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STEP4NAMs

## TERMS OF REFERENCE

UNIVERSITÉ DU LUXEMBOURG

# Pilot IV Parkinson's Disease Organoids for Predicting Drug Efficacy

## Introduction

The pilot project proposes to validate Parkinson's disease (PD) organoid models by demonstrating their potential to predict the failure of drug candidates effective in pre-clinical studies but failing in human clinical trials. Essentially, we aim to offer a case study to help leverage the relevance and applicability of organoids in the context of drug testing.

## Purpose and scope

In line with the STEP4NAM project objectives, our pilot aims to increase the confidence of established drug developing companies and SMEs in NAMs: To this end, we are looking for 4 external stakeholders from the NWE region ((Bio)Pharma sector) that would provide drug candidates/compounds to be integrated in our testing protocol. The results from this pilot study will demonstrate the efficacy of drugs without the unnecessary use of animal models and by showcasing a cheaper and more efficient testing platform.

## Approach and methodology

The testing protocol will be based on the treatment of midbrain organoids from 3 PD patient and control age and sex-matched cell lines. We will make use of cell lines derived from familial, gene-mutation driven cases which have been shown to recapitulate the main hallmarks of PD (e.g. dopaminergic neuron loss). The effect of the drugs will be assessed by qualitative and quantitative analysis of key PD disease-associated phenotypes, mainly through high content imaging of cell markers. These results will determine the efficacy of drugs based on their ability to slow or rescue PD phenotypes in the PD-derived organoid model. After careful investigation of our drug testing pool, we will computationally determine the predicted value of the PD midbrain organoid model compared to the pre-clinical animal model outcome.

**Pre-requisite for participation**

The interested stakeholders (company or SME) should have drug compounds targeted at neurodegenerative disorders (mainly PD) that were tested in a pre-clinical setting and with either confirming or contradicting results in a clinical study. Having access to both types of drugs will further strengthen the potential predicting value of organoid models, showing that results based on organoids can be transferred to a clinical setting. The pilot project is also open to include compounds that were not tested yet or are in the process of being tested in clinical studies.