Clinical trial results:
A phase 3, open-label, randomized, multicenter, 12 months, efficacy and safety study of weekly mod-4023 compared to daily genotropin® therapy in pre-pubertal children with growth hormone deficiency

Summary

EudraCT number	2016-003874-42
Trial protocol	GB DE BG FR PL ES GR IT
Global end of trial date	01 May 2024

Results information

Result version number	v1 (current)
This version publication date	16 April 2025
First version publication date	16 April 2025

Trial information

Trial identification

Sponsor protocol code	CP-4-006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02968004
WHO universal trial number (UTN)	-
Other trial identifiers	IND number: 79,745

Notes:

Sponsors

Sponsor organisation name	OPKO Biologics Ltd.
Sponsor organisation address	Ashlagan 16, Kiryat Gat,, Israel, 8211804
Public contact	OPKO Health, Inc., OPKO Health, Inc., 305 5754100, contact@opko.com
Scientific contact	OPKO Health, Inc., OPKO Health, Inc., 305 5754100, contact@opko.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 May 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 August 2019
Global end of trial reached?	Yes
Global end of trial date	01 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that annual (12 month) HV from weekly somatrogon administration is noninferior to daily Genotropin administration in children with GHD.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all ICH GCP Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.
The investigator, or a person designated by the investigator, obtained a signed and dated ICD from each subject's parent(s)/guardian(s) before any study-specific activity was performed. Informed consent was collected as detailed in the protocol.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	Bulgaria: 4
Country: Number of subjects enrolled	Belarus: 2
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Colombia: 8
Country: Number of subjects enrolled	Georgia: 6
Country: Number of subjects enrolled	Greece: 3
Country: Number of subjects enrolled	India: 26
Country: Number of subjects enrolled	Israel: 15
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	New Zealand: 4
Country: Number of subjects enrolled	Poland: 19
Country: Number of subjects enrolled	Korea, Republic of: 12
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	Taiwan: 2

Country: Number of subjects enrolled	Türkiye: 1
Country: Number of subjects enrolled	Ukraine: 24
Country: Number of subjects enrolled	United States: 42
Country: Number of subjects enrolled	United Kingdom: 3
Worldwide total number of subjects	224
EEA total number of subjects	45

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)	224
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of the 228 subjects who were randomized, 4 subjects (3 in the somatrogon group; 1 in the Genotropin group) did not receive study drug (3 withdrawal by parent/guardian, 1 lost to follow-up during the screening phase). Therefore, 224 subjects were randomized and received at least 1 dose of study drug.

Period 1

Period 1 title	Main Study
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	MOD-4023 Main Study

Arm description:

Once weekly subcutaneous injection of long acting r-hGH (MOD-4023)

Arm type	Experimental
Investigational medicinal product name	MOD-4023
Investigational medicinal product code	Somatrogon
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Once weekly subcutaneous injection using pre-filled pen device.

Arm title	Genotropin Main Study

Arm description:

Once daily subcutaneous injection of Somatropin (r-hGH; Genotropin)

Arm type	Active comparator
Investigational medicinal product name	Genotropin
Investigational medicinal product code	Somatropin
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Once daily subcutaneous injection of Genotropin

Number of subjects in period 1	MOD-4023 Main Study	Genotropin Main Study
Started	109	115
Completed	108	114
Not completed	1	1
Consent withdrawn by subject	-	1
Adverse event, non-fatal	1	-

Period 2	
Period 2 title	OLE Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms	
Arm title	MOD-4023 OLE Peiod

Arm description:

Once weekly subcutaneous injection of long acting r-hGH (MOD-4023)

Arm type	Experimental
Investigational medicinal product name	MOD-4023
Investigational medicinal product code	Somatrogon
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Once weekly subcutaneous injection of long acting r-hGH (MOD-4023).
MOD-4023: Once weekly subcutaneous injection using pre-filled pen device.

Number of subjects in period 2[1]	MOD-4023 OLE Peiod
Started	212
Completed	95
Not completed	117
Closure of Epiphyseal Plates	1
Consent withdrawn by subject	19
Local Crisis	21
Adverse event, non-fatal	9
Miscellaneous Other	4
Non-Compliance With Study Drug	1
Prohibited Treatments	1
Sponsor Discontinuation of Study	56
Bone Age Reached	5

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 10 Subjects which completed the main period, did not continue to OLE peiod

Baseline characteristics

Reporting groups	
Reporting group title	MOD-4023 Main Study
Reporting group description:	
Once weekly subcutaneous injection of long acting r-hGH (MOD-4023)	
Reporting group title	Genotropin Main Study
Reporting group description:	
Once daily subcutaneous injection of Somatropin (r-hGH; Genotropin)	

Reporting group values	MOD-4023 Main Study	Genotropin Main Study	Total
Number of subjects	109	115	224
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)	109	115	224
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	7.83	7.61	
standard deviation	± 2.66	± 2.37	-
Gender categorical Units: Subjects			
Female	27	36	63
Male	82	79	161
Race Units: Subjects			
White	81	86	167
Black or African American	0	2	2
Asian	24	21	45
American Indian or Alaska Native	1	0	1
Native Hawaiian or Other Pacific Islander	0	1	1
Other	3	5	8
Unknown	0	0	0
MULTIRACIAL	0	0	0
Not reported	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	11	13	24
Not Hispanic or Latino	98	102	200

End points

End points reporting groups

Reporting group title	MOD-4023 Main Study
Reporting group description:	
Once weekly subcutaneous injection of long acting r-hGH (MOD-4023)	
Reporting group title	Genotropin Main Study
Reporting group description:	
Once daily subcutaneous injection of Somatropin (r-hGH; Genotropin)	
Reporting group title	MOD-4023 OLE Peiod
Reporting group description:	
Once weekly subcutaneous injection of long acting r-hGH (MOD-4023)	
Subject analysis set title	MOD-4023 OLE Year 1
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects entered OLE period Year 1	
Subject analysis set title	MOD-4023 OLE Year 2
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects entered OLE period Year 2	
Subject analysis set title	MOD-4023 OLE Year 3
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects entered OLE period Year 3	
Subject analysis set title	MOD-4023 OLE Year 4
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects entered OLE period Year 4	
Subject analysis set title	MOD-4023 OLE Year 5
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects entered OLE period Year 5	

Primary: Annual Height Velocity 12 months

End point title	Annual Height Velocity 12 months
End point description:	
Annual Height Velocity in cm. Annual Height Velocity at 12 months is based on the difference between the heights at 12 months and baseline.	
End point type	Primary
End point timeframe:	
52 weeks	

End point values	MOD-4023 Main Study	Genotropin Main Study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	115		
Units: centimetre				
arithmetic mean (confidence interval 95%)	10.10 (9.58 to 10.63)	9.78 (9.29 to 10.26)		

Statistical analyses

Statistical analysis title	Annual HV at 12 Months
Comparison groups	Genotropin Main Study v MOD-4023 Main Study
Number of subjects included in analysis	224
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	ANCOVA

Secondary: Height Velocity at 6 Months

End point title	Height Velocity at 6 Months

End point description:

Height velocity in cm measured after 6 months of treatment. Annualized Height velocity after 6 months is calculated based on the difference between the heights at 6 months and baseline.

End point type	Secondary

End point timeframe:

After 6 months of treatment

End point values	MOD-4023 Main Study	Genotropin Main Study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	115		
Units: centimetre				
arithmetic mean (confidence interval 95%)	10.59 (9.96 to 11.22)	10.04 (9.47 to 10.62)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Height Standard Deviation Score (SDS)

End point title	Change in Height Standard Deviation Score (SDS)

End point description:

Change in height Standard Deviation Score (SDS) after 6 and 12 months is calculated based on the

difference between the heights at 6 and 12 months and baseline.

End point type	Secondary

End point timeframe:

After 6 and 12 months

End point values	MOD-4023 Main Study	Genotropin Main Study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	115		
Units: centimeter				
arithmetic mean (confidence interval 95%)				
6 mobths	0.54 (0.48 to 0.61)	0.48 (0.42 to 0.54)		
12 months	0.92 (0.82 to 1.02)	0.87 (0.78 to 0.96)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Bone Maturation (BM)

End point title	Change in Bone Maturation (BM)

End point description:

Annual change in bone age measurements as per Gruelich-Pyle method

End point type	Secondary

End point timeframe:

52 weeks

End point values	MOD-4023 Main Study	Genotropin Main Study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	102		
Units: year				
arithmetic mean (standard deviation)	0.05 (± 0.09)	0.06 (± 0.10)		

Statistical analyses

No statistical analyses for this end point

Secondary: Insulin-like Growth Factor-1 (IGF-1) Standard Deviation Score (SDS) Baseline

End point title	Insulin-like Growth Factor-1 (IGF-1) Standard Deviation Score

	(SDS) Baseline
End point description: Via central lab analysis	
End point type	Secondary
End point timeframe: Baseline	

End point values	MOD-4023 Main Study	Genotropin Main Study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	115		
Units: ng/m L				
arithmetic mean (standard deviation)	-1.95 (± 0.89)	-1.72 (± 0.90)		

Statistical analyses

No statistical analyses for this end point

Secondary: Insulin-like Growth Factor-1 (IGF-1) Standard Deviation Score (SDS) 12 Months

End point title	Insulin-like Growth Factor-1 (IGF-1) Standard Deviation Score (SDS) 12 Months
End point description:	
End point type	Secondary
End point timeframe: 12 months	

End point values	MOD-4023 Main Study	Genotropin Main Study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	110		
Units: ng/ml				
arithmetic mean (standard deviation)	0.65 (± 1.32)	-0.69 (± 1.09)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Annualized Height Velocity at Each 12 Months in the OLE Period

End point title	Annualized Height Velocity at Each 12 Months in the OLE Period

End point description:	
Annualized HV (cm/year): Annualized HV at each 12 months, based on the difference between the height at each 12 months and the height at the previous 12 months.	
End point type	Other pre-specified
End point timeframe:	
12 months	

End point values	MOD-4023 OLE Year 1	MOD-4023 OLE Year 2	MOD-4023 OLE Year 3	MOD-4023 OLE Year 4
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	173	173	162	75
Units: centimeter				
arithmetic mean (standard deviation)	8.11 (± 1.84)	7.91 (± 1.84)	7.02 (± 1.75)	6.56 (± 1.91)

End point values	MOD-4023 OLE Year 5			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: centimeter				
arithmetic mean (standard deviation)	5.05 (± 1.10)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in Height SDS in the OLE Period

End point title	Change in Height SDS in the OLE Period
End point description:	
Change in height SDS, calculated as the difference between the height SDS at each scheduled visit in the OLE period and the height SDS at the main period baseline.	
End point type	Other pre-specified
End point timeframe:	
12 months	

End point values	MOD-4023 OLE Year 1	MOD-4023 OLE Year 2	MOD-4023 OLE Year 3	MOD-4023 OLE Year 4
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	173	173	162	75
Units: centimeter				
arithmetic mean (standard deviation)	1.36 (± 0.75)	1.61 (± 0.78)	1.87 (± 0.85)	2.01 (± 0.75)

End point values	MOD-4023 OLE Year 5			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: centimeter				
arithmetic mean (standard deviation)	2.14 (± 0.38)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in Bone Maturation at Each Visit in the OLE Period

End point title	Change in Bone Maturation at Each Visit in the OLE Period

End point description:

End point type	Other pre-specified

End point timeframe:

12 months

End point values	MOD-4023 OLE Year 1	MOD-4023 OLE Year 2	MOD-4023 OLE Year 3	MOD-4023 OLE Year 4
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	165	170	156	74
Units: year				
arithmetic mean (standard deviation)	0.12 (± 0.13)	0.18 (± 0.16)	0.22 (± 0.16)	0.22 (± 0.16)

End point values	MOD-4023 OLE Year 5			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: year				
arithmetic mean (standard deviation)	0.17 (± 0.18)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Insulin-like Growth Factor-1 (IGF-1) Standard Deviation Score (SDS) OLE Period

End point title	Insulin-like Growth Factor-1 (IGF-1) Standard Deviation Score (SDS) OLE Period

End point description:

IGF-1 levels and IGF-1 SDS levels on Day 4 (-1) after somatrogon dosing at every scheduled visit in the OLE Year 1 and at every 6 months thereafter. Change in IGF-1 SDS, calculated as the difference between the IGF-1 SDS values in the OLE period and the IGF-1 SDS at the main period baseline.

End point type	Other pre-specified

End point timeframe:

6 months

End point values	MOD-4023 OLE Year 1	MOD-4023 OLE Year 2	MOD-4023 OLE Year 3	MOD-4023 OLE Year 4
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	155	169	155	70
Units: SDS +/- SD				
arithmetic mean (standard deviation)	2.96 (± 1.20)	2.97 (± 1.20)	3.08 (± 1.21)	3.20 (± 1.06)

End point values	MOD-4023 OLE Year 5			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: SDS +/- SD				
arithmetic mean (standard deviation)	3.43 (± 0.16)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
1 year	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22

Reporting groups	
Reporting group title	MOD-4023 Main Study
Reporting group description:	
Once weekly subcutaneous injection of long acting r-hGH (MOD-4023)	
Reporting group title	Genotropin Main Study
Reporting group description:	
Once daily subcutaneous injection of Somatropin (r-hGH; Genotropin)	
Reporting group title	MOD-4023 OLE Period
Reporting group description:	
Once weekly subcutaneous injection of long acting r-hGH (MOD-4023)	

Serious adverse events	MOD-4023 Main Study	Genotropin Main Study	MOD-4023 OLE Period
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 109 (2.75%)	2 / 115 (1.74%)	14 / 212 (6.60%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Kawasaki's disease			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Noninfective sialoadenitis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Scrotal Varicose Veins			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 109 (0.00%)	1 / 115 (0.87%)	0 / 212 (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
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delayed puberty			

subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Chronic tonsillitis			
subjects affected / exposed	1 / 109 (0.92%)	0 / 115 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 109 (0.92%)	0 / 115 (0.00%)	0 / 212 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 109 (0.92%)	0 / 115 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 109 (0.00%)	1 / 115 (0.87%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	4 / 212 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Croup infectious			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			

subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	1 / 212 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	MOD-4023 Main Study	Genotropin Main Study	MOD-4023 OLE Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	92 / 109 (84.40%)	90 / 115 (78.26%)	192 / 212 (90.57%)
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	9 / 109 (8.26%)	0 / 115 (0.00%)	11 / 212 (5.19%)
occurrences (all)	49	0	23
Injection Site Induration			
subjects affected / exposed	4 / 109 (3.67%)	1 / 115 (0.87%)	0 / 212 (0.00%)
occurrences (all)	7	1	0
Injection Site Pain			
subjects affected / exposed	43 / 109 (39.45%)	29 / 115 (25.22%)	66 / 212 (31.13%)
occurrences (all)	293	80	853
Injection site pruritus			
subjects affected / exposed	6 / 109 (5.50%)	0 / 115 (0.00%)	6 / 212 (2.83%)
occurrences (all)	10	0	13
Injection Site Swelling			
subjects affected / exposed	5 / 109 (4.59%)	0 / 115 (0.00%)	6 / 212 (2.83%)
occurrences (all)	9	0	9
Pyrexia			
subjects affected / exposed	18 / 109 (16.51%)	16 / 115 (13.91%)	40 / 212 (18.87%)
occurrences (all)	35	28	116
Vaccination Site Pain			

subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	5 / 212 (2.36%)
occurrences (all)	0	0	8
Immune system disorders			
Seasonal Allergy			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	6 / 212 (2.83%)
occurrences (all)	0	0	11
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 109 (8.26%)	9 / 115 (7.83%)	24 / 212 (11.32%)
occurrences (all)	10	11	37
Nasal congestion			
subjects affected / exposed	1 / 109 (0.92%)	3 / 115 (2.61%)	8 / 212 (3.77%)
occurrences (all)	1	3	11
Oropharyngeal pain			
subjects affected / exposed	6 / 109 (5.50%)	4 / 115 (3.48%)	18 / 212 (8.49%)
occurrences (all)	8	6	29
Rhinitis allergic			
subjects affected / exposed	3 / 109 (2.75%)	1 / 115 (0.87%)	5 / 212 (2.36%)
occurrences (all)	8	1	7
Rhinorrhoea			
subjects affected / exposed	3 / 109 (2.75%)	4 / 115 (3.48%)	12 / 212 (5.66%)
occurrences (all)	3	7	15
Psychiatric disorders			
Attention Deficit/Hyperactivity Disorder			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	7 / 212 (3.30%)
occurrences (all)	0	0	8
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 109 (1.83%)	8 / 115 (6.96%)	0 / 212 (0.00%)
occurrences (all)	3	8	0
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 109 (0.00%)	3 / 115 (2.61%)	0 / 212 (0.00%)
occurrences (all)	0	3	0
Free fatty acids increased			

subjects affected / exposed	5 / 109 (4.59%)	1 / 115 (0.87%)	11 / 212 (5.19%)
occurrences (all)	7	1	16
Insulin-Like Growth Factor Increased			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	5 / 212 (2.36%)
occurrences (all)	0	0	6
Low Density Lipoprotein Decreased			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	5 / 212 (2.36%)
occurrences (all)	0	0	6
Coronavirus Test Positive			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	15 / 212 (7.08%)
occurrences (all)	0	0	15
Thyroxine Free Decreased			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	7 / 212 (3.30%)
occurrences (all)	0	0	7
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	6 / 109 (5.50%)	1 / 115 (0.87%)	0 / 212 (0.00%)
occurrences (all)	11	1	0
Ligament Sprain			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	7 / 212 (3.30%)
occurrences (all)	0	0	9
Limb Injury			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	6 / 212 (2.83%)
occurrences (all)	0	0	6
Skin Abrasion			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	6 / 212 (2.83%)
occurrences (all)	0	0	8
Contusion			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	5 / 212 (2.36%)
occurrences (all)	0	0	6
Fall			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	5 / 212 (2.36%)
occurrences (all)	0	0	6
Traumatic Fracture			

subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	5 / 212 (2.36%)
occurrences (all)	0	0	5
Nervous system disorders			
Headache			
subjects affected / exposed	18 / 109 (16.51%)	25 / 115 (21.74%)	41 / 212 (19.34%)
occurrences (all)	39	65	107
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 109 (6.42%)	7 / 115 (6.09%)	5 / 212 (2.36%)
occurrences (all)	8	7	9
Iron deficiency anaemia			
subjects affected / exposed	3 / 109 (2.75%)	2 / 115 (1.74%)	0 / 212 (0.00%)
occurrences (all)	3	2	0
Thrombocytopenia			
subjects affected / exposed	0 / 109 (0.00%)	3 / 115 (2.61%)	0 / 212 (0.00%)
occurrences (all)	0	3	0
Basophilia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	6 / 212 (2.83%)
occurrences (all)	0	0	7
Eosinophilia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	11 / 212 (5.19%)
occurrences (all)	0	0	16
Neutropenia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	5 / 212 (2.36%)
occurrences (all)	0	0	5
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	2 / 109 (1.83%)	7 / 115 (6.09%)	7 / 212 (3.30%)
occurrences (all)	2	9	10
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	3 / 109 (2.75%)	0 / 115 (0.00%)	0 / 212 (0.00%)
occurrences (all)	3	0	0
Myopia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	6 / 212 (2.83%)
occurrences (all)	0	0	7
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	4 / 109 (3.67%)	2 / 115 (1.74%)	9 / 212 (4.25%)
occurrences (all)	4	3	13
Abdominal pain upper			
subjects affected / exposed	2 / 109 (1.83%)	6 / 115 (5.22%)	12 / 212 (5.66%)
occurrences (all)	2	9	19
Constipation			
subjects affected / exposed	2 / 109 (1.83%)	4 / 115 (3.48%)	5 / 212 (2.36%)
occurrences (all)	3	4	6
Diarrhoea			
subjects affected / exposed	3 / 109 (2.75%)	4 / 115 (3.48%)	14 / 212 (6.60%)
occurrences (all)	3	4	24
Nausea			
subjects affected / exposed	3 / 109 (2.75%)	1 / 115 (0.87%)	6 / 212 (2.83%)
occurrences (all)	5	2	12
Vomiting			
subjects affected / exposed	8 / 109 (7.34%)	9 / 115 (7.83%)	23 / 212 (10.85%)
occurrences (all)	16	15	41
Toothache			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	6 / 212 (2.83%)
occurrences (all)	0	0	8
Dental Caries			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	5 / 212 (2.36%)
occurrences (all)	0	0	9
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 109 (0.92%)	3 / 115 (2.61%)	0 / 212 (0.00%)
occurrences (all)	1	4	0
Rash			
subjects affected / exposed	2 / 109 (1.83%)	3 / 115 (2.61%)	0 / 212 (0.00%)
occurrences (all)	2	3	0
Rash generalised			
subjects affected / exposed	3 / 109 (2.75%)	2 / 115 (1.74%)	0 / 212 (0.00%)
occurrences (all)	3	2	0
Urticaria			

subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	5 / 212 (2.36%)
occurrences (all)	0	0	5
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	7 / 109 (6.42%)	3 / 115 (2.61%)	12 / 212 (5.66%)
occurrences (all)	7	3	12
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 109 (4.59%)	8 / 115 (6.96%)	10 / 212 (4.72%)
occurrences (all)	8	12	18
Pain in extremity			
subjects affected / exposed	5 / 109 (4.59%)	5 / 115 (4.35%)	10 / 212 (4.72%)
occurrences (all)	5	8	13
Scoliosis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	8 / 212 (3.77%)
occurrences (all)	0	0	8
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 109 (2.75%)	9 / 115 (7.83%)	15 / 212 (7.08%)
occurrences (all)	4	14	18
Enterobiasis			
subjects affected / exposed	4 / 109 (3.67%)	2 / 115 (1.74%)	0 / 212 (0.00%)
occurrences (all)	5	4	0
Gastroenteritis			
subjects affected / exposed	4 / 109 (3.67%)	3 / 115 (2.61%)	8 / 212 (3.77%)
occurrences (all)	5	3	12
Gastroenteritis viral			
subjects affected / exposed	0 / 109 (0.00%)	3 / 115 (2.61%)	0 / 212 (0.00%)
occurrences (all)	0	3	0
Influenza			
subjects affected / exposed	5 / 109 (4.59%)	3 / 115 (2.61%)	22 / 212 (10.38%)
occurrences (all)	8	5	28
Molluscum contagiosum			
subjects affected / exposed	3 / 109 (2.75%)	0 / 115 (0.00%)	0 / 212 (0.00%)
occurrences (all)	4	0	0
Nasopharyngitis			

subjects affected / exposed	25 / 109 (22.94%)	29 / 115 (25.22%)	66 / 212 (31.13%)
occurrences (all)	54	52	164
Otitis externa			
subjects affected / exposed	4 / 109 (3.67%)	4 / 115 (3.48%)	0 / 212 (0.00%)
occurrences (all)	4	4	0
Otitis media			
subjects affected / exposed	4 / 109 (3.67%)	7 / 115 (6.09%)	9 / 212 (4.25%)
occurrences (all)	6	8	28
Otitis media acute			
subjects affected / exposed	1 / 109 (0.92%)	3 / 115 (2.61%)	0 / 212 (0.00%)
occurrences (all)	1	4	0
Pharyngitis			
subjects affected / exposed	7 / 109 (6.42%)	5 / 115 (4.35%)	7 / 212 (3.30%)
occurrences (all)	10	7	14
Rhinitis			
subjects affected / exposed	6 / 109 (5.50%)	1 / 115 (0.87%)	10 / 212 (4.72%)
occurrences (all)	9	2	19
Tonsillitis			
subjects affected / exposed	5 / 109 (4.59%)	6 / 115 (5.22%)	6 / 212 (2.83%)
occurrences (all)	6	7	8
Conjunctivitis			
subjects affected / exposed	3 / 109 (2.75%)	3 / 115 (2.61%)	0 / 212 (0.00%)
occurrences (all)	3	3	0
Corona Virus Infection			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	37 / 212 (17.45%)
occurrences (all)	0	0	52
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	12 / 212 (5.66%)
occurrences (all)	0	0	17
Pharyngitis Streptococcal			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	7 / 212 (3.30%)
occurrences (all)	0	0	12
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	7 / 212 (3.30%)
occurrences (all)	0	0	12

Pneumonia			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	5 / 212 (2.36%)
occurrences (all)	0	0	5
Sinusitis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	5 / 212 (2.36%)
occurrences (all)	0	0	7
Viral Infection			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	5 / 212 (2.36%)
occurrences (all)	0	0	5
Viral Pharyngitis			
subjects affected / exposed	0 / 109 (0.00%)	0 / 115 (0.00%)	5 / 212 (2.36%)
occurrences (all)	0	0	7
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	3 / 109 (2.75%)	0 / 115 (0.00%)	0 / 212 (0.00%)
occurrences (all)	3	0	0
Hypoinsulinaemia			
subjects affected / exposed	4 / 109 (3.67%)	3 / 115 (2.61%)	6 / 212 (2.83%)
occurrences (all)	4	3	8
Iron deficiency			
subjects affected / exposed	1 / 109 (0.92%)	3 / 115 (2.61%)	0 / 212 (0.00%)
occurrences (all)	1	3	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 January 2018	ROW Version 3.0 (23 January 2018) Protocol Amendment 1 Countries used: Taiwan, Argentina, Colombia, Bulgaria, Greece, Turkey Increased the frequency and timing of the serum sampling schedule for immunogenicity assessment (at 10-14 days; at 1, 3, 6, 9, and 12 months. Updated statistical analyses sections to align with the SAP (Amendment 2, Version 3.0, 23 January 2018).
21 February 2018	ROW+QoL Version 2.0 (21 February 2018) Protocol Amendment 1 Countries used: Spain, Australia, New-Zealand, Russia, UK Increased the frequency and timing of the serum sampling schedule for immunogenicity assessment (at 10-14 days; at 1, 3, 6, 9, and 12 months. Updated statistical analyses sections to align with the SAP (Amendment 2, Version 3.0, 23 January 2018).
09 May 2018	ROW Version 4.0 (09 May 2018) Protocol Amendment 2 Countries used: Georgia, Poland, Taiwan, Argentina, Mexico, Bulgaria, Greece, Turkey, Israel, Canada The subject of this amendment is the inclusion of an open label extension (OLE) to the study to capture those patients that have successfully completed the 12 months of dosing in the Main Study and continue to meet inclusion / exclusion criteria.
09 May 2018	ROW+QoL Version 3.0 (09 May 2018) Protocol Amendment 2 Countries used: Spain, Australia, New Zealand, Russia, UK, Ukraine, Belarus The subject of this amendment is the inclusion of an open label extension (OLE) to the study to capture those patients that have successfully completed the 12 months of dosing in the Main Study and continue to meet inclusion / exclusion criteria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported