ADDENDUM TO STATISTICAL ANALYSIS PLAN (SAP)

Protocol Title	**A Phase 3, Twelve-week, Multi-Center, Multinational, Randomized, Double-Blind, Double-Dummy, Parallel Group Study to Determine the Efficacy, Safety and Tolerability of P2B001 Once Daily Compared to its Individual Components in Subjects With Early Parkinson's Disease and to a Calibration Arm of Pramipexole ER**
Protocol Date:	**October 7, 2020, Version 3.0**
SAP Date:	**October 21, 2021, Version 2.0**
Addendum Date:	**November 11, 2021**

Approved by:

Name	Role	Date	Signature
Sheila Oren	CEO	11 NA 21	
Pninit Litman	Study Director	pninit litman	Digitally signed by pninit litman Date: 2021.11.11 20:55:04 +02'00'
Shaul E. Kadosh	Statistician	12/Nov/2021	
Hadas Friedman	VP QA/RA		

This addendum to Statistical Analysis Plan (SAP Version 2.0) dated October 21, 2021 was written and approved prior to study unblinding. Furthermore, all personnel approving this SAP are currently fully blinded to the randomization scheme.

The SAP currently defines the modified Intent-to-Treat (mITT) Analysis Set in section 8.2 as follows:

*"The mITT Analysis Set is a subset of the ITT Analysis Set and includes subjects who were randomized, have taken at least one dose of study drug, and have at least one post-Baseline UPDRS (UPDRS II+III) measurement score at the planned **scheduled** visits. The mITT Analysis Set will use treatment according to the group to which subjects were originally randomized to. The mITT Analysis Set will serve as the principal analysis set for efficacy assessments."*

Addendum topics:

1. Based on review of blinded data, the above definition of the mITT Analysis Set would exclude a total of 13 randomized subjects that took at least one dose of study drug but early terminated the treatment/study (ETT/EST) prior to the first planned **scheduled** post baseline visit (End of Week 5 visit) and therefore have no **scheduled** post baseline UPDRS (UPDRS II+III) measurements at all. However, in line with protocol guidelines, a post-treatment UPDRS (UPDRS II+III) was collected at the **unscheduled** ETT/EST visit.
2. Consistent with the intent-to-treat principle, these 13 subjects should be included in the mITT population, since they were randomized, took at least one dose of study drug, and completed at least one post-treatment efficacy assessment, even though it occurred at an **unscheduled**, rather than a **scheduled** visit. Therefore, in order to be as thorough and complete as possible, we will interpret the early termination visit for these specific subjects as a **scheduled** visit in order to include these patients in the primary MMRM analysis.
3. The data collected from these 13 subjects at the earlier of ETT/EST visit will be mapped to End of week 5 visit.
4. In order to explore the impact of this modification, an additional sensitivity analysis will be conducted, repeating the principal analysis of the primary endpoint while excluding these 13 patients.
5. One subject with no baseline UPDRS (UPDRS II+III) measurement will be excluded from the mITT Analysis Set as the endpoint, change of total UPDRS score (defined as sum of parts II and III, scores (0-160) cannot be calculated.