Clinical trial results:
A Phase II Multicenter, Randomized, Double-Blind, 12-Week Treatment, 3-Arm, Parallel-Group, Placebo-Controlled Study to Investigate the Efficacy, Safety, and Tolerability of RO7017773 in Participants Aged 15-45 Years With Autism Spectrum Disorder (ASD)

Summary

EudraCT number	2019-003524-20
Trial protocol	IT
Global end of trial date	15 May 2024

Results information

Result version number	v1 (current)
This version publication date	30 November 2024
First version publication date	30 November 2024

Trial information

Trial identification

Sponsor protocol code	BP41316

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04299464
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4058
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
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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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study is to evaluate the efficacy of alogabat compared with placebo in participants with ASD.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 March 2021
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	Canada: 16
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	United States: 70
Worldwide total number of subjects	104
EEA total number of subjects	18

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	17
Adults (18-64 years)	87
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study across 26 investigative sites in 4 countries (United States, Canada, Spain, and Italy) from 31 March 2021 to 15 May 2024.

Pre-assignment

Screening details:

A total of 104 participants diagnosed with ASD were randomized in 1:1:1 ratio to receive alogabat 20 mg, 60 mg and placebo.

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, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received alogabat matching placebo, orally, once daily (QD) up to 12 weeks during the treatment period.

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:

Alogabat matching placebo tablets, administered orally, QD for 12 weeks.

Arm title	Alogabat 20 mg

Arm description:

Participants received alogabat, 20 milligrams (mg), orally, QD up to 12 weeks during the treatment period.

Arm type	Experimental
Investigational medicinal product name	Alogabat
Investigational medicinal product code	RO7017773
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Alogabat, 20 mg tablets, administered, orally, QD for 12 weeks.

Arm title	Alogabat 60 mg

Arm description:

Participants received alogabat, 60 mg, orally, QD up to 12 weeks during the treatment period.

Arm type	Experimental

Investigational medicinal product name	Alogabat
Investigational medicinal product code	RO7017773
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Alogabat, 60 mg tablets, administered, orally, QD for 12 weeks.

Number of subjects in period 1	Placebo	Alogabat 20 mg	Alogabat 60 mg
Started	34	34	36
Completed	32	30	29
Not completed	2	4	7
Non-compliance with Study Drug	1	-	-
Physician decision	-	1	1
Consent withdrawn by subject	-	2	1
Adverse event, non-fatal	1	-	2
Reason not Specified	-	1	3

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received alogabat matching placebo, orally, once daily (QD) up to 12 weeks during the treatment period.	
Reporting group title	Alogabat 20 mg
Reporting group description:	
Participants received alogabat, 20 milligrams (mg), orally, QD up to 12 weeks during the treatment period.	
Reporting group title	Alogabat 60 mg
Reporting group description:	
Participants received alogabat, 60 mg, orally, QD up to 12 weeks during the treatment period.	

Reporting group values	Placebo	Alogabat 20 mg	Alogabat 60 mg
Number of subjects	34	34	36
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	25.3	24.8	25.0
standard deviation	± 8.1	± 7.1	± 7.5
Sex: Female, Male Units: participants			
Female	9	8	9
Male	25	26	27
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	4	3
White	31	28	27
More than one race	0	0	2
Unknown or Not Reported	2	1	3
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	11	6	6
Not Hispanic or Latino	22	28	29
Unknown or Not Reported	1	0	1

Reporting group values	Total		
Number of subjects	104		
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	- 		
Sex: Female, Male Units: participants			
Female	26		
Male	78		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	3		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	7		
White	86		
More than one race	2		
Unknown or Not Reported	6		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	23		
Not Hispanic or Latino	79		
Unknown or Not Reported	2		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received alogabat matching placebo, orally, once daily (QD) up to 12 weeks during the treatment period.	
Reporting group title	Alogabat 20 mg
Reporting group description:	
Participants received alogabat, 20 milligrams (mg), orally, QD up to 12 weeks during the treatment period.	
Reporting group title	Alogabat 60 mg
Reporting group description:	
Participants received alogabat, 60 mg, orally, QD up to 12 weeks during the treatment period.	

