Clinical trial results:
A Randomized, Double-blind, Placebo-controlled, Multi-center, 2-part, Phase 2 Study to Evaluate Efficacy, Safety, and Tolerability of RGH-706 in Prader-Willi Syndrome

Summary

EudraCT number	2021-004262-35
Trial protocol	ES CZ IT
Global end of trial date	10 April 2024

Results information

Result version number	v1 (current)
This version publication date	11 June 2025
First version publication date	11 June 2025

Trial information

Trial identification

Sponsor protocol code	RGH-706-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05322096
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number: 154209

Notes:

Sponsors

Sponsor organisation name	Gedeon Richter Plc.
Sponsor organisation address	Gyömrői út 19-21, Budapest, Hungary, H-1103
Public contact	Head of Global Regulatory CMC & Operation, Gedeon Richter Plc., +36 204162804, ra.ctarichter@richter.hu
Scientific contact	Information Scientific Service, Gedeon Richter Plc., +36 15057032, medinfo@richter.hu

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?	Yes
Primary completion date	10 April 2024
Global end of trial reached?	Yes
Global end of trial date	10 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives were:
• To explore short-term efficacy of RGH706 on hyperphagia in patients with Prader-Willi syndrome (PWS)
• To explore the effect of RGH-706 on body weight and biomarkers
• To explore pharmacokinetics (PK), safety, and tolerability of RGH-706 in patients with PWS
• To explore the effect of RGH-706 on caregiver burden and on caregiver and clinician global impressions of severity and change

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and its most recent update, and the International Council for Harmonisation (ICH) E6 Good Clinical Practice (GCP) guideline. The study was also conducted in accordance with local legal and regulatory requirements of the countries involved, and with standard operating procedures in place.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 September 2022
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	39
EEA total number of subjects	31

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	39
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients were screened for their eligibility to participate in the study during the screening period. The primary caregiver was screened to ascertain his/her commitment to complete all study assessments during the study.
A total of 70 patients were screened during the study.

Period 1

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

Blinding implementation details:

The study included a single-blind placebo run-in period followed by a double-blind treatment period.
- Single-blind (patient/caregiver) placebo was dispensed to the eligible patients orally once daily for 2 weeks during the run-in period.
- At the start of the double-blind (patient/caregiver and investigator/study personnel) treatment period, the investigator reconfirmed patients' eligibility based on screening results and treatment compliance during the run-in period.

Arms

Are arms mutually exclusive?	Yes
Arm title	RGH-706

Arm description: -

Arm type	Experimental
Investigational medicinal product name	RGH-706
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

22.5 mg once daily for 4 weeks
5 identical RGH-706 capsules/day: 2.5 mg (4 capsules) and 12.5 mg (1 capsule)

Arm title	Placebo

Arm description: -

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

Dosage and administration details:

Placebo once daily for 4 weeks
5 identical placebo capsules/day

Number of subjects in period 1	RGH-706	Placebo
Started	21	18
Completed	20	18
Not completed	1	0
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	RGH-706
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	RGH-706	Placebo	Total
Number of subjects	21	18	39
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	21	18	39
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	30.1	26.1	
standard deviation	± 8.76	± 6.93	-
Gender categorical Units: Subjects			
Female	9	11	20
Male	12	7	19

End points

End points reporting groups	
Reporting group title	RGH-706
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Change from Baseline in the 9item HQCT Total Score at Visit 5	
End point title	Change from Baseline in the 9item HQCT Total Score at Visit 5
End point description: Hyperphagia Questionnaire for Clinical Trials [HQ-CT] The HQ-CT is a questionnaire designed to measure symptoms of food-related preoccupations, problems, and behaviors. It was administered electronically via an electronic handheld device. 9-item-level responses (which ranged from 0 to 4) for a maximum score of 36. Higher scores represent increased hyperphagia.	
End point type	Primary
End point timeframe: from Baseline to Visit 5 (after a 4 weeks treatment period)	

End point values	RGH-706	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	18		
Units: HQ-CT Total Score				
least squares mean (standard error)	-2.10 (± 1.514)	-0.11 (± 1.695)		

Statistical analyses

Statistical analysis title	LS Mean Difference
Comparison groups	Placebo v RGH-706
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.3295
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	2.1

Variability estimate	Standard error of the mean
Dispersion value	2.02

Notes:

[1] - LS means, SEs, 95% CI and p-values are from an ANCOVA model on the response variable change from baseline in 9-item HQ-CT total score with fixed factors for treatment arm and geographical location and a covariate for baseline 9-item HQ-CT total score.
Difference is calculated as LS Mean in RGH-706 22.5 mg – LS Mean in Placebo.

Primary: Absolute change from baseline in body weight at each visit

End point title	Absolute change from baseline in body weight at each visit

End point description:

End point type	Primary

End point timeframe:

From baseline at each visit

End point values	RGH-706	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	18		
Units: kg				
least squares mean (standard error)				
Visit 4 (Day 28)	0.09 (± 0.279)	0.41 (± 0.313)		
Visit 5 (Day 42)	-0.29 (± 0.497)	1.16 (± 0.512)		
Visit 6 (Day 56)	-0.08 (± 0.474)	0.35 (± 0.505)		
Visit 7 (Day 98)	1.47 (± 0.483)	0.95 (± 0.524)		
Visit 8 (Day 133)	1.75 (± 0.519)	1.48 (± 0.552)		

Statistical analyses

Statistical analysis title	LS Mean Difference

Statistical analysis description:

From baseline to End of treatment

Comparison groups	RGH-706 v Placebo
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.0456
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.73
upper limit	-0.03

Variability estimate	Standard error of the mean
Dispersion value	0.664

Notes:

[2] - LS means, SEs, 95% CI and p-values are from an ANCOVA model on the response variable change from baseline in body weight with fixed factors for treatment arm and geographical location and a covariate for baseline body weight value.
Difference is calculated as LS Mean in RGH-706 22.5 mg – LS Mean in Placebo.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline to the end of the trial.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Safety set - Placebo Run-in

Reporting group description: -

Reporting group title	Safety set - RGH-706

Reporting group description:

The number of patients with at least one TEAE for this group in the overall trial is 12.
However, the number of Subjects affected by non-serious adverse events reported below is 5 in order to avoid validation errors; as the information reported in this record represents the Treatment-emergent Adverse Events by Preferred Term Reported for ≥2 Patients in Overall Population (Safety Set).

Reporting group title	Safety set - Placebo

Reporting group description: -

Serious adverse events	Safety set - Placebo Run-in	Safety set - RGH-706	Safety set - Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 21 (0.00%)	0 / 18 (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: 4 %

Non-serious adverse events	Safety set - Placebo Run-in	Safety set - RGH-706	Safety set - Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	5 / 21 (23.81%)	13 / 18 (72.22%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 21 (4.76%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Fall			
subjects affected / exposed	0 / 2 (0.00%)	1 / 21 (4.76%)	1 / 18 (5.56%)
occurrences (all)	0	1	1

Vascular disorders Haematoma subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 21 (0.00%) 0	2 / 18 (11.11%) 2
Nervous system disorders Somnolence subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 21 (0.00%) 0	2 / 18 (11.11%) 2
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 21 (0.00%) 0	2 / 18 (11.11%) 2
Psychiatric disorders Dermatillomania subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 21 (0.00%) 0	3 / 18 (16.67%) 3
Anxiety subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 21 (0.00%) 0	2 / 18 (11.11%) 2
Behaviour disorder subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 21 (0.00%) 0	2 / 18 (11.11%) 2
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 21 (4.76%) 1	1 / 18 (5.56%) 1
Infections and infestations Cellulitis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	2 / 21 (9.52%) 2	0 / 18 (0.00%) 0
Metabolism and nutrition disorders Hyperphagia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 21 (0.00%) 0	2 / 18 (11.11%) 2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 December 2021	Protocol Version 1.1 – Global • Age of male and female patients enrolled in the study was changed from ≥16 years to ≥17 years at screening
16 December 2021	Protocol Version 2.0 – Global • An additional study visit was included in Part B of the study • Every week or every 2 weeks phone calls in Parts A and B starting from Study Day 7 ±1 (where personal attendance visits were not required) were included • Contraception measures for male patients with female partners of childbearing potential were included • Text on C-SSRS was updated • Follow-up thyroid function tests at end of study visit were included • Thyroid function tests were moved from metabolic biomarkers under secondary endpoints to safety endpoints • The study visits for Part B were updated • Study schema was revised • The metabolic biomarkers leptin, ghrelin, and adiponectin were moved from secondary objectives/endpoints to exploratory objective/endpoint
09 November 2022	Protocol Version 3.0 – USA/ Protocol Version 3.1 – EU • Addition of requirement of informed consent by legally authorized representative and an assent by the adult patients who were not able to provide informed consent • The PK endpoint was described in detail in synopsis and protocol main body and time windows for collection of PK sample were added to protocol main body and Appendix 5 Schedule of Assessments. • Clarification added that no nonclinical data from Prader-Willi-specific animal models were available • The process to manage delayed reporting of SAEs and COVID-19 crisis was described • Appendix 2: Clinical Laboratory Evaluations and Appendix 5 Schedule of Assessments were revised • Added a section on SRC and its role • Instances that mentioned 'Covance' were updated to 'Labcorp' on the Title Page, Section 7.2.2, and Appendix 3
24 March 2023	Protocol Version 4.0 – USA/ Protocol Version 4.1 – EU • Revisions were made in inclusion criteria and exclusion criteria • Reconfirmation of eligibility of the patients at Visit 3 • Revisions for better clarity regarding retesting and added the possibility to rescreen patients one time • Clarification added regarding administration of HQ-CT at screening visit • Revision of concomitant medication section and clarification regarding timeframe for prohibited medication • Clarification added regarding time window for collection of predose PK sample at Visit 5 in Part A and Visit 7 in Part B prior to on-site dosing • Clarification added regarding study drug storage conditions • Revisions in visit windows for Visits 7 and 8 in Part A and Visit 8 in Part B
14 December 2023	Protocol Version 5.0 – USA/ Protocol Version 5.1 – EU • Part B of the study was removed • The sample size of the study was reduced • The study design, objectives, and endpoints were revised to reflect removal of Part B from the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported