



Clinical trial results:

A Phase 3, Double-Blind, Randomized, Placebo Controlled, Parallel Group, Flexible-Dose, 27 Week Trial to Evaluate the Efficacy, Safety, and Tolerability of Tavapadon in Early Parkinson's Disease (TEMPO 2 Trial)

Summary

EudraCT number	2019-002950-22
Trial protocol	FR HU IT
Global end of trial date	01 October 2024

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	CVL-751-PD-002
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04223193
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4UB
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.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	01 October 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to assess the efficacy, safety, tolerability and pharmacokinetics (PK) of flexible doses of tavapadon in participants with Parkinson's Disease.

Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 January 2020
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	Poland: 47
Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Germany: 42
Country: Number of subjects enrolled	Hungary: 10
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Serbia: 8
Country: Number of subjects enrolled	Thailand: 18
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	Ukraine: 25
Country: Number of subjects enrolled	United States: 86
Worldwide total number of subjects	304
EEA total number of subjects	148

Notes:

Subjects enrolled per age group

In utero	0
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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)	159
From 65 to 84 years	145
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In this Phase 3, Double-Blind study, a total of 304 subjects with Parkinson's Disease (PD) were randomized in a 1:1 ratio to either Placebo, or tavapadon 5 mg to 15 mg once daily (QD) for 27 Weeks.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Treatment assignments were blinded to the investigators and other trial site personnel, the subjects, and all sponsor personnel who are involved in the conduct of the trial (including trial monitoring, data management, and data analysis). Access to the treatment codes will be restricted to personnel who are responsible for generating and maintaining the randomization code, packaging the IMPs, operating the IVRS/IWRS, analyzing the PK blood samples, or reporting serious adverse events (SAEs)

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received placebo matching to Tavapadon tablet once daily (QD) orally for 27 weeks.

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

Dosage and administration details:

Subjects will receive placebo matching to tavapadon tablet QD orally for 27 weeks.

Arm title	Tavapadon
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Arm description:

Subjects received Tavapadon 5 mg to 15 mg tablet QD orally for 27 weeks.

Arm type	Experimental
Investigational medicinal product name	Tavapadon
Investigational medicinal product code	
Other name	PF-06649751, CVL-751
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received tavapadon 5 mg QD to 15 mg QD tablet once daily orally for 27 weeks.

Number of subjects in period 1	Placebo	Tavapadon
Started	153	151
Completed	130	94
Not completed	23	57
Treatment with Prohibited Concomitant Medications	3	-
Consent withdrawn by subject	5	6
Non- Compliance with Study Drug	-	1
Physician decision	-	1
Failure to Meet Continuation Criteria	1	-
Adverse event, non-fatal	6	36
Other	3	6
Protocol Violation	1	1
Site Terminated by Sponsor	1	3
Lost to follow-up	1	1
Lack of efficacy	2	2

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matching to Tavapadon tablet once daily (QD) orally for 27 weeks.	
Reporting group title	Tavapadon
Reporting group description:	
Subjects received Tavapadon 5 mg to 15 mg tablet QD orally for 27 weeks.	

Reporting group values	Placebo	Tavapadon	Total
Number of subjects	153	151	304
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	62.6	63.1	
standard deviation	± 9.43	± 8.98	-
Gender categorical			
Units: Subjects			
Female	68	67	135
Male	85	84	169
Ethnicity (NIH/ OMB)			
Units: Subjects			
Hispanic or Latino	11	5	16
Not Hispanic or Latino	137	141	278
Unknown or Not Reported	5	5	10
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	15	17	32
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	0	2
White	134	134	268
More than one race	0	0	0
Unknown or Not Reported	1	0	1
MDS-UPDRS Score at Baseline (Parts II and III Combined)			
The MDS-UPDRS rating tool was used to follow longitudinal course of Parkinson's Disease and consisted of 4 parts.Part 1:Non-motor aspects of experiences of daily living[13 items,Score range(SR):0-52];Part 2:Motor aspects of experiences of daily living(13 items,SR:0-52);Part 3:Motor examination(18 items,SR:0-132);Part 4:Motor complications(6 items,SR:0-24.Not collected).Each item has 0-4 rating on scale from 0(normal)-4(severe).Higher values represent a worse outcome.Parts 2 and 3 combined is the sum of Part 2 and Part 3 scores at each assessment time for each participant(31 items,SR:0-184).			
Units: units on a scale			
arithmetic mean	30.0	31.1	
standard deviation	± 11.11	± 11.21	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received placebo matching to Tavapadon tablet once daily (QD) orally for 27 weeks.	
Reporting group title	Tavapadon
Reporting group description:	
Subjects received Tavapadon 5 mg to 15 mg tablet QD orally for 27 weeks.	

