

CIRM's Neuroscience Strategy

Neuro **Discovery** (ReMIND) Concept



Research using Multidisciplinary, Innovative approaches in Neurological Diseases

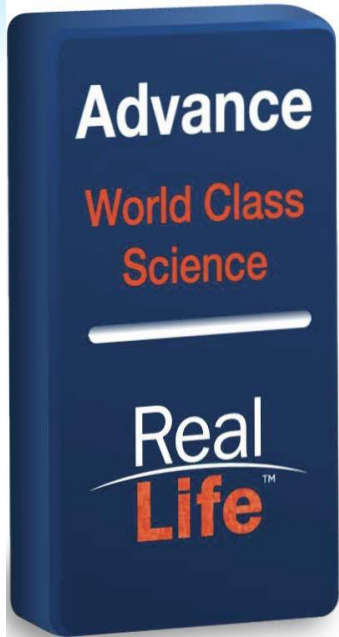
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CIRM's Scientific Programs and Education Team
Neuro-DISC (ReMIND) Concept Plan Discussion
June 27, 2023

CIRM
CALIFORNIA'S STEM CELL AGENCY

OUR MISSION

Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world





- **Develop Competency Hubs**
- **Build Knowledge Networks**



- Advance therapies to marketing approval
- Create a manufacturing partnership network
- Expand Alpha Clinics Network
- Create Community Care Centers of Excellence



- Build a diverse and highly skilled workforce
- Deliver a roadmap for access and affordability

ReMIND is the discovery phase of CIRM's Neuro Strategy. FIRST?



ReMIND



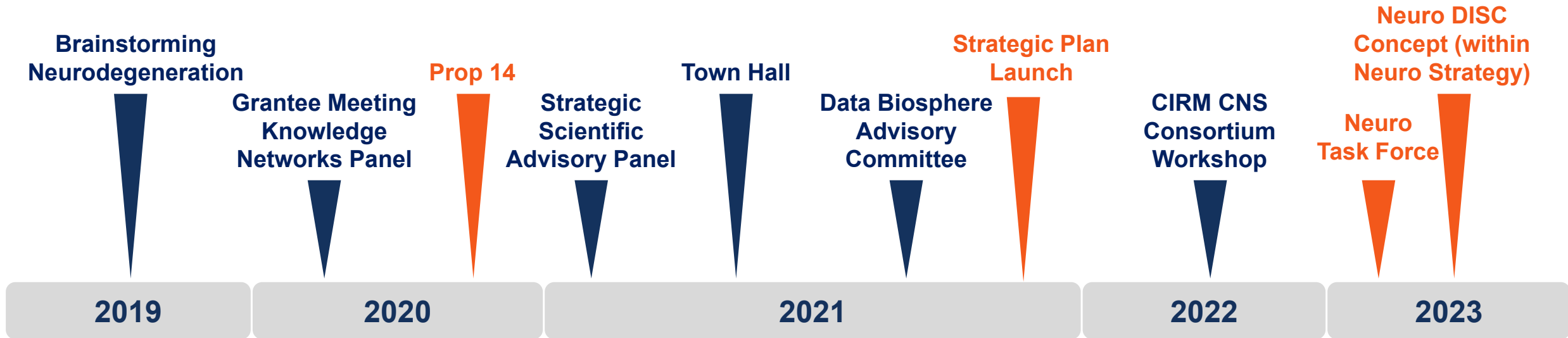
Prop 14 – \$1.5B Neuro focus

TEXT OF PROPOSED BOND

(b) Dedicating \$1.5 billion for the support of research and the development of treatments for diseases and conditions of the brain and central nervous system, such as Alzheimer's disease, Parkinson's disease, stroke, dementia, epilepsy, depression, brain cancer, schizophrenia, autism, and other diseases and conditions of the brain.

