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Memorandum

To: Members of the Science Subcommittee of the ICOC

From: Rosa Canet-Avilés, PhD, Chief Science Officer, Gil Sambrano, PhD., VP Review

Re: FY26/27 Program Guiding Principles & Review Process

Date: March 5, 2026

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Executive Summary

Over the past months, the CIRM team has gathered feedback from Board members, applicants, and reviewers regarding the implementation of program Preferences and their role in application volume control and portfolio steering. This memo reflects that feedback, incorporates early-cycle outcome data from PDEV, CLIN2, and DISC4, and proposes refinements to ensure that CIRM's funding processes remain scientifically rigorous, strategically aligned with the Strategic Allocation Framework (SAF), and operationally sustainable.

At the March 26 ICOC Meeting, we will be asking the ICOC to approve updated concepts for DISC4, PDEV, and CLIN2 to update how CIRM approaches application volume control and portfolio building, and to determine the area of focus for our upcoming DISC4 application cycle. This memo provides the ICOC with a structured review of the Preference-based approach implemented in FY25/26 and a forward-looking proposal to transition to a Guiding Principles-based framework applied consistently across the application and review lifecycle.

We are requesting that the Board:

- Provide direction on what CIRM should fund via feedback on the program-specific Guiding Principles
- Provide direction on how and where application filtering or volume control should occur
- Approve an area of focus for the next DISC4 cycle
- Approve opening the PDEV funding opportunity once per year

Summary of Feedback on Preferences

The ICOC and applicants raised concerns about the use of a point-based application of Preferences to filter volume of applications prior to full GWG review. Board members expressed discomfort that a threshold of Preference points effectively determined which proposals advanced to scientific merit review. The Board questioned the use of different score weighting mechanisms across the programs and whether these had unintended effects on the selection of projects. In particular, based on applicant feedback, the Board was concerned that the processes excluded entire categories of modalities or diseases areas.

At the same time, there was clear acknowledgment that CIRM cannot fund every scientifically meritorious application and that volume control is necessary in high-demand programs. Board members and applicants understood that preferences were introduced as a process efficiency tool to focus review on applications aligned with strategic priorities. They also recognized that such tools must be adjustable based on outcomes.

Transitioning from Preferences to Guiding Principles

The current DISC4, PDEV and CLIN2 programs are designed to respond to specific recommendations in the Strategic Allocation Framework. Each program has Guiding Principles for what it will fund, which are described in the Background and Objective sections of the Program Concept Plans and Program Announcements. Program Preferences were derived from Guiding Principles and were intended to be transparent and specific in order to facilitate an objective application volume filtering mechanism for each program. The Program

Preferences were thus playing double duty as prioritizing what each program funds and as filtering for application volume control.

The CIRM Team's analysis of Preference-based volume filtering outcomes is detailed in Appendix A. Our conclusions are largely aligned with the board's primary concerns about the Preference-based application volume filtering prior to GWG review. In addition, this Preference-based approach requires continual adjustment to align the portfolio with Guiding Principles. In summary, we concluded that the Preference-based approach is not a sustainable solution for achieving the dual goals of strategic funding prioritization and application volume control.

We are proposing to remove Preferences in favor of consistently applying each program's Guiding Principles across the application lifecycle to ensure that each program funds scientifically meritorious projects that are aligned with its funding priorities.

Today we are seeking Board feedback on three topics:

1. The nature of the projects we should fund as expressed in program-specific guiding principles
2. Ensuring that the Guiding Principles are applied most effectively throughout the review process, i.e., by the right party with the right information at the right time
3. Other updates to the PDEV and DISC4 Programs

Program Guiding Principles

Guiding Principles are how CIRM translates SAF recommendations into portfolio outcomes. As DISC4, PDEV and CLIN2 programs address different SAF Goals, it follows that these principles are tailored to the specifics of each program (shown below).

Each program's Guiding Principles are embedded within the fabric of the program. They are encompassed within program objectives, the review criteria by which projects are scientifically evaluated, and they help inform the recommendations that CIRM teams bring to the ARS to support funding decisions.

Here, we present Guiding Principles for CLIN2, PDEV, and DISC4. Appendix A and Appendix B include granular portfolio data (early cycle outcomes and active portfolio distribution) to aid the Board's consideration of Guiding Principles.

CLIN2

The CLIN2 portfolio will:

- Offer transformative impact for patients, meaning therapies that provide significant benefits over existing therapies
- Address known barriers to access and affordability* of stem cell-based and genetic therapies

* Refer to CIRM Access and Affordability Planning Requirements for definitions of key terms, program-specific requirements, and evaluation criteria.

- Broadly address both prevalent and rare diseases affecting Californians

PDEV

The PDEV portfolio will:

- Have potential to deliver transformative improvements in patient outcomes by leveraging cutting-edge therapeutic technologies
- Address known barriers to access and affordability* of stem cell-based and genetic therapies
- Broadly address both prevalent and rare diseases affecting Californians

DISC4

The DISC4 portfolio will:

- Create multidisciplinary research approaches that integrate diverse sources of evidence
- Innovate through collaboration, network synergy, and data leverage
- Implement Neuro Task Force & other organizational priorities

Proposed Plan to Implement Guiding Principles Across the Application and Review Lifecycle

To ensure that Guiding Principles are applied by the right party with the right information and at the right time, we are proposing the following implementation plan:

1. Volume Control: A volume control step in which GWG select projects using scientific value criteria defined from guiding principles;
2. Merit Review: Continued use of existing GWG review criteria, which were informed by program objectives and Guiding Principles; and
3. Funding Decision: Use of a standardized information package based on Guiding Principles to support CIRM Team recommendations that, along with GWG recommendations, will inform ARS's funding decisions.

This proposal preserves scientific review of applications and ensures that portfolio decisions are made transparently at the Board level. It also preserves the strategic focus established through the SAF by ensuring that portfolio outcomes help achieve Impact Goals. Each aspect of the above plan is summarized in Table 1 and elaborated in the memo sections below.

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Table 1. Summary of Guiding Principles Implementation Plan. Improved or changed processes shown in red.

	Volume Control	Merit Review	Funding Decision
Responsible Party	GWG	GWG	ARS
How Guiding Principles Are Applied	Selection Criteria	Review Criteria	Programmatic Factors
How CIRM Team Supports	• Define Selection Criteria • GWG Composition • Selection Process (Assignments, Feedback)	• Application • Define Review Criteria • GWG Review Process	• GWG Recommendation • Guiding Principles Summary • CIRM Team Recommendation

1. Guiding Principles in Volume Control

Scientific review of CIRM applications by the Grants Working Group (GWG) is time and resource intensive, effectively limiting the number of applications that can be fully reviewed in a single cycle. It is often the case that the number of applications received in response to a funding opportunity exceed this limit and strategies to narrow the pool of applications are required. Over CIRM's history, different strategies have been tested and utilized such as setting limits on the number of applications that CIRM would accept from any given organization; implementing a preliminary application process; or filtering applications through a positive selection process. This challenge is not unique to CIRM, and many funding agencies utilize different strategies to narrow the pool of applications received including NIH, NSF, CPRIT, and others.

The number of applications that are targeted for review by the full GWG (i.e., the number we wish to narrow the pool to) is based on preserving a high level of rigor in performing the evaluations by the 15 appointed scientific members of the working group along with the 7 patient advocate members. The number of available awards and expected success rate may also be considered in determining the number that advances to full review to ensure that the pool is sufficient while allowing for robust time and discussion during the GWG meeting phase.

GWG panels are tailored in their composition to the specific set of applications reviewed to ensure that the expertise is well matched. Recruitment of appropriate reviewers includes identifying specialists that can enhance the expertise of the panel. For CIRM, a complete evaluation may include elements not always present in other funding programs such as elements of population impact and access and affordability.

Over the last year, CIRM used "pre-submissions" (DISC4 & PDEV) and "qualification" (CLIN2) as methods to control volume that were dependent on the use of strict objective Preference criteria (Table 2). Although these methods proved effective in narrowing the pool, the use of preferences, in particular, has limited advancement of applications based on a set of unrefined characteristics rather than on a scientific assessment of the proposals.

Table 2. FY25/26 Volume Control Approaches

	DISC5	DISC4	PDEV	CLIN2
Current Process	Positive Selection	Pre-Submission	Pre-Submission	Qualification
Submission	Full Application	Pre-Sub Form	Pre-Sub Form	Full Application
Selection by	GWG	CIRM	CIRM	CIRM/GWG
Basis for selection	Scientific value	Objective preferences	Objective preferences	Objective preferences Scientific value

Goals of the Proposed Process

In examining the feedback and outcomes from the preferences-based approach to volume control, there are key goals we sought to accomplish in proposing a different approach as follows:

- Refocus the selection of applications on science rather than strict preferences.
- Align programs with a more consistent volume control process:
    - Applicants can use a unified procedure to apply across programs with minimal variability.
    - Leverage the long-standing learnings of positive selection process (since 2015) to continue making improvements.
- Increase efficiency and the opportunity to learn and implement improvements across programs.
- In Table 2 above are the varied volume control processes that were utilized over the past year across the noted funding opportunities. There is variability in the operational aspects of the process itself but also who makes the selections and the basis for the selections.

The proposed approach which we term “GWG selection” is a slight modification of the existing positive selection process utilized by the GWG to narrow a pool of applications. The process can be adapted to each of the different funding opportunities, but with some differences related to the expected application volume as shown in the table 3 below.

Table 3. Proposed Use of GWG Selection for Volume Control. Proposed changes from current process are in red.

Selection Process	Positive Selection (existing)	GWG Selection DISC4	GWG Selection PDEV	GWG Selection CLIN2
Submission	Full App	Pre Sub Form	Full App	Full App
Reviewer Scoring	Advance or Not	Select & Rank	Select & Rank	Select & Rank
Expected Reviewer Number	15	15-30	15-20[†]	15
Assignments	Optional	Required	Required	Required
Number of Apps per Reviewer	Open but must review minimum number	Fixed, must review same as all others	Fixed, must review same as all others	Fixed, must review same as all others

To illustrate the process, we provide an example where the application volume is 200 applications (such as DISC5) and the pool is narrowed to 50 applications that advance to GWG panel review. The other example demonstrates a narrowing of a smaller number of applications from 20 to 10, as might occur with CLIN2.

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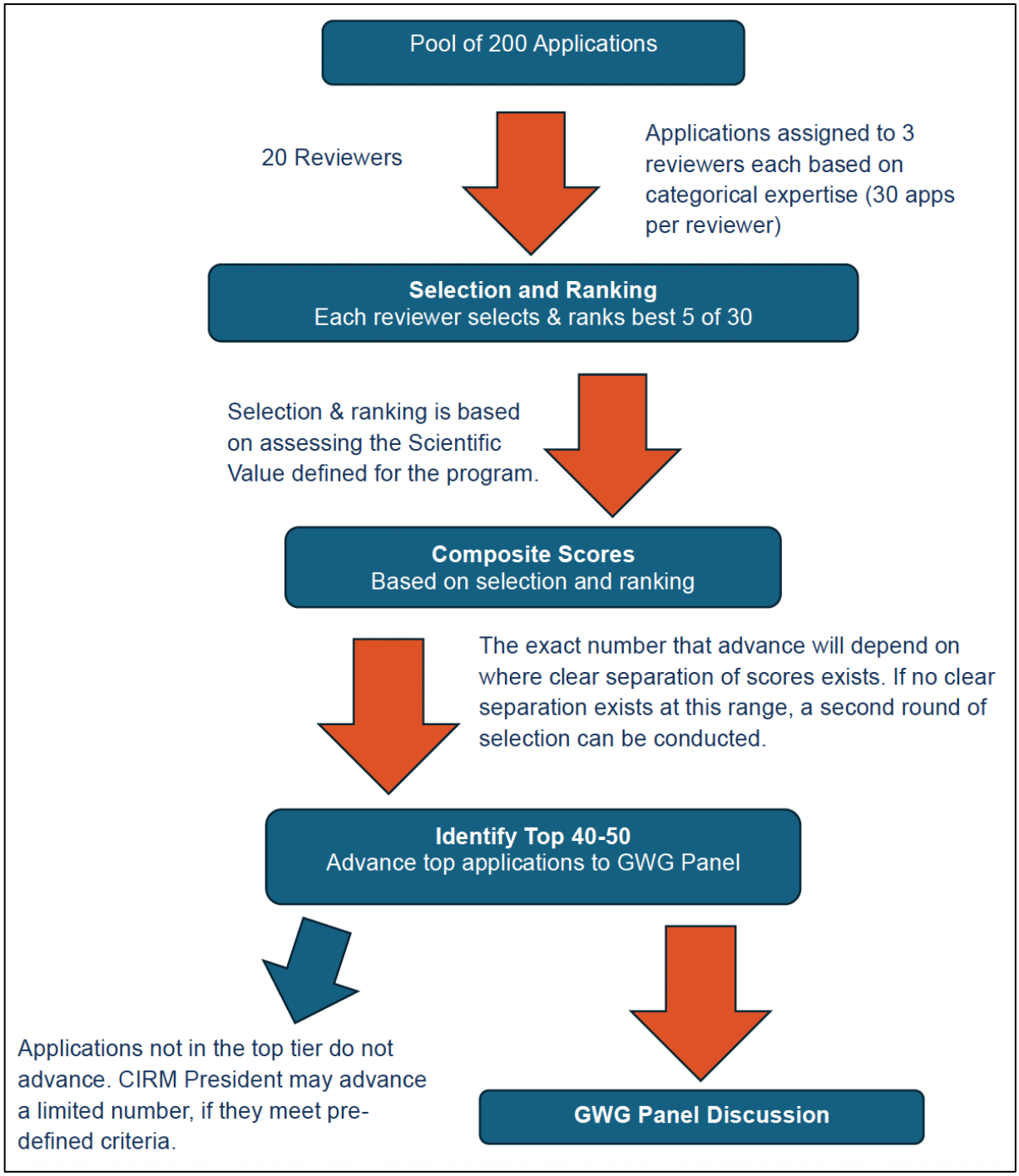
[†] This number assumes two PDEV cycles per year. If ICOC approves one PDEV cycle per year, the expected review number would be 30-40.

