Application #	INFR8-20450
Title (as written by the applicant)	Establishing a CIRM Community Care Center of Excellence in Northern California
Project Objective (as written by the applicant)	To establish a self-sustaining, FACT-accredited Community Care Center of Excellence in Northern California capable of safely delivering decentralized clinical trials and advanced cell and gene therapies to historically underserved rural populations.
Summary (as written by the applicant)	The proposed Community Care Center of Excellence (CCCE) will serve as a regenerative medicine hub for a vastly underserved, rural region in California. Spanning a multi-county catchment with poverty rates exceeding 40%, this area currently lacks localized access to advanced cell and gene therapies (CGTs) and academic research centers. Our primary objective is to safely decentralize FDA-approved CGTs and complex investigational trials, dismantling the socioeconomic and geographic barriers that historically exclude rural, low-income, agricultural, and Native American populations from these life-saving treatments. The CCCE utilizes a highly integrated Hub-and-Spoke architecture. A regional community medical center serves as the decentralized clinical execution site (the Spoke), operating under the centralized regulatory oversight, Quality Management System, and Single IRB of an established academic Alpha Clinic (the Hub). This maximizes local patient access while guaranteeing world-class safety and strict adherence to FDA and FACT standards. The project is driven by four core pillars: 1] Clinical Execution and Safety: Using a phased activation model, the CCCE will leverage centralized academic leukapheresis and intensive care tele-escalation protocols to safely launch operations. Over five years, the center will systematically transition to independent, FACT-accredited in-house apheresis and autonomous trial execution. 2] Health Equity Navigation: To eliminate the logistical burdens driving rural trial attrition, we will deploy an advanced patient navigation system. Social Drivers of Health (SDOH) screening embedded into electronic medical records will proactively identify vulnerabilities, triggering immediate wrap-around care and financial assistance to eliminate out-of-pocket transit costs. 3] Community-Based Governance: Outreach will be governed by a Community Advisory Board and executed with a grassroots coalition of community-based organizations. This ensures engagement strategies are culturally safe and tailored to the region's agricultural workforce and indigenous populations, actively dismantling medical mistrust. 4] Workforce Development: The CCCE will cultivate a specialized local workforce by integrating CGT curricula into rural medical residencies, cross-training clinical research coordinators, and establishing a pipeline of culturally competent Community Health Workers (Promotores). Ultimately, this project transforms a marginalized region into a self-sustaining clinical research hub, providing the state network with a highly replicable blueprint for delivering decentralized regenerative medicine to frontier environments.
Statement of Benefit to California (as written by the applicant)	This project extends life-saving cell and gene therapies to California's underserved rural and agricultural populations, bridging a critical healthcare vacuum. By expanding the clinical trial pipeline, it ensures trial data reflects the state's true diversity. Furthermore, this model alleviates patient bottlenecks at urban academic hubs and establishes a permanent, highly specialized biotechnology and regenerative medicine workforce within California from the ground up.
Funds Requested	$9,000,000
GWG Recommendation	**Recommended: Exceptional merit and warrants funding, if funds are available**
Process Vote	All GWG members unanimously affirmed that "The review was scientifically rigorous, there was sufficient time for all viewpoints to be heard, and the scores reflect the recommendation of the GWG." Patient advocate members unanimously affirmed that "The review was carried out in a fair manner and was free from undue bias."

SCORING DATA

Final Score: 90

Up to 15 scientific members of the GWG score each application. The final score for an application is the median of the individual member scores. Additional parameters related to the score are shown below.

