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Project Title: Preclinical proof of concept of TFEB in Parkinson Disease.

Study Rationale: Parkinson's disease is characterized by the loss of specific neurons and the abnormal accumulation of a protein (alpha-synuclein) in the brain. The objective of the project is to prevent neuron degeneration in patients by using gene therapy to overexpress selectively in deep brain structures the gene TFEB, a major regulator of the protein degradation in cells (Autophagy Lysosomal Pathway).

Hypothesis: Proof of concept in animals that TFEB expression in the neurons will lead to alpha-synuclein degradation in those neurons and can delay or even stop the Parkinson Disease progression.

Study Design: The best gene therapy product with the right expression level of TFEB in neurons will be selected. Experiments in animal models will be performed with the selected gene therapy product to show an effect on alpha-synuclein degradation and preservation of neuron degradation. Biological markers will be identified to follow efficacy of the treatment in animal models and eventually in human during clinical trial.

Impact on Diagnosis/Treatment of Parkinson's disease: There is no cure of the Parkinson Disease so far, only mitigation of symptoms. The gene therapy TFEB project aims at stopping the disease progression.

Next Steps for Development: After the demonstration of its activity, the product would be evaluated for its potential toxicity in an animal model. All those results will then constitute part of the filing of the first in human study authorization.

Pre-clinical development stage: Early