Primary: Change From Baseline in the Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts II and III Combined Score

End point title	Change From Baseline in the Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts II and III Combined Score
End point description:	
The MDS-UPDRS rating tool was used to follow longitudinal course of Parkinson's Disease. It was made up of 4 parts: Part 1: Non-motor aspects of experiences of daily living (13 items. Score range: 0–52); Part 2: Motor aspects of experiences of daily living (13 items. Score range: 0–52); Part 3: Motor examination (18 items. Score range: 0–132); Part 4: Motor complications (6 items. Score range: 0–24. Part 4 was not collected in this trial). Each item has 0–4 rating on scale from 0 (normal) to 4 (severe). Higher values represent a worse outcome. A negative change from baseline represents an improvement in motor function. Parts 2 and 3 combined is the sum of Part 2 score and Part 3 score at each assessment time for each participant. The combined score assesses 31 items with score range: 0–184. mITT Population includes subjects who receive at least 1 dose of study drug and have both a baseline and at least 1 postbaseline MDS-UPDRS assessment.	
End point type	Primary
End point timeframe:	
Week 26	

End point values	Placebo	Tavapadon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	99		
Units: score on a scale				
least squares mean (standard error)	-1.2 (± 0.89)	-10.3 (± 0.99)		

Statistical analyses

Statistical analysis title	Week 26: Placebo, Tavapadon
Comparison groups	Placebo v Tavapadon

Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[1]
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-9.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.7
upper limit	-6.5
Variability estimate	Standard error of the mean
Dispersion value	1.31

Notes:

[1] - LS Means, SE, difference from placebo, and CI's are estimated using a mixed effects repeated measures model with fixed effects for treatment group, visits, treatment by visit interaction and MAO-B inhibitor use with the baseline value as a covariate.

Secondary: Change From Baseline in the MDS-UPDRS Part II Score

End point title	Change From Baseline in the MDS-UPDRS Part II Score
End point description:	The Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) rating tool was used to follow longitudinal course of Parkinson's Disease. It was made up of 4 parts: Part 1: Non-motor aspects of experiences of daily living (13 items. Score range: 0–52); Part 2: Motor aspects of experiences of daily living (13 items. Score range: 0–52); Part 3: Motor examination (18 items. Score range: 0–132); Part 4: Motor complications (6 items. Score range: 0–24. Part 4 was not collected in this trial). Each item has 0–4 rating on scale from 0 (normal) to 4 (severe). Higher values represent a worse outcome. A negative change from baseline represents an improvement in motor function.
Analysis Population Description:	mITT Population
End point type	Secondary
End point timeframe:	
Week 26	

End point values	Placebo	Tavapadon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	99		
Units: score on a scale				
least squares mean (standard error)	0.0 (± 0.30)	-1.5 (± 0.33)		

Statistical analyses

Statistical analysis title	Week 26: Placebo, Tavapadon
Comparison groups	Placebo v Tavapadon

Number of subjects included in analysis	233
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0007 ^[2]
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-0.6
Variability estimate	Standard error of the mean
Dispersion value	0.44

Notes:

[2] - LS Means, SE, difference from placebo, and CI's are estimated using a mixed effects repeated measures model with fixed effects for treatment group, visits, treatment by visit interaction and MAO-B inhibitor use with the baseline value as a covariate.

Secondary: Percentage of Responders With "Much Improved" or "Very Much Improved" on Participant Global Impression of Change (PGIC)

End point title	Percentage of Responders With "Much Improved" or "Very Much Improved" on Participant Global Impression of Change (PGIC)
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End point description:

The Patient Global Impression of Change (PGIC) is a 7-point response scale. The participant response to the question, "Compared to your condition at the beginning of treatment, how much has your condition changed?" was assessed. Scores ranged from 1–7 on a scale of 1 (very much improved) to 7 (very much worse). Higher values represent a worse outcome.

Analysis Population Description: mITT Population

End point type	Secondary
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End point timeframe:

Week 26

End point values	Placebo	Tavapadon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	99		
Units: participants	25	46		

Statistical analyses

Statistical analysis title	Week 26: Placebo, Tavapadon
Comparison groups	Tavapadon v Placebo

Number of subjects included in analysis	233
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	Odds ratio (OR)
Point estimate	3.942
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.209
upper limit	7.037

Secondary: Change From Baseline in the MDS-UPDRS Parts II and III Combined Score

End point title	Change From Baseline in the MDS-UPDRS Parts II and III Combined Score
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End point description:

The Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) rating tool was used to follow longitudinal course of Parkinson's Disease. It was made up of 4 parts: Part 1: Non-motor aspects of experiences of daily living (13 items. Score range: 0–52); Part 2: Motor aspects of experiences of daily living (13 items. Score range: 0–52); Part 3: Motor examination (18 items. Score range: 0–132); Part 4: Motor complications (6 items. Score range: 0–24. Part 4 was not collected in this trial). Each item has 0–4 rating on scale from 0 (normal) to 4 (severe). Higher values represent a worse outcome. A negative change from baseline represents an improvement in motor function. Parts 2 and 3 combined is the sum of Part 2 score and Part 3 score at each assessment time for each participant. The combined score assesses 31 items with score range: 0-184.

Analysis Population Description: mITT Population

End point type	Secondary
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End point timeframe:

Week 5, 8, 11, 14, 18, 22, 26, and 27

End point values	Placebo	Tavapadon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	150		
Units: score on a scale				
least squares mean (standard error)				
Week 5 (n = 148, 127)	-2.1 (± 0.58)	-5.5 (± 0.63)		
Week 8 (n = 145, 119)	-2.4 (± 0.64)	-8.5 (± 0.69)		
Week 11 (n = 141, 111)	-2.3 (± 0.71)	-9.5 (± 0.77)		
Week 14 (n = 140, 110)	-2.2 (± 0.76)	-10.3 (± 0.84)		
Week 18 (n = 138, 107)	-2.2 (± 0.85)	-10.0 (± 0.93)		
Week 22 (n = 137, 99)	-1.3 (± 0.82)	-10.1 (± 0.92)		
Week 26 (n = 133, 99)	-1.2 (± 0.89)	-10.3 (± 0.99)		
Week 27 (n = 134, 100)	-1.2 (± 0.89)	-10.4 (± 0.99)		

Statistical analyses

Statistical analysis title	Week 26: Placebo, Tavapadon
Comparison groups	Placebo v Tavapadon
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[3]
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-9.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.7
upper limit	-6.5
Variability estimate	Standard error of the mean
Dispersion value	1.31

Notes:

[3] - LS Means, SE, difference from placebo, and CI's are estimated using a mixed effects repeated measures model with fixed effects for treatment group, visits, treatment by visit interaction and MAO-B inhibitor use with the baseline value as a covariate.

Secondary: Change From Baseline in the MDS-UPDRS Parts I, II and III Combined Score

End point title	Change From Baseline in the MDS-UPDRS Parts I, II and III Combined Score
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End point description:

The Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) rating tool was used to follow longitudinal course of Parkinson's Disease. It was made up of 4 parts: Part 1: Non-motor aspects of experiences of daily living (13 items. Score range: 0–52); Part 2: Motor aspects of experiences of daily living (13 items. Score range: 0–52); Part 3: Motor examination (18 items. Score range: 0–132); Part 4: Motor complications (6 items. Score range: 0–24. Part 4 was not collected in this trial). Each item has 0–4 rating on scale from 0 (normal) to 4 (severe). Higher values represent a worse outcome. A negative change from baseline represents an improvement in motor function. Parts 1, 2, and 3 combined is the sum of Part 1, Part 2, and Part 3 scores at each assessment time for each participant. The combined score assesses 44 items with score range: 0-236.

Analysis Population Description: mITT Population

End point type	Secondary
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End point timeframe:

Week 5, 8, 11, 14, 18, 22, 26, and 27

End point values	Placebo	Tavapadon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	150		
Units: score on a scale				
least squares mean (standard error)				
Week 5 (n = 148, 127)	-2.7 (± 0.67)	-5.2 (± 0.72)		
Week 8 (n = 145, 119)	-3.2 (± 0.73)	-8.3 (± 0.79)		
Week 11 (n = 141, 111)	-3.2 (± 0.82)	-9.3 (± 0.89)		
Week 14 (n = 140, 110)	-3.0 (± 0.88)	-10.4 (± 0.96)		
Week 18 (n = 138, 107)	-2.9 (± 0.96)	-10.1 (± 1.05)		
Week 22 (n = 137, 99)	-1.8 (± 0.96)	-10.1 (± 1.07)		
Week 26 (n = 133, 99)	-1.6 (± 1.03)	-9.9 (± 1.15)		
Week 27 (n = 134, 100)	-1.8 (± 1.03)	-10.2 (± 1.14)		

Statistical analyses

Statistical analysis title	Week 26: Placebo, Tavapadon
Comparison groups	Placebo v Tavapadon
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[4]
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-8.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.3
upper limit	-5.3
Variability estimate	Standard error of the mean
Dispersion value	1.52

Notes:

[4] - LS Means, SE, difference from placebo, and CI's are estimated using a mixed effects repeated measures model with fixed effects for treatment group, visits, treatment by visit interaction and MAO-B inhibitor use with the baseline value as a covariate.

