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Thursday

Phase 1/2 Study Update of an AAV9-Based Gene Therapy for Fronto-Temporal Dementia with Pathogenic GRN Mutations (PROCLAIM Trial)

Olga Uspenskaya, Erin Mahoney, Jenny Velaga, Patricia Sondergaard, Mark Lowrey, Jeffrey Sevigny

The PROCLAIM trial is designed to assess the safety, efficacy and immunogenicity of a recombinant adeno-associated virus serotype 9 (rAAV9) vector-based gene therapy candidate transducing a copy of the human GRN gene. Patients suffering from fronto-temporal dementia with GRN mutations (FTD-GRN) carry a single mutation in the GRN gene, resulting in haploinsufficiency and an approximately 50% reduction in PGRN levels. GRN mutation carriers have an approximately 90% risk of developing FTD by age 75. In FTD-GRN patients, the delivery of a functional copy of the GRN gene by rAAV9 directly to the CNS may normalize PGRN levels, potentially restoring lysosomal function and decreasing downstream neurodegeneration, thus resulting in modification of disease progression. The PROCLAIM study is evaluating three dose levels of PR006 in ascending dose cohorts. A total of 15 patients with symptomatic-stage FTD ascertained by the CDR plus NACC FTLD sub of boxes score will receive PR006 at a low, mid or high dose, administered sub-occipitally intra cisterna magna. The primary objective is to evaluate safety and tolerability of PR006, as well as to quantify the change in PGRN levels in blood and CSF.
The PROCLAIM trial has completed the low-dose cohort and is continuing to dose escalate based on ongoing safety and efficacy data. PR006 in the low-dose cohort was shown to be safe and well-tolerated.
PROCLAIM will continue to assess dose, safety, tolerability, biomarker and efficacy effects of PR006 in order to inform its further clinical development.

Conflicts of interest

full time Eli Lilly employee