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February 11, 2019

John Thomas, PhD, JD
Chair, Governing Board of the CIRM (ICOC)
210 King Street
San Francisco, CA 94107

Re: CLIN2-11431: A monoclonal antibody that depletes blood stem cells and enables chemotherapy free transplants

Dear Dr. Thomas,

I am writing in vigorous and enthusiastic support of the research study being performed at Stanford and UCSF to develop a non-chemotherapy based bone marrow conditioning regimen using antibody to c*kit*. I am a pediatric bone marrow transplant physician at UCLA and perform research to develop new methods to treat genetic blood cells diseases by autologous hematopoietic stem cells transplantation using gene therapy techniques to replace or repair the underlying genetic cause. From earlier studies, we determined that it is necessary to apply some degree of marrow cytoreductive conditioning to allow re-engraftment of the *ex vivo* edited stem cells. For diseases such as SCID, where there is a selective expansion of functional lymphocytes from a small number of gene corrected stem cells, a “relatively” low amount of chemotherapy may be given. However, this exposure of infants and children to even low dosages of toxic, potentially mutagenic agents such as busulfan, melphalan etc probably poses the largest component of risk of the treatment. For other disorders where there is little or no selective advantage for gene-corrected stem cells or their blood cell products, such as sickle cell disease and chronic granulomatous disease, even higher amounts of chemotherapy have been needed to ensure sufficient engraftment of the corrected stem cells to modify the diseases. This conditioning leads to severe neutropenia, thrombocytopenia, infection risks, mucositis, hair loss, etc, and also potential life-long risks of malignancies, infertility, etc.

Thus, I have long considered the development of alternative methods of cytoreduction that avoid chemotherapy to be one of the highest research priorities for the field. I have followed the work using antibody to c*kit* since first published by the Weissman group and appreciate the logic and great potential. In fact, I serve as a Clinical Advisory Panel member for their CIRM-funded project as I am eager to provide whatever assistance or guidance I may for their development of this critical new technology. I am very excited and impressed with their results to date in the low dose cohort and am quite interested to hear the results they will be presenting at the ASBMT/TCT meeting on their next patient cohort.

Therefore, I strongly urge CIRM to continue to provide support to this project as needed for the most rapid developemtn. It truly has transformative potential for the field and for patients. It would be a great credit to CIRM to have enabled this scientific achievement and would be an important component of CIRM fulfilling its mission to provide safer and better stem cell therapies for patients in need.

Thank you for your consideration,

Sincerely,

Donald B. Kohn, M.D.
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