Primary: Change from Baseline to Week 12 in the Adaptive Behavior Composite Score of the Vineland Adaptive Behavior Scales, Third Edition (Vineland-3)

End point title	Change from Baseline to Week 12 in the Adaptive Behavior Composite Score of the Vineland Adaptive Behavior Scales, Third Edition (Vineland-3)
End point description:	
The Vineland-3=assessment tool that uses a semi-structured interview to evaluate an individual's adaptive behaviors across 3 domains: communication, socialization and daily living skills. Items are rated on a 3-point scale (0=never; 1=sometimes; 2=usually). Each adaptive behavior domain consists of 3 subdomains. The raw scores from these subdomains are used to calculate Standard Scores and Growth Scale Values (GSVs). Standard scores are scores relative to normative age group and can range from 20-140. A GSV=person-ability score that is used to track an individual's progress and can range from 10-197. Higher score indicates better adaptive functioning. A positive change from baseline score indicates greater improvement in adaptive functioning. Composite GSV score is reported here. Efficacy population=participants who gave informed consent, were randomized, and received at least one dose of double-blind study medication. Number analyzed=participants with data available for analysis.	
End point type	Primary
End point timeframe:	
Baseline to Week 12	

End point values	Placebo	Alogabat 20 mg	Alogabat 60 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	27	28	
Units: score on a scale				
arithmetic mean (confidence interval 80%)	3.250 (2.011 to 4.490)	2.819 (1.469 to 4.169)	2.807 (1.499 to 4.115)	

Statistical analyses

Statistical analysis title	Placebo vs Alogabat 20 mg
Comparison groups	Placebo v Alogabat 20 mg

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.765
Method	ANCOVA
Parameter estimate	Difference in Adjusted Mean
Point estimate	-0.432
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-2.291
upper limit	1.428

Statistical analysis title	Placebo vs Alogabat 60 mg
Comparison groups	Placebo v Alogabat 60 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7517
Method	ANCOVA
Parameter estimate	Difference in Adjusted Mean
Point estimate	-0.4444
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-2.25
upper limit	1.363

Secondary: Number of Participants Discontinuing Treatment due to AEs

End point title	Number of Participants Discontinuing Treatment due to AEs

End point description:

An AE is an untoward medical occurrence in a participant administered a pharmaceutical product and regardless of the causal relationship with the treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom/disease temporally associated with the use of an investigational product, whether or not considered related to the investigational product. Safety population included all participants randomized to study treatment and who received at least one dose of the study treatment, whether prematurely withdrawn from the study or not.

End point type	Secondary

End point timeframe:

Day 1 up to Week 12

End point values	Placebo	Alogabat 20 mg	Alogabat 60 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	34	36	
Units: participants	1	0	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with at least One Adverse Events (AEs)

End point title	Number of Participants with at least One Adverse Events (AEs)

End point description:

An AE is an untoward medical occurrence in a participant administered a pharmaceutical product and regardless of the causal relationship with the treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom/disease temporally associated with the use of an investigational product, whether or not considered related to the investigational product. Safety population included all participants randomized to study treatment and who received at least one dose of the study treatment, whether prematurely withdrawn from the study or not.

End point type	Secondary

End point timeframe:

Up to Week 18

End point values	Placebo	Alogabat 20 mg	Alogabat 60 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	34	36	
Units: participants	24	22	22	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with at least One Serious Adverse Events (SAEs)

End point title	Number of Participants with at least One Serious Adverse Events (SAEs)

End point description:

An AE is an untoward medical occurrence in a participant administered a pharmaceutical product and regardless of causal relationship with the treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom/disease temporally associated with the use of an investigational product, whether or not considered related to investigational product. A SAE is any significant hazard, contraindication, side effect that is fatal or life-threatening, requires hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, is medically significant or requires intervention to prevent one or other of the outcomes listed above. Safety population included all participants randomized to study treatment and who received at least one dose of the study treatment, whether prematurely withdrawn from the study or not.

