

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

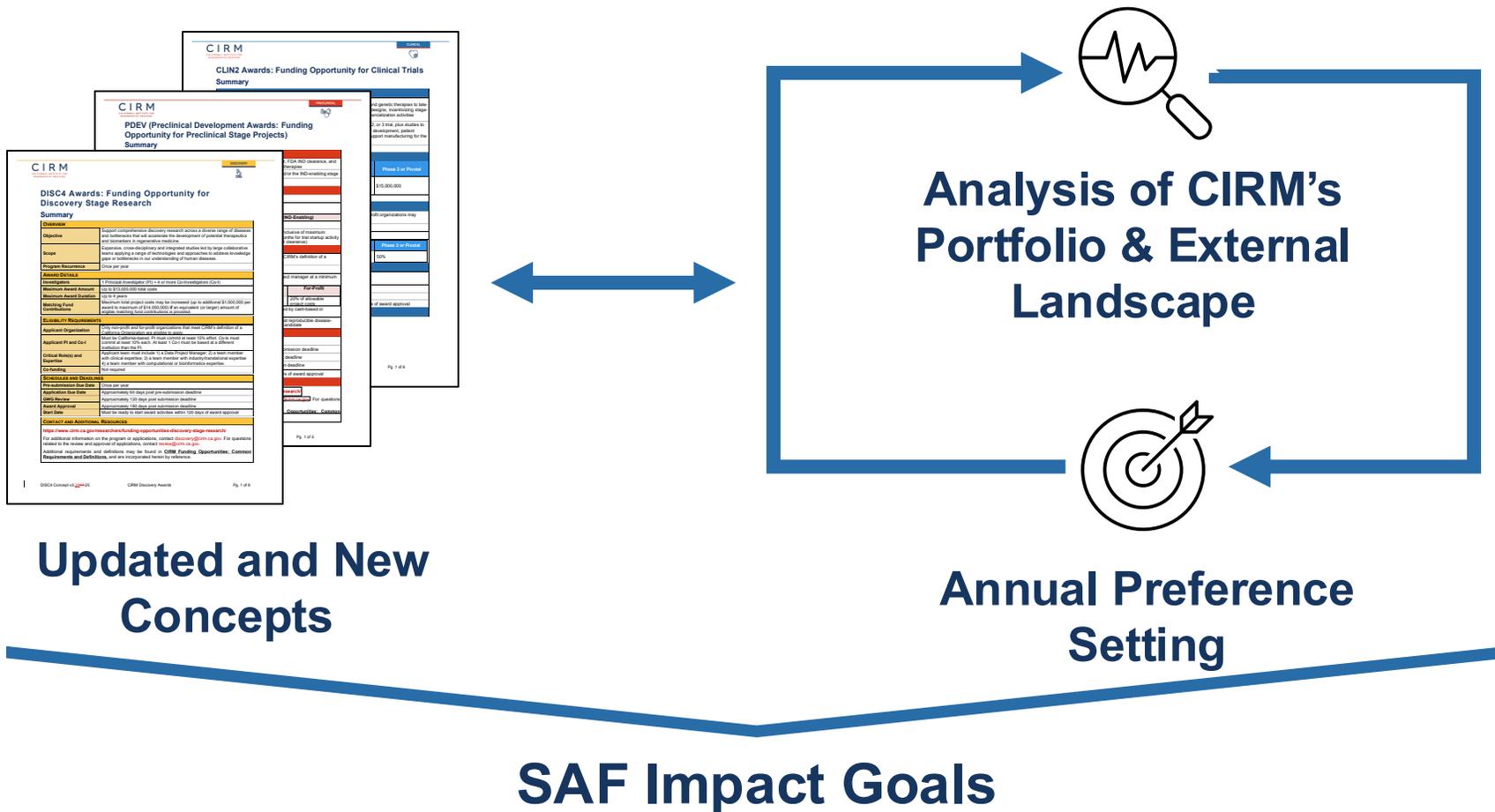
3 Portfolio Progressions

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

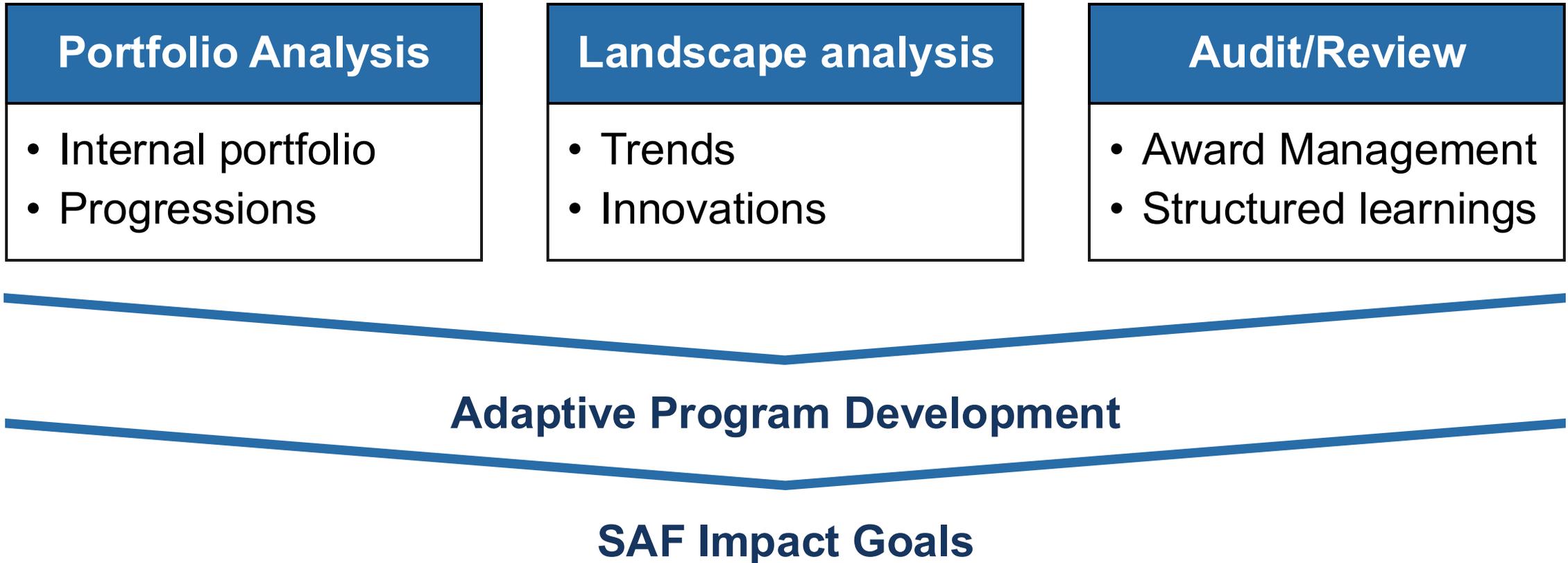
5. **Ensure** that every BLA-ready program has a strategy for access and affordability

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



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

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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

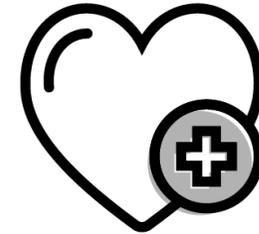
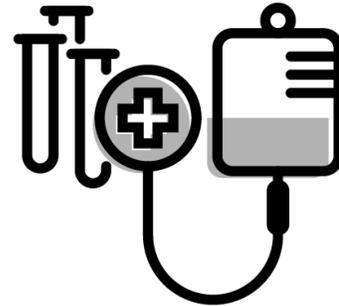
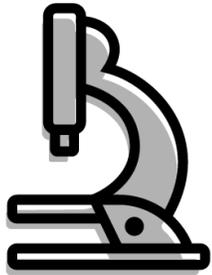
Individual award level:

- 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**

CIRM's Active Portfolio & Current Funding Opportunities



Discovery

DISC0

DISC4 (ReMIND-L)

Updated DISC4

DISC5

Preclinical Development

DISC2

TRAN

CLIN1

PDEV

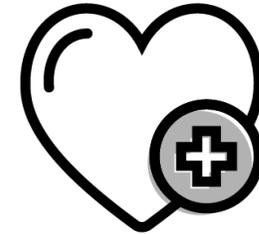
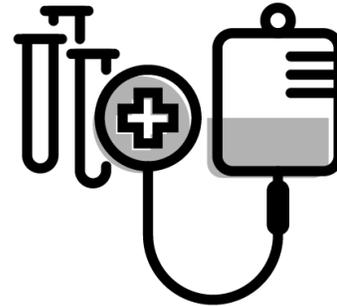
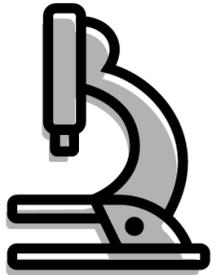
Clinical Development

CLIN2

Updated CLIN2

Portfolio Audit/Review | Current Scope

Focus based on award amounts & operational milestone structure



Discovery

Preclinical Development

Clinical Development

DISC0

DISC2

TRAN

CLIN1

CLIN2

DISC4 (ReMIND-L)

PDEV

Updated CLIN2

Updated DISC4

DISC5

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

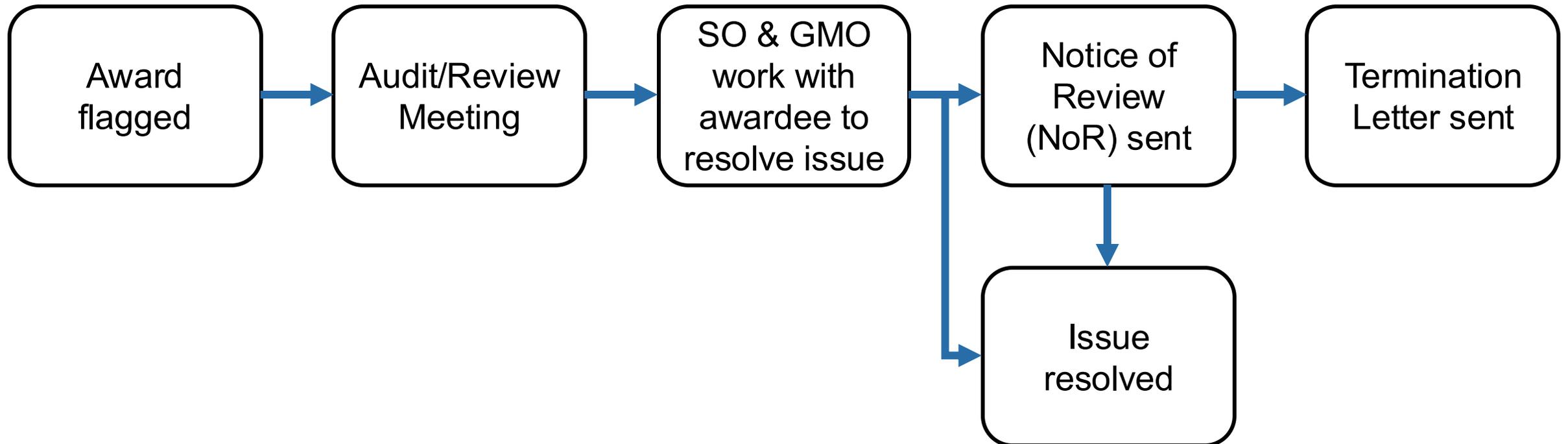
Clinical progression likelihood
Delay > 4 months



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

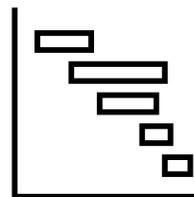
Delay Drivers	Clinical	Preclinical
Enrollment delays <ul style="list-style-type: none"> • Rare disease indications • Changes to SOC/clinical trial landscape 	✗	
Subcontracting Delays <ul style="list-style-type: none"> • Manufacturing • Trial Sites • Tech Transfer • Institutions 	✗	✗
Team lacks experience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

Solutions | Program & Process Changes



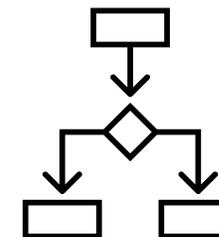
Review & Preference Criteria

- ✓ 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

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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

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Diverse Workforce Development

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Updated Progression Definitions

Focus for Today

Progression Example:



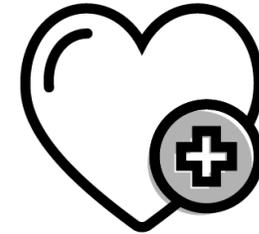
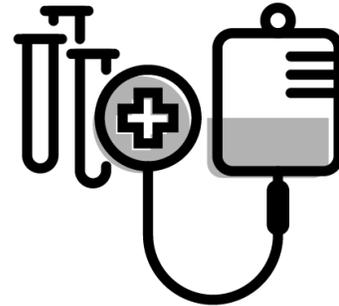
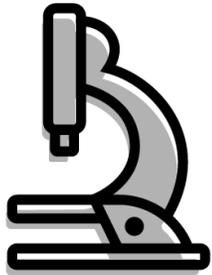
Expansion Example:



Next-Generation Example:



Context | Current Portfolio & New Programs



Discovery

DISC0

DISC4 (ReMIND-L)

Updated DISC4

DISC5

Preclinical Development

DISC2

TRAN1

CLIN1

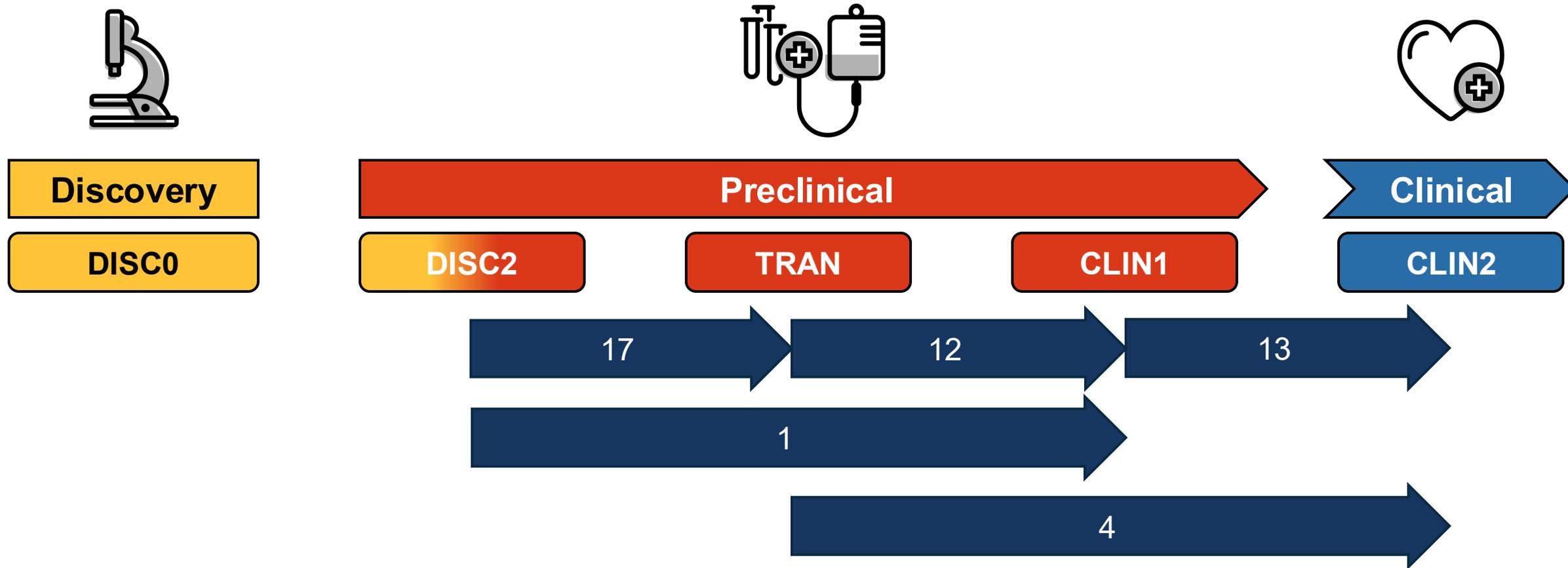
PDEV

Clinical Development

CLIN2

Updated CLIN2

Progressions from CIRM2.0 Funding Programs*



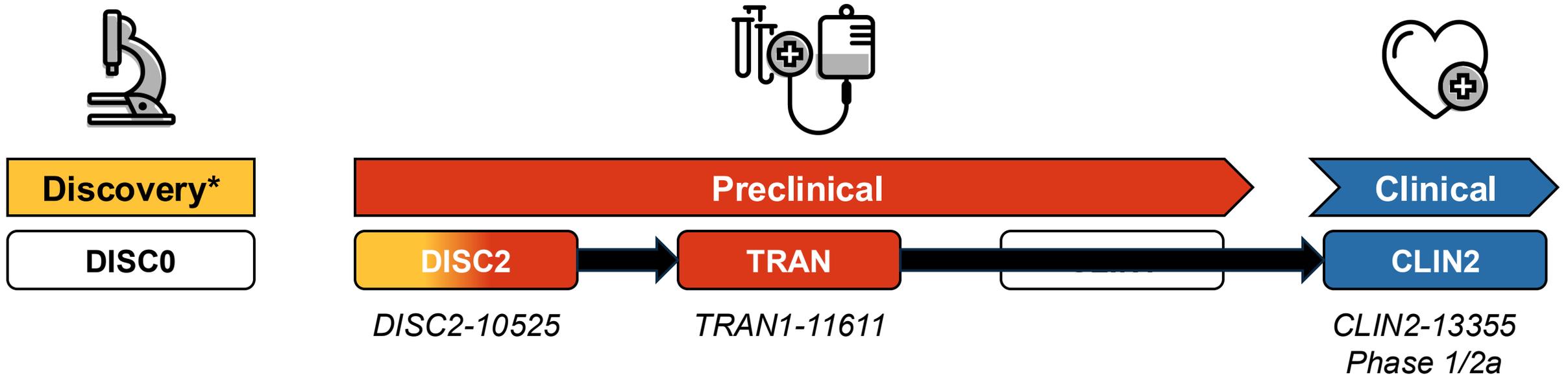
*Excludes equivalent historical programs, next generation candidates, and expansions to new indications
Data as of May 2025

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

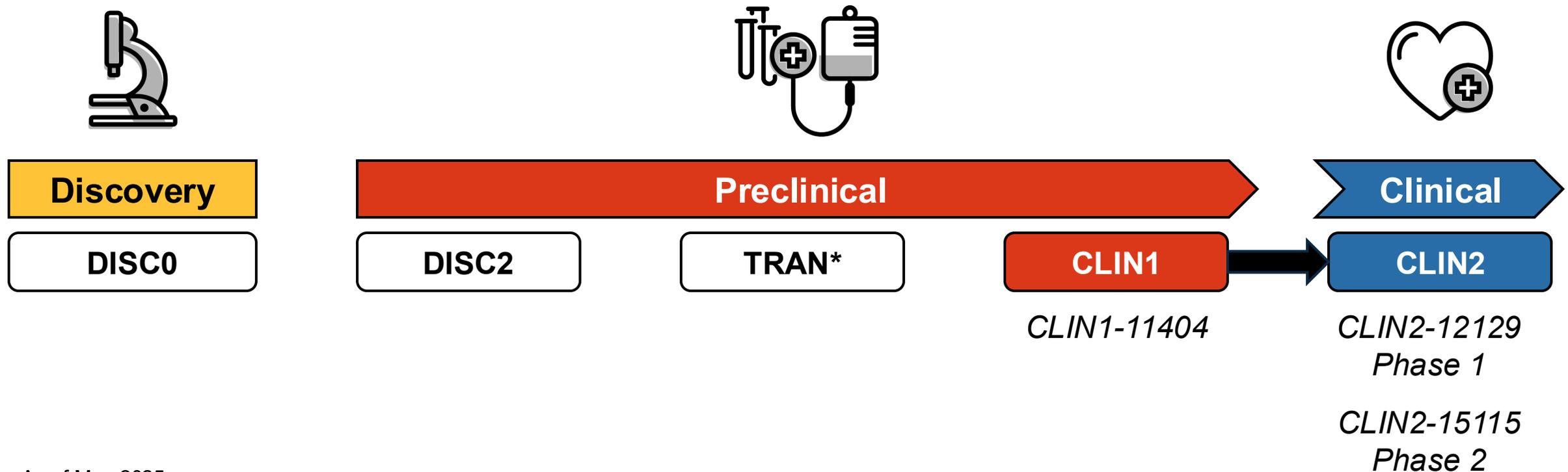
* DISC2 progressed from several basic awards to the founders of Neurona Therapeutics

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)

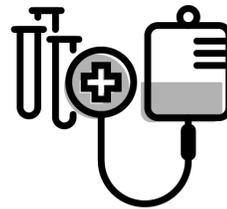
Indication: Cystinosis

PI: Stephanie Cherqui



Discovery

DISC0



Preclinical

DISC2

TRAN



Clinical

CLIN1

CLIN1-09230

CLIN2

CLIN2-11478
Phase 1/2

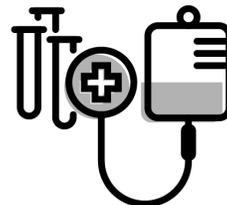
Progressions | Learnings and Adaptations



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?