PRECLINICAL

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

PDEV (Preclinical Development Awards): Funding Opportunity for Preclinical Stage Projects

Reference Proposal Template

This is a past proposal template for applicants to reference only. Proposal template in the application may change. Do not use this proposal template in your application.

07.17.2025

PDEV Preclinical Development Awards

This document is the proposal template for PDEV applicants. Please edit the footer text with your application number (i.e., replace 'XXXXX' with '12345') and save your copy with a custom filename (i.e., PDEV-12345 Proposal.docx).

The template includes full instructions, sample tables, tables to be populated by the applicant, and open sections for applicant responses. Applicants can add figures and tables to this document.

Applicants must download this template directly from the active application's 'Document Uploads' webpage. Do not re-use a proposal template from a prior application.

Do not modify template settings. This includes, but is not limited to, the template font (Arial), font size (10 pt), margins (1" all around), and paragraph and table properties. No appendices are allowed.

Applicants should not delete instructions. Do not modify template settings. This includes, but is not limited to, the template font (Arial), font size (10 pt), paragraph formatting, margins, table properties, or page orientations. No appendices are allowed. Content that exceeds the template page limits will be deleted from the application.

When you have finished the proposal, fill in the page number for each proposal section in the Table of Contents, save as a PDF, and upload the document to your online application, along with requested documentation, on the 'Document Uploads' page.

Project Information

Application Number:

PI Name:

Email:

Project Title:

Contact

For inquiries about applying please contact preclinical@cirm.ca.gov.

For inquiries about the review process please contact review@cirm.ca.gov.

Table of Contents

Resubmission Statement

Are you resubmitting a substantially similar proposal that addresses Grants Working Group (GWG) reviewer comments on a previous CIRM application?

☐ Yes.
☐ No, this is a new application.

If "Yes", please summarize your responses to the GWG reviewers and the changes you have made in the application.

Retain the instructional text. Response length can be the rest of this page plus up to 1 additional page. Content exceeding page limits will be deleted.

Project Summary

Briefly describe the project for which you seek funding, highlighting what you believe is most important for reviewers to consider.

Retain the instructional text. Response length can be the rest of this page. Content exceeding this page will be deleted.

Target Product Profile

Populate the template Target Product Profile (TPP) below to create a product 'label' describing achievable, appropriate base case and optimal specifications for use of the proposed product. The TPP should not be limited to the goals of this specific proposal. Include your goals for the overall product development program.

Base case: Minimally acceptable specifications that support attaining FDA approval, that differentiate the treatment from standard of care and other treatment options, and that provide a medically and commercially viable value proposition.

Optimal: Ideal specifications for the approved product that would meaningfully improve upon the base case profile.

For **validation,** list any planned or completed preclinical or clinical studies (using a brief titular description plus study identifier) or FDA correspondence (using date, correspondence addressee, and brief contents) that indicate your proposed base case **and** optimal product specifications are achievable and appropriate. Studies and FDA correspondence listed in the TPP should be described more fully in subsequent sections of the proposal.

FDA's draft guidance document on TPPs may be a helpful resource. An archived version is viewable at this link:

https://wayback.archive-it.org/7993/20190918100706/https://www.fda.gov/media/72566/download

Retain the instructional text and enter your responses in the <brackets> in the table below. Response length can be the rest of this page and up to 3 additional pages. Content exceeding page limits will be deleted.

Target Product Profile (TPP)

Patient Population / Therapeutic Indication		
***Base case**: Define the base case patient population.*	***Optimal**: Define the optimal patient population.*	***Validation**: Describe diagnostic information to be used to make the treatment decision. List studies or FDA correspondence that justify your base case and optimal specifications.*
<delete and enter text here>	<delete and enter text here>	<delete and enter text here>
Clinical Efficacy Endpoints		
***Base Case:** Define base case values for your proposed clinical efficacy endpoints.*	***Optimal:** Define optimal values for your proposed clinical efficacy endpoints.*	***Validation**: Describe method(s) to be used to measure clinical efficacy endpoints. List studies or FDA correspondence that justify your base case and optimal specifications.*
<Delete and enter text here. Define the clinical efficacy endpoints you will use for obtaining marketing approval, and base case values for these endpoints.>	<Delete and enter text here. Define the clinical efficacy endpoints you will use for obtaining marketing approval, and optimal values for these endpoints.>	<delete and enter text here>
Identity, Content & Purity		

***Base Case**: Define base case values for identity, content & purity of your product.*	***Optimal**: Define optimal values for identity, content & purity.*	***Validation**: Propose assay(s) for identity, content & purity. List studies or FDA correspondence that justify your base case and optimal specifications.*
<delete and enter text here>	<delete and enter text here>	<delete and enter text here>
Biological Activity		
***Base case**: Define base case values for biological activity.*	***Optimal**: Define optimal values for biological activity.*	***Validation**: Propose method(s) for measuring biological activity. List studies or FDA correspondence that justify your base case and optimal specifications.*
<Delete and enter text here. Include protein expression, electrophysiology, cell labeling, etc., as appropriate for informing the potential therapeutic utility of the product.>	<Delete and enter text here. Include protein expression, electrophysiology, cell labeling, etc., as appropriate for informing the potential therapeutic utility of the product.>	<delete and enter text here>
Safety Risks		
***Base case**: Describe the base case safety profile.*	***Optimal**: Describe the optimal safety profile.*	***Validation**: List studies or FDA correspondence that justify your base case and optimal specifications.*
<delete and enter text here>	<delete and enter text here>	<delete and enter text here>
Contraindications		
***Base case**: Describe the base case set of contraindications.*	***Optimal**: Describe the optimal set of contraindications.*	***Validation**: List studies or FDA correspondence that justify your base case and optimal specifications.*
<delete and enter text here>	<delete and enter text here>	<delete and enter text here>
Dose & Regimen		
***Base case**: Describe the base case dosing—include minimum, maximum and schedule.*	***Optimal**: Describe the optimal dosing—include minimum, maximum and schedule.*	***Validation**: Propose method(s) for evaluating dosing. List studies or FDA correspondence that justify your base case and optimal specifications.*
<delete and enter text here>	<delete and enter text here>	<delete and enter text here>
Dosage Form & Route of Delivery		
***Base case**: Describe base case dosage form and route of delivery.*	***Optimal**: Describe optimal dosage form and route of delivery.*	***Validation**: Propose decision criteria to determine which form/route of delivery to utilize. List studies or FDA correspondence that justify your base case and optimal specifications.*
<delete and enter text here>	<delete and enter text here>	<delete and enter text here>

Value Proposition

Describe the value proposition of your proposed therapy. Address each of the following points:

1. Describe the unmet medical need addressed by the proposed therapy.
2. Describe any known differences in detection/diagnosis, disease burden, care, or health outcomes across the affected population.
3. Describe the current standard of care for the intended patient population.
4. Describe how the proposed therapy will result in meaningful and substantial improvements in clinical outcomes for the intended patient population.
5. Describe the potential for the proposed therapy to be more accessible and affordable compared to available therapies or therapies currently in clinical development for the intended patient population and healthcare system.
6. Describe the landscape of related or competitor treatments or therapeutics that are currently available or in development and why the proposed therapy will be more acceptable, beneficial, feasible or practical for patients, caregivers, and the healthcare system.
7. Describe the potential risks of using the proposed therapy for the treatment of the target indication. Summarize your mitigation strategies.

Respond to all prompts above. Avoid discussing the scientific rationale for the proposed product and/or completed investigational studies conducted with the proposed product or surrogate – these should be discussed in their respective sections, below.

Resources:

- CA Community Burden of Disease and Cost Engine (https://skylab.cdph.ca.gov/communityBurden/), CDC WONDER (https://wonder.cdc.gov/), Global Burden of Disease Study (https://vizhub.healthdata.org/gbd-results/), and CAL*Explorer (cancer only; https://explorer.ccrcal.org/).
- Recent demographic data for California can be found here: https://www.census.gov/quickfacts/fact/table/CA,US.

Retain the instructional text. Response length can be the rest of this page plus up to 4 additional pages. Content exceeding the page limit will be deleted.

Scientific Rationale

Describe the proposed therapy, using schematics as needed. Explain the scientific and clinical rationale for the development and use of the proposed product for the treatment of the target indication. Include justification for the proposed indication, therapeutic approach, regimen, and route of administration. Describe the key translational, preclinical, and clinical (if any) studies that support or otherwise impact rationale. Discuss the strengths and limitations of data presented and/or the models utilized. Describe if and how the proposed therapy and/or study designs were informed by an understanding of the impact of genetic, environmental and other external factors that may impact the adoption, effectiveness, or safety of the proposed therapy. Describe whether any prior activities incorporated perspectives and experience from patients and individuals affected by the target indication.

Data from related products and citations from the literature may be included in support of the approach, but data obtained with the proposed product should be included as part of the rationale for taking the product itself to the clinic. Clearly indicate which supporting studies are the work of the PI or other Key Personnel.

Summarized data from regulatory correspondence or other application uploads should reference the page number(s) where the data can be viewed.

Retain the instructional text. Response length can be the rest of this page plus up to 7 additional pages. Content exceeding the page limit will be deleted.

Completed Nonclinical/Preclinical Studies

Summarize the nonclinical/preclinical studies that have been conducted using your proposed product or a related test article. Studies may include (but are not limited to) toxicity, efficacy, distribution, tumorigenicity, and immunogenicity.

Replicate the table as needed. In the last row, direct reviewers to study identifiers, publications, or specific pages in this proposal or other application uploads (e.g., regulatory correspondence) where data from each study can be viewed.

