Application #	INFR5-14562 #2
Title (as written by the applicant)	UCSD Advanced Cell Therapy Laboratory
Project Objective (as written by the applicant)	The project plan outlines key operational enhancements, development of specialization areas, and support for new workforce development initiatives that will enable our GMP cell manufacturing facility be a key component of the new CIRM Cell and Gene Therapy Manufacturing Network.
Summary (as written by the applicant)	Our facility aims to participate in phase one of the CIRM Cell and Gene Therapy Manufacturing Network to expand our scope of services and better coordinate with key centers in this important field. Since the establishment of our California GMP facility and receipt of our manufacturing license in 2018, we have become an integral part of the academic research and clinical trials infrastructure to enable more patients to be treated with novel cell-based therapies. Our project plan outlines key advances that we will pursue in all areas project areas: facility enhancements, development of new areas of expertise, and building and sustaining the workforce in the biomanufacturing field. Our operational enhancements include improvements in the Quality Management System (QMS), but most importantly, we propose to establish a new process development (PD) group within our facility. We will initially support 3 new hires (one a manager with experience in this area) for this PD group and expand as needed. This group will directly interface with internal and external clients to facilitate translation of research projects from the lab to GMP suitable conditions. This project also enables our facility to build on our expertise in established areas such as culture and differentiation of human pluripotent stem cells, as well as develop its expertise in important new areas. The first new area is HSC gene engineering focused on treatment of non-hematopoietic disease. This focus will allow us to better serve local clients who have done pioneering work in this area. For this work, we aim to have the new PD group work with the other academic medical institutes to gain expertise in HSC engineering. Additionally, we will develop a new Data Capture system for our products that can be used for quality control and to inform many projects. Additionally, this data capture system will better connect our program with CIRM supported clinical and biomanufacturing center. For example, this data capture system can be utilized to better define key cell characteristics that may mediate improved patient outcomes. Workforce development and support is perhaps the most import need to support the growth of the field. Here, we will develop a new Internship program for current students or recent college graduates to spend a year with our facility and partner CDMOs to learn and gain expertise in the field. Parts of this internship will be coordinated with the CIRM Bridges training program. We also aim to support interns and other outreach activities to students who are from under-represented minorities. Other initiatives will support training and educational opportunities of leadership and staff. These quality operational enhancements solidify our facilities foundation to prepare and build upon for next phase in CIRM Cell and Gene Therapy Manufacturing Network.
Statement of Benefit to California (as written by the applicant)	Support for this project will enable our facility to expand our capabilities and workforce development to better provide cell and gene therapy products for patients in California with otherwise untreatable or incurable diseases. Additionally, we will be better able to work with both California academic groups and biotechnology companies to support manufacturing of GMP cell therapies, as is much needed for both pre-clinical studies and early-stage clinical trials.
Funds Requested	$2,000,000
GWG Recommendation	Tier 1: warrants funding
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: 1

Up to 15 scientific members of the GWG score each application. The final score for an application is the majority score of all of the individual member scores. If there is no majority score, the final score is 2. Additional parameters related to the score are shown below.

Highest	1
Lowest	1
Count	12
Votes for Tier 1	12
Votes for Tier 2	0
Votes for Tier 3	0

- A score of "1" means that the application has exceptional merit and warrants funding
- A score of "2" means that the application needs improvement and does not warrant funding but, at the applicant's option, may be resubmitted to address areas for improvement if the Application Review Subcommittee has not approved an application for funding following the Grants Working Group's review
- A score of "3" means that the application is sufficiently flawed that it does not warrant funding, and the same project should not be resubmitted for review for at least six months after the date of the GWG's recommendation

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.

GWG Votes	**Does the project offer a significant value proposition that would contribute to the creation of a California Cell and Gene Therapy Network capable of accelerating manufacturing development, advancing industry standards in manufacturing and building an inclusive manufacturing workforce?**
Yes: 12	• I believe that the revised application adequately addresses the comments made by the reviewers of the original application. In particular, they have emphasized the importance and need for the process development group and stated that approximately 50% of their work is connected with PD. They also mentioned that the lease on the additional 5,000 sq ft has now been finalized. • The applicant has addressed all of the outstanding issues from the previous round of submissions. Overall, this is a stronger application. • With some other minor updates, I believe that this application is now suitable for funding. • The goals to be achieved are well articulated and detailed (enhancing cell fitness, optimizing electroporation, enhancing expansion), as are the test methods to be used. • Within the first 2 years, the plan is to share open source protocols for production and testing of nonviral CAR-T therapies. It is clear how progress and impact will be measured. • The program has significant expertise with the specialized projects listed and could eventually lend this expertise to other programs within the network. • Creating a PD group and tech transfer services addresses bottlenecks. • The implementation of eBRs will improve workflow and address bottlenecks. • EM is critical, as is data capture system with data integrity. • The specialization areas are critical areas of expertise to develop new therapies - TILs, iPS cells, gene engineering.

