rapport therapeutics

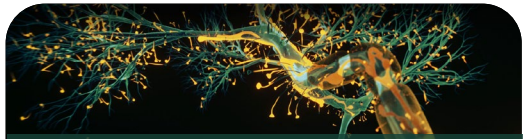
Corporate Overview

January 2024

NON-CONFIDENTIAL

Executive Summary

Vision: To become the leader in precision neuroscience through the discovery and development of transformational medicines for patients suffering from neurological disorders



Receptor Associated Proteins (RAPs)

New Era of Precision Neuroscience

- Road-tested capability of identifying key mediators of receptor function
- Differentiated pharmacology with unprecedented selectivity and specificity
- Ability to transform the treatment of neurological disorders

Scientific Innovators & Company Builders

Seasoned Team

- A pioneering discovery team
- Industry-proven leadership, company builders
- Foundational Pharma/VC collaboration

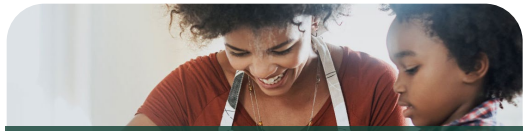
THIRD ROCK VENTURES

janssen Neuroscience
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Clinical & Discovery Pipeline

First in Class Programs

- Non-sedative forebrain restricted AMPA-γ8TARP modulator - initial indication in **focal onset seizures represents blockbuster opportunity** with multi-indication potential
- Medicinal Chemistry-enabled portfolio for neuropathic pain, hearing loss and vestibular dysfunction



Value Creation Trajectory

Clinical Stage

$100M Series A
Closed in Dec-2022

$150M Series B
Closed in Aug-2023

Lead Asset
Advances through Phase 2 POC

- Funds early clinical work for indication expansion and matures discovery effort

rapport therapeutics

Team: Track Record Of Innovation & Expertise

Management Team

David Bredt, MD, PhD
Founder, Chief Scientific Officer

20 years neuroscience drug discovery
Former Global Head of Neuroscience Research, Janssen

Johnson&Johnson Lilly

Abe Ceesay
Chief Executive Officer

20+ years commercial and executive leadership, Former President, Cerevel Therapeutics

cerevel Ironwood genzyme
TIBURIO THERAPEUTICS scPharmaceuticals

Brad Galer, MD
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

Tara Reagan
Interim CPO

Vice President, Third Rock Ventures

Swamy Yeleswaram, PhD
Chief Development Officer

25+ years drug discovery experience
Founding scientist of Incyte

Incyte Bristol Myers Squibb

Board of Directors

Steve Paul, MD
Board Chair
Co-founder Karuna, Voyager, Sage

Terry-Ann Burrell
Director
CFO, Beam Therapeutics

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

Reid Huber, PhD
Director
Partner, Third Rock Ventures

Raymond Kelleher, M.D., Ph.D.
Director
Managing Director, Cormorant Asset Management

Sanjay Mistry, PhD
Director
Vice President, J&J Innovation

Jeff Tong, PhD
Director
Partner, Third Rock Ventures

rapport therapeutics

The Clinical Problem Compels The Creation Of Rapport

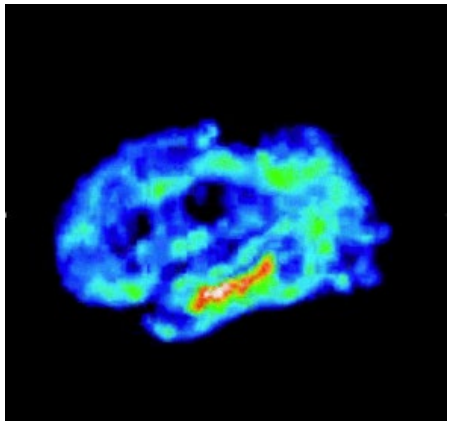
Current State of CNS Medications	The Promise of RAPs
Interact with neuronal receptors that are ubiquitous in the brain and body	RAPs create unique binding sites targetable by novel pharmacophores with increased selectivity
Lack precision for disease-specific neuroanatomic site and disease-specific receptors	Targeting RAPs can provide cell-type and/or neuro-anatomical specificity
Suffer from limited efficacy and drug interactions, which contribute to adverse events, noncompliance and discontinuation	Small molecules with unprecedented pharmacology enabling optimal efficacy, safety, and administration profiles

rapport therapeutics

γ8-TARP and RAP-219 Validates Approach and Represents "Pipeline in a Target" Opportunity

Neuroanatomical specificity

Cerebellar Sparing & Forebrain Selective



γ8-TARP Clinical PET
ACNP 2018 27.6: 536

Optimized γ8-TARP PET tracer from Janssen was transferred to Rapport to support our development programs.

Lead γ8-TARP Program RAP-219

Blockbuster Opportunity

Focal Onset Seizure

Precision treatment with optimal profile - effective, no sedation or motoric impairment, no DDIs, no titration

Indication Expansion

Large populations with high unmet needs

Psychiatry
- *Bipolar*

Chronic Pain
- *Neuropathic*
- *Inflammatory (e.g., OA)*

Formulation

Long-acting injectable expands clinical utility

Profile enables the first anticonvulsant depot formulation for epilepsy and offers appealing administration alternative for additional indications

rapport therapeutics

Seizure (2014) 23:732

Advancing Our Precision Neuroscience Pipeline

- RAP-219 program has blockbuster potential in epilepsy alone; follow on indications exponentially increase opportunity
- Pipeline programs targeting large populations with significant unmet (pain, hearing, psychiatry)
- RAP platform creates an ongoing innovation engine
- Strong IP with worldwide rights to all programs

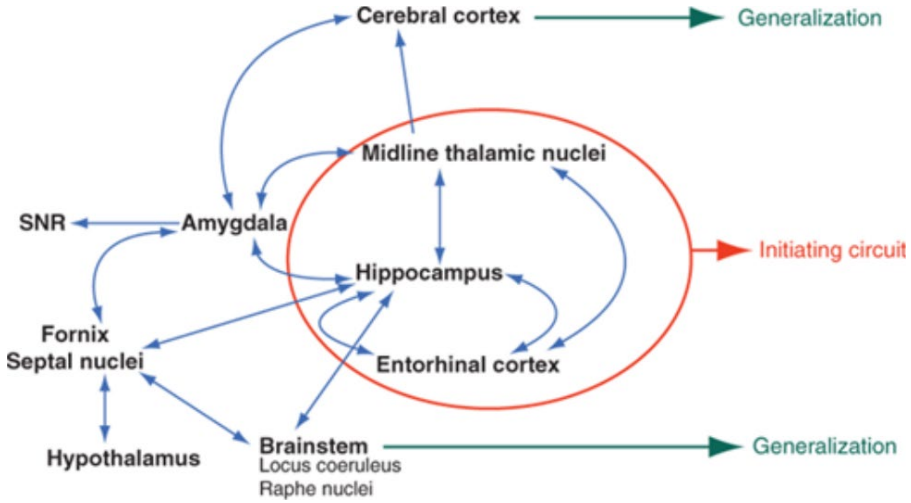
Category	Program	Discovery	Candidate Selection	IND	Phase 1	Phase 2	Next Milestone
AMPA modulator	**RAP-219*** *Epilepsy*						Ph1 MAD data 1H '24 PET (RO) data 1H '25 Ph2a Top-Line results MID'25
	RAP-219 *2nd Indication TBA*						Ph2a results 1H'26
	γ8 TARP *Indication TBA*						Ph1 results 2H'25
Discovery Stage RAPs	*Chronic pain*						Development Candidate
	Hearing/vestibular disorders						Development Candidate
	Psychiatry						Lead Optimization
RAP Platform	*Undisclosed*						Lead Optimization