Mean	88
Median	90
Standard Deviation	2
Highest	90
Lowest	84
Count	15
Tier 1 (85-100): Exceptional merit and warrants funding, if funds are available	14
Tier 2 (1-84): Not recommended for funding	1

KEY QUESTIONS AND COMMENTS

Proposals were evaluated and scored based on the key questions shown below, which are also described in the PA/RFA. Following the panel's discussion and scoring of the application, the members of the GWG were asked to indicate whether the application addressed the key question and provide brief comments assessing the application in the context of each key question. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

Key Strengths and Weaknesses
• The biggest strength of this application is that it will bring access to a remote population with socioeconomic disparities. The project is also feasible and not overly ambitious. The application could have been improved with a better description of how it will handle a sustained growth. • Strength: The population served by the clinic includes disproportionate clusters of complex auto immune disorders, hematologic malignancies and rare genetic diseases, suggesting the site will be well suited to enroll CIRM trials. The population is 21% rural (compared to the state average of 5.8%) and includes high poverty rates among Black (45%), Native Hawaiian/Pacific Islander (33.1%), and Native American (15.9%) populations who may not otherwise have the opportunity to access regenerative medicine or CIRM funded clinical trials. • Strong application with many strengths. Primary weaknesses have to do with an underdeveloped evaluation plan for several components (navigators, bias training, workforce development, etc). • Strength: To ensure clean revenue cycle management across the network, the applicant's lead Northern California Alpha Clinic partner retains billing responsibility for centralized leukapheresis collection at their site; the applicant retains autonomy over commercial biologic purchasing and local infusion billing. • Weakness: Some concerns about understaffing, particularly as the applicant tries to scale and build capacity. The reviewer appreciates the hyper-efficiency of the applicant's clinical research coordinator (CRC) to establish the baseline clinical performance of the center, but as the site builds capacity, additional resources/staffing may be required. This reviewer acknowledges that the budget includes one additional Clinical Research Coordinator. • Weakness: Sustaining the CCCE seems largely dependent on proposed plans for industry sponsored trials as noted on p18 of the proposal. This is a very practical pathway forward, but the panelist is curious about contingency plans should commercial cell and gene therapy delivery plans not meet expected revenue. During discussion with the applicant, contingency plans described indicated that the hospital would pick up unmet cost. This is satisfactory, but hopefully, other contingency plans will also be considered. • The applicant is building upon and expanding their current partnership with a Northern California university that has an active Alpha Clinic. • This is a strong application in an area of need with an established relationship with an Alpha Clinic. • The presented timeline is too conservative and outcome measures are underdeveloped. • Weakness: The applicant did not predict the number of patients likely to be affected by this CCCE. This would have been possible by population estimates and disease prevalence. • Weakness: They team did not provide numbers for the workforce to be created. This is a gap in the proposal. • Strengths--a) very well-written grant which addresses the key questions posed by the RFA; 2) such suggests a well-organized team and commitment; 3) clear responses to pre-mtg questions; 4) linkages to

Alpha Clinic infrastructure for operationalizing clinical trials, and a CTSA (community engagement, logic model methodology, etc.) are valuable.

- Weaknesses: 1) depth of talented, committed clinical personnel; 2) ability to operationalize the complexity of cell-therapy (adverse events, etc. despite availability of sub specialists and 24 hour 'on call' individual at the lead Alpha Clinic collaborator site).
- The key strength of this proposal is the ability to create a community cell therapy center, approximately 100 miles north of the Bay Area academic hospitals, that would meet the needs of a heavily minority and financially challenged patient population. Nearly 40% of the patient population falls under 2 times the federal property level. Also, there are many minority populations that generally have been challenged and suspicious of large centers including the Native American, African-American and Hmong communities that are part of the catchment area served by the applicant center. The hospital is a level 2 trauma center and has adequate specialty services to provide support for the initiatives. The partnership with an Alpha Clinic would assure a strong academic training and support. It is a major concern that the ability to deliver the appropriate care to the appropriate patient cannot be served by the current model. Expansion to a community specialty center as proposed here should be encouraged.
- There are some weaknesses which likely reflect the fact that the center has not yet been established. These include the need for well-defined, cell therapy QA and QI management strategies, but this would be put in place when the center gains FACT accreditation. Maintaining a cell therapy program can be costly, and, if not active, can become a financial burden. More detailed financial planning is needed. Finally, assurance that the clinical trial participation would be welcome from industry sponsors at this type of site would strengthen the application.

