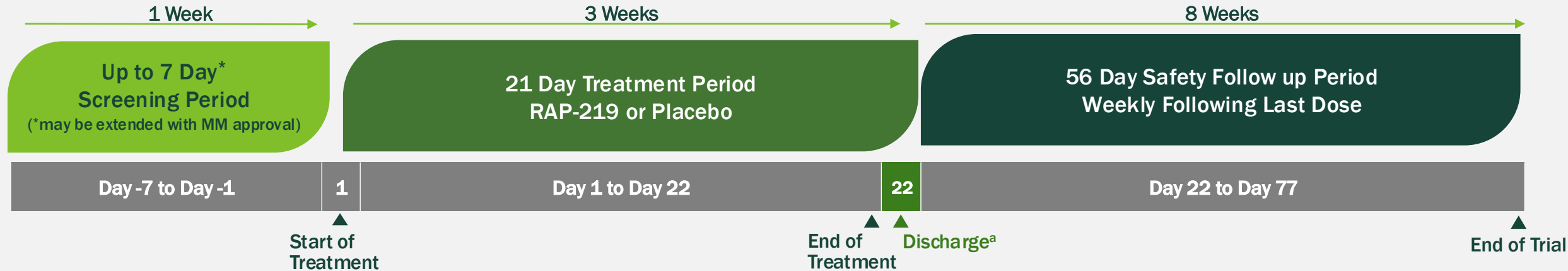
Targets glutamatergic hyperactivity in cortico-limbic networks

Increased Cerebral Metabolism in Manic Patients Relative to Healthy Controls



- Bipolar mania is characterized by **increased glutamate levels and hypermetabolism** in cortico-limbic networks^{a,b,c}
- Glutamate signaling is primarily **mediated by AMPA receptors**, which accounts for most fast excitatory transmission in the brain^d
- Lithium, valproate, and lamotrigine - **approved therapies for bipolar** - act in part by attenuating glutamatergic transmission, including reducing glutamate release and downregulating AMPA receptor function^{e,f}
- **RAP-219 selectively modulates TARPγ8-dependent AMPA receptor activity**, potentially reducing excitatory glutamatergic drive in limbic neuronal populations that correspond to manic network hyperactivity

Phase 2 proof-of-concept trial in bipolar mania



Population

- Bipolar mania
- N = ~250

Key Entry Criteria

- Meets the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) diagnosis of bipolar I disorder, with or without mixed features, with or without psychotic symptoms, as confirmed by the Structured Clinical Interview for DSM-5, Clinical Trials Version (SCID-5-CT)
- At least one prior documented manic episode (with or without psychotic symptoms) that required treatment, within 5 years prior to Visit 1

Key Endpoints

- Change from baseline to Week 3 in Young Mania Rating Scale (YMRS) total score
- Change from baseline to Week 1 in YMRS total score
- Change from baseline to Week 3 in Clinical Global Impressions–Bipolar Version (CGI-BP) Severity of Illness-Mania score

Dose Regimen

- Participants randomized 1:1:2 to RAP-219 with 2-day titration, RAP-219 with 4-day titration, or placebo
 - 0.25mg x 1 day, 0.5mg x 1 day, 0.75mg x 19 days
 - 0.25mg x 2 days, 0.5mg x 2 days, 0.75mg x 17 days

nAChR Programs

$\alpha 6\beta 4$ in Chronic Pain and Migraine

$\alpha 9\alpha 10$ in Hearing and Vestibular Disorders

Use of RAPs enables targeting of diverse nicotinic receptors

RAP-641 – $\alpha 6\beta 4$ nAChR

Expressed selectively in sensory neurons position it as a genetically-validated precision non-opiate non-CNS target for pain and migraine

$\alpha 9\alpha 10$ nAChR

Expressed selectively in auditory and vestibular and hair cells position it as a genetically-validated precision target for hearing and vestibular disorders