rapport therapeutics

Lead Program: RAP-219

AMPA Receptor Antagonism Validated Approach For Drug-Resistant Epilepsy

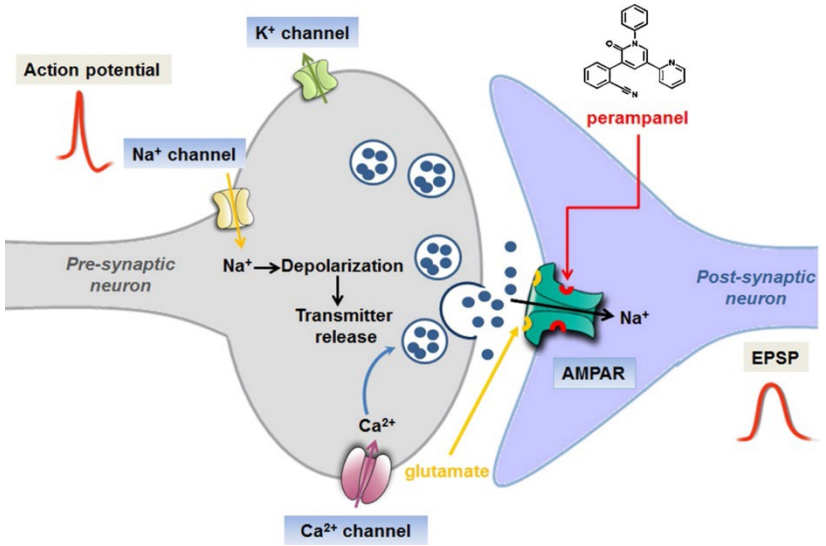
Focal Onset Seizures



ISBN 978-0-07-129621-6

- Hippocampus is a common initiation site and perpetuates seizure generalization

AMPA Receptors in Epilepsy

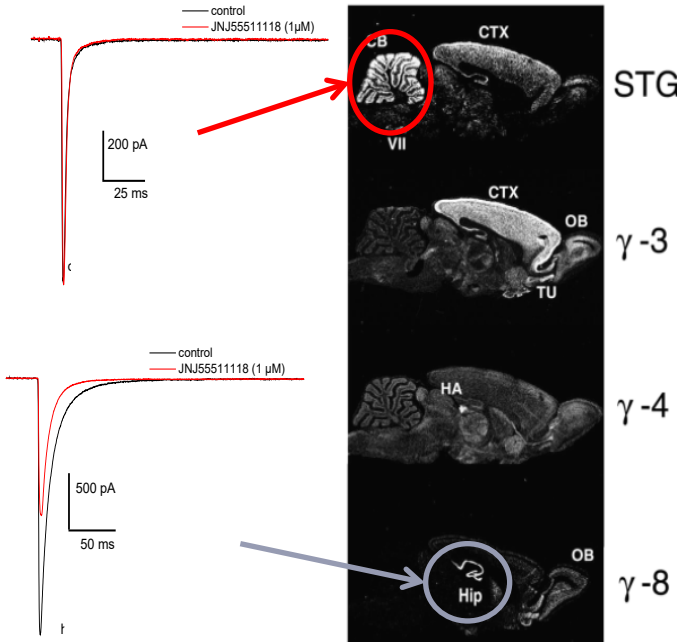


- AMPA type glutamate receptors mediate seizure initiation and spread
- **Target clinically validated** - Perampanel (Fycompa®) is an FDA/EMA approved pan-AMPAR antagonist for the treatment of FOS and generalized seizures

rapport therapeutics

RAP-219: Inhibits AMPA Currents From Hippocampal Neurons But Not From Cerebellar AMPA Neurons

Selective Hippocampal Pharmacology



JPET 2016 **657**:394

Potent and γ-8 Specific

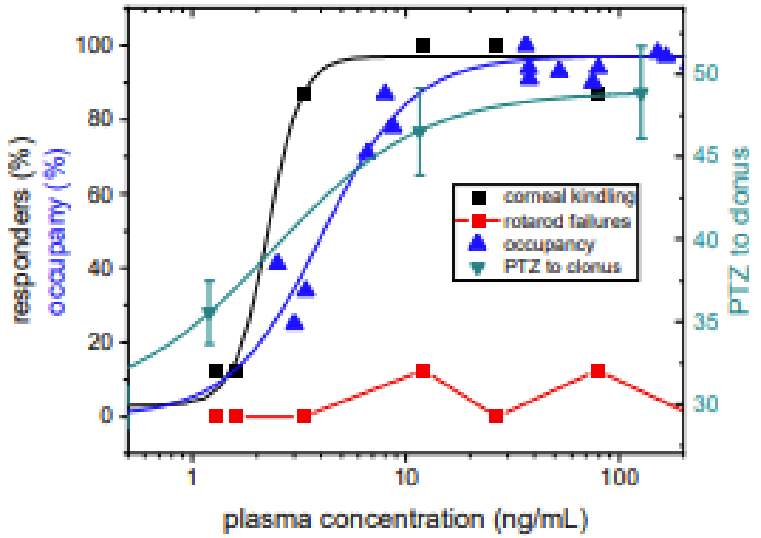
	RAP-219 IC_{50}
GluA1o + γ8	90 pM
GluA1o + γ2	>10 μM
GluA1o + γ3	>10 μM
GluA1o + γ4	>10 μM
GluA1o + γ7	>10 μM

rapport therapeutics

RAP-219: Differentiated Precision Profile

Non-Sedating Anticonvulsant

Precision Creates Unprecedented Treatment Margin



- RAP-219 effective in multiple epilepsy models at low ng/ml plasma levels corresponding to 70% receptor occupancy
- RAP-219 is not sedating or motorically impairing at the highest doses

rapport therapeutics

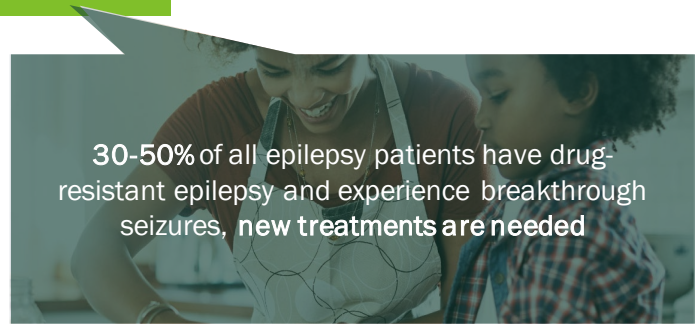
Focal Epilepsy: Large Market With High Unmet Needs Despite Current Treatments

U.S. Focal Epilepsy Market

3.1M U.S. Epilepsy Patients *(ages 18+)*

60% Focal Epilepsy % of Total Epilepsy

1.9M Focal Epilepsy Patients



>$10B

2023 global market size of general epilepsy therapies (generic & branded)

Internal Market Research, 2023

~$2.8B

2022 total branded U.S. market for general epilepsy

Internal Market Research, 2023

Limitations of Current Therapies

- Limited efficacy with up to 50% of patients still experiencing breakthrough seizures
- Tolerability issues including CNS side effects, sedation and motoric impairment
- Potential for serious adverse events
- Administration challenges including dosing, drug<>drug interactions, and lab monitoring

rapport therapeutics

Focal Epilepsy: Optimal Target Profile Emerging For RAP-219

Efficacy
- Significant seizure reduction in validated epilepsy models

Safety
- Highest dose evaluated in IND-enabling studies were considered NOAEL

Tolerability
- Target exposures achieved in Ph1 MAD exhibit no sedation, motoric impairment or other CNS side effects

Drug<>Drug Interaction
- Low to no potential as RAP-219 does not interact with CYP enzymes

Dosing
- Projected dose is oral .5mg – 1 mg with QD dosing

Long Acting Injectable (LAI)
- RAP-219 is ideally suited for LAI; first in epilepsy

rapport therapeutics

Internal Market Research, 2023

Innovative Trial Design for Proof of Concept (PoC): RNS Patients

RNS: Responsive Neurostimulation

RNS Overview

- Responsive neurostimulators are FDA approved for treatment of refractory focal epilepsy in patients who are not surgical candidates
  - ~ 6,000 patients in US
- RNS monitor and record seizure activity within brain seizure focus and detect EEG biomarker “Long Episodes” that correlate with clinical seizures
- Study Objective – reduction of long episodes by pharmacologic treatment with RAP-219
  - Exploration of several other important biomarkers

