THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

LAY ABSTRACT TEMPLATE FOR AWARDEES

Principal Investigator(s): Dr Manuel Blanc

Project Title: Glunomab: a novel immunotherapy for the treatment of Parkinson's disease

Study Rationale: Disease modification in Parkinson's disease (PD) represents an unmet medical need. The therapeutic being developed, Glunomab, is a monoclonal antibody (mAb) which inhibits a toxic interaction between two proteins recently characterized to be involved in PD pathophysiology. As its main target is on vascular endothelial cells inside the blood vessels, Glunomab does not need to cross the blood brain barrier (BBB) to exercise its therapeutic effect on the central nervous system (CNS), a major development advantage over most mAb approaches to PD.

Hypothesis: Preliminary data demonstrated that Glunomab reduced microglia activation and T-cell infiltration into the CNS, and subsequently prevented dopaminergic neuron degeneration and behavioral deficits in an AAV α-Synuclein mouse model of PD; we therefore hypothesize that Glunomab is acting on vascular endothelial cells to exercise its therapeutic effects on neurodegeneration, acting on BBB permeability and associated transmigration of inflammatory cells into the brain.

Study Design: This 2-part Program seeks to use two complementary gold-standard preclinical mouse model of PD to: 1) confirm Glunomab efficacy via systemic route in two independent laboratories with new efficacy endpoints, 2) validate the absence of sex impact on treatment efficacy, 3) assess delayed-treatment starts to target different stages in PD progression, 4) perform a dose-response study, and 5) identify new biomarkers of target engagement.

Impact on Diagnosis/Treatment of Parkinson's disease: Glunomab has a remarkable potential and we anticipate that these experiments will provide a strong proof of concept for its potential use as a treatment for PD and will accelerate its clinical testing as a disease-modifying drug.

Next Steps for Development: Glunomab has been humanized toward GMP manufacturing, and the preparation of the preclinical package (PK/PD, ADME, safety-tox) is underway. If successful, this intended Program will beneficiate from these ongoing CMC and regulatory efforts and will be of high value for the IND dossier supporting the future SAD/MAD Phase 1 and later clinical studies.