

#### Executive Summary

This report provides the statistical operating characteristics of the EPAD Proof-of-Concept (POC) phase II study. The design of the PoC study is a platform trial in which there is a master protocol. The master protocol describes the aspects of the trial that are globally specified and which all interventions follow. Each intervention will have a specific appendix that allows flexibility for the protocol parameters for that intervention. This flexibility includes the population to enrol; among the four distinct populations identified by the crossing of ApoE4 status (+/–) and preclinical/prodromal, the sample size, length of following research participants, and the choice of subarms (doses, frequency, etc). This document presents the operating characteristics for a range of these protocol parameters for the primary analysis of slowing cognitive decline.

The operating characteristics presented in this document are based on clinical trial simulations. These simulations are based on the construction of software that recreates the full parameters of the trial that allows a realistic virtual creation of the trial, including accrual rates, drop outs, realizations of the cognitive outcomes, and complete analysis of the trial as specified. The results of each simulated trial are then tabulated and summarized. These virtual trials create a Monte Carlo integration calculation of the trial operating characteristics.

This document allows the evaluation of different parameter selection choices to be made for potential interventions. The power of the trial for different design selections can be evaluated. This document is based on the current expectations or estimates for the trial parameters at the initiation of the POC trial. It is expected these simulations will be updated as the PoC trial and the longitudinal cohort study evolve providing more accurate understanding of these parameters. As new simulations and assumptions are explored this report will be updated.

For more information: [info@epad.org](mailto:info@epad.org)

