Joint
Science Subcommittee / Neuro Task Force Meeting

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Presentation Overview

1. Pre-read: Background
2. Pre-read: SAF Overview
3. Goals 1 & 2
4. Discussion/Next Steps

Please note:
To ensure ample time for discussion, the Background and SAF Overview will not be presented during the meeting on July 11th. For those interested, these sections were previously presented at the June 27th ICOC meeting. Please review these slides accordingly.
(6:52:15 timepoint)

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5-Year Strategic Plan (2022-2027) | 3 Themes

Advance World Class Science

- Develop shared resources
- Build knowledge networks

Deliver Real World Solutions

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

Provide Opportunity for All

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

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Background & Rationale

CIRM must allocate remaining resources to maximize its impact by considering available funds and reviewing past strategies

- CIRM has established itself as a leader in stem cell and regenerative medicine, funding basic research, infrastructure, education/training, and regenerative medicine discovery and clinical development
- Since CIRM's inception, the regenerative medicine field has grown exponentially
- CIRM has finite resources
- Demand for CIRM funding exceeds available resources

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SAF Mandate

- September 2023 Science Subcommittee: Prioritization Kickoff Discussion (BM Fischer-Colbrie)
  - **Outcome:** Ask for CIRM staff to develop an approach and recommendations for prioritization
- March 2024 Science Subcommittee and ICOC: Presented SAF and continued process with September 2024 target for recommendations

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

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SAF | Design Questions

Determine:

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

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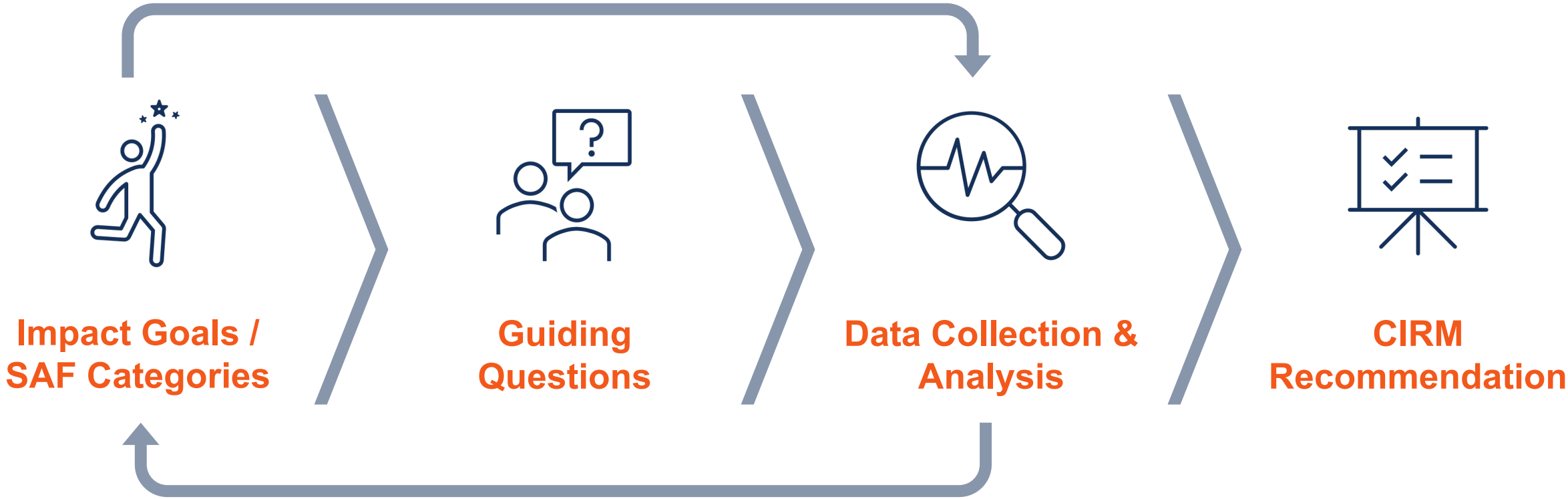
SAF | Process*

CIRM Staff



*Science Subcommittee, NTF, AAWG will inform specific aspects of the Recommendations

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SAF Categories

SAF Categories

1. Cell and Gene Therapy Approvals
2. Accessibility and Affordability of CIRM-Funded Cell and Gene Therapies
3. Discovery of Novel Disease Mechanisms
4. Diverse Workforce Development

*NTF will inform specific aspects of the Recommendations

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CIRM Preliminary* Impact Goals

Accelerating Discovery & Translation

1. **Catalyze** the identification and validation of at least X novel targets and biomarkers, ensuring integration into preclinical or clinical research for diseases in California
2. **Accelerate** development and utilization of X technologies that demonstrate improvements in safety, efficacy, and quality of cell and gene therapies

Cell & Gene Therapy Approvals

3. **Advance** at least X rare disease projects to BLA
4. **Propel** X therapies targeting distinct diseases in California to late-stage trials, including a neurological condition, to significantly reduce morbidity and mortality

Accessibility & Affordability of CIRM-Funded Cell & Gene Therapies

5. **Ensure** that every CIRM funded project completing a late-stage clinical trial has a strategy that enables access and affordability by all California patients, particularly underserved populations

Diverse Workforce Development

6. **Enhance** the integration and real-world application of training programs through strategic partnerships

**Preliminary Impact Goals to be refined through September ICOC*

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SAF Timeline

TODAY

	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep
ICOC / Sci. Sub. / NTF Meetings	2/22/24 ICOC	3/26/24 Sci. Sub.; 3/28/24 ICOC; 3/22/24 NTF ND	4/22/24 Sci. Sub.; 4/17/24 NTF ND	5/21/24 Sci. Sub.; 5/14/24 AAWG	6/27/24 ICOC; 6/14/24 Sci. Sub./NTF	7/11/24 Sci. Sub./NTF	8/7/24 AAWG; 8/16/24 Sci. Sub./NTF	9/26/24 ICOC; 9/13/24 Sci. Sub./NTF
Flow Control	CLIN1/2 Flow Control Starts				Flow Control Evaluation			
SAF Milestones					SAF Update Interim FY24/25 Research Budget Full FY24/25 Operations Budget			SAF Recommendations FY24/25 Research Budget
SAF Analysis		Formation of SAF Analysis Group	*Collect data & analyze*				*Provide recommendations*	

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Category: Accelerating Discovery & Translation

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

Goal 2 - Accelerate development and utilization of X technologies that demonstrate improvements in safety, efficacy, and quality of cell and gene therapies

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Objective of Today

Review Preliminary Goals 1 & 2:

1. High-Level Questions
2. Data & Analysis
3. Recommendations
4. Discussion

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Preliminary Goal 1

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

High-Level Questions

- **Portfolio Scope and Disease Representation:**
  - Which diseases in California would benefit most from the identification and validation of novel targets and biomarkers?
  - What does the disease burden and prevalence data indicate about priority health concerns in the state?
  - Which of these are more amenable to discovery of targets/biomarkers utilizing stem cells and/or genetic research?
- **Collaboration:** How can CIRM leverage and incentivize multi-stakeholder collaboration to accelerate the discovery and validation of novel targets and biomarkers?
- **Innovation and Technology:** What new technologies and research methods could advance the discovery and validation of novel targets and biomarkers?

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Preliminary Goal 2

Goal 2 - Accelerate development and utilization of X technologies that demonstrate improvements in safety, efficacy, and quality of cell and gene therapies

High-Level Questions

- **Current Development Bottlenecks**: What are the current translational bottlenecks for CGT ?
- **Innovation and Technology**: What innovative technologies and research methodologies could be utilized or developed to address development/translational bottlenecks?
- **Infrastructure Utilization:** How will clinical, manufacturing, and patient support infrastructures be optimized to support these objectives?
- **Fostering Collaboration**: How can CIRM foster collaboration between academic and industry stakeholders to advance the development and utilization of the novel technologies?

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SAF Data Sources

- 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
- Neuro Task Force survey results and analysis

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SAF Data Gathering and Analysis Team

- **Janie Byrum**
- Jim Campanelli
- **Rosa Canet-Avilés** *
- Lila Collins
- **Abla Creasey**
- Uta Grieshammer
- **Dongjin Lee**
- Lisa Kadyk
- Hayley Lam
- **Lisa McGinley**
- Ross Okamura
- **Shyam Patel** *
- **Kelly Shepard**
- **Sara Taylor** *
- Sohel Talib
- Chan Tan
- **Thomas Trinh** *
- Paul Webb
- Daisy Xin

* core team

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Goal 1 & 2 | Summary Table 1/2

Disease	Patient Count	Stem Cell Models	Biomarker Need	CA Economic Burden	NIH Spend in 2023
Hypertension	4,468K	✗	Low	$20.1B	$0.5B
Type II Diabetes	2,988K	✓	Medium	$42.4B	$1.2B
Depression	1,747K	✗	High	$33.9B	$0.7B
Chronic Ischemic Heart Disease & Heart Failure	1,354K	✓	Medium	$68.0B	$5.8B
Asthma	1,154K	✗	High	$16.0B	$0.3B
Stroke	892K	✗	High	$65.1B	$0.4B
Osteoarthritis (knee)	698K	✓	Medium	$5.3B	$0.1B
Type I Diabetes	290K	✓	Medium	$42.4B	$1.2B
Liver Fibrosis / Cirrhosis	113K	✓	High	$3.8B	$0.4B
Alzheimer Disease and Related Dementias	91K	✓	High	$47.2B	$3.5B
Multiple Sclerosis	39K	✓	High	$12.3B	$0.1B

X = amenable to stem cell models
✓ = validated stem cell models exist

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Goal 1 & 2 | Summary Table 2/2

Disease	Patient Count	Stem Cell Models	Biomarker Need	CA Economic Burden	NIH Spend in 2023
Breast cancer	224K	✓	Medium	$4.1B	$0.8B
Melanoma	202K	✓	High	$0.8B	**
Prostate cancer	152K	✓	Medium	$3.2B	$0.3B
Lung cancer	71K	✓	Medium	$3.4B	$0.5B
Colorectal cancer	67K	✓	Medium	$3.4B	$0.4B

✓ = validated stem cell models exist

***No publicly available data in this category*

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Technology Gaps | Summary Table

	Cell Differentiation	Delivery/ Specificity	Immune Evasion	Scalable Manufacturing	CQA/Potency	In Vivo Models
Asthma		✓		✓	✓	
Stroke		✓	✓	✓	✓	✓
Heart Disease	✓	✓	✓	✓		
Osteoarthritis (knee)		✓			✓	
Type I Diabetes			✓	✓		✓
Liver Fibrosis/Cirrhosis	✓	✓	✓	✓		
Alzheimer's Disease		✓				✓
Multiple Sclerosis		✓			✓	
Selected Cancers*		✓		✓		

Selected Cancers include breast cancer, melanoma, prostate cancer, lung cancer, and colorectal cancer

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Knowledge Gaps | Summary Table

	Disease Heterogeneity	Mechanism of Disease	Immune Response	Microenvironment
Type II Diabetes	✓			
Asthma	✓	✓	✓	
Stroke			✓	
Depression	✓	✓		
Chronic Ischemic Heart Disease & Heart Failure	✓		✓	
Osteoarthritis (knee)		✓		
Type I Diabetes		✓	✓	
Liver Fibrosis/Cirrhosis			✓	
Alzheimer's Disease	✓	✓	✓	
Multiple Sclerosis	✓	✓	✓	
Selected Cancers*	✓			✓

Selected Cancers include breast cancer, melanoma, prostate cancer, lung cancer, and colorectal cancer