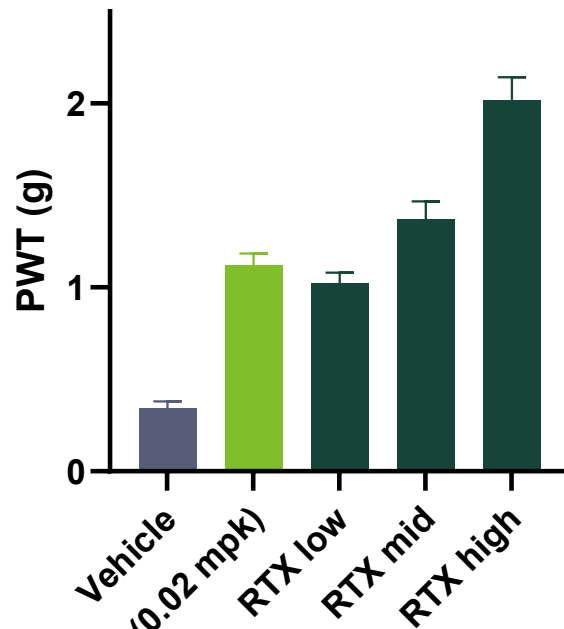
- Pan nAChR agonists are clinically validated in pain
- A broad-spectrum nicotinic agonist (ABT-594^a) was effective in a Phase 2 diabetic neuropathic pain trial – tolerability prevented further development
- Studies identified $\alpha 6\beta 4$ as the nAChR subtype that mediates nicotine and ABT-594 analgesia – a drug specific for this sensory neuron target should be better tolerated than previous nAChR approaches
- Rapport's platform unlocked the $\alpha 6\beta 4$ target and enabled us to create potent and selective first in class $\alpha 6\beta 4$ agonist compounds
- RAP-641, Rapport's $\alpha 6\beta 4$ agonist candidate, showed robust efficacy in translatable models of pain and migraine
- IND-enabling activities are currently underway

RAP-641: $\alpha 6\beta 4$ nicotinic receptor

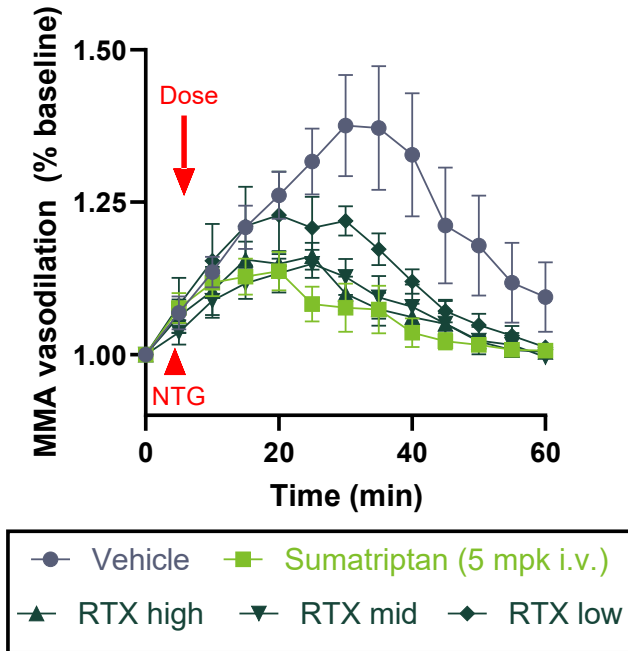
precision non-opiate non-CNS target for pain relief

Rapport Selective $\alpha 6\beta 4$ Agonist (RTX) Exhibited Robust Activity in Preclinical Pain Models^a

