Application #	CLIN1-14070 #2
Title (as written by the applicant)	Development of cryopreserved interferon-gamma primed allogeneic MSCs, for treatment of steroid refractory acute graft versus host disease
Therapeutic Candidate (as written by the applicant)	Cryopreserved, interferon-gamma-primed bone marrow mesenchymal stem cells (BM-MSCs)
Indication (as written by the applicant)	Acute Graft versus host disease (aGVHD) resulting from hematopoietic cell transplantation
Unmet Medical Need (as written by the applicant)	Systemic steroid therapy is the standard first-line treatment for aGVHD; however, the disease becomes refractory to systemic steroid therapy in 35–50% of patients. Mortality rates for patients who fail to respond to first-line steroid therapy are 80% due to very limited alternative treatments.
Major Proposed Activities (as written by the applicant)	• Address clinical hold manufacturing issues, including OSSM-007 manufacturing reproducibility and stability of product • Develop a matrix of predictive potency assays and demonstrate utility in a mouse aGVHD model • Refine the clinical dosing regimen by conducting a dose escalation study in a humanized mouse model of aGVHD
Funds Requested	$3,457,858
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	13
Votes for Tier 1	13
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 project hold the necessary significance and potential for impact?
Yes: 13	• Graft vs host disease is an ongoing problem without satisfactory treatments. • There are no other successful treatment options for steroid refractory GVHD.

	• In this resubmission, the applicant addressed the reviewers' concerns quite well. • The revised application gives improved insight in the applicant's plans for demonstrating improved potency of their activated MSCs through characterization, release testing, and pre-clinical testing • Part of the rationale for the development of this product is the improved consistency compared to standard of care. The data to support this statement has not yet been fully provided, thus this is a risk to be considered with the program.
No: 0	*none*
GWG Votes	**Is the rationale sound?**
Yes: \13	• Previous literature and the applicant's studies support the rationale. • From a manufacturing perspective, concerns around potency are being addressed appropriately. • This re-submission clarified the rationale by including plans to decrease variability with use of carefully screened cadaveric donor vertebrae, testing, extension to adult (and pediatric) patients, and a detailed plan based on prior FDA review of a related product.
No: 0	*none*
GWG Votes	**Is the project well planned and designed?**

Yes:
13
	• In this resubmission, the applicant addressed many of the prior critiques.
	• The revised application addressed concerns and provided a strategy to avoid issues encountered by a related product by providing the following key details:
	  ○ The revised application included detailed improvements to potency assays, including addressing variability and developing numerous potency assays that will be incorporated into the final release criteria for each lot of the product.
	  ○ The applicants discussed plans for validation in animal GVHD mouse models (which was also a prior FDA concern).
	  ○ The application includes a plan to engage with FDA during the potency assay validation process to gain feedback on the suitability of matrix potency assays for predicting in vivo activity.
	  ○ The applicants discussed that they do not expect additional optimization for yield but will engage with FDA if needed.
	  ○ The applicants discussed plans to increase donor selectivity related to using cadaveric vertebral bodies and a process for selection to reduce donor-to-donor variability.
	  ○ The revised application clarified plans to incorporate outcomes and clinical biomarker data from early clinical studies, as well as concurrent results from preclinical studies, and plans to incorporate FDA feedback.
	  ○ The revised proposal will only generate one additional master cell bank, and the budget is updated accordingly.
	• When contemplating commercial production, the future plan should be able to accommodate the number of lots needed during clinical development to confirm the consistency and availability of product.
	• There are remaining concerns regarding predicting donor suitability and availability as the product moves into larger clinical trials. The number of master cell banks may need to be increased, but human data collected as this study progresses are necessary to answer this question, and analytics for potency continue to be developed.

