



**Universiteit
Leiden**
The Netherlands

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

Vissers, M.F.J.M.

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Stellingen behorende bij het proefschrift

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

- 1 We are at the forefront of a paradigm shift in the treatment of neurodegenerative disorders. (*this thesis*)
- 2 First-in-man studies with potential disease-modifying drugs for neurodegenerative disorders should not be performed without using pharmacodynamic biomarkers. (*this thesis*)
- 3 Despite its large within- and between-subject variability in PBMCS, pRAB10 is a suitable pharmacodynamic biomarker for measuring LRRK2 kinase activity. (*this thesis*)
- 4 LRRK2 inhibition is a promising therapeutic strategy to slow down Parkinson's disease, especially in LRRK2-mutation carriers, but also in idiopathic Parkinson's disease. (*this thesis*)
- 5 As long as we do not fully understand the molecular mechanisms underlying neurodegenerative disorders, it remains extremely difficult to develop effective pharmacologic interventions.
(*The problem is that we don't understand the problem – Paul MacCready*)
- 6 Development of neurodegenerative disorders likely requires simultaneous activation of more than one pathogenic pathway, and multi-targeted, personalized therapies are therefore our best shot to effectively halt disease progression.
- 7 The COVID-19 pandemic often did not change the evaluation of the four basic principles of medical ethics and thus it was essential that clinical trials were restarted as soon as possible. (*Vissers et al. Br J Clin Pharmacol. 2021;87:837-844*)
- 8 Improving clinical trial efficiency is our best strategy to safeguard affordability of new treatments in the future.
- 9 Pole Pole (*Swahili*), you will reach the summit if you just keep climbing.
- 10 Management is both an art and a science.
- 11 Investing in knowledge always creates most value in the end.
(*adapted from Benjamin Franklin*)
- 12 All truly great thoughts are conceived while cycling.
(*adapted from Friedrich Nietzsche*)