End point type	Secondary

End point timeframe:

Up to Week 18

End point values	Placebo	Alogabat 20 mg	Alogabat 60 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	34	36	
Units: participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Post-baseline Suicidal Ideation or Suicidal Behaviour as Measured Using the Columbia-Suicide-Severity Rating Scale (C-SSRS)

End point title	Number of Participants With Post-baseline Suicidal Ideation or Suicidal Behaviour as Measured Using the Columbia-Suicide-Severity Rating Scale (C-SSRS)

End point description:

C-SSRS=assessment tool used to assess lifetime suicidality of participant (at baseline) as well as any new instances of suicidality (C-SSRS since last visit). Structured interview prompts recollection of suicidal ideation, including intensity of ideation, behavior, and attempts with actual/potential lethality. Categories have binary responses (yes/no) and include Wish to be Dead; Non-specific Active Suicidal Thoughts; Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act; Active Suicidal Ideation with Some Intent to Act, without Specific Plan; Active Suicidal Ideation with Specific Plan and Intent, Preparatory Acts and Behavior; Aborted Attempt; Interrupted Attempt; Actual Attempt (non-fatal); Completed Suicide. Suicidal ideation/behavior is indicated by a "yes" answer to any of the listed categories. Score of 0=no suicide risk is present. Score of ≥1 = suicidal ideation or behavior. Categories with non-zero values are only reported here. Safety population.

End point type	Secondary

End point timeframe:

Baseline up to Week 18

End point values	Placebo	Alogabat 20 mg	Alogabat 60 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	34	36	
Units: participants				
Wish to be Dead	2	1	1	
Non-specific Active Suicidal Thoughts	1	1	1	
Self-Injury Behavior Without Suicidal Intent	1	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Karolinska Sleepiness Scale (KSS) Score for Assessing Daytime Sleepiness

End point title	Change from Baseline in Karolinska Sleepiness Scale (KSS) Score for Assessing Daytime Sleepiness

End point description:

The KSS measures the subjective level of sleepiness at a particular time during the day. On this scale, participants (or support persons for adolescents aged 15 to 17 years and low-functioning participants) indicate which level best reflects the psycho-physical state experienced in the last 5 minutes. The KSS is a 9-point scale (1=extremely alert, 9=very sleepy, great effort to keep awake, fighting sleep). A decrease in KSS score or negative change from baseline indicate an improvement in sleepiness. Safety population included all participants randomized to study treatment and who received at least one dose of the study treatment, whether prematurely withdrawn from the study or not. Number analyzed is the number of participants with data available for analysis. "n"=number of participants with data available for analysis at the specified timepoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1 Predose), 3-4 hours (hrs) post-dose on Day 1, Predose and 3-4 hours post-dose on Days 14, 42, and 84

End point values	Placebo	Alogabat 20 mg	Alogabat 60 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	34	36	
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (Day 1 Predose) (n=33,34,36)	4.97 (± 2.10)	4.88 (± 2.28)	4.17 (± 2.37)	
Change at Day 1: 3-4 hrs Post Dose (n=33,33,31)	-0.88 (± 2.00)	-0.58 (± 2.12)	0.19 (± 2.20)	
Change at Day 14: Predose (n=33,32,31)	-0.03 (± 1.91)	-0.13 (± 2.12)	-0.03 (± 2.15)	
Change at Day 14: 3-4 hrs Post Dose (n=33,32,32)	-0.76 (± 1.70)	-0.84 (± 2.60)	0.34 (± 2.72)	
Change at Day 42: Predose (n=32,31,31)	-0.50 (± 2.05)	-0.94 (± 2.66)	-0.94 (± 1.82)	
Change at Day 42: 3-4 hrs Post Dose (n=31,31,31)	-0.74 (± 1.77)	-1.00 (± 2.79)	-0.26 (± 2.34)	
Change at Day 84: Predose (n=31,29,29)	-1.52 (± 2.23)	-0.83 (± 2.65)	-0.48 (± 2.13)	
Change at Day 84: 3-4 hrs Post Dose (n=31,30,27)	-1.13 (± 2.00)	-0.83 (± 2.80)	-0.30 (± 2.45)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Epworth Sleepiness Scale Score (ESS) for Assessing Daytime Sleepiness