Value Proposition

- The center's reach is expected to extend beyond applicant's primary service area to expand across the broader region to the Oregon border and coast. This reportedly vastly underserved area has no major academic medical center, Alpha Clinic, or CCCE, resulting in a significant gap in the ability to conduct cell and gene therapy (CGT) protocols.
- The center will increase access to clinical trials through a centralized referral network that handles more than 89,000 specialty referrals each year. The applicant will identify and refer eligible patients for early-phase studies to their partner Alpha Clinic while delivering trial-related care locally. To mitigate socioeconomic barriers, the CCCE will embed Social Drivers of Health (SDOH) assessments, linked to ICD-10 Z-codes, within Epic workflows to detect and address patient needs early in the screening process. The reviewer is unclear who will address issues identified through the SDOH questionnaire.
- The application does a good job establishing need, geographic challenges, and health equity concerns. More explicitly connecting these barriers to access regenerative medicine clinical trials and providing clearer evidence for some of the disease burden claims would strengthen the application. There is a fair amount of dependence on outside partners for critical components. While this is an appropriate model for low resource settings, the lack of a robust evaluation of these efforts diminishes the strengths in this area.
- The Logic Model includes necessary components (activities and outcomes); however, the plan to assess factors contributing to the outcomes are not defined well. Overall, the evaluation component of this proposal is under-developed.
- Strength: To sustain a regenerative medicine hub, the CCCE will establish dedicated CGT curricula focused on rigorous FACT-accredited cellular handling, chain-of-custody tracking, and the safety tenets of risk evaluation and management strategies (REMS). Requirements will be structurally enforced through the shared QMS at the lead Alpha Clinic collaborator hub, helping to develop and sustain the specialized workforce required.
- Strength: With a large rural population, CIRM diversifies the genomic and socioeconomic Real-World Data (RWD) available for long-term tracking and post-market surveillance.
- The project will expand access to a population that would currently have to travel quite far. This is a significant value. The reviewer doesn't see any current weaknesses for this area.
- The major strength of this program is its location in a desired area for the CCCE RFA.
- The Northern California CCCE application, in partnership with a Northern California Alpha Clinic, proposes to develop a cell therapy initiative for an underserved patient population. The proposal to develop a cell therapy program that will meet the needs of the CCCE's primary and secondary catchment area will catalyze offering cell therapy options to a patient population that has 42% of the residents who fall below 200% of the federal poverty level.
    - The recent publication by Chung et al, Blood Advances, 2024, examining a Medicare database, suggests that access to cell therapy decreases by 6.2% for every 10 miles further from the closest authorized treatment center.
    - Recognizing that average distances for “poor access” states where an average distance was over 100 miles, it was felt that expanding cell therapy to regional cell therapy centers would increase by nearly 40% the number of patients likely to receive CAR-T therapy and other cell therapies. It is approximately this distance from the applicant's site to the nearest Alpha Clinic.

Recognizing the underserved population, this distance can be a very significant barrier to treatment. Thus, it is justified to develop a Community Care Center of Excellence for Cell Therapy that can reach into Northern California. The current status of cell therapy delivery is that there are no authorized treatment centers between Sacramento, California and Portland, Oregon, a distance of almost 600 miles.

- There are currently 3 approved CIRM CCCEs, 1 in Central Valley (South of San Francisco) in Fresno and 2 in the Los Angeles area. Creating a fourth community center for cell therapy in northern California would extend the reach of the network. The commitment to develop a hub and spoke model for research trial participation should be congratulated, with expectations that the project will naturally lead to the development of a clinical center using standard of care products.
- There has been recognition that in many clinical trials the populations recruited are not representative of the US population; many minorities are not included. There are many reasons why this maldistribution of patient populations occurs. An obvious reason is that rural populations tend to have a higher percentage of individuals who have socioeconomic challenges. The proposed model will facilitate recruitment of minority populations into clinical trials for cellular therapy. That would be an important outcome for trial sponsors and for the cellular therapy field.
- The authors have clearly demonstrated a commitment to a collaborative venture and information sharing that should lead to a successful venture. Without a doubt, breaking down barriers of distance between academic centers and access to trials should increase participation but most importantly, having the patient's own primary hematologist/ oncologist participating actively in the trial will enhance enrollments. What remains to be determined is whether cell therapy industry sponsors will endorse the community treatment center as partner to the alpha center and to allow novel products be tested in the community center.
- This CCCE would serve as the only entity to offer cell and gene therapy delivery and support in Northern California and would provide meaningful navigation, workforce development programs, and key infrastructure and operational capacity to the county.
- The county's population is 21% rural as compared to a state average of 5% with 42% of the population living at below 200% of federal poverty level. Expecting the residents to travel to urban centers for CGT creates an extreme financial strain.
- The area also has high clusters of hematological malignancies, complex autoimmune disease, and rare genetic disorders.
- The applicant proposes meaningful collaborations with not only the lead Alpha Clinic collaborator but also other Alpha Clinics and the CCCE network, relying on the lead Alpha Clinic for a hub and scope model to help with accreditations and work force development.

