November 17, 2021

California Institute for Regenerative Medicine (CIRM)
1999 Harrison Street,
Suite 1650
Oakland, CA
94612

RE: Application Review Subcommittee Meeting for TRAN1-12889 Application

Dear Members of the Independent Citizens Oversight Committee,

On behalf of Ray Therapeutics, we are grateful to the reviewers for the excellent feedback they provided with respect to our TRAN1 grant application 12889, "Optogenetic therapy for treating retinitis pigmentosa and other IRDs."

It was extremely exciting and encouraging for us to see unanimous votes in favor of the scientific rationale and significance for our optogenetics program for treating patients who have lost most or all of their vision from devastating inherited retinal diseases like retinitis pigmentosa. While there are promising cell and gene therapy programs in the clinic for these indications (in part thanks to CIRM), our approach addresses those patients who may be left behind, either because they are too far along in the disease, or because they do not have one of the targeted genetic mutations. Restoration of vision represents an important and high unmet need, and we would profoundly appreciate CIRM's support to get our therapy, Ray-001, to patients.

In consideration of the updates and responses we provide below, we ask the ICOC members to consider approving our application even though our score of 80 was slightly below the required threshold of 85, primarily due to CMC development timelines. Kindly note that the scores ranged from 80 to 90, with not a single score lower than 80.

We agree entirely with the reviewers' comments that our original timelines were too ambitious. This was driven by our desire to get our therapy to patients as quickly as possible. I am pleased to report that over the past several months since we wrote and submitted the grant, we achieved a major milestone by selecting our manufacturing partner (CDMO), upon completion of a rigorous diligence process. We accelerated meetings with our CDMO (including an in-person technical and quality site visit) to pressure test the manufacturing plan, including process optimization and analytical capabilities. This information, in conjunction with feedback from additional gene therapy CMC experts that we brought on, provided the guidance needed to refine our timeline estimates and risk management planning, which again, is consistent with the reviewers' remarks. To mitigate issues that may cause delays, we have designed the development work packages to include additional studies and activities that will optimize production, purification and release of clinical supplies. While our budget remains the same, our project timelines have been extended but are still well within the 30-month window of the grant.

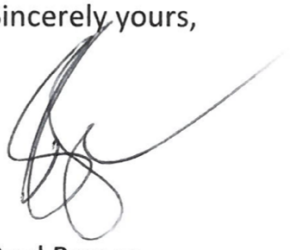
Although the emphasis of the reviewers' feedback was on CMC timelines, other valuable comments were made, with which we agree. For example, the immunogenicity of our selected capsid will be carefully studied and considered in our planned non-GLP studies and during the GLP phase of development. We have engaged some of the country's top thought leaders and subject experts who are scientifically and technically equipped to help us manage these important topics.

Some of my team members and I will be attending the subcommittee meeting on November 23rd to reinforce the merits of Ray-001 and answer any questions you may have. I have faith that our appeal will be heard, and I am hopeful that we will partner with CIRM to create a robust program that will lead to a successful preIND meeting with the FDA and beyond.

My personal experience over the last decade has been to appreciate and follow the collective advice of CIRM's staff, reviewers and advisors. I hope to have the same opportunity to take this collaborative approach with CIRM in managing the Ray Therapeutics program to bring Ray-001 to the many diverse blind patients of California, who are desperately awaiting treatment. I ask that you approve funding for our application at the subcommittee meeting. For these patients, time is critical.

As always, I have nothing but gratitude for CIRM, and all that CIRM does for patients in the state of California and worldwide.

Sincerely yours,



Paul Bresge
CEO, Ray Therapeutics