Completed Nonclinical/Preclinical Studies

Study Identifier or Title	Study Objective(s)	Test Article and Manufacturing Process Used	Animal Model, Number of Animals per Treatment Group, Route of Delivery	Key Outcome(s) *(cite underlying data)*
<Sample. The contents of this row can be deleted.> Non-clinical study report #1 LV mediated gene X phenotypic correction proof of concept	*Establish in vivo POC for approach*	*Research process otherwise same as clinical lentiviral vector*	*Gene X deficient mouse model 10 animals/group Single IV delivery of 0, 3e4, 1e5 or 3e5 vg/animal*	*Correction of gene x deficiency phenotype as assessed by T cell function in vitro, and resolution of vulnerability to virus Y. All mice develop long, coats. See regulatory upload A, pages 25-30.*
<Sample. The contents of this row can be deleted.> Non-clinical study report #2 In vivo toxicology and biodistribution	*To evaluate the safety and biodistribution of proposed product*	*Clinical lentiviral process, Produced under GMP conditions by CDMO*	*Nude mice 10 animals/sex/condition 0 or 3e5 vg/animal. Safety assessments daily, sacrifice at 6 months for PCR-based biodistribution assessment*	*No toxicity or early animal losses observed. See regulatory upload A pages 35-40*

Clinical Studies

Describe any completed, ongoing, or proposed clinical trials in humans using the proposed therapeutic candidate or a closely related product.

Replicate the table as needed. In the last row, direct reviewers to study identifiers, publications, or specific pages in this proposal or other application uploads (e.g., regulatory correspondence) where data from each study can be viewed.

If none have been conducted or initiated, please skip this section.

Clinical Studies

	<Sample Study #1 The contents of this column can be deleted.			
Status	*Ongoing*			
Trial Phase	*2b*			
Trial Population	*patients with Stage IIIb or Stage IV non-small cell lung cancer*			
Objective(s)	*safety and efficacy*			
Primary Endpoint	*PFS*			
Trial Design	*randomized, double-blind, controlled*			
Control Arm	*placebo*			
Randomization Scheme	*randomized, 2: test article to placebo*			
Blinding	*double blinded*			
Participants Enrolled	*45*			

Participants Treated with Product	*50*			
Number of Sites	*10*			
Route of Delivery	*i.v.*			
Dose(s)	*50e6*			
Is/was the manufacturing process the same as in the proposed studies?	*yes*			
Outcomes / Major Findings	*No tx induced SAEs, 6 mth PFS as compared to placebo*			
Study identifiers, publications, proposal page #s, or application upload page #s.	*'Scientific Rationale' section of this Proposal, pg. 20.>*			

Project Plan

Describe all activities proposed to achieve the objective of the PDEV Program Announcement. Make sure that the plan includes the objective itself: completion of preclinical development and attaining IND clearance.

Applicants requesting funding for Early PDEV and Late PDEV studies must describe plans for Late PDEV stage activities (i.e., IND-enabling activities) in sufficient detail to facilitate scientific review, and to clearly indicate what study designs will be pending FDA feedback.

Each activity described in the plan should match an activity outlined in the Project Timeline upload. Retain the same activity name and numbering (ex. 'Regulatory primary activity 1') across all documents to facilitate cross-referencing. Major expected activity categories are Nonclinical/Preclinical, CMC, and Clinical Planning. Appendix A of the PDEV Program Announcement provides examples of allowable activities. You may reorder the categories, add more or fewer activities as appropriate, provide alternate organization, etc.

- Nonclinical/Preclinical
- Chemistry, Manufacturing & Controls
- Clinical Planning
- Regulatory
- Access & Affordability Planning

For each project activity include the following, as applicable:

- Objective: Describe the specific objective of the activity, indicating how it will efficiently and effectively progress the project.
- Design: Proposed design with rationale for the choice of design and explanation of how it will achieve robust and unbiased results. Include test article, manufacturing process, animal model, number of animals per treatment group, route of delivery, etc.
- Methods: Methods to be used, with rationale for each choice of method and sufficient methodological detail for reviewers to assess validity.
- Success Criteria/Expected Outcome: Clearly state and provide a rationale for the proposed success criteria/expected outcome for each activity.
- Population Impact: Describe how relevant study designs are informed by an understanding and consideration of genetic, environmental and other external factors that may impact the adoption, effectiveness or safety of the proposed therapy.
- Population Impact: Describe how the proposed activity incorporates perspectives and experience from patients and individuals affected by the target indication. Clearly indicate how these activities will inform clinical development.
- Timeline: Specify whether the activity is Early PDEV or Late PDEV. Indicate how the planned dates for initiation and completion of the proposed activity align with the overall project budget and timeline. Discuss any planned preventive measures that make this timeline robust and describe mitigation strategies for timeline failures. Note: Optional candidate optimization activities must be limited to 6 months. Trial Start-Up activities may extend a maximum of 6 months after IND clearance.
- Funding: State whether CIRM funds are requested to fund all or part of the activity. If non-CIRM funds will be utilized, state the source(s).

Retain the instructional text. Response length can be the rest of this page plus up to 7 additional pages. Content exceeding page limits will be deleted.

