September 2026

Dear Prion Disease Community,

Ionis is pleased to inform you that we have completed enrollment of Regimen 3 of PrProfile, an early-stage (Phase 1/2) clinical trial designed to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of ION717 in people with symptomatic prion disease.[1]

PrProfile Clinical Development Timeline

December 2023: Ionis initiated PrProfile, enrolling people with symptomatic prion disease into Regimen 1 and Regimen 2. Participants in Regimens 1 and 2 received multiple injections of study drug (ION717 and placebo) during a 30-week double-blind Treatment Period during which the order of injections (i.e., ION717 or placebo) was blinded. Individuals who complete the double-blind Treatment Period were eligible to transition to an open-label extension (OLE) Treatment Period.[1]

December 2024: Ionis completed enrollment of Regimens 1 & 2.[2]

March 2026: Ionis expanded PrProfile to explore an additional dosing regimen (known as Regimen 3) and extend the OLE for participants enrolled in Regimen 1 & 2. The decision to implement these changes was based on a pre-planned review of interim data showing an encouraging safety and tolerability profile and that ION717 is engaging with its target biology (i.e., prion protein). Unlike earlier regimens, Regimen 3 is open-label, meaning there is no placebo received during the Treatment Period – only ION717.[3]

August 2026: Ionis completed enrollment of Regimen 3. PrProfile remains ongoing, with participants from across all Regimens continuing to receive doses of ION717 and complete assessments per the study protocol.[1]

Ionis thanks all PrProfile participants, their caregivers, and site investigators and staff for their tremendous collaboration and efforts in helping advance this research. We also wish to express our gratitude to the global prion disease community for your support throughout this program and look forward to providing updates in the future.

Sincerely,

The ION717 Team

The following page contains additional information you may find helpful:

What is ION717?

ION717 is an investigational-stage RNA-targeted medicine called an antisense oligonucleotide (ASO). It is designed to target and bind to the messenger RNA responsible for producing the normal prion protein (PrP), potentially reducing the production of the protein at its source.[4]

When will Ionis share data from PrProfile with the prion disease community?

We understand there is significant interest among the prion disease community in seeing data from our clinical trial. Because the trial remains ongoing, we must continue to collect sufficient data for our planned analyses before sharing results. Ionis will share data from PrProfile at future medical and community conferences. We anticipate that to occur after the trial reaches its estimated primary completion date of April 2027. Due to the complex nature of clinical trials, this date is subject to change.[1]

Is there a way to receive ION717 outside the clinical trial, such as for people not eligible for this clinical trial?

Evaluation of the safety and efficacy of ION717 in clinical trials is essential to establishing whether ION717 can help people diagnosed with prion disease. For this reason, ION717 is not available outside this clinical trial at this time. We are working diligently to conduct the clinical trials necessary to evaluate ION717 in individuals with prion disease.[5]

___

The CJD Support Group Australia and the CJD International Support Alliance are community resources that provide education and support to those affected by prion disease. For more information about Ionis, visit www.ionis.com or email padvocacy@ionis.com.

Abbreviations: OLE, open-label extension; ASO, antisense oligonucleotide; RNA, ribonucleic acid; CJD, Creutzfeldt-Jakob disease

References: 1. Clinicaltrials.gov NCT06153966 PrProfile, 2. Community Statement December 2024, 3. Community Statement March 2026, 4. Ionis.com Pipeline August 2026, 5. Ionis.com Expanded Access Policy August 2026.

PA-AU-PRNP-260001 v1 09/2026