Levodopa therapy remains the cornerstone of Parkinson’s disease (PD) management. However, it also has a high potential for complications. To address this, two Phase II studies were performed to assess the pharmacokinetic profile derived from continuous subcutaneous levodopa/ carbidopa (ND0612) regimen that promotes stable levodopa plasma levels, and its impact on motor complications.

### Methods

#### Study 1: ND0612-003

- **Study Design:** Double-blind, placebo-controlled study, in which 30 PD patients with motor fluctuations were randomized to either 50 mg or 100 mg of ND0612 or placebo, all of whom received carbidopa 20 mg along with levodopa at a ratio of 3:1.
- **Study Duration:** 28 days.
- **Endpoints:** Primary endpoints included determination of steady-state levodopa and carbidopa plasma concentrations, levodopa plasma levels, and the impact of fluctuations.

#### Study 2: ND0612-004

- **Study Objectives:** To determine the efficacy and safety of ND0612 in reducing fluctuations in 16 PD patients who were previously treated with oral levodopa/carbidopa.
- **Study Design:** Randomized double-blind 2 weeks intermittent treatment paradigm in these patients.

### Results

**Study 1: ND0612-003**

- **Study Duration:** 28 days.
- **Endpoints:** Primary endpoints included determination of steady-state levodopa and carbidopa plasma concentrations, levodopa plasma levels, and the impact of fluctuations.

**Study 2: ND0612-004**

- **Study Objectives:** To determine the efficacy and safety of ND0612 in reducing fluctuations in 16 PD patients who were previously treated with oral levodopa/carbidopa.
- **Study Design:** Randomized double-blind 2 weeks intermittent treatment paradigm in these patients.

### Conclusions

- Continuous SC infusion of ND0612 at low and high doses was well tolerated.
- The ND0612 regimen significantly reduced levodopa plasma level fluctuations in comparison with oral levodopa/carbidopa therapy.
- Inclusion of entacapone in the ND0612 regimen further increased plasma levodopa levels.
- Adding ND0612L to standard of care provides clinically significant improvements in motor complications.

### References


### Figure 1: ND0612 significantly reduces OFF time by 2 hours

- Baseline (days 1-7) was 1.89±0.94h in the placebo group and 0.37±0.26h in the ND0612 group.

### Figure 2: ND0612 significantly reduces OFF time by 2 hours

- Baseline (days 1-7) was 1.89±0.94h in the placebo group and 0.37±0.26h in the ND0612 group.

### Figure 3: Levodopa plasma levels following administration of ND0612 L (0.14 mg/mL) with or without entacapone

- Study 1: ND0612-003
- Study 2: ND0612-004

### Figure 4: Camidge plasma levels following administration of ND0612 L and with or without entacapone

- Study 1: ND0612-003
- Study 2: ND0612-004

### Figure 5: Pharmacokinetics of levodopa following continuous SC administration of ND0612 L and ND0612 H (60/14 mg/mL)

- (a) Individual patient from ND0612 L group
- (b) Individual patient from ND0612 H group