Plan and Design

- The application clearly describes a strong Hub-and-Spoke model that balances decentralized patient care with centralized regulatory oversight. The phased approach leverages the lead Alpha Clinic partner's established expertise, infrastructure, and quality systems while allowing the applicant CCCE to progressively build local capacity for CGT delivery. The planned transition of leukapheresis services and eventual assumption of clinical trial execution and commercial CGT delivery by Year 5 demonstrates a thoughtful strategy for long-term sustainability and regional access to advanced therapies.
- Clinical support and logistics are described as a well-structured and patient-centered approach to rapidly implementing CGT services. The phased model leverages strong coordination with an Alpha Clinic partner, robust safety protocols, local treatment capacity, and integrated remote monitoring to ensure timely access to advanced therapies while maintaining high standards of clinical oversight and patient safety.
- There seems to be a well-defined partner network, clear organizational partner roles, a justified staffing model, and an academic pipeline component. However, the current description indicates that partners will provide referrals, but not the operational detail of how this process works. The application mostly decribes activities but not expected outcomes.
- There are several pathways for career development described. The collaboration with a community-based organization will lead to interaction and opportunities for medical residents, while the lead Alpha Clinic partner's community engagement core will assist with training of navigators to address SDOH. The application does not describe how success in these areas will be measured and if and how process evaluations will be utilized to course correct as needed.
- Strength: the CCCE will initiate operations via the FACT Provisional Accreditation pathway, which will permit 120-day activation while providing the stepwise runway to achieve the five-patient volume required for full FACT Community Accreditation.
- Strength: Will deploy standardized Patient-Reported Experience Measures (PREMs) adapted for clinical trial participants, to evaluate and improve the cultural and operational competence of Northern California CCCE’s care teams

- Strength: Monitoring the successful completion of protocol-specific competency checklists for key operational functions, including chain of identity and chain of custody procedures, investigational product handling, and Epic Research Module/OnCore workflow proficiency
- Strength: Planning to track the number of allied health professionals who successfully complete the CGT-credentialing program and monitor the internal staff retention rate.
- The proposed Northern California CCCE will serve highly vulnerable subgroups such as rural, low-income, Hispanic, and Native American communities who experience disproportionately high rates of hematological malignancies (e.g., leukemias, lymphomas),
    - complex autoimmune diseases, and rare genetic disorders.
- The applicant center is already fully integrated into the lead university collaborator's Cancer Care Network Management System (QMS), and Single IRB oversight by the university OCR. By leveraging this OCR backbone, the applicant has access to the Alpha Clinic's portfolio of clinical trials.
- The applicant's payer mix consists significantly of Medicare and Medicaid patients, 54% and 22 %, respectively. Caveats: Medicare and Medicaid cover lifesaving cell and gene therapies (CGTs) but grapple with their multimillion-dollar price tags. CMS uses Outcomes-Based Agreements (OBAs) to negotiate directly with manufacturers, where Medicaid pays for treatments only if they yield promised health outcomes.
- The applicant is well positioned to manage the project. The proposal could have benefited from as stronger evaluation plan and plan to handle growth.
- The authors and leadership of the proposed program have experience and have recruited a significant number of team members who can assure that the cell therapy products can be delivered safely over time. The timeline is conservative, and this reviewer would anticipate a more rapid adoption of cell therapy that would lead to earlier onsite apheresis procedures and earlier clinical delivery of advanced commercial cellular therapies. Obtaining the FACT certification for cellular therapy by the end of year 3 (if not sooner) will certainly enhance the likelihood of this occurring.
- The clinical operations are appropriately planned and designed to provide care for regenerative medicine treatments. Appropriate commitment from specialty services has been obtained. Developing the specialized personnel who conduct chain of custody during product development and the mandatory 15 year follow up for individuals requiring gene therapies has been set in place. More in-depth description of the post grant, financial solvency and sustainability section would be helpful. In the current financial climate in the US, centers can generate significant revenue and positive margin and cell therapy space, but not understanding the complex care models can lead to significant losses. It is expected that the CIRM Alpha Clinics should provide guidance to the community center.
- In the strategic partnership, regarding the operations, there should be commitment to the financial education of the treatment center. The applicant has an effective plan to manage the clinical aspects of investigational and approved products. The commitment of the Alpha Center to identify industry partners that will allow the shared care model to occur is present but needs to be demonstrated. The career development activities to develop a workforce are defined. Applicants will leverage universities to set up cell therapy education. The reviewer advises describing a plan to join national and international societies focused on cell therapy such as ASH, ASCO, ASGCT, ISCT and ASTCT. The principal investigator and several members of their extensive team could benefit longitudinally by these efforts.
- Overcoming Barriers to Participation: the CCCE proposes a primary CBO and partner in the region to reach the diverse population in the county. With deep ties to the community, this primary CBO is a trusted partner. Minority patients are often left out of trial participation due to systemic issues. The CBO partner's strong relationships with local providers and members of the community ensures a broader outreach to include all eligible persons. The CBO will help with education, including health literacy and language barriers. At the CCCE, nurse navigators, social workers, and financial advocates walk patients through screening and consent, with professional interpreters involved throughout. The biggest reason patients from rural areas drop out of trials is practical = travel, cost and time off work. Patients will fill out social needs survey and will be referred to either a social worker or financial navigator. The CBO will also step in to provide rides, meals and lodging.
- If a participant drops out a trial, it triggers an automatic root cause review so the team can figure out what went wrong.
- Network Integration: Partnership with the main Alpha Clinic partner is central to their operation and integration into the CIRM Infrastructure Network. The main Alpha Clinic partner would handle regulatory issues - quality systems and IRB - and patients would receive treatment locally at the CCCE. Co-patient care ensures that if something were to go wrong, both teams would be in contact with partner Alpha Clinic, providing needed backup. Medical records would be shared to ensure continuity of care.
- The applicant is also partnering with an Alpha Clinic with the most complex cases referred there. This Alpha Clinic would be instrumental in the workforce development training CCCE staff and sharing patient screening tools. Follow up care would be provided locally at the CCCE.

- The CCCE also plans to work with the other CIRM CCCEs, meeting regularly to share best practices on outreach, patient support, and training. The goal is to increase rural and minority participation in trials by 25% in three years.

Feasbility

- Timeline and execution appear feasible. The environment has experience conducting clinical trials to the extent needed to establish skill for the current proposal.
- Strength: Applicant is actively constructing a Comprehensive Cancer Center to scale capacity of their center to initiate oncology clinical trials. Existing infusion infrastructure is capable of executing Year 2 CGT milestones without dependency on the Comprehensive Cancer Center's completion.
- Strength: The main Alpha Clinic partner serves as primary academic hub for clinical trials infused locally at the center; reliance on the partner Alpha Clinic's QMS and Single IRB facilitate both academic and industry-sponsored trial accrual.
- The team is appropriate to carry out the proposal. There are many partners and collaborators that bring a wealth of expertise.
- The project plan is quite feasible. If anything, it is conservative. Given the rapid growth of the field and the dissemination of available information, it is anticipated that the CCCE will be fully functional before the 5-year target. Funding for 5 years is still appropriate recognizing that the current advances are accelerating and new indications for cellular therapy are rapidly emerging. Having established the treatment center will position the CCCE to offer these new procedures. The Center currently participates in clinical research. The Center reports enrolling 24 active trial participants between 2024 and the present. These enrollments are performed under the governance of the main Alpha Clinic partner's Office of Clinical Research. This number of clinical trial accruals is modest, but what is most important is that the data management and collection are accurate.
- With the oversight of the partner Alpha Clinic research PI, team, and a commitment that there will be 3 Alpha Clinic clinical trial professionals (clinical research coordinator, clinical research supervisor, regulatory affairs coordinator and quality assurance officer), onsite training will assure that the clinical research team develops appropriately to meet the needs of the patients on clinical trial. A more dedicated effort for ongoing quality assurance and quality improvement in the program is needed. These efforts are mandated under FACT approval. More detailed description of this requisite activity would strengthen the proposal. The applicant team as described is appropriate to successfully develop and operate the proposed CCCE.
- It does appear that all necessary resources are available. Again, it is recommended that the CCCE identify not just the PI, but also an administrative leader, as well as nursing representative to commit to seek educational opportunities available through membership in professional societies.

