

CASE STUDY

Development of a PK/PD Model for Gene Therapy for a Rare Neurodegenerative Disease

Background and Problem

Allucent's client requested support to bring an Adeno-associated virus (AAV) gene therapy for a rare neurodegenerative disease into the clinic for a Phase 1b study in patients. Dose scaling from preclinical safety and efficacy studies by brain volume led to human doses without a safety margin and jeopardized clinical development.

Our Solution

Allucent evaluated the preclinical data and developed a PK/PD model that related dose to brain distribution of vector genome, transduction of brain tissue, and transgene expression to preclinical safety and efficacy outcomes. With this approach, differences in transduction efficiency between the rodent pharmacology studies and the NHP toxicology studies became apparent and revealed a large safety margin. An FIH (first-in-human) starting dose and dose escalation strategy with potential clinical and safety benefit, for the Phase 1b study was provided to support the IND and clinical protocol.

Outcome

The IND and clinical protocol submitted to the FDA were approved for initiation of the clinical study. The FDA agreed with the starting dose and dose escalation rationale to enable the Phase 1b study to start.

Services

Allucent has broad and deep expertise and experience to support the discovery, preclinical and clinical development of cell and gene therapy (CGT) products. From translational modeling and simulation to clinical pharmacology, regulatory consulting, and conducting clinical trials, Allucent has the scope to help sponsors bring your CGT product into the clinic and then forward to marketing approval.