Nonclinical/Preclinical

Preclinical activity 1A

Objective:
Design:
Methods:
Success Criteria/Expected Outcome:
Population Impact:
Timeline:
Funding:

Chemistry, Manufacturing & Controls (CMC)

Clinical Planning

FDA Correspondence

Summarize all regulatory correspondence directly related to the proposed product that you have had to date. Add your plans to address any FDA concerns or requests.

Be sure to upload copies of official FDA meeting minutes and/or relevant FDA emails in the 'Regulatory Correspondence' section of the 'Document Uploads' page in the online application.

Below the table, you will be instructed to provide an explanation of your regulatory strategy.

FDA Correspondence

	Date	Document Upload	FDA Feedback and/or Concern(s)	Plan to Address FDA Concern
Sample Entry (these two rows can be deleted)				
Sample: Pre-IND meeting minutes	01/05/19	'Regulatory Correspondence 12345'	GLP Toxicology study required.	Toxicology Study #1, above, was conducted in accordance with this request.

Summarize your regulatory strategy and explain how it addresses each regulatory concern in the table.

Retain the instructional text. Response length can be up to 1 page. Content exceeding 1 page will be deleted.

Manufacturing Plan Synopsis

Applicants requesting only Late PDEV funding must complete all sections; Applicants requesting Early and Late PDEV funding must complete any sections for which there is information.

Provide a synopsis of the Manufacturing Plan (with any redactions you feel necessary), as well as any FDA correspondence regarding the plan, as application uploads.

You must make table entries for every cGMP component of your product. For example, if your product is a genetic therapy delivered within a stem cell, you should provide integrated responses or make two sequential entries throughout the table.

Retain the instructional text. Enter your responses in the Table below. Table length can be the rest of this page plus up to 6 additional pages. Content exceeding page the limit will be deleted.

Test Article
Describe the test article.
<delete and enter text here>
Manufacturing Plan
Provide a summary description of the manufacturing process from starting material source to final test article.
<delete and enter text here>
cGMP Manufacturing Facilities
List the facilities where cGMP manufacturing of the test article will be performed. Describe the relevant expertise and track record of each manufacturing facility and summarize the Quality Assurance Plan in place.
<delete and enter text here>
Release Testing Facility
List the facilities where release testing of the test article will be performed. Describe the expertise and track record of each testing facility and summarize the Quality Assurance Plan in place.
<delete and enter text here>
Starting Material
Specify the starting cell line, cellular source, and/or component materials.
<delete and enter text here>
High-level Manufacturing, Testing, and Release Flow Diagram
Below this table, provide a high-level flow diagram that outlines the pathway from starting material source → manufacturing facility → release testing facility → clinical sites. This should include material, unit operations, and analytical methods for in-process and release testing. Describe the contents of the flow diagram here.
<delete and enter text here>

Manufacturing Tech Transfer and Scalability Planning
Briefly summarize your CMC development strategy that will enable supply of the proposed therapeutic product for the first-in-human clinical trial. Describe any completed manufacturing process development, analytical process development and GMP technology transfer.
<delete and enter text here>
Process Duration
Specify and briefly justify the duration of a manufacturing run and the time required to test and release a lot.
<delete and enter text here>
Quality Controls / Product Release
Briefly describe the identity assay(s), purity assay(s), potency assay(s) and any other release assays, and indicate the acceptance criteria for product release. Describe the development status and performance of all release assays. For cell-based products, include whether the test article will be fresh or frozen/thawed, and note the timing of each test relative to harvest, freeze/thaw (where applicable), and treatment.
<delete and enter text here>
Additional Characterization
Briefly describe any additional characterization assays routinely performed (but not required for lot release).
<delete and enter text here>
Clinical Site QC
Briefly describe the plan for managing product quality control at clinical sites.
<delete and enter text here>
Manufacturing Risks
Identify potential manufacturing setbacks (e.g., lot failure), and briefly describe risk mitigation and contingency plans. The “Plans for Risk Mitigation…” section of the proposal should be referenced for further details as needed.
<delete and enter text here>
Supply Chain Security
Briefly describe the plan for ensuring supply chain security.
<delete and enter text here>

Lot Size	Lot requirements for trial	Lot failure rate
Specify the average lot size (number of doses/treatments).	Indicate the projected number of lots needed to support the proposed clinical work.	Specify the % failure of lot release.
<delete and enter text here>	<delete and enter text here>	<delete and enter text here>

Retain the instructional text. Use this page (only) for your Manufacturing, Testing, and Release Flow Diagram. Content exceeding the page limit will be deleted.

Clinical Protocol Synopsis

Applicants requesting only Late PDEV funding must complete all sections; Applicants requesting Early and Late PDEV funding must complete any sections for which there is information.

Provide a synopsis of any components of the clinical protocol that you have drafted at this stage. If you have one, upload the current draft clinical trial protocol, as well as any regulatory correspondence regarding the draft, on the 'Document Uploads' page of the online application.

In the table below, provide a synopsis of the protocol. Include protocol page numbers to guide reviewers to the relevant sections.

Retain the instructional text. Enter your responses in the Table below. Table length can be the rest of this page plus up to 7 additional pages. Content exceeding the page limit will be deleted.

Study Title
Provide the registered title of the study.
<delete and enter text here>
Study Objectives
Provide a brief description of the trial's primary, secondary, and exploratory objectives.
<delete and enter text here>
Primary Endpoint(s)
Provide the primary endpoint(s) for the trial.
<delete and enter text here>
Secondary & Exploratory Endpoint(s)
List any secondary and/or exploratory endpoints for the trial.
<delete and enter text here>
Trial Design
Summarize the trial design, including type of trial (e.g., 3 X 3 X 3, dose escalation), trial arms, trial stages, and control or comparator groups.
<delete and enter text here>
Patient Population
Indicate the patient population you have chosen for the trial, with brief rationale.
<delete and enter text here>
Dose & Dose Justification
Specify the dose level(s), number of doses, and dosing frequency. Summarize how dosing was determined.
<delete and enter text here>

Route of Delivery
Specify how the doses will be delivered (e.g., IV, oral).
<delete and enter text here>
Eligibility Criteria
List the main inclusion and exclusion criteria for the trial.
<delete and enter text here>
Trial Enrollment Targets
Provide the planned number of trial participants for each study arm and a brief justification for the sample size. Include the demographic trial enrollment targets from the Trial Participation Goals table of this Proposal.
<delete and enter text here>
Treatment Duration
Specify the length(s) of the treatment period.
<delete and enter text here>
Schedule of Evaluations
List the required evaluation visits with a brief description of what each visit will involve.
<delete and enter text here>
Duration of Follow Up
Specify the length of the protocol-specified follow up period. If a longer-term follow up period will be covered by a companion protocol, state this here and describe more fully below.
<delete and enter text here>
Safety Considerations & Stopping Rules
Identify potential risks associated with trial participation and mitigation strategies. Specify stopping rules. Describe and justify the plan for immunosuppression and immune monitoring (if applicable).
<delete and enter text here>
Data & Safety Monitoring (DSM)
Summarize the DSM plan for this application. Include any specific adverse events that you anticipate; plans for surveillance and medical intervention; and any plans for convening an independent safety monitor or data safety monitoring board (DSMB).
<delete and enter text here>
Secondary Studies
Summarize any additional pre-planned studies (e.g., imaging, biomarker analyses, cell phenotyping, or gene expression analyses) that are part of this clinical study. Explain how these will inform decisions on continued clinical development.
<delete and enter text here>

Assays & Methodologies
Briefly describe any specialized assays or methodologies that will be used in this clinical study or associated secondary studies. Indicate the (trial or other) sites where specialized testing will be conducted.
<delete and enter text here>
Statistical Analysis
Summarize the statistical analysis plan for the trial data. Include (i) planned data analyses (statistical tests and any subgroup analyses) including interim analyses; (ii) planned interpretation (with any provisions for multiple testing and any pre-specified thresholds for a clinically meaningful effect); and (iii) endpoint-based criteria for continued development of the proposed product.
<delete and enter text here>
Long Term Follow Up
If a longer-term follow up period will be covered by a companion protocol, provide a brief rationale, timeline, and plans for interpretation of results.
<delete and enter text here>

Trial Population Goals

Required for applicants requesting only Late PDEV funding, optional for applicants requesting Early and Late PDEV funding

Use the table below to develop trial population goals for *the series* of trials leading to market authorization for the proposed product, rather than an individual trial. The trial population should seek to be reflective of those living with the indication, based upon your understanding as described under "Value Proposition". Trial population goals should be applicable to California's population.

The table is fully editable to allow modifications based on available data; we provide suggested categories.

- CA population percentages for each demographic group are provided from US Census 2020.
- **Provide benchmarks for your target indication.** Leave blank any cells for which there are no credible estimates.
    - You can find mortality rates by searching the US Vital Statistics dataset using the CDC WONDER tool (https://wonder.cdc.gov/).You can find mortality rates by sing the US Vital Statistics dataset using the CDC WONDER tool (https://wonder.cdc.gov/).
    - If other, more relevant sources for the case rate for your target indication(s) exist, edit the columns as needed and enter the data below.
- **Enter any past or current trial enrollment data** you have access to in the 'Percent (%) of Current/Past Trial Participants' column. Edit the column header or delete the column as needed.
    - Data can be from current/prior trial experience, a disease-specific trials registry or other relevant sources.
    - Patient advocacy organizations, trials networks, or CROs may have this information to share with you.
- **Set trial enrollment targets** as percentages of participants from each demographic group. Again, these goals should be for the overall series of trials leading to market authorization.

Provide citations for all data sources in the References section of this proposal.

Please note that CIRM CLIN2 (Clinical Trial Stage) awardees are required to collect and report trial participation data using the expanded categories under race shown below.

Retain the instructional text. Make your entries in the table below. You can edit this table as needed.

Trial Enrollment Targets

	Percent (%) California Population (2020)	Case Rate or Mortality Rate	Percent (%) of Current/Past Trial Participants	Trial participation goal (%)
Ethnicity				
Hispanic or Latino	40%			
CIRM notes: As shown, the 'Hispanic or Latino' category includes all individuals who identify with these ethnicities regardless of race. All race categories, below, include only individuals who are not Hispanic or Latino. This approach aligns with many datasets. Recent CDC WONDER mortality data incorporate race and Hispanic ethnicity independently. Edit the table as needed to best align with your data source(s).				
Race				
Asian	13%			

Asian Indian				
Cambodian				
Chinese				
Filipino				
Japanese				
Korean				
Laotian				
Vietnamese				
Other Asian				
Black or African American	6%			
American Indian or Alaska Native	<1%			
Native Hawaiian or Other Pacific Islander	<1%			
Guamanian				
Hawaiian				
Samoan				
Tahitian				
Other Pacific Islander				
White	38%			
CIRM notes: Five race categories (far left) are used in US Census 2020, the CA Burden of Disease & Cost Engine, CAL*Explorer, and the CDC WONDER dataset through 2017. The expanded race categories (indented) are used in the CDC WONDER dataset from 2018 to present. Edit the table as needed to best align with your data source(s).				
Sex				
Female Sex				
Male Sex				
Age				
Age < 5 years	5.8%			
Age 5 to 19	19.8%			
Age 20 to 64	58.6%			
Age 65 to 84	13.8%			
Age 85 and over	2.0%			

Trial Population Goals - Rationale

Explain how the trial population goals you entered in the table above fit into your long-range goals for collecting patient data characterizing the potential influence of demographic factors on the utility of the proposed therapy. Consider any differences in diagnosis, disease burden, care and health outcomes across the affected population. Justify exclusion of any groups at risk for the target indication.

Applicants proposing trials for very rare indications should describe relevant practical limitations here.

If applicable, describe any ways in which completed discovery-stage and/or translational-stage studies of the proposed product inform your trial participation goals.

Retain the instructional text. Response length can be up to 1 full page. Content exceeding one page will be deleted.

Clinical Operations Synopsis

Required for applicants requesting Late PDEV (IND-enabling) funding only, optional for applicants requesting Early and Late PDEV funding

Using the table template, summarize any elements of the plan to operationalize and execute the proposed clinical trial that you have drafted at this stage.

Retain the instructional text. Enter your responses in the table below. Table length can be the rest of this page plus up to 7 additional pages. Content exceeding the page limit will be deleted.

Clinical Operational Plan Synopsis

Study Title
Provide the registered title of the study.
<delete and enter text here>
Protocol Feasibility
Discuss the medical feasibility of the protocol, including the appropriateness of endpoints, diagnostic tests, treatments, and procedures.
<delete and enter text here>
Discuss the operational feasibility of the protocol, including patient enrollment feasibility, the level and logistics of screening required for timely enrollment, and whether tests and procedures can be implemented with ease.
<delete and enter text here>
Trial Leadership & Accountability
Indicate who will lead clinical operations and have overall accountability for trial execution. Briefly note other Key Personnel who will have accountability for key tasks or study deliverables.
<delete and enter text here>
Medical Monitoring
Describe the medical monitoring plan for the trial. Indicate who will provide medical input to trial sites and how medical review of the database will be performed.
<delete and enter text here>
Quality Management
Describe the plan to ensure quality of the study and the study data, including adherence to the clinical protocol and to cGCP. Briefly describe SOPs and training requirements for trial site staff. Describe the plan for monitoring the sites and for performing site audits during the study.
<delete and enter text here>
Data Collection and Handling
Append a flow diagram of data collection, data entry, data handling, data validation, data review, and query resolution for data sharing. Briefly summarize the data management process here. Include the database model (or note if the database is custom-built).
<delete and enter text here>

CRO/Vendor Selection
Describe the criteria for selection of CROs/vendors. Indicate how CROs/vendors will be vetted for capabilities, resources, and processes. Indicate who on the sponsor team will be responsible for CRO/vendor selection.
<delete and enter text here>
Selection of Central & Specialty Labs
Describe the criteria for selection of central and specialty labs. Indicate how labs will be vetted for capabilities, resources, and processes. Indicate who on the sponsor team will be responsible for lab selection.
<delete and enter text here>
Selection of Trial Sites
List all the proposed sites (CIRM-funded or not) for the trial, with a brief description of why each site is suitable for the trial. Include the criteria for selection of sites and the team member(s) who are responsible for site selection.
<delete and enter text here>
Outreach, Engagement, Enrollment & Retention
Briefly describe the plans in place to support the enrollment projection timeline(s). Describe the outreach plan to ensure that trial demographics match those of the patient demographics at large, including outreach to communities that are impacted by the condition being studied and to those who don't traditionally participate in clinical trials. Include description of approaches and resources to be leveraged to ensure outreach to potential participants is comprehensive across demographic groups. Summarize your strategies for mitigating slower than anticipated enrollment or unexpectedly high participant attrition.
<delete and enter text here>
Detail the project activities you propose to resolve barriers to trial enrollment and retention faced by the proposed trial participants, such as language differences, costs and logistics of trial-associated transportation, lodging and meals, need for patient navigators, need for child, elder or pet care, lost wages, etc.
<delete and enter text here>
Partner Oversight & Communication
Describe plans for effective oversight and communication between the study sponsor, CROs/vendors, labs, and trial sites. Include who on the proposed team will be responsible for management and oversight of each partner, processes for routine reporting, event reporting, tracking and audits, and plans for remediating lapses such as protocol deviations or breaches to cGCP.
<delete and enter text here>
Randomization & Unblinding
Where applicable, describe plans for the conduct of randomization and subsequent unblinding.
<delete and enter text here>

Product Preparation at Clinical Site
Briefly summarize the test article processing, formulation, and/or handling steps that will take place at the clinical site. Indicate who will be responsible for performing them, who will provide training and oversight, and who will have overall accountability.
<delete and enter text here>
Briefly describe any Standard Operating Procedures (SOPs), training documents, or other relevant source documents.
<delete and enter text here>
Participant Schedule of Events
Outline the schedule of events for trial participants. Include recruitment visits, pre-screening steps, screening steps, enrollment activities, treatment visits, assessment visits and planned follow up. Alternatively, provide the protocol page numbers where the schedule can be viewed.
<delete and enter text here>

Commercialization Plan

Describe your plan for commercialization of the proposed product. The plan must describe your current progress (if any) on the following components of commercialization planning and must indicate what aspects of the plan will be further developed over the course of a CIRM-funded PDEV project. As part of access and affordability planning requirements, market landscape research and market access strategy development activities described in the Project Plan section will be incorporated in Operational Milestones. Please consult CIRM's guidance on Access and Affordability Planning Requirements, which includes a description of Commercialization Activities to be considered at each stage of development.

Clearly indicate which of these efforts (if any) is a proposed activity for the PDEV project. Provide the activity name and number in the Project Plan and Project Timeline upload.

Summarized information from the Value Proposition, Project Plan or other application sections/uploads should reference the document and page number(s) where the information can be viewed.

- Product Development Plan: Timeline to approval and initial commercialization.
- Market Landscape: Market size, competitive landscape, provider landscape, payer landscape, key patient advocacy organizations.
- Market Access Strategy: Reimbursement landscape and relevant pricing models, assessment of barriers to patient access and affordability, preliminary plan for incorporating health economic evidence generation in clinical trial designs, preliminary plan for early payer engagement, preliminary sales & distribution strategy.
- Regulatory Strategy: Pre-IND/IND submission strategy, clinical development strategy, planned FDA designation requests, timeline to FDA BLA/NDA submission, ex-US regulatory strategy.
- CMC Strategy: Preliminary plan for scale-up and commercial process development, potency assay and overall analytical development strategy, identification and engagement of potential manufacturing partners, cost and lead-time reduction strategy, reagent/raw material sourcing and procurement plan, preliminary supply chain planning.
- Intellectual Property (IP) Portfolio Strategy: Summary of IP portfolio (filed applications, issued patents), description of executed license agreements, summary of any completed freedom-to-operate (FTO) analyses.
- Fundraising & Partnering Strategy: Fundraising plan to support preclinical and clinical development of proposed therapy, identification and engagement of potential strategic and commercialization partners.

Retain the instructional text. Response length can be the rest of this page plus up to 3 additional pages. Content exceeding the page limit will be deleted.

Data Sharing Overview

Describe how raw data, processed data and metadata produced from the award activities will be made available to the research community consistent with FAIR data sharing principles.

The description should include the type(s) of activities proposed to produce data (e.g., assay development, PK/PD studies etc.), how the data will be managed, what raw data, processed data, metadata (data dictionaries, data identifiers, unique identifiers, etc.) and any associated documentation (e.g., study protocols) will be shared and how (i.e., repositories), or justification for not sharing certain data.

Retain the instructional text above. Response length can be the rest of this page plus up to 1 additional page. Content exceeding the page limit will be deleted.

<Sample text. Replace this text with your response.

Our team recognizes that data generated with CIRM funding to support pre-IND and IND data packages must be shared in accordance with FAIR and CARE data principles, unless classified as confidential. Additionally, we are committed to collaborating with CIRM to ensure alignment with knowledge sharing processes as they are implemented.

Preclinical Animal Studies: Data will include clinical signs, clinical chemistries, necropsy summaries, histology reports, imaging results, and behavioral assessments.

Assay Development: Data will include product release criteria and standard curves for the target protein expression. Processed data and assay protocol will be gathered and documented.

CMC: Our partner CDMOs will provide batch records, complete manufacturing protocols (SOPs included), and QC testing data encompassing cell viability, purity, potency, flow cytometry, microplate reader outputs, and droplet digital PCR results. The genotoxicity assessment will produce sequencing data from multiple sequencing instruments.