Peripheral nerve injury model



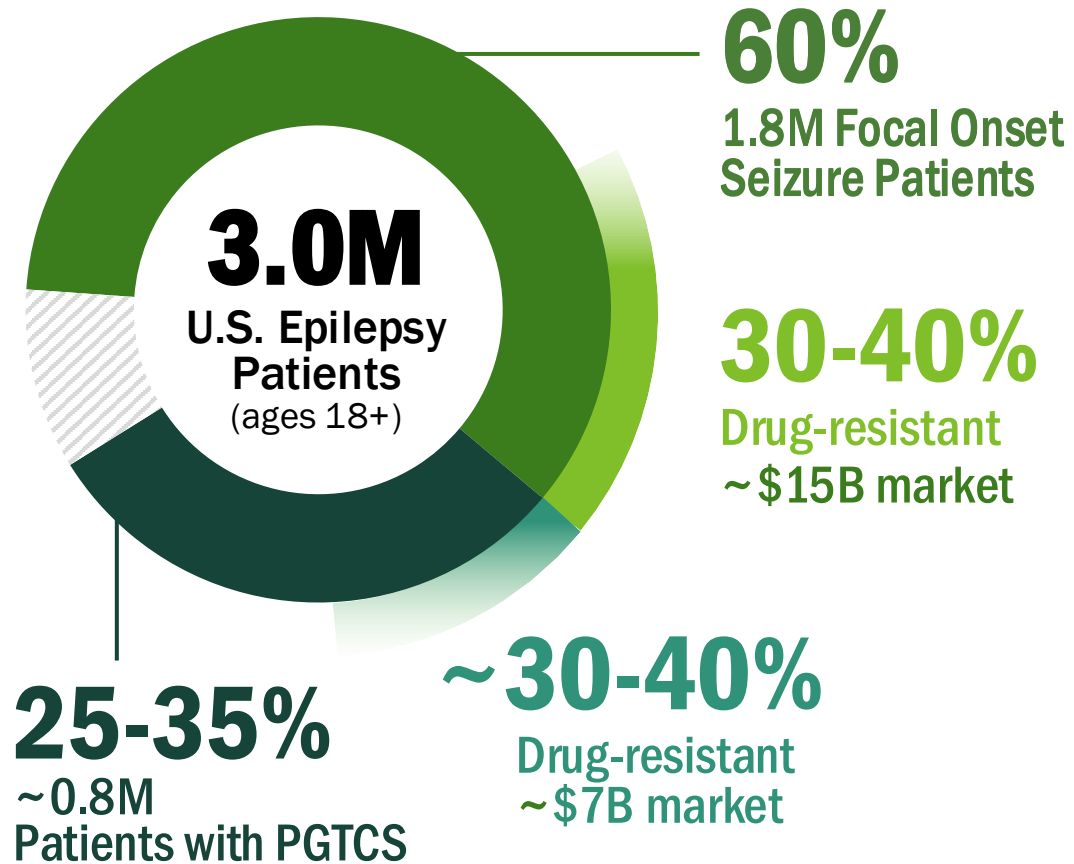
Migraine model



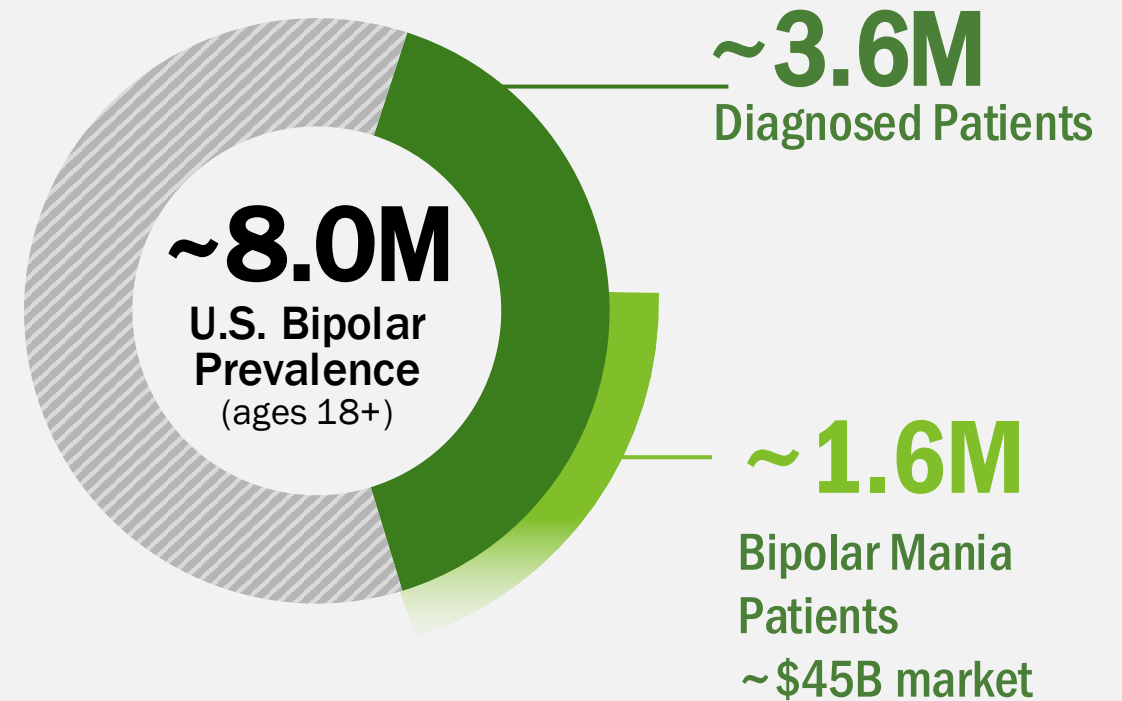
Market Opportunity & Milestones

Growing epilepsy and neurological disorder franchise (U.S.)

Epilepsy



Bipolar



Long-acting injectable: *potential to double peak revenue across franchise; extends exclusivity into late 2040s*

Multiple anticipated catalysts over next 24 months

Cash balance of \$436.1M (as of 6/30/26) supports Rapport into 2H 2029

RAP-219 Epilepsy Portfolio

- ✓ RAP-219 Phase 3 FOCUS 1 & FOCUS 2 trials initiated
- ✓ RAP-219 FOS open-label long-term safety trial initiated
- ✓ RAP-219 NDA-enabling activities underway
- ✓ LAI IND-enabling activities underway

RAP-219 Bipolar Program

- ✓ RAP-219 Phase 2 bipolar mania trial initiated

Oct 2026

RAP-219 bipolar mania Phase 2 topline results

4Q 2026

RAP-219 FOS OLE long-term safety trial initial data

1H 2027

RAP-219 PGTCs Phase 3 trial initiation

2027

RAP-219 long-acting injectable Phase 1 topline results (PK)

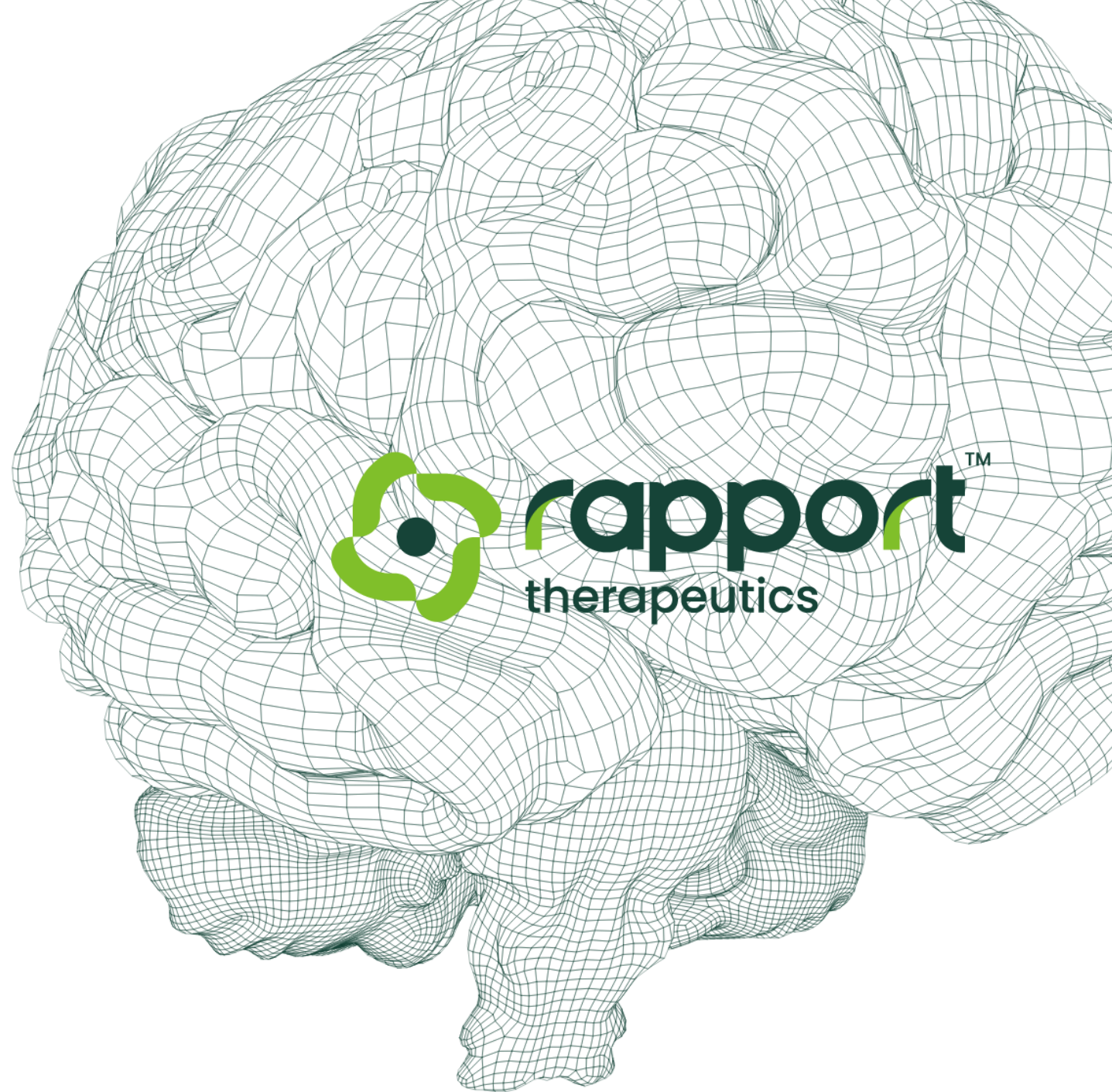
2025

2026

2027

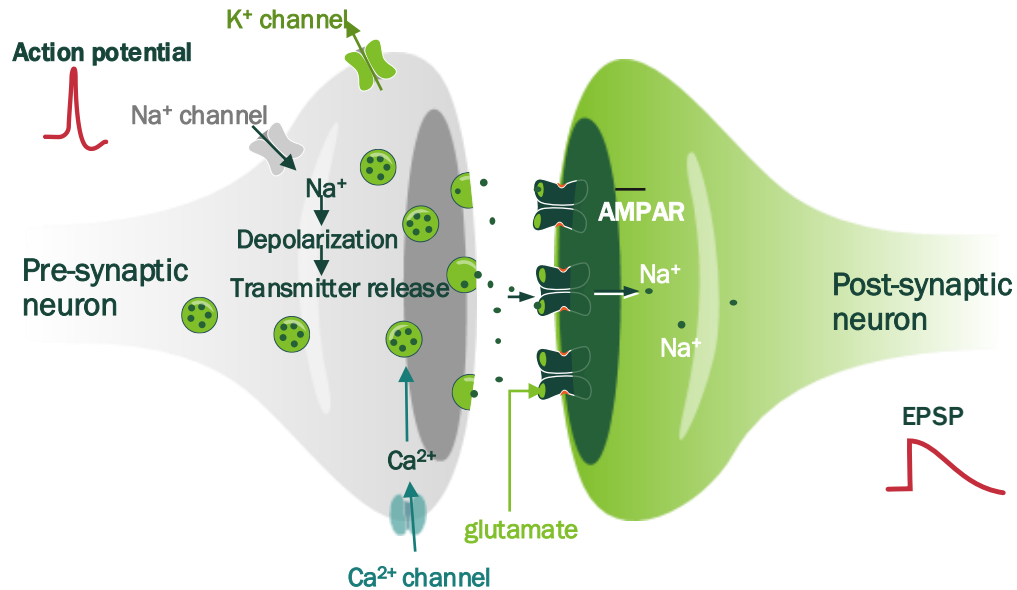
Additional catalysts: RAP-641 ($\alpha 6\beta 4$) Phase 1 trial initiation

Appendix



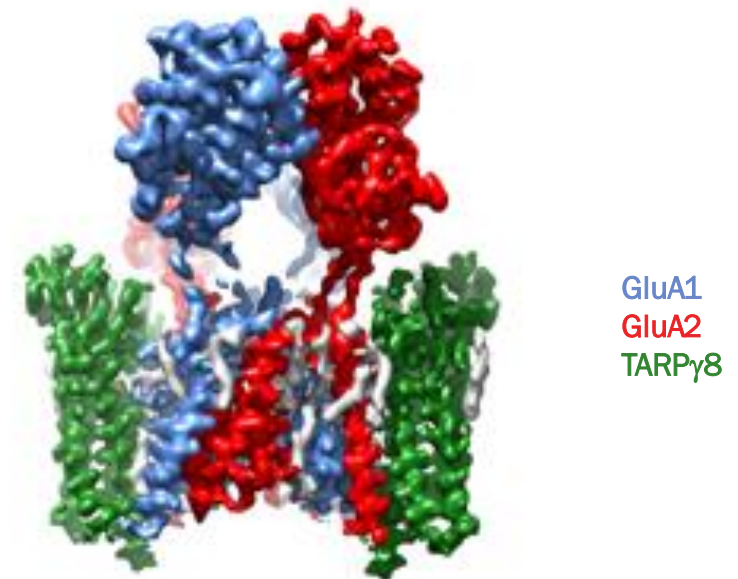
RAP-219 selectively binds to TARPy8, representing a potential first-in-class precision medicine for neurological and psychiatric disorders

AMPA Receptors (AMPA) in Epilepsy



- AMPA type glutamate receptors at excitatory synapses can mediate the initiation and propagation of seizures

Cryogenic Electron Microscopy of GluA1/2 + TARPy8 Complex

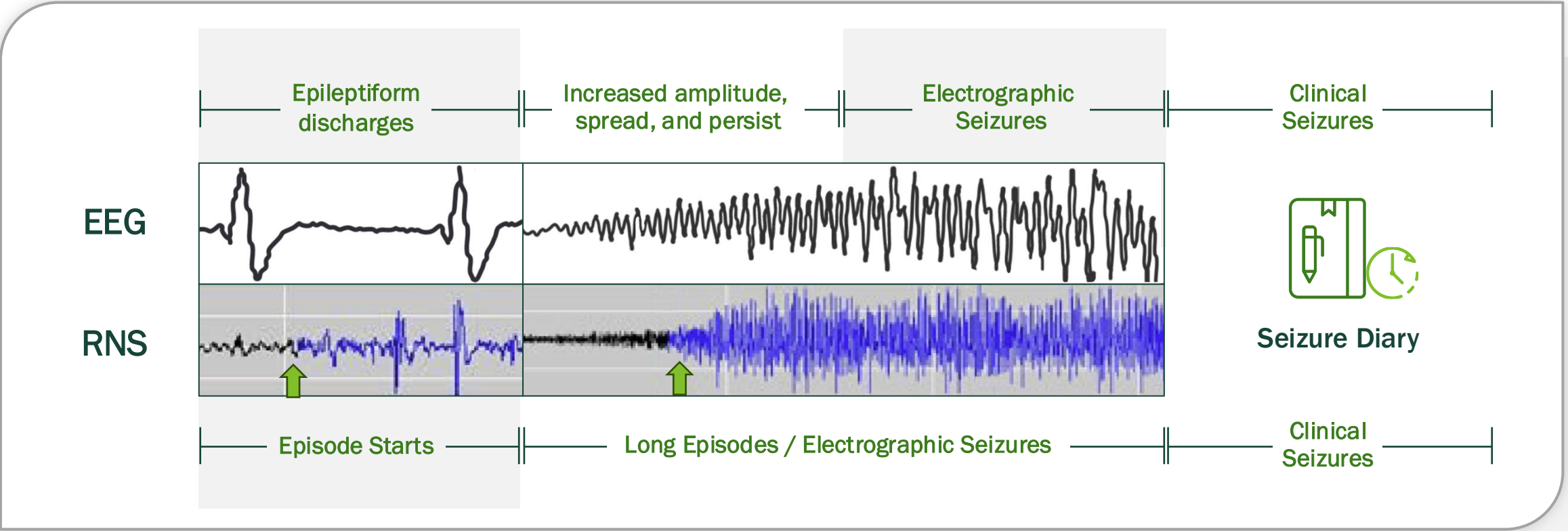


- TARPs regulate the trafficking, subcellular localization and gating of AMPA receptors

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	✓	>10,000 X target affinity
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

Progression of epileptiform activity to clinical seizures



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

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

- Skarpaas (2018)^a: significant correlation exists between reduction in long episodes and clinical seizure frequency
- Quraishi (2020)^b: ASMs resulting in a $\geq 20\%$ decrease in long episodes were clinically efficacious ($\geq 50\%$ reduction in seizures)
- Gammaitoni (2024)^c: 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

