CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Memorandum

To: Members of the ICOC
From: CIRM Leadership
Re: Consideration of the Strategic Allocation Framework Recommendations
Date: September 23, 2024

PRIORITIZATION / STRATEGIC ALLOCATION FRAMEWORK OVERVIEW

1 – EXECUTIVE SUMMARY

The California Institute for Regenerative Medicine (CIRM) has established itself as a leader in propelling stem cell research and regenerative medicine, dedicated to accelerating scientific discoveries into transformative treatments. Yet, with the rapid evolution of the field, CIRM is presented with a pivotal challenge: the strategic allocation of limited resources across a spectrum of initiatives to optimize impact and further propel the field.

To enhance the efficacy of its funding strategy, CIRM's approach to resource allocation is more crucial than ever. We must consider the current balance of available funds for research programs and review historical allocations to inform the development of potential scenarios for resource utilization. This process is compounded by the reality that the demand for funding greatly exceeds the available resources.

The **Strategic Allocation Framework (SAF)** is a structured and data-driven approach to prioritize resource allocation and provide recommendations to the ICOC for continued implementation of CIRM's strategic plan and maximize CIRM's impact, focusing on areas where it can significantly advance the field of regenerative medicine.

This memo summarizes the SAF process, defining its rationale, objectives, scope, and key recommendations for the Board's consideration.

2 – BACKGROUND & RATIONALE

Since its inception, CIRM's contributions have been vast, funding vital research, bolstering infrastructure development, advancing educational initiatives, and facilitating the discovery and development of regenerative medicine therapies.

An overview of CIRM's budget allocations and remaining funds for key initiatives and programs is presented, serving as a central figure in our discussions on the continued implementation of CIRM's strategic plan and prioritization for future research endeavors and funding allocations.

A. Current Financial Overview for CIRM

B. Scope of CIRM Funding

With approximately $3.86 billion in remaining funds, CIRM has developed the SAF to ensure its resources are allocated effectively and aligned with the Agency's mission. CIRM's mandate directs us to concentrate on research using stem and progenitor cells, as well as genetic research and genetic therapies, particularly in areas that are not generally supported by the NIH and the Federal Government.

As we enter this new phase of implementing CIRM's strategic plan, our focus should be on identifying and supporting projects that will cement our long-term impact over the next decade. In doing so, we face the challenge of balancing a diverse portfolio of investments while directing a concerted effort toward unique and high-potential opportunities. This strategic funding allocation will ensure that CIRM not only contributes to the current landscape of regenerative medicine but also shapes its future.

C. Landscape of Regenerative Medicine

The landscape of regenerative medicine is marked by an accelerating pace of scientific breakthroughs (Fig. 2 & Fig. 3), the emergence of innovative therapeutic products, and an expanding array of clinical trials targeting a wide spectrum of diseases and injuries. This dynamic environment presents both opportunities and challenges for funding bodies like CIRM.

