PUBLIC COMMENTS IN SUPPORT OF "TRAN1-12388 Targeting stromal progenitors to prevent the development of heart failure after myocardial infarction"

Heart Failure (HF) is currently a global epidemic with 20 million people suffering from heart failure worldwide with 7 million people in the US alone. Almost 700,000 patients are diagnosed annually in the United States and once a diagnosis of heart failure is made, the 5 year survival on current medical regimens is approximately 50%, a survival rate that is significantly worse than many cancers. California itself has an enormous burden of HF and in contrast to declining deaths from heart disease nationally, mortality secondary to HF has increased in California.

Despite the burgeoning importance of HF, no therapeutic innovations have been made for HF over the last 2-3 decades. In this regard, CIRM does not have a strong portfolio of TRAN grants that are aimed for the therapy of heart failure.

"**TRAN 12388 Targeting stromal progenitors to prevent the development of heart failure after myocardial infarction**" is a proposal which provides an entirely new therapeutic approach, a monoclonal antibody against a specific molecular target in HF. The mechanism of action is entirely novel as it augments the way the heart heals (tissue repair) after heart attacks or other forms of heart disease owing to genetic defects or other chronic insults. **Currently there is not a single drug that enhances tissue repair as a mechanism to avoid heart failure**.

This monoclonal antibody is already **humanized** and thus the quick development of this antibody (as proposed in the application) could represent a **game changer** in the treatment of heart failure. Reviewers agreed on the "**high relevance of the study", "unmet HF needs for the residents of California"** and **"potential for the application of this therapy across a broad range of heart failure causes".** All reviewers agreed that there was **enormous potential for rapid acceleration to first in human therapies**.

40% of the reviewers thought that the grant should get funded with issuance of accompanying minority report which emphasized the "**enormous benefit the treatment could bring to underserved communities disproportionately impacted by heart failure in California"**. Critiques were minor and related to aspects of study design, broadening the applications of this therapeutic agent and streamlining the large animal studies.

Moreover, the **scientific team is diverse and inclusive** comprising individuals from **lower socio economic and underserved minorities** who would participate in the development of a therapeutic agent that would benefit the very communities they ca
me from.

Overall, TRAN12388 **fills an empty niche in the CIRM portfolio of TRAN therapeutic grants for the treatment of HF**. While most funded TRAN grants addresses various cancers, TRAN12388 with a therapeutic agent (humanized monoclonal antibody) ready for large scale manufacturing and acceleration to first in human use, is potentially poised to be a game changer for the treatment of heart failure, targeting a new mechanism of tissue repair, that has never been used previously.

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May 12, 2021