Application #	CLIN2-12379 #2
Title (as written by the applicant)	Safety and Tolerability Study of Neural Stem Cells in Subjects with Chronic Ischemic Subcortical Stroke
Therapeutic Candidate (as written by the applicant)	A human embryonic derived, non-genetically modified neural stem cell, originally derived from the Wi-Cell H-9 line
Indication (as written by the applicant)	Patients with chronic motor deficits, from 6 to 60 months after stroke. Cells will be injected into the brain near the site of the stroke.
Unmet Medical Need (as written by the applicant)	Strokes are a leading cause of adult disability. There is no medical therapy able to promote recovery in chronic stroke patients, establishing stroke as a major unmet medical need. These cells will be the first stem cell-derived therapy directed towards improving disability for this disease.
Major Proposed Activities (as written by the applicant)	• Complete a Phase 1 / Phase 2a Clinical Trial for the cell treatment after stroke and initial data analysis • Manufacture a cGMP working cell bank and clinical lot • Complete the potency assay and stability program development
Funds Requested	$11,998,988
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	3
Count	12
Votes for Tier 1	11
Votes for Tier 2	0
Votes for Tier 3	1

- 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. 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: 12	• The only treatments for stroke (tPA and mechanical thrombectomy) are only effective in the acute setting. Therefore, there is a great need for new treatment modalities. A neural stem cell product provides a possible new way to treat stroke through local secretion of paracrine factors that influence inflammation and cell survival. • There are no approved treatments for chronic stroke. Thus, there is only rehabilitation and plasticity offered to augment recovery. This defines a huge unmet need. • Stroke is a devastating condition that effects large numbers of people, particularly the elderly. • This a very hard to treat problem and impacts quality of life. Any successful treatment would be very beneficial. • The approach is a reasonable value proposition given the devastating consequences of the disease. • There is currently little to offer chronic stroke patients with stable motor defects. Even small improvements in use of fingers, arms, or legs will have major bearing on quality of life. The applicants summarize the current clinical situation accurately. A single dose treatment that restored any degree of movement would be welcomed. • The proposal has potential for impact. Unclear mechanism of action (MOA), but compelling preclinical data and rationale. • The potential for impact is potentially limited by the concerns for the preliminary data that form the scientific premise. • One drawback to the proposed therapy is the need to develop specialized surgical centers for delivery of the cell product. Applicant hypothesizes that putting together 100 or so such centers would not be difficult. Given the enormous medical need, this could be the case. But certainly, a therapy approach that did not require a patient population with reduced mobility to travel would be preferable. This is especially true when one considers the high prevalence of stroke in underserved communities who may find travel difficult for economic reasons.
No: 0	*none*
GWG Votes	**Is the rationale sound?**
Yes: 7	• The rationale is built on the premise that neural progenitor cells, delivered into a site injured by stroke will provide a supportive environment for both regeneration of the host tissue and damping down of local inflammation. • The rationale of decreasing inflammation and supporting local cell survival has been around for many years and is supported by a lot of scientific evidence. The mode of treatment is the new aspect of this application. • The MOA is still incompletely understood, but there are compelling nonclinical data. The applicants responded to the previous review with a very comprehensive data package. • Great team, rigorous preclinical work.
No: 5	• The strongest rationale for doing the trial is the convincing portfolio of animal studies showing proof of concept for efficacy. The explanation for this efficacy remains unclear. • The preclinical data are not convincing. Much of the work was done with animals treated in the acute stroke setting, one week after stroke. This is particularly important in the case of the plasticity experiment. No electrophysiology was presented for the synaptogenesis assay. The inflammatory/infiltration studies are very preliminary and can be interpreted to show potentially pro-inflammatory effects of the treatment. • The pro-inflammatory macrophage (M1) conversion to anti-inflammatory macrophage (M2) data is gaining traction in several other studies for several different indications, but the data in this proposal are not very convincing. The data doesn't appear to show a huge shift from M1 to M2.

