DISCOVERY FOUNDATION AWARDS (DISC2): WEBINAR Q&A

WEBINAR REGISTRANT QUESTIONS AND ANSWERS

CONTENTS

WEBINAR ATTENDEE SUBMITTED QUESTIONS

PROJECT SCOPE AND FUNDING

1. **For therapeutic candidates, is it necessary for the project to last up to 3 years to budget for $1.5 million, or can a project last 2 years but still requires $1.5 million?**

   *No, it is not necessary- you are allowed to propose a $1.5 budget for a therapeutics project that is **up** to three years in duration, but could be shorter. The numbers we cited are caps, i.e. a for therapeutic candidate project, up to 3 years is allowed and for tool/tech candidate projects, up to 2 years is allowed; you only need to propose a duration that is necessary to achieve the Expected Outcome of your project. Be sure the funds calculator, budget justification, project plan, and timeline for all project acitivites align across the application components. Reviewers pay attention to whether proposed costs are reasonable.*

2. **Will the development of new programs, including the CIRM Neuro Strategy, affect the priorities and scope of the Discovery programs in the future?**

   Most likely, yes. The way that this will affect the programs will be by focusing their scope. Any such changes would first be approved by CIRM's Governing Board and subsequently reflected by updates to the Program Announcements.

3. **Would DISC2 fund a project testing a stem cell-based therapeutic candidate in combination with another drug?**

   Yes, provided the stem cell therapeutic candidate is novel.

4. **Does disease-modifying activity have to be demonstrated in an animal model, or can it be in an iPSC model?**

   Disease-modifying activity may be demonstrated in a human iPSC disease model, where relevant.

5. **For small molecules that enhance the differentiation of endogenous stem cell progenitors, is there a particular emphasis on any type of progenitor? Neural, muscle, glial?**

   There is currently no particular emphasis/priority for a specific progenitor cell.

6. **Is there a percentage of applications that will be allocated to therapeutic candidate vs. diagnostic/tool/medical device track?**

   No, there are no pre-defined quotas for therapeutic candidates vs. technolog candidates.

7. **Is my particular stem/progenitor cell type supported under the DISC2 mechanism?**

   Please review definitions of stem cells and progenitor cells that are provided in the DISC2 PA. If you provide an argument that these cells meet this definition, or it is largely established that they do, then they can be an eligible subject of study for applying to CIRM.

8. **Can a cancer vaccine be considered as a therapeutic candidate?**

   A cancer vaccine is eligible if the vaccine relies on stem cells for its therapeutic effect, or if stem/progenitor cells are used in its manufacture.

9. **Budget: Is annual salary escalation allowed in the budget? Is full tuition rate allowed for this grant type?**

   You may account for salary escalation in the budget you request, but be aware there are salary and stipend caps posted on CIRM's website that should not be exceeded within CIRM-grant support.

10. **How critical is it to show solvency for for-profit enterprises? How long of cash run is sufficient for the purposes of this grant?**

    For-profit organizations must provide documentation that shows 180 days cash on hand from date of application submission and the financial ability to meet the cofunding, if applicable, for the term of the project. The determination of solvency will be made at CIRM's sole discretion.

11. **Is there an indirect rate that is acceptable without further financial review over the direct costs?**

    For-profit organizations cannot claim indirect costs. For non-profit organizations, indirect costs are limited to 20% of allowable direct research funding costs awarded by CIRM (i.e., project costs and facilities costs), exclusive of the costs of equipment, tuition and fees, research patient care costs, as well as the costs of each individual subcontract, consultant, and service agreement in excess of $25,000. The indirect cost rate budgeted at the time of application is to be applied to the entire award project period.

12. **Do you need to have 50% of employees in California at the time of application or the time of award?**

    You must have 50% of employees in California at the time of application.

13. **Does DISC2 require a project manager and what is the minimum % effort?**

    There is currently no requirement for a Project Manager in DISC2, although it may be a good idea to include one if the project involves complex interdependencies. Data sharing and management is also an activity where project management may be helpful. CIRM may implement a requirement for Data Project Manager in future DISC2 opportunities, so be sure to peruse the most recent edition of the DISC2 program announcement if considering a future application.

14. **In the case of large, collaborative team science, does each person need to be in the budget or can personnel commit time without requesting compensation?**

    Key Personnel may have committed time without requesting CIRM funding, however, it is important to clearly indicate this in the budget justification.

15. **Can an out-of-state collaborator get salary support or only for lab supplies, etc?**

    Out-of-state collaborators may receive salary support in addition to lab supplies, etc.

16. **Any IP arising from the work funded by CIRM will be based at a CA institution. Is it okay for the IP that the preliminary data is based on to be based at a non-CA institution?**

    Yes, this is allowed. If you require any special licenses or permissions to use this IP in your project, you should consider uploading any applicable information about IP, licenses, and/or material transfer agreements that support the feasibility of your proposal.

17. **How important is a collaboration between an industry entity and academia for a compelling DISC2 application?**

    The value that a such a collaboration adds is likely project-dependent. There is no requirement for such a collaboration in DISC2, but depending on the type of project and stage and the vision for translation, having a partnership in place might be viewed as a strength, depending on what the partner brings to the program. There are, however, many examples of DISC2 programs that progressed into our TRAN1 program without any involvement of an industry partner, and many successful programs have chosen not to partner until a later stage of development.

18. **How is the clinical translatability of a DISC2 project evaluated? Is there a specific matrix/rubric?**

    If this question is referring to how Grants Working Group (GWG) members make this determination during the scientific review process, there is no specific rubric, rather they will apply the review criteria described on pages 12-13 of the DISC2 Program Announcement (see, especially, Criteria 1, 3 and 4.).

    If this question is referring to how CIRM defines "readiness" for eah of our R&D Pillar Programs, (e.g. DISC2/TRAN/CLIN), then please see the eligibility criteria for each of those individual programs. For DISC2, eligible proects must propose a research plan that will achieve the Expected Outome by the end of the DISC2 award period. This Expected Outcome, and associated deliverables, is defined for different candidate types on pages 5-6 of the DISC2 Program Announcement. Achieving these deliverables means the candidate should meet a minimal bar of "readiness" for initiation of translational stage activites. However, other considerations are important, for example, candidates may not be translatable if they include certain sequences, such as GFP that could be problematic, or if they are prepared using donor materials that will not be in compliance with FDA's requirements for Good Tissue Pratices.

19. **Can preliminary results include data from animal studies?**

    Yes. Preliminary data from animal studies can be used to support the rationale for pursuing a development candidate for use in humans, or with human materials .

20. **Do cancer stem cells fall within the scope of DISC2 awards?**

    Therapeutic candidates targeting cancer stem cells, where the proposed candidate is not itself a stem cell therapy or a genetic therapy, may be considered in scope if a) the proposed therapeutic effect is dependent on targeting human cancer stem cells for its mechanism of action and b) the proposal cites

convincing evidence that the targeted cells meet a definition of cancer stem cells. Cancer stem cells are defined experimentally by their ability to generate and recapitulate the cellular hierarchy of a continuously growing tumor, most often through serial xenotransplantation into animal models. If such evidence is weak or lacking, the proposal may be viewed as less responsive or in some cases, ineligible.

APPLICATIONS AND RESUBMISSIONS

21. What is the historical funding success rate for DISC2?

The historical funding rate for DISC2 varies from cycle to cycle, but is 18% when averaged over the last 7 years (10 competitions). The highest funding rate in a given cycle was 29%, and the lowest was 9%, when the program first debuted.

22. What are the page limits, formatting requirements for the Proposal sections described in the Program Announcement?

The full instructions (with page limits) are provided in the blank Proposal Template, which you will find within the DISC2 online application form in CIRM's Grants Management System (GMS; also called the CIRM Portal). ***This can only be accessed by creating a CIRM login, creating a new application, navigating to the Uploads section, and downloading the Word template.***

Proposal Templates can only be downloaded once applications become live in GMS, typically 4-6 weeks prior to the due date. See the DISC2 webinar slides for screenshots of the Proposal Template and templates for other required documents.

Please be sure to download and use the most current version of all CIRM templates- as they may be updated or changed in future calls.

23. How much preliminary data are required for DISC2?

Preliminary data are required to support the rationale and establish the feasibility of a given proposal. The amount of data required will be project-specific and may depend on many factors. The strongest types of preliminary data tend to support the rationale for the project, and the feasibility of executing the Research Plan to achieve the Expected Outcome in the course of the Award.

24. I'm uncertain whether to apply to Foundation (DISC0) or Quest (DISC2). How can I decide?

DISC0 and DISC2 are different with respect to expected outcome, application requirements, and review criteria. They are not interchangeable.

DISC0 Program Announcement (9.11.22)
DISC2 Program Announcement (3.15.23)

Generally speaking, the DISC0 program targets foundational or mechanistic studies that address a key knowledge gap or bottleneck in the field, whereas DISC2 awards support projects that are designed to culminate in a candidate therapeutic or prototype medical device, diagnostic or tool that is ready for translational stage activities (early development) by the end of the award period.

It is best to consult with CIRM about a specific project if you are uncertain whether it is a better fit for DISC0 or DISC2.

25. **Will CIRM have two rounds of DISC2 grants in 2023, and will the submission dates be the same as in 2022?**

    It has not yet been determined whether CIRM will have two rounds of application review for DISC2 in 2023, nor what the exact application deadlines would be. Because of the implementation of two large CIRM Infrastructure (INFR) programs, CIRM may only offer one round of DISC2 funding in 2023.

26. **What should I prioritize when revising and resubmitting a proposal that has been scored by the Grants Working Group?**

    Our advice is to be respectful of reviewer comments/feedback and address them to the best of your ability throughout your proposal, while summarizing your overall response using the Resubmission Statement page in the beginning of the Proposal Template.

27. **If I previously submitted a DISC2 application that was not funded, but think the project may be more suited to DISC0 (or *vice versa*), should I submit a new application or a resubmission?**

    Submitting a former DISC2 proposal under DISC0 (or vice versa) is not considered a resubmission since these two programs have distinct objectives, application requirements and review criteria. This would require an entirely new submission for DISC0.

    If your prior DISC2 (or DISC0) proposal was reviewed, our advice is to consider the Grants Working Group (GWG) feedback holistically while conceiving your new DISC0 (or DISC2) application. Some of the same individual GWG reviewers may evaluate the new application, but they will use distinct review criteria. The review criteria can be found in the Program Announcements (DISC0 pgs. 9-10, DISC2 pg. 13).

    Bear in mind that while there is minor overlap in the allowable activities for DISC0 and DISC2, applications that appear to be copy-pasted from one program to another will be considered ineligible and will not be reviewed by the GWG.

28. **Does the $1,500,000 budget cap for DISC2 awards pertain to the total award amount or the direct project costs only?**

    $1,500,000 is the maximum allowed total for direct project costs. Non-profit applicants may request indirect costs in addition to direct costs, and all applicants may additionally request facilities costs. Thus, for a project with $1.5M direct costs, the total award amount may be somwaht higher. The CIRM Funds Calculator in the online application should make this clearer. Please consult the Grants Management FAQ on CIRM's website for more information about direct and indirect project costs.

29. **Does CIRM grant extensions to the submission deadline?**

    No. CIRM does not have a mechanism for illness, bereavement, or other types of deadline extension for applicants.

30. **Research can take longer than anticipated; what happens if the project team doesn't meet an aim or milestone on time?**

If project aims and timelines are delayed due to technical challenges or other unexpected issues that may arise, CIRM expects grantees to communicate promptly with their assigned Science Officer and find solutions as early as possible. A No Cost Extension (NCE) can be requested with appropriate justification.

PRINCIPAL INVESTIGATORS AND KEY PERSONNEL

31. Does DISC2 allow Co-Principal Investigators?

'Co-PI' is sometimes meant to describe a Key Person who separately receives fund distributions. CIRM does not offer a 'co-PI' role nor support this type of arrangement. A DISC2 award is only given to a single PI / institution. However, collaborators, including investigators who share scientific and administrative leadership responsibilities with the PI, are allowed, and can be paid from the grant via a subcontract or as a Key Person. The specific roles and responsibilities each Key Person can be defined in the online portion of the DISC2 application.

32. Can a faculty member be a PI on one proposal and a collaborator on another proposal?

Yes. A Principal Investigator on one CIRM application can be a collaborator (subcontractor or Key Person) on another application(s), even if the applications are submitted in response to the same PA/RFA or in the same application review cycle. CIRM rules state that a PI can submit only one application per round, but this person can be a collaborator on a separate application(s) in the same round.

33. As a PI, can I commit 10% and have a Co-PI/collaborator who commits 10% to meet the 20% effort requirement?

No. The PI must commit 20% effort, salaried or not.

34. Can a postdoc be a PI on a CIRM application?

CIRM requires that a PI must be an employee of the applicant organization or be accountable for the conduct of the proposed project to the applicant organization through a formal contract. Also, the PI must be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI. There have been occasional circumstances where the applicant organization has provided a post-doc with the support and authority to act as a PI, but this not typical.

OUT-OF-STATE COLLABORATORS

35. Can my DISC2 grant support out-of-state collaborators?

Yes, out-of-state collaborators can receive funds from a CIRM award through a subcontract. However, CIRM requires that the California Organization exercises direction and control over the subcontracted activities. The funded CA organization must retain any new intellectual property generated from the CIRM funding, and the out-of-state organization cannot retain independent publication rights in any intellectual property (e.g., invention, technology, data) arising out of the CIRM funded project.

36. If we have a collaborator who is outside California, how should we address this in a DISC2 application?

An out-of-state collaborator should be entered in the Consultants/Subcontracts section of the online application, along with the budget associated with the subcontract (which will be justified in the Budget Justification section). You will need to provide a name, institution, and describe the role/responsibilities for

each collaboration. If the collaborator's specific expertise or resources are important components of your project, a biosketch should be included.

Reminder: Any new IP generated from the use of CIRM funds outside the State of California must either stay, via assignment if necessary, with the California applicant organization/awardee or such rights must be waived. One option is to put into place an agreement wherein the out-of-state contractor will assign rights to any new IP to the CIRM applicant/awardee that comes from the CIRM funded project if they agree to take CIRM funds and receive a license-back for research development purposes. Any commercialization with CIRM-funded intellectual property may trigger revenue requirements in the CIRM IP regulations, which are on the CIRM website (link here). This link is to CIRM's IP FAQ .

REVIEW PROCESS

37. How are confidentiality and IP maintained by CIRM during the review process, especially for pre-DCs structures? Should a composition of matter patent be filed in advance of submission or are structures not required?

DISC2 PA page 12 addresses confidentiality. Ultimately, applicants must decide whether they are comfortable with submitting a complete application to CIRM with the information needed for the project to be assessed in the review process.

38. What are CIRM reviewers looking for in the Diversity, Equity, and Inclusion (DEI) section?

CIRM provides guidance to reviewers for evaluating Diversity, Equity and Inclusion (DEI) in the Program Announcement, under 'Does the project uphold principles of diversity, equity and inclusion (DEI)?' (pg. 10). This guidance is in the form of subquestions and is provided in the application critique form that reviewers fill out in advance of the review meeting.

"Does the project plan and design adequately address and account for the influence of race, ethnicity, sex, gender, and age diversity? Would the project outcomes extend or validate the applicability of regenerative medicine discoveries to underserved populations, including underserved racial/ethnic communities? Has the applicant described prior efforts or proposed plans for outreach, partnership, or educational activities to inform the development of DEI within the research project?"

Our general advice is:

- ***Focus on CIRM's Mission:** Accelerating world class science to deliver transformative regenerative medicine treatments to a diverse California and world. Determine how the project fits into CIRM's mission and make this very clear in the proposal.*
- ***Be specific**, e.g., instead of stating that you will ensure the use of a collection of cell lines representing diverse genetic ancestries, delineate the exact cell lines you will be using, and the genetic ancestries they represent. Provide a rationale for the genetic ancestries you seek to include. Describe where you anticipate hurdles in achieving that diversity, and how you plan to overcome those hurdles – either at the DISC2 stage or, if necessary, in future work.*
- ***Be intentional**, e.g., instead of stating the access you may have to samples or participants from diverse backgrounds, explain how you will go about ensuring that samples / participants from diverse backgrounds are actually included / recruited into your study.*
- ***Convey that you understand key issues related to diversity, equity, and inclusion.** If unfamiliar or inexperienced with how best to approach this subject, work with an expert to articulate and execute your DEI approach. Remember, you can propose to use CIRM funds for activities intended to promote and uphold principles of Diversity, Equity, and Inclusion (DEI) in the conduct of your study.*

- ***Tap into your institution's resources****, but don't rely on your institution's website text. The reviewers do not expect you to create a sea change on your own, but they are attentive to the project-specific nature of your DEI statement.*
- ***Don't neglect the third subquestion (above).*** *Even if the Research Plan fully incorporates DEI principles, your DEI statement (and the budget) should include activities intended to inform further development of DEI within the project. These, too, should be specific and intentional.*

  Please note: Because CIRM is prohibited from taking race, ethnicity, national origin, and gender into account in making grant decisions, applicants should refrain from including race, ethnicity, national origin, or gender in describing the applicant team personnel.

39. If a project proposal focuses on a research area far outside/beyond the expertise of the review panel, will external reviewers be invited?

The CIRM GWG currently comprises about 200 reviewers with expertise in many subject areas; a listing is here: https://www.cirm.ca.gov/board-and-meetings/grants-review-working-group-members. When necessary, CIRM's Review Office recruits Specialist reviewers to provide expertise that is not fully covered by available members of the GWG. Feel free to send general suggestions to review@cirm.ca.gov; note that an expert you refer may not be invited to review your application(s) if a potential conflict exists.

CIRM'S HIPSC REPOSITORY

40. Is CIRM interested in funding studies of diseases that are not represented in the CIRM hiPSC repository? Apart from central nervous system (CNS) disorders, does CIRM have other disease priorities?

Yes. The CIRM hiPSC Repository comprises cell lines for 17 diagnoses for which multiple patient and familial samples were obtained and is hopefully a valuable resource for California researchers. It is not meant to promote the study of these diseases above others.

With the passage of Prop 14 in 2020, California voters earmarked $1.5 billion of CIRM's $5 billion in funding for disease affecting the central nervous system (CNS). While we encourage submission of DISC2 proposals focused on therapeutic candidates or tools for CNS disorders, the DISC2 review process remains open and unbiased with regard to disease or system.

In accordance with Prop 14, CIRM may stipulate priorities for basic CNS research in future calls for Discovery applications.

41. Can cells from the CIRM hiPSC Repository be used to develop a therapeutic in my DISC2 proposal?

This depends. The hiPSCs in the CIRM Repository *are for research use only, meaning, they are not appropriate for use in the manufacture of an allogenic cell therapy candidate*. However, if you are developing an autologous, iPSC-derived cell therapy candidate, these lines could be useful for establishing reproducibility of your therapeutic approach. Such lines could also be useful for testing of other types of candidates.*

> ** Information about cell lines that* may *be appropriate for developing allogeneic PSC-derived cell therapies can be found on CIRM's Information for Applicants Website.*

42. Are the primary cells from these individuals available?

No, the primary cells (PBMCs/fibroblasts) are not available from CIRM's hiPSC repository.

43. Are there any isogenic iPSC repositories available to non-profit institutions through CIRM?

Not yet. However, this effort is underway we will update this section if/when that occurs.

44. Does the CIRM hiPSC repository have any lines with Bulk/SC RNA Seq Data?

There are no single cell RNA sequencing data available via the repository for any of its hiPSC lines. However, as several of these lines have been used in published research, single cell RNA seq data may be available in association with the published articles.

45. Can the CIRM hiPSCs be used without licenses by California companies?

No, research or commercial use by for-profit entities and commercial use by non-profit entities requires the entity to take a commercial license. Unlike other repositories, the commercial license terms were negotiated before the bank was made. If an entity takes a commercial license, that license applies to the entire bank whether the entity uses one line or all of the lines. The commercial license terms can be requested through fcdi-licensing@ fujifilm.com.

CIRM GRANTS MANAGEMENT OFFICE

46. I've heard that CIRM-funded researchers who don't meet aims or milestones on schedule have to self-pay for their studies using alternate funds. Is this true?

You may be thinking of CIRM's later stage programs (TRAN1/2/3/4, CLIN1/2), where grant payments are linked to Operational Milestone achievement. Applicants to those later stage programs are required to have access to contingency funds so their projects can continue if an Operational Milestone is significantly delayed.

Discovery Stage programs such as DISC0 and DISC2 do not use the Operational Milestone model at this time. Instead, grant payments are issued at scheduled intervals as defined in the Notice of Award, contingent on grantee maintaining compliance with CIRM's post-award reporting requirements. If milestones are substantially delayed, CIRM expects grantees to communicate promptly with their assigned Science Officer and find solutions as early as possible. Grantees may request a one-time no cost extension with appropriate justification.

47. Other questions about Post Award Management: see Grants Management FAQ at link below.

https://www.cirm.ca.gov/researchers/managing-your-grant