

Subject: **PRiSM trial pre-symptomatic arm now open**

Community Statement for Patient Advocacy Organizations

October 14, 2026

Dear Prion Disease Community,

The PRiSM clinical trial is now recruiting pre-symptomatic participants at high genetic risk of prion disease.

Earlier this year we initiated PRiSM as a first-in-human clinical trial to evaluate an investigational drug called PrP-siRNA. 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.

Up to now, PRiSM has only recruited symptomatic patients diagnosed with prion disease. Today, we are adding a separate arm of the trial to test the drug in pre-symptomatic individuals. It is important to test the drug separately in both groups of people, because the safety and pharmacology of drugs can differ between patient populations, and because our ultimate goal in developing this drug is to serve both populations. As before, this is still a single dose, Phase 1 trial. The trial is designed to identify a dose level of PrP-siRNA that is safe enough and lowers PrP enough in spinal fluid, to help inform the possible further development of PrP-siRNA in later stages of clinical trial. We hope that participants who enroll will do so as a contribution to research, and not out of an expectation of direct health benefits. There are not yet any human data to demonstrate a benefit of PrP-siRNA, and this early stage trial is not designed to determine whether the drug benefits people.

PRiSM continues to also enroll symptomatic patients. Our ability to open a pre-symptomatic arm is thanks in part to acceptable safety data from the initial results in symptomatic patients. Future escalation to higher doses in the pre-symptomatic arm will be gated on testing each dose level first in symptomatic patients.

The trial is enrolling at 5 U.S. sites. The sites and updated trial details including inclusion criteria for the new pre-symptomatic arm are available on the study's ClinicalTrials.gov listing:

<https://clinicaltrials.gov/study/NCT07444580>

Individuals interested in enrolling may wish to discuss it 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.

A short list of a few frequent questions is provided on the following page of this statement. We have also posted online a more comprehensive Frequently Asked Questions for this trial: <https://www.cureffi.org/2026/10/14/prism-faq/> . CJD Foundation (cjd.foundation.org) and CJD International Support Alliance (cjdusa.com) are helpful additional resources for education, support, and conversations about prion disease.

As always, we are immensely 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.

Sincerely,

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



Frequently Asked Questions:

Q. Who developed PrP-siRNA?

A. 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 formally sponsored by the Broad Institute and is being funded by the National Institutes of Health through the NeuroNEXT program. There is currently no pharmaceutical company sponsoring this trial.

Q. Who is eligible for this trial?

A. As of October 14, 2026, both pre-symptomatic and symptomatic individuals can enroll. Other eligibility criteria apply, including that for pre-symptomatic individuals, only those with genetic variants causing a high lifetime disease risk are eligible, and for symptomatic individuals, only those in early disease stages are eligible.

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.