No: 0	*none*
GWG Votes	**Is the project feasible?**
Yes: 13	• The technologies and experience of the team support the successful execution of the clinical trial.
No: 0	*none*

GWG Votes	Does the project uphold principles of Diversity, Equity, and Inclusion (DEI)?
Yes: 13	• The DEI plan is well articulated and includes translating study materials and training sites in cultural sensitivity. • The proposed study is small, however, the applicant has plans to address DEI. • The applicant has an adequate plan to address potential barriers to participation.
No: 0	*none*

DIVERSITY, EQUITY, AND INCLUSION IN RESEARCH

Following the panel's discussion of the application, the patient advocate and nurse 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

Up to 7 patient advocate and nurse 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 & Nurse Votes	Does the project uphold principles of Diversity, Equity, and Inclusion (DEI)?
9-10: Outstanding response	0	*None*
6-8: Responsive	5	• The application includes an appropriate DEI plan. • The applicant provides a thoughtful analysis of patient population assessment and critical needs to activate and support enrollment. • The investigators note that the literature is somewhat ambiguous on whether ethnicity impacts the development of GVHD after transplant. However, access to well-matched donors and good hospital care are not uniformly available. • One study noted that 61% of Black recipients compared to 36% of White recipients developed severe GVHD. • There are no sex differences in the occurrence rates for GVHD. However, older adults are more likely to develop GVHD. • The applicant's plan to recruit clinical sites reflects attention to DEI. • The applicant's activities reflect a good faith effort and have the potential to be effective in outreach and engagement. • The applicant is developing plans to implement cultural competency training for the Clinical Operations team. • The investigators list several strategies to enlist community engagement in their larger clinical trials. Some of these activities include appointing a dedicated Diversity Manager, translation of educational materials, educating site staff in DEI principles, decreasing the frequency of clinic visits, reimbursing patients for housing and transportation, providing support for family caregivers, and providing reimbursement to patients who participate in the trial.
3-5: Not fully responsive	0	*none*
0-2: Not responsive	0	*none*

Application #	CLIN1-14300
Title (as written by the applicant)	Allogeneic iPSC derived Dopaminergic Drug Product for Parkinson's disease
Therapeutic Candidate (as written by the applicant)	Allogeneic iPSC derived dopamine progenitors delivered to the brain of Parkinson's disease patients
Indication (as written by the applicant)	Idiopathic Parkinson's disease
Unmet Medical Need (as written by the applicant)	There are currently no disease modifying therapies for Parkinson's disease. This approach is intended to be disease modifying.
Major Proposed Activities (as written by the applicant)	• FDA requested large animal study of cells delivered to the brain with device • FDA requested glial maturation assay development • FDA recommended single cell RNA sequencing data
Funds Requested	$4,000,000
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	2
Count	14
Votes for Tier 1	11
Votes for Tier 2	3
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 project hold the necessary significance and potential for impact?
Yes: 13	• The project team is spectacular and has dedicated three decades of work leading up to this trial. • The project addresses an urgent unmet medical need. • The focus is highly significant as there is no cure for the progressive neurodegenerative process (dopaminergic cell loss) in Parkinson's disease (PD)

	• The value proposition includes the use of a proprietary device to neurosurgically administer the dopaminergic precursor cellular product, which promises to be off-the-shelf and scalable for use in PD patients with moderate to severe disease who have few good treatment options. • The standard of care (SOC) for Parkinson's disease can be effective but may be of limited duration. The proposed allogenic dopaminergic product could rescue patients no longer responding to SOC, or could be used for patients that are not eligible or appropriate for current SOC. • If the cost of goods provided in the proposal are accurate, the proposed product would appear to be of moderate to high financial value for the PD community. • The potential ease of portability of the proposed product to underserved communities would provide meaningful value to PD patients. • If successful, this treatment is likely to be for a subset of patients who are in the more advanced stage of the disease but healthy enough to undergo neurosurgery, immunosuppression, and other requirements, limiting the applicability of the approach.
No: 0	*none*
GWG Votes	**Is the rationale sound?**
Yes: 13	• The rationale is sound based on the known depletion of dopamine in PD. • The applicants present significant animal data, including published nude rat studies which show proof of principle. • At this early stage of development, animal data suggests likely success. • The specific approach proposed is based on use of iPSC approaches supported by multi-dose pre-clinical data. • The data presented convincingly support the continued development of the treatment, specifically into large animals and then filing for an IND and human clinical trials. • Specific to nonclinical efforts, the completed studies in rodents support the proof of concept and mechanism of action needed for justification. • Data from rat models of Parkinson's disease have adequately "de-risked" the program and provided reasonable estimates of dose and tolerability for clinical trials. • The proposal appears to be sound from a manufacturing, nonclinical, and clinical perspective. • The proposed large animal study has been designed to meet regulatory expectations and can be expected to provide the information needed to qualify the dose and device prior to clinical trials. • Further information about immune suppression would be helpful. The optimal approach to immunosuppression in this population is not known, and is a notable risk factor.
No: 0	
GWG Votes	**Is the project well planned and designed?**
Yes: 10	• In context of the program as a whole, there is a clear potential to meet CIRM objectives of providing novel and/or much needed options to patients. • The project is appropriately planned in the context of specific efforts, general scope, and time frame (duration of specific tasks and parallel vs. sequential time frames). • The proposed nonclinical efforts are appropriate and essential to the development plan. • The proposed timelines balance the need to move quickly with sufficient caution to provide a reasonable assurance of product quality, supporting nonclinical data, and a reasonable expectation of moving into clinical trials with data to inform acceptable safety and tolerability. • Additional description of the glial assay and transcriptomics methods, as they relate to the glial component in the cell product and any impacts on graft efficacy, would be helpful.
No: 3	• The comprehensive plan for the six activities proposed is commensurate with the CIRM's mission. • The application could benefit from additional clarification regarding the need for and selection of immunosuppressive regimens that will be used in future studies. • The project is appropriately planned but the plan itself is not balanced, with most attention given to Activity 1 and far less attention to the other activities, including justification and details of key methods (e.g., scRNAseq methods and analytic approach in Activity 3).

	• From a manufacturing perspective, there are several concerns regarding the feasibility and even the understanding of the quality control assays that will be required, along with the necessary GMP activities needed to support development and qualification of such assays. QC analytical support for this portion of the project is recommended, as this accounts for two major project activities.
GWG Votes	**Is the project feasible?**
Yes: 13	• The objectives are likely to be achieved within the three-year timeline proposed, as foundational work has already been conducted including the development of the device and approach. • The proposed timeline appears to be appropriate for the scope and objectives. • The assembled team, and plans for expansion, appear to be appropriate for completing the development plan. • The contingency plan appears to be viable. • Additional deep dives and development into the manufacturing requirements, notably from an analytical perspective, would promote feasibility. • The draft protocol for the human phase 1b clinical trial is reasonable for this stage but needs to address immunosuppression (what protocol to use, what risks are involved, and how will risks be managed) and consider the development of cognitive complications (both from PD itself but also from the intervention). • The follow-up of up to 10 years is laudable but there are inconsistencies in the descriptions of the follow-up throughout the proposal (18 months, 2 years, and longer, up to 10 years). • The project could benefit from additional team members with better disease expertise and clinical experience. • The team has significant strengths in many of the required areas to ensure success of the program, but there are several areas that are not covered. Specifically, there is no movement disorders neurologist, no expert in clinical trials, or expert in some of the specific areas/methods proposed (e.g., glial cell research, scRNAseq, etc.) • The team should consider a biomarker to monitor the health of allogeneic cells with immunosuppression to address whether immunosuppression is effective.
No: 0	
GWG Votes	**Does the project uphold principles of Diversity, Equity, and Inclusion (DEI)?**
Yes: 13	• There is a well-defined distribution of PD by race and ethnic background at the treating centers. • The written plan is reasonably supportive of DEI principles, and the long-term project plan is to offer the treatment to all eligible patients. • DEI appears to be adequately addressed in the clinical development plan. The highlighted diversity of patients, and potential clinical trial sites, has the potential to address meaningful concerns for diversity in demographics and provide options for previously underserved regions and or populations. • The applicant demonstrates an understanding of the potential barriers to participation in the clinical trial. • The PI states they have experience in DEI, but specific information is not provided. • The actual implementation of the DEI plan could be better articulated.
No: 0	

DIVERSITY, EQUITY, AND INCLUSION IN RESEARCH

Following the panel's discussion of the application, the patient advocate and nurse 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: 7

