Application #	CLIN2-12823 #2
Title (as written by the applicant)	Phase 1, open label, dose escalation study of oncolytic virus (OV)-loaded cytokine induced killer (CIK) cells in patients with advanced solid tumors
Therapeutic Candidate (as written by the applicant)	Immune cells loaded with a cancer-killing virus that targets cancer tissue but not healthy tissue.
Indication (as written by the applicant)	Advanced, refractory solid tumors: colorectal cancer (CRC), hepatocellular carcinoma (HCC), osteosarcoma, triple negative (NNN) breast cancer, ovarian cancer, gastric cancer
Unmet Medical Need (as written by the applicant)	We address the unmet need of resistant and recurring cancers by combining activated cytokine-induced killer cells (CIK) and an oncolytic virus (OV). These have been thoroughly tested in humans and have excellent safety profiles but, when taken as individual therapies, have limited efficacy.
Major Proposed Activities (as written by the applicant)	• Manufacture OV-CIK cell product • Assess Safety and Tolerability • Determine Maximum Tolerated Dose
Funds Requested	$7,999,689
GWG Recommendation	***Tier 1: Has exceptional merit and warrants funding, if funds are available.***
Process Vote	All GWG members unanimously affirmed that "The review was scientifically rigorous, there was sufficient time for all viewpoints to be heard, and the scores reflect the recommendation of the GWG." Patient advocate members unanimously affirmed that "The review was carried out in a fair manner and was free from undue bias."

SCORING DATA

Final Score: 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	2
Count	15
Votes for Tier 1	14
Votes for Tier 2	1
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 at this time but could be resubmitted to address areas for improvement
- 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 proposal have the necessary significance and potential for impact?
Yes: 14	• Yes. Resistant, recurring, and incurable cancers including those the applicant proposes to address represent an area of unmet need. • Yes. Oncolytic virus (OV)-loaded cytokine induced killer (CIK) cells (OV-CIK) pose a unique approach to immunotherapy. The applicants are testing the approach in diseases for which the available data do not robustly support currently available immune approaches. • Overall, yes. However, in the applicant's current clinical protocol, the patient must undergo therapeutic infusion of OV-CIK very near a specialized production facility due to time constraints on the product's viability in transit. This limits the current geographic reach of the treatment. • The application clearly details the proposed therapeutic's significance and potential for impact.
No: 0	*none*
GWG Votes	**Is the rationale sound?**
Yes: 14	• Yes. The rationale for the treatment is that intravenous (IV)-administered OV alone infects only tumor cells surrounding the vasculature, while OV-CIK can carry the oncolytic virus into the tumor mass. The CIK cells also protect the OV from virus-neutralizing antibodies. • The application includes a reasonable rationale for the planned dosing, based on pre-clinical and clinical studies of the individual components (OV and CIK). • The applicant has addressed my concerns from the first round of review: (i) references related to mechanisms of action are now provided, (ii) data that describe the cellular composition of OV-CIK are now included, and (iii) the applicants have provided a detailed plan for the development of the potency assay. • Overall, yes. I do recommend that, before proceeding further, the applicants characterize the viral transduction efficiency of OV-CIK and the potential rate of viral shedding within patients. • References related to mechanisms of action were provided in the revision. • The rationale is generally sound.
No: 0	*none*
GWG Votes	**Is the proposal well planned and designed?**
Yes: 13	• The tumor-related, exploratory endpoint to assess viral presence in the TME seems critical for this study. It does not appear that any subjects have had this biopsy to date, as the biopsy is optional. I recommended that the biopsies be mandatory in the expansion phase of this program. • It is important that the study outcomes are independently and objectively reviewed. The safety monitoring committee (SMC) members may not be sufficiently objective. As of now, the applicants plan to convene an independent data safety monitoring board (DSMB) after the successful recruitment of five patients. • The protocol needs amendments. An independent DSMB is now being convened after CIRM's original feedback, but it would be nice to see the proposed DSMB charter draft. • Note that FDA does not have to review protocol amendments in active INDs. The sponsor seems to believe FDA approval is required for amendments. However, I appreciate that communication with FDA is wise to facilitate cooperation and collaboration, to avoid any unexpected clinical holds, and to incorporate FDA feedback in a timely manner. • Sponsor should consider amending the protocol or Investigator's Brochure (IB) or both to ensure documentation of expectations on handling risks (e.g., late arrival of cells). The applicant is working to address these issues and has amended the CIRM proposal, but it will be important to have clear instructions in the investigator-facing trial documents. • Data sharing has been enhanced in the revised proposal. Data that will be required for successful patent filing will not be shared; all other data, including sequencing data, will be shared.

	• It would improve the application (and the research program generally) if that applicant (i) stated that qualified researchers would have access to de-identified trial data and (ii) outlined the criteria for a 'qualified researcher.' They do mention data sharing opportunities through American Association for Cancer Research (AACR). Publication is effective, and clinicaltrials.gov posting is useful, but access to raw datasets allows others to validate conclusions and conduct exploratory studies.
	• While the second therapeutic infusion is justified, it may result in substantially different toxicities as compared to the first infusion. I encourage the applicants to collect adverse events (AEs), toxicity and safety issues from the second infusion separately. These separate data will be invaluable in the future when the applicants must decide whether to proceed with a second infusion in the treatment protocol.
	• Given that patients with superficial cutaneous lesions receiving the parent OV had vaccinia necrosum, the investigators should collect data on any toxicities seen in patients with cutaneous involvement of their cancer.
	• The GWG had a substantial discussion about the safety, infectivity, and potential for reversion of the proposed OV to a competent virus. It would be valuable to include a discussion of all clinical findings to date on prior intratumoral or intravenous (IV) exposure to the parent OV or the OV-CIK product, including any FDA safety review(s).
	• The applicants need to improve the organization of the grant. Reviewers were provided voluminous information and literature sources; however, these were not laid out in a user-friendly manner.
	• The applicant should plan for detection and management of safety signals related to OV-CIK. The plan should include a method for residual OV detection in the blood, urine, and ascites, and describe safeguards to prevent infection of normal tissues.
	• A few questions about manufacturing/CMC remain:
	  ◦ The transduction efficiency of CIK with OV should be defined.
	  ◦ The minimal % CIK cells in the product could be adjusted to 10% based on the results of engineering runs and experience with the first four patients
	• The potency assay for fresh product should be performed as close to the harvest day/day of infusion as possible.

No: 1	• The applicant should plan for risk mitigation related to viral shedding and uncontrolled growth of virus.
GWG Votes	**Is the proposal feasible?**
Yes: 14	• The dose escalation part of the trial appears to be feasible and, in fact, is near completion. • The industry - academia collaborations appear to be working well. • In clinical practice, the required delay for product ex vivo activation and handling of the autologous product may be significantly problematic for patients with aggressive cancers. • The requirement that infusion needs to be done at a geographically close location due to transfer time from production facility limits the geographic applicability of this treatment, at least using current manufacturing and transfer requirements. • Biopsies need to be mandatory in situations where access to malignant tissue is possible.
No: 0	*none*
GWG Votes	**Does the project serve the needs of underserved communities?**
Yes: 14	• The revised proposal now includes a reasonable outreach plan with clear goals. A key limitation is the reliance on the enrolling clinics to recruit and retain members of underserved communities. Outreach could be strengthened with IRB-approved advertising through social media or direct communication to community oncologists. However, the plan represents a significant improvement. • The revised application includes targets for patient enrollment and recruitment that include underserved and underrepresented patient populations. • The applicant will utilize Diversity Coordinators at the clinical sites along with training for the clinical site teams, including the Principal Investigators (PIs). The budget also

	includes company-internal Diversity Coordinators that will perform outreach to the PIs and the sites. Outreach to patient advocacy groups is also planned. • The applicant has developed inclusive enrollment targets: eight women with ovarian cancer including two from underserved populations; five women with colorectal cancer (CRC) including two from underserved populations; five women with triple negative (NNN) breast cancer including two from underserved populations; two women with gastric cancer, two women with osteosarcoma, and two women with hepatocellular carcinoma (HCC). • As of January 2022, the applicant has enrolled five patients with a total of two indications across three clinical sites. Of the five enrolled participants, three are women and two represented a racial or ethnic minority. • The applicant has a well-developed approach for recruiting trial participants from underserved communities.
No: 0	*none*

DIVERSITY, EQUITY, AND INCLUSION IN RESEARCH

Following the panel's discussion of the application, the patient advocate members of the GWG were asked to indicate whether the application addressed diversity, equity and inclusion, and to provide brief comments. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

DEI Score: 8.0

Up to 7 patient advocate members of the GWG score each application. The final score for an application is the median of the individual member scores. Additional parameters related to the score are shown below.

Score	Patient Advocate Votes	Has the applicant sufficiently addressed how they have or will incorporate perspectives from individuals with diverse experience and from underserved groups in the implementation of the proposed project?
9-10: Outstanding response	0	*none*
6-8: Responsive	4	• The patient inclusion criteria and clinical site selection are designed to facilitate inclusion of trial participants from underserved groups. • The applicant states their intention to recruit from both underrepresented and underserved populations, and proposes the budget, training, outreach, and participant services they will need to achieve their recruitment goals. • The applicant will collaborate with diversity programs to facilitate the enrollment and treatment of a trial population that is representative of the patient population. • The applicant states that all three of their clinical trial sites prioritize diversity and inclusion of underrepresented and underserved communities in both trial recruitment and hiring practices. • The applicant provides enrollment targets for women and minority participants. • The Proposal includes provision to participants of reimbursement for transportation and lodging. • The inclusion of a Diversity Coordinator is a strength of this application. • Strengths include the catchment areas, strong track record of success in recruiting from underserved populations at two of the clinical trial sites, and the patient demographic analysis included in the application. • If the therapy is approved for marketing, it may be advantageous to patients from underserved groups for these reasons: one hour infusion, no overnight stay, and potential for reimbursement.
3-5: Not fully responsive	0	*none*
0-2: Not responsive	0	*none*

Application #	CLIN2-13017 #2
Title (as written by the applicant)	A Double-Blind Randomized Placebo-Controlled Investigation of Autologous Muscle Derived Progenitor Cells for the Treatment of Dysphagia
Therapeutic Candidate (as written by the applicant)	Autologous Muscle Derived Progenitor Cells (AMDC) isolated from skeletal muscle biopsy
Indication (as written by the applicant)	Subjects with dysphagia (swallowing difficulties) that develops following treatment for head and neck cancer
Unmet Medical Need (as written by the applicant)	Consequences of dysphagia include malnutrition, dehydration, social isolation, feeding tube dependency, depression, aspiration pneumonia, pulmonary abscess, and death. Despite the devastating consequences caused by treatment for head and neck cancer, few effective therapeutic options exist.
Major Proposed Activities (as written by the applicant)	• Manufacture 62 AMDC products to supply the trial • Administer two doses of AMDCs to 31 subjects and two doses placebo to 31 additional subjects • Assess safety and efficacy of AMDC for the treatment of tongue dysphagia (TD) that develops following treatment for head and neck cancer
Funds Requested	$11,015,936
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 at this time but could be resubmitted to address areas for improvement
- 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 proposal have the necessary significance and potential for impact?
Yes: 15	• Dysphagia occurs in patients who have received treatment for head and neck cancer. It occurs in just under half a million patients in the USA with a five-year survival of 60%. There is no effective treatment apart from total laryngectomy which ablates the ability of the patient to speak. • Dysphagia has a significant negative impact on quality of life for affected patients following cancer therapy. The lack of rigorous studies on the efficacy of rehabilitation and exercise therapy complicates understanding standard of care and how high the bar is for new treatments. • There is a true unmet need. Swallowing dysfunction reduces independence and creates risks for aspiration. • Given the lack of truly successful interventions in this patient population and the presence of potential clinical equipoise, a randomized controlled trial is warranted. • As proposed, the treatment could address an unmet medical need expeditiously. The procedure for manufacturing and administration is relatively simple and is already in Phase 3 trials for another indication. • The cost benefit ratio would appear to be positive and, if successful, the approach could be adapted to other indications where increased muscle strength is needed. • The applicant was responsive to feedback and improved the Target Product Profile in the revision. I also appreciated the review of the tongue strength measurements.
No: 0	*none*
GWG Votes	**Is the rationale sound?**
Yes: 15	• Yes. The applicant has presented well-described preliminary data and has an industry partner. • There have been extensive changes to the Target Product Profile, the Manufacturing Section, the clinical endpoints and the diversity sections. • While still limited, I think the rationale is acceptable because it seems hard to do better preclinical swallowing models. There is a reliance on the clinical data in another indication, which seems appropriate for this unmet need. • The preclinical animal modeling is lacking. However, the stress incontinence reduction data supports the recovery potential. • I found the clinical data from the stress urinary incontinence interesting. Admittedly, it is post hoc analysis in a subgroup, the subgroup being patients with prior surgery, but there is a good effect size, 44% vs 16% placebo, and the data supported a regenerative medicine advanced therapy (RMAT) designation from the FDA. • There is a lingering question around the optimal dose, but this seems to be limited by what a safe volume is to inject into the tongue base. • Why run a phase 1 trial comparing the low dose versus high dose single injection if safety and efficacy results from that study will not be used to determine the best dose to move forward with? • Enrollment projection may be overly optimistic.
No:	*none*

