

# Portfolio Assessment and Progressions

Sara Taylor, Ph.D., Program Manager  
Elizabeth Noblin, Ph.D., Fellow  
Rosa Canet-Avilés, Ph.D., CSO

Programs and Portfolio Management Team  
June 26th, 2025  
ICOC



# Presentation Overview

1 Context (SAF)

2 Portfolio Audit/Review

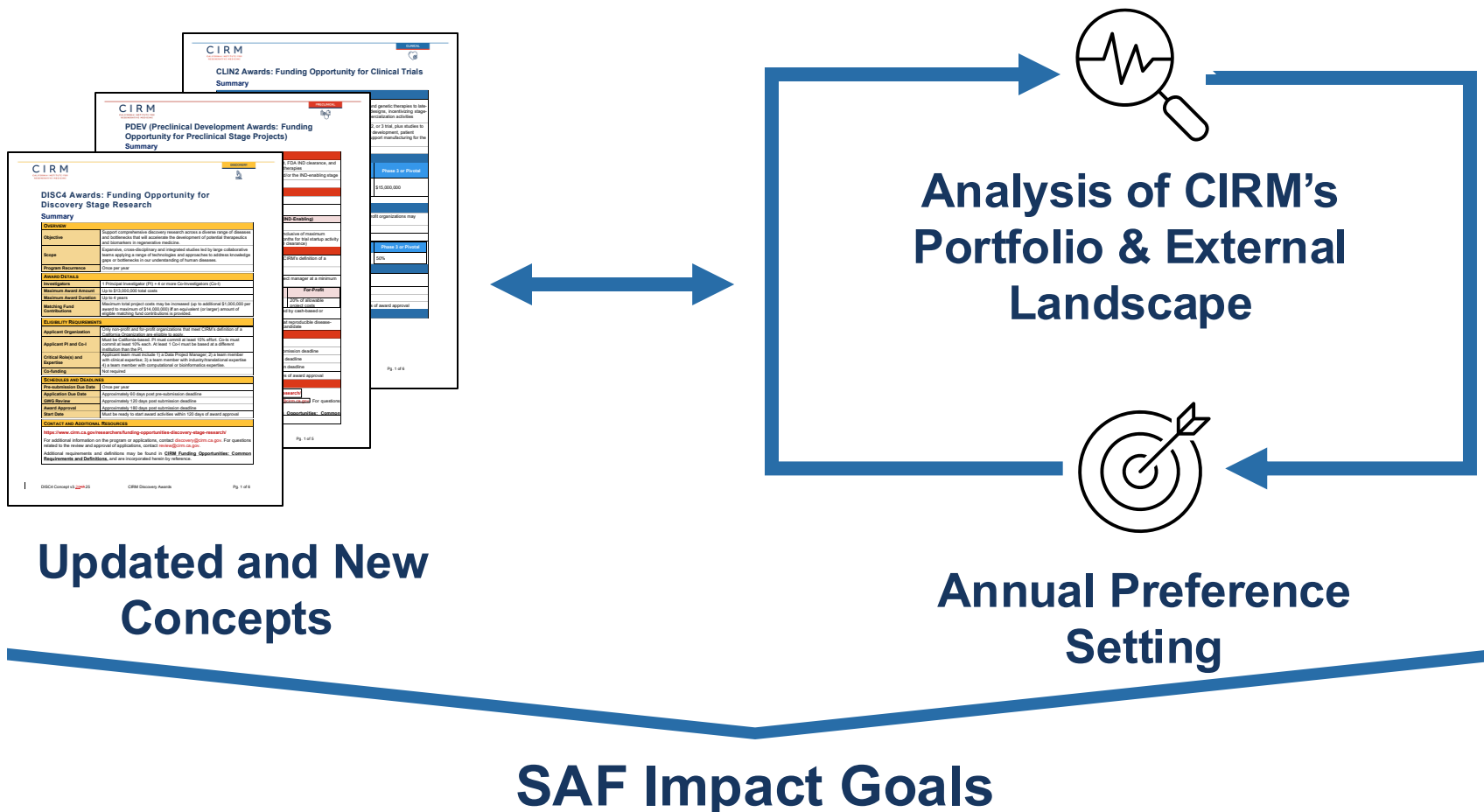
3 Portfolio Progressions

# SAF

- Responds to changes in the field & Prop 14
- Established quantifiable impact goals
- Initial projection of 6–10-year timeline
- Adaptive Model
  - Focuses resources on reaching impact goals
  - Supported by annual portfolio analysis & preference setting

# Preference Setting for Programs

Board-approved concepts include **annual adaptive preference setting** based on **portfolio analysis & external landscape** to enable **SAF goals**



# CIRM's 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

# Portfolio Assessments and SAF

*Multifaceted approach to track and adapt to progress*

## Portfolio Analysis

- Internal portfolio
- Progressions

## Landscape analysis

- Trends
- Innovations

## Audit/Review

- Award Management
- Structured learnings

**Adaptive Program Development**

**SAF Impact Goals**

# Content for ICOC Presentations

## June 2025 ICOC

- Portfolio Audits – Overview, Initial Results & Learnings
- Progressions – Overview & Examples

## January ICOC *(yearly)*

- Portfolio Audit Results & Learnings
- Internal Portfolio
- External Landscape
- Progressions

# Presentation Overview

1 Context (SAF)

2 Portfolio Audit/Review

3 Portfolio Progressions



# CIRM Award Management

## Award Management

- Periodic progress reporting (milestone-based updates & fund disbursements, financial reports)
- Continuous compliance monitoring
- Collaborative oversight by Grants Management and Science Officers

*Ongoing through CIRM lifetime*



## Portfolio Audits

- Recurring structured meetings to review award management findings
- Framework to incorporate learnings into programs & processes

# Portfolio Audit Impacts

*Strategic tool to advance SAF goals, promote success, & strengthen oversight*

## Individual award level:

- Support timely, coordinated responses to **address delays and compliance issues**
- Direct **promising programs** toward impactful outcomes
- Provide **shared visibility** into delays, misalignment, and funding risks

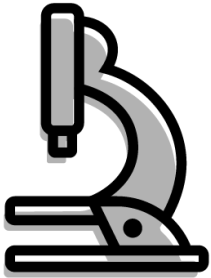
## Program/Portfolio level:

- Inform impactful **program development** as the field and portfolio mature
- Ensure **resource allocation aligns with** impact and progress
- Promote **transparency, accountability, and cross-functional learning**



**SAF Impact Goals**

# CIRM's Active Portfolio & Current Funding Opportunities



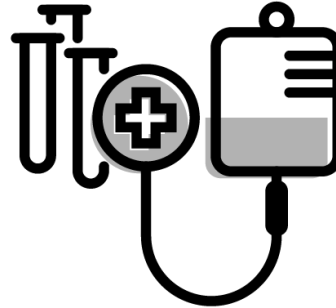
## Discovery

DISC0

DISC4 (ReMIND-L)

Updated DISC4

DISC5



## Preclinical Development

DISC2

TRAN

CLIN1

PDEV



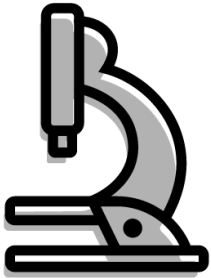
## Clinical Development

CLIN2

Updated CLIN2

# Portfolio Audit/Review | Current Scope

*Focus based on award amounts & operational milestone structure*



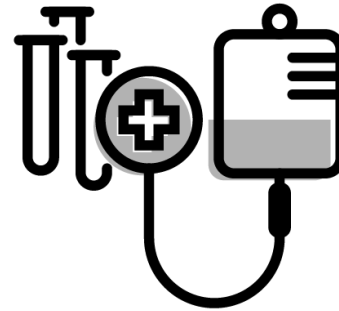
## Discovery

DISC0

DISC4 (ReMIND-L)

Updated DISC4

DISC5



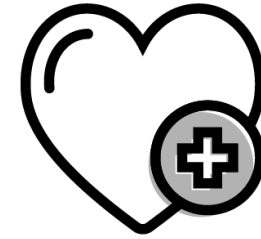
## Preclinical Development

DISC2

TRAN

CLIN1

PDEV



## Clinical Development

CLIN2

Updated CLIN2

# Portfolio Audit/Review | Process & Criteria

## Tailored by Award Type:

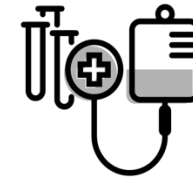
- Focused on complexity, regulatory stage, & financial exposure
- Started with: CLIN2, CLIN1, & TRAN
  - Stakes and maturity are higher
- Next: Discovery awards (*not today's presentation*)

## Criteria:



### CLIN2

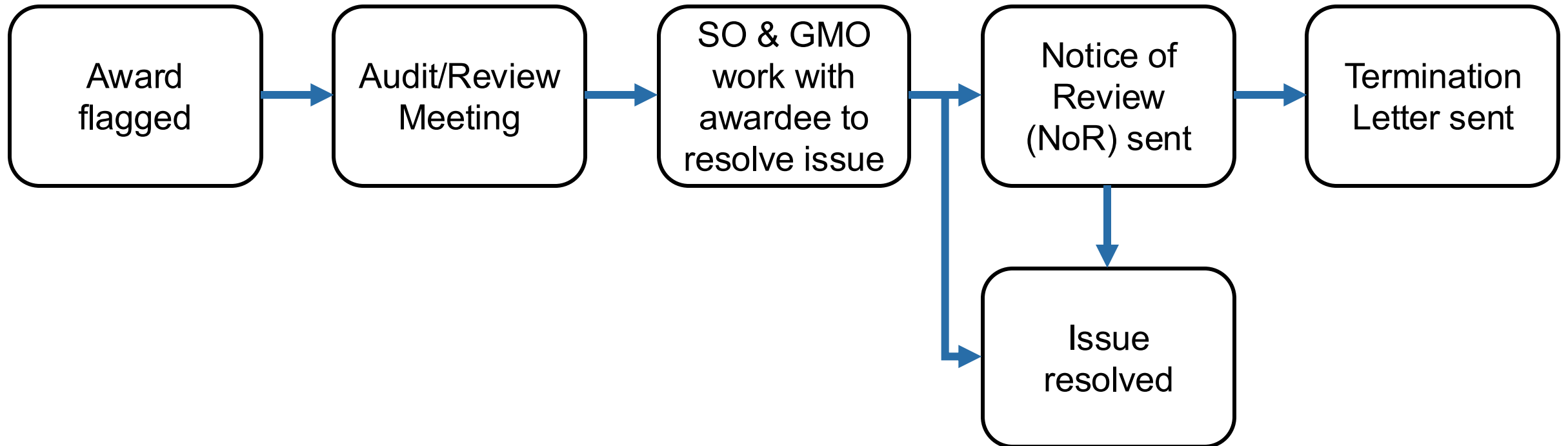
Clinical progression likelihood  
Delay > 4 months



### CLIN1 & TRAN

Delay > 4-6 months

# Portfolio Audit/Review | Process Overview



# Portfolio Audit/Review | Outcomes

Program	Total Awards*	Audited/ Reviewed	Notice of Review	Termination Letter**
CLIN2	67	32	14	3
CLIN1	31	29	3	1
TRAN	66	13	4	1

\*Awards open from September 2024 through present; \*\*Termination letter count is for awards surfaced through audits  
Data as of May 2025

# Example | TRAN1 Resolved *Without* Notice of Review

## Audit Findings

- **Reason flagged:** Issue identified in OM1 progress report
- **Delay length:** N/A
- **Delay drivers:**
  - Candidate optimization not part of original award

## Actions

- Since data supported change in scope, requested **PAR to revise OMs and success criteria** without changing payments or timeline

## Outcome

- Award **back on track**
  - Candidate finalized (optimized compared to the original)
  - Only 1 month behind original NOA timeline
- **New PDEV program** designed to allow **candidate optimization**



# Example | CLIN1 Resolved *After* Notice of Review

## Audit Findings

- **Reason flagged:** Delay
- **Delay length:** 8 month
- **Delay drivers:**
  - Manufacturing delay
- **Status:** First 3 OMs behind schedule

## Actions

- Sent **Notice of Review**
  - Manufacturing issue resolved
  - CRO paperwork delay didn't block next steps
- While addressing manufacturing delay with support from experts, SO identified potential animal study delays
  - **PAR** to holistically adjust OMs & disbursements

## Outcome

- Adjusting OMs & disbursements via a PAR helped **avoid additional delays** going forward

# Example | CLIN2 Termination

## Audit Findings

- **Reason flagged:** unlikely to progress clinically & delay
- **Delay length:** 42 months
- **Delay drivers:**
  - Slow enrollment & protocol amendment due to new SOC
  - COVID-19
- **Status:** Patient milestones met & waiting on CSR

## Actions

- Grantee proposed **expanded correlative studies** and **increased personnel costs** 42 months after completing original scope
- Additions not approved through PAR process
- Notice of Review issued to address compliance
- Sent Termination Letter

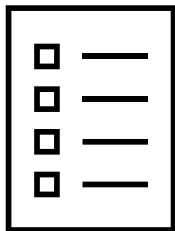
## Outcome

- Award **close out in process** (*pending submission of final documents*)

# Learnings | Delay Drivers

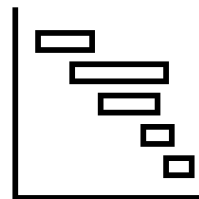
Delay Drivers	Clinical	Preclinical
Enrollment delays <ul style="list-style-type: none"><li>• Rare disease indications</li><li>• Changes to SOC/clinical trial landscape</li></ul>	×	
Subcontracting Delays <ul style="list-style-type: none"><li>• Manufacturing</li><li>• Trial Sites</li><li>• Tech Transfer</li><li>• Institutions</li></ul>	×	×
Team lacks experience in therapeutic development and/or lacks a commercial partner	×	×
CMC Issues	×	×
Slow CSR submission	×	

# Solutions | Program & Process Changes



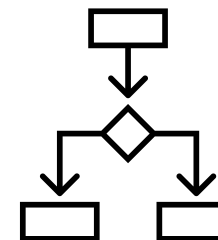
## Review & Preference Criteria

- ✓ Emphasize SOC & competitive landscape in review criteria
- ✓ Inclusion of therapies with potential to address barriers to access & affordability as preference criteria



## CMC & Commercialization

- ✓ Add stage-appropriate commercialization plans/activities to PDEV & CLIN2
- ✓ Focused leveraging of external SMEs to advance projects
- Manufacturing lead to report progress independent of PI



## Internal Process Updates

- ✓ Increase size of withheld final payment to encourage award close out
- ✓ Regular audit/review meetings to proactively monitor portfolio

## Portfolio Audit/Review | Next Steps

- Expand Audit/Review scope
- Continue sharing and implementing learnings
  - Updates included in annual January portfolio reports

# Presentation Overview

1 Context (SAF)

2 Portfolio Audit/Review

3 Portfolio Progressions

# Internal Progressions

Scope: CIRM 2.0 through SAF

## June 2025 ICOC

- **Context** for identifying & reporting progressions
- **Subset** of progressions
- **Example** of internal progression

## January 2026 *(yearly)*

- Progression **metrics and learnings** (as part of annual portfolio report)

# Context | Progression Metrics

- SAF reflects changes in the field and CIRM's expanded role under Prop 14
  - Updates CIRM's goals to match current needs
- Pre-SAF progression definitions and reports were based on earlier goals
- Detailed definitions support assessment of today's impact goals



# SAF 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

# Updated Progression Definitions

## Focus for Today

### Progression Example:



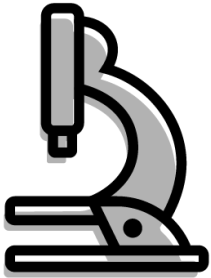
### Expansion Example:



