Strategic Allocation Framework Recommendations

Rosa Canet-Avilés, Ph.D., Vice President, Scientific Programs & Education

ICOC Meeting, San Diego, CA

September 26, 2024

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Recap of Prior SAF Presentations

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

- Since the June ICOC meeting, these goals and recommendations have been reviewed by the Science Subcommittee and Neuro Task Force, which committees have recommended approval of the goals and recommendations to the full board

- Today's presentation recaps details that can be reviewed here:
  - June ICOC – Background & SAF Overview
  - July Science Subcommittee / Neuro Task Force – Goals 1 & 2
  - August Science Subcommittee / Neuro Task Force – Goals 3 & 4
  - September Science Subcommittee / Neuro Task Force – Goals 5 & 6

Actions Today

1. Present & discuss SAF Goals & Recommendations
2. Obtain approval of SAF Goals & Recommendations

Presentation Overview

1. SAF Overview
2. Goals 1 & 2
3. Goals 3 & 4
4. Goal 5
5. Goal 6
6. Additional Recommendations
7. Discussion/Next Steps

Presentation Overview

1. SAF Overview
2. Goals 1 & 2
3. Goals 3 & 4
4. Goal 5
5. Goal 6
6. Additional Recommendations
7. Discussion/Next Steps

SAF Mandate

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

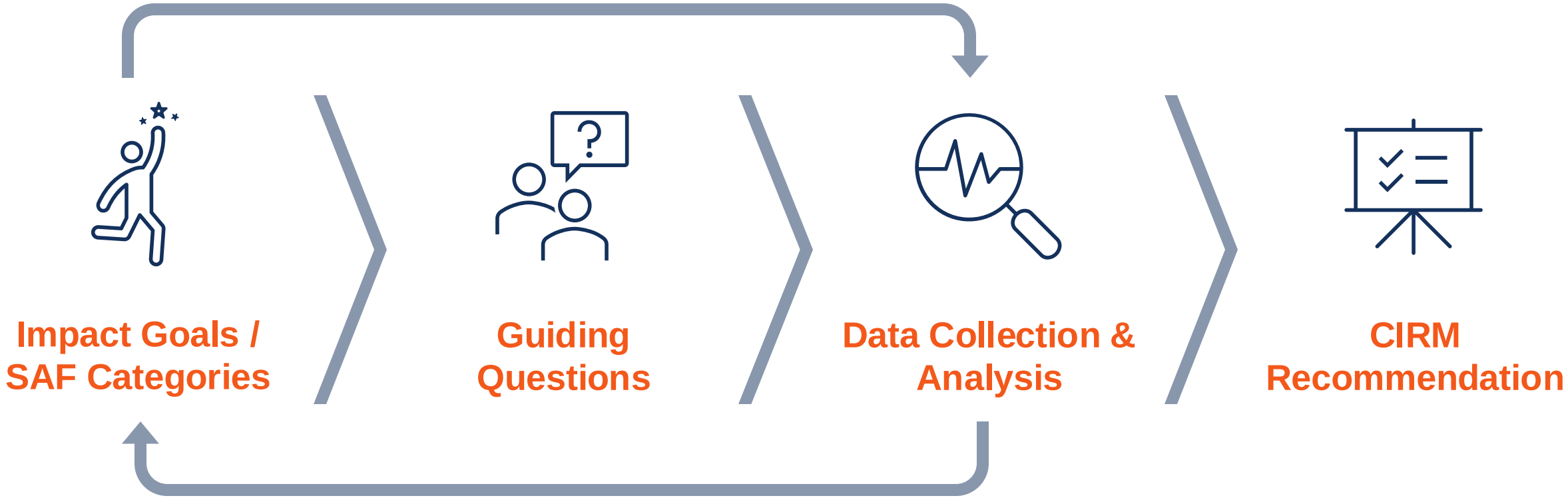
SAF | Design Questions

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?

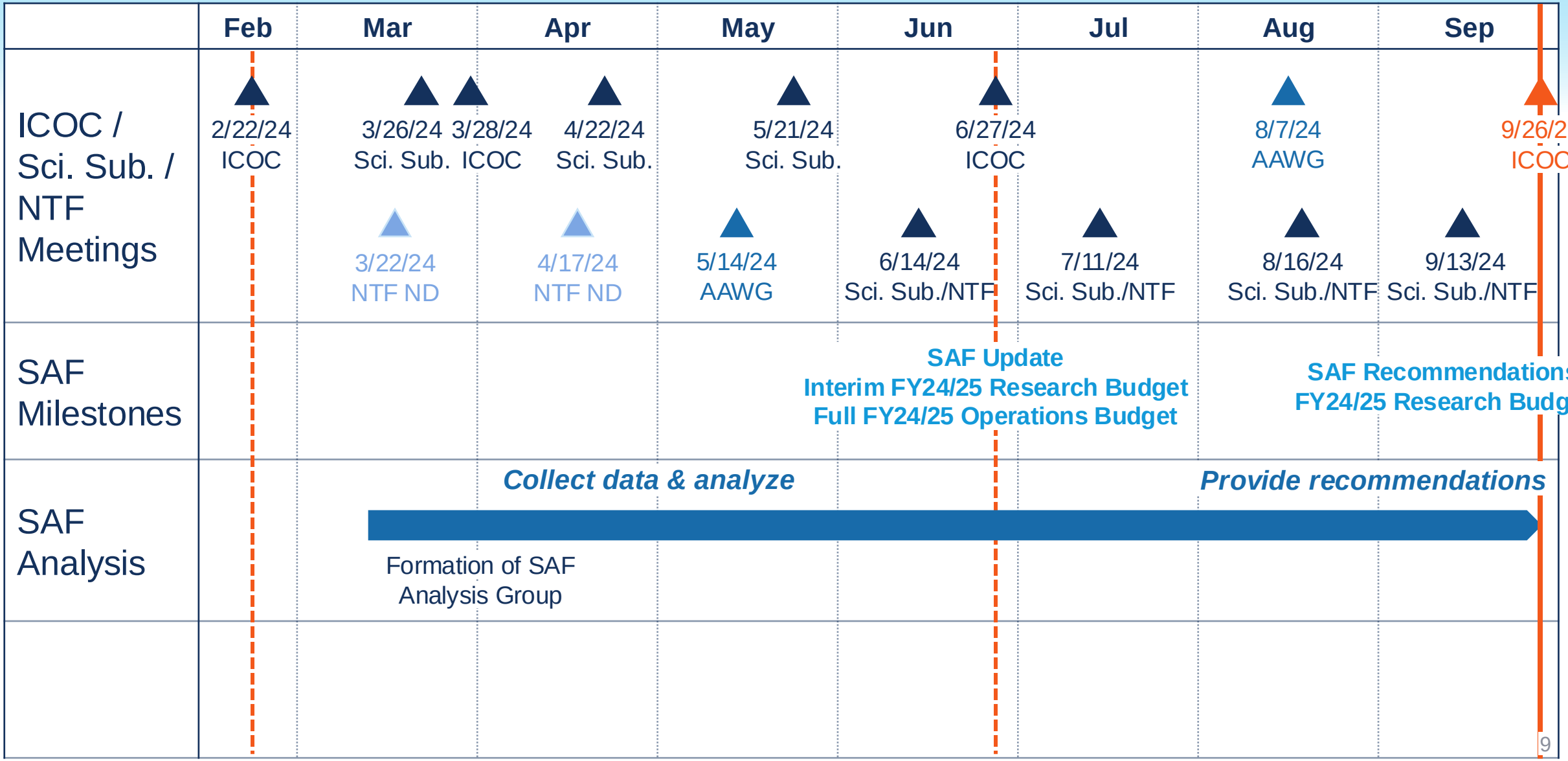
SAF | Process

CIRM Staff



SAF Timeline

TODAY



CIRM Impact Goals

Accelerating Discovery & Translation

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
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

Cell & Gene Therapy Approvals

3. **Advance** 4-7 rare disease projects to BLA
4. **Propel** 15-20 therapies targeting diseases affecting Californians to late-stage trials

Accessibility & Affordability of CIRM-Funded Cell & Gene Therapies

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

Diverse Workforce Development

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

Presentation Overview

1. SAF Overview
2. Goals 1 & 2
3. Goals 3 & 4
4. Goal 5
5. Goal 6
6. Additional Recommendations
7. Discussion/Next Steps

Goals 1 & 2

Category: 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

Goal 1 | High-Level Questions

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

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?

Goal 2 | High-Level Questions

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

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?

Goals 1 & 2 | 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

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Goals 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	$34.0B *	$2.9B
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 ** = Combined burden for T1 T2 diabetes, and chronic ischemic heart disease & heart failure*

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Goals 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*

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

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

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

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

Goal 1 | Recommendations

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

Support comprehensive discovery research through DISC4 & DISC5 funding structures

- Encourage collaborative, multidisciplinary innovation in stem cell and genetic research across diverse disciplines & disease indications with early engagement of industry to address reproducibility & scalability issues

Establish a Data Coordinating and Management Center (DCMC) to streamline data management & enhance the utility of cross-disease data

- Fund and develop a central hub for data coordination, facilitating better integration with consortia & research initiatives and enabling data science collaborative efforts via dedicated grants

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Proposed Changes to Discovery Funding Programs

Current	Proposed
DISC0: Foundational Research	**DISC4**
• No disease mechanism focus • Small collaborations (1-2 investigators) • No leveraging of external resources • No requirement for academic-industry collaboration	• Large, collaborative projects focused on disease mechanisms that leverage external resources and academic-industry partnerships
	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 • Data science initiatives to re-use data

Goal 2 | Recommendations

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

Pilot INFR Technology Platform Program to bridge the gap between research & commercialization

- Foster partnerships between academic researchers & industry professionals to support multi-stakeholder technology incubation programs that achieve defined technology readiness levels thereby facilitating rapid application in cell & gene therapy development

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

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 or academic-industry collaborations	• New initiative to develop platform technologies • Specific focus/scope to address key bottlenecks • Leverage multidisciplinary and academic-industry collaborations • Link specific outcomes to relevant technology readiness levels

Presentation Overview

1. SAF Overview
2. Goals 1 & 2
3. Goals 3 & 4
4. Goal 5
5. Goal 6
6. Additional Recommendations
7. Discussion/Next Steps

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE | Goals 3 & 4

Category: 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

Goal 3 | High-Level Questions

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

High-Level Questions

- **Current Portfolio:**
  - What proportion of the current portfolio supports rare diseases?
  - What proportion of CIRM-funded rare disease grants are likely to attain FDA approval in the next five years?
- **Infrastructure Utilization:**
  - How can CIRM's previous investment in clinical, manufacturing, and patient support infrastructure support this goal?
  - Are there any additional infrastructure investments necessary to support the unique requirements of rare disease therapy development and BLA filings?
- **Approach:**
  - What mechanisms can be adopted to facilitate the scalable development of accessible and sustainable rare diseases therapies?
- **Partnerships:** Are strategic partnerships necessary to achieve this goal?

Goal 4 | High-Level Questions

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

High-Level Questions

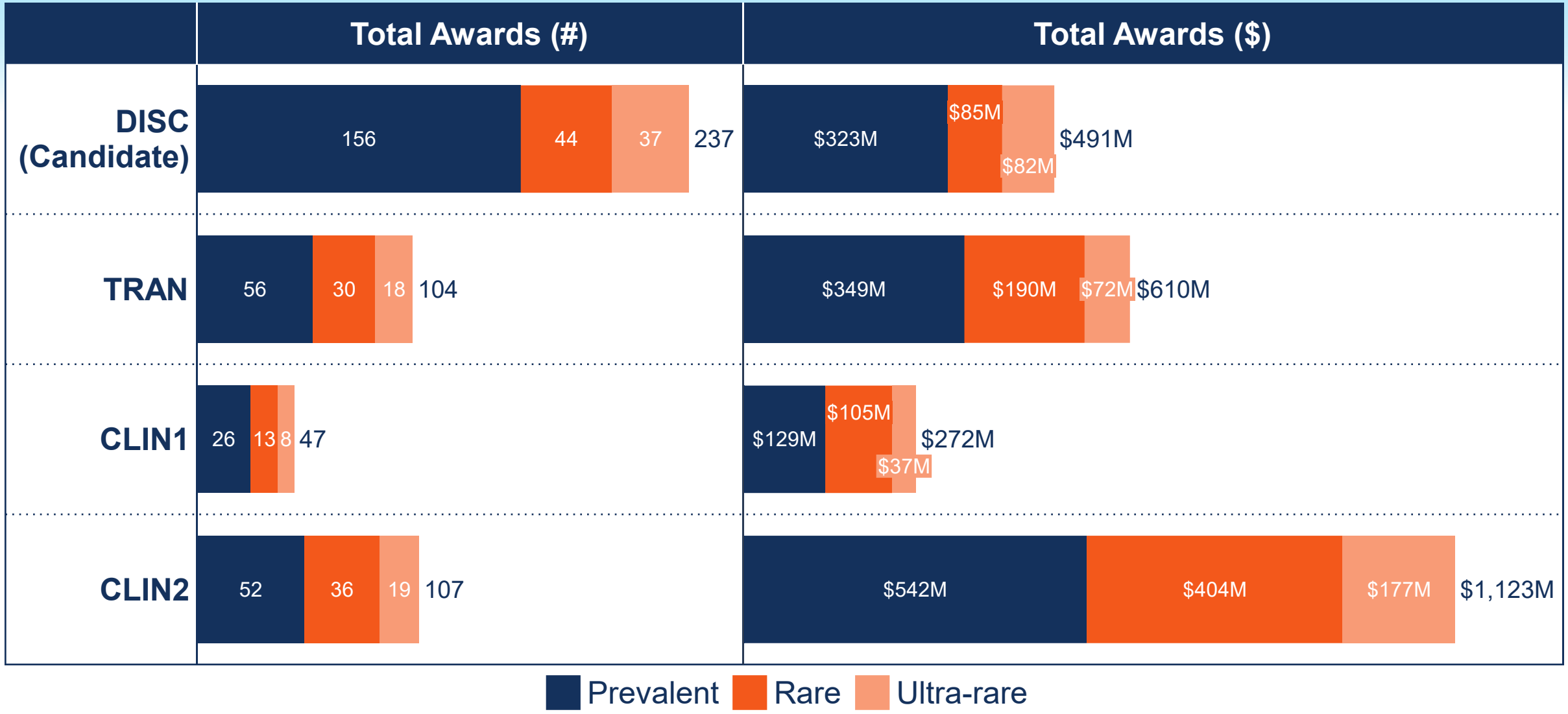
- **Disease Impact:** What diseases relevant to CA populations are amenable to CGT therapies?
- **Current Portfolio:**
  - What diseases relevant to California's population have been or are in the current CIRM clinical pipeline?
  - How many have progressed to later stage development?
  - What are the challenges facing the current portfolio?
- **Approach:** What types of enhancements to our funding programs are necessary to address these challenges and optimize the pathway for candidates towards late-stage clinical development?
- **Partnerships:** Are there strategic partnerships necessary to achieve this goal?

Goals 3 & 4 | 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
- Meetings with federal agencies

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

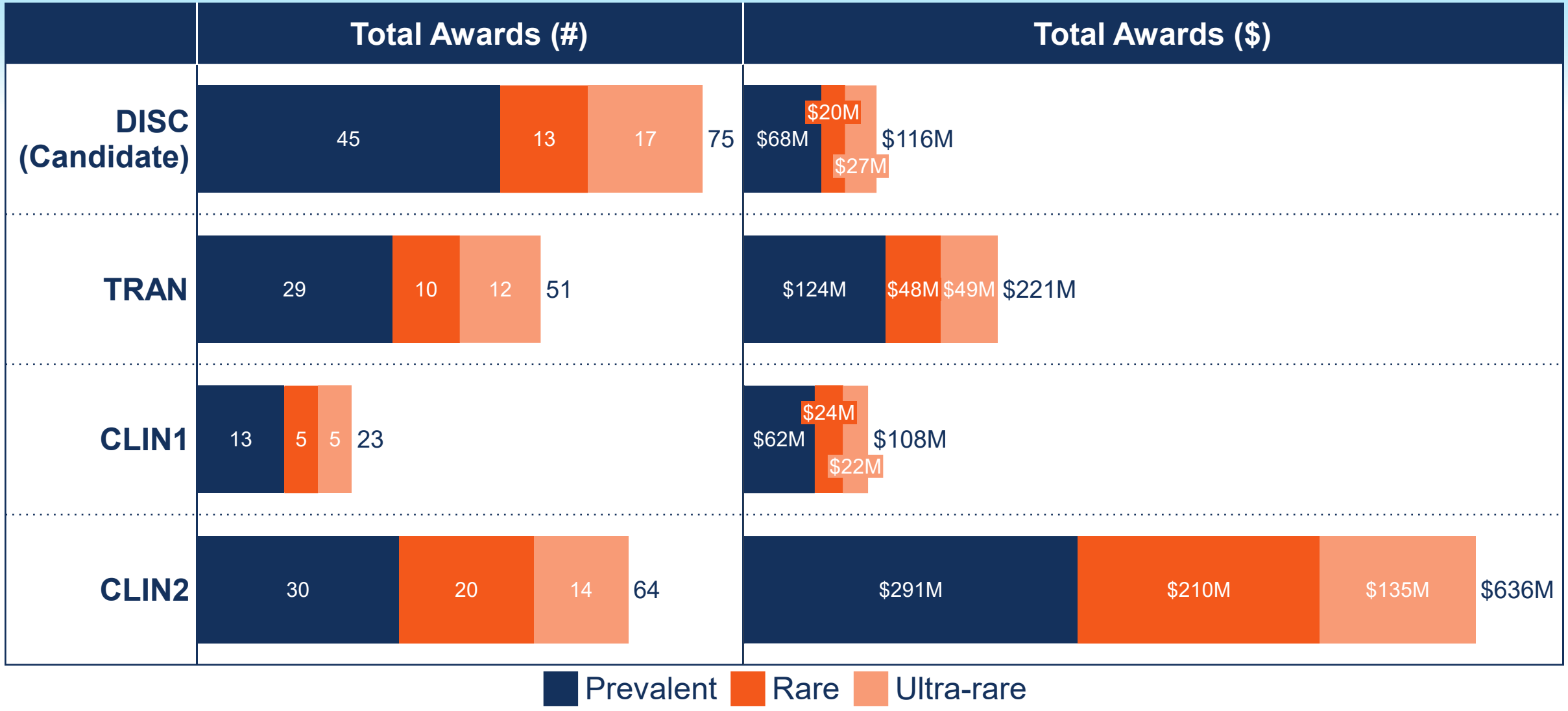
CIRM Historical Portfolio | Prevalent vs. Rare Disease



Source: CIRM Portfolio as of May 2024 excluding Foundational/Basic Research

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

CIRM Active Portfolio | Prevalent vs Rare Disease



Source: CIRM Portfolio as of May 2024 excluding Foundational/Basic Research

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Goal 4 | Summary Table 1/2

Disease	Patient Count	CA Economic Burden	Global CGT Pipeline	US Approvals
Hypertension	4,468K	$20.1B	44	0
Type II Diabetes	2,988K	$42.4B	95	0
Depression	1,747K	$33.9B	7	0
Chronic Ischemic Heart Disease & Heart Failure	1,354K	$68.0B	199	0
Asthma	1,154K	$16.0B	51	0
Stroke	892K	$65.1B	110	0
Osteoarthritis (knee)	698K	$5.3B	129	0
Type I Diabetes	290K	$42.4B	164	1
Liver Fibrosis / Cirrhosis	113K	$3.8B	94	0
Alzheimer Disease and Related Dementias	91K	$47.2B	172	0
Multiple Sclerosis	39K	$12.3B	114	0

Approved (Global) Clinical Pre-Clinical/Discovery Inactive/Discontinued/Unknown

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Goal 4 | Summary Table 2/2

Disease	Patient Count	CA Economic Burden	Global CGT Pipeline	US Approvals
Stroke	892K	$65.1B	110	0
Breast cancer	224K	$4.1B	521	0
Melanoma	202K	$0.8B	412	1
Prostate cancer	152K	$3.2B	254	1
Lung cancer	71K	$3.4B	668	0
Colorectal cancer	67K	$3.4B	330	0

Approved Clinical Pre-Clinical/Discovery Inactive/Discontinued/Unknown

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Challenges and Opportunities in CIRM R&D Pipeline

Prop 14 mandates support for therapies for diseases affecting Californians

Development of gene therapies is costly & time consuming, which makes it difficult to scale for thousands of rare diseases

Approved cell and gene therapies often face patient access challenges

Discovery | Translational | Clinical

DISC2 → **TRAN1/2/3/4** → **CLIN1** → **CLIN2** → **CLIN4**

Single Product Candidate

Pre-IND Meeting or Equivalent

IND Filing & Approval

End of Phase 2 Meeting or Equivalent

BLA Filing

- Discontinuity between early & late translational phases
- Preclinical development of cell and gene therapies can be streamlined as the field matures

Regulatory innovation can enable clinical studies of multiple therapies for multiple diseases via master protocols

Late-stage programs often require extensive investment, especially in CMC, that prevent or delay BLA readiness

Goal 3 | Recommendations

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

Accelerate Current Rare Disease Therapy Pipeline

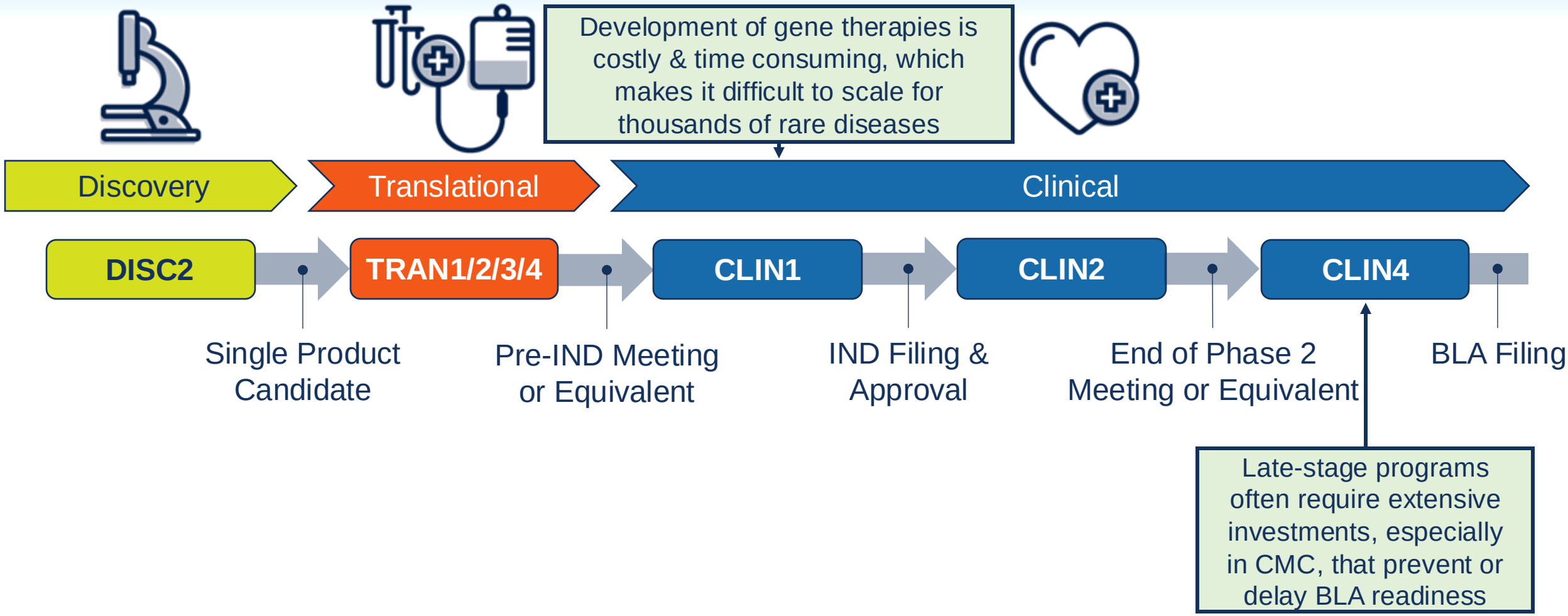
- **Increase and scale** CLIN4 funding to comprehensively address BLA readiness gaps in manufacturing, clinical/non-clinical research, and pre-commercialization*

Pilot Platform-Based Therapy Development

- **Implement pilot platform-based approach** for gene therapy development using life-threatening monogenic neurological disorders as a test case

*Not exclusive to rare disease, but majority of programs near BLA in CIRM's portfolio are in rare disease

Challenges and Opportunities in CIRM R&D Pipeline



Goal 4 | Recommendations

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

Streamline Preclinical Development Programs

- **Consolidate DISC2, TRAN1-4, and CLIN1** to accelerate the preclinical development incentivizing multidisciplinary collaborations and rapid progression to IND
- Incorporate **prioritization of innovative therapies for diseases that affect Californians**

Update CLIN2

- Allow for support of emerging **novel clinical trial designs** in CLIN2 program
- Incentivize stage-appropriate **market access strategy** development and **pre-commercialization** activities in CLIN2 program
- Incorporate **prioritization of innovative therapies for diseases that affect Californians**

Challenges and Opportunities in CIRM R&D Pipeline

Prop 14 mandates support for therapies for diseases affecting Californians

Approved cell and gene therapies often face patient access challenges

Discovery | Translational | Clinical

DISC2 → TRAN1/2/3/4 → CLIN1 → CLIN2 → CLIN4

- Single Product Candidate
- Pre-IND Meeting or Equivalent
- IND Filing & Approval
- End of Phase 2 Meeting or Equivalent
- BLA Filing

- Discontinuity between early & late translational phases
- Preclinical development of cell and gene therapies can be streamlined as the field matures

Regulatory innovation can enable clinical studies of multiple therapies for multiple diseases via master protocols

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Proposed Changes to Programs

Current	Proposed
CLIN2 and CLIN4 Programs • Prevalent, rare, and ultra-rare diseases are eligible for the same funding opportunities • **CLIN2** supports individual clinical trials for single candidates and supports a subset of pre-commercialization activities • **CLIN4** funding is insufficient for all activities needed to reach BLA readiness	**Updated Clinical Programs** • **CLIN2** supports innovative clinical trial design and incentivizes market access strategy development & pre-commercialization activities • **CLIN4** funding increases & scales to comprehensively address BLA readiness gaps • Prioritize innovative therapies for diseases that affect Californians **Pilot Rare Disease Platform Program** • Rare and ultra-rare diseases (focus) • Requirement for academic-industry partnership
Multi-Program Preclinical Path • Separate DISC2, TRAN1/2/3/4, CLIN1 Programs with their own applications • Prevalent, rare, and ultra-rare diseases are eligible for the same funding opportunities	**Streamlined Preclinical Program** • Consolidated preclinical program • Prioritize innovative therapies for diseases that affect Californians

Presentation Overview

1. SAF Overview
2. Goals 1 & 2
3. Goals 3 & 4
4. Goal 5
5. Goal 6
6. Additional Recommendations
7. Discussion/Next Steps

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE | Goal 5

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

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

Goal 5 | High-Level Questions

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

High-Level Questions

- **Landscape**
  - What are the most impactful factors for achieving access and affordability?
  - What are the barriers to access and affordability for CGTs?
  - What research is needed to understand the landscape for access and affordability?
- **CIRM Program Enhancements**
  - What activities within CIRM could be developed to facilitate access and affordability?
  - At what stage should the applicants provide an access and affordability strategy?
  - How can strategies be scaled if the therapy is successful?
- **External Engagements**
  - Who are the most important partners to impact policy change?

Goal 5 | Data Sources

- **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)
- **ICER (Institute for Clinical and Economic Review)/NEWDIGS (New Drug Development Paradigms) white papers:** Accessibility of CGT approved therapies (2024)

CIRM's Clinical Infrastructure Programs

Program	Overview	Barriers to Access				
		Clinical Expertise	Cohort Dev	Geography	Patient Knowledge	Financial
Alpha Clinics	• Launched 2015 • Support CGT clinical trials • 275+ clinical trials (71 CIRM-funded)	✓	✓			
Community Care Centers of Excellence (CCCEs)	• Launching 2025 • Support patient access to clinical trials		✓	✓	✓	
Patient Support Program (PSP)	• Launching 2025 • Address financial & logistical needs of patients in CIRM-funded trials			✓	✓	✓

Patient Access Programs are nascent but aim to reduce patient barriers to clinical trials

Source: CIRM Portfolio as of February 2024

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

CGT Access Challenges

Approved CGT Access Challenges
Limited clinical evidence generated prior to approval to inform long-term efficacy & durability vs. SOC
Very high initial cost of treatment compared to small molecules or biologics
Necessity of specialized treatment centers for delivery of treatment
Variability in coverage & reimbursement rates across Medicare, Medicaid, private insurers
Complex manufacturing & supply chains, particularly for autologous gene-modified cell therapies

Goal 5 | Recommendations (1/2)

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

Strengthen Clinical Infrastructure Connectivity

- Build interconnectivity & performance metrics between CIRM Clinical Infrastructure (Alpha Clinics, CCCEs, PSPs) to ensure enhanced referral, enrollment, & retention of California patients in clinical trials

Support Development of Market Access and Reimbursement Strategies

- Resource clinical programs to support stage-appropriate planning & evidence generation to inform robust market access & reimbursement strategies

Goal 5 | Recommendations (2/2)

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

Influence Policy

- Deploy AAWG resources to advocate for policies that advance access & reimbursement for regenerative medicines

Enhance Partnerships

- Engage state & national partners to align initiatives that expand sustainable access to regenerative medicines

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

CGT Access Challenges & CIRM Programs

Approved CGT Access Challenges	CIRM Programs & Initiatives
Limited clinical evidence generated prior to approval to inform long-term efficacy & durability vs. SOC	**Update CLIN2** to incentivize access strategy development and provide **AAWG support**
Very high initial cost of treatment compared to small molecules or biologics	**Patient Assistance Fund** will support access to CIRM-funded treatments
Necessity of specialized treatment centers for delivery of treatment	Expand capacity through **CCCE-Alpha Clinic partnerships**
Variability in coverage & reimbursement rates across Medicare, Medicaid, private insurers	Engage **policy partners** & deploy AAWG resources for **advocacy**
Complex manufacturing & supply chains, particularly for autologous gene-modified cell therapies	**Technology Platform Program & Manufacturing Network** will address manufacturing bottlenecks

Presentation Overview

1. SAF Overview
2. Goals 1 & 2
3. Goals 3 & 4
4. Goal 5
5. Goal 6
6. Additional Recommendations
7. Discussion/Next Steps

Goal 6

Category: Diverse Workforce Development

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

Goal 6 | High-Level Questions

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

High-Level Questions

- **Identifying Competency Gaps**
  - What competencies are currently lacking in the CGT workforce?
  - What types of roles or positions are most in demand for these areas of need?
  - What training is needed for these competencies, and how/where is it obtained?
- **Increasing Diversity/Representation**
  - What groups have challenges to enter and stay in the CGT workforce?
  - How can these challenges be addressed through education and training?
  - How can CIRM increase availability of opportunities to these groups?
- **Leveraging Collaborations & Best Practices**
  - What synergies exist between CIRM's EDUC and other Infrastructure programs?
  - How can CIRM leverage investments and external infrastructure/resources to expand the reach and scope of EDUC programs?

Goal 6 | Data Sources

- **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
- **Meetings with education stakeholders**

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Competencies vs. Training Availability

Competency	Academic Training in CA	CIRM EDUC/INFR Training						
		SPARK	COMPASS	Bridges	Scholars	Manf	Alpha	SRL
Process Development	Limited		✓	✓	✓	✓		
Manufacturing	Limited		✓	✓		✓		
Quality Assurance/Control	Limited		✓	✓		✓		
Data Science for Bio	Some		✓	✓	✓			
Research, General	Many	✓	✓	✓	✓			
Research, CGT	Some	✓	✓	✓	✓			
Clinical Research	Limited		✓	✓			✓	
Stem Cell Modeling	Some	✓	✓	✓	✓			✓

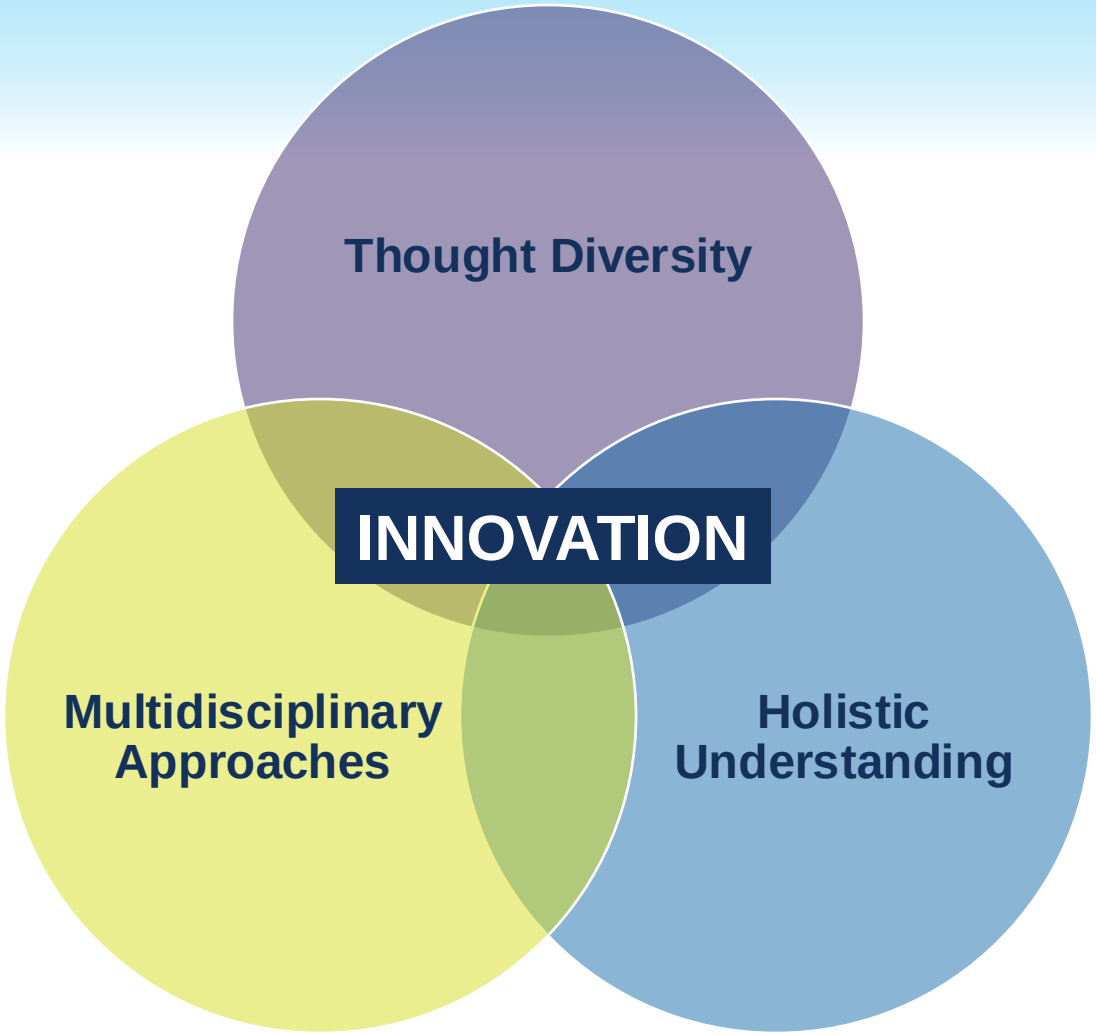
✓ = Some trainees get this opportunity; ✓ = Most trainees get this opportunity

