



Universiteit  
Leiden  
The Netherlands

## **Mechanistic early phase clinical pharmacology studies with disease-modifying drugs for neurodegenerative disorders**

Vissers, M.F.J.M.

### **Citation**

Vissers, M. F. J. M. (2023, June 21). *Mechanistic early phase clinical pharmacology studies with disease-modifying drugs for neurodegenerative disorders*. Retrieved from <https://hdl.handle.net/1887/3621076>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/3621076>

**Note:** To cite this publication please use the final published version (if applicable).

MECHANISTIC EARLY PHASE CLINICAL PHARMACOLOGY STUDIES WITH  
DISEASE-MODIFYING DRUGS FOR NEURODEGENERATIVE DISORDERS

*For Mia and Lotta  
never stop exploring*

**MECHANISTIC EARLY PHASE  
CLINICAL PHARMACOLOGY STUDIES  
WITH DISEASE-MODIFYING DRUGS  
FOR NEURODEGENERATIVE  
DISORDERS**

Proefschrift

ter verkrijging van  
de graad van doctor aan de Universiteit Leiden,  
op gezag van rector magnificus prof.dr.ir. H. Bijl,  
volgens besluit van het college voor promoties  
te verdedigen op woensdag 21 juni 2023  
klokke 15.00 uur

door  
Maurits Frederick Johan Maria Vissers  
geboren te Amsterdam  
in 1987

© Maurits F.J.M. Vissers, 2023

Design: Caroline de Lint, Den Haag (caro@delint.nl)

Images: Generated using DALL·E, OpenAI software (labs.openai.com).

Publication of this thesis was financially supported by the foundation Centre  
for Human Drug Research in Leiden, the Netherlands.

**Promotor**

Prof. dr. G.J Groeneveld

**Co-promotor**

Dr. J.A.A.C. Heuberger

**Leden promotiecommissie**

Prof dr. J.J. van Hilten

Prof. dr. T. van Gelder

Prof. dr. E.L. Swart (*Amsterdam Universitair Medisch Centrum*)

Dr. M. van Es (*Universitair Medisch Centrum Utrecht*)

**CHAPTER 1**

7 Introduction

**CHAPTER 2**

23 Targeting for success: demonstrating proof-of-concept with mechanistic early phase clinical pharmacology studies for disease-modification in neurodegenerative disorders

**CHAPTER 3**

61 Safety, pharmacokinetics and target engagement of novel RIPK1 inhibitor SAR443060 (DNL747) for neurodegenerative disorders: randomized, placebo-controlled, double-blind phase 1/1B studies in healthy subjects and patients

**CHAPTER 4**

87 A leucine-rich repeat kinase 2 (LRRK2) pathway biomarker characterization study in patients with Parkinson's disease with and without LRRK2 mutations and healthy controls

**CHAPTER 5**

113 LRRK2 inhibition by BIIB122 in healthy participants and patients with Parkinson's disease

**CHAPTER 6**

155 General discussion and conclusion

**APPENDICES**

165 Nederlandse samenvatting

177 Curriculum vitae

178 List of publications