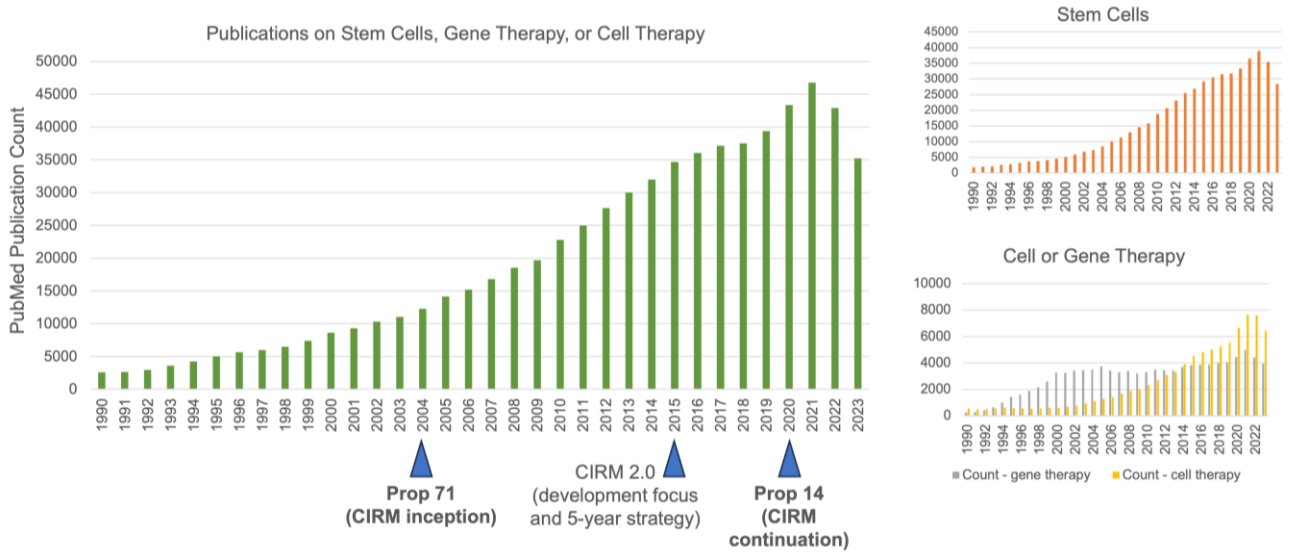
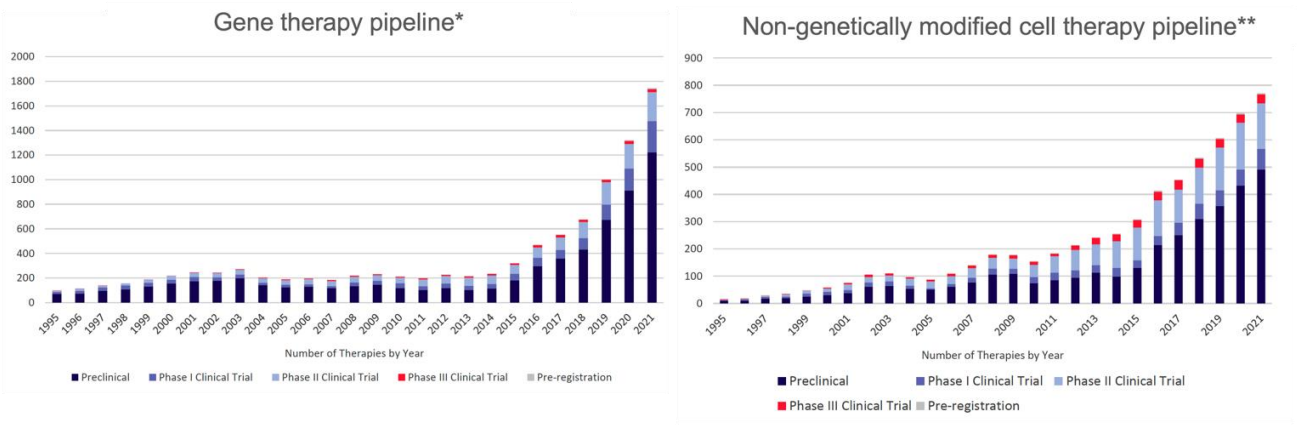


Fig 2. **Growth of the regenerative medicine field:** The field's rapid academic activity is evidenced by the significant rise in publications on stem cells, cell therapy, & gene therapy, from a few thousand in 2005 to over 40,000 by 2020.



American Society of Gene & Cell Therapy (ASGCT).- Quarterly Report, Q2, July 2021 (https://asgct.org/global/documents/asgct-pharma-intelligence-quarterly-report-july-20.aspx)

Data derived from Citeline (Pharmaprojects and Trialtrove)
*Gene therapies: gene therapy; cellular therapy – chimeric antigen receptor; cellular therapy – T cell receptor; lytic virus
**Cell therapies: cellular therapy – other; cellular therapy – stem cell; cellular therapy – tumor-infiltrating lymphocyte
Excluded from analysis: nucleic acid therapies (mRNA, oligonucleotides, RNAi, ASO)

Fig. 3: **Growth of cell and gene therapy development:** There has been a substantial growth in cell and gene therapy development, from pre-clinical research to market authorization in the past 20 years. The expansion of regenerative medicine companies and stem cell-related clinical trials underscores a growing industry and clinical engagement. The data reveals an increasing number of gene therapies and non-genetically modified cell therapies advancing through the stages of clinical trials, showcasing the sector's rapid innovation and the push towards real-world applications.

D. Finite Resources and Increasing Demand

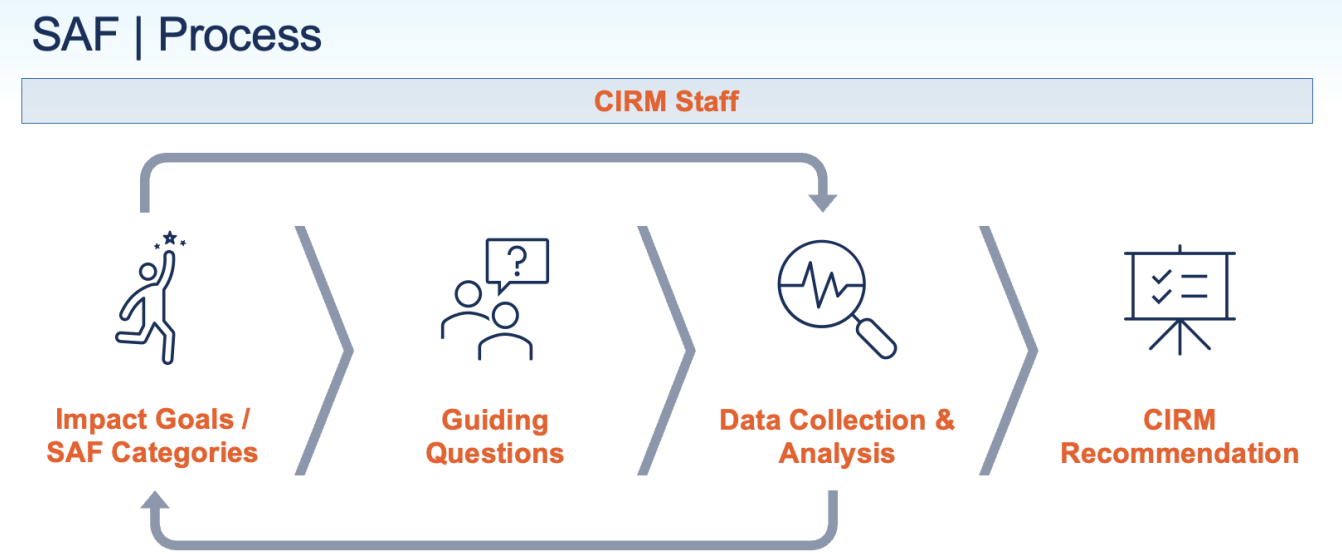
Despite the promise and progress in regenerative medicine, CIRM's resources are finite, and the demand for funding has been growing at an unprecedented rate. The situation in FY 2023–2024 serves as a clear example of a deeper problem. The CLIN program began the fiscal year with $252 million allocated. By July 2023, $50.1 million had already been approved, reducing the remaining balance to $201.8 million. As funding rounds progressed, approvals continued to erode the budget, and by February 2024, pending approvals could result in a deficit of $89.9 million. Additionally, new applications submitted in February and March totaled $107.5 million in potential funding requests, further amplifying the strain on available resources.

This scenario highlights a deeper issue in the system that goes beyond annual budget constraints. The temporary pause on new CLIN1 and CLIN2 applications, initiated in July, offered a short-term reprieve. However, this was more of a patch than a sustainable solution. A comprehensive reassessment through the SAF is necessary to craft long-term solutions. This will involve revisiting CIRM's review processes and refining strategic priorities to ensure that resources are deployed where they can have the greatest impact.

3 – STRATEGIC ALLOCATION FRAMEWORK

The Strategic Allocation Framework (SAF) originated from a request by the Science Subcommittee in September 2023, where a prioritization kickoff discussion led by Board Member Mark Fischer-Colbrie resulted in a directive for CIRM to develop a structured approach and recommendations for resource allocation. By June 2024, the SAF was presented to the Science Subcommittee and the ICOC, with a target set for final recommendations by September 2024.

The **SAF process** at CIRM is an iterative, data-driven approach to ensure the alignment of initiatives with CIRM's overall mission. The framework relies on several key steps the CIRM team used to guide decision-making and recommendations.



