



Sept 18, 2026

ATTN: Brenda L. Reggett, PharmD
Senior Regulatory Health Project Manager, Neurology 1

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
[REDACTED]

Beltsville, MD 20705-1266

RE: IND 167326 – PrP-lowering divalent siRNA 2439-exNA
Protocol Amendment
Serial 0016

Dear Brenda:

The Mass General Brigham Human Research Committee, which serves as the single Institutional Review Board of record for this study, has reviewed and approved a revision to our patient protocol now titled "An open-label, single ascending dose study to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of intrathecally administered PrP-siRNA in adults diagnosed with symptomatic prion disease and in pre-symptomatic adults at genetic risk for prion disease.", version 4.0 dated August 3, 2026. I am submitting Track Changed versions and Summaries of Changes for the protocol, the Arm 2 (symptomatic) Informed Consent Form, and the Arm 3 (pre-symptomatic) Informed Consent Form. We intend to begin enrolling participants under this protocol immediately after this submission.

Respectfully submitted,

Eric V. Minikel, PhD
Director, Prion Therapeutic Science
Broad Institute of MIT and Harvard
415 Main Street
Cambridge, MA 02142
cc: IND 167326 Regulatory File