Figure 1. Example 1: 200 Applications



In this example, 200 applications make use of 20 GWG reviewers with varied expertise to cover broad categorical areas. Each reviewer is assigned to 30 applications which results in 3 reviews per application (600 total reviews for the pool). Each reviewer identifies and ranks the top 5 applications within their pool. The number of reviewers in this model, balances good overlap of applications among reviewers and representation

of the larger pool to reduce batch-strength distortion, reviewer bias effects, and luck of assignment. The goal is to advance about 25% of the pool or about 50 applications.

The selection frequency and rankings can be normalized to produce a composite score for each application. For example, rankings can be assigned points (i.e., ranking of 1= 5pts, ranking of 2 = 4 pts, etc). Overall rankings using this model are expected to generate sufficient granularity to discern the top 40 to 50 applications. However, if a clear separation does not exist, a second round of selection of the top and/or next level tier can be performed.

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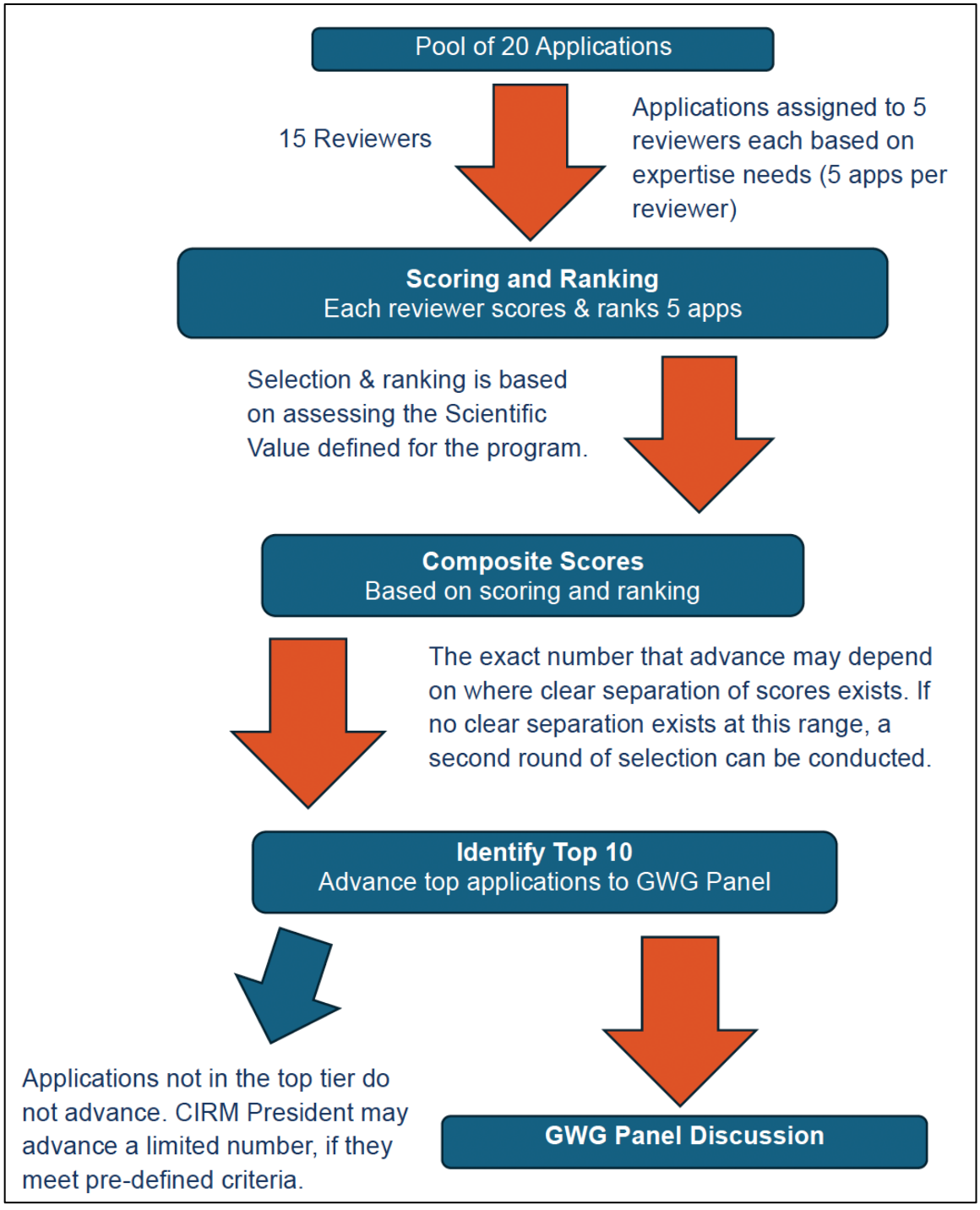
Figure 2. Example 2: 20 Applications



In this example, 20 applications make use of 15 GWG reviewers with varied expertise to cover more specific categorical areas. Each reviewer is assigned to 5 applications which results in 5 reviews per application (75 total reviews for the pool). Each reviewer scores and ranks all applications within their pool. The number of

reviewers in this model allows a greater degree of coverage and greater precision in determining the cutoff. The goal in this example is to advance 50% of the pool or 10 applications.

The rankings can also be normalized to produce a composite score for each application. As with the previous example, if a clear separation does not exist, a second round of selection can be performed.

GWG Selection Criteria

The Selection Criteria to be used by the GWG (i.e., to select which ones advance to full evaluation) will be aligned with the guiding principles for that program and will also incorporate the first element of the full review criteria defined in the Program Announcement for that funding opportunity. Applications that advance will be reviewed and scored against the full set of criteria by the GWG. The Criteria for GWG selection of applications for each program are listed below.

The GWG Selection process for each program will be guided by GWG Selection Criteria, which are derived from the Program Guiding Principles.

Criteria for GWG selection of CLIN2 applications: Scientific Value

- Impact of the proposed treatment for patients if successfully developed
- Significance of the unmet need that is being addressed
- Practicality and feasibility of the proposed treatment to be adopted by patients and healthcare providers
- Readiness of project to advance and complete a successful clinical trial

Criteria for GWG selection of PDEV applications: Scientific Value

- The therapy's potential to provide a meaningful and substantial improvement in clinical outcomes for the intended population as compared to therapies currently available or in trials.
- Impact of addressing the unmet medical need on patients, caregivers, and the healthcare system
- The therapy's potential to be more accessible and affordable compared to available treatments or therapeutics currently in clinical development.
- Feasibility and practicality of the therapy's uptake by patients, caregivers, and healthcare system.

Criteria for GWG selection of DISC4 applications: Scientific Value

- Impact of the proposed project in advancing understanding of a human disease, generating data/resources, or where outcomes rapidly advance a therapeutic or biomarker.
- Innovation relative to the current state of research such as applying novel frameworks to study of disease, cutting across silos, employs unique synergy of technologies, or utilizing innovative approaches.

Applying GWG Selection on Full Applications vs. Pre-submissions

Applying GWG Selection on a full application benefits programs where the assessment of readiness elements and availability of supporting project information is critical to the selection. For PDEV and CLIN2, benefits of GWG selection on a full application include:

- Completeness of project information for GWG selection. Survey of GWG reviewers indicates that the majority (95%) use the full application to make final selections.
- Ensures that eligibility can be fully determined: unlikely that an ineligible application takes up a valuable slot.
- Ensures selected projects are at the appropriate stage of readiness with all regulatory, CMC, and product development elements in place (PDEV & CLIN2).
- The time from submission to award is significantly shorter and mitigates project changes and "staleness" over time.

In DISC4, where a new focus area is selected annually and success hinges on forming novel multi-disciplinary teams, GWG selection on a pre-submission allows new teams more time to form and respond to a focus area once it is announced.

2. Guiding Principles in GWG Review

The GWG evaluates selected applications based on review criteria defined in each Program Announcement. These criteria are designed to provide a thorough scientific evaluation grounded in program objectives and guiding principles. Full review criteria for DISC4, PDEV, and CLIN2 programs are provided in Appendix C for reference.

3. Guiding Principles in ARS Decisions

The CIRM team has historically provided recommendations and analysis to support the ARS in making informed funding decisions. The ARS may consider these recommendations along with GWG summaries and public comment in its funding decisions. Here, we describe an updated CIRM Team Recommendation framework that provides standardized analysis grounded in Guiding Principles to support the ARS at this critical portfolio decision-making step.

Following GWG Merit Review, the CIRM Team will prepare Guiding Principles Summaries evaluating each application scoring >80 points, as well as applications with a Minority Report (issued when 35% or more GWG reviewers score an application 85 or above).

In the case of the PDEV and CLIN2 programs, each summary will address the Guiding Principles as follows:

PDEV/CLIN2 Guiding Principle Addressed	Information Provided to ARS
Transformative Clinical Impact	• Summary of GWG sentiment • Comparison to active awards & external landscape within the same indication
Accessibility & Affordability	• Summary of GWG sentiment • Summary of A&A reviewer sentiment • CIRM knowledge of the modality / route of administration
Disease Representation	• Disease area representation of active CIRM portfolio

In the case of the DISC4 program, each summary will address the Guiding Principles as follows:

DISC4 Guiding Principle Addressed	Information Provided to ARS
Multidisciplinary research approach	• Summary of GWG sentiment
Collaboration, network synergy, & data leverage	• Summary of GWG sentiment • Comparison of research approaches and topic areas to active DISC portfolio • Potential to enhance DISC4 networks
Neuro Task Force & other organizational priorities	• Fit within annual focus area • Additional considerations concerning evolving research landscape and funding need

In addition, the CIRM team will generate a Funding Recommendation that incorporates the following:

- Available program budget
- GWG score & comments
- Guiding Principles summary (as shown above)
- Prior awardee performance
- New information available to CIRM after GWG review

This information will be delivered in a memo to the ARS. Applicants will also be informed of the CIRM Team recommendation at the time they receive their GWG review outcomes. A sample ARS memo is provided in Appendix D.

The Application Review Subcommittee (ARS) will make final funding determinations informed by both the GWG's assessment of scientific merit and the CIRM team's structured analysis.

Proposal for DISC4 FY26/27 Funding Area

Strategic Focus as a Catalytic Instrument

DISC4 supports coordinated, multidisciplinary research at a larger scale and level of maturity within the Discovery Program.

Its purpose is not to preserve breadth across the entire discovery landscape, but to enable concentrated investment in defined scientific areas where coordinated effort may accelerate discovery and facilitate transition toward downstream development. Selection of this scientific area is informed by DISC4 Guiding Principles.

In the FY25/26 Program Announcement, DISC4 remained open to all eligible discovery-stage proposals but prioritized neurological diseases (including disorders of the brain, spinal cord, and peripheral nervous system) during the pre-submission and programmatic consideration stages. This cycle-specific prioritization was informed by NTF recommendations and portfolio analysis, while preserving the broader discovery scope of the program.

DISC4 FY26–27 Proposal: Immune–Tissue Interplay in Disease, Homeostasis, and Repair

This thematic focus:

- Applies across a broad spectrum of diseases affecting Californians (fibrosis, autoimmune disease, inflammatory disorders, neurodegeneration, organ failure, oncology, injury)
- Naturally lends itself to multidisciplinary and omics-driven approaches characteristic of DISC4
- Enables identification of novel targets and biomarkers distinguishing maladaptive versus productive repair
- Supports development of improved human stem cell and organoid models
- Creates strong opportunities for network synergy across funded programs

As with prior cycles, implementation would occur at the pre-submission stage, with topic clarity provided upfront. Pre-submissions will be filtered to final invited applications by the GWG Selection process described above.

PDEV Cycle Recurrence

When the Preclinical Development Program (PDEV) was approved by the ICOC on March 27, 2025, the concept plan had specified two application funding cycles per fiscal year. After careful evaluation of the application cycle frequency for this program as detailed below, the CIRM Team seeks Board approval to revise the PDEV concept plan to specify one application funding cycle per fiscal year.

Two Application Cycles Per Fiscal Year

Some of the key advantages of incorporating two application funding cycles per fiscal year are listed below along with their applicability to the PDEV Program. As the table indicates, due either to the features of the PDEV program or practical implications of the CIRM application lifecycle, most of these advantages don’t apply to the PDEV program.

Potential Benefit of Two Cycles per Fiscal Year	Applicability to PDEV Program
Alignment of application cycle availability with project readiness	The PDEV program is designed to allow for application submission at any entry point across the preclinical development lifecycle. In the two cycles to date, applications have ranged from very early projects starting with candidate optimization activities to later-stage projects that have conducted a pre-IND meeting and have started IND-enabling activities.
Applications can be resubmitted in the next application cycle with limited delay	In the two cycles to date, due to partial overlap of submission cycles, it was not possible for an application to immediately resubmit in the next cycle. The length of the application lifecycle from submission through ARS approval does not make it feasible to incorporate two non-overlapping application cycles in the same fiscal year.
Batching of application review, ARS review, and award launch throughout the fiscal year	The first PDEV cycle allocated $117.6M of the $160M Fiscal Year Program Budget leaving only $42.4M for the second PDEV cycle. Given this experience, we expect the first cycle of the fiscal year to have much higher applicant demand than the second cycle.

Practical Implications of One PDEV Cycle Per Fiscal Year

The shift to a single PDEV application funding cycle per fiscal year has the following practical implications:

- All submitted applications compete for the full program budget.
- Unfunded applications may re-submit in the next fiscal year application cycle (approximately 6 months later)
- Higher volume of applications reviewed to account for full program budget
- Program updates are efficiently implemented in the next fiscal year application cycle.
- Application availability, application due date, review cycles and award contracting timelines are optimized to meet PA requirements and minimize calendar conflicts (i.e. holiday periods).

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Requested Action

The CIRM team requests Science Subcommittee's recommend approval of the concept amendments to CLIN2, PDEV, and DISC4 programs, incorporating the changes to Guiding Principles, Guiding Principles implementation, DISC4 focus area, and PDEV once-per-year cycle occurrence presented here.

Exhibits to Memo:

- CLIN2 Concept Plan 5MAR2026 Clean Copy
- CLIN2 Concept Tracked Changes 5MAR2026
- PDEV Concept Plan 5MAR2026 Clean Copy
- PDEV Concept Tracked Changes 5MAR2026
- DISC4 Concept Plan 5MAR2026 Clean Copy
- DISC5 Concept Tracked Changes 5MAR2026

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Appendix A. Outcomes of preference scoring from the first cycles of PDEV, CLIN2, and DISC4

Original Intent of Preferences

Preferences were introduced in FY25/26 as a tool for volume control and portfolio shaping, not as a replacement for scientific merit review.

As presented to the Board in January, Preferences were intended to shape portfolio trajectory early in the application lifecycle (i.e. before full GWG review) while maintaining scientific rigor as the central evaluative mechanism.

The design assumption was that strategic steering and review efficiency could be integrated into a single process step. The first cycles provided an opportunity to test that assumption.

Implementation of Preferences in PDEV and CLIN2 Programs

For both PDEV and CLIN2 programs, the preferences were implemented in application volume filtering mechanisms prior to Grants Working Group Review. The implementation of application volume preferences differed between the two programs.

The CLIN2 program retained the prior Qualification mechanism but with the incorporation of preferences as objective scoring criteria.

The PDEV Program incorporated a pilot of a new Pre-submission process that allowed for staff filtering based on preferences and other criteria prior to invitation for submission of full applications. The PDEV Pre-Submission Process incorporated objective scoring of preferences as well as scoring for under-represented disease area and novelty of therapeutic approach to allow for a balanced portfolio of applications for GWG review.

For FY 25/26, the preferences were designed to enrich the portfolio for:

1. Therapeutic technologies that could address known A&A barriers
2. CNS diseases
3. Project acceleration potential (progressions, regulatory milestones, late-phase trials)

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Summary of FY 25/26 PDEV and CLIN2 Application Cycle Volume Filtering Outcomes

CLIN2

Across two CLIN2 application cycles, the qualification process resulted in applications that were enriched for in vivo genetic therapy, PSC-derived therapies and CNS diseases compared to the application pool. Of the 13 applications that were forwarded to GWG Review, 12 met in vivo gene therapy and/or CNS disease preference. The single application that did not meet either of these preferences was selected by the GWG via the tie-breaking process.

PDEV

The PDEV Pre-Submission process deployed a weighted scoring process across four criteria: Prop 14 preferences (PSC-derived, in vivo GT, CNS), Other Preferences, Under-Represented Disease Area, Novelty of Approach. This rubric was intended to allow for a broad range of projects to be invited for submission, including novel therapeutic approaches that did not specifically meet preference scoring. The rubric was slightly modified between Cycle 1 and Cycle 2: the weight of the under-represented disease area preference was reduced from 2 to 1, and the comparator set for under-represented disease area and novelty scoring was expanded from active CLIN2 awards to active TRAN1/CLIN1/CLIN2 awards. In both cycles, an objective tie-breaker was used to achieve the target application volume in applications with an identical score. For cycle 1, the tie-breaker was used on pre-submissions scoring 6 points and pre-submissions that met the CNS and progressions preferences were selected. For cycle 2, the tie-breaker was used on pre-submissions scoring 5 points and pre-submissions with the highest disease prevalence were selected.

Cycle 1 (168 submitted, 33 invited): The pre-submission process resulted in enrichment for in vivo genetic therapies, PSC-derived therapies, non-viral nucleic acid delivery, under-represented disease area and portfolio progression preferences compared to the full pre-submission pool. The process resulted in under-representation of projects that utilized autologous cell therapy modalities or projects that targeted the oncology disease areas compared to the full pre-submission pool. It resulted in no representation of projects that targeted the hematology disease area. Hematology and oncology are two of the highest represented disease areas in the CIRM active awards portfolio. With respect to the influence of novelty scoring, only one invited pre-submission did not meet one of the Prop 14 preferences. The novelty scoring selected for novel approaches within the pool of pre-submissions that scored for the Prop 14 preferences.

Cycle 2 (126 submitted, 23 invited): The pre-submission process resulted in enrichment for PSC-derived therapies, non-viral nucleic acid delivery and portfolio progressions. With respect to the influence of novelty score, no pre-submissions were invited for application that did not meet one of the Prop 14 preferences. The novelty scoring did select for novel approaches within the pool of pre-submissions that scored for the Prop 14 preferences. With respect to disease area representation, the metabolic disease area was over-represented and oncology disease area was under-represented in the invited pre-submissions compared to the pre-submission pool.

CIRM Team Observations on the Preferences and Volume Filtering Process for PDEV & CLIN2

The preferences and volume filtering processes as currently designed, while effective in rapidly filtering the volume, have the following limitations:

- The specificity of preferences, while advantageous for transparency and objectivity, result in a subset of preferences having a disproportionate effect on the filtering outcomes.
- The preferences and preference-based volume filtering process, as currently designed, will require continuous monitoring and adjustment by CIRM and the ICOC to align with strategic portfolio goals.

Implementation of Preferences in DISC4: Strategic Focus as a Catalytic Instrument

Where PDEV and CLIN2 function as broad translational programs requiring portfolio-level steering, DISC4 was approved as part of a complementary discovery-stage award structure designed to support coordinated, multidisciplinary research at a larger scale and level of maturity within the Discovery Program. Its purpose is not to preserve breadth across the entire discovery landscape, but to enable concentrated investment in defined scientific areas where coordinated effort may accelerate discovery and facilitate transition toward downstream development.

Thus, in DISC4, “Preference” is not a tool to shape portfolio balance but rather a strategic instrument to implement a scientific focus. As conceived in the DISC4 concept, the board will approve an area of focus on an annual basis. In March 2025, CIRM’s board selected “Neurological Diseases (including conditions and disorders of the brain, spinal cord, and peripheral nervous system) as the preference topic for the FY 25-26 Cycle.

The DISC4 concept also piloted use of a Pre-submission process to help enrich for proposals that would be best suited to benefit from the DISC4 grant mechanism, where the nature and scale of investment is most likely to yield transformative impact. Pre-submissions were short project summaries that were evaluated by the CIRM team using an objective rubric to determine which would be invited to submit a full application (shown below). Thus, similar to the processes developed for PDEV and CLIN2, the use of Preferences served the dual purpose of prioritization and volume control.

Within CIRM’s Discovery Program:

- DISC5 supports comprehensive discovery research across a diverse range of diseases and bottlenecks, funding exploratory and innovative foundational research that employs human stem cells and/or genetic research as a central approach. It is not topic-restricted.
- DISC4 was structured as a focused discovery opportunity, operating at a different scale and supporting multidisciplinary teams aligned around defined scientific themes, affording the potential to leverage data and resources across a network to maximize scientific impact

DISC4's focused structure traces back to the ReMIND Program, developed in response to Proposition 14's CNS mandate and refined in partnership with the Neuroscience and Medicine Task Force (NTF). While ReMIND-L strategically focused on neuropsychiatric disorders based on scientific opportunity and portfolio considerations at that time, the broader ReMIND vision was to catalyze multidisciplinary networks addressing fundamental gaps across CNS diseases. That experience demonstrated the value of defined thematic calls in driving convergence and shared infrastructure. The current DISC4 iteration builds on that structural model through a rotating focus approach that preserves NTF-driven scientific prioritization within the CNS mandate while maintaining DISC4 as an open, all-comers discovery platform. Thematic emphasis alternates by cycle and is informed by NTF recommendations, portfolio analysis, and annual Board consideration. Its focused elements therefore reflect intentional program design and Board-level strategy.

In the FY25/26 Program Announcement, DISC4 remained open to all eligible discovery-stage proposals but prioritized neurological diseases (including disorders of the brain, spinal cord, and peripheral nervous system) during the pre-submission and programmatic consideration stages. This cycle-specific prioritization was informed by NTF recommendations and portfolio analysis, while preserving the broader discovery scope of the program.

Summary of FY 25/26 DISC4 Application Cycle Volume Filtering Outcomes

The results of the 2025-2026 cycle indicate that prospective applicants understood that DISC4 was focused on a defined scientific topic and that this area of focus would be implemented through the use of a rubric. Of the 138 pre-submissions received, 86% were focused on neurological conditions encompassing a broad array of topics including neurodegeneration, neurodevelopment, and neuro-oncology. The remainder focused on non-neurological systems. Topics and score distribution across all pre-submissions can be viewed in Table 4B.

Due to the anticipated size and complexity of DISC4 applications, CIRM targeted 20 to 24 projects for Grants Working Group Review. Following the use of the rubric, the top scoring teams were invited to submit full applications. All 24 addressed the neurological focus area and like the starting pool, reflected a broad diversity of topics. However, given the high number of pre-submissions, the practical effect was that projects outside the defined focus area (even those with potential for high impact) had limited opportunity to advance.

This was not the result of hidden gating mechanics, but rather the predictable outcome of a tightly scoped thematic call combined with high demand.

This highlights a different strategic insight than that observed in PDEV and CLIN2. For DISC4, the central question is not how to refine gating mechanics, but how to calibrate scope and thematic breadth when the Board wishes to signal openness to a wider range of high impact science.

CIRM Team Observations on the DISC4 Implementation Process

- A clearly defined focus area attracted a highly targeted pool of applications
- Scientific quality remained strong under the focused call
- Defined themes promote scientific leverage within and across projects
- Defined themes allowed a review panel with more specialized and relevant expertise to be assembled
- When demand is high, a thematic focus functions as a practical filter

The strategic question for DISC4 is therefore different from that of PDEV and CLIN2 Preferences. It is not whether upstream gating is appropriate; it is how focus should be defined, calibrated, and iterated over time to maximize impact.

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Table 1. FY25/26 Preferences & Volume Control by Program

	PDEV	CLIN2	DISC4
Preferences	• Pluripotent stem cell-derived therapies • In vivo genetic therapies • Therapies using non-viral nucleic acid delivery • Projects addressing diseases of the brain and CNS • Projects progressing from DISC2 & TRAN1 Awards • Projects in which a pre-IND or INTERACT meeting has been conducted	• Pluripotent stem cell-derived therapies • In vivo genetic therapies • Therapies using non-viral nucleic acid delivery • Projects addressing diseases of the brain and CNS • Applications from California organizations • Projects progressing from CIRM-funded IND-enabling or earlier phase clinical trial awards • Projects with Fast Track, RMAT or Breakthrough designations • Projects proposing pivotal clinical trials (as agreed-to by the FDA)	• FY25-26 Focus Area: Neurological Diseases • Relevance to human disease biology • Cross-disciplinary and systems biology • Stem cell or genetic research innovations
Volume Control Method	• Point-based preference scoring of pre-submissions	• Point-based preference scoring of applications • GWG tie-breaking	• Point-based preference scoring of pre-submissions

CNS: Central Nervous System; IND: Investigational New Drug Application; INTERACT: INitial Targeted Engagement for Regulatory Advice on CBER/CDER ProducTs; RMAT: Regenerative Medicine Advanced Therapy

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Table 2A. PDEV FY25/26 Preference Scoring Rubric

Preference	Points
At least one of the following: • PSC-derived therapies • In vivo genetic therapies • Diseases of the CNS	3
• Non-viral nucleic acid delivery	1
• Pre-IND or INTERACT meeting conducted	1
• Progression from DISC2 or TRAN1	1
• Targeting disease area under-represented in CIRM active awards portfolio	1
• Novelty of therapeutic approach compared to CIRM active awards portfolio	0-2

PSC: Pluripotent Stem Cell; CNS: Central Nervous System; IND: Investigational New Drug Application; INTERACT: INitial Targeted Engagement for Regulatory Advice on CBER/CDER ProducTs

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Table 2B. PDEV Cycle 1 Preference Scoring Results (1 of 4)

Modality	Disease Area	Total Score	Invited*	Funded
Genetic therapy (cell free)	Muscle Disorders	3 1 1 2 2 = 9	✓	✗
Autologous cell therapy	Other;Urinary disorders	3 1 1 2 2 = 9	✓	✓
Genetic therapy (cell free)	Muscle Disorders	3 1 2 2 = 8	✓	✗
Genetic therapy (cell free)	Muscle Disorders	3 1 2 2 = 8	✓	✓
Allogeneic cell therapy	Muscle Disorders	3 1 2 2 = 8	✓	✗
Genetic therapy (cell free)	Respiratory Disorders	3 1 2 2 = 8	✓	✗
Genetic therapy (cell free)	Cardiovascular Disorders	3 1 2 2 = 8	✓	✗
Genetic therapy (cell free)	Respiratory Disorders	3 1 2 2 = 8	✓	✓
Allogeneic gene-modified cell therapy	Cardiovascular Disorders	3 1 2 2 = 8	✗	✗
Autologous gene-modified cell therapy	Neurologic Disorders	3 1 1 1 2 = 8	✓	✓
Genetic therapy (cell free)	Skin Disorders	3 1 2 2 = 8	✗	✗
Allogeneic cell therapy	Muscle Disorders	3 1 2 2 = 8	✓	✗
Genetic therapy (cell free)	Cardiovascular Disorders	3 1 1 2 1 = 8	✓	✓
Genetic therapy (cell free)	Cardiovascular Disorders	3 1 1 2 1 = 8	✓	✓
Genetic therapy (cell free)	Cardiovascular Disorders	3 1 2 2 = 8	✓	✓
Genetic therapy (cell free)	Bone & Cartilage Disorders	3 1 2 2 = 8	✓	✗
Allogeneic cell therapy	Bone & Cartilage Disorders	3 1 2 2 = 8	✓	✓
Allogeneic cell therapy	Cardiovascular Disorders	3 1 2 2 = 8	✓	✗
Autologous gene-modified cell therapy	Neurologic Disorders	3 1 1 2 = 7	✓	✗
Genetic therapy (cell free)	Metabolic Disorders	3 1 1 2 = 7	✓	✗
Autologous gene-modified cell therapy	Respiratory Disorders	1 1 1 2 2 = 7	✓	✗
Genetic therapy (cell free)	Metabolic Disorders	3 1 1 2 = 7	✓	✗
Genetic therapy (cell free)	Metabolic Disorders	3 1 1 2 = 7	✓	✗
Allogeneic cell therapy	Neurologic Disorders	3 1 1 2 = 7	✓	✓
Genetic therapy (cell free)	Muscle Disorders	3 2 2 = 7	✓	✗
Genetic therapy (cell free)	Metabolic Disorders	3 1 1 2 = 7	✓	✓
Genetic therapy (cell free)	Kidney Disease	3 1 1 2 = 7	✓	✗
Genetic therapy (cell free)	Cardiovascular Disorders	3 1 2 1 = 7	✓	✗
Allogeneic gene-modified cell therapy	Metabolic Disorders	3 1 1 2 = 7	✓	✗
Genetic therapy (cell free)	Neurologic Disorders	3 1 2 = 6	✓	✗
Genetic therapy (cell free)	Neurologic Disorders	3 1 1 1 = 6	✓	✗
Small molecule	Brain Cancers	3 1 1 1 = 6	✓	✗
Genetic therapy (cell free)	Neurologic Disorders	3 1 1 1 = 6	✓	✓
Allogeneic gene-modified cell therapy	Neurologic Disorders	3 1 1 1 = 6	✗	✗
Allogeneic cell therapy	Eye/Vision Disorders, Neurological	3 1 1 1 = 6	✓	✗
Genetic therapy (cell free)	Neurologic Disorders	3 1 2 = 6	✗	✗
Small molecule	Neurologic Disorders	3 1 2 = 6	✗	✗
Autologous gene-modified cell therapy	Neurologic Disorders	3 1 2 = 6	✗	✗
Autologous gene-modified cell therapy	Neurologic Disorders	3 1 2 = 6	✗	✗
Autologous gene-modified cell therapy	Neurologic Disorders	3 1 2 = 6	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3 1 2 = 6	✗	✗
Allogeneic gene-modified cell therapy	Neurologic Disorders	3 1 2 = 6	✗	✗

PSC / Neuro / In vivo | Non-Viral Nucleic Acid | Meeting Conducted | Progression | Under-Represented Disease Area | Novelty**

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Table 2B. PDEV Cycle 1 Preference Scoring Results (2 of 4)

Modality	Disease Area	Total Score	Invited*	Funded
Genetic therapy (cell free)	Neurologic Disorders	3 1 2 6	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3 1 2 6	✗	✗
Genetic therapy (cell free)	Eye/Vision Disorders, Neurological	3 1 2 6	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3 1 2 6	✗	✗
Biologic, excluding gene therapy	Cardiovascular Disorders	1 1 2 2 6	✗	✗
Biologic, excluding gene therapy	Cardiovascular Disorders	1 1 2 2 6	✗	✗
Biologic, excluding gene therapy	Metabolic Disorders	3 1 1 1 6	✗	✗
Autologous cell therapy	Hematology Disorders	3 1 2 6	✗	✗
Allogeneic cell therapy	Cardiovascular Disorders	3 1 2 6	✗	✗
Genetic therapy (cell free)	Solid Tumors	3 1 2 6	✗	✗
Allogeneic cell therapy	Cardiovascular Disorders	3 2 1 6	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3 1 2 6	✓	✓
Genetic therapy (cell free)	Solid Tumors	3 1 1 5	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3 1 1 5	✗	✗
Genetic therapy (cell free)	Cancers, Multiple Types/Sites	3 1 1 5	✗	✗
Genetic therapy (cell free)	Hematologic Malignancies	3 1 1 5	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3 2 5	✗	✗
Small molecule	Neurologic Disorders	3 2 5	✗	✗
Allogeneic gene-modified cell therapy	Metabolic Disorders	3 1 1 5	✗	✗
Genetic therapy (cell free)	Bone & Cartilage Disorders	3 2 5	✗	✗
Genetic therapy (cell free)	Eye/Vision Disorders, Neurological	3 1 1 5	✗	✗
Genetic therapy (cell free)	Cardiovascular Disorders	3 2 5	✗	✗
Biologic, excluding gene therapy	Brain Cancers	3 1 1 5	✗	✗
Autologous cell therapy	Neurologic Disorders	3 2 5	✗	✗
Autologous cell therapy	Neurologic Disorders	3 1 1 5	✗	✗
Genetic therapy (cell free)	Eye/Vision Disorders, Non-neurological	3 1 1 5	✗	✗
Allogeneic gene-modified cell therapy	Bone & Cartilage Disorders	1 2 2 5	✗	✗
Allogeneic cell therapy	Neurologic Disorders	3 1 1 5	✗	✗
Allogeneic cell therapy	Cardiovascular Disorders	3 2 5	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3 2 5	✗	✗
Genetic therapy (cell free)	Hematologic Malignancies	3 2 5	✗	✗
Genetic therapy (cell free)	Cardiovascular Disorders	3 2 5	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3 2 5	✗	✗
Genetic therapy (cell free)	Cardiovascular Disorders	3 2 5	✗	✗
Genetic therapy (cell free)	Brain Cancers	3 1 1 5	✗	✗
Genetic therapy (cell free)	Cardiovascular Disorders	3 2 5	✗	✗
Small molecule	Brain Cancers	3 1 1 5	✗	✗
Genetic therapy (cell free)	Brain Cancers	3 1 1 5	✗	✗
Genetic therapy (cell free)	Brain Cancers	3 1 1 5	✗	✗
Allogeneic cell therapy	Neurologic Disorders	3 1 1 5	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3 1 4	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3 1 4	✗	✗

PSC / Neuro / In vivo | Non-Viral Nucleic Acid | Meeting Conducted | Progression | Under-Represented Disease Area | Novelty**

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Table 2B. PDEV Cycle 1 Preference Scoring Results (3 of 4)

Modality	Disease Area	Total Score	Invited*	Funded
Genetic therapy (cell free)	Infectious Diseases	4	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	4	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	4	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	4	✗	✗
Genetic therapy (cell free)	Eye/Vision Disorders, Neurological	4	✗	✗
Small molecule	Neurologic Disorders	4	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	4	✗	✗
Small molecule	Neurologic Disorders	3	✗	✗
Allogeneic cell therapy	Eye/Vision Disorders, Neurological	3	✗	✗
Small molecule	Brain Cancers	3	✗	✗
Autologous gene-modified cell therapy	Hematology Disorders	3	✗	✗
Allogeneic cell therapy	Bone & Cartilage Disorders	3	✗	✗
Autologous gene-modified cell therapy	Brain Cancers	3	✗	✗
Allogeneic cell therapy	Other;liver failure	3	✗	✗
Biologic, excluding gene therapy	Neurologic Disorders	3	✗	✗
Genetic therapy (cell free)	Eye/Vision Disorders, Neurological	3	✗	✗
Allogeneic gene-modified cell therapy	Skin Disorders	3	✗	✗
Allogeneic cell therapy	Neurologic Disorders	3	✗	✗
Allogeneic gene-modified cell therapy	Other, Gastrointestinal	3	✗	✗
Autologous gene-modified cell therapy	Neurologic Disorders	3	✗	✗
Small molecule	Brain Cancers	3	✗	✗
Allogeneic cell therapy	Neurologic Disorders	3	✗	✗
Genetic therapy (cell free)	Cancers, Multiple Types/Sites	3	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3	✗	✗
Genetic therapy (cell free)	Solid Tumors	3	✗	✗
Autologous gene-modified cell therapy	Neurologic Disorders	3	✗	✗
Genetic therapy (cell free)	Hematologic Malignancies	3	✗	✗
Autologous cell therapy	Brain Cancers	3	✗	✗
Allogeneic cell therapy	Eye/Vision Disorders, Non-neurological	3	✗	✗
Small molecule	Neurologic Disorders	3	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3	✗	✗
Genetic therapy (cell free)	Hematologic Malignancies	3	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3	✗	✗
Allogeneic gene-modified cell therapy	Cardiovascular Disorders	3	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3	✗	✗
Allogeneic gene-modified cell therapy	Brain Cancers	3	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3	✗	✗
Autologous gene-modified cell therapy	Brain Cancers	3	✗	✗
Genetic therapy (cell free)	Neurologic Disorders	3	✗	✗
Allogeneic gene-modified cell therapy	Hematologic Malignancies	2	✗	✗
Allogeneic cell therapy	Other, genitourinary	2	✗	✗

PSC / Neuro / In vivo | Non-Viral Nucleic Acid | Meeting Conducted | Progression | Under-Represented Disease Area | Novelty**

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Table 2B. PDEV Cycle 1 Preference Scoring Results (4 of 4)

Modality	Disease Area	Total Score	Invited*	Funded
Allogeneic gene-modified cell therapy	Bone & Cartilage Disorders	2	✗	✗
Allogeneic cell therapy	Other; Liver	2	✗	✗
Small molecule	Cardiovascular Disorders	2	✗	✗
Autologous cell therapy	Kidney Disease	2	✗	✗
Biologic, excluding gene therapy	Cardiovascular Disorders	2	✗	✗
Allogeneic cell therapy	Metabolic Disorders	2	✗	✗
Autologous gene-modified cell therapy	Solid Tumors	2	✗	✗
Small molecule	Respiratory Disorders	2	✗	✗
Small molecule	Infectious Diseases	1	✗	✗
Allogeneic gene-modified cell therapy	Solid Tumors	1	✗	✗
Autologous gene-modified cell therapy	Hematologic Malignancies	1	✗	✗
Allogeneic gene-modified cell therapy	Solid Tumors	1	✗	✗
Autologous gene-modified cell therapy	Cancers, Multiple Types/Sites	1	✗	✗
Autologous gene-modified cell therapy	Cancers, Multiple Types/Sites	1	✗	✗
Biologic, excluding gene therapy	Hematology Disorders	1	✗	✗
Autologous gene-modified cell therapy	Metabolic Disorders	1	✗	✗
Autologous gene-modified cell therapy	Solid Tumors	1	✗	✗
Autologous cell therapy	Solid Tumors	1	✗	✗
Autologous gene-modified cell therapy	Solid Tumors	1	✗	✗
Small molecule	Hematologic Malignancies	1	✗	✗
Allogeneic gene-modified cell therapy	Hematology Disorders	0	✗	✗
Autologous gene-modified cell therapy	Solid Tumors	0	✗	✗
Autologous gene-modified cell therapy	Hematologic Malignancies	0	✗	✗
Allogeneic gene-modified cell therapy	Solid Tumors	0	✗	✗
Allogeneic cell therapy	Hematologic Malignancies	0	✗	✗
Biologic, excluding gene therapy	Solid Tumors	0	✗	✗
Autologous cell therapy	Cancers, Multiple Types/Sites	0	✗	✗
Allogeneic cell therapy	Eye/Vision Disorders, Non-neurological	0	✗	✗
Autologous gene-modified cell therapy	Cancers, Multiple Types/Sites	0	✗	✗
Allogeneic cell therapy	Cancers, Multiple Types/Sites	0	✗	✗
Autologous gene-modified cell therapy	Solid Tumors	0	✗	✗
Biologic, excluding gene therapy	Solid Tumors	0	✗	✗
Autologous cell therapy	Solid Tumors	0	✗	✗
Allogeneic gene-modified cell therapy	Solid Tumors	0	✗	✗
Biologic, excluding gene therapy	Hematologic Malignancies	0	✗	✗
Autologous gene-modified cell therapy	Hematology Disorders	0	✗	✗
Autologous cell therapy	Cancers, Multiple Types/Sites	0	✗	✗
Allogeneic cell therapy	Hematologic Malignancies	0	✗	✗
Allogeneic cell therapy	Solid Tumors	0	✗	✗
Small molecule	Hematologic Malignancies	0	✗	✗
Allogeneic gene-modified cell therapy	Hematologic Malignancies	0	✗	✗
Autologous cell therapy	Hematologic Malignancies	0	✗	✗

PSC / Neuro / In vivo | Non-Viral Nucleic Acid | Meeting Conducted | Progression | Under-Represented Disease Area | Novelty**

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Table 2C. PDEV Cycle 2 Preference Scoring Results (1 of 3)

Modality	Disease Area	Total Score	Invited*
Genetic therapy (cell free)	Metabolic Disorders	8	✓
Genetic therapy (cell free)	Bone & Cartilage Disorders	7	✓
Genetic therapy (cell free)	Other;Kidney Disease	7	✓
Allogeneic gene-modified cell therapy	Metabolic Disorders	7	✓
Allogeneic gene-modified cell therapy	Other;Liver Disorders	7	✓
Allogeneic gene-modified cell therapy	Other;Liver disorder	7	✓
Genetic therapy (cell free)	Metabolic Disorders	6	✓
Allogeneic cell therapy	Other;Liver Disorders	6	✗
Genetic therapy (cell free)	Muscle Disorders	6	✓
Genetic therapy (cell free)	Neurologic Disorders	6	✓
Allogeneic cell therapy	Cardiovascular Disorders	6	✓
Autologous gene-modified cell therapy	Neurologic Disorders	6	✓
Small molecule	Eye/Vision Disorders, Neurological	6	✓
Allogeneic cell therapy	Hematology Disorders	6	✓
Genetic therapy (cell free)	Cancers, Multiple Types/Sites	6	✓
Allogeneic cell therapy	Cardiovascular Disorders	6	✓
Allogeneic cell therapy	Neurologic Disorders	6	✓
Genetic therapy (cell free)	Brain Cancers	6	✓
Genetic therapy (cell free)	Bone & Cartilage Disorders	6	✗
Genetic therapy (cell free)	Brain Cancers	6	✓
Genetic therapy (cell free)	Hematologic Malignancies	6	✓
Allogeneic gene-modified cell therapy	Neurologic Disorders	6	✓
Allogeneic cell therapy	Metabolic Disorders	5	✓
Genetic therapy (cell free)	Cardiovascular Disorders	5	✗
Allogeneic gene-modified cell therapy	Cancers, Multiple Types/Sites	5	✗
Small molecule	Brain Cancers	5	✗
Genetic therapy (cell free)	Brain Cancers	5	✗
Genetic therapy (cell free)	Eye/Vision Disorders, Neurological	5	✗
Genetic therapy (cell free)	Eye/Vision Disorders, Neurological	5	✗
Genetic therapy (cell free)	Neurologic Disorders	5	✗
Allogeneic cell therapy	Eye/Vision Disorders, Neurological	5	✗
Genetic therapy (cell free)	Neurologic Disorders	5	✗
Genetic therapy (cell free)	Solid Tumors	5	✗
Genetic therapy (cell free)	Neurologic Disorders	5	✗
Genetic therapy (cell free)	Neurologic Disorders	5	✗
Allogeneic cell therapy	Neurologic Disorders	5	✗
Genetic therapy (cell free)	Metabolic Disorders	5	✗
Biologic, excluding gene therapy	Brain Cancers	5	✗
Allogeneic cell therapy	Neurologic Disorders	5	✓
Genetic therapy (cell free)	Neurologic Disorders	5	✗
Genetic therapy (cell free)	Infectious Diseases	5	✗
Genetic therapy (cell free)	Cancers, Multiple Types/Sites	5	✗

PSC / Neuro / In vivo | Non-Viral Nucleic Acid | Meeting Conducted | Progression | Under-Represented Disease Area | Novelty**

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Table 2C. PDEV Cycle 2 Preference Scoring Results (2 of 3)

Modality	Disease Area	Total Score	Invited*
Genetic therapy (cell free)	Eye/Vision Disorders, Neurological	5	✗
Allogeneic cell therapy	Neurologic Disorders	5	✗
Autologous cell therapy	Neurologic Disorders	5	✗
Allogeneic cell therapy	Metabolic Disorders	5	✓
Genetic therapy (cell free)	Eye/Vision Disorders, Neurological	5	✗
Genetic therapy (cell free)	Neurologic Disorders	5	✗
Genetic therapy (cell free)	Bone & Cartilage Disorders	5	✗
Allogeneic cell therapy	Cardiovascular Disorders	5	✗
Genetic therapy (cell free)	Cardiovascular Disorders	5	✗
Small molecule	Neurologic Disorders	5	✗
Small molecule	Eye/Vision Disorders, Neurological	5	✗
Allogeneic cell therapy	Neurologic Disorders	4	✗
Genetic therapy (cell free)	Neurologic Disorders	4	✗
Autologous gene-modified cell therapy	Brain Cancers	4	✗
Genetic therapy (cell free)	Neurologic Disorders	4	✗
Autologous gene-modified cell therapy	Neurologic Disorders	4	✗
Genetic therapy (cell free)	Eye/Vision Disorders, Neurological	4	✗
Allogeneic cell therapy	Neurologic Disorders	4	✗
Genetic therapy (cell free)	Cancers, Multiple Types/Sites	4	✗
Genetic therapy (cell free)	Muscle Disorders	4	✗
Allogeneic cell therapy	Neurologic Disorders	4	✗
Genetic therapy (cell free)	Neurologic Disorders	4	✗
Genetic therapy (cell free)	Eye/Vision Disorders, Neurological	4	✗
Allogeneic cell therapy	Neurologic Disorders	4	✗
Genetic therapy (cell free)	Neurologic Disorders	4	✗
Genetic therapy (cell free)	Eye/Vision Disorders, Neurological	4	✗
Small molecule	Neurologic Disorders	4	✗
Genetic therapy (cell free)	Neurologic Disorders	4	✗
Genetic therapy (cell free)	Neurologic Disorders	4	✗
Genetic therapy (cell free)	Metabolic Disorders	4	✗
Genetic therapy (cell free)	Brain Cancers	4	✗
Genetic therapy (cell free)	Hematologic Malignancies	3	✗
Genetic therapy (cell free)	Neurologic Disorders	3	✗
Allogeneic gene-modified cell therapy	Neurologic Disorders	3	✗
Autologous gene-modified cell therapy	Infectious Diseases	3	✗
Small molecule	Neurologic Disorders	3	✗
Genetic therapy (cell free)	Neurologic Disorders	3	✗
Genetic therapy (cell free)	Neurologic Disorders	3	✗
Autologous cell therapy	Neurologic Disorders	3	✗
Biologic, excluding gene therapy	Neurologic Disorders	3	✗
Biologic, excluding gene therapy	Cardiovascular Disorders	3	✗
Genetic therapy (cell free)	Solid Tumors	3	✗

PSC / Neuro / In vivo | Non-Viral Nucleic Acid | Meeting Conducted | Progression | Under-Represented Disease Area | Novelty**

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Table 2C. PDEV Cycle 2 Preference Scoring Results (3 of 3)

Modality	Disease Area	Total Score	Invited*
Autologous cell therapy	Brain Cancers	3	✗
Genetic therapy (cell free)	Neurologic Disorders	3	✗
Allogeneic cell therapy	Neurologic Disorders	3	✗
Small molecule	Neurologic Disorders	3	✗
Autologous gene-modified cell therapy	Brain Cancers	3	✗
Genetic therapy (cell free)	Solid Tumors	3	✗
Genetic therapy (cell free)	Solid Tumors	3	✗
Genetic therapy (cell free)	Neurologic Disorders	3	✗
Allogeneic gene-modified cell therapy	Solid Tumors	3	✗
Allogeneic gene-modified cell therapy	Solid Tumors	2	✗
Allogeneic cell therapy	Respiratory Disorders	2	✗
Allogeneic gene-modified cell therapy	Solid Tumors	2	✗
Allogeneic gene-modified cell therapy	Other;Type 1 Diabetes and Transplantation	2	✗
Autologous gene-modified cell therapy	Solid Tumors	2	✗
Allogeneic cell therapy	Metabolic Disorders	2	✗
Autologous gene-modified cell therapy	Other;Immune System disorder	2	✗
Allogeneic gene-modified cell therapy	Other, gastrointestinal	2	✗
Autologous gene-modified cell therapy	Cancers, Multiple Types/Sites	2	✗
Small molecule	Other;Dupuytren's & related immune-fibrotic diseases	1	✗
Small molecule	Hematologic Malignancies	1	✗
Allogeneic cell therapy	Solid Tumors	1	✗
Small molecule	Hematologic Malignancies	1	✗
Autologous gene-modified cell therapy	Hematology Disorders	1	✗
Allogeneic gene-modified cell therapy	Hematologic Malignancies	1	✗
Biologic, excluding gene therapy	Cardiovascular Disorders	1	✗
Autologous gene-modified cell therapy	Solid Tumors	1	✗
Autologous cell therapy	Solid Tumors	1	✗
Small molecule	Respiratory Disorders	1	✗
Small molecule	Bone & Cartilage Disorders	1	✗
Autologous gene-modified cell therapy	Solid Tumors	1	✗
Biologic, excluding gene therapy	Hematology Disorders	1	✗
Allogeneic cell therapy	Other;Gastrointestinal disorders	1	✗
Small molecule	Muscle Disorders	1	✗
Allogeneic gene-modified cell therapy	Solid Tumors	0	✗
Allogeneic gene-modified cell therapy	Solid Tumors	0	✗
Autologous cell therapy	Solid Tumors	0	✗
Autologous cell therapy	Hematology Disorders	0	✗
Autologous cell therapy	Cancers, Multiple Types/Sites	0	✗
Autologous gene-modified cell therapy	Hematologic Malignancies	0	✗
Allogeneic cell therapy	Solid Tumors	0	✗
Biologic, excluding gene therapy	Hematology Disorders	0	✗
Allogeneic gene-modified cell therapy	Solid Tumors	0	✗

PSC / Neuro / In vivo | Non-Viral Nucleic Acid | Meeting Conducted | Progression | Under-Represented Disease Area | Novelty**

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Table 3A. CLIN2 FY25/26 Qualification Rubric

Preference	Points
• PSC-derived therapies	1
• Diseases of the CNS	1
• In vivo genetic therapy	1
• Non-viral genetic therapy	1
• Accelerated regulatory designation (RMAT, Breakthrough, Fast Track)	1
• Progression from earlier stage CIRM award	1
• California Organization	1
• Pivotal trial	2

PSC: Pluripotent Stem Cell; CNS: Central Nervous System; RMAT: Regenerative Medicine Advanced Therapy

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Table 3B. CLIN2 Cycle 1 Qualification Results

Description	Total Score	GWG Tie Break	Full Review	Funded
Allogeneic oligodendrocyte progenitor cells for spinal cord injury	4	N/A	✓	✗
Allogeneic neural stem cells for Huntington's disease	4	N/A	✓	✓
AAV-delivered gene regulation therapy for Dravet Syndrome	4	N/A	✓	✓
AAV-based gene therapy for CMT4J	4	N/A	✓	✓
Allogeneic dopamine-producing neurons for Parkinson's disease	4	N/A	✓	✓
Allogeneic retinal progenitor cells for retinitis pigmentosa	3	132.5	✓	✗
AAV gene therapy for CLN6 disease	3	122.5	✗	✗
NK cell therapy for Alzheimer's disease	3	112.5	✗	✗
Allogeneic CAR-T for solid tumors	3	104	✗	✗
AAV-delivered epigenetic therapy for facioscapulohumeral muscular dystrophy	3	102.5	✗	✗
Allogeneic breast cancer cell-based immunotherapy for breast cancer	3	80	✗	✗
Small molecule for venous leg ulcers	2	N/A	✗	✗
Small molecule for AML/myelofibrosis	2	N/A	✗	✗
AAV-delivered genetic therapy for neuropathy	2	N/A	✗	✗
Antibody for myocardial infarction	2	N/A	✗	✗
Autologous CAR-T for multiple myeloma	2	N/A	✗	✗
Autologous CAR-T for lymphoma	2	N/A	✗	✗
Autologous CAR-T for B-cell cancers	2	N/A	✗	✗
Autologous cancer vaccine for AML	2	N/A	✗	✗
Antibody-based biologic for solid tumors & multiple myeloma	2	N/A	✗	✗
Allogeneic MSC cancer vaccine	2	N/A	✗	✗
Allogeneic HCST for Crohn disease	1	N/A	✗	✗
Extracellular vesicles for acute respiratory distress syndrome	0	N/A	✗	✗

PSC-derived | In vivo genetic therapy | Non-viral | CNS | Progression | CA organization | FDA designation | Pivotal trial

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Table 3C. CLIN2 Cycle 2 Qualification Results

Description	Total Score	GWG Tie Break	Full Review
Genetic therapy for Pitt Hopkin's Syndrome	4	N/A	✓
AAV-based optogenetic gene therapy for Stargardt disease	4	N/A	✓
Autologous B cells for rare lysosomal storage disorder	4	N/A	✓
Autologous iPSC-derived cell therapy for blinding eye diseases (geographic atrophy, Stargardt, etc.)	4	N/A	✓
Genetic therapy for rare metabolic disorder	3	102.5	✓
Epigenetic therapy for FSHD	3	103.5	✓
Autologous cancer vaccine for AML	3	100	✗
Autologous CAR-T for brain & B-cell cancers	3	120.5	✓
Autologous MSC cancer vaccine	3	90	✗
AAV-based gene therapy for dilated cardiomyopathy	2	N/A	✗
Allogeneic CAR-T for lymphoma	2	N/A	✗
Allogeneic MSC for pediatric dilated cardiomyopathy	2	N/A	✗
Autologous gene-modified HSCs for SCD	2	N/A	✗
Small molecule for venous leg ulcers	2	130	✗
Autologous adipose-derived stem cells for Alzheimer's disease	2	N/A	✗
Autologous CAR-T for multiple myeloma	2	N/A	✗
Antibody for myocardial infarction	2	N/A	✗
Allogeneic CAR-Treg for multiple sclerosis	2	N/A	✗
Small molecule for myelofibrosis & AML	1	N/A	✗
Allogeneic HCST for Crohn's disease	1	N/A	✗
Allogeneic breast cancer cell-based immunotherapy for breast cancer	0	N/A	✗

PSC-derived | In vivo genetic therapy | Non-viral | CNS | Progression | CA organization | FDA designation | Pivotal trial

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Table 4A. DISC4 Preference Scoring Rubric

Criteria	Description (listed in program announcement)	Points
Preference Topic: Neuro	Does the project align with the cycle-specific preference topic?	9
Relevance to human disease biology	Does the project hold strong relevance for understanding or addressing human diseases?	6
Cross disciplinary and systems biology	Does the project integrate cross-disciplinary approaches?	6
Stem cell or genetic research innovations	Does the project incorporate innovative approaches particularly in stem-cell or genetic research?	4

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Table 4B. DISC4 Cycle 1 Preference Scoring Results (1 of 3)

Disease Areas	Total Score	Invited*
Neurologic Disorders	9.00 5.50 4.50 4.00 23.00	✓
Brain Cancers	8.00 5.00 4.50 4.00 21.50	✓
Brain Cancers	9.00 5.00 3.50 3.50 21.00	✓
Neurologic Disorders	9.00 4.67 4.67 2.67 21.01	✓
Brain Cancers	7.50 4.50 4.50 4.00 20.50	✓
Neurologic Disorders	7.00 5.50 5.00 2.00 19.50	✓
Neurologic Disorders	7.00 4.50 4.00 4.00 19.50	✓
Neurologic Disorders	9.00 3.50 3.00 4.00 19.50	✓
Eye/Vision Disorders, Non-neurological	7.50 5.50 3.00 3.00 19.00	✓
Neurologic Disorders	7.00 4.50 3.50 4.00 19.00	✓
Cardiovascular Disorders	8.00 3.50 4.50 3.00 19.00	✓
Neurologic Disorders	9.00 3.50 3.50 3.00 19.00	✓
Neurologic Disorders	6.67 5.00 3.00 4.00 18.67	✓
Neurologic Disorders	8.00 5.00 2.50 3.00 18.50	✓
Neurologic Disorders	8.00 4.50 2.00 4.00 18.50	✓
Neurologic Disorders	8.00 4.50 2.00 4.00 18.50	✓
Neurologic Disorders	7.00 4.00 5.00 2.50 18.50	✓
Neurologic Disorders	7.50 4.00 4.50 2.50 18.50	✓
Neurologic Disorders	7.00 4.00 3.50 4.00 18.50	✓
Neurologic Disorders	8.00 4.00 3.00 3.50 18.50	✓
Neurologic Disorders	7.00 4.33 4.67 2.33 18.33	✓
Neurologic Disorders	6.33 4.33 4.33 3.00 17.99	✓
Brain Cancers	7.00 4.33 3.33 3.33 17.99	✓
Neurologic Disorders	8.00 3.00 3.00 4.00 18.00	✓
Neurologic Disorders	7.33 4.33 4.00 2.00 17.66	✗
Neurologic Disorders	8.67 3.33 2.33 3.33 17.66	✗
Neurologic Disorders	7.00 4.67 3.33 2.33 17.33	✗
Neurologic Disorders	6.33 4.33 3.67 3.00 17.33	✗
Neurologic Disorders	7.33 4.33 3.67 2.00 17.33	✗
Neurologic Disorders	7.00 3.67 3.00 3.67 17.34	✗
Neurologic Disorders	8.33 3.67 3.00 2.33 17.33	✗
Brain Cancers	9.00 3.33 3.00 2.00 17.33	✗
Neurologic Disorders	7.00 5.00 2.50 2.50 17.00	✗
Neurologic Disorders	7.00 5.00 2.50 2.50 17.00	✗
Neurologic Disorders	6.50 4.50 3.00 3.00 17.00	✗
Neurologic Disorders	7.00 4.50 2.50 3.00 17.00	✗
Neurologic Disorders	6.50 4.50 2.00 4.00 17.00	✗
Neurologic Disorders	7.00 4.50 1.50 4.00 17.00	✗
Brain Cancers	6.33 4.33 3.33 3.00 16.99	✗
Brain Cancers	7.00 4.00 3.50 2.50 17.00	✗
Bone & Cartilage Disorders	7.00 3.50 3.50 3.00 17.00	✗
Neurologic Disorders	7.00 3.50 3.50 3.00 17.00	✗
Neurologic Disorders	7.50 3.50 3.50 2.50 17.00	✗
Neurologic Disorders	8.50 2.50 4.00 2.00 17.00	✗
Neurologic Disorders	8.00 2.50 3.50 3.00 17.00	✗
Neurologic Disorders	7.67 3.67 2.67 2.67 16.68	✗

Neuro Topic | Relevance to Human Disease Biology | Cross-Disciplinary & Systems Biology | Stem Cell or Genetic Research Innovations

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Table 4B. DISC4 Cycle 1 Preference Scoring Results (2 of 3)

Disease Areas	Total Score	Invited*
Neurologic Disorders	6.67 + 3.67 + 2.33 + 4.00 = 16.67	✗
Neurologic Disorders	7.00 + 5.00 + 2.00 + 2.50 = 16.50	✗
Neurologic Disorders	7.00 + 5.00 + 1.50 + 3.00 = 16.50	✗
Neurologic Disorders	7.50 + 4.00 + 1.50 + 3.50 = 16.50	✗
Neurologic Disorders	8.00 + 3.50 + 2.00 + 3.00 = 16.50	✗
Neurologic Disorders	7.00 + 2.50 + 4.00 + 3.00 = 16.50	✗
Neurologic Disorders	7.00 + 2.50 + 3.00 + 4.00 = 16.50	✗
Eye/Vision Disorders, Neurological	8.00 + 2.00 + 3.00 + 3.50 = 16.50	✗
Brain Cancers	7.00 + 5.00 + 3.00 + 1.00 = 16.00	✗
Neurologic Disorders	8.00 + 4.33 + 2.00 + 1.67 = 16.00	✗
Neurologic Disorders	6.67 + 3.33 + 2.67 + 3.33 = 16.00	✗
Neurologic Disorders	7.00 + 2.50 + 3.50 + 3.00 = 16.00	✗
Neurologic Disorders	7.00 + 2.50 + 3.50 + 3.00 = 16.00	✗
Neurologic Disorders	7.00 + 2.50 + 3.00 + 3.50 = 16.00	✗
Neurologic Disorders	6.50 + 4.00 + 3.50 + 1.50 = 15.50	✗
Neurologic Disorders	6.50 + 3.50 + 3.50 + 2.00 = 15.50	✗
Neurologic Disorders	6.50 + 3.00 + 3.00 + 3.00 = 15.50	✗
Neurologic Disorders	7.33 + 3.33 + 1.33 + 3.33 = 15.32	✗
Cardiovascular Disorders	7.33 + 1.67 + 3.33 + 3.00 = 15.33	✗
Neurologic Disorders	6.50 + 3.50 + 3.00 + 2.00 = 15.00	✗
Neurologic Disorders	7.00 + 3.50 + 2.00 + 2.50 = 15.00	✗
Neurologic Disorders	7.00 + 3.50 + 0.00 + 4.00 = 15.00	✗
Neurologic Disorders	7.50 + 3.50 + 4.00 = 15.00	✗
Neurologic Disorders	8.00 + 3.00 + 1.50 + 2.50 = 15.00	✗
Eye/Vision Disorders, Neurological	9.00 + 2.50 + 1.50 + 2.00 = 15.00	✗
Metabolic Disorders	6.50 + 1.50 + 4.00 + 3.00 = 15.00	✗
Eye/Vision Disorders, Neurological	9.00 + 1.50 + 1.50 + 3.00 = 15.00	✗
Cardiovascular Disorders	7.00 + 4.50 + 2.00 + 1.00 = 14.50	✗
Neurologic Disorders	7.50 + 4.00 + 2.00 + 1.00 = 14.50	✗
Eye/Vision Disorders, Neurological	6.00 + 3.50 + 2.50 + 2.50 = 14.50	✗
Eye/Vision Disorders, Neurological	6.50 + 3.50 + 2.50 + 2.00 = 14.50	✗
Brain Cancers	6.50 + 3.00 + 3.00 + 2.00 = 14.50	✗
Neurologic Disorders	7.50 + 2.50 + 2.00 + 2.50 = 14.50	✗
Neurologic Disorders	7.50 + 2.00 + 2.50 + 2.50 = 14.50	✗
Neurologic Disorders	7.00 + 1.50 + 4.00 + 2.00 = 14.50	✗
Bone & Cartilage Disorders	5.33 + 3.67 + 3.00 + 2.33 = 14.33	✗
Neurologic Disorders	5.00 + 3.67 + 2.67 + 3.00 = 14.34	✗
Brain Cancers	7.00 + 2.67 + 1.67 + 3.00 = 14.34	✗
Neurologic Disorders	= 14.33	✗
Neurologic Disorders	= 14.00	✗
Neurologic Disorders	= 14.00	✗
Neurologic Disorders	= 14.00	✗
Brain Cancers	= 14.00	✗
Neurologic Disorders	= 13.66	✗
Eye/Vision Disorders, Neurological	= 13.66	✗
Neurologic Disorders	= 13.50	✗

Neuro Topic | Relevance to Human Disease Biology | Cross-Disciplinary & Systems Biology | Stem Cell or Genetic Research Innovations

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Table 4B. DISC4 Cycle 1 Preference Scoring Results (3 of 3)

Disease Areas	Total Score	Invited*
Neurologic Disorders	6.00 + 3.00 + 2.50 + 2.00 = 13.50	✗
Neurologic Disorders	6.50 + 3.00 + 2.00 + 2.00 = 13.50	✗
Neurologic Disorders	5.50 + 1.50 + 4.00 + 2.50 = 13.50	✗
Eye/Vision Disorders, Neurological	7.00 + 1.50 + 3.00 + 2.00 = 13.50	✗
Eye/Vision Disorders, Neurological	6.50 + 3.50 + 2.00 + 1.00 = 13.00	✗
Cardiovascular Disorders	7.00 + 3.50 + 1.00 + 1.50 = 13.00	✗
Brain Cancers	6.00 + 2.50 + 2.00 + 2.50 = 13.00	✗
Neurologic Disorders	6.00 + 2.50 + 2.00 + 2.50 = 13.00	✗
Neurologic Disorders	7.00 + 1.50 + 1.50 + 3.00 = 13.00	✗
Neurologic Disorders	7.00 + 3.00 + 1.00 + 1.67 = 12.67	✗
Cancers, Multiple Types/Sites	4.50 + 5.00 + 3.00 = 12.50	✗
Neurologic Disorders	5.50 + 2.50 + 2.00 + 2.50 = 12.50	✗
Neurologic Disorders	7.50 + 1.00 + 1.00 + 3.00 = 12.50	✗
Other	4.00 + 5.00 + 1.67 + 1.67 = 12.34	✗
Neurologic Disorders	6.00 + 3.50 + 1.50 + 1.00 = 12.00	✗
Neurologic Disorders	6.00 + 3.00 + 2.50 = 12.00	✗
Neurologic Disorders	5.00 + 2.50 + 2.50 + 2.00 = 12.00	✗
Eye/Vision Disorders, Neurological	7.00 + 2.50 + 2.50 = 12.00	✗
Neurologic Disorders	6.50 + 1.00 + 2.50 + 2.00 = 12.00	✗
Neurologic Disorders	6.00 + 4.00 + 1.50 = 11.50	✗
Brain Cancers	6.00 + 2.50 + 1.50 + 1.50 = 11.50	✗
Cancers, Multiple Types/Sites	5.50 + 1.50 + 3.50 + 1.00 = 11.50	✗
Eye/Vision Disorders, Neurological	6.50 + 1.50 + 1.50 + 2.00 = 11.50	✗
Neurologic Disorders	8.00 + 1.50 + 1.50 = 11.50	✗
Other	3.50 + 5.00 + 2.50 = 11.00	✗
Neurologic Disorders	5.50 + 3.00 + 2.50 = 11.00	✗
Neurologic Disorders	5.00 + 2.50 + 1.50 + 2.00 = 11.00	✗
Brain Cancers	5.00 + 2.50 + 3.50 = 11.00	✗
Other	5.00 + 4.00 + 1.50 = 10.50	✗
Muscle Disorders	6.50 + 2.00 + 1.50 = 10.50	✗
Metabolic Disorders	6.00 + 1.00 + 1.50 + 1.50 = 10.00	✗
Cardiovascular Disorders	5.50 + 2.50 + 1.50 = 9.50	✗
Cancers, Multiple Types/Sites	4.50 + 2.50 + 2.50 = 9.50	✗
Other	4.00 + 3.00 + 2.50 = 9.50	✗
Muscle Disorders	4.00 + 2.33 + 1.67 + 1.33 = 9.33	✗
Neurologic Disorders	5.00 + 2.00 + 2.00 = 9.00	✗
Neurologic Disorders	3.33 + 2.67 + 3.00 = 9.00	✗
Muscle Disorders	5.00 + 1.50 + 2.00 = 8.50	✗
Metabolic Disorders	2.50 + 3.50 + 2.50 = 8.50	✗
Cardiovascular Disorders	2.00 + 4.50 + 2.00 = 8.50	✗
Brain Cancers	3.00 + 1.50 + 3.50 = 8.00	✗
Cardiovascular Disorders	2.50 + 2.50 + 3.00 = 8.00	✗
Cancers, Multiple Types/Sites	3.67 + 2.00 + 1.33 = 7.00	✗
Cancers, Multiple Types/Sites	1.00 + 2.00 + 2.00 = 5.00	✗
Cardiovascular Disorders	3.00 + 1.00 = 4.50	✗
Cancers, Multiple Types/Sites	2.50 + 1.50 = 4.00	✗

Neuro Topic | Relevance to Human Disease Biology | Cross-Disciplinary & Systems Biology | Stem Cell or Genetic Research Innovations

Appendix B. Portfolio composition across Preclinical and Clinical Programs (PDEV, TRAN1, CLIN1, CLIN2)

Preclinical Portfolio

Preclinical Programs (TRAN1, CLIN1, PDEV):

- Disease and modality diversity are strong
- Portfolio progression to IND clearance has increased significantly
- Progression from IND clearance to active trial execution is increasingly dependent on CIRM funding

CIRM's active portfolio of preclinical stage programs (TRAN1, CLIN1, CLIN2) has significant diversification across modalities and disease areas. The predominant disease areas represented in the active portfolio of preclinical stage programs are neurological disorders, hematology and oncology. The predominant modalities represented in the active portfolio of preclinical stage programs are autologous gene-modified cell therapies, in vivo genetic therapies and allogeneic cell therapies. The primary challenge at this stage is in increasing the likelihood that projects transition successfully from IND clearance to clinical trial launch and patient enrollment.

Clinical Portfolio

CLIN2:

- CLIN2 is increasingly serving as the primary bridge from IND to patient.
- First-in-human (FIH) trials remain the stage where CIRM can most effectively de-risk programs
- Trial activation speed, sponsor durability, capital continuity, and regulatory momentum differentiate advancing programs from stalled ones
- External progression post-FIH has decreased relative to prior years, increasing reliance on CLIN2 funding

At this stage, scientific novelty alone does not determine impact. Execution strength, regulatory trajectory, and financing sustainability are the primary determinants of whether programs ultimately reach patients.

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Figure 1. Preclinical & Clinical Portfolio Composition by Modality

Modality	Active Awards
Allogeneic	6 5 2 18 31
Allogeneic, Gene-Modified	4 1 7 12
Autologous	2 1 4 7
Autologous, Gene-Modified	17 6 1 18 42
Biologic (excl. gene therapy)	3 2 5
Genetic Therapy (cell-free)	12 4 7 9 32
Small Molecule	2 1 3
Technology/Tools	1 1

TRAN CLIN1 PDEV CLIN2

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Figure 2. Preclinical & Clinical Portfolio Composition by Disease Area

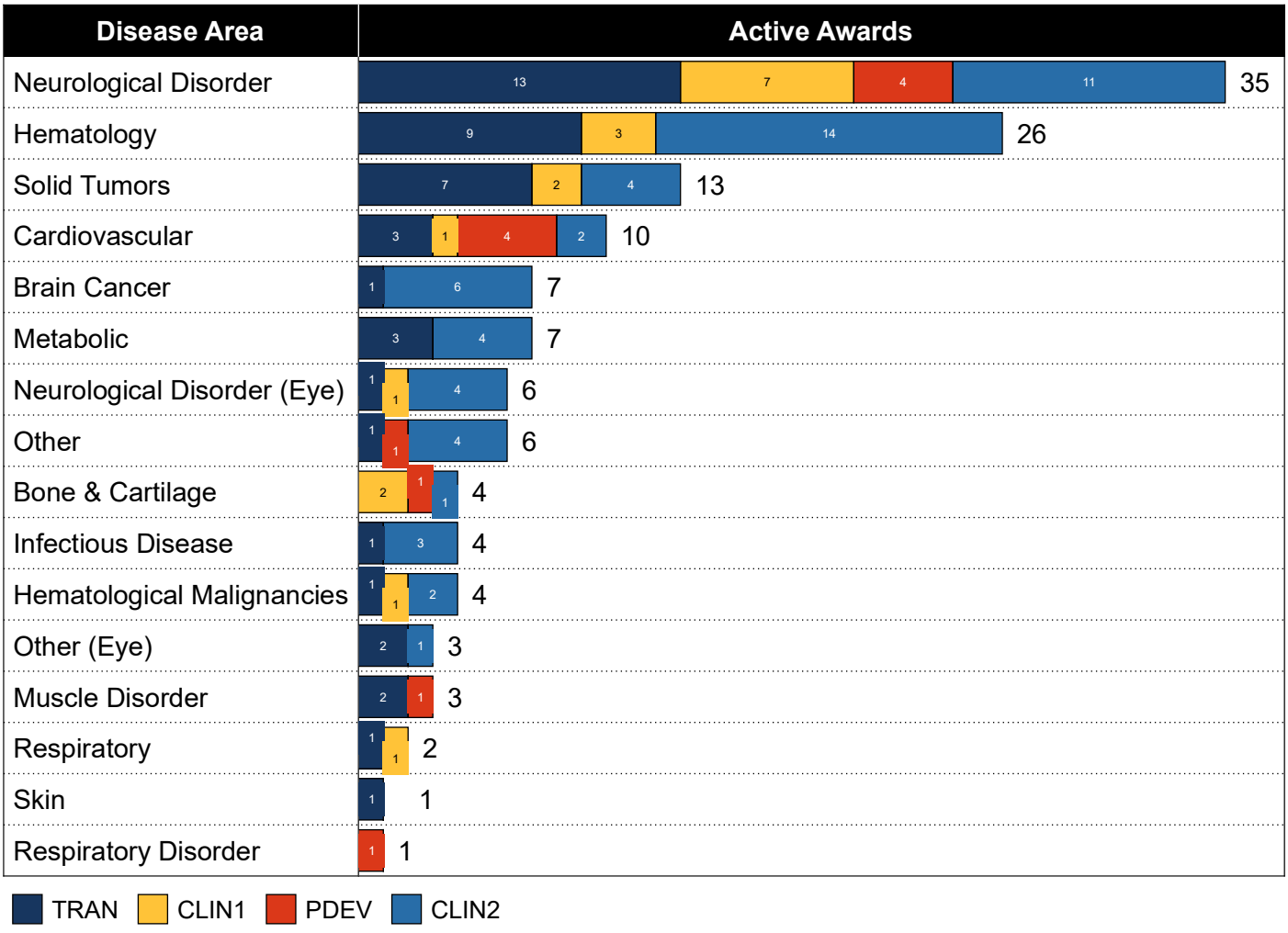

Figure 3. Preclinical & Clinical Portfolio Composition by Rare Disease

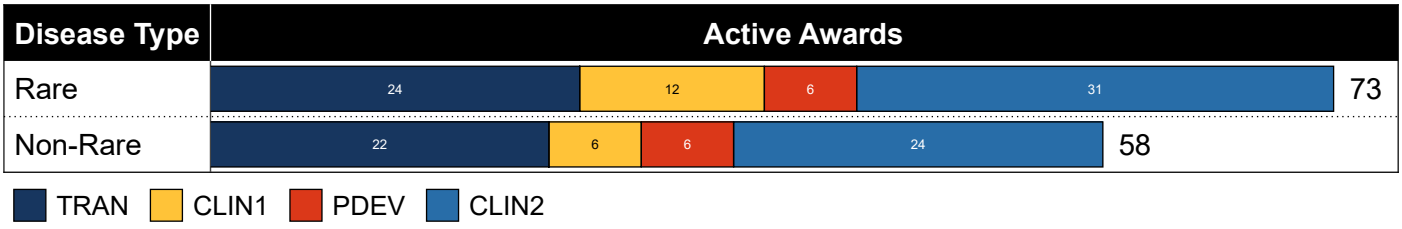

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Figure 4. Active CLIN2 Trial Phase by Modality

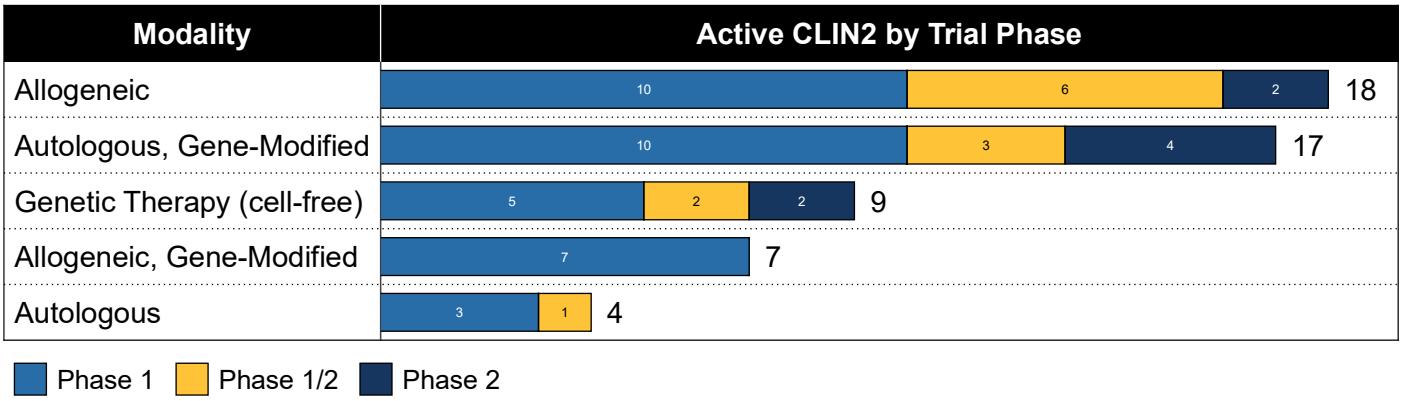

Figure 5. Active CLIN2 Trial Phase by Disease Area

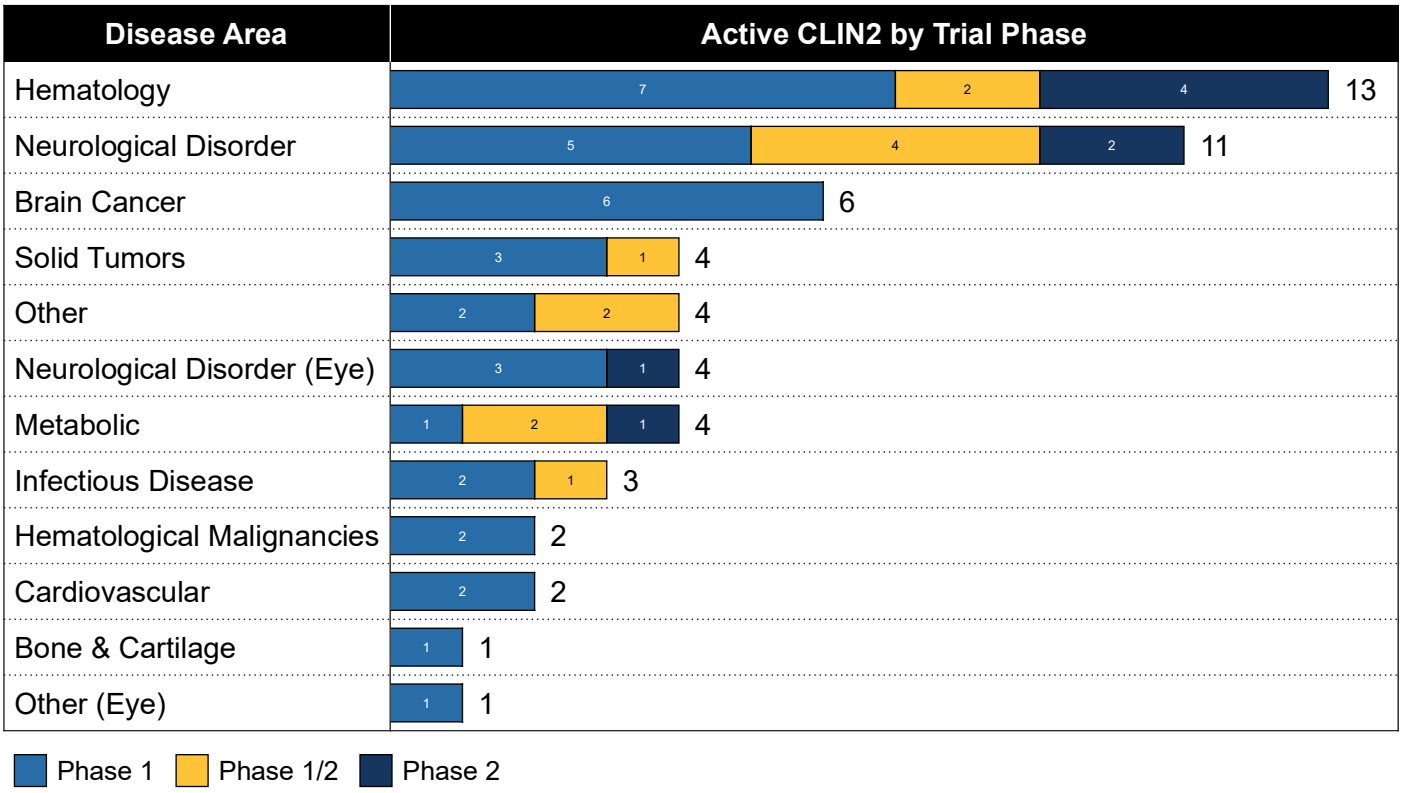

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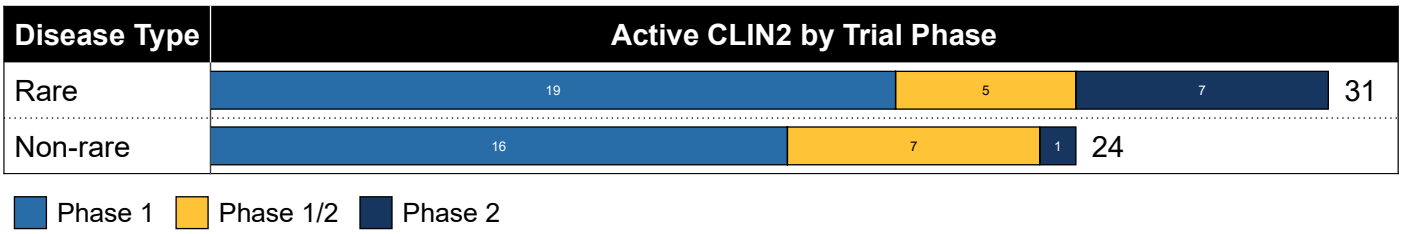
Figure 6. Active CLIN2 Trial Phase by Rare Disease



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Appendix C. GWG Review Criteria

Full GWG Review Criteria

The following are the respective review criteria for DISC4, PDEV and CLIN2 programs utilized by the GWG in evaluating and scoring applications during the Merit Review stage. For the volume control selection step, reviewers focus on the first criterion shown for each funding opportunity, which we collectively refer to as the "scientific value".

DISC4

The DISC4 funding opportunity supports comprehensive discovery research across a diverse range of diseases and bottlenecks that will accelerate the development of potential therapeutics and biomarkers in regenerative medicine.

The GWG evaluates and scores DISC4 applications based on the following:

1. **Significance: Evaluate the project's significance and potential for impact**
   - Assess the extent to which a successful project outcome would advance understanding of human disease.
   - Assess the extent to which a successful project outcome would have broader impact, for example through the generation of shareable resources/data.
   - Assess the likelihood that a successful project outcome would rapidly advance to new therapeutic or biomarker development (including consideration of the applicant's vision for progression).
2. **Innovation: Evaluate the project for innovation relative to the current state of research**
   - Assess the extent to which the project applies novel frameworks to the study of human disease.
   - Assess the extent to which the project cuts across silos or employs a unique synergy of technologies or disciplines to understand human disease.
   - Assess the extent to which the project employs innovative stem cell or genetic research approaches.
3. **Rationale: Evaluate the scientific rationale in the proposal**
   - Assess the fundamental soundness of the scientific rationale for conducting the proposed research.
   - Assess the extent to which the rationale is supported by the body of available data.
   - Evaluate the scientific rationale for choice of proposed experimental approaches (including non-human models).
   - Assess the extent to which the feasibility of carrying out the proposed experiments is supported by the preliminary data.
4. **Plan & Design: Evaluate the project plan and design**
   - Assess the extent to which the project is planned and designed to give meaningful results.
   - Assess the validity of the potential pitfalls identified and alternative approaches presented.

- Evaluate the appropriateness of the budget and timeline for the research proposed.
- Evaluate the appropriateness of leadership, expertise, resources and staffing for the research proposed.
- Assess the effectiveness of the plan for team communications and management of the collaborative effort.

5. **Population Impact: Evaluate the extent to which the project considers the potential impact of successful outcomes across affected populations**
   - Assess how effectively the experimental design accounts for genetic, environmental and other external factors that may influence research findings.
   - Assess the extent to which the project may extend or validate the potential applicability of discoveries to additional affected populations or communities.
   - Assess how effectively the applicant team's prior or proposed outreach, partnership, or educational efforts inform study design and enhance the population relevance of potential discoveries.

PDEV

The PDEV funding opportunity supports activities leading to the completion of preclinical development, FDA IND clearance, and clinical trial startup for stem cell-based and genetic therapies.

The GWG evaluates and scores PDEV applications based on the following:

1. **Value Proposition** - *Evaluate the extent to which the therapy offers a compelling value proposition based on holistic consideration of the following.*
   - Assess the therapy's potential to provide a meaningful and substantial improvement in clinical outcomes for the intended population as compared to therapies currently available or in trials (e.g., efficacy, safety, patient burden).
   - Assess the expected impact of addressing the unmet medical need on patients, caregivers, and the healthcare system.
   - Assess the therapy's potential to be more accessible and affordable compared to available treatments or therapeutics currently in clinical development for the intended patient population and healthcare system.
   - Evaluate the feasibility and practicality of the therapy's uptake by patients, caregivers, and the healthcare system.
2. **Rationale** - *Evaluate the scientific rationale for the proposed therapy and the strength of the supporting data.*
   - Assess the fundamental robustness of the scientific rationale, including justification for the indication, therapeutic approach, and route of administration.
   - Assess the extent to which the rationale is supported by the body of available data. For example, consider whether there is compelling evidence of disease modifying activity in a relevant model.

- Consider the strengths & limitations of the data presented and/or the models utilized in completed studies.

3. **Project Plan & Design** - *Evaluate the project's plan and design to achieve an active IND.*
   - Evaluate the extent to which the proposed activities are necessary and appropriate to efficiently and effectively progress the project to IND clearance. For example, consider proposed preclinical studies, IND-enabling studies, process and analytical development/testing, clinical protocol drafts and trial startup activities as stage-appropriate.
   - Consider whether the PDEV objective will be achieved within the proposed budget and timeline.
   - Assess the validity of the potential project risks identified along with the mitigation and contingency plans presented.
   - Assess how well the project incorporates stage-appropriate access and affordability planning to support future market access.
4. **Project Team and Resources** - *Evaluate the expertise and resources that will be deployed to achieve the project deliverables.*
   - Evaluate the appropriateness of the team's leadership, expertise, and staffing plan to successfully navigate to IND clearance. For example, consider team leadership, expertise and staffing in relevant functional areas such as non-clinical, GMP manufacturing, analytical, regulatory and clinical.
   - Consider whether a robust plan for coordination and execution of the project has been clearly outlined.
   - Assess the extent to which the team has access to all necessary resources and facilities, including manufacturing facilities, to successfully conduct the proposed activities.
   - Consider whether the collective team, including consultants and subcontractors, have a demonstrated track record of supporting stem cell-based and genetic therapy projects to clinical trials.
5. **Population Impact** - *Evaluate the extent to which the project considers the potential impact of the proposed therapy across affected populations.*
   - Evaluate the applicant's understanding and consideration of genetic, environmental and other external factors that may impact on the adoption, effectiveness or safety of the proposed therapy.
   - Assess the appropriateness of the intended clinical study population in the context of the project stage and current knowledge of demographic groups at risk for the target indication.
   - Evaluate the extent to which the applicant's prior or proposed activities incorporate perspectives and experience from patients and individuals affected by the target indication.

CLIN2

The CLIN2 funding opportunity supports projects that will accelerate clinical development of stem cell-based and genetic therapies to late-stage trials by encouraging innovative clinical trial designs, and incentivizing stage-appropriate market access strategies and pre-commercialization activities.

The GWG evaluates and scores CLIN2 applications based on the following:

1. **Value Proposition** - *Evaluate the extent to which the therapy offers a compelling value proposition based on holistic consideration of the following:*
   - Assess the therapy's potential to provide a meaningful and substantial improvement in clinical outcomes for the intended population as compared to therapies currently available or in trials (e.g., efficacy, safety, patient burden).
   - Assess the expected impact of addressing the unmet medical need on patients, caregivers, and healthcare system.
   - Evaluate the feasibility and practicality of the therapy's uptake by patients, healthcare providers and payors.
2. **Rationale** - *Evaluate the scientific rationale for the proposed therapy and the strength of the supporting data*
   - Assess the fundamental robustness of the scientific rationale including justification for the indication, therapeutic approach, regimen and route of administration.
   - Assess the extent to which the rationale for clinical development of the proposed therapy is supported by the body of available data, including compelling evidence of disease modifying activity in relevant disease models and any available clinical trial data generated using the proposed therapeutic approach.
   - Consider the strengths and limitations of the data presented and/or the models utilized in completed studies.
3. **Project Plan and Design** - *Evaluate the project's plan and design.*
   - Evaluate the extent to which the proposed activities are necessary and appropriate to efficiently and effectively drive clinical development of the proposed therapy. For example, the applicant should consider:
     - whether the project will generate data to enable stage appropriate go/no-go decision making for further investment in the approach;
     - the feasibility of achieving timely full enrollment of the trial; and
     - the appropriateness of the manufacturing process, plan and analytical development plans.
   - Consider the whether the project's objective is likely to be achieved within the proposed budget and timeline.
   - Assess the validity of the potential project risks identified and contingency plans presented.
4. **Project Team and Resources** - *Evaluate the expertise and resources that will be deployed to achieve the project deliverables.*
   - Evaluate the appropriateness of the team's leadership, expertise and staffing to successfully complete all aspects of the project.
   - Consider whether a robust plan for coordination and execution of the project has been clearly outlined.
   - Assess the extent to which the team has access to all the necessary resources and facilities, including manufacturing facilities, to successfully conduct the proposed activities.

- Consider whether the collective team, including consultants and subcontractors, have a demonstrated track record of supporting stem cell-based and genetic therapy projects through clinical trials and/or towards licensure, as stage-appropriate.

5. **Population Impact** - *Evaluate the extent to which the project considers the potential impact of the proposed therapy across affected populations*
   - Evaluate the applicant's understanding and consideration of the affected population for the target indication, including any differences in detection/diagnosis, disease burden, care, and health outcomes across the affected population.
   - Assess the appropriateness of the proposed trial study population in the context of current knowledge of demographic groups at risk for the target indication.
   - Consider the applicant's goals to achieve a comprehensive distribution of subjects appropriate to the proposed indication and whether key criteria to disqualify any at-risk groups are justified.
   - Evaluate the extent to which the applicant’s plan for participant outreach, engagement, enrollment and retention addresses key barriers to trial participation by all affected population groups, is well-matched to the proposed study population and is feasible in the proposed time frame.

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Appendix D. ARS Memo Template

To: Members of the Application Review Subcommittee

From: [insert name or team authoring the memo]

Re: CIRM Team Recommendations: [Program Name]

Date: [ARS Meeting Date]

Introduction:

The CIRM team's role during Application Review Subcommittee (ARS) meetings is to assist the ARS in making well-informed funding decisions. The ARS is provided the funding recommendations of the GWG, which include the final scores, assessment against the review criteria, and summary of specific strengths and weaknesses. Beyond these recommendations, the ARS may also consider:

1. Programmatic factors
2. Recommendations from the CIRM Team
3. Public comment

This memo details the CIRM Team Recommendations for applications to CLIN2 which the ARS will consider on [DATE]. CIRM assessed all applications with a median GWG score of 80 or above based on available program budget, GWG score and comments, program guiding principles, prior awardee performance (if available), and any new information available to CIRM after the GWG review.

Summary of Program Budget Considerations:

Available Program Budget (Annual)	$XXX M
Budget Utilization – GWG Recommended	$XX M
Budget Utilization – CIRM Recommended	$XXM
Remaining Program Budget	$XX M (GWG Recommended) / $XX M (CIRM Recommended)

Summary of CIRM Team Recommendations:

Application	Median GWG Score	CIRM Recommendation
CLIN2-12345	90	Fund
CLIN2-XXXXX	80	Fund
CLIN2-XXXXX	75	Not Fund

Application Assessments:

1. Application number: CLIN2-12345

Title: *Phase I/II Clinical Trial for [Indication]*

GWG Outcome:

Median	Mean	High	Low	Scores to fund	Scores not to fund
80	81	86	70	4	10

CIRM Team Recommendation:

CIRM **does** recommend that the ARS fund application CLIN2-12345. CLIN2-12345 represents the only CGT approach to treating [Indication], a disease which has no other treatments available. CLIN2-12345 is unique in its modality and target in the CIRM portfolio and the external landscape. The applicant has a successful track record in CNS-directed AAV therapies. The Access and Affordability activities can be further developed during PFAR using CIRM's A&A specialists.

Guiding Principles Summary:

Transformative Clinical Impact	- GWG note the lack of other therapies for [indication] and the high unmet need in this patient population. GWG sentiment indicates that the therapy proposed in this application has the potential for transformative impact.
	- CIRM's active PDEV portfolio contains 0 awards that address [indication] and the active CLIN2 portfolio contains 0 awards that address [indication]
	- Outside of CIRM (based on Globaldata), there are
	  ○ 1 Phase 2 clinical program addressing a different subtype of this disease
	  ○ 0 approved US treatments.

Access & Affordability	Based on A&A expert review, the application under consideration **has not** provided a sufficiently detailed plan to achieve A&A goals.
Disease Representation	The application under consideration addresses a rare disease (200,000 patients in the US) not represented in CIRM's portfolio