Up to 7 patient advocate and nurse 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 & Nurse Votes	Does the project uphold principles of Diversity, Equity, and Inclusion (DEI)?
9-10: Outstanding response	0	*none*
6-8: Responsive	5	• The applicants provide a good discussion on ameliorating barriers to trial participation. • The California PD population is well characterized. • The proposal describes how the applicants embrace DEI and its importance with regard to recruitment and barriers to participation. • The DEI plan relies too heavily on the sites, which have not been selected. It would have been preferable to see the DEI plan of the applicant, rather than a dependency upon the DEI plans of unspecified trial sites.
3-5: Not fully responsive	0	*none*
0-2: Not responsive	0	*none*

APPLICATION #	CLIN2-14416
Title (as written by the applicant)	A Phase I Open Label Study to Evaluate the Safety and Tolerability of a Candidate in Patients with Mucopolysaccharidosis Type 1
Therapeutic Candidate (as written by the applicant)	B cells will be isolated from patients suffering MPSI. These will be transformed with a normal copy of the gene and re-introduced into the patient
Indication (as written by the applicant)	Mucopolysaccharidosis I (MPSI) is a rare disease that affects predominantly children. Untreated, these patients typically die by the age of 10.
Unmet Medical Need (as written by the applicant)	The approach of turning the patient's B cells into drug-producing B cells offers the promise of continuous and sustained delivery of therapeutic levels of alpha-L-iduronidase (IDUA). The resulting drug levels mimic normal physiological conditions, and to penetrate tissues that do not receive sufficient levels of IDUA.
Major Proposed Activities (as written by the applicant)	• First in human dosing of adult patients using IDUA transformed B cells • Complete a long term (6 month) pharmacology study in mice to determine safety and efficacy of the product, enabling dosing of pediatric patients • Transfer production of product to a third party commercial manufacturer, and prepare material for larger pediatric study
Funds Requested	$8,000,000
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	2
Count	13
Votes for Tier 1	11
Votes for Tier 2	2
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 project hold the necessary significance and potential for impact?**
Yes: 12	• MPSI is a lysosomal storage disease resulting from mutations in the IDUA gene with subsequent deficiency of the IDUA enzyme. The severity of disease varies from Hurler's syndrome (most severe) to Hurler-Scheie syndrome to Scheie syndrome. Current therapy for

	Hurler's syndrome is limited to hematopoietic stem cell transplantation (HSCT). Current therapy for moderate and milder forms of MPSI is limited to enzyme replacement therapy. • MPSI is a multiorgan disease affecting cardiac function and respiratory function, and which causes skeletal deformities, enlarged liver, and neurodevelopmental/cognitive dysfunction. Early treatment initiation leads to better outcomes. Unfortunately, despite treatment, components of the disease remain difficult to treat, including skeletal deformities (present in all disease types) and neurocognitive disease (Hurler's syndrome). Thus, there is a significant unmet need. • The current therapy is aimed at treating the mild and moderate forms of disease and seeks to improve upon the current treatment option of ERT. Specifically, the downsides of ERT are that it requires weekly infusions (lasting 3-4 hours) for the life of the patient. In addition, the half-life of the ERT is very short and thus the patient is only briefly exposed to peak enzyme levels post transfusion. The investigators and others hypothesize that one of the reasons for the lack of efficacy of ERT treating some manifestations of the disease (especially the musculoskeletal manifestations) is due to insufficient enzyme levels to treat hard to reach tissues (bone). • Use of plasma B cells as a source of production of IDUA seeks to address the limitations of current treatments in two ways. First, plasma B cells are long-lived and thus multiple treatments are not likely necessary. Second, plasma B cells are "protein producing factories" and thus are hypothesized to be able to secrete high levels of IDUA and maintain peak levels for longer periods of time, therefore having a therapeutic effect on difficult to reach tissues. • The investigators have been through multiple rounds of review with the FDA and have obtained approval for the first in human trial in adult patients to demonstrate safety of the approach prior to moving to a pediatric trial. In the context of their conversations with the FDA, they have acquired the support of key opinion leaders, patient advocacy groups and patients for the proposed therapy. • If demonstrated to be safe and effective, particularly in children who are not eligible for hematopoietic stem cell transplantation, the product could significantly improve treatment if it can be administered as an annual infusion to replace the current weekly ERT infusions. In children with Hurler's syndrome, it has the potential to replace HSCT and its associated complications. • Even though there are approved treatment modalities for MPSI (ERT and bone marrow transplantation), they have significant limitations. Therefore, improvement of therapeutic options is warranted. • Cell-based gene therapy for MPSI can offer long-term disease control and prevent debilitating complications. • The product proposed here can impact care and burden of disease as well as cost. • The proposed treatment supports adoption by healthcare providers because it offers pharmacoeconomic benefits. According to calculations presented in the proposal, the course of treatment would be cheaper than the current ERT course per year. However, competition in the area of enzyme replacement therapy and other technologies could be a cause for concern.
No: 0	*none*
GWG Votes	**Is the rationale sound?**
Yes: 11	• Data presented in the proposal support further development. Multiple animal studies were conducted to demonstrate the efficacy and safety of the product-candidate. The application benefits from a good immunocompromised humanized mouse model to test efficacy, toxicity, biodistribution, and dose range. • The rationale for the proposed studies is sound. Specifically, the goals of the proposed studies are to demonstrate safety of a novel therapeutic for the treatment of MPSI in adult patients and to demonstrate the ability of the therapeutic to prevent the development of musculoskeletal pathology in the mouse model of MPSI. Accomplishing these two goals will lay the foundation of a future trial of the therapeutic in the pediatric population (a potential source for future grant applications). This patient population will likely benefit most from the proposed therapeutic as compared to adults. • The rationale for the science behind the therapeutic product is sound and strongly supported by studies in the mouse disease model. ○ The transformation system proposed by this group is believed to be safer than other approaches.

	○ The group has robust preliminary data supporting their ability to use this transformation system and produce plasma B cells for long-term production of the therapeutic product. ○ The group also provides robust in vivo mouse data, on which their IND application was based and ultimately approved. • The rationale for this phase 1 appears sound based on the existing nonclinical data and need for alternative treatment in this patient population, although FDA has asked for an additional nonclinical study evaluating skeletal response prior to trials in pediatric patients. • The autologous cell therapy proposed here provides a lower risk approach compared to stem cell transplant, providing a significant advance for treatment. • Long lived autologous plasma cells are expected to provide benefit via long term secretion of the functioning enzyme. • One minor consideration is that the applicants propose a single dose in the adult patients without any conditioning. This proposal is based on studies in mice with multiple doses and an additional cell infusion to support engraftment of human cells in mice. For current autologous HSCT in clinical trials, conditioning regimens are required. Thus, some information or preliminary data as to why no conditioning regimen is required for the current protocol would be useful. However, the current protocol has been approved by the FDA supporting the work.
No: 1	• It is unclear if the data from a trial in two patients will be translatable and sufficiently enable subsequent studies.
GWG Votes	**Is the project well planned and designed?**
Yes: 11	• The applicants have a long history of interaction with FDA for product development. • This phase 1 study in adults with the Hurler-Scheie or Scheie subtypes of MDSI represents a small first step in the clinical testing of the product and was arrived at following extensive interactions with FDA. • The trial will include only a few patients, but this is reasonable given the rarity of the condition and limited understanding of the agent in humans. • Manufacturing activities are planned well. • The project is well planned. The group has had multiple conversations with the FDA to develop the current clinical trial plan. It is logically developed with the assessment of the results from the first patient prior to the dosing of the second patient. • The team of experts includes a world leader in cell and gene therapy for MPSI, and CROs have been contracted to aid in the execution of the trial and ensure access of the trial to patients. • As per the request of the FDA, the trial only contains a small number of adult patients. This limits a robust analysis of the results but it is important to remember that the purpose of the trial is to demonstrate safety of the product and lay the foundation for a future pediatric trial. • The trial is well planned with primary and secondary endpoints consisting of short term and long term safety and additional endpoints to assess functional effects of the therapy. • A significant amount of funding is directed to mouse work to provide the foundation for a future clinical trial in the pediatric population. • In the protocol, assessments for the exploratory clinical endpoints are not clearly specified. Although this is a phase 1 protocol, it would benefit from additional detail. • The clinical trial design, expansion to the pediatric population, and additional toxicology study are guided by FDA and seem very well planned. However, the risk of insertional mutagenesis remains. • This phase 1 trial will provide only very limited data on safety, plasma and urine biomarkers, and preliminary proof of concept data from functional endpoints. It is hoped that these data will be sufficient to move into a pediatric population despite FDA's concerns regarding the lack of nonclinical data demonstrating functional improvement in the mouse model and the risk of Epstein-Barr virus (EBV)-associated lymphoma. • Given the potential risk of EBV-induced lymphoma, the applicants should consider testing for EBV reactivation in peripheral blood regularly and adding a risk-mitigation strategy to the protocol.
No: 1	• The applicants should provide a more complete clinical development plan to demonstrate that the product will be able to get to the patient population with the highest unmet need.

