BROAD INSTITUTE

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Subject: **Community Statement for Patient Advocacy Organizations**

April 22, 2026

Dear Prion Disease Community,

We have initiated a first-in-human clinical trial to evaluate an investigational drug called PrP-siRNA in patients diagnosed with prion disease. PrP-siRNA is a divalent siRNA drug administered intrathecally, meaning, by a lumbar puncture or spinal tap, designed to lower the amount of PrP produced in the brain. PrP is the protein that causes prion disease.

PrP-siRNA was developed as a collaboration between the Broad Institute and UMass Medical School, funded by National Institutes of Health grants and by donations from members of the prion disease community to the Broad Institute and to Prion Alliance. This clinical trial is being funded by the National Institutes of Health through the NeuroNEXT program.

The goal of this clinical trial is to evaluate the safety and tolerability of a single dose of PrP-siRNA, as well as to determine whether this single dose of PrP-siRNA lowers the amount of PrP detectable in spinal fluid. The results of this trial will help to inform the possible further development of PrP-siRNA and advancement into future clinical trials. Like many drug trials, this trial has pauses built in for safety assessments; as such, it will not always be possible to enroll patients in the drug treatment arm. The study also includes an observational arm, in which patients can volunteer to contribute to research without receiving study drug. At times when enrollment in the treatment arm is paused, eligible participants will be offered an opportunity to participate in the observational arm.

Trial details including inclusion criteria and study site locations are available and will be updated over time on the study's ClinicalTrials.gov listing: https://clinicaltrials.gov/study/NCT07444580

Patients interested in enrolling should discuss with their own physician and should contact the individual study sites and speak with a coordinator there about screening for study eligibility. Enrollment in the study is the responsibility of the site investigator. We as the sponsor are not directly involved in enrollment decisions and are not able to intervene or adjudicate on behalf of individual volunteers interested in enrolling.

CJD Foundation (cjdfoundation.org) and CJD International Support Alliance (cjdisa.com) are helpful additional resources for education, support, and conversations about prion disease.

We are grateful to patients and families for their participation in research. We plan to broadly share data and learnings from this study in order to help catalyze drug development in prion disease and inform the design of future clinical trials. **See below for frequently asked questions.**

Sincerely,

Eric Minikel
Director, Prion Therapeutic Science
Broad Institute of MIT and Harvard

PRiSM
PrP-targeting siRNA Safety & Mechanism Study

NeuroNEXT

Frequently Asked Questions:

Q. Are pre-symptomatic at-risk individuals eligible?

A. Not at this time.

Q. Can patients receive PrP-siRNA outside of this clinical trial?

A. No. This is a first-in-human trial of a drug with no prior human safety data. U.S. Food and Drug Administration regulations do not permit us to offer an Expanded Access program nor to support Right to Try requests.

Q. Can patients receive PrP-siRNA outside of the United States?

A. No. This study is funded by the National Institutes of Health, which supports us to offer trial sites in the United States.

Q. How long will the trial continue?

A. The National Institutes of Health grant supporting the study has a duration of 4 years. If the study enrolls rapidly and is not subject to unanticipated pauses, it may complete sooner. The end date will be kept updated on ClinicalTrials.gov at the link provided above. Analysis of samples and data from the trial will take some time. We will make every effort to share results with the community at the earliest practical moment.

Q. Will participants receive drug again after the study ends?

A. Not at this time. The U.S. Food and Drug Administration has cleared us to provide only a single dose to each participant.

Q. If the trial is successful, what is the next step?

A. We hope that successful trial data will make it possible to advance PrP-siRNA to a next stage clinical trial in a larger number of patients. The future of PrP-siRNA will depend on many variables including the data from this trial, the results of additional animal studies being conducted on PrP-siRNA, and the ability to secure funding for future stages of clinical development.