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Saturday

Design of INFRONT-3: A phase 3 randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of latozinemab in FTD-*GRN*

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State of the Art:

A heterozygous mutation in the progranulin gene (*GRN*) reduces progranulin (PGRN) protein levels and is a known cause of FTD. Latozinemab (AL001) is a human monoclonal IgG1 antibody that blocks and downregulates the sortilin receptor, the primary degradation pathway of PGRN. Restoring PGRN levels by blocking Sortilin may be an effective therapeutic approach in treating FTD-*GRN* patients.

Methodology:

INFRONT-3 is a pivotal Phase 3 study to assesses the efficacy and safety of latozinemab in *GRN* mutation carriers at risk of developing FTD or with symptomatic FTD. The primary objective of this study is to demonstrate slowing of disease progression as measured by change in the CDR® plus NACC FTLD sum of boxes (CDR®-FTLD-SB). Participants are randomized to receive 60 mg/kg AL001 or placebo (3:2 ratio), via IV infusion every 4 weeks, for 96 weeks. Randomization is stratified based on CDR®-FTLD-SB score at baseline.

Results:

This ongoing global study will enroll approximately 180 participants (NCT04374136). Pharmacodynamic endpoints include MRI measures and fluid biomarkers (blood and optional CSF). PK in serum is also being assessed. Routine safety monitoring includes assessment of AEs, laboratory and vital signs, ECGs, MRIs, and suicidal ideation and behavior. An independent Data Monitoring Committee is reviewing the progress of the study and performing ongoing safety reviews.

Conclusions:

INFRONT-3 is designed to provide confirmatory evidence of efficacy and safety for latozinemab, a novel first-in-class neuro-immunological approach for treating FTD-*GRN*. Global enrollment is ongoing.

Conflicts of interest

Stella McCaughey, Julie Y. Huang, Michael Ward, Yijie Liao, Felix Yeh, Whedy Wang, Lawrence Carter and Arnon Rosenthal are equity stakeholders in Alector, Inc and/or employees of Alector, LLC.