Secondary: Change From Baseline in the MDS-UPDRS Parts I, II and III Individual Score

End point title	Change From Baseline in the MDS-UPDRS Parts I, II and III Individual Score
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End point description:

The Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) rating tool was used to follow longitudinal course of Parkinson's Disease. It was made up of 4 parts: Part 1: Non-motor aspects of experiences of daily living (13 items. Score range: 0–52); Part 2: Motor aspects of experiences of daily living (13 items. Score range: 0–52); Part 3: Motor examination (18 items. Score range: 0–132); Part 4: Motor complications (6 items. Score range: 0–24. Part 4 was not collected in this trial). Each item has 0–4 rating on scale from 0 (normal) to 4 (severe). Higher values represent a worse outcome. A negative change from baseline represents an improvement in motor function.

Analysis Population Description: mITT Population

End point type	Secondary
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End point timeframe:

Week 5, 8, 11, 14, 18, 22, 26, and 27

End point values	Placebo	Tavapadon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	150		
Units: score on a scale				
least squares mean (standard error)				
Part I: Week 5 (n = 148, 127)	-0.6 (± 0.23)	0.4 (± 0.25)		
Part I: Week 8 (n = 146, 120)	-0.8 (± 0.25)	0.2 (± 0.27)		
Part I: Week 11 (n = 141, 111)	-0.8 (± 0.25)	0.2 (± 0.27)		
Part I: Week 14 (n = 141, 111)	-0.7 (± 0.25)	-0.1 (± 0.27)		
Part I: Week 18 (n = 138, 107)	-0.7 (± 0.25)	-0.2 (± 0.27)		
Part I: Week 22 (n = 137, 99)	-0.5 (± 0.27)	0.0 (± 0.30)		
Part I: Week 26 (n = 134, 99)	-0.4 (± 0.29)	0.3 (± 0.32)		
Part I: Week 27 (n = 134, 100)	-0.6 (± 0.28)	0.2 (± 0.31)		
Part II: Week 5 (n = 148, 127)	-0.6 (± 0.22)	-1.0 (± 0.24)		
Part II: Week 8 (n = 146, 120)	-0.4 (± 0.23)	-1.5 (± 0.25)		
Part II: Week 11 (n = 141, 111)	-0.2 (± 0.26)	-1.4 (± 0.28)		
Part II: Week 14 (n = 141, 111)	-0.4 (± 0.26)	-1.7 (± 0.29)		
Part II: Week 18 (n = 138, 107)	-0.3 (± 0.27)	-1.5 (± 0.30)		
Part II: Week 22 (n = 137, 99)	0.2 (± 0.29)	-1.4 (± 0.32)		
Part II: Week 26 (n = 134, 99)	0.0 (± 0.30)	-1.5 (± 0.33)		
Part II: Week 27 (n = 134, 100)	0.0 (± 0.30)	-1.3 (± 0.34)		
Part III: Week 5 (n = 148, 127)	-1.5 (± 0.48)	-4.5 (± 0.52)		
Part III: Week 8 (n = 145, 119)	-2.0 (± 0.53)	-7.0 (± 0.58)		
Part III: Week 11 (n = 141, 111)	-2.2 (± 0.58)	-8.1 (± 0.64)		
Part III: Week 14 (n = 140, 110)	-1.9 (± 0.63)	-8.6 (± 0.69)		
Part III: Week 18 (n = 138, 107)	-1.9 (± 0.69)	-8.4 (± 0.77)		
Part III: Week 22 (n = 137, 99)	-1.5 (± 0.68)	-8.7 (± 0.76)		
Part III: Week 26 (n = 133, 99)	-1.2 (± 0.71)	-8.9 (± 0.80)		
Part III: Week 27 (n = 134, 100)	-1.2 (± 0.71)	-9.0 (± 0.80)		

Statistical analyses

Statistical analysis title	Part I: Week 26 - Placebo, Tavapadon
Comparison groups	Placebo v Tavapadon
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0766 ^[5]
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	0.42

Notes:

[5] - LS Means, SE, difference from placebo, and CI's are estimated using a mixed effects repeated measures model with fixed effects for treatment group, visits, treatment by visit interaction and MAO-B inhibitor use with the baseline value as a covariate.

Statistical analysis title	Part II: Week 26 - Placebo, Tavapadon
Comparison groups	Placebo v Tavapadon
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0007 ^[6]
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-0.6
Variability estimate	Standard error of the mean
Dispersion value	0.44

Notes:

[6] - LS Means, SE, difference from placebo, and CI's are estimated using a mixed effects repeated measures model with fixed effects for treatment group, visits, treatment by visit interaction and MAO-B inhibitor use with the baseline value as a covariate.

Statistical analysis title	Part III: Week 26 - Placebo, Tavapadon
Comparison groups	Placebo v Tavapadon
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[7]
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-7.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.7
upper limit	-5.6
Variability estimate	Standard error of the mean
Dispersion value	1.05

Notes:

[7] - LS Means, SE, difference from placebo, and CI's are estimated using a mixed effects repeated measures model with fixed effects for treatment group, visits, treatment by visit interaction and MAO-B inhibitor use with the baseline value as a covariate.

Secondary: Change From Baseline in the Clinical Global Impression - Severity of Illness (CGI-S) Score

End point title	Change From Baseline in the Clinical Global Impression - Severity of Illness (CGI-S) Score
End point description: The Global Impression – Severity of Illness (CGI-S) Score is a clinician's impression of a participant's severity of illness on a 7-point scale. Scores ranged from 1-7 on a scale of 1 (normal) to 7 (among the most extremely ill participants). Higher values represent a worse outcome. Analysis Population Description: mITT Population	
End point type	Secondary
End point timeframe: Week 5, 8, 11, 14, 18, 22, 26, and 27	

End point values	Placebo	Tavapadon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	150		
Units: score on a scale				
least squares mean (standard error)				
Week 5 (n = 147, 126)	0.0 (± 0.04)	-0.2 (± 0.05)		
Week 8 (n = 145, 119)	0.0 (± 0.05)	-0.2 (± 0.05)		
Week 11 (n = 141, 110)	0.0 (± 0.05)	-0.3 (± 0.06)		
Week 14 (n = 140, 110)	0.0 (± 0.05)	-0.3 (± 0.05)		
Week 18 (n = 138, 106)	0.0 (± 0.05)	-0.3 (± 0.06)		
Week 22 (n = 137, 98)	0.0 (± 0.05)	-0.4 (± 0.06)		
Week 26 (n = 134, 98)	0.0 (± 0.06)	-0.4 (± 0.06)		
Week 27 (n = 134, 99)	0.0 (± 0.05)	-0.3 (± 0.06)		

Statistical analyses

Statistical analysis title	Week 26: Placebo, Tavapadon
Comparison groups	Placebo v Tavapadon
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[8]
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.08

Notes:

[8] - LS Means, SE, difference from placebo, and CI's are estimated using a mixed effects repeated measures model with fixed effects for treatment group, visits, treatment by visit interaction and MAO-B inhibitor use with the baseline value as a covariate.

Secondary: Clinical Global Impression - Improvement (CGI-I) Score

End point title	Clinical Global Impression - Improvement (CGI-I) Score
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End point description:

The Clinical Global Impression – Improvement (CGI-I) Score is a clinician's impression of how much the participant's illness has improved or worsened relative to the baseline on a 7-point scale. Scores ranged from 1-7 on a scale of 1 (very much improved) to 7 (very much worse). Higher values represent a worse outcome.

Analysis Population Description: mITT Population

End point type	Secondary
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End point timeframe:

Week 5, 8, 11, 14, 18, 22, 26, and 27

End point values	Placebo	Tavapadon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	150		
Units: units on a scale				
least squares mean (standard error)				
Week 5 (n = 148, 127)	3.6 (± 0.06)	3.3 (± 0.07)		
Week 8 (n = 146, 120)	3.5 (± 0.07)	3.1 (± 0.08)		
Week 11 (n = 141, 111)	3.5 (± 0.08)	3.0 (± 0.09)		
Week 14 (n = 140, 111)	3.6 (± 0.08)	2.9 (± 0.09)		
Week 18 (n = 138, 107)	3.7 (± 0.09)	2.8 (± 0.10)		
Week 22 (n = 137, 99)	3.6 (± 0.09)	2.8 (± 0.10)		
Week 26 (n = 134, 99)	3.7 (± 0.10)	2.7 (± 0.11)		
Week 27 (n = 134, 100)	3.7 (± 0.09)	2.8 (± 0.11)		

Statistical analyses

Statistical analysis title	Week 26: Placebo, Tavapadon
Comparison groups	Placebo v Tavapadon
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[9]
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.7

Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[9] - LS Means, SE, difference from placebo, and CI's are estimated using a mixed effects repeated measures model with fixed effects for treatment group, visits, treatment by visit interaction and MAO-B inhibitor use with the baseline value as a covariate.

Secondary: Change From Baseline in the PGIC Score

End point title	Change From Baseline in the PGIC Score
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End point description:

The Patient Global Impression of Change (PGIC) is a 7-point response scale. The participant response to the question, "Compared to your condition at the beginning of treatment, how much has your condition changed?" was assessed. Scores ranged from 1-7 on a scale of 1 (very much improved) to 7 (very much worse). Higher values represent a worse outcome.

Analysis Population Description: mITT Population

End point type	Secondary
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End point timeframe:

Week 5, 8, 11, 14, 18, 22, 26, and 27

End point values	Placebo	Tavapadon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	150		
Units: score on a scale				
least squares mean (standard error)				
Week 5 (n = 148, 127)	3.5 (± 0.08)	3.3 (± 0.09)		
Week 8 (n = 145, 120)	3.6 (± 0.09)	3.1 (± 0.09)		
Week 11 (n = 140, 111)	3.6 (± 0.09)	3.1 (± 0.10)		
Week 14 (n = 141, 111)	3.6 (± 0.10)	2.9 (± 0.11)		
Week 18 (n = 138, 107)	3.7 (± 0.10)	2.9 (± 0.12)		
Week 22 (n = 137, 99)	3.7 (± 0.10)	2.9 (± 0.12)		
Week 26 (n = 134, 99)	3.8 (± 0.11)	2.8 (± 0.12)		
Week 27 (n = 134, 100)	3.8 (± 0.11)	2.8 (± 0.12)		

Statistical analyses

Statistical analysis title	Week 26: Placebo, Tavapadon
Comparison groups	Placebo v Tavapadon
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.16

Secondary: Epworth Sleepiness Scale (ESS)

End point title	Epworth Sleepiness Scale (ESS)
End point description:	
The ESS is an 8-question, participant questionnaire that is intended to measure daytime sleepiness. It assesses the likelihood of dozing off or falling asleep in the following common situations: sitting and reading, sitting inactive in a public place as a passenger in a car for an hour or more without stopping for a break, lying down to rest when circumstances permit, sitting and talking to someone, sitting quietly after a meal without alcohol, and in a car while stopped for a few minutes in traffic or at a light. Each situation is rated on a 4-point (0-3) scale with scores ranging from 0 (would never nod off) to 3 (high chance of nodding off). Higher values represent a worse outcome. Analysis Population Description: FAS population includes all randomized participants who received at least 1 dose of study drug.	
End point type	Secondary
End point timeframe:	
Week 26	

End point values	Placebo	Tavapadon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	98		
Units: score on a scale				
least squares mean (standard error)	-0.1 (± 0.22)	-0.1 (± 0.24)		

Statistical analyses

Statistical analysis title	Week 26: Placebo, Tavapadon
Comparison groups	Placebo v Tavapadon
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9795 ^[10]
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.6

Variability estimate	Standard error of the mean
Dispersion value	0.32

Notes:

[10] - LS Means, SE, difference from placebo, and CI's are estimated using a mixed effects repeated measures model with fixed effects for treatment group, visits, treatment by visit interaction and MAO-B inhibitor use with the baseline value as a covariate.

Secondary: Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale (QUIP-RS)

End point title	Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale (QUIP-RS)
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End point description:

QUIP-RS is a questionnaire for impulse-compulsive disorders in Parkinson's disease rating scale to assess impulse control disorders (ICD). The QUIP-RS has 4 primary questions that pertain to commonly reported thoughts, urges/ desires, and behaviors associated with ICDs, each of which is applied to 4 ICDs (compulsive gambling, buying, eating, sexual behavior) and 3 related disorders (medication use, punning, and hobbyism). The QUIP-RS uses a 5-point Likert scale (score 0–4 [0 means "never" and 4 means "very often"] for each question) to gauge the frequency of behaviors. Scores for each ICD and related disorder range from 0 to 16, with a higher score indicating greater severity (frequency) of symptoms. The total QUIP-RS score for all ICDs and related disorders combined ranges from 0 to 112. A higher score indicating greater severity of symptoms.