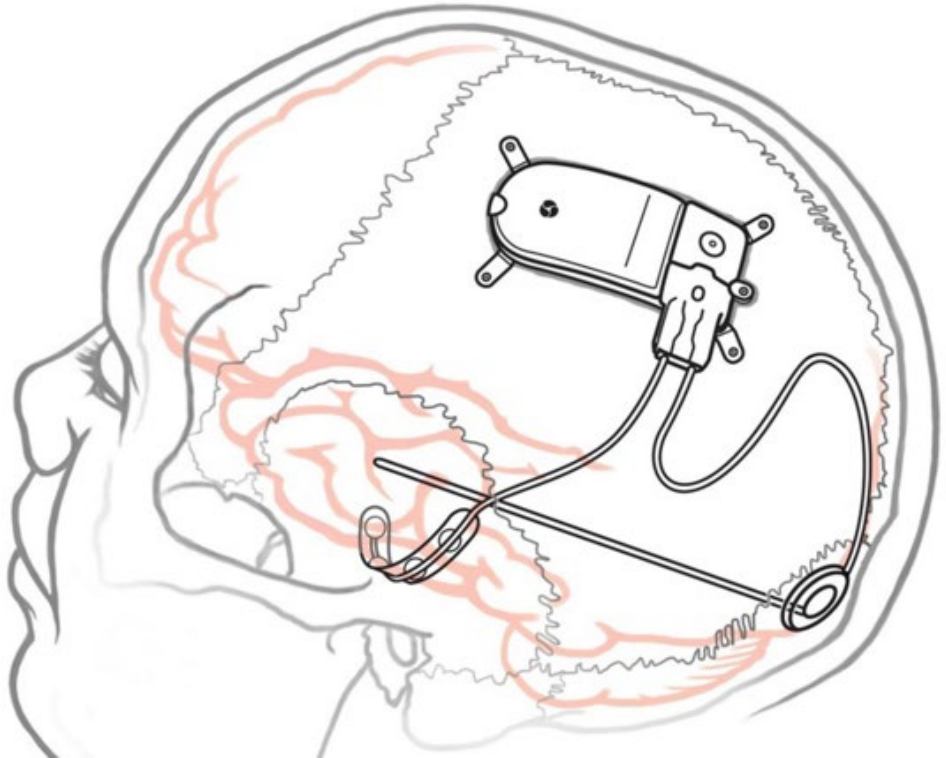
Advantages for RAP-219 PoC

Highly Translatable

- RNS focal epilepsy patients similar to those enrolled in future phase 2b/3 studies

Validated Biomarker

- Sensitive outcome measure reflective of electrographic seizure activity responsible for clinical seizures