### Next-Generation Example:



# Context | Current Portfolio & New Programs



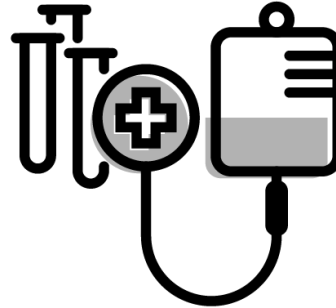
## Discovery

DISC0

DISC4 (ReMIND-L)

Updated DISC4

DISC5



## Preclinical Development

DISC2

TRAN1

CLIN1

PDEV

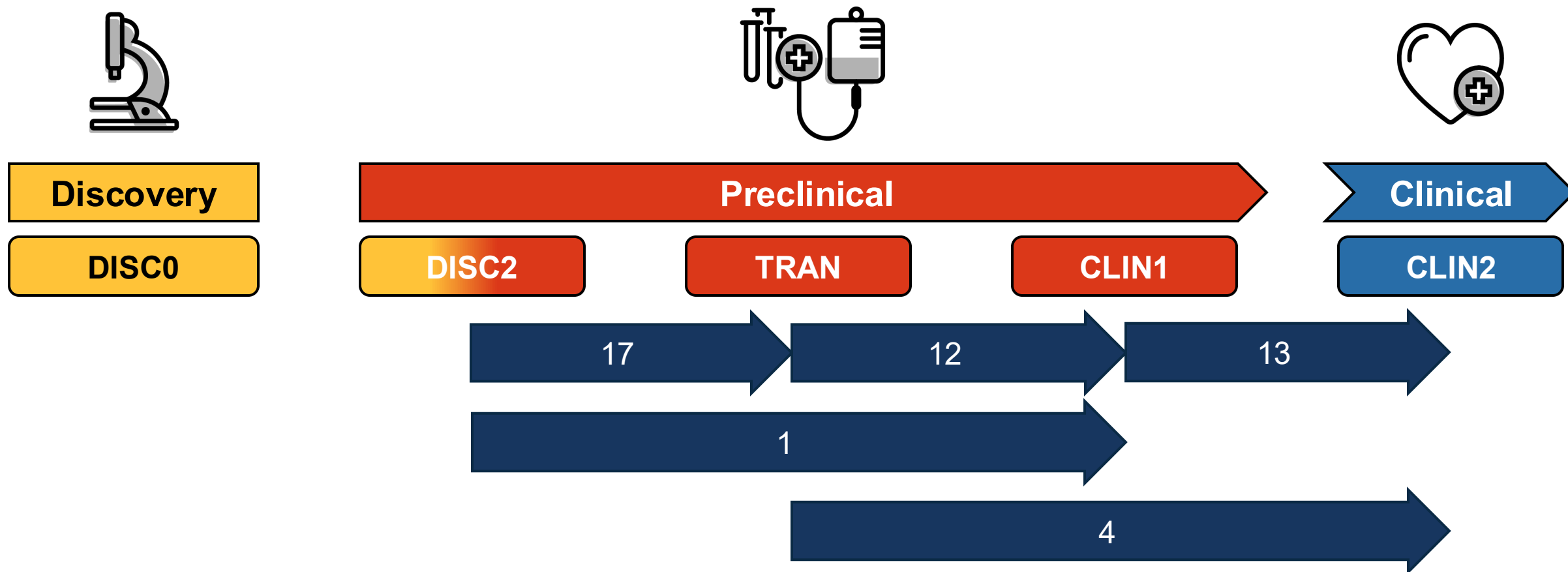


## Clinical Development

CLIN2

Updated CLIN2

# Progressions from CIRM2.0 Funding Programs\*



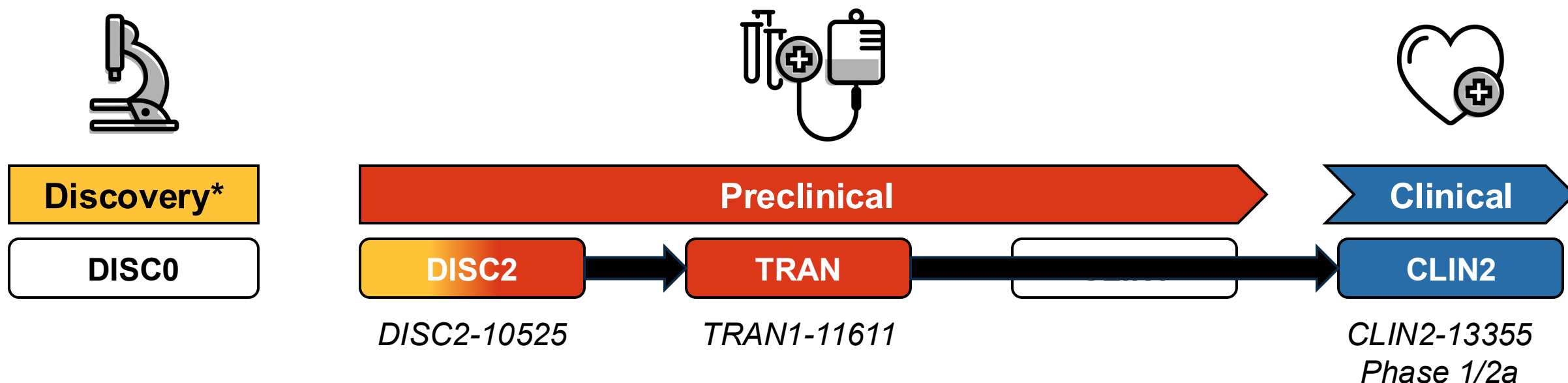
\*Excludes equivalent historical programs, next generation candidates, and expansions to new indications  
Data as of May 2025

# Progression Example: Neurona Therapeutics

**Candidate:** Inhibitory Interneuron Cell Therapy (NRTX-1001)

**Indication:** Drug-resistant Unilateral Mesial Temporal Lobe Epilepsy

**PI:** Cory Nicholas



As of May 2025; Neurona has received additional awards from CIRM outside of the direct progressions included on this slide

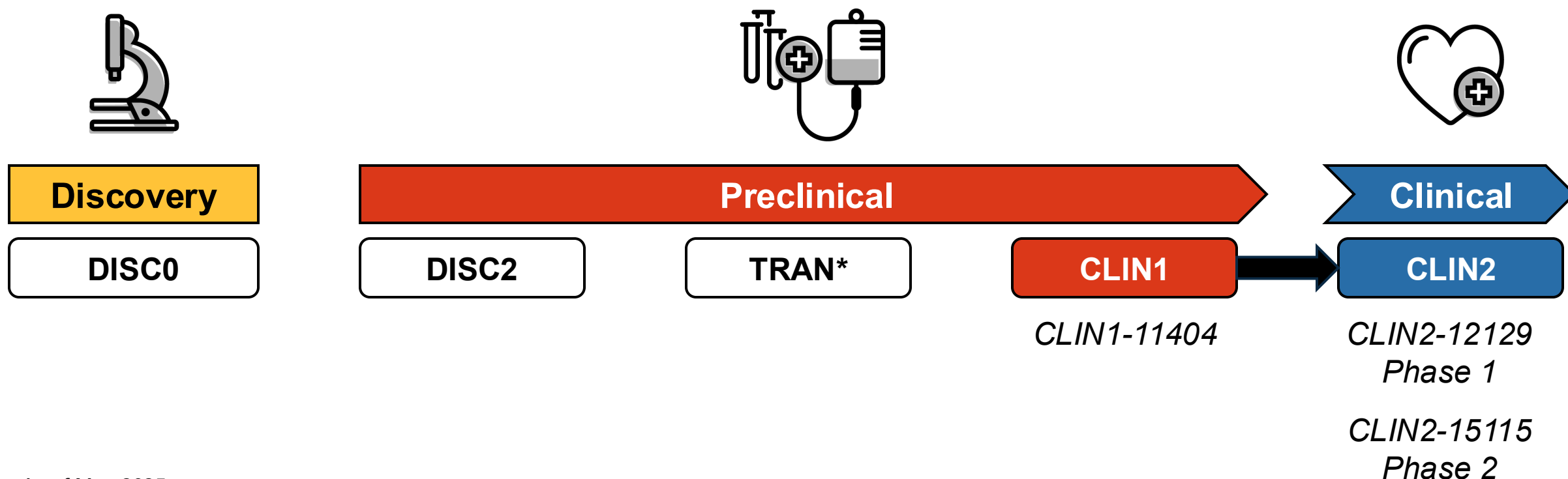
\* DISC2 progressed from several basic awards to the founders of Neurona Therapeutics

