Efficacy and safety of P2B001 in the management of early Parkinson's disease. Results from a phase 3, randomized, double-blind, double-dummy controlled trial

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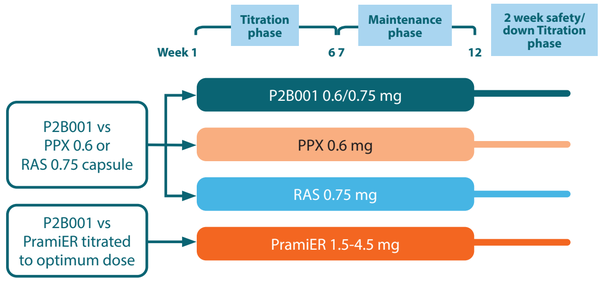
Objective

- P2B001 is an investigational, fixed-dose, once-daily combination of extended release (ER) formulations of pramipexole and rasagiline (0.6mg/0.75mg), in development as once-daily treatment for the signs and symptoms of Parkinson's disease (PD).[1,2]
- The combination of low-dose pramipexole and rasagiline aims to improve striatal dopaminergic transmission via distinct and potentially synergistic mechanisms.[2]
- Phase 2 data demonstrated significant symptomatic efficacy of P2B001 versus placebo, with a benign safety profile that was similar to placebo.[1]
- The aim of this Phase 3, pivotal study was to evaluate the efficacy and safety of P2B001 compared with its components and with marketed Extended-Release pramipexole (PramiER, calibration arm) in untreated PD.

Study Design

A 12-week, multi-center, multinational, randomized, double blind, double-dummy, active-controlled, parallel group study



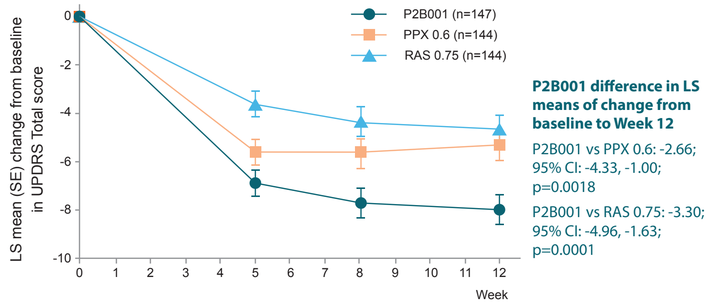
Key inclusion criteria

- Male or female, aged 35-80 years
- PD consistent with the UK Brain Bank Criteria
- Hoehn-Yahr <3
- Disease duration <3 years since diagnosis
- Not on PD medication

Untreated patients were randomized double-blind (2:2:2:1) to 12-weeks treatment with P2B001, pramipexole-ER (PPX) 0.6mg, rasagiline-ER (RAS) 0.75mg, or marketed ER-PPX (titrated).

Primary outcome measure

P2B001 showed superior efficacy to each of its individual components on change from baseline in UPDRS Total (Parts II+III) scores



P2B001 difference in LS means of change from baseline to Week 12

P2B001 vs PPX 0.6: -2.66; 95% CI: -4.33, -1.00; p=0.0018

P2B001 vs RAS 0.75: -3.30; 95% CI: -4.96, -1.63; p=0.0001

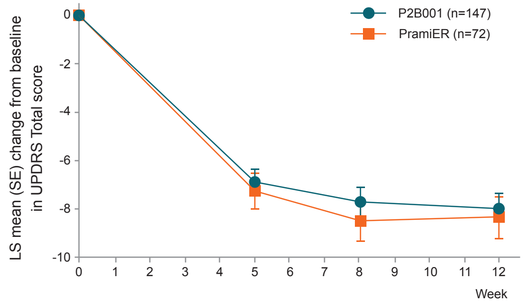
TEAEs occurring in ≥5% of patients in any treatment group

Fewer dopaminergic adverse events were reported with P2B001 vs marketed PramiER

MedDRA preferred term	P2B001 (n=150)	PPX 0.6 (n=148)	RAS 0.75 (n=147)	PramiER (n=74)
At least one TEAE	112 (74.7%)	109 (73.6%)	87 (59.2%)	64 (86.5%)
TEAEs occurring in ≥5% of patients in any treatment group				
Nausea	28 (18.7%)	24 (16.2%)	10 (6.8%)	17 (23.0%)
Fatigue	23 (15.3%)	22 (14.9%)	2 (1.4%)	13 (17.6%)
Somnolence	22 (14.7%)	27 (18.2%)	7 (4.8%)	23 (31.1%)
Dizziness	16 (10.7%)	14 (9.5%)	19 (12.9%)	7 (9.5%)
Insomnia	13 (8.7%)	9 (6.1%)	4 (2.7%)	7 (9.5%)
Headache	9 (6.0%)	14 (9.5%)	9 (6.1%)	5 (6.8%)
Constipation	6 (4.0%)	11 (7.4%)	9 (6.1%)	7 (9.5%)
Fall	6 (4.0%)	8 (5.4%)	5 (3.4%)	1 (1.4%)
Orthostatic hypotension	4 (2.7%)	5 (3.4%)	4 (2.7%)	9 (12.2%)
Decreased appetite	3 (2.0%)	2 (1.4%)	2 (1.4%)	4 (5.4%)
Pain in extremity	2 (1.3%)	10 (6.8%)	2 (1.4%)	4 (5.4%)
Memory impairment	0 (0.0%)	0 (0.0%)	1 (0.7%)	4 (5.4%)

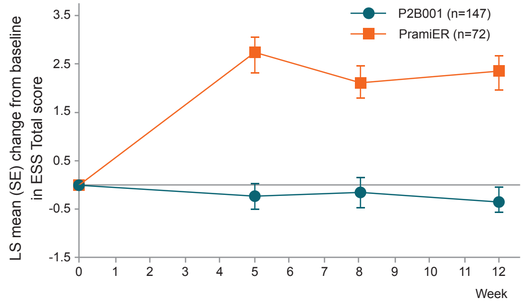
P2B001 treatment resulted in:

(a) Comparable efficacy to PramiER (mean dose 3.2mg) on improving symptoms of PD (UPDRS Total scores)



Change from baseline UPDRS Total score (P2B001 vs PramiER): **-7.98** ± 0.60 points vs **-8.35** ± 0.86; p=0.7197

(b) Significantly less daytime sleepiness (Epworth Sleepiness Scale [ESS] score, 1st secondary outcome)



-2.66 point difference on ESS for P2B001 vs PramiER **p<0.0001**

Baseline demographics

	P2B001 (n=157)	PPX 0.6 (n=156)	RAS 0.75 (n=154)	PramiER (n=77)
Age, years (SD)	63.9 (9.4)	64.9 (8.4)	65.1 (9.5)	63.9 (8.8)
Male, n (%)	106 (67.5%)	104 (66.7%)	106 (68.8%)	53 (68.8%)
White, n (%)	150 (95.5%)	147 (94.2%)	145 (94.2%)	74 (96.1%)
Time since diagnosis, months (SD)	5.1 (7.6)	4.4 (5.8)	5.8 (7.9)	5.8 (8.2)
Hoehn & Yahr stage ≥2, n (%)	120 (76.4%)	123 (78.8%)	118 (76.6%)	59 (76.6%)
UPDRS Total score (SD)	30.7 (9.9)	31.3 (11.0)	31.3 (10.2)	28.8 (10.0)
ESS score (SD)	5.5 (4.0)	6.2 (4.0)	5.7 (4.3)	6.1 (4.1)

Conclusions

- The study met its primary and secondary endpoint and treatment with P2B001 was well-tolerated with fewer dopaminergic AEs than PramiER.
- These findings support the potential of P2B001 as a first-line, once-daily treatment for people with PD that may offer effective symptomatic control with a favorable safety profile and no need for titration.

References

1. Olanow et al. Mov Disord 2017; 32(5):783-789. 2. Hauser et al. Adv Ther 2022; doi: 10.1007/s12325-022-02097-2.

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