A. Impact Goals/SAF Categories

At the outset of our strategic planning process, we began with a working hypothesis built around the **four key categories** that drive our overarching mission. This initial hypothesis formed the basis for developing a comprehensive set of impact goals.

A very important part of this refinement process involved in-depth engagement and robust discussions with the members of the ICOC through the Science Subcommittee and the Neuro Task Force meetings over the past 6 months. These deliberations were crucial in shaping the direction and scope of our efforts, ensuring alignment with CIRM's objectives and the evolving landscape of regenerative medicine.

The result was a set of **six final recommended impact goals** (framed within the **four categories**) that will guide our actions and funding priorities. These goals are designed to accelerate the discovery and translation of therapies, advance critical approvals for cell and gene therapies, improve accessibility and affordability, and ensure a diverse and skilled workforce capable of sustaining advancements in regenerative medicine.

Category 1 - Accelerating Discovery & Translation

Goal 1 - Catalyze the identification and validation of at least 4 novel targets and biomarkers, ensuring integration into preclinical or clinical research for diseases in California.

Goal 2 - Accelerate development and utilization of 5-8 technologies that have the potential to improve safety, efficacy, and/or quality of cell and gene therapies.

Category 2 - Cell & Gene Therapy Approvals

Goal 3 - Advance 4-7 rare disease projects to BLA.

Goal 4 - Propel 15-20 therapies targeting diseases affecting Californians to late-stage trials.

Category 3 - Accessibility & Affordability of CIRM-Funded Cell & Gene Therapies

Goal 5 - Ensure that every BLA-ready program has a strategy for access and affordability.

Category 4 - Diverse Workforce Development

Goal 6 - Bolster CIRM's workforce development programs to address gaps and meet evolving demands in regenerative medicine.

B. Guiding Questions

The **Design Questions** have served as the foundation for guiding the SAF, ensuring that every step in the process is aligned with the mission and strategic goals of the organization:

- **How can CIRM make the greatest impact on its mission?**
- **How might CIRM effectively allocate its remaining budget of $3.86B?**
- **Within these, how might CIRM effectively allocate its remaining Neuro budget of $1.14B?**

The CIRM team used these high-level questions as the departing point to derive guiding questions for each of the six goals. These questions (see ***Appendix A,*** *p10*), have been discussed and designed to ensure a thorough analysis of whether a particular initiative supports CIRM's goals and priorities, offering a structured way to evaluate the alignment of a project with CIRM's strategic vision.

C. Data Collection & Analysis

Once guiding questions were established, data collection began. This involved gathering relevant information and metrics needed to assess progress and impact. The team conducted thorough analyses to draw insights and develop a well-rounded understanding of the potential outcomes of each recommendation.

D. CIRM Recommendation

Based on the data collected and analyzed, the CIRM team formulated recommendations that are designed to align with the original impact goals and guiding questions. These

recommendations were developed to ensure that every initiative funded under the SAF process contributes to the overarching strategic goals of advancing regenerative medicine, increasing patient access and affordability of therapies.

The recommendations emphasize a data-driven, mission-aligned approach to resource allocation. They also provide flexibility to adapt to emerging opportunities and challenges, ensuring that CIRM can continue to drive innovation while staying responsive to the evolving needs of the scientific and medical communities.

4 – TIMELINE

The SAF process has been built around a robust schedule of key meetings with the ICOC, Science Subcommittee (Sci. Sub.), and the Neuro Task Force (NTF). These meetings have been instrumental in shaping the SAF recommendations and ensuring alignment with CIRM's strategic goals.

From February through September, CIRM has strategically scheduled regular touchpoints to collect critical data, provide updates, and gather feedback to refine our recommendations.

At each key milestone, the Board's input has been crucial in refining these recommendations. The SAF process has emphasized transparency, with consistent updates shared with both the Board and committees throughout the year. This iterative approach ensures that the SAF recommendations are not only data-driven but also responsive to the Board's evolving priorities and concerns.

As we approach the final presentation of SAF recommendations on September 26th, we will continue to incorporate feedback to ensure that these recommendations best serve CIRM's mission and long-term goals.

June NTF/Science Subcommittee	• SAF Overview - NTF Background • Present Neuro Survey Results – Discussion • Provide a high-level overview of how this fits within Strategic Analysis Framework (SAF)
June ICOC	• Provide an update on the process, aligning with the June NTF/Science Subcommittee • Offer an example of analysis that will inform recommendations
July NTF/Science Subcommittee	• Present four overarching SAF Goals and delve into Goals 1 & 2 • Review relevant data associated with Goal 1 & 2 • Discuss potential recommendations for Goal 1 & 2
August AAWG	• Present updates on Goal 5 • Discuss considerations for Goal 5
August NTF/Science Subcommittee	• Present updates based on feedback received on Goal 1 & 2 • Introduce Goal 3 & 4 and discuss associated data • Discuss potential recommendations for Goals 3 & 4

September NTF/Science Subcommittee	• Full SAF presentation:
	  • Present updates based on feedback received on Goals 1, 2, 3, & 4
	  • Present Goals 5 & 6
	  • Discuss overall recommendations in preparation for September ICOC

September ICOC	• Overall Presentation of SAF recommendations

5– SUMMARY OF RECOMMENDATIONS

The **SAF** was designed to focus CIRM's resources on measurable impact goals, ensuring that every dollar allocated contributes to advancing the agency's vision. These goals were framed within four key categories, aligning with CIRM's strategic plan and Proposition 14: **Accelerating Discovery & Translation**, **Cell & Gene Therapy Approvals**, **Accessibility & Affordability**, and **Diverse Workforce Development**.

The development process involved defining high-level questions and measurable success metrics to prioritize resources. This collaborative effort spanned CIRM teams, external consultants, and community inputs. The following are the goals and recommendations:

Accelerating Discovery & Translation

Goal 1: Catalyze the identification and validation of at least 4 novel targets and biomarkers, ensuring integration into preclinical or clinical research for diseases in California.

- Recommendations:
  - Support comprehensive discovery research through DISC4 & DISC5 funding structures, fostering multidisciplinary innovation with early industry engagement.
  - Establish a Data Coordinating and Management Center (DCMC) to streamline data management and enhance the utility of cross-disease data.

Goal 2: Accelerate development and utilization of 5-8 technologies that have the potential to improve safety, efficacy, and/or quality of cell and gene therapies.

- Recommendations:

- Pilot the INFR Technology Platform Program to bridge the gap between research and commercialization, fostering partnerships and multi-stakeholder technology incubation programs.

Cell & Gene Therapy Approvals

Goal 3: Advance 4-7 rare disease projects to BLA.

- **Recommendations:**
  - Accelerate the current rare disease therapy pipeline by increasing CLIN4 funding to address BLA readiness gaps in manufacturing and research.
  - Pilot platform-based therapy development for life-threatening monogenic neurological disorders.

Goal 4: Propel 15-20 therapies targeting diseases affecting Californians to late-stage trials.

- **Recommendations:**
  - Streamline preclinical development programs by consolidating DISC2, TRAN1-4, and CLIN1, incorporating the prioritization of innovative therapies for Californians.
  - Update CLIN2 to support emerging clinical trial designs, incentivizing market access strategy development and pre-commercialization.

Accessibility & Affordability of CIRM-Funded Cell & Gene Therapies

Goal 5: Ensure that every BLA-ready program has a strategy for access and affordability.

- **Recommendations:**
  - Strengthen clinical infrastructure connectivity, ensuring enhanced referral, enrollment, and retention of California patients in clinical trials.
  - Support the development of market access and reimbursement strategies.
  - Deploy resources to influence policies that advance access and reimbursement.
  - Enhance partnerships with state and national organizations to expand sustainable access.

Diverse Workforce Development

Goal 6: Bolster CIRM's workforce development programs to address gaps and meet evolving demands in regenerative medicine.

- Recommendations:
  - Provide high-demand technical training via updates to the Bridges and COMPASS programs, increasing internships and integration with CIRM R&D grants.
  - Create a new EDUC program to develop hybrid skillsets, focusing on cross-disciplinary internships.

- Launch outreach campaigns to increase workforce diversity and public education on regenerative medicine.

Additional Recommendations

- Restart Grantee Conference to report SAF goal progress, serving as a platform to showcase ongoing developments.
- Maintain Conference Grants for specific CIRM needs (EDUC1 Mechanism 2), ensuring collaboration with grantees to meet CIRM's strategic objectives.

