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1 - SUMMARY NEURO TASK FORCE ACTIVITY

CIRM Task Force on Neuroscience and Medicine, led by Dr. Larry Goldstein, comprises 13 ICOC members, including scientific experts and representatives from patient advocacy organizations. The goal of the CIRM Task Force on Neuroscience and Medicine is to generate a general plan for the $1.5 billion set aside for neuroscience and related medicine as specified in Proposition 14. In addition to generating a general plan for Neuroscience and related medicine, the task force aims to identify unusual opportunities for high impact in these areas for enhanced investment.

Over the past 8 months, in close collaboration with CIRM's Scientific staff, the Task Force initiated its work with an overview of the current CIRM grant portfolio, confirming compliance with Proposition 14's allocation mandate. However, it was noted that neuropsychiatric disease research was underrepresented in the CIRM portfolio with zero grants. Given the large and growing unmet need for effective treatment in the US and California, the Task Force set out to explore this area's potential by gathering insights from eminent scientists who underscored the advantages of utilizing genetic and stem cell technologies to study neuropsychiatric disorders, as well as recent progress in understanding the genetic architecture of these disorders. The above considerations together with the considerations from the past 2.5 years of stakeholder discussions, drove led to the development of the current concept plan to support Research using Multidisciplinary, Innovative approaches in Neuro Diseases (ReMIND) ReMIND responds to the pressing need to address these challenges while harnessing the opportunities within neuroscience, stem cells and genetic research. This plan aligns with CIRM's mission to foster groundbreaking scientific advancements and represents a significant step toward accelerating the discovery of treatments and therapies for CNS disorders.

With the goal of creating an overall plan for the proposition 14 mandate to fund at least $1.5 billion of neuroscience and neuromedicine projects, **the proposed next steps for the task force are to continue with the potential identification of high impact opportunities in areas of neuroscience and neuromedicine other than neuropsychiatric disease** and to ensure that the spending rate and allocation for neuroscience and neuromedicine continues to be consistent with the 27% minimum directive in Proposition 14.

2 - NEURO TASK FORCE – UPCOMING ACTIVITIES – DESIGN BRIEF

As we embark on the next series of meetings for our Neuro Task Force, it's important to recognize the transformation our field has undergone since 2019. Breakthrough techniques and collaborative platforms have revolutionized our approach to discovery and development in neurodegenerative diseases, fostering stronger ties among researchers and institutions. However, this rapid evolution also presents unique challenges; strategies and knowledge from just five years ago may not entirely match today's innovative landscape. The NTF upcoming sessions will concentrate on addressing these changes, ensuring that our collective efforts are informed by the most current science as we continue to strive for advances in treating neurodegenerative conditions.

In the upcoming months, **the TF will embark on a series of presentation and discussions that will address key knowledge gaps in neurodegenerative diseases (ND) from genes to circuits within each predetermined focus area.** This design brief establishes the objectives, intent, guiding questions, scope, and stakeholders that are relevant for conceptual program design.

The goal of these NTF discussions is to surface key knowledge gaps and bottlenecks in the study and treatment of neurodegenerative diseases (ND) within each predetermined focus area and how might the advancements in stem cell and genetic research be leveraged to catalyze research that will lead to transformational, rather than incremental, change in the neurodegenerative (ND) disease.

This **design brief establishes** the objectives, intent, guiding questions, scope, and potential stakeholders that will help us further delineate CIRM's Neuro strategy. One of the potential paths to consider is to utilize the funding framework established by the ReMIND program initiative, which was designed to incentivize and support cross-disciplinary research and knowledge-sharing. The ReMIND program framework could be easily extended to also include neurodegenerative conditions tackling the knowledge gaps identified through the following series of discussions.

DESIGN BRIEF

Category	Criteria
Design Question	How might the advancements in stem cell and genetic research be leveraged to catalyze discovery stage research that will lead to transformational, rather than incremental, change in the neurodegenerative (ND) disease field over the next decade?

Category	Criteria
Intent	The intent for these sessions is four-fold: 1. Identify the bottlenecks/knowledge gaps that would uniquely benefit from multidisciplinary solutions and knowledge sharing – which can be tactically developed by CIRM through the ReMIND platform initiative. 2. Cross-Disease Analysis - Encourage discussions on how insights from stem cell and genetic research in one neurodegenerative disease can be applied to others, potentially revealing common pathways and targets for therapy. 3. Identify areas that are already funded by others and do not require CIRM support 4. Discuss a potential role for CIRM in addressing the above points – Is there something for CIRM to do something unique?
Key Knowledge Gaps	***Please prioritize 3 key knowledge gaps that need addressing within your field (i.e., disease area within ND)*** CIRM's NTF strategic discussion will be anchored to a core set of knowledge gaps. Within the program, we expect a clear idea of the knowledge gaps being addressed by each presenter group and how a potential ReMIND program could address those gaps.
Guiding Questions	***We request that each presenter/group answer the following questions in their presentation:*** General Questions for All Topics: 1. What are the three critical knowledge gaps in the current understanding and treatment of [specific neurodegenerative disease]? 2. What are the most important bottlenecks in the development process for your therapeutic programs and what kinds of innovations could be most impactful? (only for more translational researchers) 3. How will your presentation today contribute to closing these gaps? 4. Which new technologies (e.g., through new PI collaboration) that were developed in other fields can now be adapted to answer questions in neurodegeneration with the right partner? 5. Which new conceptual framework would you propose to be tested? Especially new hypotheses regarding common mechanisms that cut across disease indications? 6. How can collaboration between academia, industry, and clinical practice be improved to address these knowledge gaps more effectively? 7. Are there particular types of public data or biological resource infrastructure that would benefit from added investment in CA?

Category	Criteria
Potential sessions / participant list	**Comment**: Might be useful to hear from industry groups (Neurona?) what were the key pain points during the development of your program? Are there innovations/tools that could be a game-changer that we should invest in now with a 3-8 year horizon? What about inviting companies working on different CNS targeting modalities – ASOs/siRNAs (Biogen, Ionis, Alnylam), Cell therapy (Bluerock, Neurona, Sana Tx), Gene editing (Crispr tx) Neurodegeneration across diseases – Comment: a group discussing common issues across diseases might be a good place to either start or end. • Biomarkers: Henrik Zetterberg, Kaj Blenow • Disease mechanisms (Cellular/Molecular): Mark Cookson, Clive Svendsen, • Genetics: Andy Singleton, Beth Stevens • Ignacio Muñoz-Sanjuan (CHDI/now CajalNeuro), Update on ALS • Merit Cudowicz, Jeff Rothstein, Don Cleveland, Gene Yeo Update on Parkinson's Disease • Early changes in disease – Lorenz Studer • Late changes in disease and cell therapy – Patrick Brundin • Others: Andy Singleton (Genetics), Mark Cookson (Cell Biology), Randy Schekman/Ekemini Riley (ASAP -leveraging others-) Update on Alzheimer's Disease • Randy Bateman (Biomarkers), Reisa Sperling, Eric Reiman • Tony Wyss Coray, Jonathan Kipnis, David Gate (T-cell-microglia axis in aging, AD/PD) • Genetics: Alison Goate, John Hardy Huntington's Disease • Leslie Thompson • Ignacio Muñoz-Sanjuan (CHDI/now CajalNeuro), • Robert Pacifici (CHDI) Other Neurodegenerative Diseases and Possible Therapies • Stephanie Cherqui (Cystenosis) • Rosa Rademakers (FTD and related disorders and epilepsy)