PROPOSITION 14 CONTINUED

(c) The institute shall allocate at least one billion five hundred million dollars (\$1,500,000,000) of the proceeds of the bonds authorized pursuant to Section 125291.110 to make grants for research, therapy development, and therapy delivery involving diseases and conditions of the brain and central nervous system, including, but not limited to, Alzheimer's disease, Parkinson's disease, stroke, dementia, epilepsy, schizophrenia, depression, traumatic brain injury, brain cancer, and autism, and for grant oversight and general administration costs associated with these grants and loans, subject to the limits in subparagraph (C) of paragraph (1) and subparagraph (A) of paragraph (2) of subdivision (a).



Key Takeaways of Previous Meetings

- There are **major gaps** in our understanding of the mechanisms underlying disease processes in the brain (including **neuropsychiatric**)
- Benefits of collaborative **consortium approach** – integrating -omics, novel stem cell models, and patient data
- We need to **promote knowledge sharing** and **expand shareable resources** to accelerate research of complex diseases



\$1.2B

➤ Invested in Discovery programs by CIRM to date

28%

➤ Neuro funded studies within Discovery portfolio

4%

➤ Of all grants investigate mechanisms underlying CNS disorders

Generation of novel therapies for neurological disease requires uncovering the underlying mechanisms



Neuro DISC (ReMIND) Concept – Goal

Accelerate the discovery of mechanisms underlying **CNS** disorders leading to **identification** and **validation** of novel **targets** and **biomarkers** with the goal that these efforts will provide new avenues and rigorous foundations for other translational and clinical development work.

ReMIND = Research using Multidisciplinary, Innovative approaches in Neurological Diseases



1. Advance **foundational scientific understanding** of **neurological disease mechanisms**
2. Catalyze **multi-disciplinary innovation** and **attract new talent and ideas** into the study of neuro diseases
3. Incentivize **open and collaborative science** through **data and knowledge sharing infrastructures**
4. Develop **transformative models, tools and technologies** that address challenges in the study of neuropsychiatric diseases
5. Leverage and connect with **CIRM's existing infrastructure** of programs




- **Prop 14's \$1.5B** earmarked for **Neurological diseases**
- **Scientific strength, innovation and expertise** in genetics, stem cell biology and molecular neuroscience in California – **Revolution how we study the brain**
- World-class **CA stem cell research infrastructure**, including CIRM-funded Shared Resource Labs, iPSC BioBank, and planned data infrastructure (DCMC)
- **Potential to leverage large amounts of data and resources** from other Neuro focused consortia/initiatives
- **Advances in stem cell technologies** can address limitations in traditional models and improve diversity

Neuropsychiatric diseases

Series of **Neuro Task Force** meetings made the case that **neuropsychiatry** space is **primed** for **rapid progress**, due to several recent advancements:

Neuro Task
Force
Meetings

- 
- (#2) Genetic risk architecture starting to be defined
 - (#3) Demonstrated utility of human stem cell models
 - (#4) Advancements in related research technologies



	ReMIND-L		ReMIND X
Types of study	Large collaborative projects		Exploratory projects
Preliminary Data	Required		Not required
Award structure	4 years		2 years
Direct costs per award	Base component		\$0.5M/ year \$1.0M total
	Up to \$2.0M/ year \$8.0M total		
Expected number of awards	6		15
Total budget per cycle (w/indirect costs)			\$18M
Team	5 or more Investigators		2 or more Investigators



Large team collaborative projects

Program Budget: \$72M

Award Amount: up to \$2.5M / year

Duration: 4 years

Applicant team: 5 or more Investigators

of Teams awarded: 6

LARGER BUDGETS?

Opportunity for one time renewal for 4 more years in next cycle



Exploratory, high-risk, high-impact studies
Program Budget: \$18M
Award Amount: \$0.5M /year
Duration: 2 years
Applicant team: 2 or more Investigators
of Teams awarded: 15