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¹Rapport Therapeutics, Inc., Boston, MA, USA; ²NeuroPace, Inc., Mountain View, CA, USA; ³New York University Comprehensive Epilepsy Center, New York, NY, USA; ⁴New York University Grossman School of Medicine, NYU Langone Health, New York, NY, USA; ⁵Perelman School of Medicine of the University of Pennsylvania, Philadelphia, PA, USA

Background

Novel proof-of-concept (POC) designs utilizing validated biomarkers with positive predictive ability of antiseizure medication (ASM) treatment effects are needed that:

- Provide greater patient numbers with the ability to predict success of Phase 3 studies via models that closely represent clinical seizure (CS) activity¹
- Are not reliant on patient diaries, which have been shown to under- and over-report seizures²

The responsive neurostimulator (RNS® System, NeuroPace®) continuously senses electrocorticographic activity and responds to electrographic seizure onset with bursts of electrical stimulation.

The RNS® System also continuously detects long episodes (LEs), runs of focal or interictal epileptiform activity (typically 30-60 sec) that represent electrographic seizures and provide an objective surrogate for CS counts³.

A change of at least 30% in LE frequency following a new ASM start has been reported to correlate with change in CS frequency⁴.

Objectives

Using data from an open-label, long-term treatment study of the RNS® System and an anchor-based approach based on change in patient-reported 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 ($\geq 50\%$ reduction)

Methods

Retrospective data, including LE and CS frequency, were obtained from a long-term treatment study of the RNS® System⁵.

- Data inclusion criteria were based on inclusion criteria utilized for the POC Phase 2a study of RNS-29

Results

Data from 45 patients who initiated clobazam (CS; n=16, 36%), levetiracetam (LEV; n=14, 31%), or lacosamide (LCM; n=15, 33%) were included in the analysis (Table 1).

An RNS® System electrode was implanted in the mesial temporal lobe of ~70% of patients included in this analysis.

Table 1. Demographics and Baseline Characteristics

	CS (n=16)	LEV (n=14)	LCM (n=15)	Overall (n=45)
Female, n (%)	4 (25.0)	2 (14.3)	5 (33.3)	11 (24.4)
Age at ASM start, mean (range), y	36.6 (8.9)	24.5 (2.3)	38.5 (8.1)	36.5 (8.8)

Table 2. Clinical Seizure Reduction and Correlated LE Frequency Reduction

CS Frequency Reduction	LEV	LCM	Overall
<25%	0 (0.0)	0 (0.0)	0 (0.0)
25-49%	0 (0.0)	0 (0.0)	0 (0.0)
50-74%	0 (0.0)	0 (0.0)	0 (0.0)
≥75%	0 (0.0)	0 (0.0)	0 (0.0)

Table 3. Percentage of 30% LE Responders with ≥50% Reduction in CS was Similar Across ASMs

ASM	n	CS Frequency Reduction
LEV	14	0 (0.0)
LCM	15	0 (0.0)
Overall	29	0 (0.0)

Conclusions

A linear relationship was observed between change in LE frequency and change in CS frequency.

The ROC analysis identified that a 30% reduction in LE frequency was the optimal cut point associated with a clinically meaningful ($\geq 50\%$) reduction in CS frequency regardless of the ASM utilized.

- 70% of patients who achieved a 30% reduction in LE frequency following ASM initiation also experienced a clinically meaningful ($\geq 50\%$) reduction in CS.
- Higher LE response thresholds were correlated with a profound ($\geq 75\%$) reduction in CS.

LE may serve as a viable biomarker for use in POC studies with positive predictive ability for clinical meaningful efficacy in reducing CS frequency in later stages of ASM development.