	• The response to the previous critique regarding MOA data was to delete the entire section of the proposal. However, the issue remains that these were foundational preliminary data to support the scientific premise of the proposal. The macrophage data are not convincing and could even be interpreted as harmful. Meaning, the treatment increases M1 polarized macrophages in the treated patients. This is typically felt to be harmful. Activated cells by translocator protein-based imaging are thought to be principally M1 and not M2. If these cells are the proposed site of action of the secretome, then I don't see how deleting the section makes this a stronger proposal. The imaging data in Figure 6 are concerning in that it identifies amplified inflammatory responses diffusely. It is unclear to me how an amplified diffuse inflammatory response post injury is beneficial. It may be that the animals improve in spite of this, not because of it. • Not convinced this will work in older patients based on animal data in young healthy animals. Would like to see some studies in older animals. This is a large jump from rodents to humans. I would like to see another animal model showing efficacy. • In terms of the in vitro data that are foundational for the premise of the proposal, the cytokine changes in Figure 9 either show no difference between the groups, or the relative gene expression/fold changes are below 2. While statistically different, these are probably not relevant. Also concerning is the lack of a correction for false discovery by using t-tests alone when testing multiple read-outs. • CIRM should consider an early milestone for the applicant to show evidence that the four cGMP lots to be used in the trial are comparable within a predefined range in production, for example in vitro assessment of candidate secretory products or some other relevant more data dense parameter. They should also submit a plan explaining how they will proceed with the clinical trial if the lots are not comparable: Do another cohort at the same dose level with the new lot to reassess safety? Something else? This will require them to complete analytical assay validation for their candidates; that should not take a full year proposed in the application. This milestone should be accomplished before initiating clinical use of the second cGMP lot. • CIRM should clarify milestones for initiating the new manufacturing campaigns proposed in the revised proposal. Will these be tied to ongoing clinical results in any way?
GWG Votes	**Is the proposal well planned and designed?**
Yes: 11	• Overall, I think this is a well thought out study. The trial is well designed and supported by the pre-clinical data. • As far as the clinical trial is concerned, yes. • Well planned, but it is unclear if immunosuppression is really necessary. • Other reviewers have raised some concerns about the use of immunosuppression which can have hypertensive effects and I think this is a minor concern. • The immunosuppression response doesn't make much sense. I understand that the FDA approved it as such. However, the core assumption is that (1) the drugs are functional equivalents, and/or (2) there are no significant interactions with the treatment, (3) long term cell survival is negligible. In fact, in the chronic animals that mimic the clinical trial, 4/9 have cells present at day 45, and only minimal amounts at that time. This is a relatively minor-moderate critique, but it remains unclear why all of the pre-clinical data were developed under one paradigm and then switched. If the rationale for immunosuppression was so compelling as per the references cited, then why wasn't it used initially? • This is a Phase 1 safety study with secondary measurements looking for efficacy signals, but the trial is not powered to demonstrate any efficacy signals. • Need to address the qualification of the different clinical lots before use. • There was no response to increase the blood pressure monitoring of these patients. In fairness, there isn't an investigator's brochure included at this point, so this may be in that ultimate document.
No: 1	*none*
GWG Votes	**Is the proposal feasible?**
Yes: 12	• This team is very experienced and have done similar trials, so I think the project is feasible.

	• The PI and team have demonstrated the ability to do this in other similar trials. All of the necessary expertise is in place. • No change from original submission. Group has experience recruiting and treating the clinical population. Cells are banked. • There has been the development of an appropriate contingency plan for thaw/viability issues. • While I think the trial will demonstrate safety, I think there is a low probability of seeing any meaningful efficacy. Still, I do think this is an important first step in the development of a potential new treatment modality for ischemic stroke. • The issue of imaging ligand specificity in the clinical trial and the entire translocator protein activation work has been removed. • In a trial published in 2019, there was no apparent benefit in those with a baseline upper motor arm score of 4 (completely plegic). That suggests that a lower level of injury may be more tractable for therapy, yet that is not included in the current study. Why not? Would love to see exploratory serologic/imaging measures to link to the MOA.
No: 0	*none*
GWG Votes	**Does the project serve the needs of underserved communities?**
Yes: 12	• There is a plan to enroll diverse groups into the trial, so I think the diversity objectives have been satisfied. • Appears to have a robust ability and plan for enrolling a diverse population into the trial. • Exclusions are valid and risk-based/appropriate. • They do an excellent job here. • Good statement.
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

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	• No concerns.
6-8: Responsive	1	• Conformance with institutional DEI program and varied socio-economic demographics on the team allow for a high DEI score.
3-5: Not fully responsive	0	*none*
0-2: Not responsive	0	*none*