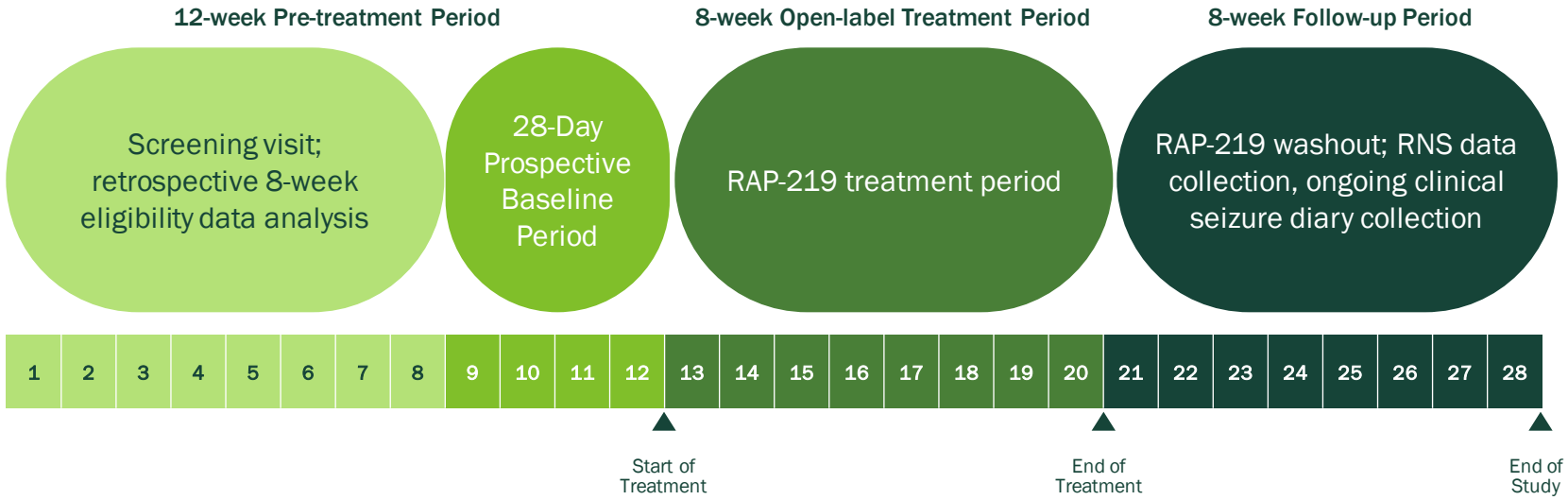
rapport therapeutics

RAP-219 Ph2a FOS Study (RNS)

Study Features

- 8 weeks of retrospective RNS data to provide historical data on electrographic event activity, clinical seizure frequency and background therapies; ensuring all therapies are stable (RNS and medications)
- 28-day prospective baseline period to establish baseline electrographic and clinical seizure frequency
- 8-week treatment period to evaluate the effect of RAP-219 on electrographic seizure and biomarker event frequency as well as establish PK/PD relationship
- 8-week follow-up period to allow for washout and potential return to baseline event frequencies

Study Schema



rapport therapeutics

Pipeline: Discovery RAPs

Validated nAChR-Targeted NeuroMedicine Portfolio

- Discovered elusive nicotinic acetylcholine receptor chaperones and auxiliary subunits
- These subunits enable functional expression of previously inaccessible targets and provide added dimension for receptor pharmacology

Target	Lead Indication
nAChR	Neuropathic pain
nAChR	Hearing disorders
nAChR	Psychiatry

rapport therapeutics

Value Creation Planning

rapport therapeutics

Building The Leading Precision Neuroscience Company

Value Creating Data Cadence

UPCOMING MILESTONE 1	**RAP-219 — Ph1: SAD/MAD** Indication: Agnostic	1Q24

SAD/MAD data demonstrating differentiated precision pharmacology and pharmacokinetic profile

UPCOMING MILESTONE 2	**RAP-219 — Ph1: PET Data** Indication: Agnostic	1H25

PET data confirming receptor occupancy targets and selectivity

UPCOMING MILESTONE 3	**RAP-219 — Ph2a: POC** Indication: Focal Onset Seizures (FOS)	MID25

POC data in highly translatable patient population utilizing seizure biomarker

UPCOMING MILESTONE 4	**RAP-219 — Ph2a: POC** Indication: Expanded Pipeline	1H26

POC studies initiated for additional indications to realize pipeline in a target opportunity

Well Financed

$100M
Series A
December 2022

$150M
Series B
August 2023

$160M
Cash Balance
As of Q3 2023

$64M Tranche 2 Pending

Investor Syndicate

Johnson & Johnson INNOVATION | JJDC
THIRD ROCK VENTURES
ARCH VENTURE PARTNERS
CORMORANT ASSET MANAGEMENT
Goldman Sachs | Asset Management
LOGOS CAPITAL
SURVEYOR
Fidelity INVESTMENTS
T.RowePrice
PERCEPTIVE ADVISORS
SOFINNOVA INVESTMENTS

rapport therapeutics