Neuropsychiatric disorders



**Neurovascular/
Neuroimmune**



Other neurological diseases



**Other focus areas
or bottlenecks**





Neuropsychiatric

Neuropsychiatric

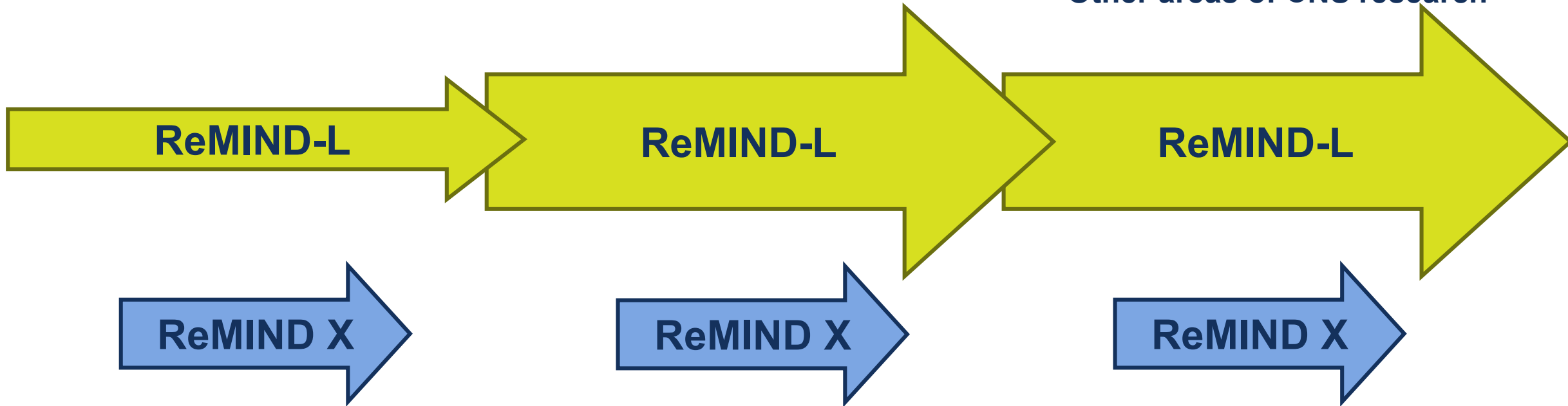
Neuropsychiatric

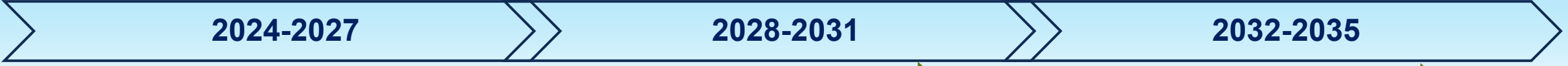
* Neurovascular • Neuroimmune

* Neurovascular • Neuroimmune

Other areas of CNS research

* Examples only





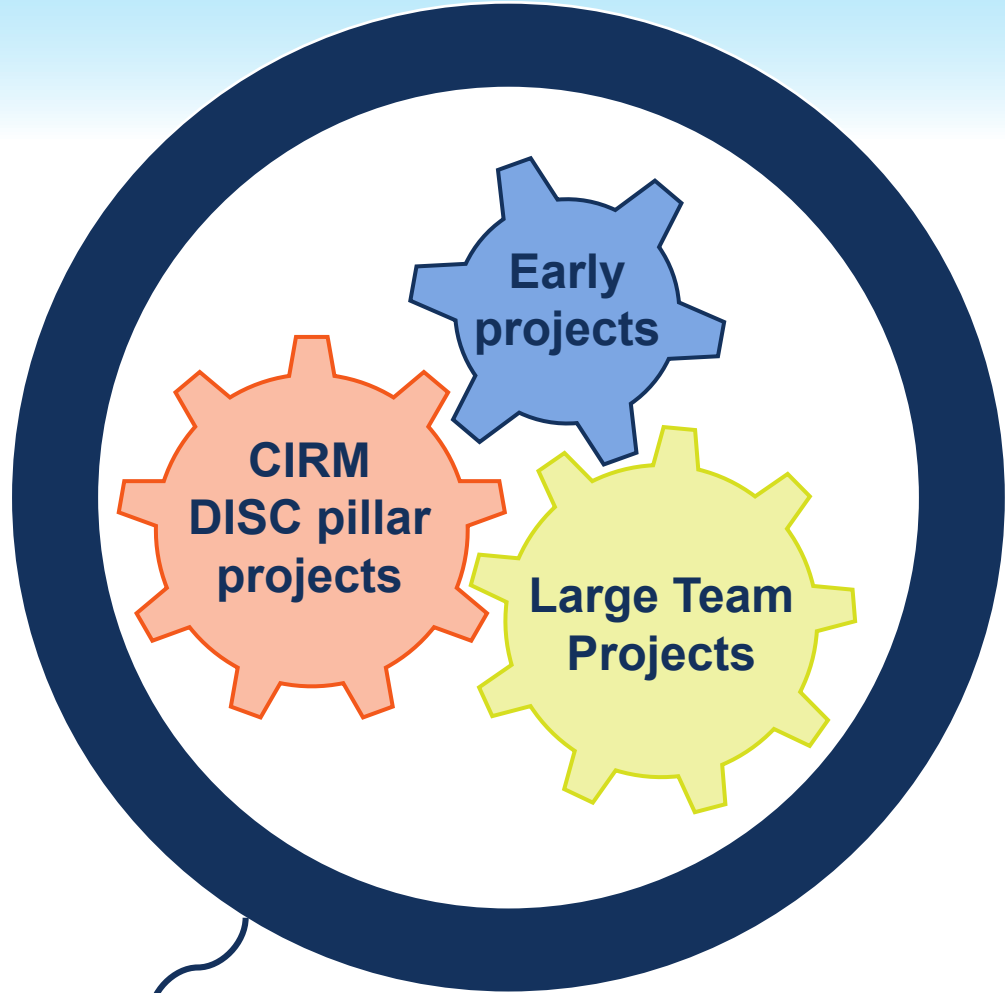
CNS projects are 28% in DISC0/2 Pillar program ~\$235M

Total: \$168M

Total: \$240M

Total: \$240M

Total DISCOVERY Neuro Funding: \$648M



Steering Committee and Data Coordinating & Management Center

- **Accelerate**
foundational scientific understanding of neuropsychiatric disease mechanisms and the development of novel tools
- **Catalyze**
multi-disciplinary innovation, attracting new talent and ideas into neuropsychiatric research and seed new partnerships
- **Drive**
open and collaborative science and align best practices through data & knowledge sharing infrastructure



