PrProfile: Phase 1/2a Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Intrathecally (IT) Administered ION717 in Patients With Prion Disease (PrD)[1]

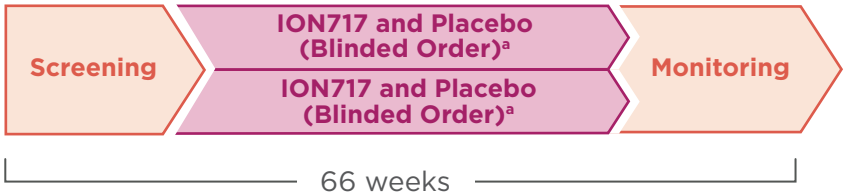
PrPROFILE

Study objective[1,2]:
To evaluate an investigational antisense RNA-targeted medicine, ION717, in patients with PrD.

Period 1[1]: ≤6-week screening period

Period 2[1]: 24-week double-blind randomized period

Period 3[1,3]: 36-week post-treatment period



This is a first-in-human, randomized, multicenter study of ION717. **Period 1** is the screening period, where eligibility for study participation will be assessed. During **Period 2**, participants will receive ION717 and placebo.[a] This is followed by **Period 3**, a 36-week post-treatment period where participants will be monitored.[1,3]

Select inclusion/exclusion criteria[1,b]:

- Patients aged ≥18 years[c]
- Confirmed diagnosis of probable or definite PrD
- Early-stage PrD at time of screening
- Patients with clinically significant abnormalities rendering them unsuitable for participation are excluded[d]

For more study information scan here:

Table: Key Clinical Endpoints[1]

Primary Endpoint	Incidence of Treatment-Emergent Adverse Events
Secondary Endpoints	• Maximum Observed Plasma Concentration and Half-Life of ION717 • Area Under the Plasma Concentration-Time Curve of ION717 • Cerebrospinal Fluid (CSF) ION717 Levels • Amount of ION717 Excreted in Urine • Percent Change in Prion Protein Levels in CSF

ION717 has not been evaluated for safety and efficacy by any regulatory authorities and is not indicated for the treatment of any disease.

[a]Administered by lumbar IT bolus injection. Participants will receive multiple doses of study drug (ION717 and placebo) during the 24-week treatment period. The order of doses is blinded. [b]List is not comprehensive. [c]At time of informed consent. Patients must have a caregiver who is ≥18 years old and who is able and willing to facilitate the patient's involvement, to the best of their ability, for the duration of the trial; caregivers must also be able and willing to provide information about themselves and the patient for the duration of the trial. [d]Abnormalities include but are not limited to: obstructive hydrocephalus, presence of a functional ventriculoperitoneal shunt for the drainage of CSF, an implanted central nervous system catheter; a known brain or spinal disease that would interfere with the lumbar puncture process, CSF circulation, or safety assessment; or any other condition which, in the opinion of the investigator, would make the patient unsuitable for inclusion or could interfere with the patient participating in or completing the study.

1. ClinicalTrials.gov. Accessed February 5, 2024. https://www.clinicaltrials.gov/study/NCT06153966/ 2. Ionis Pharmaceuticals. The Ionis antisense pipeline. Accessed February 6, 2024. https://www.ionispharma.com/ionis-technology/antisense-pipeline/ 3. Ionis Pharmaceuticals. Data on file.

IONIS®

ION717 Is an Investigational RNA-Targeted Medicine (RTM) That Has Been Designed to Reduce CNS Expression of Prion Protein (PrP)[1-5]

PrPROFILE

Proposed ION717-Mediated Downregulation of PrP[1-5]

Prnp-targeting antisense oligonucleotide administration in animal models delayed PrD onset, increased survival duration, and reversed neuronal and astrocytic damage[3,4]

ION717 has not been evaluated for safety and efficacy by any regulatory authorities and is not indicated for the treatment of any disease.

For more information or questions about participating sites, please contact us at **PrionDisease@clinicaltrialmedia.com** or **(844) 221-3587.**[6]

LEADING THE RNA REVOLUTION

in the treatment of neurologic disease

With a history of major breakthroughs in RNA-targeted technology, Ionis' robust pipeline is filled with potential.

CNS, central nervous system; dsDNA, double-stranded DNA; mRNA, messenger RNA; *PRNP*, prion protein gene.

1. Ionis Pharmaceuticals. The Ionis antisense pipeline. Accessed February 6, 2024. https://www.ionispharma.com/ionis-technology/antisense-pipeline/ 2. Bennett CF, et al. *Annu Rev Pharmacol Toxicol*. 2021;61:831-852. 3. Raymond GJ, et al. *JCI Insight*. 2019;5(16): e131175. 4. Minikel EV, et al. *Nucleic Acids Res*. 2020;48(19):10615-10631. 5. Dhuri K, et al. *J Clin Med*. 2020;9(6):2004. 6. ClinicalTrials.gov. Accessed February 5, 2024. https://www.clinicaltrials.gov/study/NCT06153966/

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