# Progression Example: Spina Bifida

**Candidate:** Allogeneic Placental Mesenchymal Stem Cells on a Biomaterial Scaffold (PMSC-ECM)

**Indication:** Myelomeningocele (Spina Bifida)

**PI:** Diana Farmer



As of May 2025

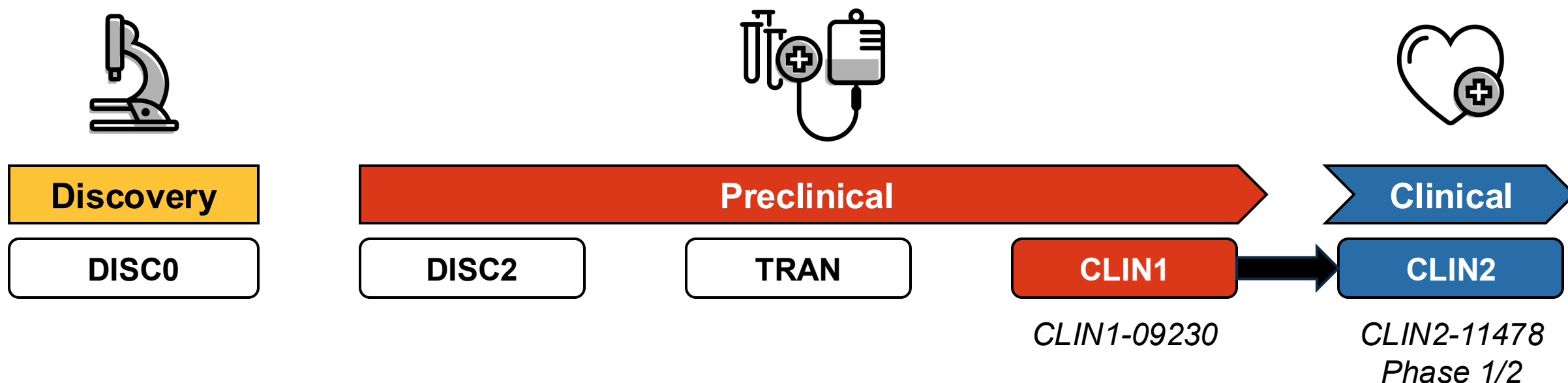
\* CLIN1 progressed from a translational CIRM1.0 award

# Progression Example: Cystinosis

**Candidate:** Autologous Gene-Modified Hematopoietic Stem Cell (DFT383)

**Indication:** Cystinosis

**PI:** Stephanie Cherqui



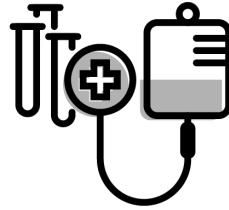
# Progressions | Learnings and Adaptations



## Discovery\*

### Updated DISC4

- Key Person with industry or translational experience required on project team
- Vision for Progression required in application



## Preclinical

### PDEV

- Single award mechanism accelerates progression to first-in-human trials
- Emphasis on comprehensive clinical planning



## Clinical

### Updated CLIN2

- Applications accepted after IND submission (progressing active CLIN1 awards)
- External expert advisors will support planning for next-stage trials



# Progression Reporting | Next Steps

- Updated progression definitions support tracking progress to SAF Impact Goals
- January ICOC will include a more comprehensive progression report
  - External progressions
  - Trends, learnings and program development

# Questions?