Metadata: A comprehensive metadata file will be compiled, detailing the experimental design, sample information (clinical, phenotypic, genotypic), sample handling specifics (library preparation, sequencing platforms) and data processing parameters (analysis pipelines, tools/software, versions). In addition, all reagents and protocols required to replicate the data generated in this project will be documented.

Under the supervision of the PI, the data project manager will oversee data management activities which include database development, maintenance, QC and reporting progress on data management and sharing for the PDEV award.

Our DSMP will prioritize transparency while also respecting legal and ethical standards. We will share the formats and locations of data mentioned to advance the knowledge of the broader scientific community. At the same time, we will withhold specific data that could pose risks related to intellectual property or confidentiality.>

Team Organization

Summarize the qualifications of the proposed team, including their track record supporting cell and gene therapy projects to clinical trials, and plans for team collaboration. Outline the plan for project coordination, communication, and execution. Include how any CMOs/CROs involved will be managed. Outline the leadership, expertise, and staffing for all relevant functional areas (nonclinical, GMP manufacturing, analytical, regulatory, and clinical). Applicants requesting funding for Early PDEV and Late PDEV activities must describe any expected changes in key personnel or subcontractor composition over the course of proposed project.

Retain the instructional text. Response length can be up to 1 page. Content exceeding 1 page will be deleted.

Plans for Risk Mitigation and Financial Contingency

Discuss the risks that could delay achievement of project milestones and jeopardize completion of the project within the proposed budget and timeline. Routine risk surveillance and mitigation costs should be included in the project budget.

Use the numbered format provided below. For each risk, do the following:

- Describe the project risk, including its potential impact on the project timeline.
- Detail plans for risk surveillance, mitigation, and contingency. (Risk surveillance and mitigation costs should be included in the project budget).
- Provide estimates of the contingency costs (e.g., the cost of an unplanned operational runs) and the investment of additional project time/operational cost required to implement the contingency plan.
- Identify a non-CIRM funding source to cover contingency costs. Provide a letter from the funder or your organization in your Letters of Support PDF upload, including acknowledgement and the dollar amount.

Use the format from these **sample entries.** At the end, sum the contingency costs into a total. This total must be included in the 'Budget Justification > Financial Contingency Funds' section of the online application.

Sample Entries

Risk #1: Lot failure of GMP manufacturing run

Mitigation Strategy (1): Built into the contract is 1 manufacture fail. The CMO will produce replacement lots within a maximum 3 months' delay. This will result in slippage of the timeline by 3 months' maximum with no cost to the applicant. A second lot failure would result in a maximum 6 months' delay and 20% of costs would be absorbed by the applicant. To avoid lot failure, we have selected an experienced CMO and are providing a non-GMP protocol with a 5% lot failure rate.

Contingency Costs (1): Costs for a single lot failure are equal to 3 months' operational costs, which would be ~$90,000 ($30,000/month). A 6-month delay and absorption of the lot run failure will be $180,000 plus $50,000 (20% of the lot run costs).

Non-CIRM Source of Funding (1): These costs are covered by the applicant organization, and we have provided demonstration of that coverage in cash-on-hand in the Financial Feasibility Assessment upload.

Risk #2: Trial enrollment lags by more than 2 quarters.

Mitigation Strategy (2): An outline of plans with the CRO to ensure enrollment is described on page 22 of this proposal, in the Project Plan section. Should enrollment lag, there are 2 additional trial sites that the company is currently working to bring online. [Description of the sites, number of patients, state of relationship with the sites, how long it would take to bring online, how this would affect the protocol, statistics, interpretation of results, etc.]. In the event these sites are needed, we anticipate a 12-month delay in fully enrolling the trial.

Contingency Costs (2): A 1 year delay, completion of FDA discussions and bringing the 2 additional sites online will result in $750,000 increased cost to complete the proposed trial.

Non-CIRM Source of Funding (2): These costs would be covered by our partner, AllTrials, Inc. A signed letter of support from AllTrials acknowledging this arrangement, with the dollar amount, is included in the Letters of Support upload.

Retain the instructional text. Response length can be up to 2 pages. Content exceeding 2 pages will be deleted.

Risk #1:
Mitigation Strategy (1):
Contingency Costs (1):
Non-CIRM Source of Funding (1):

Risk #2:
Mitigation Strategy (2):
Contingency Costs (2):
Non-CIRM Source of Funding (2):

Risk #3:
Mitigation Strategy (3):
Contingency Costs (3):
Non-CIRM Source of Funding (3):

Total Contingency Costs for the Project (sum of the costs above):

Resources & Environment

Provide a brief description of the facilities, environment(s), core services, and resources available for conducting the proposed project. Include brief descriptions of resources for data sharing.

Retain the instructional text. Response length can be the rest of this page plus up to 1 additional page. Content exceeding the page limit will be deleted.

References

List all references used in the body of the proposal.