Real Life™

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Grants Working Group DISC2 Review

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CIRM
CALIFORNIA'S STEM CELL AGENCY

Mission Statement

OUR MISSION

Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

Recurring Programs

DISCOVERY

TRANSLATION

CLINICAL

New Idea → 2/Year → Single Product Candidate → 2/Year → Pre-IND or Equivalent → 12/Year → Approved Therapy

CIRM Quest Discovery Program

Objective

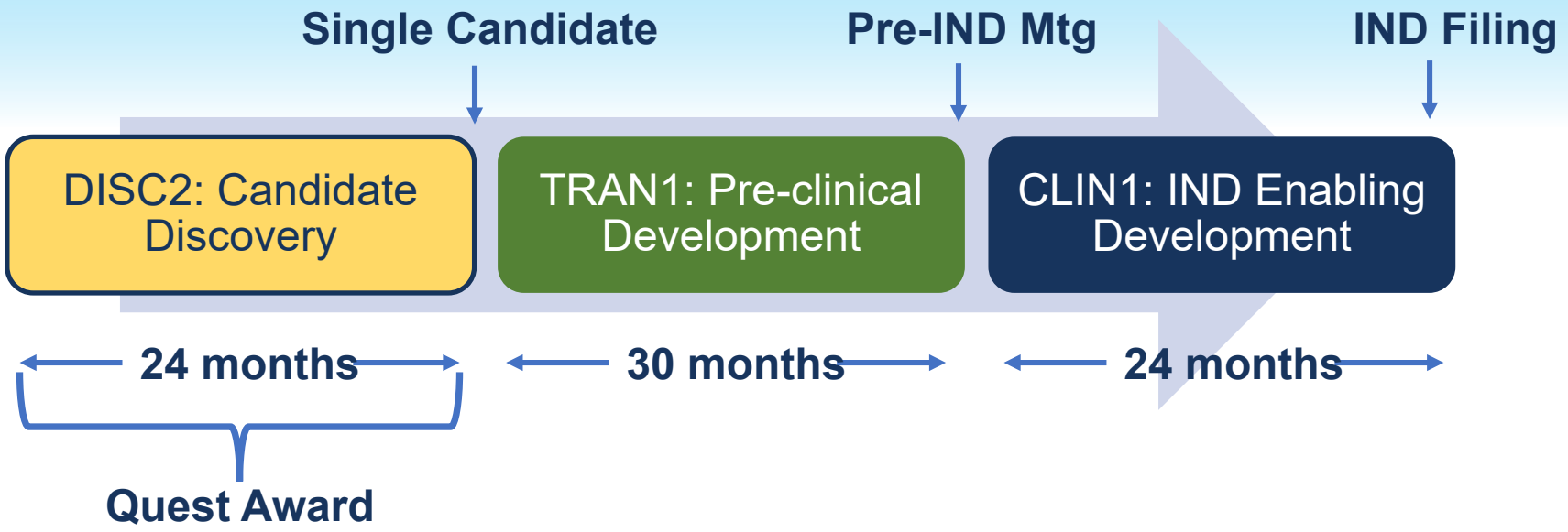
The Quest Program will promote the discovery of promising new stem cell-based and gene therapy technologies that could be translated to enable broad use and ultimately, improve patient care.

Projects funded through the Quest Awards should propose technology that is uniquely enabled by human stem/progenitor cells or uniquely enabling for the advancement of stem cell-based therapies or aimed at developing a gene therapy approach.

What are we looking for?

Candidate Type	Therapeutic	Diagnostic/Device/Tool
Expected Outcomes for a two-year project	Single candidate identified	Candidate prototype identified
	Target Product Profile drafted	Target Product Profile drafted
	Disease modifying activity demonstrated	Scientific proof-of-concept demonstrated

Accelerating Therapeutic Development



Expected **outcomes** of DISC2 applications:

- A single candidate ready for translational studies identified.
- A Target Product Profile developed.
- Demonstration of disease-modifying activity or proof of concept.

Positive Selection (Two-Stage) Review Process

- Performed when the total number of applications exceeds the capacity of the GWG to review in a single session.
- In the first stage, GWG members including patient advocates and nurse Board Members conduct a pre-review of applications and select which ones to advance to a full review.
- The CIRM President and CIRM will examine non-selected applications to determine if any merit a full review. The remainder are not considered further.
- A total of 75 eligible applications were submitted,13 bypassed the process with a previous 80-84 score, and a total of 54 advanced to the full discussion stage by GWG.

Scoring System for DISC2 Applications

- **Score of "85-100"**

  Recommended for funding, if funds are available

- **Score of "1-84"**

  Not recommended for funding

  *Applications receiving a score of **80-84** in this review cycle were deemed by the GWG to have sufficient merit to bypass the positive selection process and advance to full scientific review if resubmitted in the next review cycle*

- **Score of "1-79"**

  Not recommended for funding

Applications are scored by all scientific members of the GWG with no conflict.

The **median** of all individual GWG scores determines final score.

Review Criteria

1. Does the project hold the necessary significance and potential for impact? (i.e., what value does it offer; is it worth doing?)
2. Is the rationale sound? (i.e., does it make sense?)
3. Is the project well planned and designed?
4. Is the project feasible? (i.e., can they do it?)
5. Does the project address the needs of underserved communities?

Board members with Conflicts of Interest

Board members with Conflicts of Interest for DISC2 applications		
Haifaa Abdulhaq	Leon Fine	Christine Miaskowski
Kim Barrett	Elena Flowers	Suzanne Sandmeyer
George Blumenthal	Judy Gasson	Barry Selick
Michael Botchan	Larry Goldstein	Michael Stamos
Linda Boxer	James Kovach	Art Torres
Carol Christ	Pat Levitt	Kristiina Vuori
Deborah Deas	Linda Malkas	Karol Watson
Ysabel Duron	Shlomo Melmed	Keith Yamamoto

GWG Recommendations Summary

	Number of Apps	Total Applicant Request	Funds Available
Recommended for funding Score 85-100	17	$22,025,125	$57,890,193
Not recommended for funding Score 1-84	37		

For each award, the final award amount shall not exceed the amount approved by the ICOC Application Review Subcommittee and may be reduced contingent on CIRM's assessment of allowable costs and activities.

Minority Reports

- Under Prop 14, any application that is not recommended for funding by the GWG, but which had 35% or more members score to fund the application must include a minority report.

- The minority report is included in the review summary and provides a brief synopsis of the opinion of reviewers that scored the application 85 or above.

CIRM Team Recommendations

CIRM Team concurs with the GWG recommendations for funding.

In addition, the CIRM Team supports the minority position for applications DISC2-13510 and DISC2-13475 and recommend funding of these applications.

App Number	Title	Funds Requested	Score
DISC2-13510	An hematopoietic stem-cell-based approach to treat HIV employing CAR T cells and anti-HIV broadly neutralizing antibodies	$1,143,600	84
DISC2-13475	Developing gene therapy for dominant optic atrophy using human pluripotent stem cell-derived retinal organoid disease models	$1,345,691	84

Minority Report for DISC2-13510

Score	Num ≥85 (Fund)	Num <85 (Do not fund)	Range	Funds Requested
84	7	7	80-90	$1,143,600

TITLE: An hematopoietic stem-cell-based approach to treat HIV employing CAR T cells and anti-HIV broadly neutralizing antibodies

DISEASE INDICATION: HIV infection

PRODUCT TYPE: Cell and gene therapy

APPROACH: Develop a CAR T and B cell therapy expressing broadly neutralizing antibodies against HIV

Minority Report for DISC2-13475

Score	Num ≥85 (Fund)	Num <85 (Do not fund)	Range	Funds Requested
84	7	8	79-85	$1,345,691

TITLE: Developing gene therapy for dominant optic atrophy using human pluripotent stem cell-derived retinal organoid disease models

DISEASE INDICATION: Dominant optic atrophy

PRODUCT TYPE: Gene therapy

APPROACH: Use PSC-derived human retinal organoids to evaluate efficacy of a gene therapy

Minority Report for DISC2-13413

Score	Num ≥85 (Fund)	Num <85 (Do not fund)	Range	Funds Requested
84	6	8	70-85	$1,221,980

TITLE: In Utero Treatment of Duchenne Muscular Dystrophy with Non-viral Gene Editing

DISEASE INDICATION: Duchenne muscular dystrophy

PRODUCT TYPE: Gene therapy

APPROACH: Develop a lipid nanoparticle/mRNA complex that can safely and efficiently edit muscle stem cells in utero

Minority Report for DISC2-13442

Score	Num ≥85 (Fund)	Num <85 (Do not fund)	Range	Funds Requested
83	6	8	80-86	$1,342,606

TITLE: Microgel encapsulated iPSC-derived notochordal cells to treat intervertebral disc degeneration and low back pain

DISEASE INDICATION: Intervertebral disc degeneration

PRODUCT TYPE: Cell therapy

APPROACH: Develop an injectable microtissue-encapsulated iPSC-derived notochordal cell therapy to treat disc degeneration