Serving the Needs of California Patients and Affected Communities

- Implicit bias training will be required of all personnel but here also the execution of the training and evaluation are not clear. The CCCE will increase access to clinical trials through a centralized referral network, which is well described. The program will be resourced with community health workers but it is not clear how they will be deployed or evaluated.
- Strength: NCCCE will participate in quarterly, rapid-cycle CCCE operational working groups with Fresno Community Health System CCCE and the Loma Linda University CCCE to exchange lessons on referral pathways, rural outreach strategies, patient support workflows, workforce training, quality oversight, and telehealth-enabled care coordination. The goal of these collaborative alliances will be to shorten startup time, promote consistent safety and quality practices, and strengthen the enrollment of rural and underserved patients across diverse geographies.
- Strength: the applicant will establish MOUs with the lead CBO to coordinate annual "Return of Results" with participating community-based partners and trusted regional organizations: Aggregate CCCE trial outcomes, programmatic successes, and translated lay summaries will be shared with study participants, referring providers, community partners, and civic leaders. Feedback gathered through these sessions will be synthesized by the applicant and their lead CBO into formal recommendations and shared with the Alpha Clinic partner's OCR, ensuring a compliant, regulatory mechanism to actively refine future trial designs and recruitment strategies.
- The reviewer sees no major concerns for the project serving the needs of community it will serve. The only thing that is a minor concern would be the expansion of trials and sustainability after funding ends.
- This reviewer is enthusiastic about the application and the ability to enhance access to clinical trials in cellular therapy and regenerative medicine from otherwise disadvantaged patient populations that are unlikely to participate in trials. Barriers to trial participation can include financial, distrust of the healthcare system and inability to maintain longitudinal participation. All these barriers can be overcome by the development of community research treatment centers. The fact that the population served is approaching 50% minority, itself is a catalyst to move forth. The program at the Alpha Clinic partner site is nationally recognized and will prove to be an excellent partner for the CCCE. It is mentioned that there also will be opportunity to participate in trials at other Alpha Clinics. Having the Alpha Clinic partner team

as a mentor team, with their finger on the pulse of advancing clinical research, is likely to further facilitate trial participants from the region to pursue trials. Successful collaboration between the Alpha Clinic partner and the applicant will likely further enhance the relationships with these other CIRM Alpha Clinics. The tools and resources at the applicant team are offering should lead to patient accruals. The defined screening of the electronic record will enhance visibility of patients that might otherwise have fallen under the radar screen for early trial identification. Importantly, the leadership of the PI and the Co. investigator will be able to recruit patients from their own practices and to the trials directly. In this modern era, patient reported outcomes and obtaining patient experience directly is important for clinical research centers.

- In the described “Participant & Community Engagement Logic Model”, the applicants identify pathways for community engagement through federally qualified health centers as well as patient advocacy groups. An important participant in the research efforts will be the Director & Health Equity Lead. It is stated that individual will meet quarterly with community advisory board to review accrual demographics and co-design outreach strategies. Also, there should be a commitment to frequent meetings with the PI to assure that the targets are met.
- The applicant center currently processes over 89,000 oncology and specialty referrals annually.