APP #	TITLE	BUDGET REQ	FUND?	SCORE (Majority)	1	2	3
INFR5-14663	Laboratory for Cell and Gene Medicine: A partner in the California Cell and Gene Therapy Manufacturing Network	**$2,000,000**	**Y**	**1**	15	0	0
INFR5-14739	Enhancing California's Manufacturing of Leading-Edge Cell & Gene Therapies	**$2,000,000**	**Y**	**1**	15	0	0
INFR5-14756	Scalable Expansion for Stem Cell-Derived Therapies	**$1,998,174**	**Y**	**1**	15	0	0
INFR5-14636	A comprehensive biomanufacturing center solving bottlenecks in cell and gene therapy manufacturing to accelerate new therapies for California patients	**$2,000,000**	**Y**	**1**	13	0	0
INFR5-14719	Open Manufacturing Network for Cell and Gene Therapies	**$1,999,933**	**Y**	**1**	12	2	0
INFR5-14562	[Institution Name] Advanced Cell Therapy Laboratory	**$2,000,000**	**N**	**2**	7*	7	0
INFR5-14667	Advancing Cell Therapy Manufacturing Through Collaboration	**$1,999,964**	**N**	**2**	5*	7	0
INFR5-14779	Creating A Collaborative California Cell and Gene Therapy Manufacturing Network	**$1,496,973**	**N**	**2**	0	10	5
INFR5-14574	The [Institution Name] GMP Cell and Gene Therapy Manufacturing Facility	**$2,000,000**	**N**	**2**	0	9	5

* Qualify for Minority Report

Application #	INFR5-14663
Title (as written by the applicant)	Laboratory for Cell and Gene Medicine: A partner in the California Cell and Gene Therapy Manufacturing Network
Project Objective (as written by the applicant)	The LCGM supports process development and manufacturing for investigator initiated and select industry partner clinical trials. The objective of our proposal is to complete our project plan and enhance the LCGM value proposition positioning us competitively for the phase two funding period.
Summary (as written by the applicant)	The Laboratory for Cell and Gene Medicine (LCGM) is an innovative, state-of-the-art, multi-product manufacturing facility that develops cell and gene-based therapies in compliance with current Good Manufacturing Practices (cGMP) FDA regulations. The LCGM has a demonstrated track record of advancing cell and gene-based therapies through early-stage clinical development, from vector and process development through first-in-human Phase I/II clinical trials. The LCGM's manufacturing expertise spans the panoply of gene therapy approaches including CAR-T therapies, allogeneic CAR-T therapies, novel approaches to hematopoietic stem cell transplant, genome editing of hematopoietic stem cells, and genetically manipulated and un-manipulated T-cell therapies for immune modulation. The LCGM is currently performing process development and/or GMP manufacturing for 12 first-in-human phase I investigator-initiated clinical trials. Through CIRM INFR5 Manufacturing Network Phase I funding, we propose to implement enhancements to the LCGM operational infrastructure, specialized capabilities, and workforce development via the following projects: 1) Evaluation, selection, and implementation of electronic solutions for LCGM quality management system (QMS). This project will facilitate more efficient batch record release, labelling, kitting, manufacturing, and manufacturing document review and product release, preparing us for seamless collaborative partnerships in the Phase II funding opportunity. 2) Development, testing and preparation of technology transfer package for non-viral gene delivery platform. This project allows for a flexible gene delivery platform while reducing the dependency on long lead time and costly reagents such as viral vector. We will transfer this technology to LCGM manufacturing as well as other CIRM consortium affiliates as part of the Phase II funding opportunity. 3) Enhancement of curriculum, outreach and administration of GMP Certificate Program. This project provides a direct pipeline to LCGM of trained candidates and will provide a pool of experts for GMP manufacturing staffing across the expanding CIRM Manufacturing Network consortium, thus filling current workforce shortfalls. Importantly, the GMP Certificate program is designed to tap into the historically under-represented in healthcare demographic, fulfilling our commitment to effect diversity, equity, and inclusion change in medical education. In summary, the LCGM has a proven track record of successful process development and cGMP manufacturing for early phase clinical trials. We are now proposing to enhance and strengthen key components of the existing LCGM infrastructure and operations via the CIRM INFR5 funding opportunity. The proposed activities will add significant value to the LCGM and CIRM INFR5 Network members, and ultimately increase opportunities across the general California population.
Statement of Benefit to California (as written by the applicant)	A major roadblock in stem cell therapies is confirming efficacy in patients. As a member of the California Cell and Gene Therapy Manufacturing Network, the LCGM will: 1. offer a Northern California manufacturing hub producing transformative drug products that enable investigator-initiated stem cell trials, and 2. allow expanded access to Network trials. This program will benefit Californians, and the state of California by helping maintain its leadership position in stem cell therapies.
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 average of the individual member scores. Additional parameters related to the score are shown below.

Highest	1
Lowest	1
Count	15
Votes for Tier 1	15
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: 15	• The proposal was very well thought out addressing the three main objectives they wanted to achieve, including operational enhancements, development and tech transfer of non-viral gene transfer technologies to other institutions and organizations, and workforce development. Each area was well prepared. • Overall strong value proposition, appropriate methods and approach. • The limited capacity to manufacture investigational products is a serious bottleneck in the field of cell and gene therapy and each of the 3 aims in the current application addresses this need in different ways. • The de-risking and acceleration project involves the selection and implementation of an electronic quality management system (QMS) to facilitate GMP operations. The acceleration project will streamline functioning of the facility and position it well for its proposed large expansion. Taken together these should serve the facility well for involvement in Phase 2. • The replacement of paper manufacturing records with electronic systems represents a significant enhancement for cell manufacturing and will increase efficiency of operations. • Electronic production records could be helpful and potentially scalable. • The specialization project focuses on the development of a technology transfer package for a platform for non-viral gene delivery.

	• The development of non-viral gene delivery platforms represents a viable approach to develop more efficient and more flexible methods for manufacturing genetically modified cellular products. • The workforce development project aims to enhance a GMP Certificate program to train staff for both internal and external employment. • The lack of well-trained personnel able to manufacture cellular products and tools for genetic modification represents a significant limitation. The educational and workforce development plan proposed in this application is an excellent solution to this problem and represents an opportunity to increase the diversity of the workforce needed for further growth in this field. • From a workforce development view - loved the project and the certificate program. Glad to see they are planning to partner with two local community colleges. Definitely adds value. • Very strong workforce training plan. • The components of the project should have an overall beneficial effect beyond the project period. The de-risking and training programs are likely to have a more localized impact, whereas the specialization project could offer more widespread benefits. There is good institutional support. • The GMP facility interacts with the Alpha Stem Cell Clinic and is developing collaborations with two other institutions. It has industry collaborations and has licensing agreements with a few companies. • They report being involved in 13 clinical trials, two of which are yet to start. I believe that they are showing adequate levels of involvement with others and feel that this is likely to increase following completion of the specialization studies proposed for the current project.
No: 0	*None*
GWG Votes	**Is the project well planned and designed?**
Yes: 15	**Overall:** • Plans to double the current size of the GMP facility are appropriate and demonstrate significant institutional commitment to enhance cell and gene therapy infrastructure. • Good plan and reasonable timeline. • Well designed. **Operational Enhancements**: • The acceleration project will bring in software for quality management, which is currently paper based. They have begun working with a potential vendor on both electronic batch records and a quality management system (QMS). They will expand this interaction to include Process Development (PD), and materials and equipment management software. Milestones are provided for each of the activities in the operational enhancements section. • The proposed operational enhancements came out of a need identified in a formal gap analysis. • If one of the potential systems is not an adequate solution, there are other commercial systems that may be able to provide a more comprehensive approach to replace paper records and individual programs. • Plans for development of electronic records are a relatively weak part of the proposal. The plan is to develop different electronic solutions for different functions including inventory management and equipment management. Implementing different software solutions for different tasks will make it difficult to collect and link data on individual products and different manufacturing procedures. • There is little difference in this part of the proposal to differentiate the activities involved with the QMS system. It is somewhat buried in the descriptions of implementing other modules (batch records, PD, equipment and materials management etc.). There is no description of the requirements of the QMS system and what data it will manage. • The potential vendor for the software is a company that has many clients. Their webpage indicates that they do work with QMS but associates this activity with equipment quality management. It is not clear whether the vendor will be required to develop facility-specific software, but I feel that this is likely. I am a little concerned that this would be yet another CIRM facility that is seeking a different software vendor which will complicate

	collaborations. The potential advantages are that this could provide a useful comparison between different software. **Specialization:** ● This is an excellent specialization project, supported by good preliminary data, a detailed project plan, collaborations, and defined milestones. It is likely to be of value to all the CIRM facilities and to other cell and gene therapy centers. ● Development of non-viral gene delivery systems are a critical need for the field and the application provides detailed preliminary data supporting their expertise in this field and the progress that has already been made in developing an innovative solution in this area that can be exported to other centers in California and beyond. This is an appropriate area of specialization for this center that can benefit the CIRM Network and can be expanded in Phase 2 applications. ● The specialization project is particularly interesting. They will evaluate a non-viral gene delivery system for genomic modification and will use a selection transgene and a drug for cell enrichment. This will reduce both the time and cost of development of new products. ● They present good preliminary data based on preparation and enrichment of gene edited CAR cells. ● They present a detailed project plan to evaluate their knock in procedure and selection process and to compare efficacy against plasmid and AAV-mediated gene modification. They will also incorporate safety studies, a detailed comparison of cells generated using their new system versus cells produced using viral vectors. ● They will then finalize the technology by developing a technology transfer package for export of their method to other centers. They will collaborate on this component project with three other institutions. **Workforce Development:** ● The facilities workforce development program is exceptional and incorporates collaborations with local community colleges to enhance the diversity of the program. The Certificate program involves comprehensive and rigorous training for an 18-month period. They also have a paid summer internship program that was started in 2022 focused on minority students. They do not describe training programs for individuals at the post-doctoral degree level. ● The GMP certification program is a nice element of the proposal, and I would like to see the team consider engagement of Cell and Gene Therapy Industry experts in the curriculum formulation. The cGMPs of Cell and Gene therapy are emerging and evolving. For the certification to be beneficial to institutions and industry for filling the talent pipeline, and public-private collaboration in this effort could be beneficial. ● The workforce development component aims to supplement an 18-month GMP certificate program, enhancement of their existing GMP bootcamp curriculum, and further development of advertising and outreach activities. ● The GMP certificate activities are also proposed by other CIRM applicants, and it seems to me that the curriculum development should be shared and common to all, unless the infrastructure at each institution does not permit this. The certificate proposal shares content with those proposed by others. They also propose to enhance recruitment in Phase 2 by including applicants with a two-year associate degree, rather than the current four-year bachelor's degree. ● They propose to enroll 2 cohorts mainly from colleges with majority under-represented student bodies. The second cohort will be enrolled following review and enhancement of the curriculum offered to the 1st cohort (assisted by outside vendors) and improvement in outreach activities. The plans for the certificate and its preliminary curriculum are well described. ● The present GMP bootcamp consists of 5 modules. It contains lectures from a variety of institutions and companies. They will enhance this by addition of synchronous and asynchronous learning modules (not described) and tools to assess comprehension. They will also improve outreach and advertising activities (providing facility tours, career fairs, social media etc.). Milestones are provided for workforce development as are success criteria. ● Overall, I thought that the workforce development sub-component was good. ● A lot of thought was put into the certificate program. Great to see.
No: 0	*None*

GWG Votes	Is the project feasible?
Yes: 15	• The scope of the proposed plans is appropriate for what can be accomplished within the project timeline and will help support the facilities application for Phase 2 funding. • Feasible plan. Encourage the applicants to keep in mind the value to CIRM if the electronic documentation systems can effectively be exported to other CIRM members. • Each section of the proposal provides goals and timelines that seem appropriate for the proposed activities. The potential risks and mitigation strategies are presented. I have no major concerns about either the feasibility or completion of timelines on this proposal. • The proposed team consists of six existing staff members who have the required training and expertise. • The facilities and equipment are excellent. There is a proposal to almost double the facility size in the future. • The cell and gene therapy program at the applicant institution is growing and based on the size of the institution, its areas of interest, proposed expansion of its already substantial facilities and expertise and reputation, I do not doubt that it will continue to attract new projects. • The workforce development activities are definitely feasible. One risk is that students will leave prior to completing the certificate program due to its length. • There is a concern about software implementation - however they have a plan and an approach outlined. • The main thing to watch out for is the timeline for the implementation of the electronic infrastructure.
No: 0	*None*
GWG Votes	**Does the project effectively serve the needs of underserved and disproportionately affected communities?**
Yes: 15	• The workforce development plan will appropriately target community colleges with high percentages of underserved and minority populations for recruitment into the educational program. • Glad to see some established partnerships and intentionality around DEI. • Proponents are aware and supportive of underserved communities. • Effectively supports underserved communities. • The proposed workforce development program focuses on technical staff and does not address training individuals who already have PhD or MD degrees. These individuals could become future leaders in the field who will be able lead GMP cell manufacturing facilities.
No: 0	*None*

Application #	INFR5-14739
Title (as written by the applicant)	Enhancing California's Manufacturing of Leading-Edge Cell & Gene Therapies
Project Objective (as written by the applicant)	We will implement a new staffing model, training regimen, electronic quality management system, and outreach activities to overcome current bottlenecks and provide the foundation for manufacturing the pipeline of cell and gene therapies under development to bring treatments and cures to patients.
Summary (as written by the applicant)	Our GMP facility has a long and successful track record of supporting cell and gene therapy development. With the recent worldwide successes with CAR-T cell therapies and other gene therapies, as well as the emerging field of regenerative medicine based on stem cells, cell and gene therapy trials are expanding dramatically. This project is designed to support future growth and increase the capacity and capabilities of our GMP facility, including generation of a comprehensive training program for staff joining the GMP, as well as selection and implementation of a Quality Management System to support the training program. Other activities for this grant include generation of standardized protocols for common manufacturing processes such as isolation, genetic modification, and cryopreservation of CD34+ cells, dendritic cells and others. To address the major bottleneck created by the lack of qualified staff in the field, we will undertake a number of activities aimed at workforce development, including multiple types of outreach to raise awareness of career opportunities within GMP facilities, as well as building training programs to create a pipeline of qualified staff for the future. We will also work with partners across the network to build the appropriate payroll classifications to support recruitment and retention of staff within academic GMP facilities. The proposed synergistic project activities have a multiplying effect: they provide the foundation for addressing the near-term pipeline of cell and gene therapy clinical trials and build further into the future. At the end of the project period, this GMP will significantly increase its capacity to support cell and gene therapy manufacturing and be ready for continued growth into the future.
Statement of Benefit to California (as written by the applicant)	This project tackles current bottlenecks in manufacturing for cell and gene therapies and expands capacity and capabilities to address the growing pipeline. This positions our GMP to play an active role in the development and exchange of best practices and know-how across a network of GMPs in California. In addition to creating new jobs in the California economy, these efforts will ensure that the most promising new treatments and cures reach the patients in California who need them most.
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

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Highest	1
Lowest	1
Count	15
Votes for Tier 1	15

Votes for Tier 2	0
Votes for Tier 3	0

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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: 15	**Overall:** ● This is an excellent proposal that will enhance the overall value of the CIRM Cell and Gene Therapy Network. ● The proposal addresses debottlenecking manufacturing within the institution which is a recognized cell therapy center in California. The decentralized model employed at the institution, while complex and potentially unscalable, does serve to strengthen collaboration and shared knowledge between the research focused team and the manufacturing team. These elements should be preserved in the new model, and I encourage the sponsor to consider how to continue this important collaboration. ● Over the past 30 years the facility has manufactured quite a number of disparate products for early-stage clinical trials using phase appropriate GMP manufacturing. ● This manufacturing work has involved a decentralized model whereby individual lab staff would be trained and guided in GMP manufacture. While this model might have been practical it is inherently inefficient and impractical for GMP manufacturing particularly for later stage products. Now, they are building a state-of-the-art GMP manufacturing facility that will utilize a centralized model whereby the facility will have core staff for manufacturing as well as separate Quality Assurance (QA) and Quality Control (QC) functions. ● The facility proposal includes an extensive listing of projects, internal and industry-based, with which they have been involved. The activities proposed in the project will streamline facility operations and improve staff availability. This should have an effect beyond the project period. ● Given the applicant's long history in CGT manufacturing and their commitment to building a new facility, hiring new staff and focusing on a centralized model for GMP manufacturing I think there is considerable value and synergy between current efforts at the institution and this grant application. ● There appears to be a real commitment from the institution to build out this facility and a commitment to staff the facility. This grant will augment staff and will speed up the development of a functioning GMP facility. ● The facility collaborates with the Alpha Stem Cell Clinic and the clinical and translational science institute. It states that it is "well positioned' to collaborate with a stem cell research center and CIRM-funded EDUC programs including BRIDGES, COMPASS and SCHOLAR programs. ● It has partnered with a number of academic centers by supporting clinical trials and has received peer-reviewed funding including that from CIRM. They have also partnered with companies providing reagents and equipment. ● The proposal should have a beneficial effect on facility operations and workforce development.

- The applicant plans to transfer to centralized system and specialize in gene modified stem cells. Good workforce development curriculum. Small facility.
- Crucial to the success of the facility will be the development of realistic cost and charging models to ensure the facility can support itself over time. One can anticipate this transition will hit some bumps in the road but given the demand for GMP manufacturing (which will likely increase with time) I imagine that this facility with its trained staff will ultimately be very sustainable.
- Fiscally, the sustainability is much harder to ascertain. As the organizational model is a complete overhaul, the fiscal sustainability will likely have to transfer from a system where individual investigators are funding their own program (and their own manufacturing) to a service fee model. The service fees are not continuous (as programs come and go). As the program grows, this is less of a concern, but bridging to that point may be difficult.
- Organizationally, the proposed enhancements will be substantially more sustainable well beyond the project period.

Operational Enhancements:

- The operational enhancements clearly relieve a bottleneck (de-centralized manufacturing) that exists at this facility. The proposal to have committed, trained personnel supporting manufacturing is an industry standard and required for improving the CGT landscape at the institution and in California.
- The operational enhancement component consists of centralization of GMP facilities by providing a core of staff responsible directly to the facility rather than to research/ clinical investigators. The operational enhancements are important to this specific facility, especially the provision of a centralized GMP source. It is impractical and inefficient to use staff provided by investigators, as each must train in GMP behaviors before starting production. It also poses a liability risk to the facility, which will have overall responsibility for FDA regulations compliance.
- The plan to implement an electronic Quality Management System (eQMS) will add controls and efficiencies that are not currently in place. Implementing an eQMS will present challenges but on balance I believe it will be worth it in the long run.
- Addition of an eQMS, while time consuming to implement at the beginning, will be critical to improvement and accelerate the CGT environment. The proposal to include this will provide operational enhancement to this facility and to the network.

Specialization:

- The specialization activities will basically consist of a general expansion of manufacturing activities and sharing of protocols.
- The current list of technical specializations is extensive, and a result of the current investigator driven expertise. Coordination of these specializations and delivering them into a single centralized facility has the potential to 'platform' these technologies and expand them across the network.
- This facility will almost exclusively focus on autologous products, so the emphasis is on scaling out rather than scaling up.
- The specialization project lacks detail, but its intent seem sound, in that it should broaden and improve experience in cell manufacturing. With the new GMP facility coming online these activities should position the facility well for involvement with Phase 2.

Workforce Development:

- Workforce development involves improving staff recruitment to the facility, mentoring individuals for leadership positions, provision of career development for research staff, creation of a systematic GMP technical training system, establishment of 4 traineeships, building partnerships with industry and development of job classifications and pay structures for technical staff.
- The most impressive of the sub-components in this proposal is workforce development, which in addition to providing the usual training courses and certificates will address the widespread concern of defining job classifications and pay scales. This is a major problem for most academic GMP facilities, whose staff have unique qualifications and are constantly recruited by industry.
- I am impressed with the amount of thought given to internal staff developing and hiring of the workforce development component; while the activities may not offer broad value to the CA workforce, it is exactly what they need to develop their staff.
- Job descriptions and pay package investigation is a strength. Suggest coordination and collaboration with other institutions to develop CIRM-wide initiative.

No: 0	*None*
GWG Votes	**Is the project well planned and designed?**
Yes: 15	**Operational Enhancements:** ● The most important task of the project on operational enhancement is to provide a centralized core of technologists for the manufacturing facility. There are two existing staff, but most activities are conducted by individuals who have played a role in developing the projects. This is extremely inefficient and is a very rarely used model. It is important, especially in view of a new facility coming on-line, that this part of the proposal be implemented. ● Proposed tasks consist of 1) hiring and training additional central core staff in methods used by the individual product teams, 2) implementation of electronic quality management system which will also track projects, staff competency manage documents and assist with training and 3) enhancement and implementation of in-house and partnered analytical capabilities. Improvements in analytical capabilities will involve hiring QC staff and where possible leveraging existing analysis resources. These are logical improvements to laboratory operations and should be supported. ● The current decentralized model for manufacturing is inefficient as it requires continual training of staff from different labs who are undertaking manufacturing projects in the current facility. With dedicated core staff the manufacturing will be significantly de-risked. ● This centralized model will also be essential for late-stage manufacturing. ● The development of QC and QA, the eQMS system and the hiring and training of staff will all demonstrate the competencies needed to move to a centralized manufacturing model. ● The success criteria for this sub-component are rather basic - "complete hiring and training of central staff" but I believe that the tasks are presented and are logical so that the criteria for success are rather obvious. ● No coordination of the eQMS across the CIRM network was indicated. Strongly encourage discussion, coordination, and working with other CIRM partners to identify a eQMS system. **Specialization:** ● I really liked their plans to engage commercial manufacturers to understand large-scale manufacturing needs; it's often overlooked and smart to better align academic and industry needs. ● They offer to share protocols with other facilities and to help train their staff (IP permitting). This section is vague. It states that the facility will offer expertise on technology platforms by training the central core staff. This is not a specialization task. It does not provide a project plan, or list of tasks with success criteria. It may be that the centralization of manufacturing activities must take precedence over any specialization tasks. **Workforce Development:** ● The workforce development component has very well-articulated needs/plans. ● The workforce development sub-component is rather strong in that it contains a unique feature. They propose to raise awareness of career opportunities by developing presentation materials and offering information sessions in collaboration with three partners including the Alpha Stem Cell Clinic. In addition, they will participate in ongoing programs. Later they will include day-on-the-job opportunities and short rotations. ● They will offer training on the GMP environment to first-phase Clinical Pathology residents and Transfusion Medicine fellows using applied and didactic methods, which will include meeting participation, shadowing staff, trial audit participation, additional component will be provided on request, and the program may be eventually expanded to other components of the School of Medicine and the Graduate Division. ● They plan to hold an annual campus workshop on career development for research staff for 30-50 participants already involved in cell and gene therapy at the institution. This will be held by a commercial clinical research training and certification provider. I was able to find suitable courses from only one of the suggested providers. ● As with other applicant facilities, they propose to develop a paid training and/or certification program for technical positions, although this one appears to be for their GMP staff. The second component is establishment of formal intern-type traineeships within the facility in concert with other institutional training programs. This will leverage the

	BRIDGES and COMPASS programs. They currently offer undergraduate positions within the facility. ● Another development component will be building industry partnerships to allow trainees to gain first hand experience. In this context they mention several companies, and some letters of support are included. Again, this program seems to be focused for internal GMP staff. ● A very interesting component is that on developing job classifications and pay structures. It represents a much-needed task within the field, and I highly encourage this component. ● The workforce planning seems to be undersized. It is difficult to judge if the number of positions being proposed is sufficient to enable success of this program. I applaud the efforts presented to address the compensation and leveling initiative to improve the competitiveness of the institution as compared to industry in order to retain talent. Additional work should be done to confirm the workforce planning regarding its ability to support the full project scope.
No: 0	*None*
GWG Votes	**Is the project feasible?**
Yes: 15	● I think the project is feasible as described. ● A new GMP facility is due to come on line with 7 manufacturing rooms. It is not clear whether the existing facility will remain open. Even if it does not, the manufacturing capacity will increase from 80 to 150 products per year. The equipment and resources available will be excellent. The new facility is a collaboration between three pre-existing groups at the institution. ● With limited existing space the facility already has a good track record for manufacturing products. This is likely to be substantially improved by the switch to a centralized production core, expansion of the facility, and workforce development activities. I am sure that there will be an adequate demand for their services. ● The workforce development component is very feasible assuming they are able to find/develop the needed expertise. ● I think this plan and timeline is feasible. Crucial to the success of the project will be the identification and hiring of key managers for Manufacturing, QA and QC. These three hires are really important to the success of the program. The senior leadership is well qualified. As mentioned, hiring of the three key managers is crucial for success of the project. ● A big component of this proposal is hiring of staff to implement the centralized manufacturing core. Existing key staff are well qualified, but there is no information on the current two manufacturing GMP facility staff. There are only two key staff on the proposal; they will need a very active recruitment program. ● Overall, there is a shortage of CGT GMP manufacturing in the USA. The success of this project will be more about execution than an adequate project pipeline. ● The success criteria provided for the sub-component projects are rather generic but the tasks to be performed are, in general, well described with appropriate timelines. The exception is the Specialization sub-component, which is too vague to determine its likelihood of success within its timeline.
No: 0	*None*
GWG Votes	**Does the project effectively serve the needs of underserved and disproportionately affected communities?**
Yes: 14	● Given the institution's excellent history in this area I think the activities are likely to improve access to CGTs for underserved and disproportionately affected populations. To some extent this is one step removed from access to CGTs - meaning the group will be manufacturing for third parties and not directly involved in administering CGTs to patients. ● Based on the track record of the facility I believe that they will create advancement opportunities for underserved Californian populations. Right now, English is a second language for almost half of the team, and 15% are the first in their family to graduate from college. ● The institution has a collaborative sickle cell project. ● Clear commitment and demonstration of this value.

No: 1	• In the workforce development component, I thought this was the weakest part of the proposal. While leveraging CIRM programs and some initiatives and resources at the institution, I didn't get the sense there was a lot of internal staff commitment to DEI.

Application #	INFR5-14756
Title (as written by the applicant)	Scalable Expansion for Stem Cell-Derived Therapies
Project Objective (as written by the applicant)	A scalable induced pluripotent stem cell (iPSC) expansion, T cell expansion, and cardiomyocyte maturation/expansion process that is ready for validation in a large-scale bioreactor (25 - 2000L) and tech transfer into Good Manufacturing Practices (GMP) production.
Summary (as written by the applicant)	This proposal has three primary goals: (1) Develop reproducible, sensitive potency/functional assays to serve as Critical Quality Attributes, allowing freedom to improve and mature processes as a cellular product progresses from Phase I clinical trials to commercialization without high levels of risk or overly exhaustive comparability studies, (2) Create scalable allogeneic manufacturing processes, reducing capacity and consistency limitations while reducing cost of goods and increasing patient access, and (3) Support students during a hands-on thesis for a master's of Translational Medicine, creating a justifiable path to increase earnings potential without an overly burdensome investment of time and finances. Successful completion of this proposal will generate a scalable expansion process for induced pluripotent stem cells (iPSCs), T cells, and cardiomyocytes ready for scale-up and tech transfer into GMP production. California researchers can leverage this out-of-house, scalable manufacturing process to increase yield and decrease costs. This process, along with a workforce training program, will provide underserved populations in California access to clinical treatments and on-ramps to the cell and gene therapy workforce.
Statement of Benefit to California (as written by the applicant)	Creating low-cost, scalable allogeneic therapies democratizes cell and gene therapy, allowing underserved populations of California to access life-saving treatments and facilitating development of therapies for rare conditions. Programs to support trainees during hands-on thesis projects in cell and gene therapy lowers the financial risk associated with Masters degree programs, creating a more inclusive workforce to reflect the diversity of California.
Funds Requested	$1,998,174
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 average of the individual member scores. Additional parameters related to the score are shown below.

Highest	1
Lowest	1
Count	15
Votes for Tier 1	15
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: 15	**Overall:** ● The value proposition of the proposal lies in the applicant's aim to address the following bottlenecks: (1) potency and functional assays (2) scalable and optimized allogeneic cell expansion and (3) a lack of a qualified manufacturing workforce. These issues represent significant bottlenecks in the field of cell gene therapy. ● The proposed project includes very focused activities: (i) developing standard functional/potency assays for three cell types - pluripotent stem cells (PSCs), cardiomyocytes and T cells; (ii) developing a process development paradigm in a bioreactor system; and (iii) implementing a master's level training program. **Operational Enhancements:** ● The project on de-risking and accelerating process development and manufacturing focuses the development of meaningful reproducible and sensitive potency/functionality assays as Critical Quality Attributes. ● The wide ranging and encompassing nature of the proposed projects will benefit not only the applicant facility but the entire field beyond the project period. ● This is strong program. I liked the emphasis on potency and reference banks. ● The proposed projects will undoubtedly facilitate scaling of its activities into Phase 2 of the INFR5 funding opportunity as they provide generic enhancements to the field. ● The facility works with an Alpha Stem Cell Clinic and is working on several CIRM-funded projects. They have industry collaborations and have worked on a number of INDs, though it is not clear if any of these INDs were for commercial entities. **Specialization:** ● Specialization will involve identification of Critical Process Parameters for manufacturing allogeneic products. ● The applicant is focusing on platform technologies, which are product-agnostic and will become a foundation for the 2nd phase of funding. ● The applicant plans to develop functional assays for cardiomyocytes - voltage, contractility, and calcium - and create a matrix of assays. This "generic matrix" could be used further to define a potency assay for the final drug product. ● In the case of CAR T, TILs, and other immune cells they are planning to focus on controls, including reference material. They plan to utilize suspension bioreactors for scalable cell expansion. ● A reviewer asked a question about potency assays and the applicants responded satisfactorily. At least two assays will be developed for pluripotent stem cells as an intermediate product (at the Working Cell Bank (WCB) / Master Cell Bank (MCB) level). **Workforce Development:**

	• Workforce Development aims to support students during a hands-on thesis for a Masters in Translational Medicine. The applicant institution has focused on projects that will improve cell and gene therapy development on a broad basis. This is very laudable and to be encouraged. • The most impactful approach in workforce development is the proposed Master in Translational Medicine program. The applicant has been running this program successfully for two years. Now they plan to expand it to ten scholars, and then to twenty scholars in the second phase. • The proposed master's program is a solid program; however, to add value to the state of CA, the applicant should focus on other, more attainable degree levels. The industry is shifting away from requiring graduate degrees for manufacturing roles toward bachelor's and associate degrees. I wish this proposal acknowledged a desire to reach a broader base of talent. • I love the attention to QA in training and the thoughtfulness about benchmarking materials.
No: 0	*none*
GWG Votes	**Is the project well planned and designed?**
Yes: 15	**Overall:** • The proposal could use a little more specific read metrics for accomplishments, but overall it's very good. • With the focus and synergy of the three programs, the project seems well-planned and achievable. • The milestones plan and success criteria are clearly outlined in a table within the proposal. **Operational Enhancements:** • The acceleration project focuses on development of potency assays for cell products, an area of tremendous interest. Studies will focus on assays for iPSC and T cells. • The success criteria are quantitative with values for coefficients of variation and acceptable backgrounds. I would have liked to see more details on the component tasks of the written proposal. My concerns were mitigated by the responses of the applicants to reviewers' additional questions. • Tasks are not adequately described. **Specialization:** • The specialization project will focus on process development of hPSC suspension culture system by looking at the effects of a range of variables. The applicant will also examine enhancements for cardiac differentiation of hPSC. • Central to these studies will be the evaluation of scalable expansion systems. Preliminary data and planned tasks are provided for the specialization project and the results will be valuable to the field in general. **Workforce Development:** • Given limited access to PhD programs, the applicant proposes to expand enrollment in their Masters in Translational Medicine degree program - from 5-8 to 20 students per year. The program consists of one year of coursework and one year of hands-on thesis studies. • Recruitment will be from underserved populations and the proposal will fund a pre-doctoral NIH-level stipend. The primary GMP activity will be a rotation through the facility in addition to teaching and mentoring students. • This project would considerably expand the numbers of qualified biomanufacturing staff in California. It is unfortunate that details are very thin - e.g., curriculum, recruitment activities, rotation times, etc. • The single success criterion is recruitment of a single student to conduct a portion of their thesis project in the GMP facility. This is minimal at best and the proposed activities are very briefly described in the Workshop Development sub-component.
No: 0	*none*
GWG Votes	**Is the project feasible?**

Yes: 15	• The proposal clearly demonstrates an organizational commitment to continued development beyond the end of this funding period. As part of contingency/risk mitigation, The applicant institution will cover unplanned expenses (due to possible delays). • The institution has a long track record in manufacturing a wide variety of products. I have no doubt that this will continue beyond the proposal and that the experience gained will be beneficial in future activities. • Given the relative lack of detail in the operational enhancements and workforce development section, it is difficult to determine whether these activities will be completed on time. The specialization activities should, however, be achievable. • This is a good proposal and my concerns were mitigated by the applicant's slide presentation. I believe that their proposal to produce reference samples is particularly good. • The clarity and focus of the application along with the expertise of the staff gives confidence in the project feasibility. • There are four Key Personnel (one is TBA as replacement of a recent move). They are well-qualified but their time commitments are low. The highest percent effort (50%) is requested for the Project Manager, who has primarily administrative responsibilities. The Program Director commits either 20% or 30% effort. • The team is appropriately staffed and well-qualified to perform the work. The project has access to all the necessary facilities. • The facilities are excellent. Approval should be given for purchase of the bioreactor. • The activities can feasibly be completed within the timeframe. • This is a very thoughtful and skilled team.
No: 0	*none*
GWG Votes	**Does the project effectively serve the needs of underserved and disproportionately affected communities?**
Yes: 15	• The applicant has a lot of internal institutional diversity, equity and inclusion (DEI) programs/practices that indicate DEI is a focus; however, the workforce development program would be more accessible if it offered non-graduate degrees. • The master's degree in Translational Medicine program has been functional for about two years and is designed to include candidates from underserved communities. • The applicant hopes to improve access to cell and gene therapies (CGT) through the implementation of large-scale generation of allogeneic (off-the-shelf) cells. • A workplace social club for CGT is in place for addressing DEI issues at the facility. • The training program and track record of serving the community appear sound. • The applicant seems attentive and has addressed DEI issues. • The institution has a good track record for promoting DEI. • Yes, several facets of the proposal are DEI-oriented.
No: 0	*none*

Application #	INFR5-14636
Title (as written by the applicant)	A comprehensive biomanufacturing center solving bottlenecks in cell and gene therapy manufacturing to accelerate new therapies for California patients
Project Objective (as written by the applicant)	We aim to considerably expand access for all Californians to outstanding cell and gene therapy treatments for multiple patients. With operational enhancements to develop diverse talent from underserved communities, our GMP facility will advance all aspects of biomanufacturing within the network.
Summary (as written by the applicant)	As part of a health system with a robust academic and clinical enterprise, we are a leading GMP biomanufacturing center producing induced pluripotent stem cell (iPSC)-based and gene therapies in the growing field of regenerative medicine. Our organization has national standing with a track record of excellence in stem cell studies from bench to bedside, reflected by numerous funded studies and clinical trials. Should we gain this funding, we will manufacture cell and cell-based gene therapies compliant with current Good Manufacturing Practices (cGMPs) to support Investigational New Drug (IND)-enabling clinical trials as part of the California Cell and Gene Therapy (CGT) Manufacturing Network. Specifically, we will develop automated processes to scale up manufacturing of iPSCs and genetically engineered iPSCs to support cell-based gene therapies. Supported by our expert quality and analytical development teams, we will enhance operational efficiencies by improving (a) our all-inclusive quality management system (QMS) with revised implementation of electronic manufacturing batch records and (b) establishing a digital laboratory information and sample management system (LIMS) in the quality control laboratory. We also seek this funding to build training programs in collaboration with our partners. These programs will be tailored to specifically develop diverse biomanufacturing workforce talent from underserved communities, geared towards supporting advanced biomanufacturing. This funding will augment the GMP 'mind set', that of recognizing and managing risk and establishing Quality-by-Design (QbD) principles. This mind set will establish greater consistency of process, measurement and control, to ensure that the cell and gene therapy treatment we manufacture is safe and meets quality standards, with the ultimate goal to protect the patient. Such operational and quality improvements will make us even more attractive to trial sponsors in industry and academia, patients, and health care providers as a recognized center of excellence in biomanufacturing that is closely integrated within a large health system. With a robust academic and commercial project pipeline to develop and manufacture clinical-grade cell therapy products suitable for investigational use in humans, our ultimate "customers" will be patients in need of innovative cell and gene therapy approaches. Finally, with these improved operational efficiencies, additional value will be added by working closely with the Cell and Gene Therapy (CGT) Manufacturing Network by developing technology transfer packages surrounding iPSC banking and cellular immunotherapies, and by enhancing knowledge sharing in biomanufacturing. Contributing to this community will make a whole that is greater than the sum of its parts. In summary, this funding and our participation as expert members of the CGT Manufacturing Network will significantly alleviate constrained CGT biomanufacturing capabilities in California.
Statement of Benefit to California (as written by the applicant)	As part of the Cell and Gene Therapy (CGT) Manufacturing Network, we will bring operational enhancements and workforce development programs to advance and alleviate constrained biomanufacturing capabilities in California. Such advances will allow us to manufacture the latest CGT treatments for multiple patients with debilitating diseases and unmet needs. Californians with devastating diseases will have access to CGT products manufactured in our GMP facility for early and later 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

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Highest	1
Lowest	1
Count	13
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Votes for Tier 3	0

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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
	Overall:
	● This program has several aims:
	  ● Develop an automated system for the culture of Induced Pluripotent Stem Cells (iPSC) to include automation, use of new equipment, and increasing scale. This component leverages their world class experience in preparing and banking iPSC. They will also look at automating clonal cell screening and selection.
	  ● Improve their quality management system (QMS) and introduce electronic worksheets and a laboratory information management system (LIMS) for their quality control (QC) laboratory. This will facilitate their daily operations and potentially provide systems, processes, and procedures to other facilities in California and beyond. This facility is relatively new and it is a perfect time to implement electronic systems.
	  ● Build a workforce training system tailored to the recruitment and retention of minority and underrepresented groups.
	They propose to integrate these efforts by working closely with other CIRM programs (BRIDGES and SPARK) and facilities.

	• This proposal has the potential to provide outcomes that will be of value in Phase 2 of the program and beyond. They propose to collaborate closely with other members of the CIRM manufacturing network who also have an active interest in iPSC. The institution is providing the required matching funding and an additional contingency fund. • The applicant's iPSC platform is extremely impressive and would bring value to the California cell/gene therapy ecosystem. • During and beyond this project the applicants will 1) diversify their manufacturing portfolio, 2) invest in cutting- edge technology, 3) develop additional partnerships (academic and commercial), 4) expand global reach, 5) offer additional custom manufacturing services, 6) develop automation, 7) increase services in all aspects of operations, 8) strengthen supply chain management, 9) implement sustainability initiatives to reduce costs, and 10) expand DEI training. However, details on how this will be achieved are not provided. **Operational Enhancements:** • The proposed operational enhancements address critical manufacturing bottlenecks. These enhancements will be achieved by improvements in software, currently used for "all things manufacturing," and quality. They also are planning to implement LIMS in the QC laboratory. These enhancements will significantly improve operations. **Specialization:** • The specializations in the proposal relate to automating the workflow with iPS cells. The applicants aim to achieve automation on different levels, including scaled up manufacturing (a batch size of 10e11 to 10e12 cells) of master cell bank / working cell bank and gene-edited clonal iPS cell lines. **Workforce Development:** • Regarding the training and workforce development component, the applicants have given significant thought over time to training, mentoring, and professional development of their own staff. This is a smart strategy as there are well-understood challenges in academic cGMP laboratories when it comes to gaining industry expertise. It is great to see that they are looking to form education and training partnerships with several minority-serving institutions in their region to broaden diversity. • The application includes a great proposed partnership with a nearby academic institution to address workforce development.
No: 0	*none*
GWG Votes	**Is the project well planned and designed?**
Yes: 13	**Overall:** • The overall plan is somewhat ambitious but feasible. **Operational enhancements:** • The first focus of the de-risking component of the proposal is to enhance the capabilities of the software currently used for quality management by working with the software provider to implement new features and functions. The second focus is to evaluate and implement a commercial LIMS system and qualify analytical assays for iPSC. The required capabilities of these systems are presented and are consistent with the requirements for good quality management system software. • The project is well-planned. The proposed enhancements will lead to the improvement of operations in all stages of development. **Specialization:** • The applicants will work on the specialization project in two areas: 1) automation of iPSC culture with real time control and 2) automation of clonal cell screening and selection to generate gene-edited iPSC cell banks. This aims to mitigate the harsh effects of current screening methods on cell integrity, reduce variability of the starting materials, and improve methods for single cell isolation and dispensing. Specific tasks are listed for each or these projects. The goals are provided and potential risks and mitigations are discussed. • Additional task components include development of data capture and analytical methods. Analytical protocols for analysis will be shared with the CIRM manufacturing group and others.

- The development of new electronic software features are important in streamlining GMP operations. Several groups using the same software as the applicants are struggling with its user-unfriendly features and are working with the software provider to make improvements. While there is a letter of support from the software provider, they may not be able to provide timely and efficient resolutions to their software issues to the applicants as an individual user institution.
- The selection of a LIMS system will take time. There are software packages with huge variations in capabilities and complexity. It would be advisable to contact other GMP facilities, particularly those supported by CIRM, to seek advice. It would be disadvantageous to the GMP manufacturing group to end up with unique QMS/Batch Record software at each of its facilities.
- The specialization tasks represent an opportunity for considerable improvements in iPSC manufacturing and characterization. The manufacturing component is the more complex of the two tasks, since the characterization project essentially involves evaluation of equipment.
  The manufacturing sub-component is supported by promising preliminary data and by a logical series of tasks and criteria for evaluation. It has the potential to evolve further through a collaboration with a well-known provider of manufacturing supplies.
- The task to improve the cryopreservation method may be overly ambitions. Cell freezing methods are under continual re-evaluation but little progress has been made in the last 10 years. If a commercially-available cryoprotectant gives reasonable results, it should be chosen for use.
- It may not be possible to complete development of all of the proposed analytical assays during the period of funding, although it may be possible to work with other facilities to import them.
- The specialization area is iPS-based gene and cell therapies. The center already has preliminary data and experience with most things and areas they are proposing to enhance. The success of the proposed projects will boost competency in iPS cell-based therapies.

Workforce Development:

- The workforce development project includes:
  - Development of a Cell and Gene Therapy Manufacturing Technician Certificate in collaboration with a local college which has a 90% ethnic minority student body including 78% Hispanics. The institutions have worked together for a few years and have trained 6 students into positions at the GMP facility.
  - Biomanufacturing internships with two local institutions. The GMP facility has existing relationships with both institutions. This program will recruit about 6 students annually to paid internships. The details of this program are not provided.
- The parent institution of the new GMP facility offers additional training programs, including:
  - Two separate biomanufacturing symposia on Translational Medicine and Biomanufacturing, regular manufacturing sessions, opportunities for new employees to be mentored by experienced biomanufacturing professionals, monthly internal seminars and opportunities for paid attendance at local, national and international meetings.
  - Participation in CIRM education initiatives including the Scholar, BRIDGES and SPARK programs.
  - Degree programs such as an M.S. in Biomanufacturing, graduate education research programs, postdoctoral internal and NIH-funded training programs, and a clinical scholars program.
- The major outreach initiative is the development of the Manufacturing Technician Certificate, which has a good curriculum. They propose to graduate the first participants in June 2025.
- The applicants mention an internship to become familiar with GMP skills and techniques but further details were lacking.
- The critical components of workforce development will be the creation of the certification qualification and the internship (which is inadequately described). If both of these are successful, this will make a useful contribution to the development of a workforce with entry-level capabilities. It is good to see an emphasis on recruitment of more junior students.

	• Workforce development component of the application were well planned. One would like more detail on program implementation, but the curriculum was well planned and designed.
No: 0	*none*
GWG Votes	**Is the project feasible?**
Yes: 13	**Overall:** • With the exception of a couple of objectives referred to above, most of the goals are achievable within the proposed timeline. The tasks are organized in a logical manner. The sequence and the relative risks associated with each have been outlined and mitigation plans have been proposed. • The team who will execute this project is already on board and no additional hiring will be required. Team members all have the relevant qualifications to perform their assigned tasks, which cover the expertise required for successful completion of this project. The Program Director is extremely experienced with the range of tasks to bring this project to fruition. • The team is staffed appropriately and qualified. • The applicants have no lack of interest and have a good pipeline of projects (especially in iPS cell-based therapies area) to support all proposed enhancements. • The facility and all areas within are well supplied with the equipment required to perform the proposed tasks. • There is a description of a communication plan which is somewhat generic and indicates that mode and frequency of contact will depend on the urgency of the issue. They will, however, also evaluate the communications plan and regularly update it to ensure continued effectiveness. • The knowledge sharing plan is adequate. The team communications plan is somewhat generic. There is no funding overlap with other support. The institution is providing both matching and contingency funds. The risks are well identified and mitigation strategies are appropriate. • Several commercial collaborations exist. For a new facility this is a good start. Undoubtedly, they will attract more commercial partners. The applicants should also build up similar relationships with internal departments and centers and centers at their institution, and this can be achieved by the end of the funding period. **Specialization:** • The proposed timeline looks reasonable. But it also will depend on other companies providing tools and services. For example, the applicants have mentioned that the GMP software developer may not able to complete their part of the work to fit into the proposed timeline. It illustrates a high dependence on success and timely execution of third-party companies/collaborators. **Workforce Development:** • Regarding the workforce component, the proposed plan is feasible although not too many details were provided with respect to implementation.
No: 0	*none*
GWG Votes	**Does the project effectively serve the needs of underserved and disproportionately affected communities?**
Yes: 12	• The applicants see the needs of under-served communities as falling into two groups: 1) recruitment and retention of a diverse workforce, and 2) developing therapies and products to serve under-served communities, who are often disproportionately affected by diseased treated by cell and gene therapies. • The applicants cite DEI programs offered by their institution and the GMP facility integration with these initiatives, but do not describe this in great detail. They also cite institutional interactions with several universities which have large numbers of minority students. The interactions are not described. • The applicant institution is already collaborating with two universities with high representation of minority students on cell and gene therapy manufacturing workforce development.

	• From the workforce development perspective, it is refreshing and good to see that the applicants have 1) established true partnerships with predominantly minority institutions, 2) have hired their graduates, and 3) have plans for strengthening partnership with new internship and certificate programs.
	• It is rewarding to note that the facility has recruited some of the trainees from predominantly minority institutions.
	• The applicants indicate that their institution has many DEI committees, including LGBTQ+, and that these report DEI metrics. But how this affects their participation in programs relevant to this application is not described.
	The major involvement with DEI will be through collaboration within the institution's network, development of training programs in collaboration with two colleges that educate underserved community students, and development of iPSC lines from donors with diverse backgrounds.
	• The application provides well-detailed information on workforce development including underserved CA populations.
	• The applicants list DEI activities as developing therapies for diseases disproportionately affecting under-served communities, partnering with community based groups to increase disease awareness, including diverse patient populations in trials, providing education and training for community members, building a diverse workforce, being culturally competent with community members, collaborating with others to ensure affordable access to under-served communities, and ensuring team training in cultural sensitivity and DEI.
	  ◦ However, they detail only two of these efforts with respect to implementation during the proposed project: 1) growing iPSC lines from diverse donors by using blood bank registries and institutional clinics, which will happen during Phase 2 of the project, and 2) their collaborative training programs with colleges with high minority student representation.
	  ◦ During phase 1 of this project, the only component that may have an effect on increasing workforce diversity is the two training programs which collaborate with colleges with high proportions of minority students. Internship within the GMP facility may also serve the same purpose, but is poorly described. Increasing diversity of iPSC cell donors is deferred until phase 2.
	• The proposed DEI efforts on this project are somewhat unimpressive. This may in part be due to the relative newness of the GMP Facility program, which, during its start-up phase, has many technical and procedural tasks to accomplish.
	• The facility project team does not present a successful track record in promoting DEI, perhaps due to their newness. The project staff do not appear to include anybody with DEI experience and it is assumed that this will be obtained from other institutional staff. A QA lead is cited as responsible for coordinating personnel GMP trainings but it is assumed this is for the GMP staff members.
	• The DEI section is the weakest part of the proposal, but this could be attributed to the fact that this is a new facility that has been otherwise engaged. It is also important to recognize that a manufacturing facility can have little influence on several DEI components, such as the diversity in populations recruited for clinical trials. The host institution has multiple resources for helping the GMP DEI efforts, and these should be explored to strengthen this section.
	• This is a moderately strong program to serve underserved and disproportionately affected communities, but it could be more impactful.

No: 1	• The project may have some limitations to effectively serve the needs of underserved affected communities, likely due to the infancy of the facility. It would be helpful to understand what additional access may available to supplement and/or measure this limitation in lieu of some historical precedence. • There are potential concerns around the operational approach to address DEI. The team demonstrated progress on this as discussed in the open session, where they presented data being collected regarding trainees. Additional emphasis on examples such as this to describe the outreach programs' reach and impact would be helpful to contextualize progress.

Application #	INFR5-14719
Title (as written by the applicant)	Open Manufacturing Network for Cell and Gene Therapies
Project Objective (as written by the applicant)	An open-source network for sharing new cellular engineering platforms across manufacturing facilities; improve safety and efficacy of non-viral engineering approaches; and formalize GMP training programs for students, staff, and leaders.
Summary (as written by the applicant)	This project aims to streamline the development and implementation of new cell and gene therapy manufacturing platforms. Key activities will include 1) improving and expanding our non-viral T cell and hematopoietic stem and progenitor cell (HSPC) engineering platforms, 2) establishing an open-source manufacturing network to promote efficient transfer of these platforms across manufacturing facilities, and 3) enhancing our workforce development initiatives to train the next generation of cell and gene therapy professionals. Together, these activities will help establish a collaborative pipeline for cell therapy development, manufacturing, and technology transfer that leverages our combined expertise and resources to efficiently implement new technologies, accelerate product development, scale manufacturing platforms, and expand patient access to promising new therapies.
Statement of Benefit to California (as written by the applicant)	This project will implement new non-viral engineering platforms to improve cell therapy safety and efficacy, and will establish an open-source network to freely share these platforms across California manufacturing facilities. This approach is expected to significantly reduce development costs, accelerate the generation of new products, and expand patient access to next generation cell and gene therapies.
Funds Requested	$1,999,933
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	2
Count	14
Votes for Tier 1	12
Votes for Tier 2	2
Votes for Tier 3	0

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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	**Overall:** ● The components to this application involve (i) consolidating operations of three facilities into one open-source manufacturer, (ii) expanding capabilities in non-viral gene modification of primary cells including T cells and hematopoietic stem cells (HSCs) and developing characterization assays, and (iii) combining existing training programs while leveraging the institution's existing SPARK program. ● The proposal leverages the applicant's strong, existing collaborations with an Alpha Stem Cell Clinic and the SPARK program. There are a number of industry collaborations including with *[company names redacted].* ● Within their institution, the applicant is collaborating with a relevant therapeutics initiative and two relevant genomics institutes. The applicant also proposes a collaboration with a biotherapy center abroad. ● The applicant's plans should improve operations and training opportunities and offer new technologies to customers in Phase 2. ● Successful completion of these objectives will be of great benefit to the California network. ● The project shows vision and positions the facility for success. ● Overall, this proposal has a very high potential for impact. **Operational Enhancements:** ● The applicant plans to integrate three existing GMP facilities and develop open-source manufacturing. The proposal lays out plans for communication and regulatory functionality for this open resource. ● Their proposal to make their standard operating procedures (SOPs) freely available to others may not be practical – e.g., there may be intellectual property (IP) concerns. That said, if it works it could provide a useful SOP-sharing model for other biomanufacturers. ● Making production and analytics protocols openly available (with supporting data) provides a facile avenue for similar products to leverage previous results and translate. This allows a facility to develop product-specific foci with low barriers to entry and proven systems. ● The applicant aims to democratize the SOPs and know-how to be developed. ● The applicant provides interesting solutions (shared SOPs) to an internal bottleneck issue at the facility. **Specialization:** ● This proposal is unique because it focuses on enabling non-viral gene modification of primary cells including T cells and hematopoietic stem cells (HSCs). This area of study represents the future of gene-modified cell therapies. ● If funded, this proposal could lead to the introduction of new manufacturing and analysis methods for cell and gene therapies (CGTs), including nonviral vector-mediated gene manipulation therapies. ● The development of non-viral vectors can significantly improve production and outcomes for cell and gene therapies (CGTs). ● Platform development is already in process for handling a variety of cell lines. **Workforce Development:** ● The proposed project speaks to workforce bottlenecks. The shortage of talent in biomanufacturing has been well characterized, as has the resulting need to increase