	• There is a known workforce bottleneck in cell and gene therapy. It's great to see that they are inclusive of both community college and university students for their internship program. • The workforce development plan with a thought-out curriculum and diverse experiences. It includes advanced learning as well - masters, six sigma, and specialization. • It seems they plan to keep the workforce programs alive and have formed some good partnerships with area employers for hosting interns. • They allude to a plan to scale outreach efforts around their internship program to include other community colleges and universities in the SD region. • They have provided an example of the type of CDMO rotations that would be performed as part of the workforce development project. This provides concrete information on this aspect of the project. • There are definitely lots of linkages to existing CIRM education programs. • Collaborations are clearly defined in the proposal. • The GANTT chart has been revised, with numbers of patients updated. • A sustainability plan is included, and includes hiring a business manager and further support for space.
No: 0	*none*
GWG Votes	**Is the project well planned and designed?**
Yes: 12	• Milestones are appropriate, and the projects seem well planned and designed. • Applicants have responded to critiques. • Yes, overall well planned and designed. • Yes, the proposal is much improved. • Overall, yes, with limitations to the workforce component. While they focus on SD community colleges and universities, they rely on the inherent diversity at those institutions, not necessarily focusing on drawing in diverse talent. Also, the program impact is relatively small at only a few interns per year.
No: 0	*none*
GWG Votes	**Is the project feasible?**
Yes: 12	• There is no doubt about the ability of the project team to complete the proposed work as they have the appropriate facilities from a workforce standpoint and leverage other key partners. • It was unclear in the last submission when the applicants would secure space for their Process Development aspirations. Now that the space has been secured, a lot of perceived risk has been removed from the project. • The lease for additional space has been signed. • Reasonable milestones. • Yes, this is feasible.
No: 0	*none*
GWG Votes	**Does the project effectively serve the needs of underserved and disproportionately affected communities?**
Yes: 12	• The project effectively serves the needs of underserved populations. However, the impact could be magnified by developing programs aimed at groups rather than individuals. • The DEI plan could be improved with a more proactive, rather than passive approach to DEI. • DEI impact is minimal when you consider underserved California populations. The applicant focuses on SD community colleges and universities, but relies on the inherent diversity at those institutions rather than trying to draw in diverse talent. • The program impact is relatively small, with only a few interns per year. • The application did not have a lot of information about the applicant's track record and history in DEI as compared to other proposals in this review.
No: 1	• The applicant did not address the concerns identified in the prior review in terms of outreach to engage underserved communities.

Application #	INFR5-14574 #2
Title (as written by the applicant)	The [Institution Name] GMP Cell and Gene Therapy Manufacturing Facility
Project Objective (as written by the applicant)	To contribute to a network that will de-risk pathways to commercialization for cell and gene therapies and develop a diverse and skilled manufacturing workforce in California, we propose to develop and implement several key activities to meet these goals over the two years of this project proposal.
Summary (as written by the applicant)	We propose to meet the goals of the CIRM GMP network by developing and implementing several key activities within our GMP facility. First, quality-driven enhancements will support development and maintenance of a maximally efficient structure for operations with embedded continuous improvement processes. CIRM funding will enable our GMP facility to increase efforts toward staff training in industry quality standards, Quality by Design (QbD) principles, and compliance training to enable continuous improvement. Second, we aim to empower academic innovators to plan ahead for critical manufacturing milestones in their translational research projects. This will be accomplished through development of QbD Studios as training and project implementation tools, and establishing workflows for deep product characterization and identification of CQAs/CPPs, reducing the likelihood of project failure to accelerate and de-risk CGT manufacturing. Third, we propose to develop and implement training programs to provide a pipeline of qualified personnel to fill GMP manufacturing roles both locally and across California. A major component of this goal is to leverage current CIRM educational initiatives, including the CIRM Scholar, COMPASS, and Bridges programs. Specifically, the proposed GMP Professional Training Program element of our workforce development plan, which targets PhD and MD level scientists working on GMP process development and tech transfer, will be opened to CIRM Scholar trainees. In parallel, the proposed GMP Facility Operations Training Program has been designed to be completed as a defined element of the institution's COMPASS curriculum and will also be offered to our CIRM Bridges interns. Finally, we will pursue development of an internal/external data portal to enhance access to data and tools for deep cell characterization and enhance GMP project efficiency. Each of these approaches are designed specifically to address key bottlenecks in CGT manufacture.
Statement of Benefit to California (as written by the applicant)	This project will have a significant public impact by increasing access to cutting-edge medical treatments for Californians, and by driving economic growth by fostering innovation in the state's biotechnology industry. Consistent with our strong track record of valuing diversity, equity and inclusion as a key focus of the campus, we have sought to integrate IFNR5 program goals with opportunities to enhance the delivery of CGTs to medically underserved populations and develop a diverse workforce.
Funds Requested	$2,000,000
GWG Recommendation	Tier 1: warrants funding
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: 1

Up to 15 scientific members of the GWG score each application. The final score for an application is the majority score of all of the individual member scores. If there is no majority score, the final score is 2. Additional parameters related to the score are shown below.

Highest	1
Lowest	2
Count	12

Votes for Tier 1	10
Votes for Tier 2	2
Votes for Tier 3	0

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- A score of "3" means that the application is sufficiently flawed that it does not warrant funding, and the same project should not be resubmitted for review for at least six months after the date of the GWG's recommendation

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.

GWG Votes	**Does the project offer a significant value proposition that would contribute to the creation of a California Cell and Gene Therapy Network capable of accelerating manufacturing development, advancing industry standards in manufacturing and building an inclusive manufacturing workforce?**

Yes: 12	• This application has been extensively revised in response to the initial review, with an emphasis on several points:
	  ◦ The Facility Profile now includes a description of the procedures currently used for process development and a proposal to work with a second California institution on the implementation of an electronic Quality Management System. This section also now emphasizes staff experience.
	  ◦ The section on Operational Enhancements has been revised to provide considerable extra detail on the proposal to implement staff training in quality by design.
	• This is a revised application that addresses many of the weaknesses identified in the previous application. In some cases, plans were simply clarified but in several areas, substantive revisions of plans have improved the likelihood that the applicant will successfully contribute to the California Cell and Gene Therapy Network.
	• There is an improved description of the involvement of the institution with a cell tracking software platform and collaboration with a second California institution on the electronic quality management system.
	• The workforce development section has also been revised to provide a better description of the GMP Facility Operations Training Program and the GMP Professional Training Program, and to provide details on interactions with other CIRM programs.
	• Overall the revised application represents an improvement over the original. Plans are more clearly described and most reviewers' concerns are appropriately addressed.
	• A major focus of the application is to implement Quality by Design (QbD) principals in process development for new cell and gene therapies. Plans include educational workshops in this area that can be helpful to other facilities in the network.
	• The applicant institution's Alpha Clinic is very busy and supports a large number of innovative cell therapy trials focused primarily on neurologic and degenerative diseases. These trials are currently supported by commercial entities. As the institution's GMP facility comes online, future clinical trials will be supported by their own facility.
	• The applicant institution's facility will add capacity to the California Cell and Gene Therapy Network but the application does not otherwise address specific bottlenecks for cell and gene therapies.
	• Yes, the proposer has clarified how the operation of GMP facility will accommodate Product Development activities.
	• Yes, integrating Process Development within the GMP space could lead to acceleration of developmental timelines through process validation.

	• Yes, a shared platform across sites for an electronic Quality Management System is envisioned that will enable tech-transfer and multi-site manufacturing. • Yes, a scalable benefit to a California-wide GMP network is the potential to add a guest account structure that would enable customizable access to discrete modules on a project-by-project basis. • Workforce development efforts focus primarily on implementation of short introductory courses in different aspects of cell manufacturing with different courses for individuals at different levels of training. The revised application clarifies that these short courses are designed to interest students of various backgrounds in the opportunities available in cell manufacturing careers are various levels. Students in these courses would be eligible to apply for a longer paid in-depth training program. • From a workforce development perspective, the reworked proposal added a lot in response to prior feedback, and the outreach and engagement efforts are strong. Due to the small number of interns proposed, the overall workforce development impact of this proposal is questionable, but it is a good proposal.
No: 0	*none*
GWG Votes	**Is the project well planned and designed?**
Yes: **11**	• Yes. There have been significant changes to the proposal regarding QbD training for internal staff. All staff will complete a 3-day SixSigma QbD training course on site, with updated training on an annual or bi-annual basis. Future training of new staff will be run by a qualified team member. • There are now clear goals for QbD training: to establish these principles and enhance awareness from a process perspective, enhancing efficiency of project communication and execution. • The specialization section has been revised for clarity, expanding the rationale for the plan, and links to the proposed QbD Studios. • The proposers have also provided a more detailed plan for pilot project activity completion, and provided examples of the proposed analysis tools for greater detail. • The pilot project focuses primarily on the implementation of genomics cell tracking software and machine learning to characterize large scale cell expansion and detect genetic instability. While still at an early stage, preliminary results suggest that this may be a very useful approach to maintain production of high quality and consistent cell banks. • The applicant has made substantial commitments to support cell and gene therapy manufacturing including support for building the new 7 cleanroom facility that is now coming online. Additional space for Process Development may be available in future years. • As a newer facility with limited staff and GMP manufacturing experience, the proposal delays efforts to scale up operations until phase 2 of the funding opportunity. • Dedicated space for process development is not currently available and will not be available for several years until a new research building comes online. • The revised application explains that the 7 cleanrooms have been designed to support process development activities as well as GMP manufacturing. However, conducting process development in a GMP environment is unnecessarily cumbersome and not ideal. Using cleanrooms for process development also reduces he number of cleanrooms that can be used to support clinical manufacturing projects. • From a workforce development perspective, the application includes a well described plan for a "fundamentals" training program and related components. They added considerable detail between the first submission and now. It is encouraging to see this additional thinking and activities that meet a defined need.
No: **1**	*none*
GWG Votes	**Is the project feasible?**

Yes:
12
	• Two steps for the completion of the pilot project activities for systems for data and analytics are articulated:
	  ◦ 1) Creation of the basic portal and to enable data exchange.
	  ◦ 2) Addition of analytics access to enable pipelines for genomic/transcriptomic/proteomic analysis.

