

## **A baculovirus-produced gene therapy vector PR006A demonstrates efficacy and tolerability in mouse and NHP studies**

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GRN haploinsufficiency in humans leads to an approximately 90% risk of developing FTD-GRN. FTD-GRN is characterized by impairment of executive function, changes in behavior, and language difficulties. To address an unmet clinical need, we developed an investigative gene therapy, PR006A, with the aim of increasing human progranulin (GRN) levels to improve disease manifestations with a one-time treatment.

Our first-generation PR006A product, produced on a HEK-based platform is currently being studied in our Phase 1/2 PROCLAIM clinical trial. With improvements in product development, we utilized the Sf9-baculovirus platform to produce a second-generation product. We performed preclinical comparability studies to assess efficacy and safety. To evaluate efficacy, we used the Grn KO mice, which have a complete loss of progranulin, display age-dependent phenotypes, and key pathological features of human FTD-GRN. In a head-to-head comparison, intracerebroventricular (ICV) administration of both PR006A products to Grn KO mice reduced key FTD-GRN-related phenotypes in the brain of Grn KO mice, including accumulation of lipofuscin and ubiquitin, markers indicative of lysosomal abnormalities, and proinflammatory cytokine expression and microgliosis, markers indicative of CNS inflammation. Safety endpoints (body weight, multiple organ histopathology) captured as part of the murine efficacy experiments revealed no adverse PR006A-related histopathological findings. A 6-month GLP toxicity study in NHPs (cynomolgus macaques) revealed no adverse in-life observations or histopathological findings.

In summary, the baculovirus-produced PR006A vector was well tolerated in both the mouse and nonhuman primate (NHP) studies and demonstrated efficacy and tolerability comparable to the HEK-produced PR006A vector.

### **Conflicts of interest**

I am currently employed by Prevail Therapeutics, a wholly owned subsidiary of Eli Lilly and Company