Sources: ARM, WORKFORCE GAP ANALYSIS FOR THE CELL AND GENE THERAPY SECTOR MARCH 2023; CIRM Portfolio Analysis; CA Community College Centers of Excellence Report, 2022

Hybrid Skill Sets Are Rare But Critical For Innovation

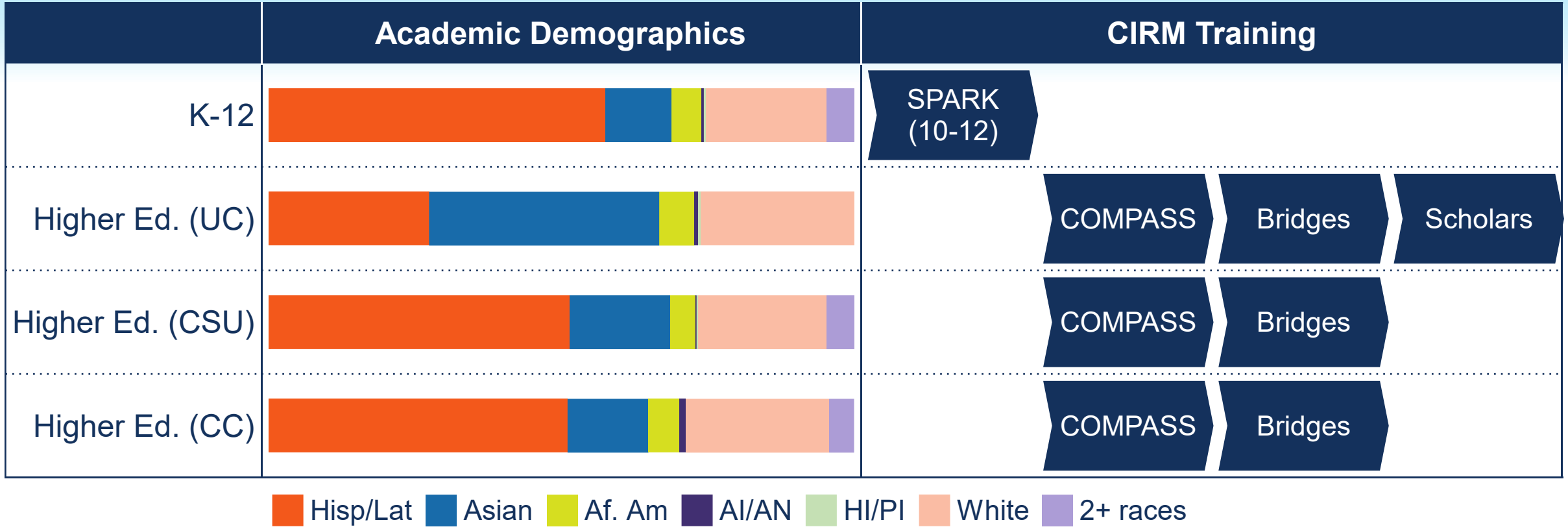
- Silos between disciplines & industries stifle innovation and limit diversity of thought
- Increased holistic understanding improves efficiency

Individuals with hybrid skill sets are highly valued for overcoming roadblocks and driving innovation



Sources: Notes from NAS Regenerative Medicine Forum, Workforce Discussion June 4-5, 2024 (Proceedings in preparation); Post et al., Capitalizing on thought diversity for innovation, Routledge, Taylor and Francis Group; 2023 Life Science TEConomy Report; NAS Press: Research at the Intersection of the Physical and Life Sciences (2010)

Demographic Attrition Begins Prior to College



Targeted and consistent outreach earlier in education (K-10th grade) is needed to prevent drop of underrepresented students in higher education

Sources: UC Accountability Report 2022, CSU Demographic Report, Education Trust West CA STEM by the Numbers 2015 report, CA Commission on Teacher Credentialing

Goal 6 | Data Analysis Summary

- **Identifying Competency Gaps**
  - Limited exposure/accessibility to manufacturing and clinical career paths in CA academic training
  - Few opportunities for:
    - Hands-on training in development, manufacture, and translation of CGT
    - Developing cross-disciplinary skillsets
- **Increasing Diversity/Representation**
  - Some populations continue to be underserved and underrepresented in the workforce
  - Attrition of diverse perspectives begins prior to college entry
- **Leveraging Collaborations & Best Practices**
  - Opportunities to increase connectivity and intra-program collaboration

Goal 6 | Recommendations

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

Provide high-demand technical training via Bridges & COMPASS program updates

- Increase training offerings, diversify internship types, & increase integration with CIRM R&D grants

Create new EDUC program to develop hybrid skillsets

- Implement new program structure to focus on cross-disciplinary internships

Launch outreach campaigns to educate the public & increase diversity of California's regenerative medicine workforce

- Develop programming to support outreach/education efforts for K-12, teachers, & community members via collaboration with key stakeholders

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Proposed Changes to Training Programs

Current	Proposed
EDUC Programs	**Increase high-demand technical training**
Bridges & COMPASS Programs: • Training/internships for in-demand competencies (manufacturing, process dev., etc.) are not widely available • Varied/limited integration with INFR programs Scholars Program	For Bridges & COMPASS relaunch: • Increase training offerings to meet industry needs • Diversify internship types • Increase integration with INFR & R&D programs
	Create hybrid skillset training program
	• Develop & launch new program that develops hybrid skillsets in trainees
Outreach & Education	**Launch education & outreach campaign**
• SPARK program (high school) • Outreach to K-12 & teachers is ad hoc	• Relaunch SPARK • Develop programming for K-12, teachers, & community members via EDUC1 (Mechanism 2) collaborations
CIRM Collaboration Hub	**Continue CIRM Collaboration Hub rollout**
• CIRM hub recently launched to link EDUC and INFR programs; rollout in progress	• Continue CIRM hub rollout to increase career path awareness for trainees

Presentation Overview

1. SAF Overview
2. Goals 1 & 2
3. Goals 3 & 4
4. Goal 5
5. Goal 6
6. Additional Recommendations
7. Discussion/Next Steps

Additional Recommendations

Additional recommendations to support all goals

Restart Grantee Conference to Report SAF Goal Progress

Restart recurring grantee conference (timing TBD) with main objective of reporting progress on SAF goals

Keep Conference Grants for Specific CIRM Needs (EDUC1 Mechanism 2)

Grantee retains the primary responsibility for planning, directing, and executing the proposed event; CIRM team will work closely with the grantee to design and implement an event responsive to a specific CIRM need

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Proposed Changes for Conferences Grants

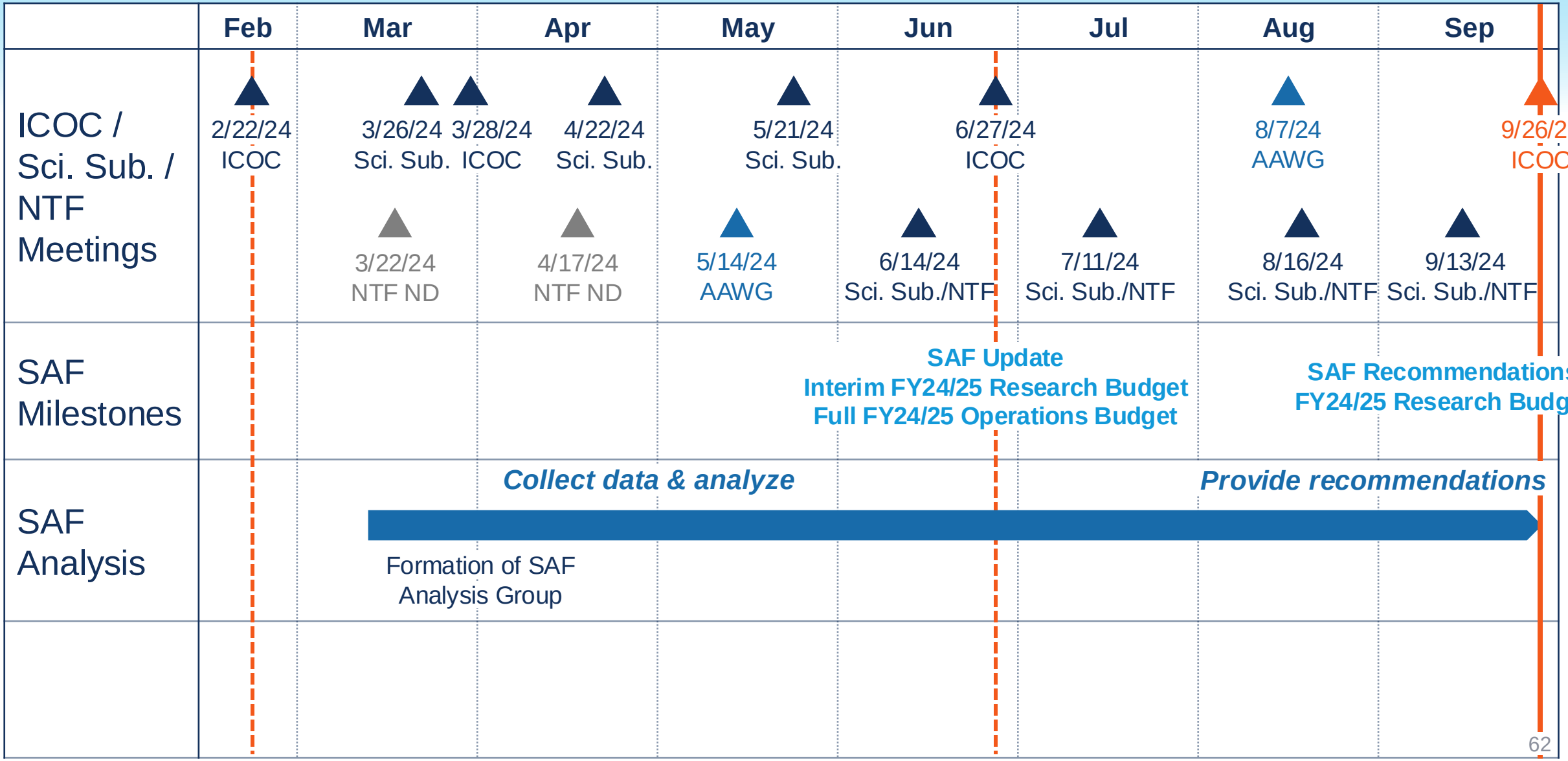
Current	Proposed
EDUC1 Conference Grants	**EDUC1 Conference Grants**
• Mechanism 1: Grantee solely responsible for the proposed conference; event must be relevant to CIRM's mission • Mechanism 2: Grantee retains primary responsibility for the proposed event, but works closely with CIRM staff to design and implement an event responsive to specific CIRM needs	• Mechanism 1 discontinued • Mechanism 2 used to fund events responsive to specific CIRM needs, including a reinstated Grantee Conference designed to report SAF Goal Progress