	• The details and the software tools available for these activities are now well-explained, and indicate feasibility of implementation. • Yes, the revised proposal has added effort for several team members and technical programming staff to a total of 45% combined time to increase support for both QbD Studios and computing for systems, data and analytics. This reflects adequate effort for these activities. • The revised application clarifies the more limited objectives of this proposal and defers some objectives to the next phase of this grant process. This increases the feasibility of implementing the current objectives. • The implementation of an electronic manufacturing system now focuses on a vendor that has already been implemented at other centers, which makes this approach more feasible. Nevertheless, implementation of these software systems is a complex process that takes considerable time. It remains unlikely that this can be implemented in this first phase of the application. • Characterization for critical quality attributes and release criteria for a human neural stem cell therapeutic candidate for chronic cervical spinal cord injury has involved developing a classifier tool to monitor GMP cell line expansion and banking, and release testing for potency, using the analytic tools that will be containerized for bulk RNAseq profiling. These analytics were used to identify molecular expression patterns, using a training data set of benchmark gene signatures from positive and negative cell lines. • Current projects focus primarily on clinical trials employing allogeneic cells for a variety of neurologic indications. This is clearly a strength of the research environment that has in many cases already been translated to the stage of clinical evaluation. The GMP facility was not directly involved in manufacturing these cellular products and it remains unclear which, if any, of the projects will rely of the new facility in the future. • The collaboration with a cell processing vendor will facilitate implementation of procedures to manufacture autologous CAR T or CAR NK cell products, but upcoming trials using these products are not described. • It is not clear what equipment is currently available in the facility and whether this is sufficient to support manufacturing of either allogeneic cell banks or autologous cell products or to manufacture viral vectors. • The proposed workforce development activities are feasible.
No: 0	*none*
GWG Votes	**Does the project effectively serve the needs of underserved and disproportionately affected communities?**
Yes: 12	• Academic investigators and industry sponsors will be able to take advantage of the institution's Alpha Clinic DEI initiatives; for example, partnership with the institution's center for clinical and translational science for community engagement, which seek to increase diversity in clinical trial participation, integrating outreach to and participation by representatives from diverse and medically underserved groups. • Yes, the institution GMP facility has developed a training program and paid internship program. B.S./M.S. level students will be recruited through the CIRM COMPASS and Bridges programs. • The applicant describes both short term workshops and paid internships. • The revised application more clearly describes proposed activities to improve access for underserved populations. • Proposed workforce development programs are focused primarily on increasing awareness, but this may be helpful in reaching different populations. • Plans for workforce training are limited in scope but may increase in subsequent phases. • The application includes a good discussion of how the applicants will recruit interns and some proactive outreach with external resources, which was great to see.
No: 0	*none*

Application #	INFR5-14667 #2
Title (as written by the applicant)	Advancing Cell Therapy Manufacturing Through Collaboration
Project Objective (as written by the applicant)	The project aims to provide tools & strategies to improve cell therapy manufacturing through collaborations, increase availability of viral vectors, train & educate underrepresented students, standardize data collection in academic GMP facilities, reduce costs and increase accessibility.
Summary (as written by the applicant)	Our initiative, "Advancing Cell Therapy Manufacturing Through Collaboration," symbolizes our strong belief that collective effort can revolutionize cell therapy manufacturing. Utilizing our advanced Good Manufacturing Practice (GMP) facility, we are committed to fast-tracking the development and application of next-generation cell therapies, thereby driving medical innovations in California and improving patient health outcomes. The bedrock of our proposal is the implementation of an electronic Quality Management System (eQMS). The integration of this cutting-edge tool into our operations is anticipated to lead to substantial improvements in data management, increase efficiency, and reduce errors, raising the bar for cell therapy manufacturing. A key focus of our strategy is to address the intricacies of both viral and non-viral cell therapy manufacturing. While these may seem at odds, they are in fact complementary approaches that cater to the diverse needs of the rapidly evolving field. Non-viral cell therapy manufacturing, with its scalability and versatility, represents an important advancement in the field of cell therapy. To accelerate its development, we plan to establish a scalable, open-source workflow, which will standardize procedures, catalyze progress, and facilitate sector-wide collaboration. We also acknowledge that many existing therapies rely on viral vectors, and as such, their production remains crucial. To meet this need, we are committed to developing in-house viral vector manufacturing platform, a significant advancement that will alleviate current supply issues and fast-track several essential projects towards clinical translation. In addition to these technical strides, we recognize the importance of nurturing a robust talent pool, particularly among underrepresented communities. Our comprehensive workforce development initiatives aim to cultivate a diverse and competent workforce, empowering them to contribute significantly to the future of cell therapy manufacturing. At the heart of our initiative lies the spirit of collaboration. We strive to foster partnerships with academic institutions and industry leaders across California and beyond, to fortify the cell therapy manufacturing network across the state. The positive impact of this collaborative endeavor will resonate throughout California, expanding patient access to advanced therapies, bolstering local biomedical industries, and consolidating California's position as a leading force in delivering life-saving cell therapy treatments.
Statement of Benefit to California (as written by the applicant)	Our proposal is driven by a deep passion for improving the lives of Californians and advancing the field of cell therapy. We intend to leverage cutting-edge technology and streamlined manufacturing methods to establish a collaborative framework for the production of cell therapies, making them more accessible and affordable. We are also committed to investing in the development of a skilled and diverse workforce. Our mission to revolutionize cell therapy for the betterment of California.
Funds Requested	$1,999,964
GWG Recommendation	Tier 1: warrants funding
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: 1

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Highest	1
Lowest	1
Count	12
Votes for Tier 1	12
Votes for Tier 2	0
Votes for Tier 3	0

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- A score of "3" means that the application is sufficiently flawed that it does not warrant funding, and the same project should not be resubmitted for review for at least six months after the date of the GWG's recommendation

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.

GWG Votes	**Does the project offer a significant value proposition that would contribute to the creation of a California Cell and Gene Therapy Network capable of accelerating manufacturing development, advancing industry standards in manufacturing and building an inclusive manufacturing workforce?**
Yes: 12	• The addition of this site will enrich the already robust stem cell and gene therapy infrastructure at the applicant institution, creating vertical integration and leading to a complete bench to bedside approach to bringing potential therapies to a large and diverse population. • Critical bottlenecks in cell and gene therapy are addressed by this proposal. The added attention to broadening cell therapy development workshops with other CA state systems, including high school and community college outreach, is significant in enabling workforce expansion and specialization. • Really impressed with changes to the program, very strong workforce component. • The applicant has a suitable approach to enable leveraged collaborative opportunities within the CIRM network. Industry partners are also brought into the application proposal with eQMS system that features interaction capabilities among multiple facilities. • New scaling activities in the updated proposal were described across the network, and this addition is likely to position the facility for continued operational enhancements. The proposal received other key additions in the update which include External User Access and an Open Access Module for SOPs and Knowledge Transfer which are designed to help support the entire CIRM network when implemented. • The proposal's commitment to include other CA university programs demonstrates organizational commitment to sustain the proposed enhancements. • Large number of new letters of support. Strong indications of collaborative environment which is critical to success of the GMP network model. • Overall responses to prior review comments were strong.

	• A significant strength of this activity is the eQMS project that is well positioned to be integrated with outside sites and even export modules. The other projects will lead to great value added to the California ecosystem, though the nonviral manufacturing project remains a significant weakness of this proposal with limited impact.
No: 0	*none*
GWG Votes	**Is the project well planned and designed?**
Yes: 12	• The details of the proposal are well outlined with clear milestones. • With removal of the plasmid manufacturing platform, the proposed enhancements are adequate to de-risk early-stage cell and gene therapy process development and manufacturing campaigns. • For operational enhancements, the success criteria are adequate to measure the impact. The enhancements to measure for performance include optimizing non-viral CAR T-cell production workflow, conduct successful engineering runs, and their providing protocols thru the electronic doc management system. • For areas of specialization, goals of achieving high titer lentiviral production and concentration following optimization of the transfection unit of operation are consistent with the expected outcome to measure impacts of enhancements. • The proposed execution of an engineering run and comprehensive analytical testing planned for the last several months of the proposals timeline and its success would demonstrate the progress toward a specialized competency in lentiviral manufacturing. • The updated project plan gave appropriate attention to create technical and career entry opportunities. And this includes outreach to provide additional resources to undeserved California residents. • Workforce development is well planned, and staff has capability to pull it off. • Only weakness is planned approach to process development for non-viral cell therapy manufacturing. Approach is fairly standard optimization assessment of a large number of potentially important variables.
No: 0	*none*
GWG Votes	**Is the project feasible?**
Yes: 12	• The project is feasible. For the non-viral manufacturing project it will be important to ensure that the overall goal of implementing the process is kept in mind, even if that means foregoing specific optimization experiments that evaluate various cytokines etc. • The proposed activities in the updated application include integrating lentiviral vector production workflow into the in-house operations as part of the specialization project. This effort includes a partnership with another institution and consultants which advance the access to the necessary resources to execute the project plan. • With attention focused on lentiviral product development and analytics, including removal of the pDNA component from the application, the proposed plan is feasible within the timeline proposed. • The staff and personnel are qualified to execute the project plan. With the addition of collaborative activities and consultants, the project plan provides access to key competencies difficult to recapitulate elsewhere. • The applicant provides a summary of cell and gene therapy projects supported by the facility and the current process of contracting several clients to develop and manufacture their products in the new cGMP facility. This presents an adequate pipeline for advanced demonstration and progress in competency. Moreover, the established facility will likely draw in more clientele as growth in the area of specialization continue at a steady rate in the cell and gene therapy community. • They have secured additional $750,000 from institution and corporate partners. • No concerns. The workforce development program is well planned. • More focused.
No: 0	*none*
GWG Votes	**Does the project effectively serve the needs of underserved and disproportionately affected communities?**
Yes: 12	• The updated application now includes a workforce development section. They incorporated a workshop and community outreach in collaboration with internal and

	external programs which will likely increase workforce participation from underserved populations in CA. ● The various workforce and DEI programs are a strength of this proposal, in particular the COMPASS program. ● Strength is workforce development, especially partnerships with COMPASS and ARM. ● Strong community outreach and DEI initiatives. ● Yes, their outreach efforts seemed designed to achieve this. ● The team has a clear track record for promoting and advancing DEI. As described in their proposal, the applicant organization is dedicated to promoting DEI in cell and gene therapy through ongoing workforce development initiatives. ● Yes, long institutional track record of strong DEI values. ● The project does bring inclusive perspectives and experiences to the proposed set of activities with demonstrated specialties amongst the team members. ● The team also includes descriptions of a "strong track record of advocating for racial equity and promoting access to safe and effective medical innovations" which further demonstrates a successful track record for promoting DEI. ● The proposal team does have a proactive DEI component that is wonderful to see. ● With a key approach in the manufacturing platform advancements enabling allogeneic products that may be used in any patient, the proposal aims to improve access to cell and gene therapy for disproportionately affected populations.
No: 0	*none*

Application #	INFR5-14779 #2
Title (as written by the applicant)	Creating A Collaborative California Cell and Gene Therapy Manufacturing Network
Project Objective (as written by the applicant)	The need for cell and gene therapy product manufacturing will be ever increasing over the next decade, and several new GMP facilities are coming online. We believe it is important to continue to advance the processes and to share our accumulated knowledge for early and late-stage clinical trials.
Summary (as written by the applicant)	The [redacted] GMP facility has been operational since 2010, funded by the first CIRM major facilities grant. We support cell and gene therapy product development and GMP manufacturing of products for Phase I-III clinical trials. We enabled investigators to translate their products from laboratory research into safe and efficacious cell and gene therapies. For this grant application, we believe it is important to share our accumulated knowledge in such a breadth of product manufacturing for early and late-stage clinical trials with other GMP facilities within the State of California. The need for cell and gene therapy product manufacturing will be ever increasing over the next decade, and several new GMP facilities are currently coming online. We agreed to collaborate with two new GMP facilities within the State of California to address manufacturing hurdles. For part 1, Infrastructure, we will address quality by design of cell and gene therapy product manufacturing for Phase I to III products and will share this project with [redacted]. We will also further develop our in-house electronic quality management system, which dramatically improved our GMP inventory system, by expanding it to include electronic batch records. For part 2, Specialization areas, we will: A) further develop comprehensive product release tests for a fresh, not cryopreserved product, with a shortened CAR-T cell manufacturing process; B) establish, qualify and generate SOPs for mobile cleanroom units in the vicinity of the medical center. We will further develop the California CAR-T program and the point of care manufacturing processes by validating mobile units; C) further develop SOPs and methods for delivery of fresh, or cryo-recovered MSC products; D) develop new technology to manufacture gene therapy vector, specifically, lentiviral vector, in a fully closed and automated cell culture and vector harvesting system which can be employed outside of an ISO 7 space. E) collaborate with the state of the art, newly constructed GMP Facility at [redacted] to help implement lentiviral vector manufacturing there. In part 3, Education/Training, the GMP training/certificate program, already existing, will be further developed to include [redacted] Compass Students and our partners coming into the huge complex next door, with a bioengineering component. By developing a specialized studies Cell and Gene Therapy Manufacturing program administered by Continuing and Professional Education, we will include a wider array of topics. This new program will be expanded to include [redacted], bringing the training to Southern California. In summary we believe that this proposal will strengthen the ability of CIRM - funded facilities to provide much needed cell and gene therapies in the coming decade.
Statement of Benefit to California (as written by the applicant)	Through the proposal a partnership with other academic GMP Facilities will be established to share the knowledge of product manufacturing to expand access to clinical trials of potentially lifesaving therapies such as CAR-T cells. The investment of CIRM into the [redacted] GMP Facility will continue to expand and be leveraged to enable the patients in need in the state of California to have a stronger possibility of receiving cutting-edge cell and gene therapy treatments.
Funds Requested	$1,719,365
GWG Recommendation	Tier 1: warrants funding
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: 1

Up to 15 scientific members of the GWG score each application. The final score for an application is the majority score of all of the individual member scores. If there is no majority score, the final score is 2. Additional parameters related to the score are shown below.

Highest	1
Lowest	2
Count	13
Votes for Tier 1	9
Votes for Tier 2	4
Votes for Tier 3	0

- A score of "1" means that the application has exceptional merit and warrants funding
- A score of "2" means that the application needs improvement and does not warrant funding but, at the applicant's option, may be resubmitted to address areas for improvement if the Application Review Subcommittee has not approved an application for funding following the Grants Working Group's review
- A score of "3" means that the application is sufficiently flawed that it does not warrant funding, and the same project should not be resubmitted for review for at least six months after the date of the GWG's recommendation

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.

GWG Votes	**Does the project offer a significant value proposition that would contribute to the creation of a California Cell and Gene Therapy Network capable of accelerating manufacturing development, advancing industry standards in manufacturing and building an inclusive manufacturing workforce?**
Yes: 13	• This proposal is from a program with a stellar track record of success and has proposed a number of initiatives that have the potential to be transformative - specifically the certification program and the point of care modular facilities. While the proposal was lacking significant details in a number of areas, the value that could be potentially provided by such a world-class facility leading these cutting-edge initiatives is an important consideration. • There is no better facility to lead these impactful initiatives than this applicant. • The revised application more clearly addresses solutions to bottlenecks in cell and gene therapies. It proposes 1) extending access to CAR therapies by improving processing strategies, extending the availability of manufacturing facilities and improving preparation of lentiviral vectors; 2) it provides additional details on improvements to its existing GMP/Certificate program and finally, 3) amplifies its proposal on the development of electronic quality management systems. • The applicant has an excellent track record for manufacturing cell and gene therapy products. It is unique amongst CIRM facilities in that it has supported Phase 3 clinical trials and has been successful in all of its IND applications. It also has a good track record in community outreach and educational activities and with interactions with commercial biotech organizations. With the initiatives that are described in the revised application, this should position it well to sustain its activities in multiple areas beyond the period of project funding. • The applicant has a very good track record in GMP production of both viral vector and cell therapy products.

	• The GMP Facility has existing collaborations with the CIRM Alpha Clinics and with the Bridges program. In this application they propose new interactions with the CIRM Facilities at [redacted] to introduce lentiviral manufacturing to the institution and with [redacted] on the development of electronic quality-by-design software. • This facility has been very active in the development of interactions with commercial entities and proposes two collaborations with existing CIRM GMP facilities. It also generically agrees to share progress and findings with other CIRM groups. Its proposed activities would certainly be of interest to other GMP manufacturers both inside and beyond the CIRM network. They have made improvements to the section on data sharing. • Will further develop the California CAR-T program and the point of care manufacturing processes by validating mobile units. • The applicant has had an excellent program in workforce education (as evidenced by the direct training of the PI on this application). • A solid proposal from the workforce development perspective. While the workforce component is largely the same as before, there is a well understood need for additional certificate-based pathways into the industry, so the approach is appreciated. • Shortening CAR-T manufacturing is a strength, but the value of next generation MSC manufacturing is questionable. • What is the regulatory pathway for mobile CAR-T cell therapy?
No: 0	*none*
GWG Votes	**Is the project well planned and designed?**
Yes: 6	• The point of care concept and certification programs provides significant strength to the application. The exact regulatory pathway for the point of care approach would benefit with additional details in the application with regard to the unit design and the expectations from the agency. • The workforce development plan is well organized and planned. • Project would benefit with additional details on deliverables in regard to the operational and process improvements.
No: 7	• The revised application is an improvement on the previous version, although there are relatively few changes. The quality by design project is still somewhat lacking in detail but contains enough terminology to indicate that the applicant is familiar with the process. A good feature is the intent to share their findings with the GMP Facility at [redacted]. The success criteria for this component are again somewhat vague consisting of a statement that a method will be "established, documented and standardized". • The second component of this part of the proposal is the establishment of electronic software that encompasses inventory management, environmental monitoring, document control and batch records. There are no details of even basic requirements for these systems, although it states that some components are already in development. The success criteria are to develop a system, train users and transfer the system to [redacted] • The second part of this proposal component is to accelerate manufacturing and release testing of CAR-T cell products and to improve access to the therapy. They indicate that they have cut the manufacturing time in half but provide no details on how this was achieved or what further experiments are to be performed. • They indicate that some release tests will be performed in advance of cell harvest, but this is a principle that has long been accepted by the FDA. They provide no description of additional or new release tests. • The next component of this section is the development of off-site manufacturing facilities in the form of specially designed trailers that could initially manufacture two products per month, expandable to four. While I find this intriguing, I have major reservations on the practicality of establishing numerous satellite manufacturing sites with respect to overall compliance with GMP regulations, staff training and competency and cost for compliance for a facility with such low manufacturing capacity. • The final section discusses improvements to lentiviral vector manufacturing. The basic system was described by the applicants in 2015 and they propose to make improvements by using PEI for transfection, tangential flow for purification followed by validation of the system. The improvements are at least described for this component, but it is a little curious that little progress has been made since the first description of their manufacturing technique in 2015.

	• As stated previously the quality by design and CAR-T cell components have very generic outcome criteria. The use of satellite CAR-T cell manufacturing is much more clearly monitored, the outcome criteria for the other two projects are adequately described. • In spite of the generally poor description of the various projects, if successful they would indeed demonstrate progress towards competency in the described areas. This facility has an excellent track record which indicates that they are able to accomplish their goals. • The revised proposal is largely unchanged from their original application. They generally have a good track record in developing and offering educational opportunities, including participating in the CIRM Bridges to Stem Cells Program. • Their current educational program consists of four online modules and an in-person, one week laboratory experience. They propose to develop a manufacturing certificate program to train technologists for academic or biotech positions. This will be developed in collaboration with the Department of Continuing and Professional Education and the curriculum will be expanded to 120 hours to include additional topics, such as Quality Control and Quality-by-Design. The establishment of the course is well described. The extension of the program will also be conducted in collaboration with a local community college. The course objectives are adequately described. • The projects continue to lack significant details about the projects and how they will be done. One example that was brought up was the modular facilities that are well designed for closed systems, but the majority (or almost all) of cell therapy processes are not entirely closed so how will this be addressed? • Application overall needed to provide more detailed descriptions for each proposed specialization. • The proposal was lacking details did not address previous concerns.
GWG Votes	**Is the project feasible?**
Yes: 10	• Although the revised proposal is still somewhat hampered by a lack of description, I believe that the majority of their objectives can be achieved within the timelines allocated. In many cases they state that they have made preliminary progress and that this grant would be used to consolidate their findings. • The team is highly experienced and well qualified to perform the activities in the proposal. I believe that [a key person's] effort has been increased which will be a distinct benefit. There is one TBD staff member who will work on the training program. • The applicants have access to all the facilities and resources required to complete the proposed projects. They have requested a system for vector purification and funds for development of the software and purchase of small piece of hardware. • This GMP Facility has an outstanding track record in manufacturing a wide variety of products for cell and gene therapy. Their proposal described 18 different manufacturing campaigns, the vast majority of which have been evaluated in Phase 1-3 clinical trials. • The certificate program definitely looks feasible given the institution's track record. • They have been actively involved in educational outreach and have successfully interacted with a number of biotechnology companies. As one of the most active CIRM GMP Facilities I have no doubt that their productivity will continue. • They have rewritten and considerably improved the Risk Mitigation and Financial Contingencies section. • Primarily I feel that the applicant is a very valuable member of the CIRM GMP Network. They have considerable experience, some of which is unique. They have been productive and collaborative and have some interesting and unique insights as to future activities. However, I am still disappointed with this application. Apart from the new mobile manufacturing project, they have still failed to provide sufficient detail on their proposed projects, in spite of the fact that they state that many are already in progress. Their criteria for evaluation for success are extraordinarily simplistic. • My belief is that the applicant is a key component of the CIRM GMP group, but that they have not given this application the attention that it deserves. The revised version did not address many of the reviewer's requests for additional detail. I do not believe it was strengthened by the addition of the mobile manufacturing project, but I have omitted that from my evaluation. These are the reasons for my continued lack of enthusiasm. I would like them to resubmit and to provide more detail on each of the subprojects. However, I would support any CIRM or Board action to base their final decision on the very good track record of this facility, rather than the failings in the revised application.

	• While the revised proposal is an improvement on the original application, I am disappointed that the component projects are not more concretely described. I find them to be rather generic and lacking the detail which the applicants should have to hand. This makes a final evaluation somewhat difficult. • The revised application details the changes that have been made to address the points raised in the original review, however, although it is indicated that additional detail has been provided, frequently it has not. • The project is feasible, especially with the track record of the facility. However, the lack of details do make this project difficult to evaluate.
No: 3	• Concerns about mobile manufacturing project. • For the mobile manufacturing aspects, it was difficult to assess since little detail was provided regarding feasibility of closing the entire manufacturing process, and what FDA regulatory pathway could be employed for commercial approval.
GWG Votes	**Does the project effectively serve the needs of underserved and disproportionately affected communities?**
Yes: 13	• The workforce development program in the previous application increased workforce participation from underserved and disproportionately affected populations. The minor enhancements made in the revised application should not affect this substantially apart from the new proposed collaboration with a nearby community college. • The DEI information provided in the last application was approved by all reviewers and there have been no changes in this section in the revised application. • I think they have a good record for serving DEI needs and communities, it's evident in the proposal and I am sure they will do well. • Programs like the certificate program serve underrepresented communities. The certification program could tie in nicely with similar approaches to offering career opportunities and training in addition to adequate healthcare. • Yes. The applicants have partnered with a company to deploy mobile manufacturing for cell and gene therapy clinical trials. The first mobile cleanroom unit will be established near their institution and then expanded throughout California. The partnership aims to decentralize therapy development and manufacturing and will expand geographic access to CIRM-supported clinical trials across California. • Expansion to include outreach for more rural communities is a strength. • The team brings together the required mixture of expertise to perform the project. I really did not see any information on diversity and inclusivity apart from that in experience. • Their track record on DEI is good. It is not clear whether the inclusion of a nearby community college will further strengthen this because they did not provide any information on this institution. • There is a certificate program however it will not engage all levels of workforce development.
No: 0	*none*