February 23, 2017

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CALIFORNIA'S STEM CELL AGENCY


# CLIN, TRAN and DISC Concept Plan Amendments Agenda Item #10

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# Eligibility Determination

Explicitly state CIRM's authority to make an eligibility determination, except with respect to the subjective clinical criteria, until the time of contract execution.

- Apply prospectively to awards approved from Feb 23, 2017 forward.
- CIRM will inform the Application Review Subcommittee if it exercises this authority on any award approved by the Subcommittee.

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# Good Standing Requirement (All concepts)

Require applicants to verify:

(1) systems in place to track CIRM funds *(limited to for-profits and non-profits in existence for < 5 years)*

(2) CEO, CFO, or PI has not been convicted of, and is not under investigation for, crimes involving fraud or misappropriation *(limited to for-profits and non-profits in existence for < 5 years)*

(3) PI is not under investigation for research misconduct and is not barred from receiving research funds by DHHS Office of Research Integrity

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# Personnel Eligibility

**PI Minimum Percent Effort**: Require a PI to propose and justify percent effort for each phase of the project timeline to match the proposed activities (but not less than 15% averaged over the project period). (CLIN 1, 2, 3)

- Ensure effort matches activity
- Ensure CIRM is not paying for unnecessary work
- Minimum based on experience of GWG clinician scientists that oversee clinical trial projects

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# Personnel Eligibility

- **Project Manager**: Allow applicants to satisfy requirement by entering into a contract with CIRM's Stem Cell Center (CLIN and TRAN 1-3)
- **Project Manager Minimum Percent Effort:** Reduce minimum percent effort for TRAN projects from 50% to 35%
  - Based on advice from independent consultants and the SCC, which are experienced in providing project management services for this stage of development.

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# Project Eligibility

**Readiness**: Reduce proposed time to file an IND for CLIN1 applicants from 24 months to 18 months

- Align with CIRM strategic goal to reduce time from discovery phase to initiation of clinical trial to 4 years (30 months TRAN +18 months CLIN1)
- Average time proposed by CLIN1 applicants is 16.8 months

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# Project Eligibility

- **Small Molecule/Biologic**: Clarify eligibility of research involving small molecules or biologics:
  - for which a stem cell is necessary to manufacture the therapy (e.g., exosomes derived from a stem cell)
  - that modifies a stem cell therapy (e.g., tracking agent)
  - Applies to TRAN 1, CLIN 1 and CLIN 2-Phase 1 trials

# Project Eligibility

- **Phase 2 Trials**: Restrict to cellular therapies where stem/progenitor cells either compose the therapy or are used to manufacture the cell therapy
- **Phase 3 Trials**: (1) Restrict to cellular therapies where stem/ progenitor cells either compose the therapy or are used to manufacture the cell therapy AND where the therapy is for rare indications; and (2) Allow applicant that has been informed by the FDA that its phase 2 trial could be used for marketing approval to apply for Phase 3 funding

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# Eligibility for Devices

- **TRAN 3**: Include studies on a device where the therapeutic mechanism of action requires the recruitment or incorporation of an endogenous human stem or progenitor cell

- **CLIN 2**: Limit device trials to feasibility studies

# CLIN3 Program Scope

Limit to awardees for new activities that would enable FDA marketing approval of the proposed stem cell treatment

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# Funding Caps (CLIN)

- CLIN 1: $6M (non-profits) & $4M (for-profits)

- CLIN 2: (1) Phase 1 trial: $5M (for-profits) and $9M (non-profits)
  (2) Phase 2 trial: $12M
  (3) Phase 3 trial: $15M

- CLIN 3: $15M

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# Clinical Award Cap Model

About $478M available. Goal is to fund 40 CLIN2 trials between 2017 and 2020

| | | | | | CY2017-2020 | |
|---|---|---|---|---|---|---|
| CLIN | Stage | NP or FP | #Awards | Award Cap | Amount | % Share |
| CLIN1 | IND | Non-Profit | 8 | $6.0 | $48.0 | 15% |
| CLIN1 | IND | For-Profit | 6 | $4.0 | $24.0 | |
| CLIN2 | Phase 1 | Non-Profit | 14 | $9.0 | $126.0 | 33% |
| CLIN2 | Phase 1 | For-Profit | 6 | $5.0 | $30.0 | |
| CLIN2 | Phase 2 | NP/FP | 16 | $12.0 | $192.0 | 40% |
| CLIN2 | Phase 3 | NP/FP | 2 | $15.0 | $30.0 | 6% |
| CLIN3 | Phase 2/3 | NP/FP | 2 | $15.0 | $30.0 | 6% |
| | | | | | $480.0 | |