This document provides a summary of the main recommendations; however, for a more detailed view, please refer to the full presentation to the ICOC on September 26, 2024. That presentation includes the specific questions that guided the development of these goals and the data derived from various sources that accompany the justification for each recommendation.

6 – MOTION REQUEST

We request a motion that the ICOC approve these goals and recommendations.

7 – APPENDICES

A. Data Sources for Analysis Leading to Recommendations

The following data sources were utilized in the analysis process that informed the SAF recommendations for each goal. These sources provide critical insights, ranging from clinical data to economic burden reports, enabling a comprehensive understanding of the landscape and ensuring that the recommendations are data-driven and well-supported.

Goals	Data Sources

Goals 1 & 2	• California Department of Public Health, CDC, Cancer Registry reports
	• CIRM internal portfolio data analysis
	• CIRM independent research by project leads and science officers
	  ○ Clinical trials
	  ○ Economic burden reports
	  ○ News reports
	  ○ Peer review papers
	  ○ Research articles
	• GlobalData database for industry analysis
	• IQVIA CA disease landscape analysis
	  ○ Anonymized 1.5B patient claims data past 12 months matched to ICD-10 medical codes
	  ○ Subject matter expert review and insights
	  ○ Health Economics and Outcomes Research (HEOR) data
	  ○ Patient Reported Outcomes (PROs) data
	  ○ NIH funding and Industry pipeline data 15
	• Neuro Task Force survey results and analysis

Goals 3 & 4	• California Department of Public Health, CDC, Cancer Registry reports
	• CIRM internal portfolio data analysis
	• CIRM independent research by project leads and science officers
	  ○ Clinical trials
	  ○ Economic burden reports
	  ○ News reports
	  ○ Peer review papers
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	  ○ Subject matter expert review and insights
	  ○ Health Economics and Outcomes Research (HEOR) data
	  ○ Patient Reported Outcomes (PROs) data
	  ○ NIH funding and Industry pipeline data
	• Neuro Task Force survey results and analysis
	• Meetings with federal agencies

Goals	Data Sources
Goal 5	• Portfolio Data (as of February 2024) • AAWG Considerations (May & August 2024) • GWG Recommendations: CLIN2 awards (2023) • Centers for Medicare & Medicaid Services (CMS): Hospital Inpatient PPS final rule (FY 2024) 4 Goal 5 • ICER (Institute for Clinical and Economic Review)/NEWDIGS (New Drug Development Paradigms) white papers: Accessibility of CGT approved therapies (2024)

Goal 6	• Biotech industry workforce gap analyses, forums, and reports: TEConomy, California Economic Impact Report, Biotechnology Skilled Needs Assessment
	• Cell and Gene Therapy workforce analysis reports: Nature Biotech, NIMBL, Alliance for Regenerative Medicine, National Academy of Sciences
	• CIRM internal portfolio and trainee analysis (2009-present)
	• Research in hybrid skillset training needs
	  ○ Research articles
	  ○ Peer review papers
	• Research in CA education landscape: CA Department of Education, US Census Bureau, CA Commission on Teacher Credentialing
	• Demographic and diversity reports
	  ○ University of California Information Center
	  ○ The California State University Enrollment
	  ○ California Community Colleges Research and Data Analytics
	  ○ Reports on diversity in biotech industry 51
	• Meetings with education stakeholders

B. Glossary of Terms

- BLA: Biologics License Application
- Master Protocol: A clinical trial protocol designed with multiple coordinated sub-studies to evaluate one or more investigational drugs for one or more diseases within the overall trial structure
  - Basket Trial: A master protocol designed to study a single investigational drug in multiple diseases or disease subtypes
  - Platform Trial: A master protocol designed to study multiple investigation drugs in a single disease in a perpetual manner, with therapies allowed to enter or leave the platform based on a decision algorithm

  - Umbrella Trial: A master protocol designed to study multiple investigational drugs in the context of a single disease
- Platform Technology: A technology that can be incorporated in multiple therapies or that can be used for the research, development, and/or manufacture of multiple therapies.
- Rare Disease: A disease with a prevalence of <200,000 patients in the US
  - Ultra-rare Disease: A disease with a prevalence of <10,000 patients in the US