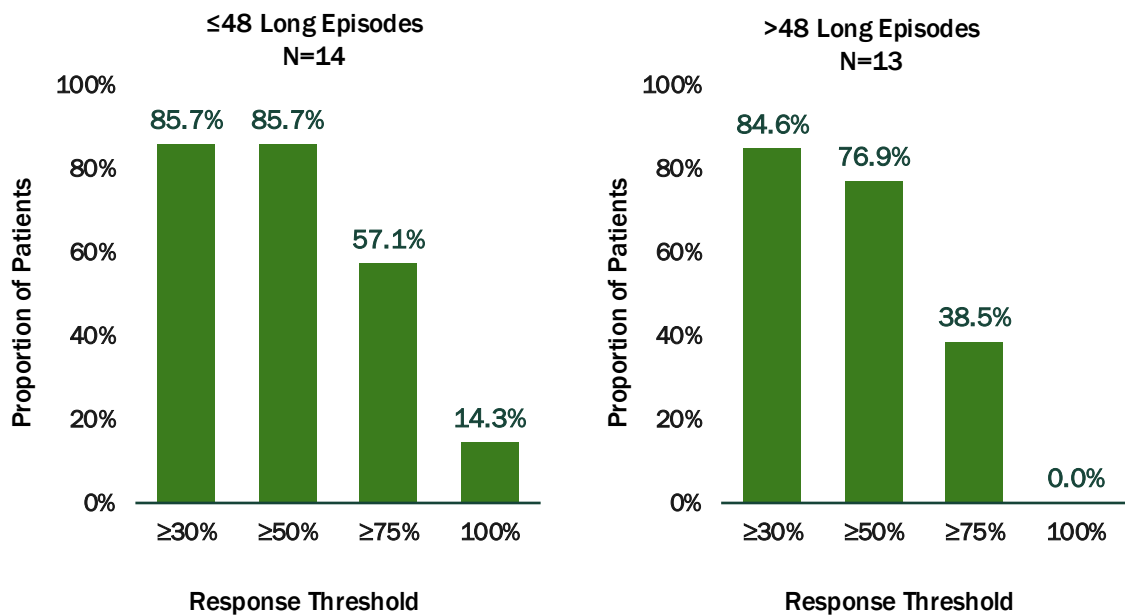


^a Skarpaas et al., Epilepsy & Behavior 83 (2018); ^b Quraishi et al., Epilepsia 61 (2020); ^c Gammaitoni et al, American Epilepsy Society (AES) 2024 Annual Meeting, Poster #1.494.

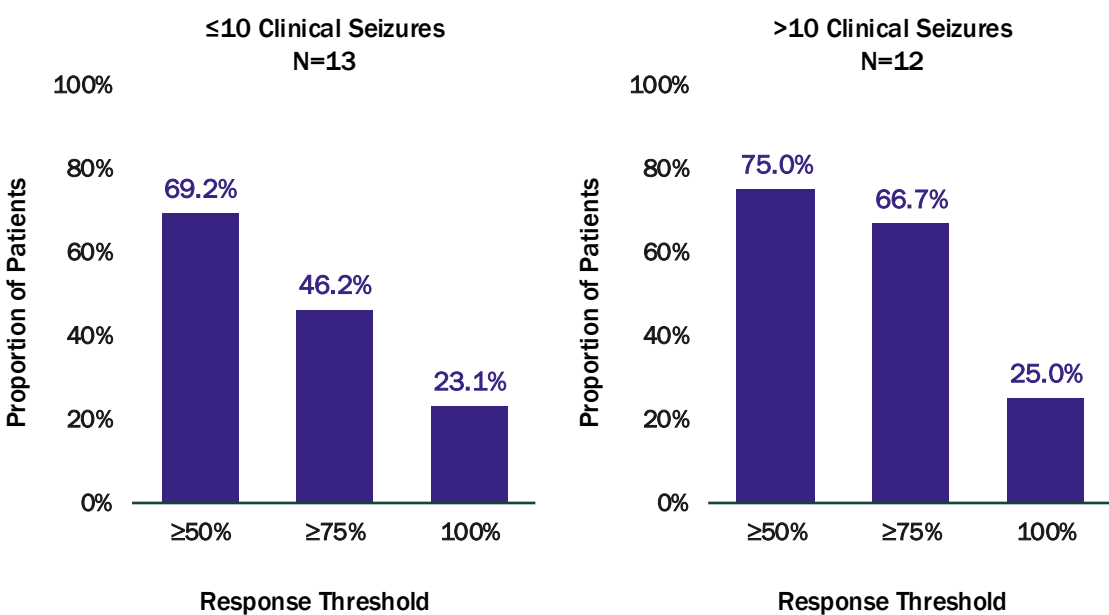
Clinically meaningful improvement demonstrated, regardless of baseline disease severity

Responder Rates by Baseline Severity

Long Episode Responder Rates



Clinical Seizure Responder Rates



RAP-219 reduced LEs and clinical seizures similarly during early and late treatment periods

Effect of RAP-219 During Treatment Weeks 1-4 and 5-8