GWG Votes	Is the project feasible?
Yes: 12	• This study in adults appears feasible at a single site as planned. • The team is knowledgeable on this type of therapy. • The team is qualified to perform the work. • Yes, the proposal includes significant preliminary data in the murine model and the team has demonstrated resources and expertise. • The proposed timeline looks reasonable. • The project is very feasible with the likely accomplishment of the intended objectives. • The collaborating institution almost ensures the ability of the team to recruit the planned number of patients for this study. • The mouse work used to obtain the IND supports the ability of the team to successfully pursue the proposed animal studies. • The group has already had multiple trial runs for production of the therapeutic and has developed the assays needed to assess safety and efficacy, again highlighting the feasibility of the proposed work. • This excellent team has detailed a number of potential risks as well as mitigation strategies. • The applicant has addressed planning for some of the concerns with manufacturing of these cells. Execution of these plans will require strong program integration with staff at the applicant's institute.
No: 0	*none*
GWG Votes	**Does the project uphold principles of Diversity, Equity, and Inclusion (DEI)?**
Yes: 12	• The applicant's planned activities reflect a good faith effort and have the potential to be effective. • There are no red flags at this point for this genetic disease. • Yes. The group makes every effort to uphold the principles of DEI. Notably, the trial only involves a few patients. This is readily acknowledged by the group. It is noted that they will make the trial broadly available. Future trials, which will include more patients, would continue to uphold the principles of DEI. • This initial study in a small number of patients precludes addressing diversity in enrollment. However, the applicant should be encouraged to prepare for ensuring the DEI of any future pediatric study. • DEI issues are not fully covered, because of the limitation that only a few adult patients are proposed for the phase 1 trial. The applicant's limited ability to further address DEI is therefore unavoidable at this time.
No: 0	*none*

DIVERSITY, EQUITY, AND INCLUSION IN RESEARCH

Following the panel's discussion of the application, the patient advocate and nurse 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: 6

Up to 7 patient advocate and nurse 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 & Nurse Votes	Does the project uphold principles of Diversity, Equity, and Inclusion (DEI)?
9-10: Outstanding response	0	*none*
6-8: Responsive	5	• The application meets the requirements for DEI analysis and assessment. • The team seems to embrace DEI principles.

		• The applicant adequately describes how the success of this project would likely lead to a therapy that positively impacts underserved or disproportionately affected communities. • An analysis of the very rare patient population indicates no difference in patient demographics compared to the background population. • Regarding outreach, retention, and community engagement, the team has selected strong clinical sites known to be outstanding in patient outreach. • The team has also contracted with a CRO with support related to patient outreach, and the team has connections with additional institutions and organizations to bolster DEI efforts. • The applicants have identified a multi-lingual consultant to support social communications and web site development. • The team has engaged a clinical vendor to address barriers to trial participation by managing patient travel, housing, and other considerations. • The small size of the trial population makes it challenging to develop a DEI plan.
3-5: Not fully responsive	0	*none*
0-2: Not responsive	0	*none*