Application #	CLIN2-12595 #2
Title (as written by the applicant)	Phase 1 Clinical Trial of Autologous GD2 Chimeric Antigen Receptor T Cells for Diffuse Intrinsic Pontine Gliomas and Spinal Diffuse Midline Glioma
Therapeutic Candidate (as written by the applicant)	Autologous T cells genetically engineered to express a Chimeric Antigen Receptor targeting GD2 (GD2-CART)
Indication (as written by the applicant)	Brain tumors in children and young adults: Diffuse Intrinsic Pontine Gliomas (DIPG) and Spinal Diffuse Midline Glioma (DMG)
Unmet Medical Need (as written by the applicant)	DIPG, the leading cause of childhood brain tumor death, is uniformly fatal. Many clinical trials have explored the use of various therapeutic agents for DIPG. However, no improvement in overall survival has been demonstrated to date. Thus, there is an urgent need for novel effective therapies.
Major Proposed Activities (as written by the applicant)	• Determine recommended Phase 2 dose of therapeutic for patients with DIPG and Spinal DMG • Assess toxicity of GD2CAR T cells • Assess clinical activity of GD2CAR T cells in children and young adults with DIPG and Spinal DMG.
Funds Requested	$11,998,310
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. 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: 13	• This a devastating disease, uniformly fatal and any therapy would be a game changer. • DIPG is a fatal disease with very bad survival. The absence of good treatment options for DIPG is an unmet medical need. • DIPG is a devastating form of glioma. With current standard of care most children die within 2 years. • Childhood pontine gliomas have insufficient effective treatments. • It is encouraging to see a proposal with potential to treat a true unmet medical need. • Due to the diffuse growth of the tumor, the only available standard treatment option is radiation. The proposed therapy offers a significant improvement over the standard treatment. The value proposition is a survival benefit. • Any new treatment modality with supporting pre-clinical evidence and a reasonable safety profile merits support. This project fits those criteria. • Good responses to previous CIRM review. Would benefit from generating characterization data from Day 11 cultures. • Pre-clinical and early clinical data indicate some level of efficacy, although it appears to be transient.
No: 0	*none*
GWG Votes	**Is the rationale sound?**
Yes: 13	• Excellent preliminary data. Some efficacy signals in patients, which is very encouraging. • The scientific rationale is well established and published. • The proposed product clearly can target disease. • The rationale is based on very compelling pre-clinical data. I don't think doing more animal work is the right way to go. This product now needs to be tested in the clinic to see if the safety profile is acceptable and there is any sign of efficacy. • A little odd that manufacturing allows for variable culture time, dependent on number of cells and dose requirement. Presumably day 7 and day 11 are not equivalent cell populations. Applicants should provide comparability studies to evaluate day 7 versus day 11 products for potential toxicity and potency changes, and how those changes could impact interpretation of dose-finding studies, especially if the need for day 11 cells is associated with patients at higher dose arms. The main concern is this clinical trial is already combining several variables with only small number of patients. This already will confuse any determination of maximum tolerated dose and ability to evaluate for any hints of efficacy. Adding another potential variable in terms of cell product potency/toxicity (day 7 versus day 11) will complicate things even further. • As the trial is progressing the authors should perform a study to assess comparability of the cell product harvested on day 7 versus day 11. Since the author demonstrated decline of potency at day 14 of manufacturing in the system, it is highly likely that the potency and phenotype of the product harvested on day 7 and 11 would be different. • Not clear how patients are screened for the specific mutation.
No: 0	*none*
GWG Votes	**Is the proposal well planned and designed?**
Yes: 13	• I believe the project is well designed and planned. The pre-clinical results are compelling and there is impressive data in a small cohort of patients - it is time to move this work fully into the clinic to test safety and efficacy. I believe the applicants have a well thought out clinical design to determine safety and hopefully some efficacy signal.

	• The project is appropriately planned and well designed. • They responded well to the previous review and the proposal is improved. • Well designed. • The work on the durability of the effect will be important. It seems like the FDA is increasingly focused on durability - which ultimately goes to the cost-benefit of the therapy. • Concern about conflating the two delivery methods in the same patient will complicate interpretation of toxicity and efficacy.
No: 0	*none*
GWG Votes	**Is the proposal feasible?**
Yes: 13	• The staff is well qualified and has all the necessary resources. • Risk assessment and mitigation strategies are described. • Study is already open, and accrual has progressed to next dose level. • I believe the proposal is feasible. The only concern would be whether they can recruit enough patients in a timely manner. • There is some concern with cell penetration and persistence but repeat dosing along with multiple dosing methods will help to address these issues.
No: 0	*none*
GWG Votes	**Does the project serve the needs of underserved communities?**
Yes: 13	• Yes, the application addresses this. • Appears fine. • Some more outreach needed.
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	• Strong focus on DEI goals. Advancing the institution's commitment to the values of diversity and inclusion is a key component of the institution's long-range vision. The institution's initiative for DEI is working across the entire institution's community, focusing on the areas of recruitment, research, education, and engagement. • More outreach is needed.
3-5: Not fully responsive	0	*none*
0-2: Not responsive	0	*none*

Application #	CLIN2-12735
Title (as written by the applicant)	A Phase I, Pilot Study of Human Embryonic Stem Cell-Derived Cardiomyocytes in PaTients with ChrOnic Ischemic Left VentRicular Dysfunction (HECTOR)
Therapeutic Candidate (as written by the applicant)	The therapeutic candidate is human embryonic stem cell-derived cardiomyocytes (hESC-CMs) as a new therapy for chronic ischemic cardiomyopathy patients
Indication (as written by the applicant)	hESC-CMs will be indicated for treatment of heart failure (HF) and for preventing progression to HF in patients with chronic ischemic cardiomyopathy.
Unmet Medical Need (as written by the applicant)	Ischemic heart disease accounts for 60% of HF. With limited availability of donor hearts and a bleak prognosis, new therapeutic strategies are needed. This trial will test the safety and feasibility of administering hESC-CMs as a therapy for treating chronic ischemic cardiomyopathy.

Major Proposed Activities
(as written by the applicant)
	• Prepare for trial initiation
	  • Complete regulatory approvals
	  • Finalize clinical study protocol, informed consent form, IRB approval
	  • Relevant training
	• Recruit and randomize participants
	  • Enroll first participant
	  • Recruit the target sample size
	  • Follow-up visit of the enrolled participants
	• Data collection and management
	  • Primary and secondary endpoint analyses
	  • Final study report and manuscript submission
	  • Results reporting

Funds Requested	$6,987,507
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	3
Count	12
Votes for Tier 1	10
Votes for Tier 2	0
Votes for Tier 3	2

- 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. 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: 12	• This is a major unmet need. If successful it would save health care costs associated with heart failure and improve quality of life. • Left Ventricular Dysfunction (LVD) represents a large unmet clinical need. The central issue with this disease is the death of large numbers of cardiomyocytes. • All FDA concerns appear to have been addressed and FDA have released the program from clinical hold, so they are now ready to begin the clinical trial. • Based on pre-clinical animal models, ESC-derived cardiomyocytes appear to have some potential for impact in heart disease. • The proposed mechanism of action is both cell replacement of dead cardiomyocytes and support of resident cardiomyocytes through the secretion of paracrine factors which promote angiogenesis and inhibit apoptosis amongst other things. • Although the preclinical data supports proceeding with this Phase 1 clinical trial, there is concern about the potential lack of engraftment. • The background of multiple trials indicates low chance of efficacy. However, this data will help to determine if there is a path forward for cell therapies or if a fundamentally new approach is required before investing in further trials. • While this is an appropriate Phase 1 safety study, it is not clear how any go/no-go decision rules regarding efficacy and proceeding to Phase 2 will be developed and/or applied. • The applicant should clearly outline the goals that would trigger the applicant to decide whether to pursue a Phase 2 clinical trial.
No: 0	*none*
GWG Votes	**Is the rationale sound?**
Yes: 9	• The rationale of the study is sound. • I echo many of the reviewers concerns that there is a high likelihood that this study generates results similar to previous cardiac cell therapy studies. However, it is reasonable to try embryonic stem cells to confirm or dispel these beliefs, and this PI and team are well positioned to do so. • The concept of replacing dead and dying cardiomyocytes has been around for a long time and I think it is sound and logical. The real question is whether one can supply enough cells to impact LVD and whether the cells can integrate to give appropriate function. Others have run into problems with arrhythmias after cellular transplantation. The applicants are aware of this potential issue and have tailored their dose accordingly. • There is concern that the effect is temporary and subsides after withdrawal of immunosuppression and disappearance of the cells. It is not clear whether a short-term paracrine effect will translate into an effective therapy. This first step is probably warranted however but could be supplemented with some concrete evaluation of whether a Phase 2 study would be likely to provide a prolonged therapeutic effect. • The pre-clinical animal data is promising enough to warrant entry into the clinic. Looking at their data I do not see convincing evidence of hESC derived cardiomyocyte survival and integration and the few "lone ranger" cells that they do show could be explained in other ways - cell fusion for example. Aside from that the animal models are far from perfect and of course in any of the large animal models one is always battling with the immune system in the context of a xeno-transplant. • The predicted effects are most likely to be paracrine with little engraftment. • Rationale for specific dose levels is only minimally justified, with no adjustments for specific patient characteristics.

