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CALIFORNIA'S STEM CELL AGENCY

Grants Working Group Public Review Summary

Create Clinical-Grade CIRM Translating Center to Leverage Stem Cell Treatment Development and Manufacturing Innovations for Progressing to the Clinic

Application Number: INFR2-09233	Review Date: October 4, 2016

Partnering Opportunity to Create a CIRM Translating Center (INFR2)

REVIEW SUMMARY

10.10.16

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Create Clinical-Grade CIRM Translating Center to Leverage Stem Cell Treatment Development and Manufacturing Innovations for Progressing to the Clinic

APPLICATION NUMBER: INFR2-09233

REVIEW DATE: October 4, 2016

REQUEST FOR APPLICATIONS: INFR2 Partnering Opportunity to Create a CIRM Translating Center

Summary

We have built a proprietary groundbreaking technology enabling large-scale production of high quality clinical-grade human pluripotent stem cell (hPSC) lines and high efficient direct conversion of hPSC by small molecule induction into lineage-committed human therapeutic products. The major goals of this project are to establish CIRM Translating Center to leverage proprietary technology innovations to provide shared clinical-grade translating capacities/assets. The proposed center will utilize the proprietary technology to provide therapeutically-viable and clinically-useful platforms for preclinical IND-enabling research and cGMP-compatible processes, design and execute a cost-effective CT product development and manufacturing strategy, and seamlessly integrate with CIRM Accelerating Center to operate through providing core services support services to ensure CIRM projects access to cutting-edge translational capabilities and successfully move through IND-enabling studies to IND filing and clinical trials.

Funds Requested

$14,917,500

Recommendation

Score: <60

Recommended = 85-100

Not Recommended = 1-84

For programs for which only one application will be funded, the application receiving the highest average scientific score of 85 or above will be deemed to be the GWG's recommendation for funding. If no application receives a score of 85 or above, all applicants shall have the opportunity to submit an amended application, based on the summary of the GWG review, to address reviewer concerns. The GWG shall conduct a supplemental review of the amended applications and re-score the applications using the same range (1-100). The application that receives the highest average score of 85 or above shall be deemed to be the application recommended for funding by the GWG.

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Review Overview

The application did not focus on how the objectives of the CIRM request for applications (RFA) (i.e., establishing a stem cell specific preclinical contract research organization that would offer core services for a variety of cell products and accelerate progression from the late preclinical stage to IND filing and conduct of clinical trials) would be achieved. Instead, the proposal focused on how the applicant's proprietary technology might advance cell therapy development. Further the applicant institution does not appear to have adequate resources to fulfill the requirements of the CIRM Translating Center. Therefore, this application was not recommended for funding.

Review Summary

Does the proposed center hold the necessary significance and potential for impact?

a) Consider whether the proposed center is likely to accelerate the progression of stem cell projects from the late preclinical stage to IND filing and conduct of clinical trials.

- The proposal is more focused on developing a single technology than establishing the envisioned CIRM Translating Center that would broadly support stem cell therapy preclinical development.
- The entire proposal is based upon the efforts of a single person, the center director (CD), and a single technology. It is therefore unlikely to accelerate progression of a large number of products using variable technologies from the late preclinical stage to IND filing and the conduct of clinical trials.

b) Consider whether the proposed center offers a sufficient, impactful, and practical value proposition for preclinical researchers, patients, and/or healthcare providers by increasing the speed and quality of preclinical stage stem cell projects.

- The applicant suggests that access to the proprietary technology is the core of the value proposition for the proposed center. Given that the technology is still in development, the extent of its impact remains to be seen, and reviewers were not convinced that access to a single technology offers a sufficient value proposition for the CIRM Translating Center as it limits its scope.
- The CD also serves as the CEO of a for-profit company that is raising funds around the same intellectual property described in this application. If the value proposition lies in exclusive access to the proprietary technology, this detracts from the value proposition and would be a conflict of interest. Further, freedom to operate is not well described nor is the claim to exclusivity, which further detracts from the described value proposition.

Has the applicant developed a plan designed to successfully establish and operationalize the center?

a) Consider whether the center is likely to seamlessly integrate with the CIRM Accelerating Center to accelerate CIRM–funded stem cell projects.

- A detailed plan to integrate with the CIRM Accelerating Center was not described in the proposal, though it was stated that the applicant organization

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intended to do so.

b) Consider whether the operation of the center is appropriately planned and designed to provide meaningful, accelerating, and impactful resources (including the required core services) for the conduct of stem cell preclinical research.

- The applicant did not estimate capacity nor the number of clients that could be supported and did not provide a well described plan to provide meaningful, accelerating, and impactful resources for the conduct of stem cell preclinical research.

c) Consider whether the project plan and timeline for establishing the center demonstrate an urgency that is commensurate with CIRM's mission?

- The applicant did not sufficiently described the plan to accommodate the expected number of projects in the CIRM pipeline. Therefore, the project plan is not commensurate with CIRM's mission.
- The timeline includes a significant delay in getting all aspects of the CIRM Translating Center operational, which is not commensurate with CIRM's mission.

d) Consider whether there is an effective plan proposed to provide specialized services that are unique to diverse stem cell and gene modified cell treatments.

- The described plan does not provide specialized services for sufficiently diverse stem cell and gene modified stem cell treatments.

e) Consider whether the business and sustainability plan is appropriate to serve CIRM projects with competitive pricing while ensuring sustainability of the center beyond five years.

- Sustainability is unlikely as the applicant institution does not have any current employees beyond the CD, a facility, or current operations and the applicant did not described resources outside of those requested from CIRM or provide an adequate plan to develop such resources.
- The proposed discounts are not described well enough to determine whether there is a competitive fee plan.

Is the project feasible?

a) Consider whether the proposed center is likely to be established within the proposed timeline.

- Given the lack of resources and experience of the applicant institution it is unlikely that the proposed center can be established within proposed timelines.

b) Consider whether the proposed team appropriately qualified and staffed.

- The proposed center appears currently to have only a single employee (the CD) and it is not clear that this employee's experience is adequate to manage all aspects of the CIRM Translating Center in all disease and product areas.
- It is not clear that the CD has direct, hands-on experience interacting with FDA, conducting IND-enabling preclinical studies, interacting with CRO and CMO organizations, etc.
- The application states the CD will hire a limited number of employees, none of

whom are named, and it is not likely that this will be sufficient to support all required core services.

- One supporting letter from a collaborator references returning the proprietary technology to the collaborators institution. It is unclear how this furthers achievement of the RFA objectives or supports feasibility of the proposed center.

c) Consider whether the team has access to all the necessary resources, including necessary collaborations and partnerships, and whether their track record support feasibility to establish, equip, operate, and maintain the center.

- The proposed center appears currently to have only a single employee, inadequate facilities, insufficient track record, and limited resources, which makes establishing, equipping, and operating the center within a reasonable timeframe challenging.

d) Consider whether the center will have the capability and resources to provide the required core services.

- The physical facilities are not well described and most employees are to be determined making evaluation of the capabilities of the center challenging.
- The expected capacity of the center is not well described in the application, but it is unlikely that a center with so few resources will be able to provide the required core services to a large and diverse clientele.

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

- The contingency plan was poorly constructed and described and difficult to understand.
- It did not appear that the applicant has a good grasp of potential risks and delays.

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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: Do Not Fund (CIRM concurs with the GWG recommendation).