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1st Recommendation for Goal 1

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

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1st Recommendation for Goal 1

1 - Discovery investment in Foundational and Mechanistic Discovery

- **Objective**: Enhance research to explore cross-disease systems and interactions, aiming for breakthroughs in new disease mechanisms, targets, and biomarkers
- **Approach**: Utilize cross-disease data and collaborate with various consortia to maximize research outcomes

Recommendation 1 - DISC4 and DISC5 as Pillars for Discovery funding - Support comprehensive discovery research through structured initiatives DISC4 and DISC5

Approach: Encourage collaborative, multidisciplinary innovation in stem cell and genetic research across diverse disciplines and disease indications.

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2nd Recommendation for Goal 1

1 - Discovery investment in Foundational and Mechanistic Discovery

- **Objective**: Enhance research to explore cross-disease systems and interactions, aiming for breakthroughs in new disease mechanisms, targets, and biomarkers
- **Approach**: Utilize cross-disease data and collaborate with various consortia to maximize research outcomes

Recommendation 2 - Establish a Data Coordinating and Management Center (DCMC) - Streamline CIRM data management to enhance the utility of cross-disease data

Approach: Fund and develop a central hub for data coordination, facilitating better integration with consortia and research initiatives

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Recommendations for Goal 2

Goal 2 - Accelerate development and utilization of X technologies that demonstrate improvements in safety, efficacy, and quality of cell and gene therapies

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Recommendations for Goal 2

1 - Investing in multidisciplinary technology platform focused initiatives

- **Objective**: To expedite the development and application of technologies that enhance the safety, efficacy, and quality of cell and gene therapies
- **Approach**: Encourage multidisciplinary multi-stakeholder collaborations to develop platform technologies that broadly impact pre-clinical and development of multiple therapies for multiple diseases

(Pilot) **INFR Technology Platform Program -** Bridge the gap between research and commercialization by fostering partnerships between academic researchers and industry professionals

Approach: Support multi-stakeholder technology incubation programs to achieve defined technology readiness levels thereby facilitating rapid application in cell and gene therapy development

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Proposed Changes to Discovery Programs

Current	Proposed
DISC0: Foundational Research	**DISC4**
• No disease mechanism focus • Small collaborations (1-2 investigators) • No leveraging of external resources	• Large, collaborative projects focused on disease mechanisms that leverage external resources
	DISC5
	• Small, exploratory projects focused on disease mechanisms
DSMP: Data Sharing & Management Plan	**DSMP + DCMC:** Data Coordination and Management Center (INFR)
• Award requirements to detail data-sharing plans	• Harmonized data sharing with a knowledge platform that enables and encourages data re-use and integration with external resources

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Proposed Changes to Technology Funding Programs

Current	Proposed
Broad Approach	**Pilot Technology Platform Program (INFR)**
• Technology gaps funded through current DISC0/2 and TRAN3/4 Funding Opportunities • No specific focus/scope • No requirement for multidisciplinary collaborations	• New initiative to develop platform technologies • Specific focus/scope to address key bottlenecks • Leverage multidisciplinary academic-industry collaborations • Link specific outcomes to relevant technology readiness levels

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Timeline & Next Steps

Meeting	SAF Topics
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 Goal 4 • Review relevant data associated with Goal 4 • Discuss potential recommendations for Goal 4
August NTF/Science Subcommittee	• Present updates based on feedback received on Goal 4 • Introduce Goal 1 & 2 and discuss associated data • Discuss potential recommendations for Goals 1 & 2
August AAWG	• Present updates on Goal 3 and discuss associated data • Discuss potential recommendations for Goal 3

September NTF/Science Subcommittee	• Full SAF presentation:
	  ◦ Present updates based on feedback received on Goals 1,2, & 4
	  ◦ Present Goal 3 (from AAWG feedback) and Goal 5 together, discussing strategies and data relevant to both

September ICOC	• Overall Presentation of SAF recommendations

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SAF Timeline