Analysis Population Description: FAS population

End point type	Secondary
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End point timeframe:

Week 26

End point values	Placebo	Tavapadon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	99		
Units: score on a scale				
least squares mean (standard error)	-1.9 (± 0.31)	-2.0 (± 0.34)		

Statistical analyses

Statistical analysis title	Week 26: Placebo, Tavapadon
Comparison groups	Placebo v Tavapadon
Number of subjects included in analysis	233
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8916 ^[11]
Method	Mixed Model for Repeated Measures (MMRM)
Parameter estimate	LS Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.8

Variability estimate	Standard error of the mean
Dispersion value	0.45

Notes:

[11] - LS Means, SE, difference from placebo, and CI's are estimated using a mixed effects repeated measures model with fixed effects for treatment group, visits, treatment by visit interaction and MAO-B inhibitor use with the baseline value as a covariate.

Secondary: Columbia-Suicide Severity Rating Scale (C-SSRS)

End point title	Columbia-Suicide Severity Rating Scale (C-SSRS)
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End point description:

The C-SSRS is a systematically administered instrument developed to track suicidal adverse events across a treatment study. The instrument is designed to assess suicidal behavior and ideation, track and assess all suicidal events, as well as the lethality of attempts. Suicidal ideation (SI) categories include the following: wish to be dead; nonspecific active suicidal thoughts; active suicidal ideation without intent to act; active suicidal ideation with some intent to act but no plan; active suicidal ideation with plan and intent. Suicidal behavior categories include the following: actual attempt; interrupted attempt; aborted attempt; preparatory acts or behavior; suicidal behavior; completed suicide.

Analysis Population Description: FAS population

End point type	Secondary
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End point timeframe:

Week 27

End point values	Placebo	Tavapadon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	151		
Units: participants				
Any Suicidal Ideations	0	5		
Any Suicidal Behaviors	0	0		
Any Suicidal Behaviors or Ideations	0	5		
Non-Suicidal Self-Injurious Behavior	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs)
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End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product which does not necessarily have a causal relationship with this treatment. The investigator assesses the relationship of each event to the use of study drug. A serious adverse event (SAE) is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the participant and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment emergent adverse events/treatment-emergent serious adverse events (TEAEs/TEAEs) are defined as any event that began or worsened in severity on or after the first dose of study drug.

Analysis Population Description: FAS Population

End point type	Secondary
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End point timeframe:

From first dose of study drug until 190 days following last dose of study drug.

End point values	Placebo	Tavapadon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	151		
Units: participants				
Any TEAE	84	115		
TESAE	2	7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality were reported from enrollment until 4 weeks after the end of study. Treatment-emergent adverse events and serious adverse events were collected from first dose of study drug until 4 weeks after the last dose of study drug.

Adverse event reporting additional description:

Mean duration on study drug was 176.7 and 144.5 days for Placebo and Tavapadon, respectively. Median time on follow up (median time subjects were followed) was 200 and 198 days for Placebo and Tavapadon, respectively.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	Tavapadon_5_to_15_mg_QD
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	Tavapadon_5_to_15_mg_QD	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 151 (4.64%)	2 / 153 (1.31%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
FEMORAL NECK FRACTURE			
subjects affected / exposed	1 / 151 (0.66%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEAD INJURY			
subjects affected / exposed	1 / 151 (0.66%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FALL			
subjects affected / exposed	2 / 151 (1.32%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
JOINT INJURY			

subjects affected / exposed	1 / 151 (0.66%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	1 / 151 (0.66%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
PRESYNCOPE			
subjects affected / exposed	1 / 151 (0.66%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME			
subjects affected / exposed	1 / 151 (0.66%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
HYPERCHROMIC ANAEMIA			
subjects affected / exposed	0 / 151 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
HYPERHIDROSIS			
subjects affected / exposed	0 / 151 (0.00%)	1 / 153 (0.65%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
DEPRESSION			
subjects affected / exposed	1 / 151 (0.66%)	0 / 153 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Non-serious adverse events	Tavapadon_5_to_15 _mg_QD	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	99 / 151 (65.56%)	59 / 153 (38.56%)	
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	8 / 151 (5.30%)	3 / 153 (1.96%)	
occurrences (all)	10	4	
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	6 / 151 (3.97%)	0 / 153 (0.00%)	
occurrences (all)	7	0	
Nervous system disorders			
PARAESTHESIA			
subjects affected / exposed	4 / 151 (2.65%)	4 / 153 (2.61%)	
occurrences (all)	5	5	
HEADACHE			
subjects affected / exposed	25 / 151 (16.56%)	8 / 153 (5.23%)	
occurrences (all)	37	11	
DYSGEUSIA			
subjects affected / exposed	12 / 151 (7.95%)	0 / 153 (0.00%)	
occurrences (all)	12	0	
DIZZINESS			
subjects affected / exposed	24 / 151 (15.89%)	5 / 153 (3.27%)	
occurrences (all)	28	7	
TREMOR			
subjects affected / exposed	3 / 151 (1.99%)	13 / 153 (8.50%)	
occurrences (all)	3	15	
SOMNOLENCE			
subjects affected / exposed	5 / 151 (3.31%)	6 / 153 (3.92%)	
occurrences (all)	6	7	
PARKINSON'S DISEASE			
subjects affected / exposed	1 / 151 (0.66%)	4 / 153 (2.61%)	
occurrences (all)	1	4	
General disorders and administration site conditions			

ASTHENIA			
subjects affected / exposed	8 / 151 (5.30%)	2 / 153 (1.31%)	
occurrences (all)	9	2	
FATIGUE			
subjects affected / exposed	12 / 151 (7.95%)	1 / 153 (0.65%)	
occurrences (all)	14	1	
Gastrointestinal disorders			
DYSPEPSIA			
subjects affected / exposed	6 / 151 (3.97%)	2 / 153 (1.31%)	
occurrences (all)	6	3	
CONSTIPATION			
subjects affected / exposed	6 / 151 (3.97%)	3 / 153 (1.96%)	
occurrences (all)	6	3	
DIARRHOEA			
subjects affected / exposed	4 / 151 (2.65%)	2 / 153 (1.31%)	
occurrences (all)	5	2	
DRY MOUTH			
subjects affected / exposed	5 / 151 (3.31%)	1 / 153 (0.65%)	
occurrences (all)	5	1	
VOMITING			
subjects affected / exposed	12 / 151 (7.95%)	0 / 153 (0.00%)	
occurrences (all)	14	0	
SALIVARY HYPERSECRETION			
subjects affected / exposed	5 / 151 (3.31%)	2 / 153 (1.31%)	
occurrences (all)	5	2	
NAUSEA			
subjects affected / exposed	45 / 151 (29.80%)	5 / 153 (3.27%)	
occurrences (all)	54	5	
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	6 / 151 (3.97%)	2 / 153 (1.31%)	
occurrences (all)	7	2	
Psychiatric disorders			
ABNORMAL DREAMS			
subjects affected / exposed	5 / 151 (3.31%)	1 / 153 (0.65%)	
occurrences (all)	5	2	
INSOMNIA			

subjects affected / exposed occurrences (all)	6 / 151 (3.97%) 6	5 / 153 (3.27%) 5	
ANXIETY subjects affected / exposed occurrences (all)	5 / 151 (3.31%) 5	2 / 153 (1.31%) 2	
Musculoskeletal and connective tissue disorders PAIN IN EXTREMITY subjects affected / exposed occurrences (all)	0 / 151 (0.00%) 0	4 / 153 (2.61%) 5	
BACK PAIN subjects affected / exposed occurrences (all)	4 / 151 (2.65%) 5	7 / 153 (4.58%) 8	
ARTHRALGIA subjects affected / exposed occurrences (all)	7 / 151 (4.64%) 7	6 / 153 (3.92%) 6	
Infections and infestations URINARY TRACT INFECTION subjects affected / exposed occurrences (all)	5 / 151 (3.31%) 5	4 / 153 (2.61%) 4	
UPPER RESPIRATORY TRACT INFECTION subjects affected / exposed occurrences (all)	3 / 151 (1.99%) 3	7 / 153 (4.58%) 7	
COVID-19 subjects affected / exposed occurrences (all)	5 / 151 (3.31%) 5	8 / 153 (5.23%) 8	
BRONCHITIS subjects affected / exposed occurrences (all)	0 / 151 (0.00%) 0	4 / 153 (2.61%) 4	
Metabolism and nutrition disorders DECREASED APPETITE subjects affected / exposed occurrences (all)	4 / 151 (2.65%) 4	1 / 153 (0.65%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 June 2020	Version 2.0: Incorporate measures into the protocol to ensure the safety of the trial subjects and the validity of the trial data in the environment of the COVID-19 pandemic and to clarify other aspects of trial conduct unrelated to the COVID-19 pandemic.
03 September 2021	Version 3.0: Correct errors and harmonize similar content across the Phase 3 tavapadon protocols via modification and clarification of eligibility criteria, procedural aspects, and statistical considerations.
06 July 2023	Version 4.0: Add eye examinations as an additional trial assessment to monitor for the new potential risk of increased intraocular pressure across the Phase 3 tavapadon protocols.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported