Clinical trial results:
A Phase 2A Safety and Biomarker Study of EPI-589 in Mitochondrial Subtype and Idiopathic Parkinson's Disease Subjects

Summary

EudraCT number	2015-001786-10
Trial protocol	GB DE
Global end of trial date	08 January 2019

Results information

Result version number	v1 (current)
This version publication date	11 November 2023
First version publication date	11 November 2023

Trial information

Trial identification

Sponsor protocol code	EPI589-15-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02462603
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	PTC Therapeutics, Inc.
Sponsor organisation address	100 Corporate Court, South Plainfield, United States, NJ 07080
Public contact	Medical Information, PTC Therapeutics, Inc., +011 44 1-866-562-4620, medinfo@ptcbio.com
Scientific contact	Medical Information, PTC Therapeutics International Limited, +353 19068700, medinfo@ptcbio.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 January 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 January 2019
Global end of trial reached?	Yes
Global end of trial date	08 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the safety of PTC589 as assessed by occurrence of drug-related serious adverse events (SAEs) in participants with Parkinson's Disease (PD).

Protection of trial subjects:

This study was conducted in full accordance with all applicable research policies and procedures, all applicable United States (US) federal and local laws and regulations including 45 Code of Federal Regulations (CFR) 46, 21 CFR Parts 50, 54, 56, 312 and 314, and the International Conference on Harmonisation (ICH) Guideline for good clinical practice E6(R2)(2016).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 May 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	United States: 29
Worldwide total number of subjects	44
EEA total number of subjects	7

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	15
From 65 to 84 years	29

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Forty-four participants (28 idiopathic and 16 genetically diagnosed) were enrolled into the study and 41 participants received treatment

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	PTC589

Arm description:

Participants with Parkinson's disease (idiopathic and mitochondrial genetic subtype participants) received PTC589 at a dose of 500 milligrams (mg) (2 tablets of 250 mg each) orally twice daily (BID) for up to 3 months unless discontinued for safety or tolerability issues.

Arm type	Experimental
Investigational medicinal product name	PTC589
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

PTC589 was administered per schedule specified in the arm description.

Number of subjects in period 1	PTC589
Started	44
Received at Least 1 Dose of Study Drug	41
EITT population	40
Completed	40
Not completed	4
Non-Compliance	1
Consent withdrawn by subject	2
Investigator Decision	1

Baseline characteristics

Reporting groups	
Reporting group title	PTC589
Reporting group description:	
Participants with Parkinson's disease (idiopathic and mitochondrial genetic subtype participants) received PTC589 at a dose of 500 milligrams (mg) (2 tablets of 250 mg each) orally twice daily (BID) for up to 3 months unless discontinued for safety or tolerability issues.	

Reporting group values	PTC589	Total	
Number of subjects	44	44	
Age categorical Units: Subjects			
Adults (18-64 years)	15	15	
Elderly (From 65-84 years)	29	29	
Sex: Female, Male Units: participants			
Female	9	9	
Male	35	35	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	1	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	43	43	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	2	
Not Hispanic or Latino	42	42	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	PTC589

Reporting group description:

Participants with Parkinson's disease (idiopathic and mitochondrial genetic subtype participants) received PTC589 at a dose of 500 milligrams (mg) (2 tablets of 250 mg each) orally twice daily (BID) for up to 3 months unless discontinued for safety or tolerability issues.

Primary: Number of Participants With Drug-Related Serious Adverse Events (SAEs)

End point title	Number of Participants With Drug-Related Serious Adverse Events (SAEs)[1]

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. Serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. A summary of other non-serious AEs and all SAEs, regardless of causality is located in the 'Reported AE section'. Safety population included any participant who received at least 1 dose of PTC589.

End point type	Primary

End point timeframe:

Baseline up to 30 days after last dose of study drug (up to 4 months)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis is descriptive in nature.

End point values	PTC589			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Movement Disorder Society Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Score at Month 3

End point title	Change From Baseline in Movement Disorder Society Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Score at Month 3

End point description:

The MDS-UPDRS is a tool for monitoring the impact of Parkinson’s disease, the degree of disability caused, and complications from treatment. Part I (13 items) evaluates nonmotor experiences of daily living (nM-EDL); Part II (13 items) evaluates motor experiences of daily living (M-EDL; Part III (18 items) is a motor examination; Part IV (6 items) examines motor complications (for example, motor fluctuations and dyskinesias). Each item was rated on a 5-point scale, ranging from 0 (normal) to 4 (severe), with higher score indicating greater severity and more impairment. Total score for Part I (nM-EDL) and Part II (M-EDL) each ranges from 0-52; for Part III (motor examination) ranges from 0-72; and for Part IV (motor complications) ranges from 0-24; with higher scores in each range for all 4 parts

reflecting greater severity. Efficacy intent-to-treat (EITT) population included any participant who received at least 1 dose of PTC589 and had a minimum of the Month 3 assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 3

End point values	PTC589			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: units on a scale				
arithmetic mean (standard deviation)				
nM-EDL Total Score: Baseline	5.0 (± 4.51)			
nM-EDL Total Score: Change at Month 3	-0.1 (± 3.93)			
M-EDL Total Score: Baseline	5.8 (± 4.13)			
M-EDL Total Score: Change at Month 3	0.1 (± 3.54)			
Motor Examination Total Score: Baseline	22.5 (± 8.60)			
Motor Examination Total Score: Change at Month 3	-0.6 (± 6.72)			
Motor Complications Total Score: Baseline	1.3 (± 2.34)			
Motor Complications Total Score: Change at Month 3	-0.1 (± 2.17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Non-motor Symptoms Scale (NMSS) Total Score at Month 3

End point title	Change From Baseline in Non-motor Symptoms Scale (NMSS) Total Score at Month 3

End point description:

Non-motor symptoms were evaluated using the NMSS which was divided into 30 questions in 9 different domains including such symptoms as dribbling saliva, constipation, depression, sleep disorders, apathy, hallucinations and dementia. Symptoms were quantified based on their severity (using a scale of 0 [none] to 3 [severe]) and frequency (using a scale of 0 [rarely] to 4 [very frequent]). Total score derived from adding up the product of the frequency score times severity score for each of the 30 questions. Total score ranged from 0 to 360, with a lower score indicating fewer symptoms. EITT population included any participant who received at least 1 dose of PTC589 and had a minimum of the Month 3 assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 3

End point values	PTC589			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	15.7 (± 14.84)			
Change at Month 3	-0.6 (± 14.79)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Parkinson's Disease Questionnaire - 39 (PDQ-39) Score at Month 3

End point title	Change From Baseline in Parkinson's Disease Questionnaire - 39 (PDQ-39) Score at Month 3

End point description:

The PDQ-39 is a self-administered questionnaire for participants with Parkinson's disease that has 39 questions grouped in 8 dimensions: mobility (items 1-10), activities of daily living (items 11-16), emotional well-being (items 17-22), stigma (items 23-26), social support (items 27-29), cognitions (items 30-33), communication (items 34-36), and bodily discomfort (items 37-39). Each item was scored on a 5-point Likert scale (0 to 4) to indicate the frequency of each event; 0 = never, 1 = occasionally, 2 = sometimes, 3 = often, and 4 = always or cannot do at all. Each dimension's total score ranged from 0-100, with lower scores indicating better health, and higher scores indicating more severe symptoms. EITT population included any participant who received at least 1 dose of PTC589 and had a minimum of the Month 3 assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 3

End point values	PTC589			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: units on a scale				
arithmetic mean (standard deviation)				
Mobility: Baseline	7.06 (± 12.543)			
Mobility: Change at Month 3	0.19 (± 7.281)			
Activities of daily living: Baseline	11.56 (± 10.096)			
Activities of daily living: Change at Month 3	0.21 (± 10.676)			
Emotional well-being: Baseline	10.84 (± 11.387)			
Emotional well-being: Change at Month 3	0.10 (± 10.180)			
Stigma: Baseline	15.96 (± 17.685)			
Stigma: Change at Month 3	-0.94 (± 16.602)			
Social support: Baseline	1.88 (± 4.811)			

Social support: Change at Month 3	3.12 (± 9.750)			
Cognition: Baseline	9.70 (± 12.085)			
Cognition: Change at Month 3	-1.24 (± 8.747)			
Communication: Baseline	6.25 (± 9.388)			
Communication: Change at Month 3	1.25 (± 10.777)			
Bodily discomfort: Baseline	16.87 (± 15.390)			
Bodily discomfort: Change at Month 3	0.01 (± 14.501)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EuroQol-5 Dimension (EQ-5D) Score at Month 3

End point title	Change From Baseline in EuroQol-5 Dimension (EQ-5D) Score at Month 3

End point description:

EQ-5D is a questionnaire designed to provide measures of health-related quality of life states, consisting of 5 domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). Each dimension has a 3 point response scale designed to indicate the level of the problem: 1 = no problems, 2 = some problems, 3 = extreme problems. A higher score indicated an increase in the level of problem. The EQ-5D also contains a visual analog scale (EQ-VAS), which records the respondent's self-rated health status on a vertical graduated visual analog scale ranging from 0 (worst imaginable health state) to 100 (best imaginable health state). Higher score indicated improvement. EITT population included any participant who received at least 1 dose of PTC589 and had a minimum of the Month 3 assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 3

End point values	PTC589			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: units on a scale				
arithmetic mean (standard deviation)				
Mobility: Baseline	1.2 (± 0.36)			
Mobility: Change at Month 3	0 (± 0.36)			
Personal Care: Baseline	1.1 (± 0.27)			
Personal Care: Change at Month 3	0 (± 0.36)			
Usual Activities: Baseline	1.2 (± 0.42)			
Usual Activities: Change at Month 3	0.1 (± 0.35)			
Pain/Discomfort: Baseline	1.3 (± 0.47)			
Pain/Discomfort: Change at Month 3	0.2 (± 0.48)			
Anxiety/Depression: Baseline	1.1 (± 0.27)			
Anxiety/Depression: Change at Month 3	0.2 (± 0.50)			
VAS Score: Baseline	81.0 (± 12.00)			
VAS Score: Change at Month 3	-1.9 (± 8.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: Montreal Cognitive Assessment (MoCA) Score

End point title	Montreal Cognitive Assessment (MoCA) Score

End point description:

MoCA is a 30-point questionnaire for cognitive dysfunction. It assesses different cognitive domains: attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation. Scores on the MoCA range from 0-30 with 26-30 indicating normal global cognition; 18-25 mild cognitive impairment; 10-17 moderate cognitive impairment; and <10 severe cognitive impairment. EITT population included any participant who received at least 1 dose of PTC589 and had a minimum of the Month 3 assessment. Here, 'Number analyzed' = participants with normal, mild, moderate, or severe cognition impairment. 'n' = participants evaluable for specified category. Data for a specific severity level was not collected if no evaluable participants were available. '99999' = data not available due to no participants.

End point type	Secondary

End point timeframe:

Month 3

End point values	PTC589			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: units on a scale				
arithmetic mean (standard deviation)				
Normal global cognition (n = 33)	28.5 (± 1.25)			
Mild cognitive impairment (n = 7)	23.4 (± 1.40)			
Moderate cognitive impairment (n = 0)	99999 (± 99999)			
Severe cognitive impairment (n = 0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Beck Depression Inventory (BDI) Score

End point title	Beck Depression Inventory (BDI) Score

End point description:

Each of the 21 items on BDI tool represent a depressive symptom. The symptoms are each scored on a 4-point Likert scale of 0 (symptom is absent) to 3 (symptom is severe). Scores for each symptom are added up to obtain the total scores for all 21 items, which are interpreted as follows 1-10 (normal); 11-16 (mild mood disturbance); 17-20 (borderline clinical depression); 21-30 (moderate depression); 31-

40 (severe depression); and >40 (extreme depression). Participants with symptom score of 0 were not included in the summary. EITT population included any participant who received at least 1 dose of PTC589 and had a minimum of Month 3 assessment. 'Number analyzed' = participants with symptom score >1 for normal, mild, borderline, moderate, severe, or extreme depression. 'n' = participants evaluable for specified category. Data for a specific severity level was not collected if no evaluable participants were available. '99999' = data not available due to no participants.

End point type	Secondary

End point timeframe:

Month 3

End point values	PTC589			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: units on a scale				
arithmetic mean (standard deviation)				
Normal (n = 24)	3.6 (± 2.41)			
Mild mood disturbance (n = 9)	13.1 (± 1.83)			
Borderline clinical depression (n = 0)	99999 (± 99999)			
Moderate depression (n = 0)	99999 (± 99999)			
Severe depression (n = 0)	99999 (± 99999)			
Extreme depression (n = 0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Montgomery and Asberg Depression Rating Scale (MADRS) Total Score at Month 3

End point title	Change From Baseline in Montgomery and Asberg Depression Rating Scale (MADRS) Total Score at Month 3

End point description:

The MADRS is a clinician-rated tool for measuring changes in depressive symptom severity. Ten core symptoms and cognitive features (feelings of sadness, lassitude, pessimism, inner tension, suicidality, reduced sleep or appetite, difficulty concentrating, and a lack of interest) were rated on a severity scale of 0 (no symptoms)) to 6 (symptoms of maximum severity). The total score was the sum of the scores on the 10 items, ranging from 0 to 60 with a higher score indicating increasing depressive symptoms. EITT population included any participant who received at least 1 dose of PTC589 and had a minimum of the Month 3 assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 3

End point values	PTC589			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	2.4 (± 2.60)			
Change at Month 3	0.1 (± 3.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time to Complete Time Up and Go (TUG) Test in ON State at Month 3

End point title	Change From Baseline in Time to Complete Time Up and Go (TUG) Test in ON State at Month 3

End point description:

Timed motor tests are simple, objective, quantitative measures for the assessment of Parkinson's disease. They include, in on-medication and off-medication state, timed recorded physical movements. Time Up and Go Test (TUG) is one of timed motor tests which is used to assess a person's mobility and requires both static and dynamic balance. This is a walking assessment. Participants start in the seated position, stand up, walk 7 meters, turn around, and sit back down. The entire process from leaving the chair to returning to the chair was timed. The total time was summarized under ON state with participants on dopamine therapy. EITT population included any participant who received at least 1 dose of PTC589 and had a minimum of the Month 3 assessment. Here, 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Month 3

End point values	PTC589			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: seconds				
arithmetic mean (standard deviation)				
Baseline	8.637 (± 1.8763)			
Change at Month 3	-0.347 (± 1.1056)			

Statistical analyses

No statistical analyses for this end point

Secondary: Level of Disease-Related Biomarker (Glutathione) in Plasma

End point title	Level of Disease-Related Biomarker (Glutathione) in Plasma

End point description:

Glutathione lowest limit of quantification (LLOQ) = 0.01 micromoles (uM) and upper limit of quantification (ULOQ) = 27.83 uM in plasma. EITT population included any participant who received at least 1 dose of EPI-589.

End point type	Secondary

End point timeframe:

Month 3

End point values	PTC589			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: µM				
arithmetic mean (full range (min-max))	1.54 (0.37 to 8.33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of PTC589

End point title	Maximum Observed Plasma Concentration (Cmax) of PTC589

End point description:

EITT population included any participant who received at least 1 dose of PTC589 and had a minimum of the Month 3 assessment. Here, 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

0 hour (predose) and 0.5, 1, 2, 4, 6, 8, and 12 hours postdose at Month 1 and 3

End point values	PTC589			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: nanograms (ng)/milliliter (mL)				
arithmetic mean (standard error)				
Month 1	3718.3 (± 311.6)			
Month 3	2903.5 (± 249.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Level of Disease-Related Biomarker (Glutathione) in Cerebrospinal Fluid (CSF)

End point title	Level of Disease-Related Biomarker (Glutathione) in Cerebrospinal Fluid (CSF)

End point description:

Glutathione LLOQ = 0.002 uM and ULOQ = 0.35 uM in CSF. EITT population included any participant who received at least 1 dose of EPI-589. Here, 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Month 3

End point values	PTC589			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: µM				
arithmetic mean (full range (min-max))	0.10 (0.04 to 0.23)			

Statistical analyses

No statistical analyses for this end point

Secondary: Level of Disease-Related Biomarker (Glutathione) in Urine

End point title	Level of Disease-Related Biomarker (Glutathione) in Urine

End point description:

Glutathione LLOQ = 0.01 uM, and ULOQ = 1.39 uM in urine. EITT population included any participant who received at least 1 dose of EPI-589.
Due to database limitations, the Arithmetic Mean and the Full Range (min-max) cannot be reported in the table below and "0.0000" are reported as placeholders. The Arithmetic Mean is: 0.000006051 and the Full Range (min-max) is: 0.00000034 to 0.00003283.

End point type	Secondary

End point timeframe:

Month 3

End point values	PTC589			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: µM				
arithmetic mean (full range (min-max))	0.0000 (0.0000 to 0.0000)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to 30 days after last dose of study drug (up to 4 months)	
Adverse event reporting additional description:	
Safety population included any participant who received at least 1 dose of PTC589.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups	
Reporting group title	PTC589
Reporting group description:	
Participants with Parkinson's disease (idiopathic and mitochondrial genetic subtype participants) received PTC589 at a dose of 500 mg (2 tablets of 250 mg each) orally BID for up to 3 months unless discontinued for safety or tolerability issues.	

Serious adverse events	PTC589		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 41 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	PTC589		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 41 (70.73%)		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Pyrexia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Pain			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Laryngeal inflammation			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Psychiatric disorders			
Nightmare			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Depressed mood			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Investigations			

Low density lipoprotein increased subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Blood cholesterol increased subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 2		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Injury, poisoning and procedural complications			
Post lumbar puncture syndrome subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 3		
Facial bones fracture subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Fall subjects affected / exposed occurrences (all)	2 / 41 (4.88%) 2		
Muscle strain subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	8 / 41 (19.51%) 15		
Dizziness subjects affected / exposed occurrences (all)	4 / 41 (9.76%) 4		
Bradykinesia subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Dyskinesia subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1		
Dystonia			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Hypoaesthesia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Hypogeusia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Peroneal nerve palsy			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	2		
Eye pain			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Dry eye			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Abnormal sensation in eye			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Ocular discomfort			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Vomiting			

subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	4		
Nausea			
subjects affected / exposed	7 / 41 (17.07%)		
occurrences (all)	9		
Abdominal pain upper			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Salivary hypersecretion			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Flatulence			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Eructation			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Arthralgia			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	7		
Muscular weakness			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Musculoskeletal stiffness			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Plantar fasciitis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Tendonitis			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Skin infection			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Respiratory tract infection viral			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Localised infection			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		

Metabolism and nutrition disorders Gout subjects affected / exposed occurrences (all) Diabetes mellitus subjects affected / exposed occurrences (all)	 1 / 41 (2.44%) 1 1 / 41 (2.44%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 September 2015	The key changes were: • Study title, objectives, and endpoints were modified; • Central nervous system (CNS) and urine biomarker assessments added; • DaTscan removed from Month-3 visit; • The Columbia Suicide Severity Scale has been added to the clinical safety assessments; • Deoxyribonucleic acid (DNA) genetic analysis has been removed from Screening assessments; • Mattis Dementia Rating Scale has been removed from efficacy variables.
04 January 2016	The key changes were: • Numerically indicated the ± day range of study treatment administration; • Additional detail for adaptive design rationale; • Added examples of contraception; • Added a post-treatment follow-up visit; • Added details of study withdrawal criteria; • Added warning about possible drug-associated phototoxicity since no data are yet available.
10 October 2016	The key changes were: • Added the new list of investigators and investigative sites; • Revision of inclusion and exclusion criteria regarding disease severity and prohibited meds; • Added the term "for idiopathic participantd" to DaTscan, "fasting" for blood-based glutathione cycle biomarkers in schedule of assessments; • Changed the MDS-UPDRS assessment from run-in to screening visit; • Changes in laboratory evaluations, National Institutes of Health common terminology criteria, etc.; • Dose modifications guidelines.
17 February 2017	The key change was: • Change in Company Name from Edison Pharmaceuticals to BioElectron Technology Corporation.
29 September 2017	The key changes were: • Fasting conditions for biomarker samples; • Added the term morning and evening dose to BID; • Non-clinical studies language; • Changed the language under pharmacokinetics (PK) section • Changed the timed motor test as ON state only (for participants on dopamine therapy); • Dose limiting toxicity; • Administration of clinical assessment; • Washout period for subjects on high doses of Vitamin E or C; • Complete blood count (CBC) differential as absolute or percentages; • Carbon dioxide (CO2) for serum chemistry; • Day 1 first dose language; • Changed the height measurement to screening visit only; • Included breast exam as part of screening physical exam; • Removed language in adverse event reporting; • Changed the AE language under post-treatment follow-up.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported