

# Safety, Tolerability, and Efficacy of NE3107 From a Phase 2, Double- Blind, Placebo-Controlled Study in Levodopa/Carbidopa-Treated Patients With Parkinson's Disease

Clarence Ahlem, Christopher Reading, Joseph Djan, Joseph Palumbo

BioVie Inc., Carson City, Nevada, USA.

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# Acknowledgments and Disclosures

## Acknowledgments

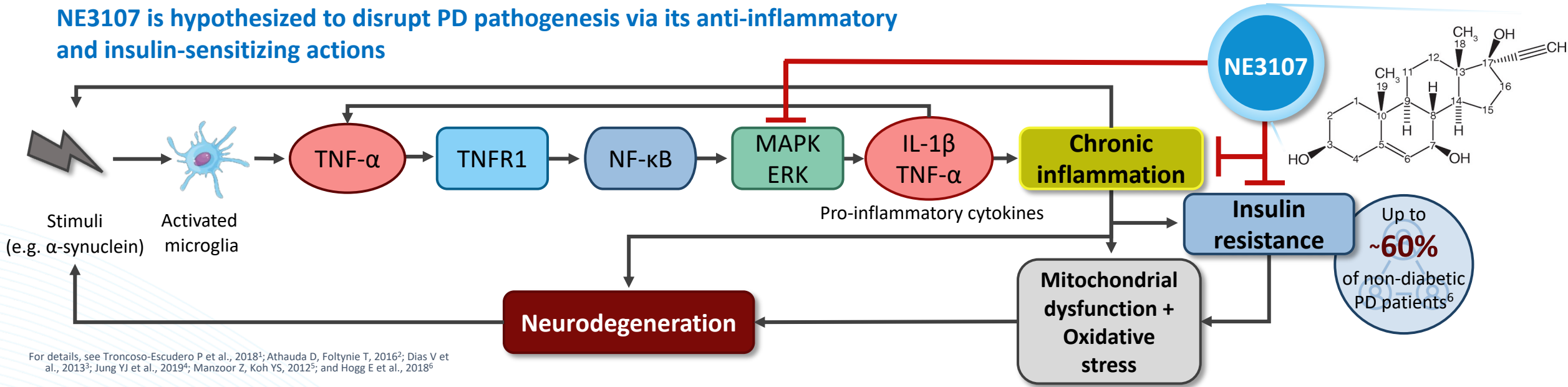
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## Disclosures

CA, CR, JD, and JP are employees of BioVie Inc.

# Background

NE3107 is hypothesized to disrupt PD pathogenesis via its anti-inflammatory and insulin-sensitizing actions



- Disrupting the feed-forward loop formed by neuroinflammation, insulin resistance, and oxidative stress may be an effective strategy to limit PD progression<sup>1-4,7,8</sup>
- NE3107 is an oral, blood-brain-permeable molecule that binds ERK and has anti-inflammatory and insulin-sensitizing activities via inhibition of inflammation-stimulated ERK and NF-κB activation and TNF-α signaling, without disrupting homeostasis<sup>9</sup>
- NE3107 has an excellent safety profile and was shown to improve insulin sensitivity and glucose metabolism and reduce CRP and HbA1c in obese and inflamed patients with impaired glucose tolerance or T2D<sup>9</sup>
- In a marmoset PD model, NE3107 was associated with improved mobility, enhanced levodopa activity, and decreased neuronal death in the substantia nigra; it also alleviated levodopa-induced dyskinesia, a side effect of long-term exposure to levodopa<sup>10</sup>
- We conducted a phase 2, double-blind, placebo-controlled study to assess the safety, tolerability, and exploratory efficacy of NE3107 in levodopa-treated PD participants and the effects of NE3107 on the PK profile of carbidopa/levodopa

# Objectives

- A **phase 2, double-blind, placebo-controlled study** to evaluate the safety, tolerability, and exploratory efficacy of NE3107 in levodopa-treated PD patients and examine the effects of NE3107 on the PK profile of concomitantly administered carbidopa/levodopa

## Safety and Tolerability

- To assess the safety and tolerability of NE3107 administration in levodopa-treated PD patients

## Pharmacokinetics

- To characterize the PK profile of carbidopa/levodopa in PD patients before and after treatment with NE3107

## Exploratory Efficacy

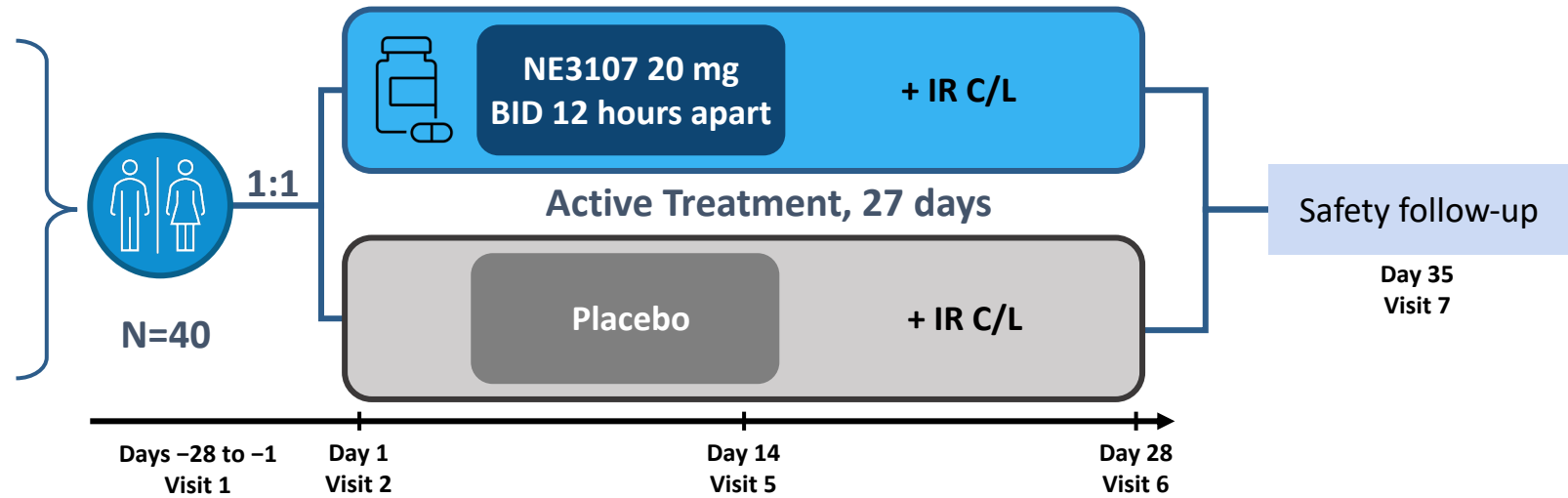
- To assess the effect of NE3107 on motor and non-motor features of PD
- To assess the effect of NE3107 on motor complications in PD

# Study Design

## Phase 2, Double-Blind, Placebo-Controlled, 28-Day Study

### Inclusion criteria

- 30-80 years old
- Diagnosis of PD
- Bradykinesia and motor response to levodopa
- History of motor fluctuations + early morning OFF episodes
- Receiving  $\geq 300$  mg of carbidopa/levodopa daily



### Safety and Tolerability Assessments

TEAEs  
SAEs  
Suicidality (C-SSRS)  
Percent completers

### Levodopa PK Assessments (Change between visits 2 and 5)

$C_{max}$   
 $T_{max}$   
AUC  
Elimination half-life

### Efficacy Assessments

(Between visit 1 and visits 2, 5, and 6 and between visit 2 and visits 5 and 6)

MDS-UPDRS Part I-III Scores  
Total daily OFF time  
Total daily ON time

# Safety Assessments

Assessed during safety follow-up  
on day 35 (visit 7)

- Incidence and temporal profile of treatment-emergent adverse events, evaluated by type/nature, severity/intensity, seriousness, and relationship
- Incidence of related TEAEs (including possibly- and probably-related) of moderate or severe intensity
- Incidence of TEAEs leading to withdrawal of study drug
- Incidence of SAEs
- Suicidality, as measured by the C-SSRS
- Changes in physical examination, vital signs (blood pressure and heart rate), 12-lead ECG, and laboratory data (hematology and blood chemistry)
- Percentage of completers

## Efficacy Assessments

Changes between visit 1 and visits 2, 5, and 6 and between visit 2 and visits 5 and 6

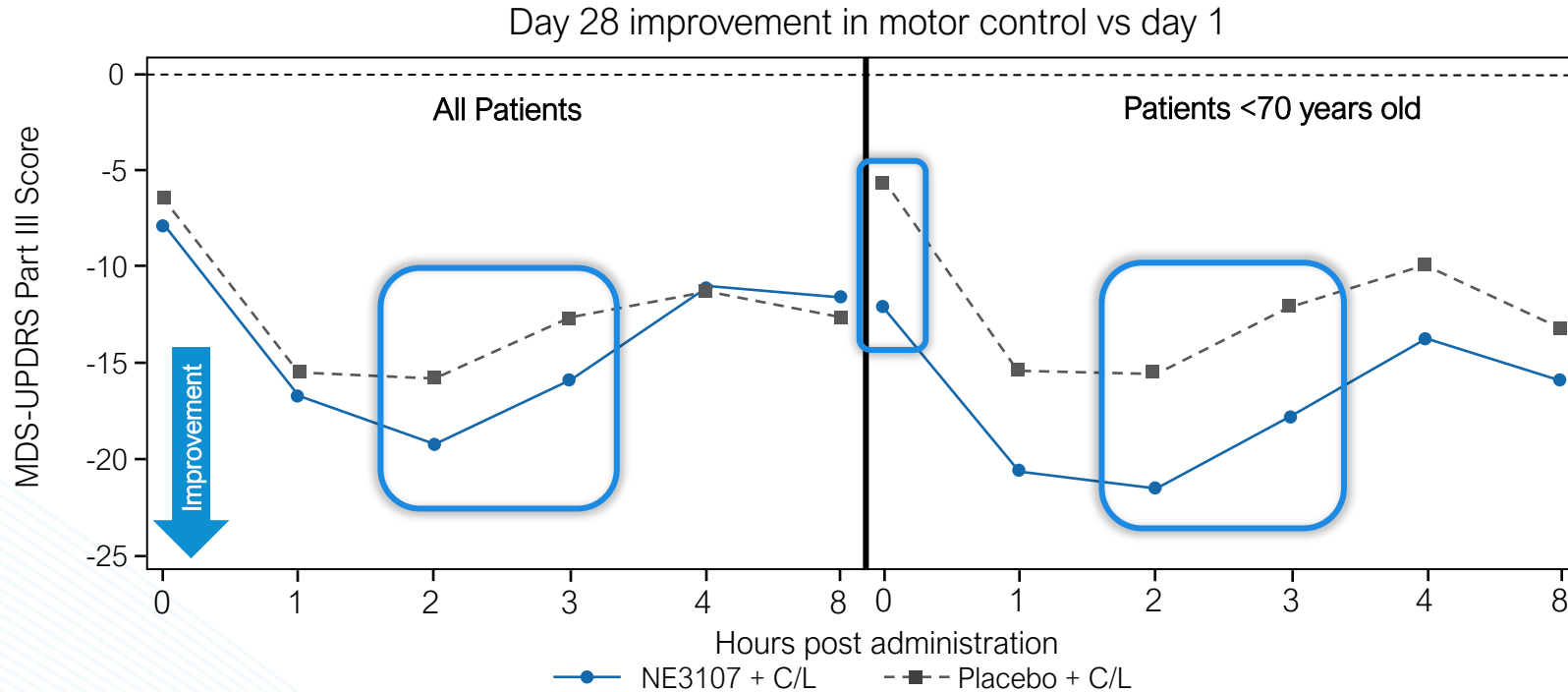
- Change in MDS-UPDRS Part III Score from baseline (practically-defined OFF) to postdose timepoints each day
- Total OFF time over the 8-hour assessment period
- Average MDS-UPDRS Part III Score when ON
- MDS-UPDRS Part I Score
- MDS-UPDRS Part II Score
- Total ON time with or without dyskinesia during the 8-hour assessment period
- Dyskinesia severity (investigator) and troublesome/non-troublesome status (participant) during the 8-hour study period (if applicable)
- Time to onset of ON time
- Non-Motor Symptom Assessment Scale for Parkinson's Disease (NMSS)

# Baseline Characteristics

Characteristic	NE3107 + IR C/L (n=22)	Placebo + IR C/L (n=23)
Age, mean (y)	67.6	66
Gender, n (%)		
Female	9 (41)	8 (35)
Male	13 (59)	15 (65)
Weight, mean (kg)	80.1	80.8
BMI, mean	28.2	27.9
Time since diagnosis, mean (years)	7.6	7.3
Total daily levodopa, mean (mg)	548	691
MDS-UPDRS Scores, mean		
Part I	6.8	7.5
Part II	9.4	8.2
Part III	28.4	25.8
ON time without dyskinesia within 4 h, mean (h)	1.95	1.93
OFF time within 4 h, mean (h)	2.1	1.7

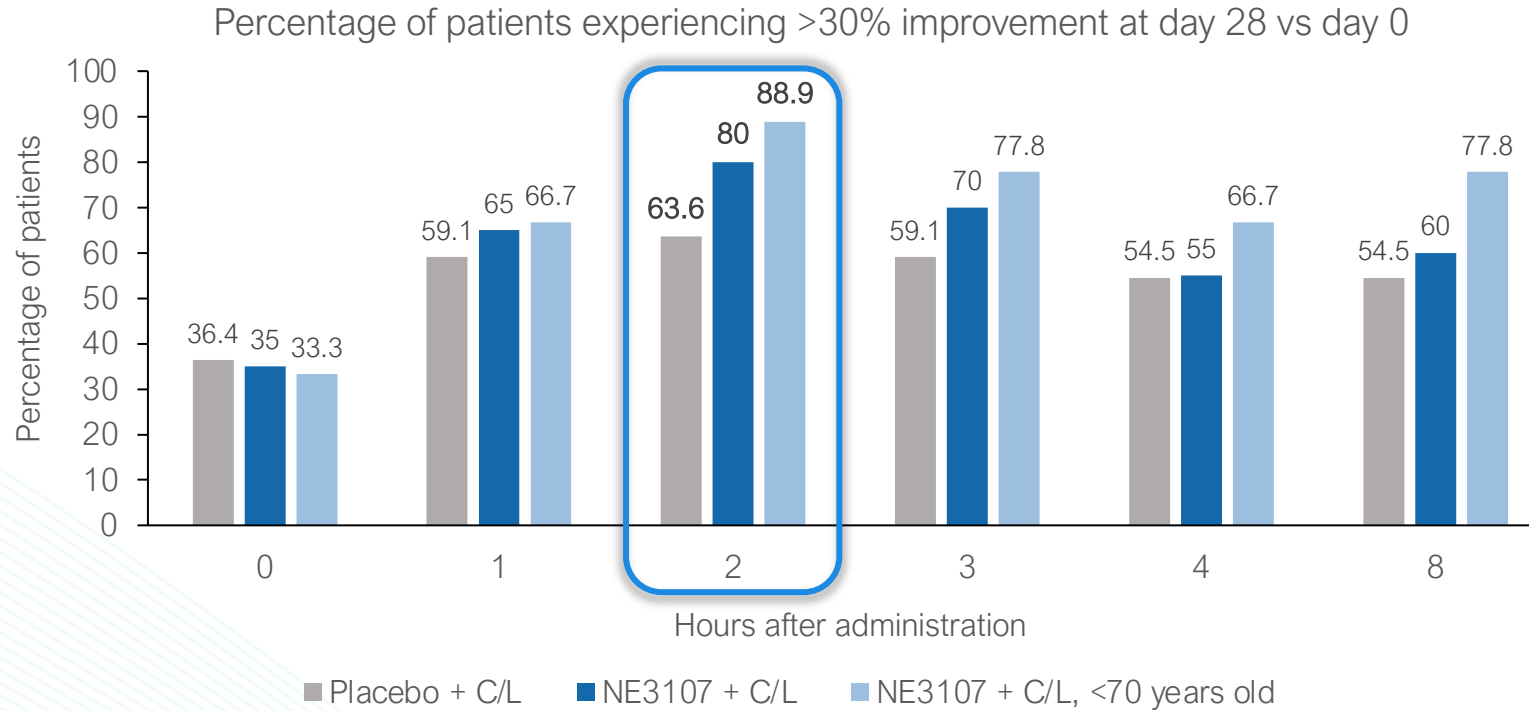


# Efficacy Assessments



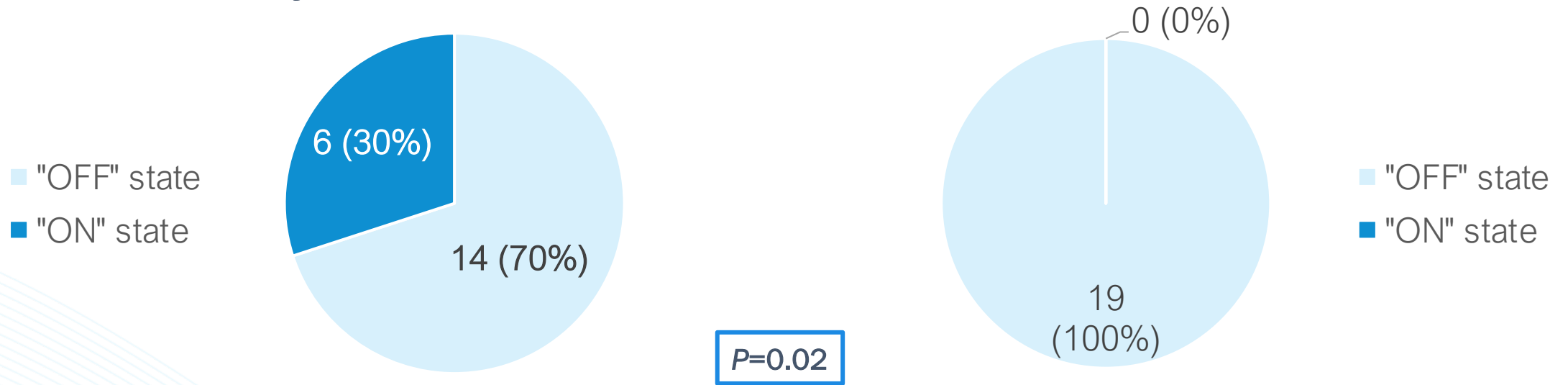
- Patients treated with NE3107 and C/L experienced greater improvements (3+ points) in their MDS-UPDRS Part III score than patients treated with placebo and C/L at the 2- and 3-hour marks
- Patients <70 years old treated with NE3107 and C/L experienced improvements that are ~6 points better than those who received placebo and C/L
  - ~50% of the total patient population was <70 years old
  - NE3107-treated patients <70 years old had lower Part III scores prior to medication administration (t=0) compared to those treated with C/L alone

# Efficacy Assessments (cont.)



- 80% of NE3107 and C/L-treated patients and 88.9% of NE3107 and C/L-treated patients <70 years of age demonstrated >30% Part III score improvements 2 hours post administration from baseline, compared to 63.6% of patients treated with placebo + C/L

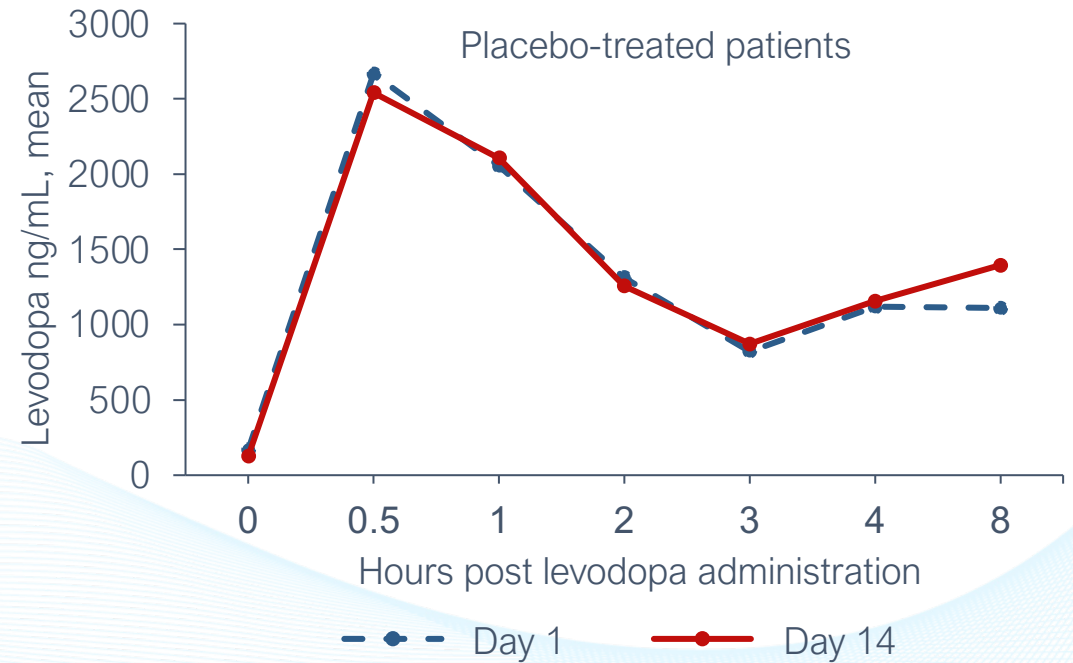
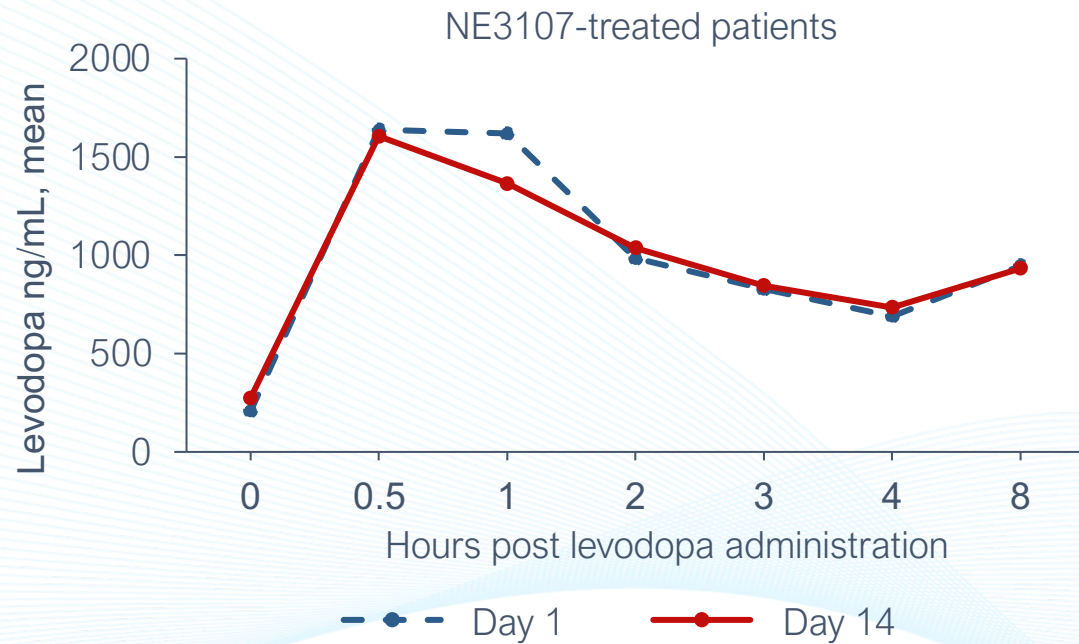
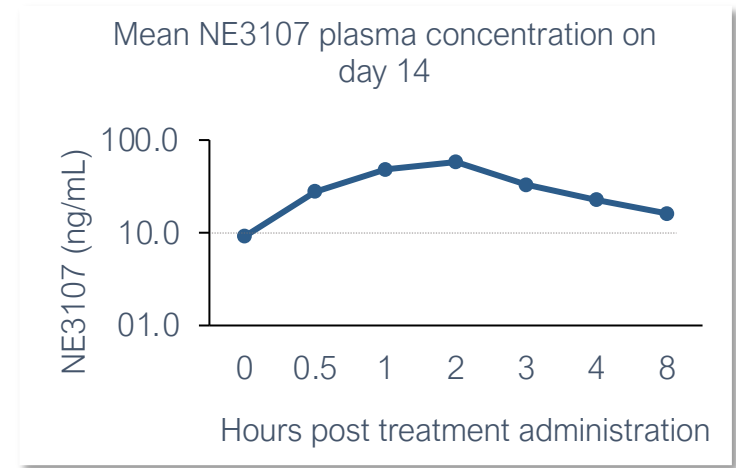
## Post Hoc Efficacy Assessment



- 30% (6/20) of patients treated with NE3107, compared to none (0/19) of the placebo-treated patients, who had a baseline of morning OFF experienced a morning ON state prior to receiving their morning medications on day 28
  - This difference was statistically significant ( $P=0.02$ )

# Safety and PK

- No drug-related adverse events were observed
- NE3107 did not affect the PK profile of levodopa



# Conclusions

- Our phase 2, placebo-controlled, double-blind study assessing the safety, efficacy, and PK of NE3107 in patients with PD **met both of its objectives**
- NE3107-levodopa combination treatment was associated with **clinically meaningful**<sup>11</sup> and **superior improvements (3+ points)** on the **motor** examination part (Part III) of the **MDS-UPDRS**
- Patients <70 years of age experienced greater motor control with NE3107, suggesting that **younger patients, presumably with less PD progression, may benefit more** from an anti-inflammatory, NE3107 intervention
- At the end of the study, only patients who received NE3107, and not levodopa alone, were assessed as being in the **morning ON state** before receiving their morning medication, an improvement in motor function that is **clinically meaningful** for patients with PD
- The observed pro-motoric effects of NE3107 were not the result of increased plasma levodopa concentrations
- The findings demonstrate the potential **intrinsic** and **levodopa-enhancing, pro-motoric activity** of NE3107 that is consistent with data from animal models and support further clinical investigation of NE3107 in late-phase trials

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