	awareness about careers at all educational levels. The project seeks to incorporate GMP and manufacturing-specific curricula and exposure into multiple touchpoints - high school, community college, university, and graduate school. • The GMP training program as envisaged is essential for ongoing development and support in the workforce.
No: 1	• The open-source project could provide great benefit, but it is unclear how open it will be or how it will be managed. • It's not clear how intellectual property (IP) will be managed with this system.
GWG Votes	**Is the project well planned and designed?**
Yes: 13	• The de-risking and acceleration of project development (PD) manufacturing projects proposes to offer open-source manufacturing by improved partnerships between the existing and new GMP facilities. The plan for this will be developed by a diverse working group. • This would integrate procedures, documentation, and other aspects of facility operations. This will be implemented through a working group who will provide the framework, followed by development of common SOPs and documents and provision of regulatory support. This is a sensible undertaking that should streamline operations and provide additional support to facility users. • The success criteria are (i) the conduct of meetings for generating a proposal summary, (ii) the generation SOPs for shared technical documents and (iii) launching of publicly accessible website. These are a little conservative, but logical. • There is a strong specialization proposal to optimize and improve non-viral engineering of T cells and HSPC. This will be partnered with the development of better analytical methods for cell characterization. This section includes valuable preliminary data and a good project plan. • The workforce development projects include (i) integration of the training programs at the GMP facilities, (ii) leveraging training offered through the SPARK program and (iii) development of a 1-year manufacturing internship with training modules in manufacturing, QA, PD, and hands-on participation. • Additionally, GMP components would be added to the SPARK curriculum including GMP experience, new therapies, introduction to careers in manufacturing, facility tours, mentoring, and research. Ethics training would also be a component. Three fellowships are available, the most relevant in Cell Therapy and Transfusion Medicine. • This should prepare a broad range of students for careers in cell and gene therapy (CGT). While the details in the proposal are somewhat limited, it's clear the graduates will be highly prized as new staff. • The overall project is focused, well-designed, and well-planned. The applicant has access to world class capabilities and infrastructure. They have the track record to enable this proposal. • Advances in non-viral gene modification will benefit the field. I am less convinced about the open-source process and the space and working relationship with their large industry partner. *[Company name redacted].* • The applicant should consider involving a legal or IP expert on the working group. • The non-viral vectors, facility and open-source knowledge will all support the transition to late-stage manufacturing. • Aim 1, phase 1 goals, as summarized in slide 6, is limited in description on governance policies.
No: 1	• Details still need to be worked out.
GWG Votes	**Is the project feasible?**
Yes: 13	**Workforce Development:** • Integration of different facilities can be more complex than initially envisaged, but the plan to involve a working group is a good one. If the working group meetings are successful, it should be possible to initiate collaboration during the course of this project. • The institution's transplantation facility has an excellent track record from a variety of projects. The institution's pediatric cell therapy laboratory is smaller but has been involved in a number of graft engineering projects. • Though the two existing facilities are rather different, the large new GMP facility from the industry partner will considerably expand the pool of qualified individuals associated with the project.

	• The partnership with the large industry partner could prove complex. The nature of the relationship does not appear to have been clearly worked out in advance. Will the institution retain IP from projects conducted at the industry facility? • Policies like tech transfer should be given early attention. The applicant should establish what constitutes a sending unit/facility for a protocol, what is the constitution of a receiving unit, who/what is involved at each stage, and what determines successful transfer. • I would like to see a clear aim to develop practices that are not specific to a CDMO or academic lab. • The only major issue is the potential for legal and IP complications associated with the Open Manufacturing Platform. Multiple stakeholders and institutions are involved with this project. • The success of Aim 1 will hinge on participants' willingness to share their SOPs. • This is a "maybe" based on the implementation of open-source and how the relationship with the industry partner will be managed. • There are some existing collaborations, but the full integration may take time. **Specialization:** • The specialization projects should be feasible since non-viral gene modification is already in progress. • The timeline for development of analytical assays will depend on whether these assays will be developed de novo or imported from collaborators. **Workforce Development:** • Workforce development will focus on adding more training modules to the SPARK program and developing an internship program. These goals should be achievable within Phase 1. • The non-fellowship workforce programs are new, so the timeline and execution represent reasonable assumptions. **Applicant Team:** • This proposal is well thought out and supported by the applicants' track record. • The team is well qualified. • There is a potential overlap with one existing grant, but the effort for the investigator on the manufacturing proposal has been reduced appropriately.
No: 1	• How will leadership from the three different facilities work together?
GWG Votes	**Does the project effectively serve the needs of underserved and disproportionately affected communities?**
Yes: 13	• Yes. Anything that reduces cost and increases successes for patients will positively impact underserved communities. • The applicant describes a focus on enabling and developing low-cost therapies for the broader community. • The team did a nice job of discussing how DEI fits into their overall mission and values. • The training programs have a mandate to serve underserved communities. • A major strength is the training across multiple learner groups. • The applicant is aware of and has addressed DEI issues.
No: 1	• Aspects of DEI are not adequately incorporated (or described) for the fellowship training or early career exposure efforts.

Application #	INFR5-14562
Title (as written by the applicant)	[Institution Name] 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 over four years ago, 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 three 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 hematopoietic stem cell (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 (DC) system for our products that can be used for quality control and to inform many projects. Additionally, this DC system will better connect our program with CIRM-supported clinical and biomanufacturing centers. For example, DC can be utilized to better define key cell characteristics that may mediate improved patient outcomes. Workforce development and support is perhaps the most important 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 for leadership and staff. These quality operational enhancements solidify our facility's foundation for the 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 2: needs improvement, could be resubmitted
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: 2

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

Highest	1
Lowest	2
Count	14
Votes for Tier 1	7
Votes for Tier 2	7
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	**Overall** • The overall aspirations reflected in the proposal align with CIRM's mission. The project will accelerate the implementation of industry standards into academic facilities, and help build an inclusive manufacturing workforce. • A strength of this application lies in the applicant team's plans for partnerships. They plan to collaborate with large, neighboring academic medical centers and with commercial contract manufacturing organizations (CMOs). • The proposal promotes collaborative efforts with existing programs at other institutions. • The proposed program would enhance the network's capabilities. **Operational Enhancements** • This is a relatively young facility, established about six years ago. The team has already demonstrated their ability to produce phase appropriate Good Manufacturing Processes (GMP) cell and gene therapy (CGT) materials. • Operational enhancement activities focus predominantly on fleshing out services - building a process development (PD) group, strengthening tech transfer (TT), and implementing systems for electronic batch records (EBR) and internal environmental monitoring (EM). • The applicant seeks to add PD, and TT, and additional manufacturing space to become a one stop shop for academic researchers who require assistance with process development.

	• A PD group could enhance and accelerate manufacturing. However, there is little detail on the remit of the PD - i.e., Which projects would go to PD? What process will be used for SOP writing? How will critical materials determinations be made? • They have two cleanrooms with 2,000 sq ft of space, which is adequate for the near term. Adding a PD function to the mix will allow more efficient use of the clean rooms and increase project throughput. • Additional manufacturing space will facilitate smoother operations. Both will be valuable for on-boarding new projects in Phase 2. • The facility is currently undergoing space expansion that will provide additional support, but will not increase the clean room manufacturing areas, making the timing of PD group formation problematic. • The applicant team has a strong understanding of electronic quality management systems (eQMS), including industry-relevant applications. Their eQMS practices will be exemplary to the network. • The network would benefit from understanding and learning from the proposed team's implementation of applications to support eQMS. • The applicants already have eQMS in place which is a real strength. They now want to add electronic batch records (EBR) to their capabilities, which is positive and puts them in line with industry standards. • EBR and environmental monitoring (EM) are industry standards. However, the proposal indicates particle counting only and does not describe or discuss surface monitoring (i.e., touchplates). Total integration of EM would be optimal. • Implementation of EBR will not accelerate manufacturing, but is a clear move to industry standards. • The applicants have been using external EM and now want to bring EM in house, which is a positive step. • Overall, yes, but I have concerns about the applicant team's readiness for EBR and eQMS. **Specialization** • The applicant team's current areas of specialization are (i) pluripotent stem cells (PSC) and (ii) tumor-infiltrating lymphocytes (TIL). The applicant team also has experience with neural stem/progenitor cells, human embryonic stem cell (hESC)-derived retinal progenitors and induced pluripotent stem cell (iPSC)-derived dopaminergic progenitor cells. The proposed activities in these areas of specialization mainly consist of more collaboration and more broadly providing the cells. • The applicant team proposes (i) to develop expertise in HSC gene engineering for treatment of non-hematopoietic cells and (ii) to develop a data capture (DC) system for product manufacture and analysis information. • The proposal includes good, specialized programs, especially the DC system. **Workforce Development** • The applicant team proposes to (i) recruit (with the aid of the CIRM BRIDGES program) two interns annually from colleges with substantial under-represented minority enrollment and (ii) offer increased training opportunities for current staff and (iii) leverage the Extended Studies program to offer Six Sigma Green Belt training for leadership candidates. • The applicant states they work closely with CIRM-funded Alpha Stem Cell Clinics, the CIRM Manufacturing Group, the BRIDGES programs, their own institutional cell and regenerative medicine team, and three local biotech companies to run the on-site training. • The proposal includes a solid mix of internal professional development opportunities as well as programs to train interns/students from area and community colleges. The applicant has taken a really interesting approach - partnering with CMOs to offer trainees experience within industry. • They propose to collaborate on training programs with CIRM-funded facilities at other academic institutions in the region.
No: 1	• This is a small facility for an ambitious plan.
GWG Votes	**Is the project well planned and designed?**
Yes: 10	**Operational Enhancements**

	• While this is a relatively new facility, I think the plans to add process development (PD) and Tech Transfer (TT) functions as well as electronic batch records (EBR) and internalize environmental monitoring (EM) are all excellent. • The operational enhancements focus on the creation of a *de novo* process development (PD) group, which would be of value for bringing on new projects. They plan to recruit a PD manager and two associates. However, this is a small facility with limited manufacturing space and staff. Will there be a sufficient number of projects to justify a group of three for PD? • It may also prove difficult to rapidly recruit PD hires, though the applicant does address this in the risk mitigation section of the proposal. They propose to use International Society for Cell & Gene Therapy (ISCT) training courses and industry partners to help train the new PD group, if needed. • They will use their currently implemented [*trade name redacted]* software for data capture (DC). • The proposal to implement internal environmental monitoring (EM) is an excellent idea. • They will also implement new software for electronic batch records (EBR) and have been looking at two options *[trade names redacted].* In my experience these are upper-level systems that may be beyond what is required. • The success criteria for operational advancements are reasonable and should be achievable if recruitment of PD staff stays on track. • In the future (beyond the timeframe of this proposal) the applicant plans to add additional clean room space. This proposal will develop invaluable functions for the current facility and allow a seamless transfer to the larger space later. Waiting for the new space would be a mistake. **Specialization** • The applicant's plans for new specialization areas are generically described, as are the criteria for success. The development of the data capture (DC) system is the strongest component of this section. • There is limited description of improvements to the applicant's current areas of specialization. **Workforce Development** • The proposed workforce development program focuses on the development of a paid internship program which will supplement training provided through CIRM BRIDGES. • This is a small program that would train two people annually. The graduates would undoubtedly find positions within the state, but the impact of the program obviously will be limited. • Recruitment of recent graduates or senior undergraduates will be through three colleges/universities with diverse student bodies. • The program would last for a year and cover basic laboratory lectures and online courses and rotations through the GMP facility and industry partners' facilities. • The institution also offers a master's degree program in drug development and product management. • The applicant provides reasonable criteria for evaluating the success of the proposed workforce development activities.
No: 4	**Operational Enhancements** • In some areas, success criteria are not clear. For example, the applicant mentions that they plan to hire and establish a PD group for more efficient translation and transfer to external partners. What are the quantitative success criteria? • The applicant wants to hire a fairly small PD group - one manager and two associates. It's unclear that this PD group will have the appropriate size and expertise to achieve the applicant's objectives. • The applicant should include their ideas for potential clients who would contract the PD service. • The applicant may not have the appropriate budget or support staff they will need to implement electronic batch records (EBR). **Workforce Development** • The proposal does not include enough detail about the proposed training partnerships with CMOs. What will these training partnerships entail?
GWG Votes	**Is the project feasible?**

Yes: 11	• This proposal is ambitious - and likely feasible. One concern is whether there will be enough staff to achieve the proposed operational enhancements in the time allotted. • The operational enhancements should be achievable within the proposed timeline, provided the PD team in recruited quickly. • The Key Personnel have the institutional acumen to achieve the goals described in this proposal. For example, the team has already implemented a highly relevant, industrially common eQMS that is not straightforward to install. • The Key Personnel are qualified to perform the tasks described. The facility director has almost 20 years experience in process development, process scaling, tech transfer and GMP manufacturing of CGTs. • Unfortunately the Program Director appears to have a weaker track record on CIRM-funded grants, with some milestones not completed or even started and timelines not met. • This is a small facility but has the appropriate equipment and staff. They will open an additional 5,000 square feet of support space during this project but this will not include clean rooms. There are longer term plans to develop a much larger GMP facility. • The facility's pipeline has been somewhat limited, partly due to the small size. This should improve with recruitment of a PD group. • Hiring the right people for the PD group will be important for the success of the project. • The specialization project is not adequately described. It is difficult to evaluate feasibility. • The workforce development component is definitely feasible as it leverages a number of existing relationships and programs. • The workforce development plan should be achievable.
No: 3	• Overall, the project is aspirational and has good objectives. But the application is missing some critical details on execution and implementation. • My concerns are about staffing and facility space. • Sustainability is questionable.
GWG Votes	**Does the project effectively serve the needs of underserved and disproportionately affected communities?**
Yes: 14	• Overall, this grant does a good job of considering underserved communities. • The applicant recognizes that recruiting/partnering with area colleges and community colleges will increase diversity. Solid plan. • It appears that the proponent is aware of and engaged in addressing DEI. • The group has strong ties to existing DEI-oriented CIRM initiatives (Alpha Clinic and BRIDGES). • The applicant will benefit from its location within a diverse community.
No: 0	*none*

MINORITY REPORT

If an application receives a Final Score of 1-84 and 35% or more of the scientific members of the GWG recommend an application for funding, then a minority report is provided that summarizes the perspective of those scientific members.

Seven out of 14 members of the GWG scored this application as Tier 1. Applications that have an even split of votes across Tier 1 and Tier 2 receive a Tier 2 score by default, which is the case with this application. The panel as a whole thought this proposal from a relatively new facility was good. In particular, reviewers thought the proposed product development expansion, environmental monitoring, and workforce development components seemed achievable and would support the growth of the facility. Reviewers who recommended the application for funding had largely the same concerns as those who did not recommend the application, namely, the project lacked details on the execution, implementation plan, and success criteria expected. However, on balance, the reviewers who scored the application as a Tier 1 thought that the concerns were not strong enough to warrant a possible resubmission, and recommended the application for funding.

Application #	INFR5-14667
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 plasmids & 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 proposal, "Advancing Cell Therapy Manufacturing Through Collaboration," aims to establish a collaborative framework for developing advanced cell therapy manufacturing techniques. Our Good Manufacturing Practice (GMP) facility aims to accelerate the development and implementation of next-generation cell therapies through collaboration with industry leaders and innovative partnerships. We strive to provide cutting-edge technology, expert knowledge, and exceptional services to support the growth and advancement of the cell therapy industry. Our objectives include: ● Developing a cutting-edge electronic Quality Management System (eQMS) ● Implementing an in-house plasmid and viral vector manufacturing platforms ● Creating a closed workflow for non-viral cell therapy manufacturing ● Introducing a GMP fellowship program for underrepresented communities ● Establishing an internship program for cancer survivors to introduce them to cell therapy manufacturing. The eQMS is expected to streamline data collection and process reporting, optimizing processes, increasing efficiency, and reducing errors. The availability of in-house plasmid and viral vectors will address the significant gap in the availability of these material for cell therapy manufacturing. Creating a closed workflow for non-viral cell therapy manufacturing can improve product quality and safety, reduce costs, and increase scalability, ultimately making these therapies more accessible and beneficial for patients. Through targeted training and education programs, particularly for underrepresented communities, we aim to address workforce shortages and provide our students with the skills and knowledge they need to succeed in the cell therapy manufacturing industry. Additionally, we are proud to offer specialized training opportunities for cancer survivors, helping them gain valuable skills and a sense of purpose as they work towards a brighter future. By implementing these activities, we will not only optimize and advance the projects our institution is working on, but also support other institutions in California in their efforts to develop life-saving cell therapy treatments for patients in need. We are deeply committed to the spirit of collaboration and partnership, and believe that we can achieve a common vision of saving lives through the development and advancement of next-generation cell therapies. Our proposal has the potential to greatly benefit the growth and development of California's cell and gene therapy industry, and we are fully committed to its success.
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 2: needs improvement, could be resubmitted
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: 2

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

Highest	1
Lowest	2
Count	12
Votes for Tier 1	5
Votes for Tier 2	7
Votes for Tier 3	0

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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: 10	**Overall:** ● The proposal positions the facility for scaling its operations and trainings with outlines to advance the production capabilities and reach of platform procedures. ● The project offers significant value and indicates untapped potential for the platform. For instance, the project proposes high titer GMP recombinant lentiviral (rLV) production at pilot-scale. This is impactful and opportunistic because demands for small scale GMP rLV are also unmet. ● The proposal demonstrates organizational commitment by providing details around orchestrating facilities, programs, education, and work-force development in very resourceful manners. Additional description of how the proposed document management system may operate in a change or version control environment would be helpful to understand the organizational commitment overall. **Operational enhancements:** ● The proposed advancement in eQMS presents an approach to address facility bottlenecks in cell and gene therapy but this approach also presents some concern in regard to the caliber of product from the vendor's computer application. ● Based on available marketing materials, the proposed software vendor demonstrates strength in inventory and monitoring controls. The proposal demonstrates suitable implementation of the inventory control systems within the facility. Next-steps with the vendor involve implementing systems for version control of documents and other quality system needs such as change control. But there is little, if any, description on the vendor's product page for services such as e-document control.

	• The inventory control tool established with the proposed vendor is suitable for this specific set of facility operations but leveraging the vendor's applications to advance to a sustainable eQMS may be limited. • For some aspects of electronic document management, providing training in an application with more industry precedence may serve to better prepare participants in the proposed education activity. • Leveraging an in-house built interface or an interface proven within the network may provide direction and additional components to an education program around electronic QMS builds. • Training and specialization around a specific computer application are presented. The impact of this training may be limited to the network of facilities that use these specific products. • The proposal describes the selected vendor as being SOC 2 Type 2 audited, but only a SOC 2 Type 1 report is available from the vendor. A SOC Type 1 report looks at whether controls systems are in place, while a Type 2 report looks at whether controls are working effectively. **Workforce Development** • From a workforce development standpoint, the partnerships and programs they are running will help introduce this industry to new professionals. That said, the benefit to the state of California may be limited as they are focused on interns and fellowships.
No: 3	• The applicants need to better clarify what value their proposed technical projects bring to the California Cell and Gene Therapy Network. ◦ For example, the development and use of an eQMS will clearly be beneficial to this institution's cGMP operations, but the applicant needs to better describe how/why the various proposed modules of this particular software should be developed and implemented across the CA CGT network (in other words, why is this vendor the best option if a goal for the network is universal use and compatibility of electronic systems)? • The value proposition of the main project is difficult to understand. The applicants may be able to provide significant value if they focused on the advancement of the non-viral genetic modification of human cells and the supply of plasmid and vectors to a broader consumer base. • The workforce and diversity components of this application are strong, but the proposal could use a more impactful specialization project and a better program addressed at increasing access to underserved populations. The value proposition would be significantly improved if the specialized project was revised to something more impactful across the community. In particular, the non viral vector delivery may be important but the gains would be incremental.
GWG Votes	**Is the project well planned and designed?**
Yes: 8	• The application includes a feasible plan and straightforward milestones. • The project is well planned and designed with established partnerships, but has limited reach.
No: 5	**Operational Enhancements:** • Overall, the proposal is planned to advance nucleic acid and vector production capabilities. Both small and pilot scale production capabilities will be built out. The timelines highlight early stages of development for technology transfer activities and block time for pilot scale development. More specific plans for small scale development would help in understanding the proposed design space. • The pilot scale pDNA activities are appropriate to trigger pilot scale vector production and are likely to demonstrate facility progress. Early progress could be demonstrated during small scale activities, especially with some early staging of small scale pDNA practices that could advance to small scale vector production. • The proposal could be improved by providing more detail around the integration of small scale activities, how these activities support the advancement to pilot scale work, and what the activities are intended to demonstrate would help in the assessment of progress. It would also be helpful to highlight the importance of the small-scale activities and give them attention in the planning process (similar to what has been given to pilot scale planning). Overall, this would help ensure that the project meets expectations to perform IND-enabling CMC activities.

	• The proposed use of pDNA to advance areas of expertise around rLV production to provide regional relief to vector bottlenecks is low cost with high reward and is appropriately fostered in this applications plan. The plan would be stronger with specific deliverables on small scale rLV production, especially ones that could meet current rLV regulatory body standards. • The proposal plans for plasmid DNA (pDNA)-expressing MCBs to be selected off-site and provided to the facility for subsequent fermentation steps. Because environmental and helper pDNA are already supplied, this template material would be transfer constructs (transgene cassette harboring pDNA). The potential variability in host bacteria expressing transgene constructs may be derisked with some defined internal practices to support product specific attributes for this starting material source. • The proposal would benefit from additional description of how the facility will access upstream MCB pDNA technologies to support drug substance product knowledge. Securing access to a nearby microbial lab could provide additional internal ownership of evolving best practices. • With advancements in pDNA construct size and antibiotic-free selection processes, understanding potential concerns for novel clinical program development at the construct stage would be beneficial. Revisions of constructs in later clinical development can be avoided with strong product-specific data supporting the rationale prior to IND-enabling clinical activities. • Segregation of MCB selection to avoid cross-contamination is the appropriate approach for dedicated room-associated activities. However, the proposal does not address product specific attributes elicited during process development that impact decisions in the product profile. • The applicant could benefit from additional consultants to address operational areas of concern regarding segregation of plasmid versus vector versus cell manufacturing within the same facility footprint. • The proposed microbial practices lack details to support career advancement. It is understandable to leverage a vendor for MCB selection, but selection practices and procedures would benefit with some internal descriptions and capabilities that may be transferable to the facility. It would also be helpful to give attention to flexibility in transgene constructs. • From a regulatory compliance perspective, it is typically preferred that Quality Assurance can operate completely independent of manufacturing. Thus, having QA report directly under the GMP director is perhaps not the best organizational structure. • The eQMS implementation proposed here is ambitious, and could be implemented well if they leveraged a wider partnership with other institutions or industry partners. **Specialization:** • The proposed area of specialization (non-viral based gene delivery) has integral needs with the proposed pDNA activities, but additional information connecting these aims would be helpful. • The project plan overall presents an approach for suitable entry, with ample late-stage opportunity for further clinical CMC development in a relevant platform. However, concerns around portability and transferability of the program arise due to vendor dependencies and disposition practices. • It is difficult to see how full integration of the electroporation and cell processing systems discussed in this application will move forward when the different vendors for these products typically do not collaborate for joint development. **Workforce Development:** • The proposed plan provides substantial technical and leadership skills for career advancement opportunities that includes training on cutting edge systems, which are highly relevant to current trends for biotechnology. • Additional career advancement opportunities may be available via participation in small scale activities. Experiences can be gained during scaling activities that involve early descriptions of process selection criteria. Descriptions can include characterization of potential product-specific process performance indicators that may be included within a typical set of results that emerge from a platform-based product development campaign. • The application describes that the institution has implemented a comprehensive training plan and records training electronically. However, the proposal to score the time taken for training using the existing control system needs more details.
GWG Votes	**Is the project feasible?**

Yes: 12	**Overall:** ● The proposed team is talented and has the appropriate skills and GMP experience (in both academic and industry settings) to deliver on the project plan. ● The project team has access to facilities and resources that are suitable to execute on the project plan. **Operational Enhancements:** ● The proposed team has some direct experience in building an electronic QMS. And the team's practiced experiences are relevant for building out a modern eQMS. The experiences provided by the team's subject matter experts are appropriate for execution of quality deliverables in relevant electronic document control. ● The proposal would benefit with additional context around how the sum of the parts would be leveraged to create value for the network. For instance, consider compiling indicators of performance to an existing process (pDNA production would include both non-viral and viral based key performance indicators). This enables monitoring new programs from multiple indicators with an aim to improve overall performance across programs and networks, leading to better decision making practices. ● The feasibility of eQMS implementation is not clear. **Specialization:** ● The project has an adequate project pipeline to support competency in their specialized area: Closed Manufacturing Platform for Non-Viral Cell Therapies. ● The proposal provides several individual areas of specialization and avenues to relieve therapeutic bottlenecks that appear to be incongruent. The interrelatedness of these areas needs to be spelled out more clearly to better appreciate the vision. ● Most activities are feasible but there are concerns about trying to tie together the electroporation and cell processing systems in the way envisioned. Even if successful, the impact of this integration is unclear. **Workforce Development:** ● Regarding workforce development, the team has the expertise needed. By leveraging a number of established programs/partnerships, success is highly likely. ● The plan is feasible, but it is difficult to appreciate the long-term impact and educational advancements. In regard to these concerns, computer applications used in the industry would likely provide more relevant training and user experience. It is crucial that systems are not disruptive during clinical/IND enabling activities.
No: 1	● Feasibility is difficult to assess since this new facility has not yet produced any qualified plasmid/vector products. ● The applicants need to better describe if there are additional aspects of their institution's "quality/regulatory ecosystem" that can be accessed to help support their cell and gene therapy efforts. For example, presumably there is an overarching quality department that manages patient clinic and hospital operations, so how will the proposed GMP QA/QC resources be integrated within that structure? ● The applicants need to clarify if there are other departments that typically handle aspects of research trials implementation, regulatory compliance, or the development of legal contracts, etc. that will also be available to the GMP facility.
GWG Votes	**Does the project effectively serve the needs of underserved and disproportionately affected communities?**
Yes: 13	● The proposal appropriately opens access to cell and gene therapies. Project plans particularly provide training and support for individuals from marginalized and under-served communities. ● The team brings broad perspectives and experience to achieve the proposed activities. The diverse and inclusive perspectives include demonstrated success from past experiences implementing activities similar to those included in this proposal. ● The team's track record is demonstrates success in advancing DEI values. This is exemplified by program leads receiving an ASGCT award for research on disproportionately affected minorities and by securing an Alpha Clinic award. ● Workforce development activities are expected to foster increased participation from underserved populations in CA. The applicant's commitment is demonstrated on a few levels which include GMP Fellows, Dream Interns, and GROW programs to support efforts to create a welcoming and inclusive environment for all individuals.

	• From a workforce perspective, the project does work to increase diversity (fellowship program) and they will be able to reach and impact other students. • The proposal includes good education components and integration with other CIRM programs. • The workforce development aspect of this proposal is strong.
No: 0	*none*

MINORITY REPORT

If an application receives a Final Score of 2 and 35% or more of the scientific members of the GWG recommend an application for funding with a score of 1, then a minority report is provided that summarizes the perspective of those scientific members.

Five out of 12 members of the GWG scored this application as Tier 1. Overall, reviewers thought the project had the potential to be impactful but were concerned about institutional support and resources for this very nascent facility. Reviewers who scored the application as a 1 expressed that, despite several weaknesses in this application, advancement of this project would benefit California. These reviewers differed in opinion from the majority of reviewers on two main points:

- The specialization focus on non-viral gene delivery is sufficiently well-planned and impactful to merit funding. However, reviewers broadly agreed that the choice of system that will be combined in this application to achieve this focus could represent a risk.
- The workforce development plans were well thought out and would be a benefit to relevant communities. However, one reviewer who gave a score of 1 based on this impact also advised the applicants to consider contributions to workforce development more broadly, rather than in ways that will specifically benefit this facility.

Application #	INFR5-14779
Title (as written by the applicant)	Creating A Collaborative California Cell and Gene Therapy Manufacturing Network
Project Objective (as written by the applicant)	The GMP Facility has demonstrated its ability to support cell and gene therapy product development and manufacturing for Phase 1-3 clinical trials. We will share our knowledge of product manufacturing for early and late-stage clinical trials with other GMP facilities within the State of California.
Summary (as written by the applicant)	The GMP facility has been operational since 2010 and was supported by a previous CIRM grant. Since then, the GMP facility has demonstrated its ability to support cell and gene therapy product development and GMP manufacturing of such products for Phase 1-3 clinical trials. We enabled investigators to translate their products from laboratory research into safe and efficacious cell and gene therapies, of which two therapies are now ready to be commercialized, with BLA applications pending. The unique design of this GMP facility, developed by its facility director, implemented already 13 years ago and still being state of the art, is compliant with all phases of product manufacturing and has been lauded as one of the best academic facilities in the country. The breadth of product manufacturing encompasses multipotent and pluripotent stem cell derived products, including mesenchymal stromal cells, hematopoietic stem cells, cord tissue derived endothelial cells, human embryonic stem cell derived neuronal stem cells and primary cells from peripheral blood, such as T cells, used for the manufacturing of a variety or novel CAR T cell products. The facility is also known for the GMP manufacturing of a variety of gene therapy vectors, such as oncoretroviral, lentiviral, AAV and adenoviral vectors, some already being used in Phase 3 clinical trials. The facility's quality system has been constantly improved to be in compliance with regulatory requirements of all phases of clinical trial product manufacturing, including Phase 3 manufacturing. 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. With our GMP facility and future collaborations, we will address the bottleneck of lentiviral vector manufacturing with a manufacturing system we developed, and we will address quality by design of cell and gene therapy product manufacturing for Phase 1-3 products; we will share this method with other academic GMP Facilities. 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. Finally, a GMP training /certificate program, already existing at our institution, will be expanded to include our collaborators, 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)	The GMP facility has been a leader in the GMP manufacturing of cell and gene therapy products in the State of California, and nationwide, for over a decade. 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, which might not otherwise be available to underserved populations in the State of California.
Funds Requested	$1,496,973
GWG Recommendation	Tier 2: needs improvement, could be resubmitted
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: 2

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

Highest	2
Lowest	3
Count	15
Votes for Tier 1	0
Votes for Tier 2	10
Votes for Tier 3	5

- 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: 7	**Overall:** ● The GMP facility has considerable experience in manufacturing a variety of products for a wide range of clients, with an emphasis on commercial collaborations. It has manufactured products for Phase 3 trials, which is unique among California facilities. ● The project plan does portray a set of activities that will likely continue with significant duration beyond the project plan. The project's overall aim is to establish educational systems around GMP for CGT with specializations in an advancing adherent culture platform with modern techniques for co-transfecting plasmids. ● The leverage of facilities, clinics, and other CIRM partners is demonstrated within the proposal and overall represent a large portion of the systems and education programs being proposed to advance. ● Industry partners are leveraged more so on the product profile and portfolio side of the proposal. The proposal outlines further internal builds of Quality Systems that does not leverage industry stalwarts for such activities. Internal builds they described are extraordinarily capable and provide opportunities for insight and education around building electronic quality systems as proposed. ● There have been collaborations with the Alpha Stem Cell Clinic with respect to DEI activities, which have also involved the center for reducing health disparities. They have worked with the CIRM BRIDGES program. ● The GMP facilities will work with another institution on implementation of the electronic Quality by Design system and with a separate institution on the specialization project on improving lentiviral manufacturing. Historically there have been multiple collaborations with industry and these are likely to continue.

	• This is an extraordinary program that has significant experience in the cell and gene therapy field. They've matured into a position where they can now offer guidance to other facilities within the California ecosystem. However, the majority of the proposal reads as a narrative about what they've done and spends little time on a few specific future projects with explicit milestones and deliverables. In particular, the first project is broad, unfocused, and difficult to evaluate objectively. • Overall, most of this proposal is poorly written and rather vague. It tends to focus on past achievements rather than detailing future tasks. • Yes, but limited in detail and not clear metrics for the use of funds. **Operational enhancements:** • The operational enhancements are focused on internal improvements that should streamline operations. • The enhancements will streamline internal operations and that should improve functioning of the facility and could be of interest to other groups. • The operational enhancement should streamline running of the facility and the collaboration with another institution should position the facility well for continued activities in Phase 2. The same is true for the collaboration for the specialization project. • The proposals description of project management systems to manage peripherals and other laboratory systems is exemplary of modern industry trends. The network will benefit from the education they hope to share in their experiences establishing this particularly friendly computer application as a utility to support significant portions of laboratory systems. **Specialization:** • The specialization project is similar to ongoing work at other GMP facilities. The unique part is the proposed tech transfer to another institution. • With the increased footprint of the operations reached by proposing a tech transfer of development activities to another institution, the proposal is providing scaling through regional expansion with specialization on key GMP processes using training programs during phase 2 of the plan. **Workforce Development:** • The applicant has good training programs in place and the proposed certificate program should further strengthen these. • The workforce development and specialization components should be of value beyond the project period as they provide resources to other facilities. • The increased workforce development activities strengthen the program and will be of value to the entire CIRM Manufacturing Group through Phase 2. • I really appreciate that the proposed certificate program is short in duration, and therefore more attainable. I would have liked to see more partnership with community colleges and other regional partners. • Yes, the proposal does address critical bottlenecks in CGT. Specifically paying attention to broadening education and providing relevant experiences in CGT, as the proposal does, will support a growing bottleneck of qualified individuals.
No: 8	• This facility is a state-of-the-art powerhouse. While the goal of transferring technology to other facilities is a good one, there are few details for how this will occur successfully. • Very little information was given on what the project was, the bulk of the application and presentation were on the past accomplishments of the program. • Application lacked specific details on what was "new" in this proposal (there was too much review of past successes at the institution). • The quality by design proposal lacks details and lacks clearly defining bottlenecks. There was a large focus on past rather than building for the future. • Key elements and a robust description of the value proposition were not included in this proposal.
GWG Votes	**Is the project well planned and designed?**
Yes: 1	*none*
No: 14	**Operational enhancements:** • The operational enhancements focus somewhat vaguely describes improvements to the management software and implementation of a quality by design (QBD) system that will

be shared with another institution. This is perhaps the poorest of the component projects due to its lack of detail. The success criteria for enhancements are far too generic i.e., a QBD system will be established, and it will be implemented at the collaborating institution.

- The proposed advancements in the operation are adequate to de-risk product development and downstream manufacturing of CGT products. The design includes a significant focus on education and training which provides a substantial portion of activities which enable late-stage capabilities to emerge from both the facilities and the individuals being trained.
- Implementation of QBD at another institution and its measure is planned to occur in the 2nd year of the proposal, where the project will likely be able to provide progress beyond the Quality-by-design and procedure definition.
- Particularly in the area of QBD and quality issues, there are too few details of what activities would be undertaken, what challenges would be addressed, what barriers exist that would be overcome, and how success would be measured.

Specialization:

- The specialization project will provide improvements to manufacturing methods for lentiviral vector manufacturing. These are not unique to this institution, and I know of other facilities that have already implemented these improvements. In fact, the applicant published much of the data in 2015. The creative section is the proposed transfer of the technology to another institution and the performance of comparison studies. Again, the success criteria are somewhat generic.
- Criteria for success are needed to demonstrate successful tech transfer and implementation of a seasoned vector production platform which are currently based on generalized comparability metrics provided in the proposal. Additional details are needed as to what constitutes success in regard to modules being tech transferred and their expected levels of demonstration, and some metrics that support independent operations to the transferred facility.
- Aside from qualitative measures, there will be limited measures of the progress during the proposals funding. Metrics around success of small-scale tech transfer that enable the facility would be helpful in understanding the timing for completion or when an unfortunate delay may occur.

Workforce Development:

- Workforce development will focus on the creation of a Cell and Gene Therapy Manufacturing Certificate that will supplement existing training programs e.g., a course on stem cell biology and manufacturing practices and a specialized course in biopharmaceutical manufacturing. The latter will be expanded as part of the certificate program. This will be done in collaboration with another institution. The program will be launched in year 2.
- The applicant has been a leader in developing training programs. The certificate project will strengthen their offerings and incorporate collaboration with another institution. They have already trained more than 100 students in the elements of GMP. The proposed improvements should be of considerable value to facilities throughout the state.
- The criteria are less than adequate to demonstrate the impact of the enhancements from the educational components proposed. These are understandably more qualitative measures but additional details as to current programs baseline and expected expansion with some focus describing what successful reach would look like are missing to provide context. What is provided is described well, but what does organic expansion look like with the additional resources requested?
- Progress for both the educational program and implementation of the electronic system are likely able to demonstrate facility progress during their implementation and qualifying activities in the 2nd yr of the proposals funding.
- There are continued aims for workforce development by creating career entry and advancement opportunities during the early-career phases of individuals in a proven setting within the California education system.
- I didn't see a lot of details or specifics on the proposed certificate program implementation which made it difficult to evaluate.

Overall:

- The description of the project plan and design is too limited to adequately assess. There is a notable lack of key metrics, and the rationale for methods is lacking.
- This proposal as well as the presentation by the applicant spent far too long telling us about the achievements of the facility in the past. We are all aware of the excellent record

	of this facility. The application should focus on future plans to describe the use of CIRM and other funds to enhance what is already recognized as a world class endeavor that has a long history of producing clinical grade CGT products. • Not enough information was provided to consider if the plan was achievable. • Again, details were missing regarding the specific projects and what metrics for success would be used to assess progress. • Details are lacking, particularly in the QBD aspects. There is also a lack of detail on viral vectors as their specialization area. • As mentioned, the various projects need to be focused onto 2-3 sub-projects that have specific milestones, deliverables, and can be assessed objectively. • Not granular enough. While clearly capable and accomplished, it wasn't clear how it would be implemented. Programming a home-grown electronic document system seems not to answer the scalable and expandable goal of the funding.
GWG Votes	**Is the project feasible?**
Yes: 7	• The proposed program is taking advantage of established systems and advancing off of the inertia from well-established systems and is likely to be implemented within the proposed timeline. • It is likely that the specialization and workforce development projects will meet their timelines. • The proposed team is renowned for their capabilities and the caliber of individuals trained under their mentorship. They are qualified to execute the project plan as described. • The team is described with experience building internal electronic systems, including abandonment of cumbersome commercial experiences portrayed, and are likely to progress appropriately in advancing their internal electronic document management systems to execute the project plan. • The team is well qualified to perform the proposed project. One of the faculty's involvement seems somewhat peripheral and I am curious as to why the previous facility director is not more closely involved with workforce development. • The facilities are excellent. Provision of the tangential flow filtration equipment is essential for completion of the specialization project. • The institution has a proven track record of attracting projects and clients. I have no doubt that this will be sustained. • The plan describes access to the facilities, personnel, and resources. Also described are access to other resources and CIRM partners which are necessary to execute on the project plan. • The proposal outline access and ongoing activities associated with over a dozen pipeline programs. These programs provide leverage for demonstrating the proposal's plan to build education programs and broaden the operational footprint of vector production and testing capabilities with specialization in upstream cell culture practices. • Some concrete metrics to understand the vision for progress would be helpful to gauge progress over the duration of funding. • Details on the QBD project are rudimentary and the success criteria are too generic so it is difficult to know whether the timeline will be achieved. • Given the lack of details, feasibility is difficult to evaluate. • It's feasible based on the history of the facility. It was not clearly feasible from the application.
No: 8	• As the proposal reads, it is very abstract and there are not objectives by which to judge whether it will be successful or not. • This is hard to judge on the technical aspects of the proposal because of lack of details. Training and DEI are much better developed. • Unable to fully assess given the lack of robust description of the plan. • I didn't see a lot of details or specifics on the proposed workforce development certificate program implementation which made it difficult to evaluate.
GWG Votes	**Does the project effectively serve the needs of underserved and disproportionately affected communities?**
Yes: 14	• The team has a demonstrated track record for promoting and advancing DEI. As described in their proposal, the institution established a center for reducing health disparities in 2005 and has a successful track record in advancing DEI values. • The team embodies and exudes DEI principles organically. Its historical contributions are exemplary of this practice. They have historically accommodated for the CGT

	community's additional needs that needed reasonable adjustments to give a novel therapeutic a fair chance at success. The same applies for their attention to reach, education, career development, and so on for workforce development. ● The plan describes access to the facilities, personnel and resources. Also described are access to other resources and CIRM partners which are necessary to execute on the project plan. ● The proposed activities are intended to provide a broader reach of education and early career training to the CGT community. The underserved and disproportionately affected populations will improve with requested resources to advance and deliver approved products to unmet needs. ● The center for reducing health disparities is an important program in this regard. ● By designing short duration certificate programs, it will inherently be more accessible to a more diverse number of participants. ● This was a strength of the proposal. The underserved population is highly targeted, which is excellent. The workforce training also partners with a number of other partners. Minor improvement would be to include more data about the percentage of underrepresented groups and metrics on whether the current approach has been successful. ● The proposal will broaden development programs and increase workforce participation to a significant extent. The level of entry into the program and/or some levels of affordable public access to publicly funded education modules is limited in its description on deliverables. ● The project team presents an unclear limitation to bring diverse perspectives and experiences during the implementation of the proposed activities. They note "It is expected that outreach for this program will be conducted at community colleges, which might be able to supply the target student population for this program." Deliverables around broadening the programs reach to community colleges can include understanding unexpected restrictions that would limit supply to the targeted population. ● Lack of detail: lots of ideas, but no firm plans. ● Limited but present in the proposal.
No: 1	*none*

Application #	INFR5-14574
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 product 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 2: needs improvement, could be resubmitted
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: 2

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

Highest	2
Lowest	3

Count	14
Votes for Tier 1	0
Votes for Tier 2	9
Votes for Tier 3	5

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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: 9	**Operational Enhancements:** ● The project offers significant value that would contribute to the CIRM network's capabilities. The applicants accept that in CGT, efficacy comes before safety. The proposal has an approach to address the universe of Chemistry, Manufacturing, and Controls (CMC) differences that comes with CGT products versus traditional products. ● From a developer's perspective, their visionary concept to pivot space from process development to GMP enables shorter runways to launch. Their approach aims to reduce product development drags derived from traditional CMC practices for biologics, such as those established for recombinant proteins where large amounts of time are dedicated to establish process history before and during safety studies. ● In campaigns where medicines are given clear trials for safety, CMC has a considerable opportunity to provide process development history to secure ample IND-enabling content. For CGT, with minimal process opportunities and additional personalized aspects, early demonstration in a dedicated facility with no expected disruption caused by moves for later-stage activities would translate to significantly shorter timelines up to and through process validation. ● The proposed approach would be novel and address unconsidered, unmet needs for easier commercialization of the most efficacious CGT products. ● There is untapped value that this proposition captures with its added flexibility, leading to a highly desirable access point for a CMC designer in CGT. ● The proposed activities should improve the functionality of the institute's GMP facility. They will have a very limited effect on the cell and gene therapy field in general. The relevance to Phase 2 of the project is generically described as more of a general acceleration by sharing QBD activities and achievements from other Phase 1 tasks. ● Overall, the application was poorly written and disorganized with excessive use of confusing acronyms. This suggests a lack of experience, with aims that were difficult to understand on one hand and also difficult to accomplish on the other. **Specialization:** ● The specialization project will work on implementation of QBD. Two examples of preliminary application of QBD to existing projects are provided. They will also implement an internal and external web-based data visualization portal that will serve multiple data storage and sharing functions. ● In the context used, the term "competency" seems to be confused with activities involved with process development and improvement, rather than its true meaning of the ability of staff to perform tasks.

	• The section on development of QBD probably belongs more appropriately in the Acceleration sub-component rather than in the Specialization section. • The program plans for acceleration and for specialization are somewhat rambling and discursive, rather than offering a clear proposition of what is to be accomplished and how this will be done. There presentation of QBD and critical parameters is contrived and does not present a good summary of their functions in quality management. The specialization tasks are poorly described except in Figure 2, which should have been used as the basis for the text section of the proposal. • The need to include QBD activities in both the acceleration and specialization sub-components projects is not evident. It appears that some of the FDA-required components of GMP training are not already in place, e.g. competency and proficiency assessment, and some quality program features. • The proposal plans to choose and implement a commercially available electronic documents system. Interestingly they also plan to partner with a genomics cell tracking company to develop a GMP version of the company's cell lineage tracking software. This product will be useful for consolidating characterization data of cell lines used in the facility, and it also has machine learning functions to predict cell line deviation from desired characteristics. No detail is given on this methodology but it is an interesting system. • The inclusion of the genomics cell tracking software partnership is unique and differentiating. It's clear that this is still an early program, so implementation is somewhat risky. However, it is a worthy effort and differentiating for this program. • Interactions with commercial entities are rather limited. A provider of cell processing systems will offer assistance with training on its equipment and a provider of genomic cell characterization tools will offer components of the electronic batch records system. • Another applicant to this Program Announcement indicated collaboration with this applicant on QBD implementation and data sharing, but this was not cross-referenced in this proposal. Instead, this application highlights a collaboration with a fellow applicant on development of an electronic records system. **Workforce Development:** • Workforce development activities will include introduction of an approved GMP Facility Operations Training Program in collaboration with the CIRM BRIDGES and COMPASS programs. This programs have been successful at the applicant institution, which has hosted intern trainees, a large percentage of which have remained in academia. The applicants will also offer a GMP Professional Training Program aimed at grad students, postdocs and research scientists, which will leverage CIRM-EDUC-funded training grants. • Although collaborations with the institution's alpha stem cell clinic were not evident, the application included interactions with the CIRM BRIDGES and COMPASS programs. There is mention of interactions with a vendor specializing in cell processing for training purposes, and with a genomics company for cell tracking, characterization, and database development. The facility also works closely with various institution centers for clinical research and care.
No: 5	• The application is lacking several details, including how the facility will scale and add to a larger network to de-risk cell manufacturing for CA. Furthermore, the facility is not offering new training. Some of the software tools that the applicants propose to integrate are very early stage. • Commenting only on workforce development component, it was great to see the applicants leverage existing partnerships and CIRM initiatives, but the broader impact of the workforce component is unclear, as this was understated in the proposal. • While the concepts of QBD, CQAs and CPPs are important, this is a poorly developed part of the proposal in that many ideas are mentioned but the connections between those ideas and the activities and products to support them are not clearly articulated. • There are few specifics provided regarding the nature or approaches to deep cell line characterization or to the analytics based on data sharing. There is a wide network of facilities that is invoked, but the connections between these goals and these facilities are not articulated.
GWG Votes	**Is the project well planned and designed?**
Yes: 1	*none*
No:	**Overall:**

13	• Mitigation of lead times and project delays is admirable. This will be addressed by cross-training and improving the workforce to enhance recruiting activities. The final section will develop electronic systems for 1) cell tracking and validation and 2) implementation of a commercial electronic records system in collaboration with other CIRM GMP facilities. • Each component has a section on dependencies, timeline, funding and impact assessment. • Future plans seem to be focused on future manufacturing projects that will come into the GMP facility, not on further developing the operational goals. • The application was rather confusing. It would be helpful to clarify how they would execute on the planned actions. **Operational Enhancements:** • The application describes extensive previous experience in process development. Investigators at the applicant institution have been active in the cell therapy field with several projects that have resulted in clinical trials of cellular therapies for retinal diseases, brain tumor vaccines, spinal cord injury and traumatic brain injury. While the range of cell therapy trials is impressive, these have all been implemented before the current GMP facility became operational. • Overall, the proposal is aspirational and it is unclear if the investigators have the requisite space and capabilities, with regard to process development, that would enable successful execution of the proposal. • The overall aims of the "accelerate" sub-component project were admirable but poorly presented. • While process development is a major focus of the application, the new facility has no dedicated space for process development activities. They propose that GMP cleanrooms will be used for process development. • Looking at the design of the facility, it will be very difficult to use unidirectional cleanrooms for process development unless this work is also carried out under GMP conditions. This will make the process development work unnecessarily cumbersome. If the process development work is not carried out using cleanroom procedures, this will compromise the clinical work being carried out in the cleanrooms. **Specialization:** • The need to implement QBD is critical to management of GMP facilities and is being undertaken by most institutions. It is unfortunate that that QBD development is a major component of the specialization project, since this puts it somewhat out of order with the activities in this section. • QBD training for staff consists only of a 3 hour session. It should consist of a much more in depth module. The involvement of a vendor who provides cell processing systems seem peripheral. Interactions with the CIRM GMP network are mentioned but not described. Operational QBD activities consist of involvement with a QBD studio. Since it appears that QBD is new to this facility it is not clear how proposed interactions with GMP QA, lead scientists, and late stage manufacturing staff will be of benefit. • The activities in this application primarily involve implementation of QBD by development of training studios. The tasks are presented in Figure 2 which describes the activities in a much more organized manner than in the accompanying text. Terms related to these activities are used in a loose manner. Competency refers to ability to do the assigned task and not to the ability to improve processes and outcomes as described herein. • Overall the aim is laudable, the description in Figure 2 is well thought-out, but the descriptive text does not match up in quality. • The commitment to QC and QBD is questionable, in that training seems to consist of brief “opportunities” for staff. It is not clear how these principles will be integrated into the manufacturing processes. QBD expertise is only 2% effort and Computing expertise is 2% of effort. This is unlikely a sufficient effort to have significant impact. • Equally somewhat vague is the proposal to develop external web-based systems for data and analytics. The data to be available are listed, but poorly described and appear to be somewhat unfocused, resulting in the impression of a catch-all system. • Using genomics to track cell line manufacturing may be helpful for manufacturing allogeneic cell lines but will not be helpful for other manufacturing procedures such as autologous CAR T cells. Other electronic systems that will be used in the facility are not well described. • The genomics approach is high risk, but possibly high reward. • The instruments proposed in this application are most useful in the manufacture of relatively small scale autologous products such as CAR T cells. Most of the examples of

	products proposed for the new GMP facility will involve manufacturing large scale allogeneic cell banks and the instruments may not be suitable for these applications. **Workforce Development:** ● It is proposed that two training programs be developed: one for BS/MS level students interested in a career in manufacturing and recruited through the CIRM BRIDGES and COMPASS programs; the second for science professionals interested in cell and gene therapy development. These programs should help attract staff to entry level GMP positions, which are likely to be at the applicant's institution. They may help recruitment at other California facilities. Other than the eligibility requirements, differentiation between the two programs is not clear. ● The workforce training for internal facility staff on GMP principles, GMP certification and QBD principles was very brief, for a new facility a more rigorous training would be important for staff particularly around more complicated concepts such as QBD. ● The plan would benefit with additional details on the metrics for success on education components and information sharing resources. ● Regarding workforce development, the applicants plan to leverage existing CIRM and related initiatives but robust planning on internal workforce development approaches was lacking. ● The limited depth of training, specific for staff on QBD aspects, is concerning. ● The product based deliverables for goals may be limited, and additional clarity on plans to scale training activities during campaigns would be helpful to provide context on progress. ● The implementation of training modules would not seem to me to add much to the training that is supposed to be performed by the facility itself. The cooperative training with a vendor who provides cell processing systems seems rather generic, apart from focused training on their equipment and systems. The continuous improvement and competency training does not describe internal tasks to be performed.
GWG Votes	**Is the project feasible?**
Yes: 8	**Operational Enhancements:** ● There are good facilities and resources to support this proposal. A key collaborator will provide expertise in facility development and management. ● The application mentions several projects currently in development. With the anticipated improvements, it is likely that additional projects will come on-line. ● The investigators are top notch and have a good track record with regard to translating cell therapies to the clinic. Yet, some aspects of the project, such as critical infrastructure, are not fully in place and would limit the overall feasibility of the proposal. The proposal seems a bit early. ● It is not clear that all of the components of the Acceleration sub-component are required. ● The inclusion of a materials management expert seems superfluous. Apart from that, the staff are well qualified with the appropriate expertise. ● The project is feasible, but this would be easier to appreciate with additional details around the projected benefits from the turn-key nature of the application and space flexibility being provided. **Specialization**: ● The activities can be completed within the proposed timelines although it would be clearer with a better description for the Specialization sub-component. ● While the plans appear feasible, they are ambitious. Little detail is given on how they would approach choosing and implementing an electronic documents system, which is no small task. **Workforce Development:** ● Commenting on workforce component only, the activities are achievable and they have the expertise needed, but the impact is questionable.
No: 6	**Operational Enhancements:** ● Feasibility appears challenging due to aggressive timelines and the early nature of their facility and staff. ● The institutional commitment to build this new GMP facility suggests a substantive long-term commitment, but it is still early to evaluate the accomplishment and sustainability of this resource.

	Specialization: • Although there are clear advantages for implementing QBD principles in cell manufacturing there are also significant limitations in applying this approach to highly regulated procedures needed for GMP manufacturing. Once products are manufactured to support IND applications and clinical production, procedures are locked down and it is very difficult to make further changes as more manufacturing and clinical experience is gained in the course of the trial • The small commitment to QBD makes it unlikely that the effort will have much impact on product development and manufacturing. It would have been great if success indicators included an improvement in product quality, or some similar metric. • Electronic record keeping wouldn't come on board until year 2, which makes achieving the data sharing goals nearly impossible. • The primary industry collaboration is with an international leader in the development of GMP-compliant manufacturing instruments and GMP-compliant reagents and supplies. Their training expertise will be helpful but is likely restricted to training in the use of their instruments and supplies and may not be useful for applications that do not use their instruments. **Workforce Development:** • The proposed workforce development program is primarily a first step and is not likely to be adequate. For example the initial undergraduate training program appears to be a 3-week summer program. This is not sufficient for adequate training in cleanroom manufacturing.
GWG Votes	**Does the project effectively serve the needs of underserved and disproportionately affected communities?**
Yes: 10	• Overall, the applicant does a good job of trying to serve the needs of underserved community members. This primarily comes across through their training programs. • The applicants present good extensions of their current activities to serve the needs of underserved communities, but not clear plan. • The applicants have established good collaborations to address this goal.
No: 4	• The workforce development plans are relatively generic, focusing on short term experiences and brief exposure to GMP processing. It is not clear how effective these programs will be in serving the needs of underserved communities. • Commenting on the workforce component only, there was no strong workforce/talent focus on recruiting or hiring from underserved communities. • The scope of the efforts in workforce development is relatively small. In principle, training for both professionals as well as traditional trainees is a great idea, and implicitly recognizes that even experienced researchers may be lacking certain fundamental knowledge regarding measurements and quality that is required for successful cell therapy products. But the amount of new training opportunities that will be provided by this proposal is minimal.