Clinical trial results:
An Open-Label Extension Study to Assess the Safety and Tolerability of Sep-363856 in Subjects with Schizophrenia.

Summary

EudraCT number	2019-000696-16
Trial protocol	LV BG HR
Global end of trial date	09 November 2023

Results information

Result version number	v1 (current)
This version publication date	23 November 2024
First version publication date	23 November 2024

Trial information

Trial identification

Sponsor protocol code	SEP361-303

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04109950
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Otsuka Pharmaceutical Development & Commercialization, Inc.
Sponsor organisation address	2440 Research Boulevard, Rockville, United States, 20850
Public contact	Clinical Transparency, Otsuka Pharmaceutical Development & Commercialization, Inc., 11 8446878522 , clinicaltransparency@otsuka-us.com
Scientific contact	Clinical Transparency, Otsuka Pharmaceutical Development & Commercialization, Inc., 11 8446878522 , clinicaltransparency@otsuka-us.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	09 November 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to the long-term safety and tolerability of flexibly- dosed SEP-363856 (25, 50, 75, 100 mg/day) in adult subjects with schizophrenia who completed Study SEP361-301 or Study SEP361-302 by the incidence of overall adverse events (AEs), serious adverse events (SAEs), and AEs leading to discontinuation.

Protection of trial subjects:

Written informed consent, assent, or both were obtained from a legally acceptable representative (e.g., guardian) or from the subject.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 November 2019
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	Serbia: 169
Country: Number of subjects enrolled	United States: 105
Country: Number of subjects enrolled	Ukraine: 86
Country: Number of subjects enrolled	Russian Federation: 60
Country: Number of subjects enrolled	Bulgaria: 38
Country: Number of subjects enrolled	Croatia: 3
Country: Number of subjects enrolled	Colombia: 1
Country: Number of subjects enrolled	Latvia: 1
Worldwide total number of subjects	463
EEA total number of subjects	42

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	11
Adults (18-64 years)	452
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at investigational sites in the United States (US), Russia, Ukraine, Bulgaria, Latvia, Croatia, Colombia and Serbia from 20 Nov 2019 to 09 Nov 2023. Sumitomo Pharma America Inc. was the former Sponsor and conducted this study.

Pre-assignment

Screening details:

A total of 452 adult & 11 adolescent subjects entered current study, after completing 6-week, double-blind treatment period in one of core studies SEP361-301 or SEP361-302. 445 adults and 11 adolescent subjects received flexible doses of SEP363856. Otsuka took over study after IND was transferred and is concluding activities with registry postings.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Adults: Prior Placebo

Arm description:

Subjects who received placebo in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	SEP-363856
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg.

Arm title	Adults: Prior SEP-363856 50 mg/day

Arm description:

Subjects who received SEP-363856 50 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	SEP-363856
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg.

Arm title	Adults: Prior SEP-363856 75 mg/day

Arm description:

Subjects who received SEP-363856 75 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	SEP-363856
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg.

Arm title	Adults: Prior SEP-363856 100 mg/day

Arm description:

Subjects who received SEP-363856 100 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	SEP-363856
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg.

Arm title	Adolescent: Prior Placebo

Arm description:

Adolescent subjects who received placebo in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. Adolescent subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was adjusted in the range of 25 – 75 mg/day, if deemed clinically necessary by the investigator, up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	SEP-363856
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was adjusted in the range of 25 – 75 mg/day. Beginning on Day 18, the dose was adjusted within the range of 25 to 100 mg/day, if deemed clinically necessary by Investigator.

Arm title	Adolescent: Prior SEP-363856 50 mg/day

Arm description:

Subjects who received SEP-363856 50 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adolescent subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was adjusted in the range of 25 – 75 mg/day, if deemed clinically necessary by the investigator, up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	SEP-363856
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was adjusted in the range of 25 – 75 mg/day. Beginning on Day 18, the dose was adjusted within the range of 25 to 100 mg/day, if deemed clinically necessary by Investigator

Arm title	Adolescents: Prior SEP-363856 75 mg/day

Arm description:

Subjects who received SEP-363856 75 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adolescent participants received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was adjusted in the range of 25 – 75 mg/day, if deemed clinically necessary by the investigator, up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	SEP-363856
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was adjusted in the range of 25 – 75 mg/day. Beginning on Day 18, the dose was adjusted within the range of 25 to 100 mg/day, if deemed clinically necessary by Investigator.

Number of subjects in period 1	Adults: Prior Placebo	Adults: Prior SEP-363856 50 mg/day	Adults: Prior SEP-363856 75 mg/day
Started	158	68	161
Completed	53	28	62
Not completed	105	40	99
Noncompliance with Study Drug	3	1	1
Consent withdrawn by subject	36	22	42

Adverse Event	15	7	15
Death	-	-	1
Pregnancy	1	-	-
Geopolitical Conflict Related	3	1	1
Lost to follow-up	10	1	5
Reason not specified	29	4	22
COVID-19 Related	2	2	2
Protocol deviation	3	1	5
Lack of efficacy	3	1	5

Number of subjects in period 1	Adults: Prior SEP-363856 100 mg/day	Adolescent: Prior Placebo	Adolescent: Prior SEP-363856 50 mg/day
Started	65	7	2
Completed	25	0	1
Not completed	40	7	1
Noncompliance with Study Drug	1	-	-
Consent withdrawn by subject	15	3	-
Adverse Event	10	1	1
Death	-	-	-
Pregnancy	-	-	-
Geopolitical Conflict Related	-	-	-
Lost to follow-up	7	1	-
Reason not specified	6	2	-
COVID-19 Related	-	-	-
Protocol deviation	1	-	-
Lack of efficacy	-	-	-

Number of subjects in period 1	Adolescents: Prior SEP-363856 75 mg/day
Started	2
Completed	1
Not completed	1
Noncompliance with Study Drug	-
Consent withdrawn by subject	1
Adverse Event	-
Death	-
Pregnancy	-
Geopolitical Conflict Related	-
Lost to follow-up	-
Reason not specified	-
COVID-19 Related	-

Protocol deviation	-
Lack of efficacy	-

Baseline characteristics

Reporting groups

Reporting group title	Adults: Prior Placebo

Reporting group description:

Subjects who received placebo in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adults: Prior SEP-363856 50 mg/day

Reporting group description:

Subjects who received SEP-363856 50 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adults: Prior SEP-363856 75 mg/day

Reporting group description:

Subjects who received SEP-363856 75 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adults: Prior SEP-363856 100 mg/day

Reporting group description:

Subjects who received SEP-363856 100 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adolescent: Prior Placebo

Reporting group description:

Adolescent subjects who received placebo in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. Adolescent subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was adjusted in the range of 25 – 75 mg/day, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adolescent: Prior SEP-363856 50 mg/day

Reporting group description:

Subjects who received SEP-363856 50 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adolescent subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was adjusted in the range of 25 – 75 mg/day, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adolescents: Prior SEP-363856 75 mg/day

Reporting group description:

Subjects who received SEP-363856 75 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adolescent participants received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was adjusted in the range of 25 – 75 mg/day, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group values	Adults: Prior Placebo	Adults: Prior SEP-363856 50 mg/day	Adults: Prior SEP-363856 75 mg/day
Number of subjects	158	68	161
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	38.1	35.1	37.6
standard deviation	± 10.66	± 8.25	± 9.69
Gender categorical Units: Subjects			
Female	73	18	72
Male	85	50	89
Ethnicity Units: Subjects			
Hispanic or Latino	4	1	8
Not Hispanic or Latino	154	67	153
Unknown or Not Reported	0	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	0
Native Hawaiian or Other Pacific Islander	2	0	2
Black or African American	30	8	27
White	125	60	131
More than one race	0	0	0
Unknown or Not Reported	0	0	1

Reporting group values	Adults: Prior SEP-363856 100 mg/day	Adolescent: Prior Placebo	Adolescent: Prior SEP-363856 50 mg/day
Number of subjects	65	7	2
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	36.5	15.7	15.5
standard deviation	± 9.59	± 1.38	± 0.71
Gender categorical Units: Subjects			
Female	24	3	0
Male	41	4	2
Ethnicity Units: Subjects			
Hispanic or Latino	4	0	1
Not Hispanic or Latino	61	7	1
Unknown or Not Reported	0	0	0

Race Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	0	1	0
Native Hawaiian or Other Pacific Islander	2	0	0
Black or African American	10	2	0
White	52	3	2
More than one race	0	0	0
Unknown or Not Reported	1	0	0

Reporting group values	Adolescents: Prior SEP-363856 75 mg/day	Total	
Number of subjects	2	463	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	14.5		
standard deviation	± 2.12	-	
Gender categorical Units: Subjects			
Female	1	191	
Male	1	272	
Ethnicity Units: Subjects			
Hispanic or Latino	0	18	
Not Hispanic or Latino	2	445	
Unknown or Not Reported	0	0	
Race Units: Subjects			
American Indian or Alaska Native	0	1	
Asian	0	2	
Native Hawaiian or Other Pacific Islander	0	6	
Black or African American	0	77	
White	2	375	
More than one race	0	0	
Unknown or Not Reported	0	2	

End points

End points reporting groups

Reporting group title	Adults: Prior Placebo

Reporting group description:

Subjects who received placebo in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adults: Prior SEP-363856 50 mg/day

Reporting group description:

Subjects who received SEP-363856 50 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adults: Prior SEP-363856 75 mg/day

Reporting group description:

Subjects who received SEP-363856 75 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adults: Prior SEP-363856 100 mg/day

Reporting group description:

Subjects who received SEP-363856 100 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adolescent: Prior Placebo

Reporting group description:

Adolescent subjects who received placebo in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. Adolescent subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was adjusted in the range of 25 – 75 mg/day, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adolescent: Prior SEP-363856 50 mg/day

Reporting group description:

Subjects who received SEP-363856 50 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adolescent subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was adjusted in the range of 25 – 75 mg/day, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adolescents: Prior SEP-363856 75 mg/day

Reporting group description:

Subjects who received SEP-363856 75 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adolescent participants received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was adjusted in the range of 25 – 75 mg/day, if deemed clinically necessary by the investigator, up to 52 weeks.

Primary: Number of Subjects With Adverse Events (AEs), Serious Adverse Events (SAEs), and AEs or SAEs Leading to Study Discontinuation

End point title	Number of Subjects With Adverse Events (AEs), Serious Adverse Events (SAEs), and AEs or SAEs Leading to Study Discontinuation[1][2]

End point description:

An AE is any untoward medical occurrence associated with the use of a drug in subjects, whether or not considered drug related. Untoward medical occurrences that occurred after signing informed consent form (ICF) of the current study SEP361-303 were considered AEs.
A SAE is an AE that meets one or more criteria: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect.

End point type	Primary

End point timeframe:

From signing of the ICF in the current study up to 7 days after last dose of study drug in the current study (approximately 53 weeks)

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: As prespecified in the protocol only descriptive statistics were planned for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was assessed only in adult population.

End point values	Adults: Prior Placebo	Adults: Prior SEP-363856 50 mg/day	Adults: Prior SEP-363856 75 mg/day	Adults: Prior SEP-363856 100 mg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	156	66	159	64
Units: participants				
AEs	89	31	92	30
SAEs	12	4	12	4
AEs or SAEs leading to study discontinuation	15	7	16	10

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signing of the ICF in the current study up to 7 days after last dose of study drug in the current study (approximately 53 weeks)

Adverse event reporting additional description:

The safety population included all the subjects that were enrolled and received at least one dose of study drug during the 52-week OLE treatment period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Adults: Prior Placebo

Reporting group description:

Subjects who received placebo in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adults: Prior SEP-363856 50 mg/day

Reporting group description:

Subjects who received SEP-363856 50 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adults: Prior SEP-363856 75 mg/day

Reporting group description:

Subjects who received SEP-363856 75 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adults: Prior SEP-363856 100 mg/day

Reporting group description:

Subjects who received SEP-363856 100 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adult subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was increased up to 100 mg/day, in increments of 25 mg, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adolescent: Prior Placebo

Reporting group description:

Adolescent subjects who received placebo in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. Adolescent subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was adjusted in the range of 25 – 75 mg/day, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adolescent: Prior SEP-363856 50 mg/day

Reporting group description:

Subjects who received SEP-363856 50 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current

study, following a dose-escalation schedule. In the current study, adolescent subjects received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was adjusted in the range of 25 – 75 mg/day, if deemed clinically necessary by the investigator, up to 52 weeks.

Reporting group title	Adolescents: Prior SEP-363856 75 mg/day

Reporting group description:

Subjects who received SEP-363856 75 mg/day in the double-blind phase 3 studies SEP361-301 [NCT04072354] or SEP361-302 [NCT04092686], received flexible doses of SEP-363856 in the current study, following a dose-escalation schedule. In the current study, adolescent participants received SEP-363856 tablets, orally, once daily at a starting dose of 50 mg on Day 1 through Day 3, followed by dose-escalation to 75 mg/day from Day 4 through Day 7. From Day 8, the dose was adjusted in the range of 25 – 75 mg/day, if deemed clinically necessary by the investigator, up to 52 weeks.

Serious adverse events	Adults: Prior Placebo	Adults: Prior SEP-363856 50 mg/day	Adults: Prior SEP-363856 75 mg/day
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 156 (7.69%)	4 / 66 (6.06%)	12 / 159 (7.55%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 156 (0.64%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	8 / 156 (5.13%)	4 / 66 (6.06%)	10 / 159 (6.29%)
occurrences causally related to treatment / all	2 / 8	0 / 4	2 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	2 / 156 (1.28%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Suicidal behavior			

subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	1 / 156 (0.64%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	1 / 156 (0.64%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Adults: Prior SEP-363856 100 mg/day	Adolescent: Prior Placebo	Adolescent: Prior SEP-363856 50 mg/day
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 64 (6.25%)	0 / 7 (0.00%)	1 / 2 (50.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 64 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Schizophrenia			

subjects affected / exposed	4 / 64 (6.25%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 64 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	0 / 64 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal behavior			
subjects affected / exposed	1 / 64 (1.56%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 64 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 64 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	0 / 64 (0.00%)	0 / 7 (0.00%)	1 / 2 (50.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Adolescents: Prior SEP-363856 75 mg/day		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Completed suicide			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicidal behavior			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychotic disorder			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Agitation			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Adults: Prior Placebo	Adults: Prior SEP-363856 50 mg/day	Adults: Prior SEP-363856 75 mg/day
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 156 (23.08%)	18 / 66 (27.27%)	39 / 159 (24.53%)
Investigations			
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Tri-iodothyronine increased			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	19 / 156 (12.18%)	12 / 66 (18.18%)	22 / 159 (13.84%)
occurrences (all)	28	16	27
Somnolence			

subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	8 / 156 (5.13%)	5 / 66 (7.58%)	9 / 159 (5.66%)
occurrences (all)	10	6	11
Initial insomnia			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	16 / 156 (10.26%)	7 / 66 (10.61%)	17 / 159 (10.69%)
occurrences (all)	20	11	23
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Corona virus infection			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 156 (0.00%)	0 / 66 (0.00%)	0 / 159 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Adults: Prior SEP-363856 100 mg/day	Adolescent: Prior Placebo	Adolescent: Prior SEP-363856 50 mg/day
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 64 (12.50%)	4 / 7 (57.14%)	2 / 2 (100.00%)
Investigations			
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 64 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Tri-iodothyronine increased			
subjects affected / exposed	0 / 64 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 64 (0.00%)	1 / 7 (14.29%)	1 / 2 (50.00%)
occurrences (all)	0	1	1
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 64 (6.25%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Somnolence			
subjects affected / exposed	0 / 64 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 64 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Constipation			

subjects affected / exposed	0 / 64 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 64 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 64 (0.00%)	3 / 7 (42.86%)	0 / 2 (0.00%)
occurrences (all)	0	3	0
Vomiting			
subjects affected / exposed	0 / 64 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 64 (0.00%)	0 / 7 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	2 / 64 (3.13%)	0 / 7 (0.00%)	1 / 2 (50.00%)
occurrences (all)	2	0	1
Initial insomnia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	2 / 64 (3.13%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 64 (0.00%)	0 / 7 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Corona virus infection			
subjects affected / exposed	0 / 64 (0.00%)	1 / 7 (14.29%)	1 / 2 (50.00%)
occurrences (all)	0	1	1
Pharyngitis			
subjects affected / exposed	0 / 64 (0.00%)	1 / 7 (14.29%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	0 / 64 (0.00%)	3 / 7 (42.86%)	0 / 2 (0.00%)
occurrences (all)	0	3	0

Non-serious adverse events	Adolescents: Prior SEP-363856 75 mg/day		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)		
Investigations			
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Tri-iodothyronine increased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Nausea			

subjects affected / exposed occurrences (all)	2 / 2 (100.00%) 2		
Vomiting subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Psychiatric disorders Agitation subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Anxiety subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Initial insomnia subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Insomnia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Infections and infestations Corona virus infection subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Pharyngitis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 July 2019	An adolescent cohort was added based on feedback from the food drug administration (FDA).
16 September 2020	• For the Positive and Negative Syndrome Scale (PANSS) and Clinical Global Impression-Severity (CGI-S), the specificity of "total score" was removed from the objectives and left for discussion under the endpoints and analysis sections. • PANSS response was added as an effectiveness endpoint. • Inclusion/exclusion criteria were updated, including the following: − Clarified that that the Medical Monitor must approve retesting of clinical laboratory tests or ECGs for use in determining eligibility. − Language regarding drug test results was clarified to indicate that positive results may not necessarily result in exclusion if the Investigator determined that the positive test was as a result of prescription medicine(s).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported