Clinical trial results:
A Phase 3 Multicenter, Open Label, Multi Cohort Study to Evaluate the Efficacy and Safety of Somatropin in Japanese Participants with Prader-Willi Syndrome (PWS).

Summary

EudraCT number	2024-000101-32
Trial protocol	Outside EU/EEA
Global end of trial date	15 April 2024

Results information

Result version number	v1 (current)
This version publication date	20 October 2024
First version publication date	20 October 2024

Trial information

Trial identification

Sponsor protocol code	A6281323

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04697381
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 July 2024
Is this the analysis of the primary completion data?	No

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

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of somatropin in participants with PWS.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 February 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	Japan: 33
Worldwide total number of subjects	33
EEA total number of subjects	0

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)	7
Adolescents (12-17 years)	5
Adults (18-64 years)	21
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants diagnosed with PWS received somatropin, a recombinant human growth hormone (r-hGH) in this study.

Pre-assignment

Screening details:

This study had 3 cohorts (GH naive pediatric cohort, GH treated pediatric cohort and adult cohort).

Period 1

Period 1 title	Treatment Period (12 Months)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	GH Naive Pediatric Cohort

Arm description:

Participants 18 years or younger, naive to GH treatment, received somatropin 0.245 milligram per kilogram per week (mg/kg/week) subcutaneously. Treatment period was of 12 months and extension period was of 36 months. Participants were followed up to 28 days.

Arm type	Experimental
Investigational medicinal product name	Somatropin
Investigational medicinal product code	PNU-180307
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Somatropin 0.245 mg/kg/week was administered.

Arm title	GH Treated Pediatric Cohort

Arm description:

Participants 18 years or younger, who continued GH treatment for at least 2 years with stable dose for the last 6 months and were on GH at time of inclusion, received somatropin 0.084 mg/kg/week subcutaneously. The dosage was adjusted according to participants symptoms and serum insulin-like growth factor-1 (IGF-1) levels with maximum dose up to 1.6 milligram/day (mg/day). Treatment period was of 12 months and extension period was of 36 months. Participants were followed up to 28 days.

Arm type	Experimental
Investigational medicinal product name	Somatropin
Investigational medicinal product code	PNU-180307
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Somatropin 0.084 mg/kg/week was administered.

Arm title	Adult Cohort

Arm description:

Adult participants who were off from GH treatment for at least 1 year, initially received somatropin 0.042 mg/kg/week subcutaneously. Dose was titrated up to 0.084 mg/kg/week from Month 1 visit. The dosage was adjusted according to participants symptoms and serum IGF-1 levels with maximum dose up to 1.6 mg/day. Treatment period was of 12 months and extension period was of 36 months. Participants were followed up to 28 days.

Arm type	Experimental
Investigational medicinal product name	Somatropin
Investigational medicinal product code	PNU-180307
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Somatropin 0.042- 0.084 mg/kg/week was administered.

Number of subjects in period 1	GH Naive Pediatric Cohort	GH Treated Pediatric Cohort	Adult Cohort
Started	6	7	20
Completed	6	7	20

Period 2

Period 2 title	Extension Period (36 Months)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	GH Naive Pediatric Cohort

Arm description:

Participants 18 years or younger, naive to GH treatment, received somatropin 0.245 milligram per kilogram per week (mg/kg/week) subcutaneously. Treatment period was of 12 months. and Extension Period was of 36 months. Participants were followed up to 28 days.

Arm type	Experimental
Investigational medicinal product name	Somatropin
Investigational medicinal product code	PNU-180307
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Somatropin 0.245 mg/kg/week was administered.

Arm title	GH Treated Pediatric Cohort

Arm description:

Participants 18 years or younger, who continued GH treatment for at least 2 years with stable dose for the last 6 months and were on GH at time of inclusion, received somatropin 0.084 mg/kg/week subcutaneously. The dosage was adjusted according to participants' symptoms and serum insulin-like growth factor-1 (IGF-1) levels with maximum dose up to 1.6 mg/day. Treatment period was of 12 months. and Extension Period was of 36 months. Participants were followed up to 28 days.

Arm type	Experimental

Investigational medicinal product name	Somatropin
Investigational medicinal product code	PNU-180307
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Somatropin 0.084 mg/kg/week was administered.

Arm title	Adult Cohort

Arm description:

Adult participants who were off from GH treatment for at least 1 year, initially received somatropin 0.042 mg/kg/week subcutaneously. Dose was titrated up to 0.084 mg/kg/week from Month 1 visit. The dosage was adjusted according to participants' symptoms and serum IGF-1 levels with maximum dose up to 1.6 mg/day. Treatment period was of 12 months. and Extension Period was of 36 months. Participants were followed up to 28 days.

Arm type	Experimental
Investigational medicinal product name	Somatropin
Investigational medicinal product code	PNU-180307
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Somatropin 0.042- 0.084 mg/kg/week was administered.

Number of subjects in period 2	GH Naive Pediatric Cohort	GH Treated Pediatric Cohort	Adult Cohort
Started	6	7	20
Completed	6	7	14
Not completed	0	0	6
Physician decision	-	-	2
Adverse events	-	-	3
Unspecified	-	-	1

Period 3

Period 3 title	Follow up period (28 days)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	GH Naive Pediatric Cohort

Arm description:

Participants 18 years or younger, naive to GH treatment, received somatropin 0.245 milligram per kilogram per week (mg/kg/week) subcutaneously. Treatment period was of 12 months. and Extension Period was of 36 months. Participants were followed up to 28 days.

Arm type	Experimental
Investigational medicinal product name	Somatropin
Investigational medicinal product code	PNU-180307
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Somatropin 0.245 mg/kg/week was administered.

Arm title	GH Treated Pediatric Cohort

Arm description:

Participants 18 years or younger, who continued GH treatment for at least 2 years with stable dose for the last 6 months and were on GH at time of inclusion, received somatropin 0.084 mg/kg/week subcutaneously. The dosage was adjusted according to participants' symptoms and serum insulin-like growth factor-1 (IGF-1) levels with maximum dose up to 1.6 mg/day. Treatment period was of 12 months. and Extension Period was of 36 months. Participants were followed up to 28 days.

Arm type	Experimental
Investigational medicinal product name	Somatropin
Investigational medicinal product code	PNU-180307
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Somatropin 0.084 mg/kg/week was administered.

Arm title	Adult Cohort

Arm description:

Adult participants who were off from GH treatment for at least 1 year, initially received somatropin 0.042 mg/kg/week subcutaneously. Dose was titrated up to 0.084 mg/kg/week from Month 1 visit. The dosage was adjusted according to participants' symptoms and serum IGF-1 levels with maximum dose up to 1.6 mg/day. Treatment period was of 12 months. and Extension Period was of 36 months. Participants were followed up to 28 days.

Arm type	Experimental
Investigational medicinal product name	Somatropin
Investigational medicinal product code	PNU-180307
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Somatropin 0.042- 0.084 mg/kg/week was administered.

Number of subjects in period 3	GH Naive Pediatric Cohort	GH Treated Pediatric Cohort	Adult Cohort
Started	6	7	14
Completed	6	7	20

Joined	0	0	6

Continue to follow up	-	-	6

Baseline characteristics

Reporting groups	
Reporting group title	GH Naive Pediatric Cohort
Reporting group description:	
Participants 18 years or younger, naive to GH treatment, received somatropin 0.245 milligram per kilogram per week (mg/kg/week) subcutaneously. Treatment period was of 12 months and extension period was of 36 months. Participants were followed up to 28 days.	
Reporting group title	GH Treated Pediatric Cohort
Reporting group description:	
Participants 18 years or younger, who continued GH treatment for at least 2 years with stable dose for the last 6 months and were on GH at time of inclusion, received somatropin 0.084 mg/kg/week subcutaneously. The dosage was adjusted according to participants symptoms and serum insulin-like growth factor-1 (IGF-1) levels with maximum dose up to 1.6 milligram/day (mg/day). Treatment period was of 12 months and extension period was of 36 months. Participants were followed up to 28 days.	
Reporting group title	Adult Cohort
Reporting group description:	
Adult participants who were off from GH treatment for at least 1 year, initially received somatropin 0.042 mg/kg/week subcutaneously. Dose was titrated up to 0.084 mg/kg/week from Month 1 visit. The dosage was adjusted according to participants symptoms and serum IGF-1 levels with maximum dose up to 1.6 mg/day. Treatment period was of 12 months and extension period was of 36 months. Participants were followed up to 28 days.	

Reporting group values	GH Naive Pediatric Cohort	GH Treated Pediatric Cohort	Adult Cohort
Number of subjects	6	7	20
Age Categorical Units: Participants			
Less than (<6) years	3	0	0
6-12 years	3	1	0
13-17 years	0	5	0
18-44 years	0	1	20
More than equal to (>=) 45 years	0	0	0
Age continuous Units: years			
arithmetic mean	5.83	14.86	23.90
standard deviation	± 2.79	± 2.67	± 5.39
Sex: Female, Male Units: Participants			
Female	2	3	13
Male	4	4	7
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	6	7	20
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	6	7	20
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0

White	0	0	0
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	33		
Age Categorical Units: Participants			
Less than (<6) years	3		
6-12 years	4		
13-17 years	5		
18-44 years	21		
More than equal to (>=) 45 years	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	18		
Male	15		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	33		
Unknown or Not Reported	0		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	33		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	0		
More than one race	0		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	GH Naive Pediatric Cohort

Reporting group description:

Participants 18 years or younger, naive to GH treatment, received somatropin 0.245 milligram per kilogram per week (mg/kg/week) subcutaneously. Treatment period was of 12 months and extension period was of 36 months. Participants were followed up to 28 days.

Reporting group title	GH Treated Pediatric Cohort

Reporting group description:

Participants 18 years or younger, who continued GH treatment for at least 2 years with stable dose for the last 6 months and were on GH at time of inclusion, received somatropin 0.084 mg/kg/week subcutaneously. The dosage was adjusted according to participants symptoms and serum insulin-like growth factor-1 (IGF-1) levels with maximum dose up to 1.6 milligram/day (mg/day). Treatment period was of 12 months and extension period was of 36 months. Participants were followed up to 28 days.

Reporting group title	Adult Cohort

Reporting group description:

Adult participants who were off from GH treatment for at least 1 year, initially received somatropin 0.042 mg/kg/week subcutaneously. Dose was titrated up to 0.084 mg/kg/week from Month 1 visit. The dosage was adjusted according to participants symptoms and serum IGF-1 levels with maximum dose up to 1.6 mg/day. Treatment period was of 12 months and extension period was of 36 months. Participants were followed up to 28 days.

Reporting group title	GH Naive Pediatric Cohort

Reporting group description:

Participants 18 years or younger, naive to GH treatment, received somatropin 0.245 milligram per kilogram per week (mg/kg/week) subcutaneously. Treatment period was of 12 months. and Extension Period was of 36 months. Participants were followed up to 28 days.

Reporting group title	GH Treated Pediatric Cohort

Reporting group description:

Participants 18 years or younger, who continued GH treatment for at least 2 years with stable dose for the last 6 months and were on GH at time of inclusion, received somatropin 0.084 mg/kg/week subcutaneously. The dosage was adjusted according to participants' symptoms and serum insulin-like growth factor-1 (IGF-1) levels with maximum dose up to 1.6 mg/day. Treatment period was of 12 months. and Extension Period was of 36 months. Participants were followed up to 28 days.

Reporting group title	Adult Cohort

Reporting group description:

Adult participants who were off from GH treatment for at least 1 year, initially received somatropin 0.042 mg/kg/week subcutaneously. Dose was titrated up to 0.084 mg/kg/week from Month 1 visit. The dosage was adjusted according to participants' symptoms and serum IGF-1 levels with maximum dose up to 1.6 mg/day. Treatment period was of 12 months. and Extension Period was of 36 months. Participants were followed up to 28 days.

Reporting group title	GH Naive Pediatric Cohort

Reporting group description:

Participants 18 years or younger, naive to GH treatment, received somatropin 0.245 milligram per kilogram per week (mg/kg/week) subcutaneously. Treatment period was of 12 months. and Extension Period was of 36 months. Participants were followed up to 28 days.

Reporting group title	GH Treated Pediatric Cohort

Reporting group description:

Participants 18 years or younger, who continued GH treatment for at least 2 years with stable dose for the last 6 months and were on GH at time of inclusion, received somatropin 0.084 mg/kg/week subcutaneously. The dosage was adjusted according to participants' symptoms and serum insulin-like growth factor-1 (IGF-1) levels with maximum dose up to 1.6 mg/day. Treatment period was of 12 months. and Extension Period was of 36 months. Participants were followed up to 28 days.

Reporting group title	Adult Cohort

Reporting group description:

Adult participants who were off from GH treatment for at least 1 year, initially received somatropin 0.042 mg/kg/week subcutaneously. Dose was titrated up to 0.084 mg/kg/week from Month 1 visit. The dosage was adjusted according to participants' symptoms and serum IGF-1 levels with maximum dose up to 1.6 mg/day. Treatment period was of 12 months. and Extension Period was of 36 months.

Participants were followed up to 28 days.

Primary: Change From Baseline to Month 12 in Lean Body Mass Measured by DEXA: GH Naive Pediatric and GH Treated Pediatric Cohort

End point title	Change From Baseline to Month 12 in Lean Body Mass Measured by DEXA: GH Naive Pediatric and GH Treated Pediatric Cohort[1][2]

End point description:

Lean body mass, a measurement of body composition, was assessed by DEXA scan, and calculated as lean body mass (%) = lean body mass (kg) / (lean body mass [kg] + fat mass [kg]) *100. Efficacy evaluable set included all participants assigned to study intervention and who took at least one dose of study intervention and had at least one efficacy evaluation. "Number of Participants Analysed" signifies participants evaluable for this endpoint measure at this time point.

End point type	Primary

End point timeframe:

Baseline, Month 12

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: No statistical analysis was planned

[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 end point is reporting statistics for the arms specified

End point values	GH Naive Pediatric Cohort	GH Treated Pediatric Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Percentage of body mass				
arithmetic mean (standard deviation)	4.59 (± 4.490)	-1.34 (± 3.238)		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline to Month 12 in Lean Body Mass Measured by Dual-Energy X-ray Absorptiometry (DEXA): Adult Cohort

End point title	Change From Baseline to Month 12 in Lean Body Mass Measured by Dual-Energy X-ray Absorptiometry (DEXA): Adult Cohort[3][4]

End point description:

Lean body mass, a measurement of body composition, was assessed by DEXA scan, and calculated as lean body mass (%) = lean body mass (kg) / (lean body mass [kg] + fat mass [kg]) *100. Efficacy evaluable set included all participants assigned to study intervention and who took at least one dose of study intervention and had at least one efficacy evaluation. "Number of Participants Analysed" signifies participants evaluable for this endpoint measure this time point.

End point type	Primary

End point timeframe:

Baseline, Month 12

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The end point is reporting statistics for the arms specified

[4] - 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 end point is reporting statistics for the arms specified

End point values	Adult Cohort			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Percentage of body mass				
least squares mean (confidence interval 95%)	3.09 (1.85 to 4.33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Month 12 in Lean Body Mass Measured by BIA-GH Naive Pediatric and GH Treated Pediatric Cohort

End point title	Change From Baseline to Month 12 in Lean Body Mass Measured by BIA-GH Naive Pediatric and GH Treated Pediatric Cohort[5]

End point description:

Lean body mass, a measurement of body composition, was assessed by DEXA scan, and calculated as lean body mass (%) = lean body mass (kg) / (lean body mass [kg] + fat mass [kg]) *100. Efficacy evaluable set included all participants assigned to study intervention and who took at least one dose of study intervention and had at least one efficacy evaluation. "Number of Participants Analysed" signifies participants evaluable for this endpoint measure at this time point.

End point type	Secondary

End point timeframe:

Baseline, Month 12

Notes:

[5] - 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 end point is reporting statistics for the arms specified

End point values	GH Naive Pediatric Cohort	GH Treated Pediatric Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: Percentage of body mass				
arithmetic mean (standard deviation)	3.32 (± 3.867)	0.58 (± 4.711)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Month 12 in Lean Body Mass Measured by Bioelectrical Impedance Analysis (BIA)-Adult Cohort

End point title	Change From Baseline to Month 12 in Lean Body Mass Measured by Bioelectrical Impedance Analysis (BIA)-Adult Cohort[6]

End point description:

Lean body mass, a measurement of body composition, was assessed by DEXA scan, and calculated as lean body mass (%) = lean body mass (kg) / (lean body mass [kg] + fat mass [kg]) *100. Efficacy evaluable set included all participants assigned to study intervention and who took at least one dose of study intervention and had at least one efficacy evaluation. "Number of Participants Analysed" signifies participants evaluable for this endpoint measure at this time point.

End point type	Secondary

End point timeframe:

Baseline, Month 12

Notes:

[6] - 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 end point is reporting statistics for the arms specified

End point values	Adult Cohort			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Percentage of body mass				
least squares mean (confidence interval 95%)	2.03 (-0.67 to 4.73)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Month 12 in Adipose Tissue Distribution Measured by Abdominal Computed Tomography (CT)

End point title	Change From Baseline to Month 12 in Adipose Tissue Distribution Measured by Abdominal Computed Tomography (CT)

End point description:

Adipose tissue distribution was measured by abdominal CT. Areas of subcutaneous adipose tissue (SAT) (centimeter square [cm^2]), visceral adipose tissue (VAT) (cm^2) were measured at the level of the umbilicus by abdominal CT. Efficacy evaluable set included all participants assigned to study intervention and who took at least one dose of study intervention and had at least one efficacy evaluation. "Number of Participants Analysed" signifies participants evaluable for this endpoint measure at this time point.

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	GH Naive Pediatric Cohort	GH Treated Pediatric Cohort	Adult Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	19	
Units: Centimeter square (cm^2)				
arithmetic mean (standard deviation)				
Change at Month 12, SAT	60.423 (± 138.2001)	102.222 (± 211.9111)	-13.764 (± 31.0212)	
Change at Month 12, VAT	4.825 (± 13.5401)	-13.403 (± 28.5490)	-4.040 (± 16.8243)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Month 12 in Body fat (Percentage) Measured by DEXA: Adult Cohort

End point title	Change From Baseline to Month 12 in Body fat (Percentage) Measured by DEXA: Adult Cohort[7]

End point description:

Body fat was assessed by DEXA scan and calculated as body fat (%) = body fat (kg) / [lean body mass (kg) + body fat (kg)] *100. Efficacy evaluable set included all participants assigned to study intervention and who took at least one dose of study intervention and had at least one efficacy evaluation. "Number of Participants Analysed" signifies participants evaluable for this endpoint measure at this time point.

