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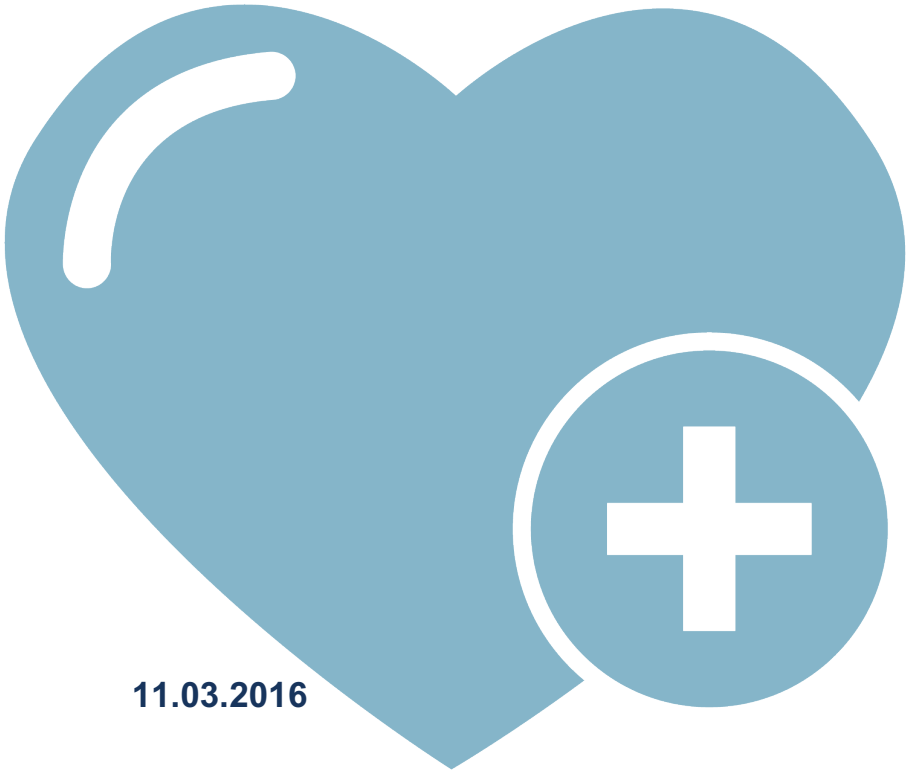
Grants Working Group Public Review Summary

A Phase 1b/2 Trial of the Anti-CD47 Antibody Hu5F9-G4 in Combination with Cetuximab in Patients with Solid Tumors and Advanced Colorectal Cancer

Application Number: CLIN2-09577	Review Date: October 25, 2016

Clinical Trial Stage Project Proposal (CLIN2)



11.03.2016

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A Phase 1b/2 Trial of the Anti-CD47 Antibody Hu5F9-G4 in Combination with Cetuximab in Patients with Solid Tumors and Advanced Colorectal Cancer

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PROGRAM ANNOUNCEMENT: CLIN2 Clinical Trial Stage Projects

Therapeutic Candidate

The treatment is a humanized monoclonal antibody, Hu5F9-G4, in combination with cetuximab.

Indication

Patients with advanced colon cancer that have a genetic mutation in the KRAS gene and those without the KRAS genetic mutation.

Unmet Medical Need

Colon cancer is the second leading cause of US cancer deaths. Only about 10% of patients survive past 5 years. Those who do not respond to initial therapy, and those with a KRAS gene mutation, have very limited treatment options. This treatment has the potential to provide benefit to these patients.

Major Proposed Activities

Determine the safety and tolerability of Hu5F9-G4 in combination with cetuximab in cancer patients

Determine the optimal dose regimen of Hu5F9-G4 when given with cetuximab in cancer patients

Determine the therapeutic efficacy of Hu5F9-G4 in combination with cetuximab in colon cancer patients

Funds Requested

$ 10,234,048 ($6,822,698 Co-funding)

Recommendation

Score: 1

Votes for Score 1 = 14 GWG members

Votes for Score 2 = 0 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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Review Overview

Reviewers thought this treatment approach could improve the standard of care in the proposed patient population and that the application described strong data to support the preclinical and clinical rationale and a well-designed, feasible, and meaningful clinical trial. Reviewers, therefore, recommended this proposal for funding.

Review Summary

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

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

- There is a major unmet medical need in the proposed patient population. While other treatments exist, survival is poor.
- The data supports that the proposed treatment holds potential to fulfill the unmet medical need.

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

- This is a promising treatment approach that, if realized, could easily exceed the standard of care for the intended patient population, possibly with reduced systemic toxicity, as compared to other treatments available.

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

- The proposed treatment offers a sufficient, impactful, and practical value proposition for patients and health care providers, though it is too early in clinical development to predict success.

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.

- There is good preclinical evidence for synergy of the two agents that, if duplicated in patients, would provide a substantial improvement in patient outcomes for both KRAS wild type and mutant colon cancer patients.
- The scientific rationale for targeting of CD47 in this patient population is sound.
- There is evidence of a pharmacodyanmic effect in the ongoing clinical studies.

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

- The clinical safety and efficacy data from the ongoing clinical trials are highly supportive of continued development of this therapeutic candidate.

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.

- The project is well planned and designed, implementing a standard and

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thoughtful development path.

- The clinical protocol is well-thought out and relies on well-established designs and principles.
- The design of the trial itself is fine, but the decision making process is suboptimal. It is critical to include clear go/no go criteria for the second phase of the trial and for the data to be evaluated by an independent, objective third party for a decision as it is unclear what toxicities are expected given the proposed new mechanism of action and use of a combination therapy.
- There are opportunities to elucidate the mechanism of action and demonstrate whether targeting of cancer stem cells and/or debulking of the tumor is occurring.

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

- This is a well-constructed and 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 both demonstrate an urgency that is commensurate with CIRM's mission but not unreasonable as the applicant moves quickly to push clinical development forward.
- There is some overlap of clinical studies that is reasonable and demonstrates urgency, but that may or may not be accepted by FDA. However, reviewers thought the applicant has a reasonable justification to move forward safely.

Is the project feasible?

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

- The timelines are ambitious, but reviewers thought the intended objectives are likely to be achieved.
- The applicant will need to monitor enrollment closely and actively in order for timelines to be met.
- Enrollment has clearly been given a lot of thought, and active mitigation strategies are in place. Reviewers did wonder why the applicant is not pursuing some of those strategies at the onset of the trial rather than waiting for enrollment to lag to implement the strategies.

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 team is well-qualified and staffed and has access to all necessary resources to conduct the proposed activities.

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

- Contingency plans are viable and appropriate to manage risks and delays. Costs are a bit high, but will be borne by the applicant.

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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).