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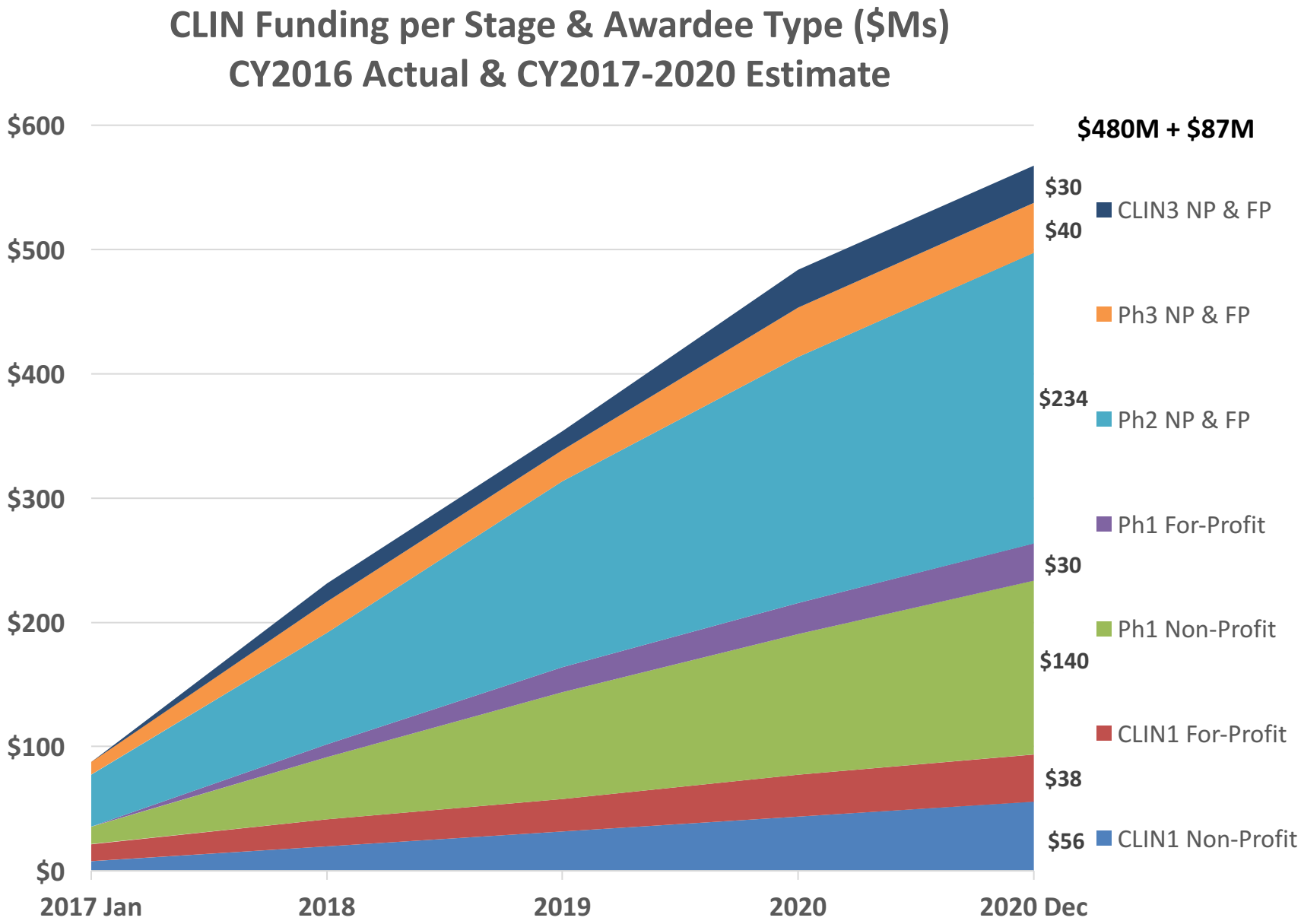
CLIN Funding per Stage & Awardee Type ($Ms)
CY2016 Actual & CY2017-2020 Estimate
$600
$500
$400
$300
$200
$100
$0
2017 Jan
2018
2019
2020
2020 Dec
$480M + $87M
$30
$40
$234
$30
$140
$38
$56
CLIN3 NP & FP
Ph3 NP & FP
Ph2 NP & FP
Ph1 For-Profit
Ph1 Non-Profit
CLIN1 For-Profit
CLIN1 Non-Profit

# Fundable Activities

- CLIN 1 and 2: Permit funding for necessary manufacturing activities for a follow-on clinical trial

- CLIN 2: Permit funding for comparability studies and commercial development activities

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# REQUESTED ACTION

Approval of proposed amendments to CLIN, TRAN and DISC concept plans

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