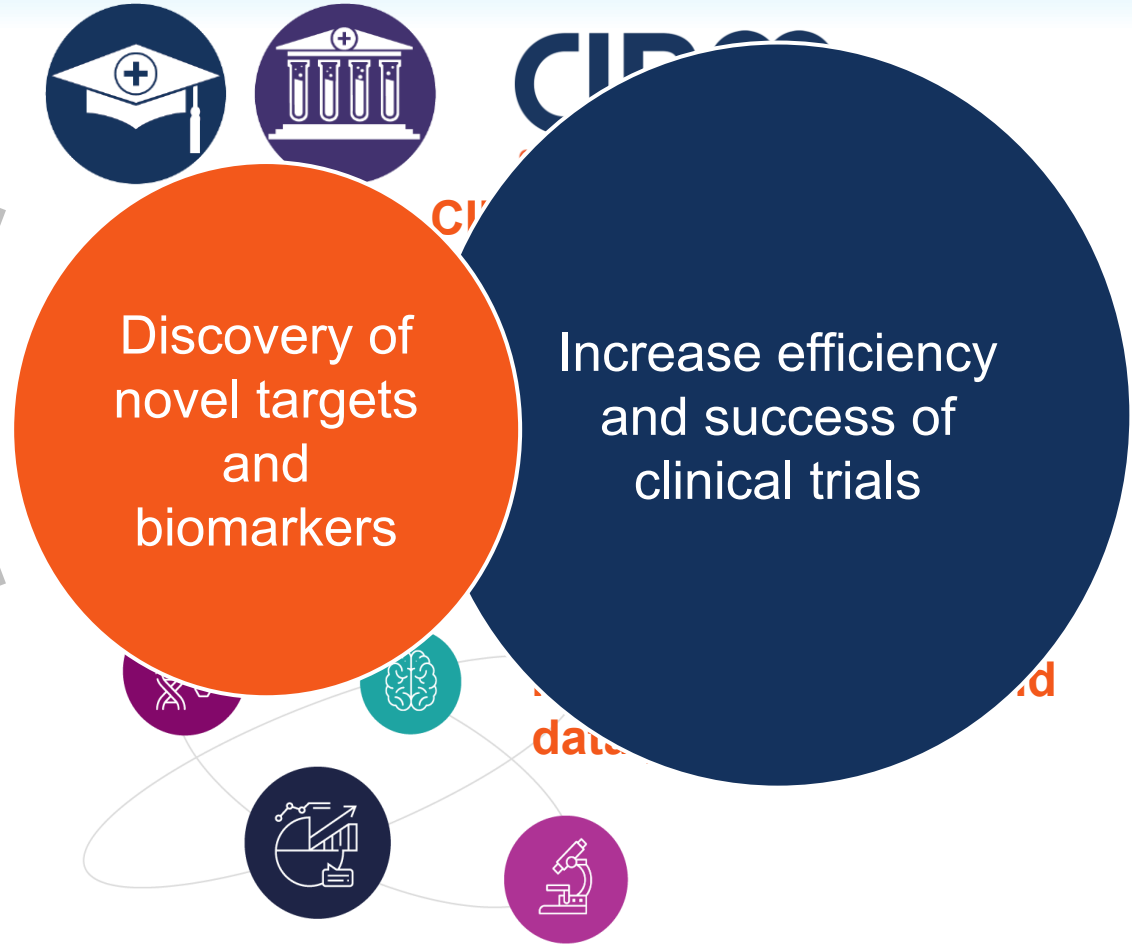
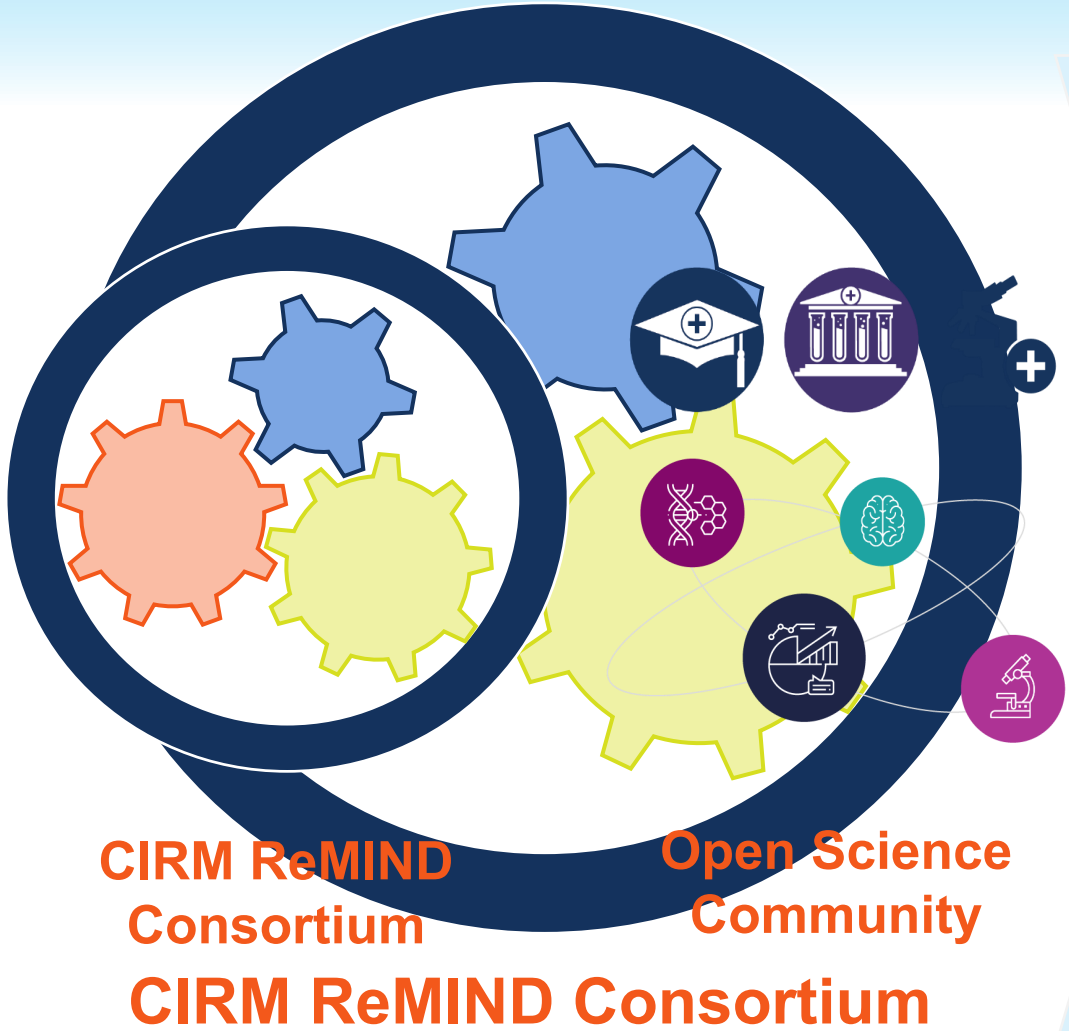
ReMIND

- Novel mechanistic insights into the biology of neuropsychiatric diseases
- Further understanding current mechanisms, including mechanisms cutting across classically defined disease boundaries
- Extension or validation of findings to diverse human populations
- Identification and validation of new therapeutic strategies, targets, and/or biomarker(s)

ReMIND X

- Proof of concept or initial validation of proposed tool, model, hypothesis

Note: Complete proposed data generation and sharing will be common to all





To be eligible, ReMIND projects **must**:

- Propose study focused on elucidation of mechanism of neuropsychiatric disease
- Include studies using human stem cells or genetic research*

Note: Any studies using non-human systems **must** be validated with a relevant human cell equivalent

* Research that alters genomic sequences of cells (edit, remove, or add DNA sequences); or Introduces or directly manipulates nucleic acids (such as mRNAs, antisense oligonucleotides) in cells.



	ReMIND	ReMIND X
Types of study	Large Collaborative projects	Exploratory, high-risk projects
CA eligibility	All Principal Investigators must be employed at California non-profit or for-profit research institutions	
Coordinating PI	One PI designated as the Coordinating PI who will manage the collaboration and will be administrative contact for CIRM and any grant partners	
Min % PI effort	Coordinating PI – 20% Other PI – 10%	Coordinating PI – 10% Other PI – 10%
Team size	5 (minimum)	2 (minimum)
Team member	<ul style="list-style-type: none"> At least one member of the collaboration should have relevant clinical expertise and one member should have relevant computational biology expertise CIRM will encourage favorable consideration of applications that include at least 1-2 early career faculty 	<ul style="list-style-type: none"> Strongly encourage applications from investigators who can bring new technologies, resources, or frameworks to the study of neuropsychiatric disease and in-vitro modeling of CNS.



Data Sharing

Must include Data Sharing and Management Plan

Describe approach to sharing and management of data generated consistent with FAIR principles

Must coordinate with Data-Coordination and Management Center (DCMC*)

Participation in DCMC steering committee and alignment of data processes with its recommendations.

Diversity, Equity, Inclusion

Applications must include plans to address DEI

*DCMC Concept to be presented to ICOC March 2024

CIRM will coordinate DAP composed of non-CA experts to provide independent, confidential, expert advice on ReMIND programs

Specific activities of the committee may include:

- Review the progress reported by large collaborative team awardees and provide non-binding advice to the awardees and CIRM
- Help CIRM staff to identify and leverage external resources to further collaborative research



Program Budget

	ReMIND	ReMIND X
Total per-cycle budget (w/indirect costs)	\$72M	\$18M

Who can apply?

- Principal Investigators at California-based non-profit and for-profit research institutions



CIRM requests the Board approve the proposed ReMIND Program Concept



ReMIND

Research using **M**ultidisciplinary, **I**nnovative
approaches in **N**eurological **D**iseases