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Assessing efficacy of a PrP-lowering Molecular Gate as a therapeutic for prion disease

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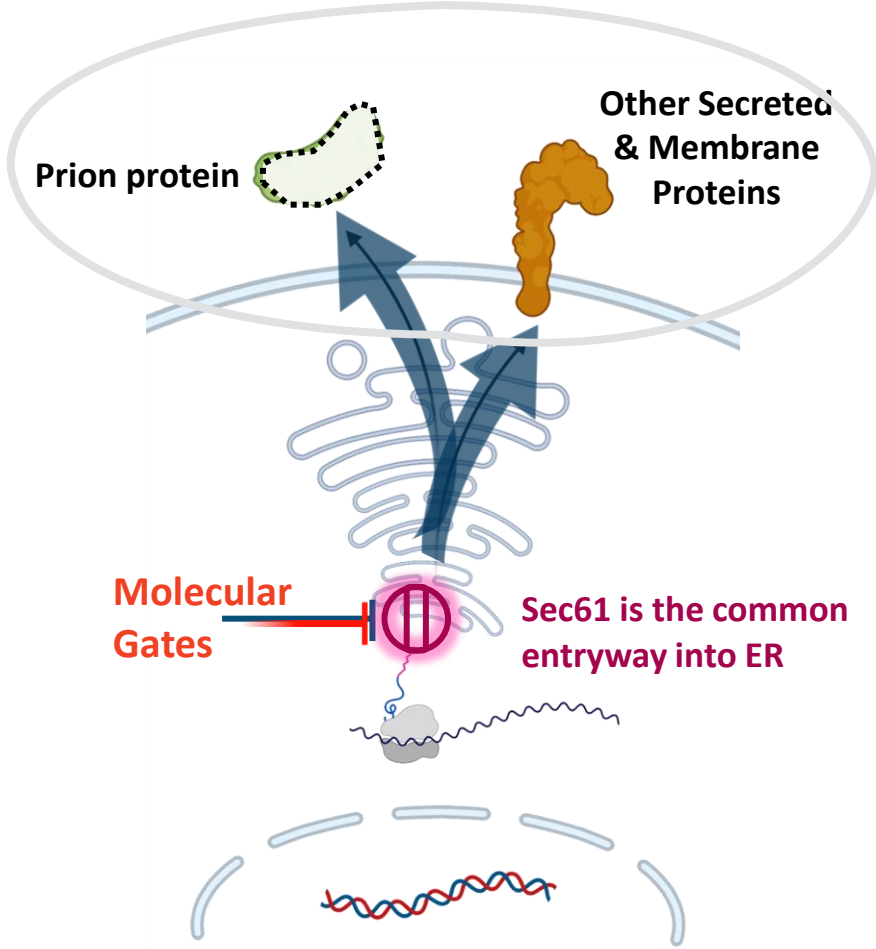
2026 CJD Foundation Family Conference, Chicago

Our platform & approach in prion disease

- **A pill to lower PrP in the brain.** Gate Bioscience is developing Molecular Gates - a new class of oral small-molecule drugs that block harmful proteins from leaving the cell, sending them to be degraded instead.
- **Lowering PrP in the brain – the best drug hypothesis in neuroscience.** Our drug lowers prion protein in the brain - the substrate misfolded prion needs to multiply and spread - to prevent, slow, or potentially reverse the disease.



Prion + 4200 other secreted and membrane proteins

Our small molecules "gate" the entryway – selectively prevent Prion from entering

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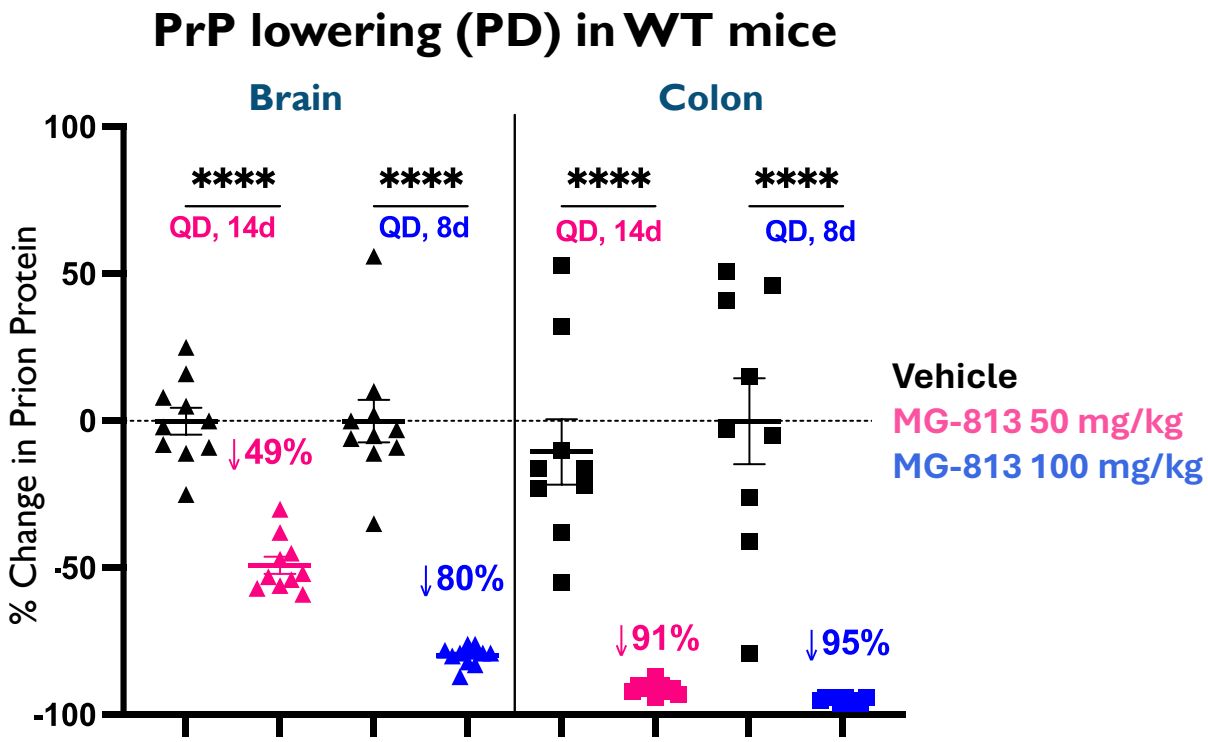
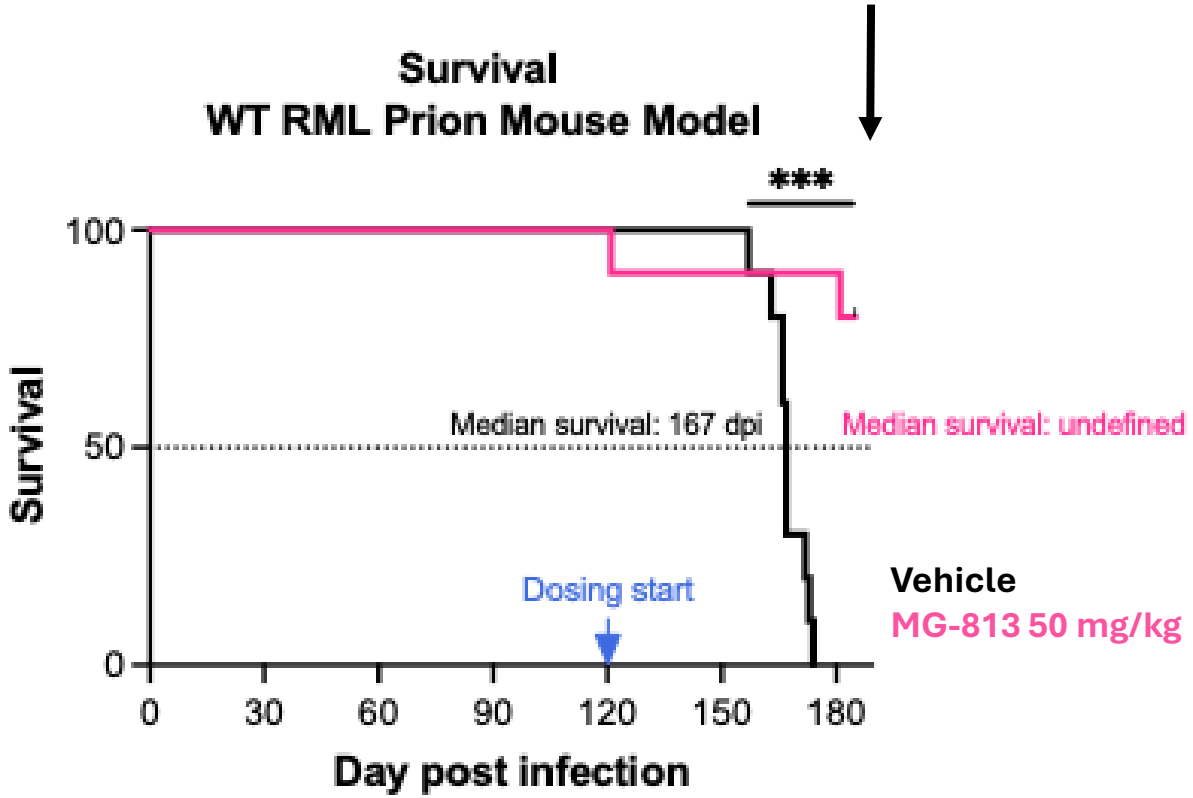
Early results

Proof-of-Concept in Mice with MG-813: 50% Prion elimination significantly extends survival of Prion infected mice when dosed after symptom onset

MG-813 was dosed by daily oral gavage for 70 days (!) – huge burden for mice & scientists. We could not complete the survival curve.
Solution: Put the compound in the animal food instead…





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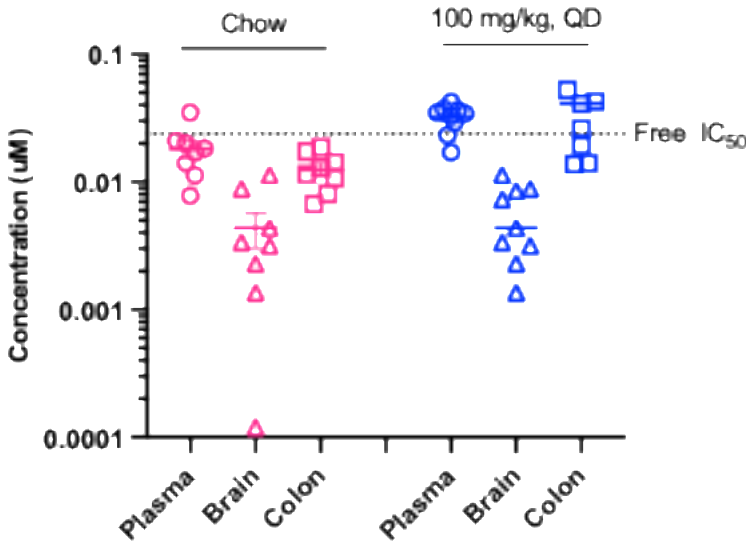
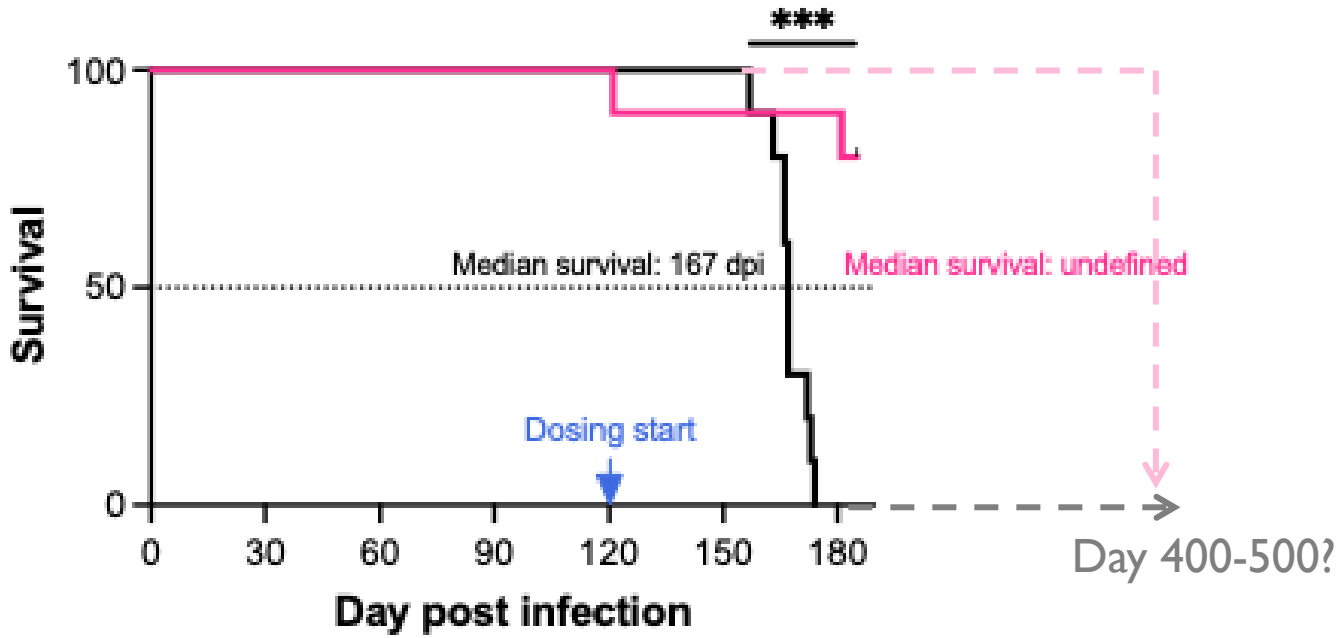
Open questions we'll answer

MG-813 is compatible with formulation into chow, it is well tolerated & gives comparable exposure to dosing by oral gavage

MG-813: Free drug concentration



- *How long will treated animals survive?*
- *What will be the difference in survival between intervening early (60dpi) vs late (120dpi)?*
- *How much additional survival benefit comes from lowering prion protein by more than 50% (compared with published ASO/siRNA/gene therapy studies)?*



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What this means for patients

- Unlike other prion-lowering drugs that require repeat spinal injections, our Molecular Gate can be **taken as a pill** from the comfort of a patients' home.
- Long-term treatment possible for both symptomatic patients and at-risk mutation carriers who may need to dose for decades.
- We are currently performing toxicological studies on our clinical candidate, to enable entry into first-in-human studies in healthy volunteers in 2027.

Oral pill

Brain penetrant

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Huge thank you to our donors

We couldn't do this without you!

The Michael H. Cole Memorial Research Grant, contributed by Jeanne Cole

The Sherry Maxwell Fabian Memorial Grant, contributed by Tom Fabian

The Chuck Fear Memorial Research Grant, contributed by Pamela Fear and Family

The Fred Glavan/Lee Gallagher Family Memorial Grant, contributed by the Glavan and Gallagher Families

The Maria D. McConnell Memorial Grant, contributed by Philip McConnell and Family

The Dora Middendorf Memorial Grant, contributed by Renee Middendorf and Family

The Daniel Nugent Memorial Grant, contributed by Carmine Cafiero, Family and Friends

The José A. Piriz and Sonia E. Piriz Memorial Research Grant, contributed by Karla Piriz and Lauren Esposito

The Marsha K. Snively Memorial Research Grant, contributed by the Snively Family

The Strides for CJD Grant, contributed by the Families of the CJD Foundation

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