GWG Recommendations for Applications Submitted to the CLIN Program

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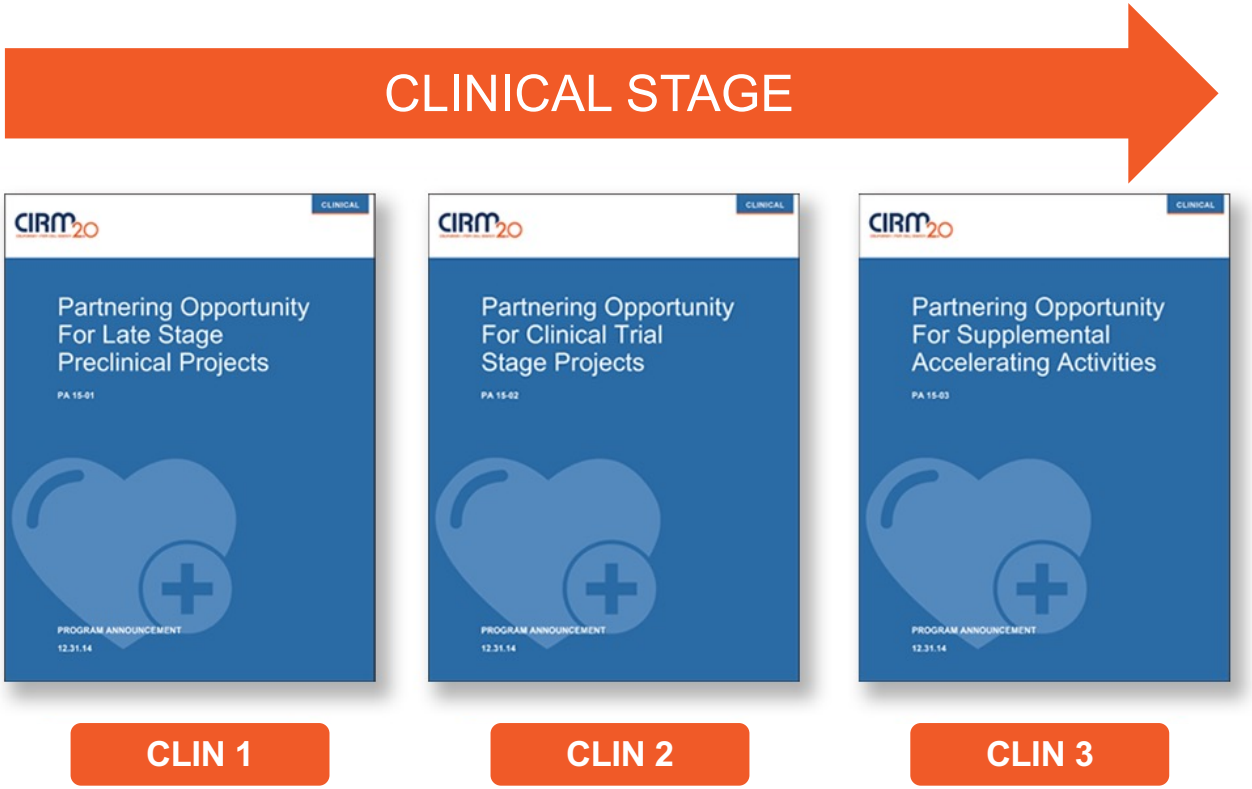
CIRM
CALIFORNIA'S STEM CELL AGENCY

Clinical Stage Programs



Jan-Jun 2021 Clinical Budget Status

Annual Allocation: $100 million

Amounts are shown in millions

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?

Scientific Scoring System for Clinical Applications

- **Score of "1"**

  Exceptional merit and warrants funding.

  May have minor recommendations and adjustments that do not require further review by the GWG

- **Score of "2"**

  Needs improvement and does not warrant funding at this time but could be resubmitted to address areas for improvement.

  GWG should provide recommendations that are achievable (i.e., "fixable changes") or request clarification/information on key concerns.

- **Score of "3"**

  Sufficiently flawed that it does not warrant funding and the same project should not be resubmitted ***for at least 6 months****.*

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

Elements in CIRM Application Review

- **Addressing the Needs of Underserved Communities**
  - **This section describes the applicant's plan for outreach and enrollment of a diverse patient cohort that accounts for racial, ethnic and gender diversity**
  - **The section is evaluated as part of the overall project and incorporated into the scientific merit score (1,2 or 3)**
- **Diversity, Equity and Inclusion**
  - **This section describes how the applicant team incorporates diverse perspectives and experiences to improve the project through the composition of the team and/or any other approaches**
  - **This section is evaluated and scored by patient advocate/nurse members of the Board (appointed to the GWG) and shown in the DEI score (0-10)**

CLIN2-12319: Cell and Gene Therapy for ALS

Therapy	Allogeneic neural progenitor cells genetically engineered to secrete GDNF
Indication	Amyotrophic lateral sclerosis (ALS)
Goal	Complete a phase 1/2a trial
Funds Requested	$11,990,372 ($0 Co-funding)

Maximum funds allowable for this category: $12,000,000

CLIN2-12319: Background Information

Clinical Background: Amyotrophic lateral sclerosis (ALS) is an incurable neuromuscular disease with progressive loss of motor neurons in the spinal cord and brain, leading to paralysis and death normally within 5 years of diagnosis.

Value Proposition of Proposed Therapy: Currently, there are no effective treatments for ALS. The proposed therapy offers a one-time treatment with the possibility of improved patient outcomes including slowing or halting of disease progression.

Why a stem cell project: The therapeutic candidate contains neural progenitor cells.

CLIN2-12319: Related CIRM Portfolio Projects

Application/ Award	Project Stage	Project End Date	Indication	Candidate	Additional Notes
Current Application	Phase 1/2a clinical trial	~Jul 2025	ALS	GDNF-secreting neural progenitor cells	Allogeneic cell therapy delivers GDNF, which has neuroprotective properties, and produces astrocytes to restore microenvironment. Advances administration to motor cortex and effect on upper extremities.
CLIN2	Phase 1 clinical trial	Jul 2021	ALS	GDNF-secreting neural progenitor cells	Initial trial with same candidate as above, but administered in lumbar region to assess safety, tolerability, and possible effect on lower extremities.
CLIN2	Phase 3 clinical trial	Jul 2021	ALS	MSC cell therapy	Autologous bone marrow-derived mesenchymal stem cells secreting neurotrophic factors that may activate neuroprotective and immunomodulatory pathways

CLIN2-12319: Previous CIRM Funding to Applicant

Project Stage	Indication	Project Outcome	Project Duration	Award Amount	Milestones*
Phase 1 clinical trial (Active)	ALS	Safety, feasibility	Apr 2017 – Jul 2021	$6,154,067	**M1-M4:** Enrollment and dosing of proposed patients (Achieved on time) **M5:** CSR submission (Minor delay)
IND-enabling (Closed)	ALS	Preclinical studies, IND filing, phase 1 trial	Feb 2013 – Apr 2017	$16,168,464	**M1-M4**: Preclinical safety/toxicity, dose-ranging studies, manufacturing, IND filing (Achieved with minor delays) **M5-M6**: Phase 1 trial not completed, but achieved under subsequent CLIN2 award
Phase 1 clinical trial (Active)	Retinitis pigmentosa	Safety, initial efficacy	Dec 2019 – Nov 2023	$10,444,063	**M1-M5** Enrollment and dosing of proposed patients (enrollment delayed by COVID-19) **M5-M6** Topline data and CSR submitted (not started)

CLIN2-12319: GWG Review

GWG Recommendation: Exceptional merit and warrants funding

Scientific Score	GWG Votes
1	10
2	3
3	0

DEI Score: 8

CIRM Team Recommendation: Fund (concur with GWG recommendation)

Award Amount: $11,990,372*

*Final award shall not exceed this amount and may be reduced contingent on CIRM's final assessment of allowable costs and activities.