Presentation Overview

1. SAF Overview
2. Goals 1 & 2
3. Goals 3 & 4
4. Goal 5
5. Goal 6
6. Additional Recommendations
7. Discussion/Next Steps

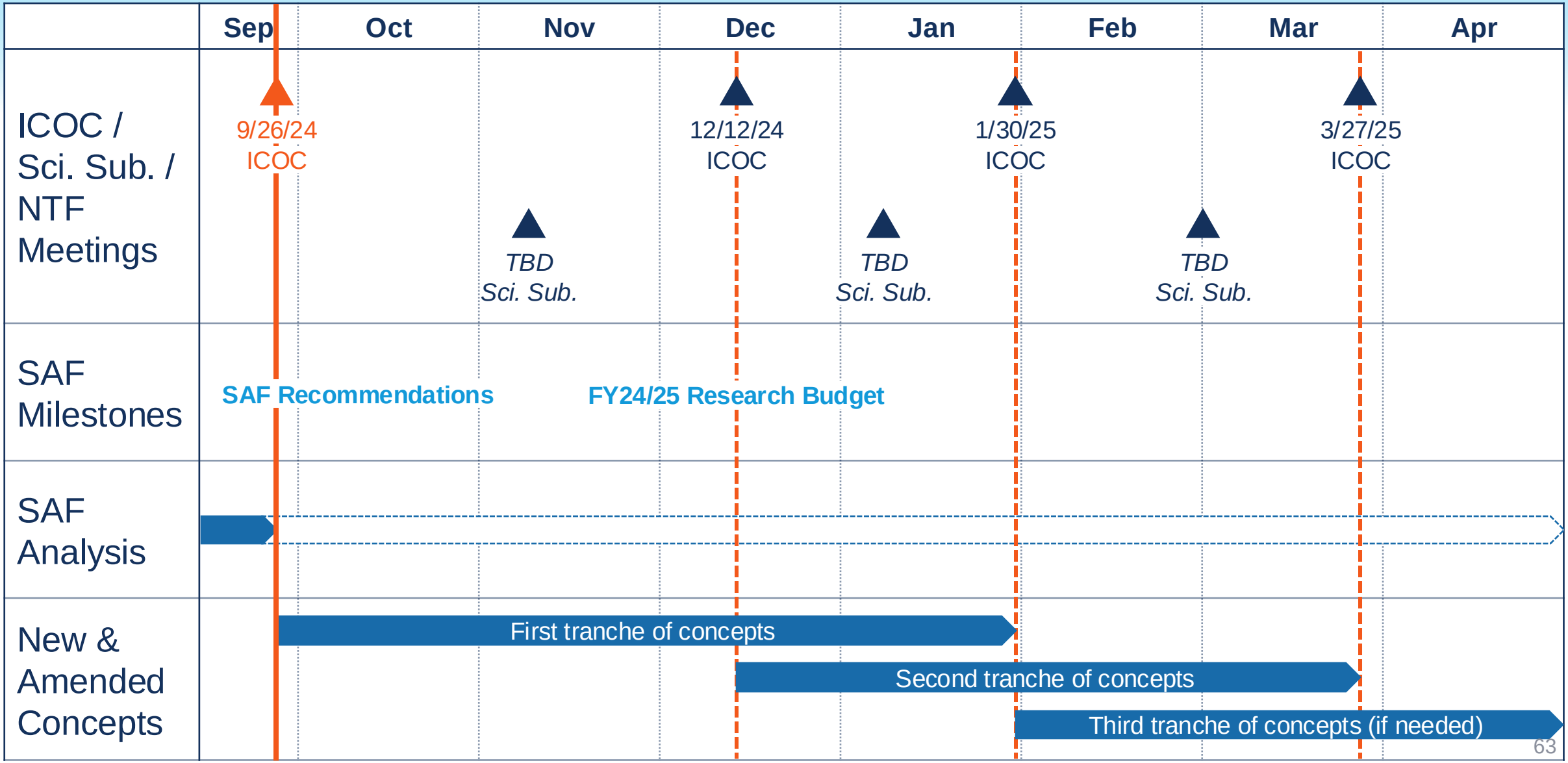
SAF Timeline (1/2)

TODAY



SAF Timeline (2/2)

TODAY



CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Next Steps | Concept Development & Amendments

Goal	Concept	Type	Tranche & ICOC Meeting
1	Revised DISC4/5 for Discovery Research	Amendment	1 - January
1	DCMC	New	TBD
2	Technology Platform Program Pilot	New	TBD
3	CLIN4 Updates	Amendment	2 - March
3	Rare Disease Platform Pilot	New	2 - March
4	Preclinical Development	New	1 - January
4/5	CLIN2 Updates	Amendment	1 - January
6	EDUC Training Program Updates	Amendment	TBD
6	EDUC Hybrid Skillset Training Program	New	TBD
Other	EDUC1 Conference Grant Updates	Amendment	2 - March

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Summary | SAF Goals & Recommendations (1/3)

Goals	Recommendations
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	**Support comprehensive discovery research through DISC4 & DISC5 funding structures** Encourage collaborative, multidisciplinary innovation in stem cell and genetic research across diverse disciplines & disease indications with early engagement of industry to address reproducibility & scalability issues **Establish a Data Coordinating and Management Center (DCMC) to streamline data management & enhance the utility of cross-disease data** Fund and develop a central hub for data coordination, facilitating better integration with consortia & research initiatives and enabling data science collaborative efforts via dedicated grants
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	**Pilot INFR Technology Platform Program to bridge the gap between research & commercialization** Foster partnerships between academic researchers & industry professionals to support multi-stakeholder technology incubation programs that achieve defined technology readiness levels thereby facilitating rapid application in cell & gene therapy development
3. Advance 4-7 rare disease projects to BLA	**Accelerate Current Rare Disease Therapy Pipeline** Increase and scale CLIN4 funding to comprehensively address BLA readiness gaps in manufacturing, clinical/non-clinical research, and pre-commercialization **Pilot Platform-Based Therapy Development** Implement pilot platform-based approach for gene therapy development using life-threatening monogenic neurological disorders as a test case

CIRM CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Summary | SAF Goals & Recommendations (2/3)

Goals	Recommendations
4. Propel 15-20 therapies targeting diseases affecting Californians to late-stage trials	**Streamline Preclinical Development Programs** Consolidate DISC2, TRAN1-4, and CLIN1 to accelerate the preclinical development incentivizing multidisciplinary collaborations and rapid progression to IND Incorporate prioritization of innovative therapies for diseases that affect Californians **Update CLIN2** Allow for support of emerging novel clinical trial designs in CLIN2 program Incentivize stage-appropriate market access strategy development and pre-commercialization activities in CLIN2 program Incorporate prioritization of innovative therapies for diseases that affect Californians
5. Ensure that every BLA-ready program has a strategy for access and affordability	**Strengthen Clinical Infrastructure Connectivity** Build interconnectivity & performance metrics between CIRM Clinical Infrastructure (Alpha Clinics, CCCEs, PSPs) to ensure enhanced referral, enrollment, & retention of California patients in clinical trials **Support Development of Market Access and Reimbursement Strategies** Resource clinical programs to support stage-appropriate planning & evidence generation to inform robust market access & reimbursement strategies **Influence Policy** Deploy AAWG resources to advocate for policies that advance access & reimbursement for regenerative medicines **Enhance Partnerships** Engage state & national partners to align initiatives that expand sustainable access to regenerative medicines

Summary | SAF Goals & Recommendations (3/3)

Goals	Recommendations
6. Bolster CIRM's workforce development programs to address gaps and meet evolving demands in regenerative medicine	**Provide high-demand technical training via Bridges & COMPASS program updates** Increase training offerings, diversify internship types, & increase integration with CIRM R&D grants
	Create new EDUC program to develop hybrid skillsets Implement new program structure to focus on cross-disciplinary internships
	Launch outreach campaigns to educate the public & increase diversity of California's regenerative medicine workforce Develop programming to support outreach/education efforts for K-12, teachers, & community members via collaboration with key stakeholders
Additional Recommendations	**Restart Grantee Conference to Report SAF Goal Progress** Restart recurring grantee conference (timing TBD) with main objective of reporting progress on SAF goals
	Keep Conference Grants for Specific CIRM Needs (EDUC1 Mechanism 2) Grantee retains the primary responsibility for planning, directing, and executing the proposed event; CIRM team will work closely with the grantee to design and implement an event responsive to a specific CIRM need

Requested Action

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

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