No: 3	• The applicants admit the cells will only transiently persist. It is difficult to envision how this could impact a chronic myocardial disease. • While the large animal studies appeared to be safe, they do not provide evidence of efficacy. While the other animal studies show efficacy, they used immunosuppression for the course of the study. Many other studies have been conducted which rely on paracrine factors, these have not proven to be helpful over the long run. Without engraftment this is unlikely to work. • I believe this will prove to be safe, similar to many other studies and cell types. However, to move the field forward I believe we really need these types of cells to engraft. I would like to see large animal studies with the short course of immunosuppression to show efficacy. • Maybe. The paracrine mechanism of action rationale with a short immunosuppressive regimen is unsubstantiated.
GWG Votes	**Is the proposal well planned and designed?**
Yes: 12	• This is an excellent proposal and well planned. • This proposal is very thought out and overall, well designed. • I think the project is well planned. • The drug product has already been produced and has undergone and passed quality control testing. The manufacturing facility is highly reputable, so I don't have concerns about the drug product. • I think the timeline is realistic and the budget is appropriate for a clinical trial of this nature. • I would encourage the applicants to predefine criteria that they would use to evaluate the success of this trial, specifically data would support a go/no-go decision and the design of a phase 2 study. • There is a need for a clear definition of go/no-go for moving to Phase 2. • There is some question about the status of catheters. The company has stopped supporting these catheters since Jan 2021. The letter of support appears to indicate this will not be an issue.
No: 0	*none*
GWG Votes	**Is the proposal feasible?**
Yes: 12	• I think the project is feasible within the timeline defined by the applicants. • The team already has qualified cell product in place, they have answered all FDA questions and have been removed from clinical hold and are therefore poised to go into the clinic. • The team is very qualified from the manufacturing of the cellular product through to the clinical team. • This is an outstanding team. • Yes. The team is felt to be excellent and the recruitment plan feasible. • Excellent team. • Data sharing plan is a model for future applicants. • They have addressed mitigation plans to manage risks and they look reasonable. • I believe this is a reasonable first step in addressing the clinical needs of LVD patients. It is primarily a safety study and therefore is not expected to (and is not powered to) show efficacy. Having said that I think there are huge hurdles to overcome with conditions like LVD. Delivering enough cells to the right location(s) and having them integrate appropriately and function is going to be difficult and take time. While I am skeptical that this sort of approach will work in the near term, I think this could be an important first step and I cannot think of anything else I would ask the applicants to do before entering the clinic. • The sample size for phase 2 is based on a variable that is not mentioned anywhere under the trial endpoints. The protocol needs to be adjusted to align objectives. • If the maximum tolerated dose is the second proposed dose, will the trial continue and if so with how many patients? • Recruitment goal may be optimistic.
No: 0	*none*
GWG Votes	**Does the project serve the needs of underserved communities?**

Yes: 12	• They do a very thoughtful job of addressing these areas. • Yes, significant effort has been made to include underserved communities. • This Phase 1 clinical trial clearly addresses this point. • The applicants have really thought through the needs of underserved communities and addressed this thoroughly in the application.
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: 10.0

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	• Investigators specified that HF is more prevalent in women and effects a disproportionately higher number of ethnically diverse individuals. They will target these groups as part of their recruitment efforts. • As noted by the applicant, research team members who will recruit patients are from racially and ethnically diverse backgrounds. • Well thought out recruitment strategy to recruit a diverse sample of patients (both gender and race/ethnicity). • Patients were included in the design of the study. • Excellent job in outreach to underserved communities: places of worship, community groups. • Community groups (places of worship, schools, community associations) were included in the design of the study. • Translation of study materials is available in numerous languages. • Patient Advisory Team, that is representative of patient demographics, will be consulted over the course of the study. • Research team members will receive education on the ethics of vulnerable populations in research.
6-8: Responsive	1	• Strong community outreach program, first time graduates, international background and goals for DEI enable a high score.
3-5: Not fully responsive	0	*none*
0-2: Not responsive	0	*none*