End point type	Secondary

End point timeframe:

Baseline, Month 12

Notes:

[7] - 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 end point is reporting statistics for the arms specified

End point values	Adult Cohort			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Percentage of body fat				
least squares mean (confidence interval 95%)	-3.09 (-4.33 to -1.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Month 6 in Lean Body Mass Measured by DEXA: Adult Cohort Only

End point title	Change From Baseline to Month 6 in Lean Body Mass Measured by DEXA: Adult Cohort Only[8]

End point description:

Lean body mass, a measurement of body composition, was assessed by DEXA scan, and calculated as lean body mass (%) = lean body mass (kg) / (lean body mass [kg] + fat mass [kg])*100. Efficacy evaluable set included all participants assigned to study intervention and who took at least one dose of study intervention and had at least one efficacy evaluation.

End point type	Secondary

End point timeframe:

Baseline, Month 6

Notes:

[8] - 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 end point is reporting statistics for the arms specified

End point values	Adult Cohort			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percentage of body mass				
least squares mean (confidence interval 95%)	2.38 (1.30 to 3.46)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in administered medicinal product, event need not necessarily have a causal relationship with product treatment or usage. A SAE was any untoward medical occurrence in a participant administered a medicinal or nutritional product (including pediatric formulas) at any dose that: resulted in death; was life-threatening; required inpatient hospitalization or prolongation of hospitalization; resulted in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions); resulted in congenital anomaly/birth defect. TEAEs were events emerged during treatment period and were absent before treatment or that worsened relative to pretreatment state. AEs included both serious and non-serious adverse events. Full analysis set included all participants assigned to study intervention and who took at least one dose of study intervention.

End point type	Secondary

End point timeframe:

From dose 1 up to 28 days after end of study treatment (maximum duration up to 49 months)

End point values	GH Naive Pediatric Cohort	GH Treated Pediatric Cohort	Adult Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	7	20	
Units: Participants				
TEAEs	5	7	19	
TESAEs	0	1	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Month 12 in Body fat (Percentage) Measured by DEXA: GH Naive Pediatric and GH Treated Pediatric Cohort

End point title	Change From Baseline to Month 12 in Body fat (Percentage) Measured by DEXA: GH Naive Pediatric and GH Treated Pediatric Cohort[9]

End point description:

Body fat was assessed by DEXA scan and calculated as body fat (%) = body fat (kg) / [lean body mass (kg) + body fat (kg)] *100. Efficacy evaluable set included all participants assigned to study intervention and who took at least one dose of study intervention and had at least one efficacy evaluation. "Number of Participants Analysed" signifies participants evaluable for this endpoint measure at this time point.

End point type	Secondary

End point timeframe:

Baseline, Month 12

Notes:

[9] - 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 end point is reporting statistics for the arms specified

End point values	GH Naive Pediatric Cohort	GH Treated Pediatric Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Percentage of body fat				
arithmetic mean (standard deviation)	-4.59 (± 4.490)	1.34 (± 3.238)		

Statistical analyses

No statistical analyses for this end point

Secondary: Bone Maturation

End point title	Bone Maturation[10]

End point description:

Bone maturation is the process whereby the tissue undergoes changes from the embryonic rudiment of bone to the adult form. Bone maturation was calculated as bone age divided by chronological age. Participants with bone maturation value greater than 1 is presented in this outcome measure. FAS included all participants assigned to study intervention and who took at least one dose of study intervention.

End point type	Secondary

End point timeframe:

12 months

Notes:

[10] - 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 end point is reporting statistics for the arms specified

End point values	GH Naive Pediatric Cohort	GH Treated Pediatric Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: Participants	4	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Laboratory Test Abnormalities

End point title	Number of Participants With Laboratory Test Abnormalities

End point description:

Criteria for abnormal laboratory values for chemistry parameters: alanine aminotransferase, alkaline phosphatase greater than (>) 3.0*upper limit of normal (ULN), albumin > 1.2*ULN, urea nitrogen millimoles per liter (mmol/L) > 1.3*ULN, HDL cholesterol mmol/L less than (<) 0.8* lower limit of normal (LLN), LDL cholesterol mmol/L >1.2*ULN, triglycerides mmol/L > 1.3*ULN, thyrotropin milliunits per liter (mU/L) <0.8*LLN and >1.2*ULN, glucose (mmol/L) >1.5*ULN, hemoglobin A1C liter of cells per liter of blood (L/L) >1.3*ULN. FAS included all participants assigned to study intervention and who took at least one dose of study intervention.

End point type	Secondary

End point timeframe:

49 months

End point values	GH Naive Pediatric Cohort	GH Treated Pediatric Cohort	Adult Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	7	20	
Units: Participants	5	3	16	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From dose 1 up to 28 days after end of study treatment (maximum duration up to 49 months)

Adverse event reporting additional description:

Same event may appear as both non-SAE & SAE. What is presented are distinct events. An event may be categorized as serious in 1 participant and non-SAE in other participant, or a participant may have experienced both SAE and non-SAE.FAS included all participants assigned to study intervention and who took at least one dose of study intervention.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	v26.1

Reporting groups

Reporting group title	GH naive pediatric cohort

Reporting group description:

Participants 18 years or younger, naive to GH treatment, received somatropin 0.245 mg/kg/week subcutaneously. Treatment period was of 12 months and extension period was of 36 months. Participants were followed up to 28 days.

Reporting group title	Adult cohort

Reporting group description:

Adult participants who were off from GH treatment for at least 1 year, initially received somatropin 0.042 mg/kg/week subcutaneously. Dose was titrated up to 0.084 mg/kg/week from Month 1 visit. The dosage was adjusted according to participants symptoms and serum IGF-1 levels with maximum dose up to 1.6 mg/day. Treatment period was of 12 months and extension period was of 36 months. Participants were followed up to 28 days.

Reporting group title	GH treated pediatric cohort

Reporting group description:

Participants 18 years or younger, who continued GH treatment for at least 2 years with stable dose for the last 6 months and were on GH at time of inclusion, received somatropin 0.084 mg/kg/week subcutaneously. The dosage was adjusted according to participants symptoms and IGF-1 levels with maximum dose up to 1.6 mg/day. Treatment period was of 12 months and extension period was of 36 months. Participants were followed up to 28 days.

Serious adverse events	GH naive pediatric cohort	Adult cohort	GH treated pediatric cohort
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	3 / 20 (15.00%)	1 / 7 (14.29%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 20 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain contusion			

subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fractured base			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Sinus node dysfunction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Affect lability			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	GH naive pediatric cohort	Adult cohort	GH treated pediatric cohort
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	19 / 20 (95.00%)	7 / 7 (100.00%)
Vascular disorders			

Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	2 / 20 (10.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
Extravasation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	4 / 20 (20.00%)	1 / 7 (14.29%)
occurrences (all)	0	8	1
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Injection site reaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 20 (10.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Testicular pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Genital tract inflammation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Sleep apnoea syndrome			

subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Snoring			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Cough variant asthma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			
subjects affected / exposed	1 / 6 (16.67%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Dissociative disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Conversion disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Dysphoria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 20 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Blood triglycerides increased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Body height increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Glycosylated haemoglobin increased			

subjects affected / exposed	1 / 6 (16.67%)	3 / 20 (15.00%)	0 / 7 (0.00%)
occurrences (all)	1	3	0
Insulin-like growth factor increased			
subjects affected / exposed	1 / 6 (16.67%)	3 / 20 (15.00%)	1 / 7 (14.29%)
occurrences (all)	2	3	2
Liver function test increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Injury, poisoning and procedural complications			
Immunisation reaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Chillblains			
subjects affected / exposed	0 / 6 (0.00%)	2 / 20 (10.00%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Contusion			
subjects affected / exposed	1 / 6 (16.67%)	4 / 20 (20.00%)	1 / 7 (14.29%)
occurrences (all)	1	5	1
Fall			
subjects affected / exposed	1 / 6 (16.67%)	4 / 20 (20.00%)	1 / 7 (14.29%)
occurrences (all)	2	7	2
Foot fracture			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Lip injury			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin abrasion			

subjects affected / exposed	0 / 6 (0.00%)	3 / 20 (15.00%)	1 / 7 (14.29%)
occurrences (all)	0	3	1
Arthropod bite			
subjects affected / exposed	0 / 6 (0.00%)	2 / 20 (10.00%)	1 / 7 (14.29%)
occurrences (all)	0	2	1
Subcutaneous haematoma			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Thermal burn			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	0 / 6 (0.00%)	2 / 20 (10.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Procedural pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	2 / 20 (10.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Dysaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	2 / 6 (33.33%)	3 / 20 (15.00%)	1 / 7 (14.29%)
occurrences (all)	5	4	1
Loss of consciousness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Ear and labyrinth disorders			
Vertigo			

subjects affected / exposed	0 / 6 (0.00%)	2 / 20 (10.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Ear pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	3	1	0
Deafness unilateral			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Ear pruritus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Ocular hyperaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Glaucoma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Eczema eyelids			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	3 / 20 (15.00%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Angular cheilitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Anal prolapse			

subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	2 / 6 (33.33%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Anal polyp			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
subjects affected / exposed	0 / 6 (0.00%)	2 / 20 (10.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Hypoaesthesia teeth			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	1 / 6 (16.67%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 6 (16.67%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Hepatic steatosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 6 (0.00%)	2 / 20 (10.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Blister			

subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Haemorrhage subcutaneous			
subjects affected / exposed	2 / 6 (33.33%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	3	0	0
Hand dermatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 20 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Ingrowing nail			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Miliaria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	2 / 20 (10.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Urticaria			
subjects affected / exposed	2 / 6 (33.33%)	1 / 20 (5.00%)	1 / 7 (14.29%)
occurrences (all)	2	3	1
Rash			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hyperkeratosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dermatitis diaper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 20 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	0 / 6 (0.00%)	2 / 20 (10.00%)	0 / 7 (0.00%)
occurrences (all)	0	6	0
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	2 / 20 (10.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Osteoarthritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Scoliosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 20 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)	4 / 20 (20.00%)	0 / 7 (0.00%)
occurrences (all)	2	9	0
Tinea pedis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 20 (10.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Rhinitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Otitis externa			
subjects affected / exposed	0 / 6 (0.00%)	0 / 20 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	4 / 6 (66.67%)	1 / 20 (5.00%)	1 / 7 (14.29%)
occurrences (all)	26	2	1
Impetigo			
subjects affected / exposed	0 / 6 (0.00%)	2 / 20 (10.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Herpes zoster			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0

Genital candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	3 / 6 (50.00%)	11 / 20 (55.00%)	1 / 7 (14.29%)
occurrences (all)	3	11	1
Bacterial infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Eczema impetiginous			
subjects affected / exposed	0 / 6 (0.00%)	2 / 20 (10.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Influenza			
subjects affected / exposed	2 / 6 (33.33%)	2 / 20 (10.00%)	2 / 7 (28.57%)
occurrences (all)	3	2	3
Herpangina			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Genital abscess			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Skin infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0

Otitis media			
subjects affected / exposed	1 / 6 (16.67%)	0 / 20 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Abnormal weight gain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Glucose tolerance impaired			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Pseudohypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 20 (5.00%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 6 (0.00%)	3 / 20 (15.00%)	0 / 7 (0.00%)
occurrences (all)	0	3	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2021	Screening period was updated to up to 28 days to make consistent with visit window for screening. also, Month 42 was added to header row to clarify and wrote down all specific visit timing in the case the extension period continued for 36 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported