

Grants Working Group Recommendations

CLIN2 Clinical Trial Awards

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Review

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Our Mission

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



Strategic Impact Goals

Accelerating Discovery & Translation	Cell & Gene Therapy Approvals	Accessibility & Affordability of Therapies	Diverse Workforce Development
Goal 1: Catalyze the identification and validation of at least four novel targets and biomarkers, ensuring integration into preclinical or clinical research for diseases in California Goal 2: Accelerate the development and utilization of 5-8 technologies that have the potential to improve safety, efficacy, and/or quality of cell and gene therapies	Goal 3: Advance 4-7 rare disease projects to Biologics License Application (BLA) Goal 4: Propel 15-20 therapies targeting diseases affecting Californians to late-stage trials	Goal 5: Ensure that every BLA-ready program has a strategy for access and affordability	Goal 6: Bolster CIRM's workforce development programs to address gaps and meet evolving demands in regenerative medicine

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Updated CLIN2

- Allows for support of emerging **novel clinical trial designs** in CLIN2 program
- Incentivizes stage-appropriate **market access strategy** development and **pre-commercialization** activities in CLIN2 program
- Incorporates **prioritization of innovative therapies for diseases that affect Californians**

CLIN2 Program Objective

To support the completion of an interventional phase 1, 2, or 3 trial for an innovative stem cell-based or genetic therapy addressing a serious unmet need and with the potential for transformative benefits to patients, families and the health care system.

CLIN2 – Key GWG Updates

- Competitive evaluation of applications within each cycle
- Scientific scoring adopted 1-100 scale
- Four cycles per year
- Scientific review criteria have been updated
- New 'Access and Affordability' proposal and evaluation by A&A reviewers
- Program preferences for CLIN2 qualification have been established and applied

CLIN2 Program Structure

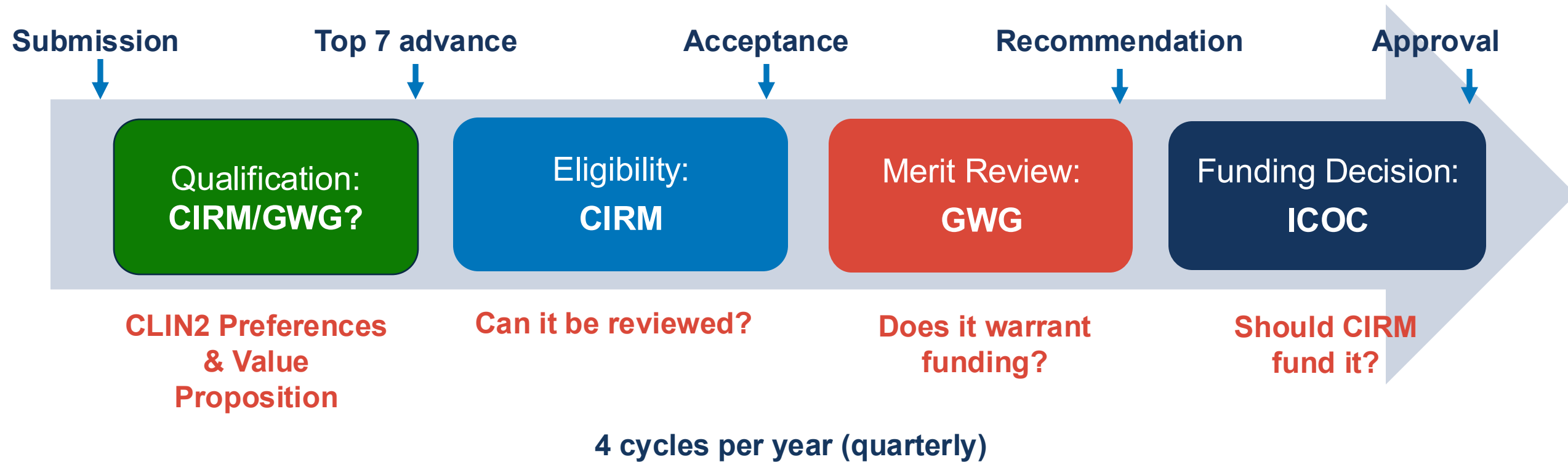
	CLIN2		
	First-in-Human	Phase 2 or subsequent*	Phase 3 or pivotal
Recurrence	4x per year		
Max Duration	4 years		
Applicant	California or non-California organizations		
Co-funding**	30% (for-profit) None (non-profit)	50% (for-profit) None (non-profit)	50%
Max Award (Total Cost)	\$8M (for-profit) \$12M (non-profit)	\$15M	\$15M
Awards/Year	9-16***		
Projection	9 x \$15M = \$135M		
Total Funds/Year	\$135M		

* Subsequent trials are Ph1 trials following a First-in-Human trial with the same candidate, disease indication and route of administration

** Co-funding is a percentage of total Allowable Project Costs

*** Number of awards is dependent on how many at each stage and organization status.

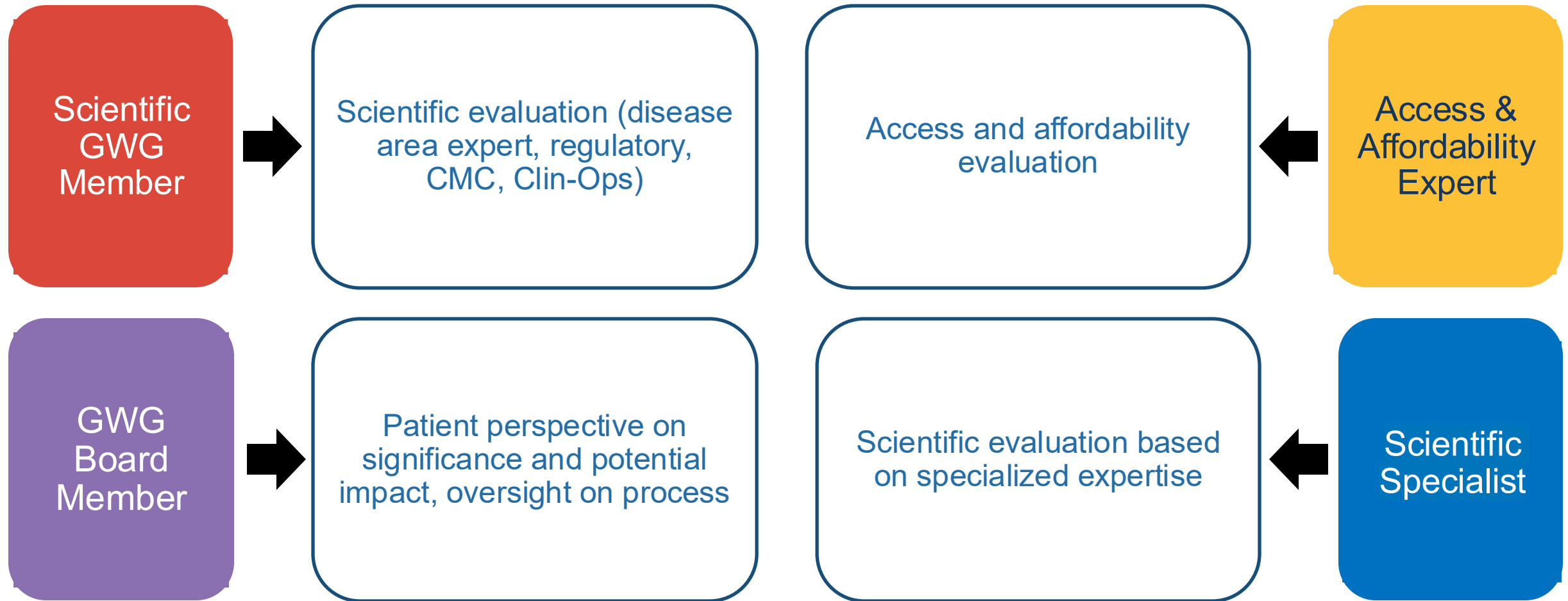
CLIN2 Application & Review Process



GWG – Grants Working Group

ICOC – Independent Citizens' Oversight Committee

CLIN2 GWG Panel Composition and Roles



Scientific Scoring System

Using the 1 to 100 scale

- **Median score of 85-100:** *Exceptional merit and warrants funding, if funds are available.*
- **Median score of 1-84:** *Not recommended for funding.*
- Scoring is holistic and based upon all facets of the expert review.
- GWG are encouraged to make full use of the scoring range to signal their enthusiasm for each project.

CLIN2 Scientific Review Criteria

1. **Value Proposition** - Evaluate the extent to which the therapy offers a compelling value proposition
2. **Rationale** - Evaluate the scientific rationale for the proposed therapy and the strength of the supporting data
3. **Project Plan and Design** - Evaluate the project's plan and design
4. **Project Team and Resources** - Evaluate the expertise and resources that will be deployed to achieve the project deliverables
5. **Population Impact** – Evaluate the extent to which the project considers the potential impact of the proposed therapy across affected populations

Access & Affordability

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

- Applicants complete an Access and Affordability (A&A) Proposal that is evaluated by a subject matter reviewer.
- A&A reviewers present their evaluations at GWG meetings along with the scientific and board reviewers.
- Access and affordability evaluations may inform scoring of the review criteria.
- For early-stage trials, deficiencies identified in A&A proposals may be addressed in the award period.

GWG Recommendations

Recommendation	Number of Apps	Total Applicant Request	Funds Available
Recommended for funding Score of 85-100	3	\$34,999,993	\$135,000,000
Not recommended for funding Score of 1-84	3		

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.

No CLIN2 applications qualified for a minority report this cycle.

CIRM Team Recommendations

App Num	Total Budget Request	GWG SCORE	Hi	Lo	Y	N	CIRM Recommendation
CLIN2-19068	\$8,000,000	90	90	75	12	2	FUND
CLIN2-18731	\$15,000,000	86	90	75	10	3	FUND
CLIN2-18595	\$11,999,933	85	90	70	8	7	FUND
CLIN2-19061	\$8,000,000	80	86	70	4	10	FUND
\$42,999,933		CIRM Team recommends funding of CLIN2-19061 in addition to those recommended by GWG.					

CIRM Team Recommendations Rationale

CLIN2-19061 proposes a gene therapy (AAV expressing FIG4 transgene) to address CMT4J.

- CIRM's active PDEV and CLIN2 portfolio contain no awards that address CMT4J.
- The proposed therapy represents a novel modality in the external landscape. There is one known phase 2 clinical trial addressing a different type of CMT and no approved treatments exist for CMT4J.
- This application is a progression from a previously CIRM-funded CLIN1 award.
- Concerns raised by GWG are readily addressable and would not prevent the project from achieving success.