From: Rich Horgan <rich@curerd.org>
Date: Thursday, March 28, 2024 at 12:22 PM
To: Claudette Mandac <cmandac@cirm.ca.gov>
Subject: Re: [EXT] Public comment time for tomorrows board meeting

Hi Claudette

This is in regards to the item concerning clin dev projects and the future plans for allowing applications:

To the CIRM ICOC,

I am the founder & CEO of Cure Rare Disease (CRD), a non-profit biotechnology company focused on the development of advanced modalities for ultra-rare diseases. Many of the diseases we seek to treat fall into the bucket of non-commercializable diseases.The mission of CRD is incredibly personal to me as I had a younger brother, Terry, who was impacted by an ultra-rare disease for which there was no cure. I formed a collaboration of researchers and clinicians to fight back given the lack of industry interest. Throughout the journey, thousands of families, patients, researchers and advocates reached out to me to express a unifying sentiment that there is no path for ultra-rare disease patients and they found, and continue to find, hope in our mission.

Regarding the situation facing CIRM of pausing Clin Dev grant applications, this action has very seriously impacted ultra-rare disease patients. Ultra-rare disease patients are generally people who are impacted by diseases for which there is insufficient population to warrant or enable commercial drug development given small populations and limited, if any, economic return expected and required by investors. Without commercial investment, there is limited to no monies available to advance drug development programs for ultra-rare disease patients. Increasingly given the lack of financing available to enable these programs, families, nonprofits and academic centers are teaming up and championing efforts to develop therapeutics for these populations.

While individual ultra-rare diseases represent few patients, the aggregate of ultra-rare disease patients represents millions of patients across America, many of whom call California home.

For Cure Rare Disease, we had prepared two applications for the Clin Dev 1 opportunity for two ultra-rare disease programs. When we discovered, at the 11th hour, the pause in the program, we communicated this to the families who are impacted by the diseases in question. One of those people is a patient with Limb girdle muscular dystrophy type 2i (LGMD2i), a neuromuscular disease that is characterized by a mutation of the FKRP gene leading to muscular degradation and ultimately leading to death. LGMD2i impacts about 1,000 Americans. Generally patients pass away due to cardiopulmonary related issues. There is no treatment or cure for LGMD2i. In 2021, we started a research partnership to

develop a next-generation gene replacement strategy that has since shown significant potential to improve the phenotype of LGMD2i animal models. In March 2024, we held our preIND meeting with the FDA and received positive affirmation about the planned preclinical and clinical program. The program is awaiting funding to begin manufacturing scale-up of the gene therapy and given the rare nature of the disease, CIRM was one of the only funding options. The intention of the CIRM Clin Dev 1 grant was to fund this and IND enabling toxicology prior to a Phase I clinical trial planned for 2H 2025. We are hopeful for LGMD2i patients that this may lend some benefit to combating the disease.

One patient in particular, Max, 23, has followed the development program closely over the last couple of years. When Max heard this news he was shattered. Max has no other option and now Max's program will be significantly delayed due to this decision by CIRM to pause funding. Max is in college and has a whole life ahead of him. Max may die from this delay. Unfortunately, Max is but one of thousands of stories all united by a lack of therapeutic options and now, a worsensed situation.

Prior to the decision to halt clin dev applications, CIRM was one of the very, very few beacons of light that ultra-rare disease patients and drug developers could look toward for the high level of funding necessary to advance a drug into the clinic - most notably, manufacturing and toxicology work streams which range from several hundred thousand dollars to millions of dollars for a drug campaign, even for an ultra-rare disease. With the recent decision to pause new applications, this has halted one of the only life lines that these patients and families have.

On behalf of the rare disease community, academic centers and others, I implore CIRM to immediately re-start accepting applications for programs that are intended to treat ultra-rare disease patients. This is very much so a life or death issue for the patients impacted and a months long delay is, and will continue to, cost lives unnecessarily. California must not leave behind ultra-rare disease patients who have already been left behind and neglected simply because of the rarity of their disease. Max should not die when technologies exist to try and stop the disease robbing them of life but is unable to be developed because the disease is not a profitable one.

Best,
Rich