End point title	Change from Baseline in Epworth Sleepiness Scale Score (ESS) for Assessing Daytime Sleepiness

End point description:

The ESS is a brief, self-administered eight-item questionnaire that measures daytime sleepiness in adults. Participants were asked to rate on a scale of 0-3 the chances that, “over the past month” and “since last visit”, he/she would have dozed in eight specific situations that are commonly met in daily life (0 = would never doze and 3 = high chance of dozing). The ESS score is the sum of eight item-scores and can range from 0 to 24. A lower ESS score or a negative change from baseline score indicates an improvement in daytime sleepiness. Safety population included all participants randomized to study treatment and who received at least one dose of the study treatment, whether prematurely withdrawn from the study or not. Number analyzed is the number of participants with data available for analysis. "n"=number of participants with data available for analysis at the specified timepoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 14, 42, and 84

End point values	Placebo	Alogabat 20 mg	Alogabat 60 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	26	
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (Day 1) (n=26,26,26)	5.00 (± 3.69)	6.15 (± 4.23)	4.54 (± 2.67)	
Change from Baseline at Day 14 (n=25,25,26)	0.24 (± 2.42)	-0.72 (± 3.36)	0.73 (± 4.58)	
Change from Baseline at Day 42 (n=26,25,24)	0.62 (± 2.52)	-2.08 (± 4.15)	0.50 (± 3.39)	
Change from Baseline at Day 84 (n=26,24,23)	0.38 (± 3.40)	-1.46 (± 4.28)	0.26 (± 3.41)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline ESS Score for Children and Adolescents (ESS-CHAD) for Assessing Daytime Sleepiness

End point title	Change from Baseline ESS Score for Children and Adolescents (ESS-CHAD) for Assessing Daytime Sleepiness

End point description:

The ESS-CHAD is a brief, support person-administered eight-item questionnaire that measures daytime sleepiness in children and adolescents. Each item asked the support persons of adolescents and participants with an IQ score <70 to rate on a scale of 0-3 the chances that "Over the past month," and “since last visit”, “your child” would have dozed in eight specific situations that are commonly met in daily life (0 to 3 where 0 = would never doze and 3 = high chance of dozing). The ESS score is the sum of eight item scores and can range from 0 to 24. A lower ESS score or negative change from baseline score indicates an improvement in daytime sleepiness. Safety population=participants randomized to study treatment and who received at least one dose of the study treatment, whether prematurely withdrawn from the study or not. Number analyzed=number of participants with data available for analysis. "n"=number of participants with data available for analysis at the specified timepoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 14, 42, 63, and 84

End point values	Placebo	Alogabat 20 mg	Alogabat 60 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	5	7	
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (Day 1) (n=5,5,7)	4.20 (± 3.83)	6.20 (± 1.30)	6.86 (± 4.53)	
Change from Baseline at Day 14 (n=5,5,6)	-1.00 (± 2.92)	-0.40 (± 3.36)	-1.00 (± 2.28)	
Change from Baseline at Day 42 (n=5,4,5)	-1.40 (± 2.70)	-2.00 (± 2.16)	1.00 (± 2.92)	
Change from Baseline at Day 63 (n=2,2,2)	-1.00 (± 1.41)	-2.50 (± 0.71)	-2.00 (± 1.41)	
Change from Baseline at Day 84 (n=5,4,4)	1.40 (± 4.51)	-1.25 (± 4.19)	-1.50 (± 1.29)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Daytime Sleepiness Assessed Using Sudden Onset of Sleep Questionnaire

End point title	Number of Participants with Daytime Sleepiness Assessed Using Sudden Onset of Sleep Questionnaire

End point description:

Sleep questionnaire was developed for this study. Each participant was asked to answer a series of 8 questions. The questions & their responses are as follows: a. Have you ever fallen asleep/have you been likely to fall asleep during your waking time? (Yes/No); b. Was this episode? (Gradual with awareness/Sudden & unpredictable/Sudden with awareness); c. Of recent episode, how often does this occur? (Every day/Less frequently/Once a week/Other); d. Do you feel worried about falling asleep during the day? (Yes/No); e. Did the episode disrupt your daily activities? (Considerably/Marginally/No); f. Did this episode disrupt your social life (Considerably/Marginally/No); g. In case of such an episode, was awakening? (Difficult/Easy/Normal). Categories with non-zero values are only reported here. Safety population.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Days 7, 14, 42, 63, and 84

End point values	Placebo	Alogabat 20 mg	Alogabat 60 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	34	36	
Units: participants				
a. Baseline: Day 1 (No)	22	28	29	
a. Baseline: Day 1 (Yes)	11	6	7	
a. Day 7 (No)	30	25	30	
a. Day 7 (Yes)	1	8	2	

a. Day 14 (No)	22	26	26	
a. Day 14 (Yes)	8	6	8	
a. Day 42 (No)	26	29	28	
a. Day 42 (Yes)	6	3	4	
a. Day 63 (No)	3	2	1	
a. Day 63 (Yes)	0	0	1	
a. Day 84 (No)	26	30	27	
a. Day 84 (Yes)	7	1	4	
b. Baseline: Day 1 (Gradual with Awareness)	10	5	6	
b. Baseline: Day 1 (Sudden & Unpredictable)	1	0	0	
b. Baseline: Day 1 (Sudden with Awareness)	1	1	1	
b. Day 7 (Gradual with Awareness)	1	7	1	
b. Day 7 (Sudden and Unpredictable)	0	1	0	
b. Day 7 (Sudden with Awareness)	0	0	1	
b. Day 14 (Gradual with Awareness)	10	5	5	
b. Day 14 (Sudden and Unpredictable)	0	2	0	
b. Day 14 (Sudden with Awareness)	0	0	3	
b. Day 42 (Gradual with Awareness)	6	3	2	
b. Day 42 (Sudden with Awareness)	1	0	2	
b. Day 63 (Gradual with Awareness)	1	0	0	
b. Day 63 (Sudden with Awareness)	0	0	1	
b. Day 84 (Gradual with Awareness)	7	1	3	
b. Day 84 (Sudden and Unpredictable)	0	0	1	
b. Day 84 (Sudden with Awareness)	0	0	1	
c. Baseline: Day 1 (Everyday)	5	1	1	
c. Baseline: Day 1 (Less Frequently)	1	1	2	
c. Baseline: Day 1 (Once a Week)	4	4	3	
c. Baseline: Day 1 (Other)	0	0	1	
c. Day 7 (Everyday)	0	0	1	
c. Day 7 (Less Frequently)	0	2	1	
c. Day 7 (Once a Month)	0	1	0	
c. Day 7 (Once a Week)	1	1	0	
c. Day 7 (Other)	0	4	0	
c. Day 14 (Everyday)	2	0	4	
c. Day 14 (Less Frequently)	0	3	0	
c. Day 14 (Once a Week)	6	2	2	
c. Day 14 (Other)	2	2	2	
c. Day 42 (Everyday)	3	0	2	
c. Day 42 (Less Frequently)	1	0	2	
c. Day 42 (Once a Month)	0	1	0	
c. Day 42 (Once a Week)	1	2	0	
c. Day 42 (Other)	1	0	0	
c. Day 63 (Everyday)	1	0	1	
c. Day 84 (Everyday)	0	0	2	
c. Day 84 (Less Frequently)	3	0	0	
c. Day 84 (Once a Week)	1	1	2	
c. Day 84 (Other)	3	0	0	
d. Baseline: Day 1 (No)	5	3	7	
d. Baseline: Day 1 (Yes)	7	4	0	
d. Day 7 (No)	0	6	2	

d. Day 7 (Yes)	1	2	0	
d. Day 14 (No)	8	6	8	
d. Day 14 (Yes)	2	1	0	
d. Day 42 (No)	4	1	3	
d. Day 42 (Yes)	2	2	1	
d. Day 63 (No)	0	0	1	
d. Day 63 (Yes)	1	0	0	
d. Day 84 (No)	4	0	4	
d. Day 84 (Yes)	3	1	0	
e. Baseline: Day 1 (Considerably)	0	1	0	
e. Baseline: Day 1 (Marginally)	8	5	1	
e. Baseline: Day 1 (No)	4	1	6	
e. Day 7 (Considerably)	0	1	1	
e. Day 7 (Marginally)	1	1	0	
e. Day 7 (No)	0	6	1	
e. Day 14 (Considerably)	0	1	1	
e. Day 14 (Marginally)	3	1	2	
e. Day 14 (No)	7	5	5	
e. Day 42 (Marginally)	1	0	0	
e. Day 42 (No)	5	3	4	
e. Day 63 (Marginally)	1	0	0	
e. Day 63 (No)	0	0	1	
e. Day 84 (Considerably)	0	0	1	
e. Day 84 (Marginally)	2	0	1	
e. Day 84 (No)	5	1	2	
f. Baseline: Day 1 (Marginally)	3	3	1	
f. Baseline: Day 1 (No)	9	4	6	
f. Day 7 (Considerably)	0	0	1	
f. Day 7 (Marginally)	0	1	0	
f. Day 7 (No)	1	7	1	
f. Day 14 (Considerably)	1	0	2	
f. Day 14 (Marginally)	0	1	1	
f. Day 14 (No)	9	6	5	
f. Day 42 (Considerably)	0	0	1	
f. Day 42 (Marginally)	0	0	1	
f. Day 42 (No)	6	3	2	
f. Day 63 (No)	1	0	1	
f. Day 84 (Considerably)	0	0	1	
f. Day 84 (Marginally)	1	0	0	
f. Day 84 (No)	6	1	3	
g. Baseline: Day 1 (Difficult)	1	0	0	
g. Baseline: Day 1 (Easy)	7	5	4	
g. Baseline: Day 1 (Normal)	4	2	3	
g. Day 7 (Easy)	1	5	1	
g. Day 7 (Normal)	0	3	1	
g. Day 14 (Easy)	6	5	3	
g. Day 14 (Normal)	4	2	5	
g. Day 42 (Easy)	4	3	3	
g. Day 42 (Normal)	2	0	1	
g. Day 63 (Easy)	1	0	0	
g. Day 63 (Normal)	0	0	1	
g. Day 84 (Easy)	6	1	2	

g. Day 84 (Normal)	1	0	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 12 in Behavior/Symptoms as Measured by all Domains of the Repetitive Behavior Scale-Revised (RBS-R) Score

End point title	Change from Baseline to Week 12 in Behavior/Symptoms as Measured by all Domains of the Repetitive Behavior Scale-Revised (RBS-R) Score

End point description:

The RBS-R is a 43-item informant-based questionnaire, assessing the variety of restricted and repetitive behaviors (RRBs) in individuals with ASD. The scale is grouped into six subscales: Stereotyped, Self-Injurious, Compulsive, Ritualistic, Sameness, and Restricted Behaviors. For each item, behaviors are rated on a 4-point scale: 0-Behavior does not occur, 1-Behavior occurs and is a mild problem, 2-Behavior occurs and is a moderate problem, 3-Behavior occurs and is a severe problem. A total RBS-R score is calculated as the sum of the scores for the 43 items. The total score ranges from 0 to 129 and higher scores are indicative of more severe RRBs. Efficacy population included all participants who gave informed consent, were randomized, and received at least one dose of double-blind study medication. Number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Placebo	Alogabat 20 mg	Alogabat 60 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	29	28	
Units: score on a scale				
arithmetic mean (confidence interval 80%)	-6.695 (-9.772 to -3.618)	-4.954 (-8.071 to -1.836)	-8.410 (-11.621 to -5.200)	

Statistical analyses

Statistical analysis title	Placebo vs Alogabat 60 mg
Comparison groups	Placebo v Alogabat 60 mg
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6228
Method	ANCOVA
Parameter estimate	Difference in Adjusted Mean
Point estimate	-1.715