0	
GWG Votes	**Is the proposal well planned and designed?**

Yes:
14
	• A controlled clinical study will be necessary due to a possible large placebo effect.
	• The applicants have provided additional information in the manufacturing section, although this aspect will not be funded by CIRM.
	  • They more clearly describe the use of the Intermediate Cell Stock in the generation of the final product.
	  • The release testing procedures are described in considerably more detail.
	  • They mention that the endotoxin limit was calculated according to USP85, but it still seems very high based on the usual FDA limit of 5 EU/kg/hour.
	  • They provide details of the myogenic differentiation - PCR and gene expression tests.
	  • They indicate that the lot failure rate has decreased by about 2 to 3% and compare it to the failure rate for another autologous cell therapy.
	  • The description of the manufacturing process is still somewhat vague, e.g., does not describe what reagents are used for enzymatic digestion, cell culture and cryopreservation.
	  • The method for shipping and handling the product at the sites not described in any detail but will not be funded by CIRM.
	• Appreciated their response on dosing. Understand the manufacturing limitations of single injections of the higher dose into the tongue. While I don't agree that two lower doses is equivalent to a single high dose, the lower dose is already a high cell concentration for injection. I do think they have better chance at efficacy with two separate doses.
	• Concerns remain regarding the specific secondary outcome measures to be collected and what specific outcome measures will be most meaningful in addition to tongue strength measures.
	• It may be difficult to complete all of the study questionnaires through the virtual interviews.
	• The clinical protocol needs to be updated to reflect the proposed changes.

No: 1	• Concerns with availability of clinical data via intended route of administration to support dose rationale. The product will likely be safe but may not be sufficiently effective for proceeding to a phase 3 pivotal trial.
GWG Votes	**Is the proposal feasible?**
Yes: 15	• The product has some safety data from the phase 1 that didn't show significant risks, and a reasonable plan for a randomized, controlled study to see if there is an effect. Worth trying for this unmet need that usually would not get much attention or support. • Appreciated that they dropped the Voice Handicap Index. There were still concerns among the reviewers about the patient burden for clinical scales. Please re-review and make sure all timepoints tested are necessary. • The protocol does not appear to be updated with their changes to the trial in the proposal. For example, the Voice Handicap Index (VHI10) is still included, June 2021 version. This would need to be resolved before moving forward. • The lot failure rate has recently declined. Recruitment issues are discussed in the Risk Mitigation strategies table. The changes made in the manufacturing section adequately respond to this reviewer's concerns, but there have been relatively few changes to the pre-clinical section and the proposed clinical protocol, and this should determine the adequacy of their responses to the previous review.
No: 0	*none*
GWG Votes	**Does the project serve the needs of underserved communities?**
Yes: 15	• Tremendous improvement, applicant's proposal reflects an incorporation of feedback provided in the original critique. • This project targets a relatively ignored population of study.

	• Yes, the outreach plan is appropriate. • The investigators propose to partner with institutional community outreach and engagement offices in outreach activities with the proposed clinical sites. They will also conduct lectures and Q&A sessions with diverse populations in the Central Valley areas. Interestingly, they will utilize community health workers to contact underserved populations by reducing barriers in translation. • Additionally, they will use a student run clinic at one clinical site as a location to make contact. They cite the disproportionately high rates of cancer and poor access to health care in the Central Valley of California as a further resource for recruitment. • Similar outreach information is not provided for one of the other clinical sites, and it is not clear whether biopsy samples will be obtained by that particular team.
No: 0	*none*

DIVERSITY, EQUITY, AND INCLUSION IN RESEARCH

Following the panel's discussion of the application, the patient advocate members of the GWG were asked to indicate whether the application addressed diversity, equity and inclusion, and to provide brief comments. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

DEI Score: 8.5

Up to 7 patient advocate members of the GWG score each application. The final score for an application is the median of the individual member scores. Additional parameters related to the score are shown below.

Score	Patient Advocate Votes	Has the applicant sufficiently addressed how they have or will incorporate perspectives from individuals with diverse experience and from underserved groups in the implementation of the proposed project?
9-10: Outstanding response	2	• CIRM-sponsored alpha-stem cell clinics would be used for this study. Use of these sites will automatically result in a patient-centered approach.
6-8: Responsive	2	• The DEI sections have been edited to reflect a robust commitment to DEI values • The description of the team's commitment to DEI is well stated. • The inclusion of Bridges graduates shows strong program continuity and return on investment related to CIRM funding.
3-5: Not fully responsive	0	*none*
0-2: Not responsive	0	*none*

Application #	CLIN2-13355 #2
Title (as written by the applicant)	Phase 1/2 Study of a Neural Cell Therapy in Subjects with Drug-Resistant Unilateral Mesial Temporal Lobe Epilepsy
Therapeutic Candidate (as written by the applicant)	An inhibitory neuron cell therapy derived from human embryonic stem cells.
Indication (as written by the applicant)	Focal epilepsy; drug-resistant mesial temporal lobe epilepsy.
Unmet Medical Need (as written by the applicant)	Current treatments for drug-resistant mesial temporal lobe epilepsy include surgical resection and ablation; both are tissue-destructive and can cause serious, irreversible adverse effects. There is a clear need to develop targeted, non-tissue-destructive, and long-lasting therapies that are safe and effective for mesial temporal lobe epilepsy.
Major Proposed Activities (as written by the applicant)	• Initiate and conduct a first in human study of the product in subjects with drug-resistant mesial temporal lobe epilepsy. Includes preclinical and technical support. • Clinical operations supporting planning of Stage 2. Includes preclinical and technical support.
Funds Requested	$7,999,999
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	14
Votes for Tier 1	14
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 at this time but could be resubmitted to address areas for improvement
- 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 proposal have the necessary significance and potential for impact?
Yes: 14	• Mesial temporal lobe epilepsy (MTLE) is a common form of epilepsy not always responsive to drugs or surgical intervention. This novel cell therapy product shows promise in animal models and may ameliorate MTLE in both the short and long term. • MTLE is the most common form of partial epilepsy in young adults and the most frequent type of epilepsy reported. • According to the applicant, each year in the U.S., ~150,000 new cases of epilepsy are diagnosed, and over 360,000 adults in California live with chronic epilepsy. • It is a novel therapy idea that may help ~12% of people with intractable temporal lobe epilepsy. • The response to the initial comments and questions was very good. • Patients and health care providers would choose this product over current surgical approaches if its overall safety profile is acceptable, and its efficacy is durable. The possible mechanism of action could prove favorable to ablating or removing neural tissue. • For patients whose response to current pharmaceutical interventions is insufficient, implantation of this product may offer a durable and more effective long-term solution than current surgical approaches.
No: 0	*none*
GWG Votes	**Is the rationale sound?**
Yes: 14	• Yes, given anti-seizure medicines are only completely effective for a subset of people with epilepsy, with just 44% of people achieving seizure freedom on currently available medications. According to the applicant, one third of people diagnosed with epilepsy have drug-resistant seizures. • It is a worthwhile idea to try given that other treatment options are all imperfect. • Pre-clinical testing in rodents and primates have shown the treatment to be safe. Rodent models of MTLE have shown the product to be efficacious and durable up to 1 year (the useful life of the rodent model). • Data suggest effect in humans could be significant and durable for those who would otherwise need current standard-of-care surgical intervention. • The sham control procedure was better explained. • There is an overall lack of adequate detail regarding the manufacturing.
No: 0	*none*
GWG Votes	**Is the proposal well planned and designed?**
Yes: 14	• The research plan is thorough and has improved from the initial proposal. Items of concern have mostly been addressed. • The protocol supports CIRM's mission to accelerate stem cell treatments to patients with unmet medical needs: Data collected from this study will be crucial in expanding clinical trials in the use of this product for MTLE and in obtaining regulatory approval and translating use of this product to a clinical standard. • The clinical plan has been reviewed by FDA and modified accordingly. I do believe that the product is now ready for clinical testing and the proposal is well planned.

	• Follow-up to observe seizure control may take a year of more, and this may be impacted if the cell survival is marginal. This makes retention in the trial very important as follow-up tends to drop off with time. • The applicants have attached a Manufacturing Process Plan which provides Certificates of Analysis and details of the lots already manufactured, in addition to a non-qualified potency assay, while not describing the manufacturing process in detail. The product has already been prepared and, in my opinion, meets all requirement for clinical use.
No: 0	*none*
GWG Votes	**Is the proposal feasible?**
Yes: 14	• Clinical protocol is well supported, well written, and feasible at the number of centers the applicant proposes. Patient accrual, although difficult (as with most small first in human trials), seems achievable and oversight from both the applicant and their contract research organization seems sufficient. • The animal data is encouraging, and I feel that there are going to be enough patients interested in avoiding a craniotomy and focal brain resection. • Team appears experienced, skilled, and prepared. A key person has prior CIRM experience. Executive, clinical, scientific, regulatory, and quality functions seem appropriately staffed with committed personnel. CIRM related award performance indicates ability to keep projects on track. Budget seems sufficient for suggested activities. • Previously, I had some concerns for the scant cell manufacturing plan, but the applicant did supply additional information that leads me to believe the project is feasible. • I did want to note that the panel requested the manufacturing plan details and this was not supplied or addressed in the resubmission. I have worked in industry for over 30 years with 20 years of that developing manufacturing processes for cell-derived products. While we understand that the manufacturing process is often a closely guarded trade secret, I think that when a applicant asks for CIRM funding (provided by the tax payers of California) it behooves them to supply whatever details are requested or else possibly not receive support from CIRM. In this case, the data supplied convinced us that the project did warrant funding but that will not always be the case when requested information is not supplied.
No: 0	*none*
GWG Votes	**Does the project serve the needs of underserved communities?**
Yes: 14	• Very thorough response. The applicant convincingly expresses intent, with examples, to be a strong advocate for diversity, equity, inclusion. Plans/ideas detail a clear purpose (for example, "outreach" is proposed, with a specific target). Engagement and outcomes are referenced along with using data to inform applicant's plan as indicated. • The applicant has revised the application and materially improved DEI oversight, planning, and engagement. The protocol requires each participant to have been previously evaluated with video EEG to confirm epileptic focus location, and this will mean that essentially all will need to be reachable through association with known tertiary epilepsy centers. Nevertheless, the applicant has detailed steps to make all reasonable efforts to actively offer the trial as broadly as possible to all who might qualify. • The updated proposal has addressed the initial concerns very well. We will see how it works out. • This section of the grant has been vastly improved and does serve the needs of underserved communities.
No: 0	*none*

DIVERSITY, EQUITY, AND INCLUSION IN RESEARCH

Following the panel's discussion of the application, the patient advocate members of the GWG were asked to indicate whether the application addressed diversity, equity and inclusion, and to provide brief comments. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

DEI Score: 9.0

Up to 7 patient advocate members of the GWG score each application. The final score for an application is the median of the individual member scores. Additional parameters related to the score are shown below.

Score	Patient Advocate Votes	Has the applicant sufficiently addressed how they have or will incorporate perspectives from individuals with diverse experience and from underserved groups in the implementation of the proposed project?
9-10: Outstanding response	3	• The applicant convincingly expresses intent, with examples, to be a strong advocate for diversity, equity, inclusion in the revised proposal (e.g., identifying a DEI expert who will act as a consultant regarding increasing diversity on the proposed trial). • A seven-point plan includes: Addressing language barriers, mitigating social determinants, site selection strategies, investigator and staff diversity, education of site staff and patients, and using demographic data to inform future cohorts. • Overall, this plan reflects an outstanding effort toward outreach and recruitment of a diverse cohort. • Strong emphasis toward recruiting appropriate personnel/expertise and budget to implement plan.
6-8: Responsive	1	*none*
3-5: Not fully responsive	0	*none*
0-2: Not responsive	0	*none*