Non-motor Effects of Bemdaneprocel for Parkinson's Disease: Results up to 18 Months From a Phase 1 Study

Henchcliffe C[1]; Sarva H[2]; Lozano A[3,4]; Fasano A[4–6]; Kalia S[3,4]; Yu K[7]; Brennan C[7]; York M[8]; Stemple W[9]; Abid N[9]; Yountz M[9]; Enayetallah A[9]; Lampron A[9]; Tabar V[7]

[1]Department of Neurology, University of California, Irvine, CA, USA; [2]Department of Neurology, Weill Cornell Medicine, New York, NY, USA; [3]Division of Neurosurgery, University of Toronto, Toronto, Ontario, Canada; [4]Krembil Brain Institute, Toronto, Ontario, Canada; [5]Division of Neurology, University of Toronto, Toronto, Ontario, Canada; [6]Edmond J. Safra Program in Parkinson's Disease, Morton and Gloria Shulman Movement Disorders Clinic, Toronto Western Hospital, UHN, Toronto, Ontario, Canada; [7]Department of Neurosurgery and Center for Stem Cell Biology, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [8]Department of Neurology, Baylor College of Medicine, Houston, TX, USA; [9]BlueRock Therapeutics LP, Cambridge, MA, USA

Introduction

- Current standard treatments for Parkinson's disease (PD) motor symptoms do not address the loss of dopaminergic neurons, an underlying cause of the disease; moreover, they do not specifically address and may even worsen some non-motor symptoms[1–3]
- Bemdaneprocel is an investigational therapy comprising dopaminergic neuronal progenitors derived from human embryonic stem cells
  - Preclinical studies in rodents support safety and proof-of-concept for bemdaneprocel[4,5]
- Results previously presented from exPDite, a Phase 1 multicenter, multisite, open-label, nonrandomized study (NCT04802733), met the primary objective of safety and tolerability, supported the feasibility of stereotactic transplantation of bemdaneprocel, and suggested stability or improvement in motor outcomes in some participants at 12 months post transplantation[6]

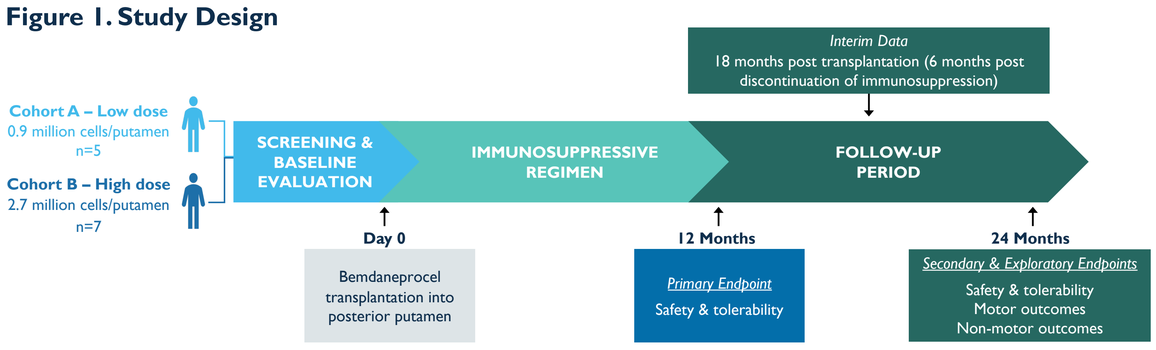
Objective

- To evaluate the impact of bemdaneprocel, compared with baseline, on non-motor outcomes up to 18 months post transplantation (6 months post discontinuation of immunosuppression) in participants with PD

Methods

- Participants with PD motor symptoms inadequately controlled by standard treatments were ≥50 to ≤78 years of age in Canada or ≥60 to ≤78 years of age in the United States
  - Eligible participants had a diagnosis of idiopathic PD (based on modified UK Parkinson's Disease Society Brain Bank criteria) with ≥3 to ≤20 years since PD diagnosis, levodopa response (defined as ≥30% improvement on Movement Disorders Society-Unified Parkinson's Disease Rating Scale [MDS-UPDRS] Part III), and a Hoehn and Yahr score of 0–3 in ON state (Canada only), or 0–2 in ON state and 3–4 in OFF state (US only)

Figure 1. Study Design



- A total of 12 participants enrolled sequentially
  - The first 5 participants were assigned to the low-dose cohort (0.9 million cells/putamen); the last 7 were assigned to the high-dose cohort (2.7 million cells/putamen)
- Bemdaneprocel was administered stereotactically into the posterior putamen bilaterally through a single burr hole on each side in a single session
  - A cannula was used to deliver a total of 9 cell deposits along 3 tracks per putamen
- Immunosuppression was initiated during transplantation and continued for 1 year post transplantation
  - **Basiliximab** (20 mg, IV) was administered intraoperatively and on postoperative day 4
  - **Methylprednisolone** (500 mg, IV) was initiated on day 0, tapered to **prednisone** (5 mg, PO), and continued at 5 mg QD for 1 year
  - **Tacrolimus** (PO, BID) was initiated on postoperative day 1 and adjusted to a target trough blood level of 4–7 ng/mL for 1 year
- Exploratory non-motor outcomes are reported as mean scores at baseline and 18 months post transplantation on the Parkinson's Disease Non-Motor Symptom Scale (PD NMSS) and 39-item Parkinson's Disease Questionnaire (PDQ-39)
- A formal neuropsychological evaluation included the Neuropsychiatric Inventory Questionnaire (NPI-Q), Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), and Frontal System Behavior Scale (FrSBe); results at baseline and 12 months post transplantation are reported

Results

Table 1. Participant Demographics and Baseline Characteristics

	Low Dose (n=5)	High Dose (n=7)	Total (N=12)
Age, years			
Mean (SD)	66.8 (6.8)	66.7 (4.8)	66.8 (5.4)
Median (Q1, Q3)	67.0 (65.0, 67.0)	68.0 (64.0, 70.0)	67.0 (64.5, 70.0)
Sex, n (%)			
Male	4 (80.0)	5 (71.4)	9 (75.0)
Female	1 (20.0)	2 (28.6)	3 (25.0)
Race, n (%)			
Asian	0	1 (14.3)	1 (8.3)
White	3 (60.0)	5 (71.4)	8 (66.7)
Other	1 (20.0)	1 (14.3)	2 (16.7)
Multiple	1 (20.0)	0	1 (8.3)
Time since PD diagnosis, years			
Mean (SD)	11.0 (3.7)	7.8 (2.2)	9.1 (3.2)
Median (Q1, Q3)	12.7 (8.9, 13.7)	8.2 (5.3, 10.2)	9.0 (5.9, 11.5)
Hoehn and Yahr Stage (OFF state), n (%)			
2	1 (20.0)	0	1 (8.3)
3	4 (80.0)	7 (100.0)	11 (91.7)
Hoehn and Yahr Stage (ON state), n (%)			
2	5 (100.0)	7 (100.0)	12 (100.0)

PD, Parkinson's disease; Q1, quartile 1; Q3, quartile 3; SD, standard deviation.

Table 2. Parkinson's Disease Non-Motor Symptom Scale (PD NMSS)

	Low Dose (n=5)		High Dose (n=7)	
PD NMSS Domain, mean (median)	Baseline	18 months	Baseline	18 months
Cardiovascular Including Falls	0.8 (1.0)	3.8 (2.0)	0.9 (0.0)	1.3 (0.0)
Sleep/Fatigue		14.8 (12.0)	8.9 (8.0)	10.9 (8.0)
Mood/Cognition		6.0 (7.0)	0.6 (0.0)	2.3 (0.0)
Perceptual Problems/Hallucinations		1.0 (0.0)	1.1 (0.0)	1.4 (0.0)
Attention/Memory		6.0 (4.0)	1.7 (0.0)	2.9 (2.0)
Gastrointestinal Tract		4.8 (1.0)	3.6 (2.0)	4.6 (3.0)
Urinary		12.8 (10.0)	11.7 (10.0)	11.0 (8.0)
Sexual Function	1.0 (0.0)	3.0 (0.0)	4.0 (0.0)	4.0 (0.0)
Miscellaneous	4.8 (1.0)	3.6 (4.0)	8.1 (1.0)	5.7 (0.0)
Total Score	**24.8 (15.0)**	**55.8 (43.0)**	**40.6 (38.0)**	**44.0 (37.0)**

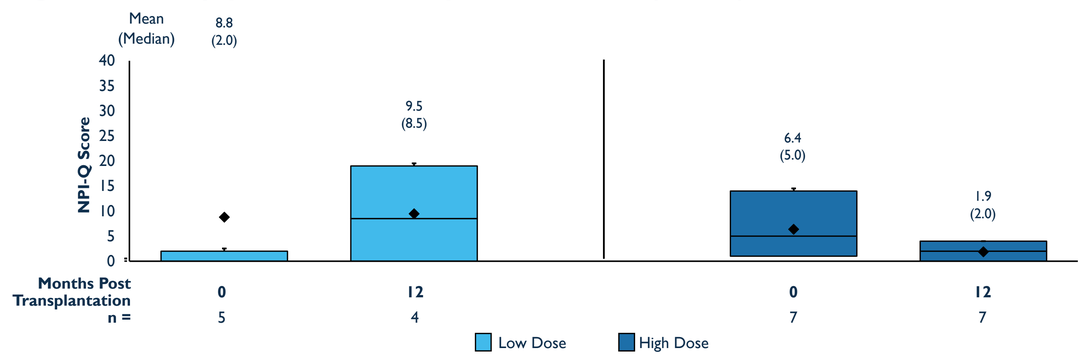
Total score range: 0–360 (lower scores indicate improvement).[7]

Table 3. 39-item Parkinson's Disease Questionnaire (PDQ-39)

		18 months	
	27.5 (30.0)	31.5 (35.0)	15.4 (12.5)
Activities of Daily Living	30.8 (33.3)	25.0 (25.0)	24.4 (20.8)
Emotional Well-being	23.3 (25.0)	27.5 (25.0)	8.9 (4.2)
Stigma	21.3 (25.0)	25.0 (25.0)	6.3 (0.0)
Social Support	20.0 (16.7)	14.2 (16.7)	4.8 (0.0)
Cognition	18.8 (18.8)	18.8 (12.5)	15.2 (12.5)
Communication	23.3 (16.7)	26.7 (25.0)	7.1 (0.0)
Bodily Discomfort	35.0 (41.7)	35.0 (25.0)	39.3 (33.3)
Summary Index			

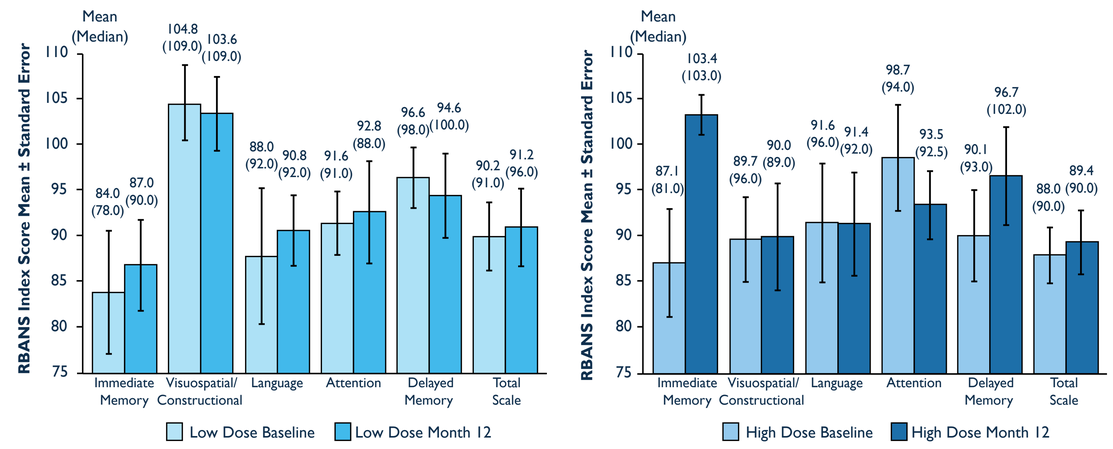
Summary index score range: 0–100 (lower scores indicate improvement).[8]

Figure 2. Neuropsychiatric Inventory Questionnaire (NPI-Q)



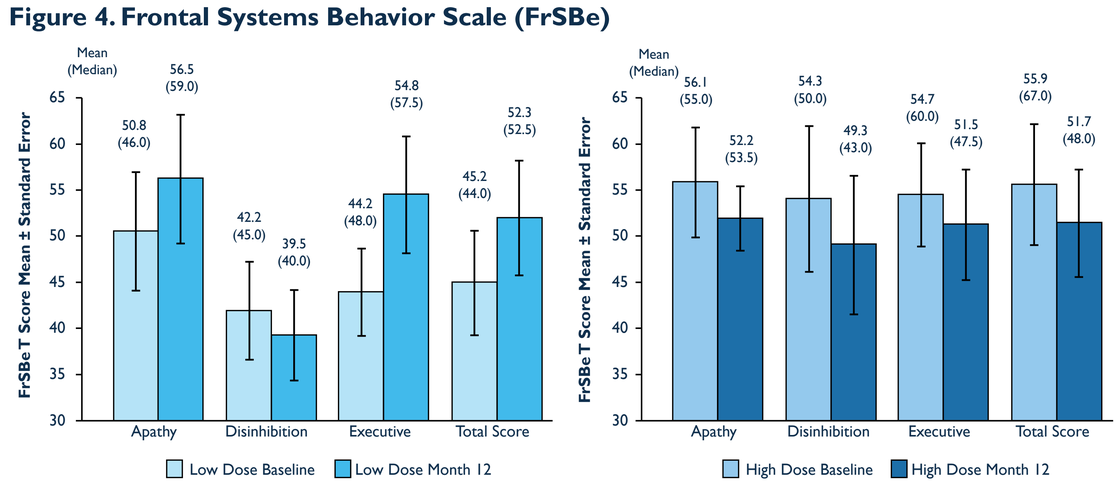
Total score range: 0–96 (lower scores indicate improvement).[9] Horizontal lines: median; diamonds: mean; boxes: quartiles 1 and 3; whiskers: extreme values.

Figure 3. Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)



Total scale score range: 40–160 (higher scores indicate improvement).[10]

Figure 4. Frontal Systems Behavior Scale (FrSBe)



Raw scores are converted to T-scores (mean 50, SD 10; T-scores ≥65 are clinically significant). Lower scores indicate improvement.[11]

References: 1. Armstrong MJ, Okun MS. *JAMA.* 2020;323(6):548-60. 2. Rascol O, Payoux P, Ory F, Ferreira JJ, Brefel-Courbon C, Montastruc JL. *Ann Neurol.* 2003;53(Suppl 3):S3-S12. 3. De Bie RMA, Clarke CE, Espay AJ, Fox SH, Lan AE. *Lancet Neurol.* 2020;19(5):452-61. 4. Kim TW, Piao J, Koo SY, et al. *Cell Stem Cell.* 2021;28(2):343-55.e5. 5. Piao J, Zabierowski S, Dubose BN, et al. *Cell Stem Cell.* 2021;28(2):217-29.e7. 6. Henchcliffe C, Sarva H, Lozano A, et al. Presented at: International Congress of Parkinson's Disease and Movement Disorders; August 27–31, 2023; Copenhagen, Denmark. 7. Ray Chaudhuri K, Rojo JM, Schapira AHV, et al. *PLoS One.* 2013;8(2):e57221. 8. Balestrino R, Hurtado-Gonzalez CA, Stocchi F, et al. *NPJ Parkinsons Dis.* 2019;5:26. 9. Cummings JL. The Neuropsychiatric Inventory Questionnaire: Background and Administration. 1994. https://www.alz.org/media/documents/npiq-questionnaire.pdf. 10. Yang C, Garrett-Mayer E, Schneider JS, Gollomp SM, Tilley BC. *Mov Disord.* 2009;24(10):1453-60. 11. Cabrera S, Edelstein K, Mason WP, Tartaglia MC. *Neurooncol Pract.* 2016;3(2):113-9.

Disclosures: Henchcliffe C has received honoraria for consulting from AskBio and Certara; stock options for scientific advisory board participation from Axent Biosciences; honoraria for scientific advisory board participation from Bayer AG, Canary Health Technologies, and ProJenX; honoraria for DSMB meetings from MeiraGTx; research support from BlueRock Therapeutics and Weston Brain Institute; and honoraria for presentations from the American Academy of Neurology, ASGCT, UCLA, IAPRD, World Congress of Neurology, and the Parkinson Study Group. **Sarva H** has performed consulting work for Novo Nordisk and Neurocrine in the past 24 months. She received research support from BlueRock, Prevail, Neuroderm, Sun Pharma, Biogen, Insightec, Bukwang, Genentech, Novo Nordisk, Samuels Foundation, and National Institute of Aging. She has received research support in the past from NIH. **Lozano A** has nothing to disclose. **Fasano A** has stock ownership in Inbrain Pharma and has received payments as consultant and/or speaker from AbbVie, Abbott, Boston Scientific, CereGate, Dompé Farmaceutici, Inbrain Neuroelectronics, Ipsen, Medtronic, Iota, Syneos Health, Merz, Sunovion, Paladin Labs, and UCB. He has received research support from AbbVie, BlueRock Therapeutics, Boston Scientific, Medtronic, Praxis, and ES and receives royalties from Springer. **Kalia S** has received consultant and/or speaker honoraria from Novo Nordisk, Abbott, Boston Scientific, and Medtronic. **Yu K** has nothing to disclose. **Brennan C** has nothing to disclose. **York M** has performed consulting work for the Michael J. Fox Foundation, the Parkinson's Foundation, and BlueRock Therapeutics; received research support from the Michael J. Fox Foundation, NIH, NASA, and the Alzheimer's Association; received honoraria for scientific advisory board participation from RAD-PD. **Stemple W, Abid N, Yountz M, Enayetallah A,** and **Lampron A** are full-time employees of BlueRock Therapeutics LP. **Tabar V** is a scientific advisor for BlueRock Therapeutics.
Support and Acknowledgments: This study was supported by BlueRock Therapeutics LP. Under the direction of the authors, Benjamin M. Hiller, PhD, of Peloton Advantage, LLC, an OPEN Health company, provided medical writing and editorial support for this poster, which was funded by BlueRock Therapeutics LP.
Bemdaneprocel is investigational and has not been approved for treatment by any health authority.

Conclusions

- Participants who received bemdaneprocel experienced stability or improvement in many exploratory non-motor, quality of life, and psychiatric outcomes
  - Participants in the high-dose cohort showed greater trends towards improvement on the NPI-Q, RBANS, and FrSBe at 12 months, suggesting positive outcomes in neuropsychiatric symptoms, cognitive functioning, and frontal lobe-related behaviors
  - The high-dose cohort demonstrated stability of PD NMSS and PDQ-39 scores at 18 months (6 months post discontinuation of immunosuppression), suggesting controlled non-motor symptom severity and health-related quality of life
  - Trends in these data must be interpreted with caution due to the small sample size and uncontrolled study design
- These results support the continued development of bemdaneprocel for the treatment of people with Parkinson's disease and the continued investigation of the impact of bemdaneprocel on non-motor outcomes

Presented at 18th International Conference on Alzheimer's & Parkinson's Diseases; Lisbon, Portugal; March 5–9, 2024