



Therapeutics for
Huntington's disease

January 25, 2025

The CIRM Independent Citizens' Oversight Committee

Via attachment to email

Re: CLIN2-17081

Dear CIRM Independent Citizens' Oversight Committee:

I am writing to express the support of CHDI Foundation for the REGEN4HD Phase 1b/2a clinical trial (CLIN2-17081) that has received an IND from the FDA.

Huntington's disease (HD) is an excellent model for studying regenerative medicine in neurological diseases. Its late onset and slow progression provide a time window to test cell transplantation engraftment after neurodegeneration but before symptoms become so debilitating restoration of function is unlikely. As an autosomal dominant disorder caused by a single known mutation in the HTT gene, the identification of cases is unambiguous. I believe a cell-based treatment for HD is exactly the type of medicine CIRM was created to enable.

Current small molecule and biologic therapeutic strategies focus on lowering the product of the mutant gene or modulating the somatic instability of the mutant CAG tract. For regulatory and other reasons, for the foreseeable future those interventions will be evaluated in people who have already suffered significant neurodegeneration. Whether or not and at what point those approaches might arrest the progression of the disease is currently unknown. For the foreseeable future there will be *at least* an important role for a complementary regenerative strategy.

Therefore, in the interest of having a comprehensive therapeutic approach to treating HD it is important to the community that these efforts proceed in parallel. I strongly urge you to give due consideration to funding CLIN2-17081.

CHDI Foundation is a privately funded, not-for-profit biomedical research organization devoted to Huntington's disease. Our mission is to enable the development of drugs that will slow the progression of HD and provide meaningful clinical benefit to patients as quickly as possible. To achieve this CHDI manages a diverse portfolio of research projects through a novel virtual model that encourages scientific collaboration to more directly connect academic research, drug

discovery and clinical development. Our activities extend from exploratory biology to the identification and validation of therapeutic targets, and from drug discovery and development to clinical studies and trials. CHDI employs more than 120 people, half of whom are scientists or clinician/scientists, and provides financial support for more than 1,000 FTEs at academic research centers, contract research organizations and clinical study sites around the world. For more information about CHDI's activities please see our websites, www.chdifoundation.org, www.HdinHD.org, and www.Enroll-HD.org. CHDI Management is the company that manages the scientific activities of CHDI Foundation.

Thank you for your consideration of this important effort,

A handwritten signature in blue ink that reads "Robi Blumenstein". The signature is written in a cursive, slightly slanted style.