

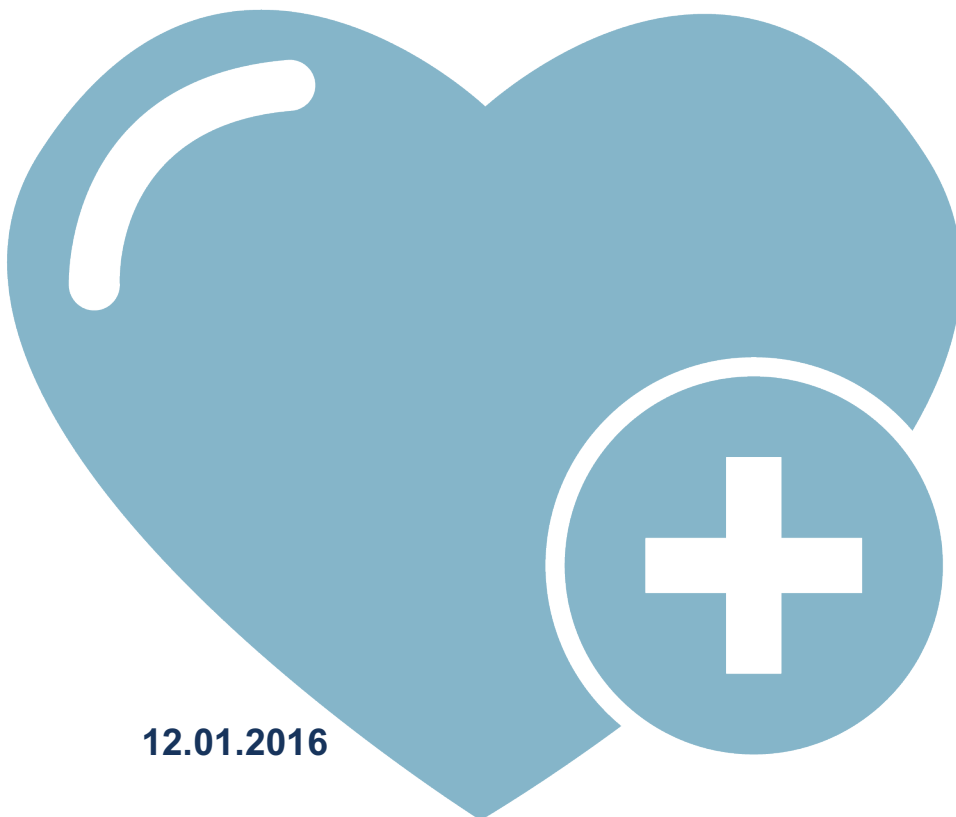
# Grants Working Group Public Review Summary

Phase 2b Clinical Study of Safety and Efficacy of Intravitreal Injection of Retinal Progenitor Cells for Treatment of Retinitis Pigmentosa

Application Number: CLIN2-09698

Review Date: November 29, 2016

Clinical Trial Stage Project Proposal (CLIN2)



12.01.2016



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Summary

# Phase 2b Clinical Study of Safety and Efficacy of Intravitreal Injection of Retinal Progenitor Cells for Treatment of Retinitis Pigmentosa

**APPLICATION NUMBER: CLIN2-09698**

**REVIEW DATE: November 29, 2016**

**PROGRAM ANNOUNCEMENT: CLIN2 Clinical Trial Stage Projects**

## Therapeutic Candidate

Allogeneic human retinal progenitor cells (hRPC)

## Indication

Retinitis Pigmentosa (RP)

## Therapeutic Mechanism

The cells are intended to remain suspended in the vitreous cavity of the eye and exert a beneficial neurotrophic effect on the degenerating retina.

## Unmet Medical Need

RP is an incurable orphan disease. There are no treatments currently available other than a retinal chip for very end stage patients. To date, there is nothing that will restore sight or slow the progression of vision loss in RP. Achieving any measurable benefits would be groundbreaking.

## Project Objective

Phase 2 trial completed

## Major Proposed Activities

Enrollment of patients in a Phase 2b clinical trial, along with patient follow up and collection of all clinical outcome measures.

## Funds Requested

\$ 8,295,750 (\$5,530,501 Co-funding)

## Recommendation

Score: 1

Votes for Score 1 = 11 GWG members

Votes for Score 2 = 4 GWG members

Votes for Score 3 = 0 GWG members

- 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.



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Public Review  
Summary

## Review Overview

The proposed treatment approach holds the potential to address a clear and urgent unmet medical need, improve the standard of care, and offer a strong value proposition for this patient population. Further, the investigators leading this study are exceptional and have proposed a well-designed trial to generate useful data that will further inform clinical development of this treatment. Although reviewers expressed minor concerns regarding the trial design and did not find the clinical efficacy data from the Phase 1/2 study to be overwhelmingly compelling, they did think the existing clinical data supports moving forward with a proof of concept study. Therefore, reviewers recommended this project for funding based on its overall potential.

## Review Summary

### Does the project hold the necessary significance and potential for impact?

#### a) Consider whether the proposed therapy fulfills an unmet medical need.

- The proposed patient population represents an urgent unmet medical need, and the proposed treatment has potential to fulfill that unmet medical need.

#### b) Consider whether the approach is likely to provide an improvement over the standard of care for the intended patient population.

- If successfully developed, the proposed treatment would provide an improvement to the standard of care for this patient population.

#### c) Consider whether the proposed therapeutic offers a sufficient, impactful, and practical value proposition for patients and/or health care providers.

- The route of delivery is simple and requires only topical anesthesia with no immunosuppression. This should result in lower treatment cost and the therapy being more broadly available.
- This treatment offers a sufficient, impactful, and practical value proposition for patients and healthcare providers, especially if a single or infrequent injections are required for therapeutic benefit.

### Is the rationale sound?

#### a) Consider whether the proposed project is based on a sound scientific and/or clinical rationale, and whether it is supported by the body of available data.

- The risk-benefit profile for the proposed project is favorable.
- The applicant provided a solid rationale that immunosuppressive drugs will not be required, and the clinical data supports that rationale.
- While reviewers did not find the efficacy data from the Phase 1/2 study overly compelling, they thought the safety data was encouraging and, overall, thought the clinical data supported moving forward with the proposed clinical trial.
- The investigator does not have a good understanding of the mechanism of action (MOA) of the product. However, it is not necessary at this stage to fully understand MOA, and the proposed project should generate good data that will inform MOA moving forward.
- Reviewers did not think data from the Phase 1/2 study demonstrated a clear dose response, and the rationale for dose selection in the proposed trial was not well described in the application.



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AGENCY

Public Review  
Summary

**b) Consider whether the data supports the continued development of the therapeutic candidate at this stage.**

- Reviewers thought the clinical data supported continued development of this treatment.
- With this type of product, there is always an issue assessing and demonstrating comparability of the product from lot to lot. A solid comparability protocol is needed for pivotal studies and commercialization. The applicant should focus on developing this before completion of the proposed project.

**Is the project well planned and designed?**

**a) Consider whether the project is appropriately planned and designed to meet the objective of the program announcement and achieve meaningful outcomes to support further development of the therapeutic candidate.**

- Reviewers found the trial design appropriate to enable identification of a clear efficacy signal.
- The trial is appropriately powered and proposes appropriate endpoints to allow the investigators to learn a great deal from the trial and to set the stage for a subsequent pivotal study.
- Reviewers thought the applicant should consider adding a third arm to the trial to test a second dose of the product given that a clear dose signal was not achieved in the preceding trial.
- Reviewers expressed some concerns regarding the proposed primary endpoint, as it is not a validated endpoint and validation of a new endpoint in this patient population may be challenging. However, reviewers agreed with the applicant that visual acuity is not an informative endpoint for this patient population, and that the proposed primary endpoint may be appropriate for a proof of concept study.
- The inclusion of a large number of secondary endpoints measuring function alleviated reviewer concerns regarding the primary endpoint. Reviewers noted that the applicant will need to carefully evaluate outcomes and work with FDA to identify an approvable endpoint that measures function as opposed to visual acuity. An approvable endpoint might end up being a composite endpoint.
- Reviewers did not think the applicant's assumptions regarding the number of patients in the control arm that would drop out from the study were realistic.

**b) Consider whether this is a well-constructed, quality program.**

- This is a well-constructed high quality program.

**c) Consider whether the project plan and timeline demonstrate an urgency that is commensurate with CIRM's mission.**

- The project plan and timeline demonstrate an urgency that is commensurate with CIRM's mission.

**Is the project feasible?**

**a) Consider whether the intended objectives are likely to be achieved within the proposed timeline.**

- Reviewers thought it likely that the intended objectives will be achieved within the proposed timelines.
- This team includes key opinion leaders in the field of clinical trial work for the



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AGENCY

Public Review  
Summary

retina, and reviewers were confident in their ability to carry out the proposed work.

- Reviewers noted that, based on enrollment rate from the Phase 1/2 trial, enrollment appears feasible.

**b) Consider whether the proposed team is appropriately qualified and staffed and whether the team has access to all the necessary resources to conduct the proposed activities.**

- The applicant has a strong track record and the team is strong.

**c) Consider whether the team has a viable contingency plan to manage risks and delays.**

- Risk and mitigation strategies are discussed in the application and are sufficient.



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Public Review  
Summary

## CIRM Recommendation to Application Review Subcommittee

The CIRM recommendation to the Application Review Subcommittee is considered after the GWG review and did not affect the GWG outcome or summary. This section will be posted publicly.

**RECOMMENDATION:** Fund (CIRM concurs with the GWG recommendation).