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-6.204
upper limit	2.774

Statistical analysis title	Placebo vs Alogabat 20 mg
Comparison groups	Placebo v Alogabat 20 mg
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6082
Method	ANCOVA
Parameter estimate	Difference in Adjusted Mean
Point estimate	1.741
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-2.631
upper limit	6.114

Secondary: Change from Baseline to Week 12 on the Vineland-3 Socialization Domain

End point title	Change from Baseline to Week 12 on the Vineland-3 Socialization Domain

End point description:

Vineland-3=assessment tool that uses a semi-structured interview to evaluate an individual's adaptive behaviors across 3 domains: communication, socialization, and daily living skills. Items are rated on a 3-point scale (0=never;1=sometimes;2=usually). Each domain consists of 3 subdomains. Raw scores from each subdomain of socialization domain (interpersonal relationships, play and leisure time, coping skills) are used to calculate Standard Scores and GSVs. Standard scores are relative to normative age group and range from 20-140. GSV=person-ability score used to track an individual's progress and range from 10-197. Higher score=better adaptive functioning. Positive change from baseline score=greater improvement in adaptive functioning. Socialization domain GSV score is reported here. Efficacy population=participants who gave informed consent were randomized and received at least one dose of double-blind study medication. Number analyzed=participants with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Placebo	Alogabat 20 mg	Alogabat 60 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	27	29	
Units: score on a scale				
arithmetic mean (confidence interval 80%)	6.298 (4.302 to 8.294)	3.315 (1.162 to 5.468)	1.824 (-0.220 to 3.868)	

Statistical analyses

Statistical analysis title	Placebo vs Alogabat 60 mg
Comparison groups	Placebo v Alogabat 60 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.046
Method	ANCOVA
Parameter estimate	Difference in Adjusted Mean
Point estimate	-4.474
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-7.326
upper limit	-1.622

Statistical analysis title	Placebo vs Alogabat 20 mg
Comparison groups	Placebo v Alogabat 20 mg
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1987
Method	ANCOVA
Parameter estimate	Difference in Adjusted Mean
Point estimate	-2.983
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-5.957
upper limit	-0.009

Secondary: Change from Baseline to Week 12 on the Vineland-3 Communication Domain

End point title	Change from Baseline to Week 12 on the Vineland-3 Communication Domain

End point description:

Vineland-3=assessment tool that uses a semi-structured interview to evaluate individual's adaptive behaviors across 3 domains: communication, socialization, and daily living skills. Items are rated on a 3-point scale (0=never;1=sometimes;2=usually). Each adaptive behavior domain consists of 3 subdomains. The raw scores from communication domain (receptive, expressive, written) are used to calculate Standard Scores and GSVs. Standard scores are scores relative to a normative age group and

can range from 20-140. GSV=person-ability score used to track an individual's progress and can range from 10-197. Higher score=better adaptive functioning. Positive change from baseline score=greater improvement in adaptive functioning. Communication domain GSV score is reported here. Efficacy population=all participants who gave informed consent, were randomized, and received at least one dose of double-blind study medication. Number analyzed=number of participants with data available for analysis.

End point type	Secondary
End point timeframe:	
Baseline to Week 12	

End point values	Placebo	Alogabat 20 mg	Alogabat 60 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	27	28	
Units: score on a scale				
arithmetic mean (confidence interval 80%)	1.624 (0.087 to 3.162)	2.903 (1.228 to 4.578)	4.321 (2.693 to 5.948)	

Statistical analyses

Statistical analysis title	Placebo vs Alogabat 60 mg
Comparison groups	Placebo v Alogabat 60 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1244
Method	ANCOVA
Parameter estimate	Difference in Adjusted Means
Point estimate	2.697
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.453
upper limit	4.94

Statistical analysis title	Placebo vs Alogabat 20 mg
Comparison groups	Placebo v Alogabat 20 mg
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4746
Method	ANCOVA
Parameter estimate	Difference in Adjusted Means
Point estimate	1.279

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-1.021
upper limit	3.578

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to Week 18	
Adverse event reporting additional description:	
Safety population included all participants randomized to study treatment and who received at least one dose of the study treatment, whether prematurely withdrawn from the study or not.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received alogabat matching placebo, orally, QD up to 12 weeks during the treatment period.	
Reporting group title	Alogabat 60 mg
Reporting group description:	
Participants received alogabat, 60 mg, orally, QD up to 12 weeks during the treatment period.	
Reporting group title	Alogabat 20 mg
Reporting group description:	
Participants received alogabat, 20 mg, orally, QD up to 12 weeks during the treatment period.	

Serious adverse events	Placebo	Alogabat 60 mg	Alogabat 20 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 34 (0.00%)	0 / 36 (0.00%)	0 / 34 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Placebo	Alogabat 60 mg	Alogabat 20 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 34 (47.06%)	17 / 36 (47.22%)	20 / 34 (58.82%)
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 34 (0.00%)	0 / 36 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Ligament sprain			

subjects affected / exposed	0 / 34 (0.00%)	0 / 36 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Nervous system disorders			
Lethargy			
subjects affected / exposed	2 / 34 (5.88%)	0 / 36 (0.00%)	1 / 34 (2.94%)
occurrences (all)	2	0	1
Hypersomnia			
subjects affected / exposed	2 / 34 (5.88%)	3 / 36 (8.33%)	3 / 34 (8.82%)
occurrences (all)	2	3	3
Headache			
subjects affected / exposed	5 / 34 (14.71%)	2 / 36 (5.56%)	3 / 34 (8.82%)
occurrences (all)	7	12	7
Dizziness			
subjects affected / exposed	2 / 34 (5.88%)	2 / 36 (5.56%)	1 / 34 (2.94%)
occurrences (all)	2	2	1
Sudden onset of sleep			
subjects affected / exposed	0 / 34 (0.00%)	2 / 36 (5.56%)	3 / 34 (8.82%)
occurrences (all)	0	3	6
Somnolence			
subjects affected / exposed	5 / 34 (14.71%)	6 / 36 (16.67%)	7 / 34 (20.59%)
occurrences (all)	8	12	7
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 34 (0.00%)	3 / 36 (8.33%)	2 / 34 (5.88%)
occurrences (all)	0	4	5
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 36 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Nausea			
subjects affected / exposed	0 / 34 (0.00%)	4 / 36 (11.11%)	1 / 34 (2.94%)
occurrences (all)	0	8	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 34 (5.88%)	1 / 36 (2.78%)	1 / 34 (2.94%)
occurrences (all)	4	1	1

Psychiatric disorders			
Irritability			
subjects affected / exposed	2 / 34 (5.88%)	4 / 36 (11.11%)	1 / 34 (2.94%)
occurrences (all)	3	4	1
Anxiety			
subjects affected / exposed	3 / 34 (8.82%)	1 / 36 (2.78%)	1 / 34 (2.94%)
occurrences (all)	3	1	1
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 36 (2.78%)	2 / 34 (5.88%)
occurrences (all)	0	1	2
Nasopharyngitis			
subjects affected / exposed	1 / 34 (2.94%)	1 / 36 (2.78%)	3 / 34 (8.82%)
occurrences (all)	1	1	3
Rhinitis			
subjects affected / exposed	2 / 34 (5.88%)	0 / 36 (0.00%)	0 / 34 (0.00%)
occurrences (all)	4	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 May 2020	A more focused safety monitoring and detailed guidance for management of AEs of somnolence, sudden onset of sleep, and gastrointestinal related events was implemented.
18 February 2021	As a response to the COVID-19 pandemic, the overall number and duration of study visits was reduced, which also resulted in a reduced study burden for participants and their caregivers.
25 October 2021	The collection of hair samples for exposome analysis was added to allow for an exploratory analysis of the dynamics of physiological metabolites and environmental factors or chemicals.
01 June 2022	To reduce the study burden for participants and their caregivers, specific exploratory assessments were removed, more flexibility to schedule study visits were provided, and the option to perform specific study assessments remotely was given. Some eligibility criteria (CGI-S removed, Children's Yale Brown Obsessive Compulsive Scale modified for ASD threshold lowered to 8 from 12) were modified, which did not impact the enrichment of the target population.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported