Dear Members of the California Institute for Regenerative Medicine Governing Board,

On behalf of the Charlotte and Gwenyth Gray Foundation, the children and families affected by CLN6 Batten disease, and the many clinicians, scientists, advocates, and partners who have dedicated themselves to this effort, we respectfully ask you to reconsider the significance, readiness, and urgency of this program as you review the recommendations presented to the Board.

First and foremost, we would like to thank the reviewers for the time, expertise, and thoughtful consideration they devoted to our application. We understand the concerns that were raised regarding Chemistry, Manufacturing, and Controls (CMC) readiness, comparability testing, potency assay development, release testing, and the risks associated with transitioning manufacturing partners. Given the information available at the time of review, those concerns were understandable.

What we hope the Board will appreciate, however, is that the application represented a snapshot of a program that was actively evolving in real time.

During the review period, our team was simultaneously implementing FDA-requested manufacturing enhancements, completing analytical development activities, advancing clinical planning, and preparing for study execution. We realize this is the definition of "building the plane while flying it", however, the reality is that ultra-rare disease development often requires exactly that approach. Families facing a relentlessly progressive and fatal disease simply do not have the luxury of waiting for a perfectly linear development pathway.

Some reviewers questioned why we submitted the application before all CMC activities had been completed. The answer is both simple and deeply personal to the families we serve: because every month matters. Had we waited until every assay, every comparability exercise, and every analytical activity were fully complete before applying, we would have lost precious time for children whose disease does not pause while we work through development milestones. We made the decision to advance these activities in parallel because we believed the urgency facing these children warranted that approach. In hindsight, we understand why that created concern for reviewers. We listened carefully to that feedback and responded by doing exactly what was asked of us.

Today, the landscape looks very different. Since submission, all comparability testing has been completed. Potency assays have been completed, release testing has been completed, and additional analytical characterization has been completed. We have generated the data requested by reviewers and regulators alike, and we have completed every activity requested by the FDA—and then some—to ensure this program is positioned for safe and successful clinical execution.

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Simply put, the program that exists today is not the same program that was reviewed several months ago. The uncertainties that understandably concerned reviewers have been resolved, and the team stands ready to move forward.

We also believe it is important to understand the rationale behind our manufacturing transition, as it was a significant focus of the review.

This decision was not made out of convenience or preference. It was made because we reached a point where our previous manufacturing strategy could no longer support the needs of the CLN6 patient community. Through the transition to our current manufacturing approach, we have established a path capable of producing sufficient material ***for more than sixty patients***. For a disease community that has historically had little reason for hope, this represents a transformational step forward and creates the opportunity to impact far more children than was previously possible.

We were also encouraged by the feedback received during our recent Type C meeting with the U.S. Food and Drug Administration. What struck us most about that meeting was not simply the scientific discussion, but the agency's clear recognition of the urgency facing these children and families. The conversation was thoughtful, collaborative, and focused on identifying a responsible path forward. FDA carefully reviewed our manufacturing strategy, analytical plans, comparability package, and proposed clinical approach. We listened to their feedback, completed the requested work, and left the meeting with confidence that we have built a program capable of moving forward responsibly and safely.

Today, if funding were available, we would be prepared to initiate this study immediately.

In many ways, that is what makes this moment so difficult. For years, the barriers standing between these children and a clinical trial were scientific, manufacturing, and regulatory in nature. Today, those barriers have been overcome. The manufacturing challenges have been solved. The FDA provided a clear path forward, and the study team stands ready to initiate the trial.The only remaining barrier is funding.

We fully appreciate the responsibility CIRM carries in stewarding limited resources and evaluating many deserving programs. We also recognize that funding decisions are rarely simple. However, should the Board believe there is a path forward involving partial funding, milestone-based funding, or another collaborative funding approach, we would enthusiastically welcome that conversation. The Charlotte and Gwenyth Gray Foundation remains fully committed to raising additional funds and doing whatever is necessary to bring this study to children as quickly as possible. Our goal is not simply to secure funding; our goal is to ensure that this trial moves forward before more time is lost for more children, more families.

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While much of the review understandably focused on scientific and operational risk, we respectfully ask the Board to also consider the human reality behind this application.

CLN6 Batten disease is a fatal pediatric neurodegenerative disorder. Children gradually lose the ability to walk, speak, learn, communicate, and engage with the people they love. Families do not experience delays in quarters, fiscal years, or grant cycles. They experience delays in birthdays that pass with new losses, milestones that are never reached, and abilities that, once lost, can never be recovered.

For these families, a funding decision deferred until 2027 is not simply a delay in a development program. It is another year of disease progression for children whose time is already painfully limited. That reality weighs heavily on all of us.

It is also important for the Board to understand who is standing behind this program. The Charlotte and Gwenyth Gray Foundation is not a pharmaceutical company, a venture-backed biotechnology organization, or an academic research institution with access to substantial capital. We are a small non-profit foundation created by parents determined to find a path forward for their children and others affected by this devastating disease. More than a decade ago, through extraordinary determination and the generosity of a community that rallied around these children, the Foundation successfully raised more than $8 million to fund the first clinical trial. While that effort helped demonstrate what was possible, it also revealed just how difficult it is for rare disease families to repeatedly shoulder the burden of funding therapy development on their own. Raising those funds once required years of work and the support of countless donors. Recreating that effort a second time in today's funding environment has proven extraordinarily challenging.

That reality was one of the reasons we brought this program to California. We believe in CIRM's mission and its commitment to helping advance transformative therapies for patients with the greatest unmet medical need. We believe there was a path to partnership that could help bridge the gap between what families can accomplish on their own and what is required to bring a promising therapy to children who cannot afford to wait.

The Charlotte and Gwenyth Gray Foundation was created because one family refused to accept that there was nothing that could be done. What began as a mother's determination to save her daughters has grown into a community of families, scientists, clinicians, and advocates united by a shared belief that children with CLN6 Batten disease deserve more than acceptance of the status quo.

Over the years, this community has navigated manufacturing setbacks, regulatory hurdles, scientific uncertainty, and financial challenges. At every turn, they have continued forward because the need remains urgent and the potential impact remains profound.

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We are not asking the Board to set aside scientific rigor. In fact, we believe the work completed since submission demonstrates our commitment to exactly that standard.

If given the opportunity, we are prepared to begin this trial this year. We are committed to doing everything within our power—including continuing to raise funds alongside our partners—to ensure that this potential therapy reaches the children who need it as quickly as possible.

California has long been a leader in advancing transformative therapies for patients with the greatest unmet medical need. We believe this program reflects that mission and embodies the very purpose for which CIRM was created.

Thank you for your consideration, your service, and your commitment to patients and families who so often have nowhere else to turn. For children with CLN6 Batten disease, time is not simply a development milestone: it is the one thing they can never get back.

With gratitude and respect,

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