



## Clinical trial results:

### An Open-label Extension Study to Assess the Long-term Safety and Efficacy of UX007 in Subjects with Glucose Transporter Type 1 Deficiency Syndrome

#### Summary

EudraCT number	2015-000389-69
Trial protocol	GB ES DK
Global end of trial date	22 October 2019

#### Results information

Result version number	v1 (current)
This version publication date	03 May 2020
First version publication date	03 May 2020

#### Trial information

##### Trial identification

Sponsor protocol code	UX007G-CL202
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02599961
WHO universal trial number (UTN)	-
Other trial identifiers	EMA/190573: Unique Product Identifier (UPI)

Notes:

##### Sponsors

Sponsor organisation name	Ultragenyx Pharmaceutical Inc.
Sponsor organisation address	60 Leveroni Court, Novato, United States, California 94949
Public contact	Medical Information, Ultragenyx Pharmaceutical Inc., +1 8887568657, medinfo@ultragenyx.com
Scientific contact	Medical Information, Ultragenyx Pharmaceutical Inc., +1 8887568657, medinfo@ultragenyx.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	22 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 October 2019
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the long-term safety of UX007 in glucose transporter type 1 deficiency syndrome (Glut1 DS) subjects.

Protection of trial subjects:

The trial was designed, conducted, recorded, and reported in accordance with the principles established by the 18th World Medical Association General Assembly (Helsinki, 1964) and subsequent amendments and clarifications adopted by the General Assemblies. The investigators made every effort to ensure that the study was conducted in full conformance with Helsinki principles, international Council for Harmonization (ICH) Good Clinical Practice (GCP) guidelines, current Food and Drug Administration (FDA) regulations, EU Clinical Trial Directive 2001/20/EC, and local ethical and regulatory requirements. Each investigator was thoroughly familiar with the appropriate administration and potential risks of administration of the study drug, as described in the protocol and Investigator's Brochure, prior to the initiation of the study. The method of obtaining and documenting informed consent and the contents of the informed consent form (ICF) complied with ICH GCP guidelines, the requirements of 21 CFR Part 50, "Protection of Human Subjects," the Health Insurance Portability and Accountability Act regulations, and all other applicable regulatory requirements. Investigators were responsible for preparing the ICF and submitting it to the Sponsor for approval prior to submission to the Institutional Review Board (IRB). All ICFs were written in regional language and contained the minimum elements for consent as mandated by the ICH guidelines. An IRB-approved ICF was provided by the Sponsor prior to initiation of the study. Investigators obtained signed written informed consent from each potential study subject prior to the conduct of any study procedures and after the methods, objectives, requirements, and potential risks of the study were fully explained to each potential subject. Consent for participation could be withdrawn at any time for any reason by the subject.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 September 2015
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	United States: 9
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Denmark: 1
Worldwide total number of subjects	15
EEA total number of subjects	4

Notes:

<b>Subjects enrolled per age group</b>	
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)	5
Adolescents (12-17 years)	5
Adults (18-64 years)	5
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study enrolled pediatric, adolescent, and adult Glut1 DS subjects who completed the UX007G-CL201 study (2013-003771-35; rollover subjects). No non-rollover subjects (subjects from other clinical studies, investigator sponsored trials, or expanded access/compassionate use treatment) enrolled.

### Pre-assignment

Screening details:

For continuing UX007G-CL201 subjects, the Week 52 visit of that study may have been conducted in conjunction with the Baseline visit for this study to avoid duplication of assessments.

### Period 1

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

### Arms

Arm title	UX007 (Triheptanoin)
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Arm description:

UX007 dosing was targeted and/or maintained at 35% of total daily caloric intake.

Arm type	Experimental
Investigational medicinal product name	triheptanoin
Investigational medicinal product code	UX007
Other name	C7 oil, glycerol triheptanoate, glycerol trienantate, 1, 2, 3-trienanthoylglycerol, trienanthin, 2,3-di(heptanoyloxy)propyl heptanoate
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Treatment was mixed with food (or formula, if appropriate) and administered orally (PO) or by gastrostomy tube at least four times per day (breakfast, lunch, dinner, and before bed).

Number of subjects in period 1	UX007 (Triheptanoin)
Started	15
Completed	0
Not completed	15
Subject Non-Compliance	2
Consent withdrawn by subject	1
Discontinuation of Study by Sponsor	9
Other, Not Specified	3

## Baseline characteristics

### Reporting groups

Reporting group title	Overall Study
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Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	15	15	
Age categorical			
Units: Subjects			
2 to < 12 years	5	5	
12 to < 18 years	5	5	
18 to < 65 years	5	5	
Age continuous			
Units: years			
arithmetic mean	15.24		
standard deviation	± 6.106	-	
Gender categorical			
Units: Subjects			
Female	11	11	
Male	4	4	
Ethnicity			
Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	13	13	
Unknown or Not Reported	1	1	
Race			
Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	1	1	
Black or African American	1	1	
White	11	11	
Other, Not Specified	1	1	
Overall Seizure Frequency Per 4 Weeks			
The number of observable seizures were recorded by the subject or caregiver via diary. Observable seizures were defined as: generalized tonic-clonic; generalized tonic; generalized clonic; generalized atonic; partial/focal with secondary generalization; myoclonic, myoclonic (astatic) atonic, myoclonic tonic; complex partial/focal; simple partial/focal motor; absence.			
Units: seizures per 4 weeks			
arithmetic mean	312.17		
standard deviation	± 528.057	-	
Baseline (2013-003771-35) Columbia Neurological Score (CNS) Total Score			
The CNS evaluates measures of neurological function and development delay, and is the sum of scores for the following domains: Weight, Height, Head Circumference, General Medical Exam, Funduscopy Exam, Cranial Nerves, Stance & Gait, Involuntary Movements, Sensation, Cerebellar Function, Muscle Bulk, Tone & Strength, Myotatic Reflexes, Toe Sign, Other Findings. The CNS is only scored when all domains are measured and ranges from 0 (abnormal exam) to 76 (normal exam). Higher scores are associated with higher neurological function.			
n=12 (subjects with a baseline assessment).			
Units: score on a scale			

arithmetic mean	38.63		
standard deviation	± 25.428	-	
Baseline (2013-003771-35) Short Form 10 (SF-10) Health Survey for Children Physical Summary Score			
<p>The SF-10 Health Survey for Children was administered to caregivers of subjects aged 5-17 years. Responses are used to generate 2 component summary scores: Physical Summary Score and the Psychosocial Summary Score. The T-score based scale scores were centered so that a score of 50 corresponds to the average score in a comprehensive 2006 sample (a combination of general population and supplemental disability and chronic condition samples). Higher scores are associated with better quality of life.</p> <p>n=10 (subjects with a baseline assessment).</p>			
Units: T-score			
arithmetic mean	32.63		
standard deviation	± 17.027	-	
Baseline (2013-003771-35) SF-10 Health Survey for Children Psychosocial Summary Score			
<p>The SF-10 Health Survey for Children was administered to caregivers of subjects aged 5-17 years. Responses are used to generate 2 component summary scores: Physical Summary Score and the Psychosocial Summary Score. The T-score based scale scores were centered so that a score of 50 corresponds to the average score in a comprehensive 2006 sample (a combination of general population and supplemental disability and chronic condition samples). Higher scores are associated with better quality of life.</p> <p>n=10 (subjects with a baseline assessment).</p>			
Units: T-score			
arithmetic mean	48.29		
standard deviation	± 10.196	-	
Baseline (2013-003771-35) SF 12 V.2 (SF-12v2) Health Survey Physical Component Summary (PCS) Score			
<p>SF-12v2 was assessed for adults ≥ 18 years. 8 domain scores were used to generate 2 component summary scores: physical health (PCS) and mental health (MCS). Scores have mean of 50 and SD of 10. T-score based scoring method scores the data in relation to U.S. general population T-scores. Therefore, all scores obtained that are below 50 can be interpreted as below the US general population T-score. Scores above 50 can be interpreted as above the U.S. general population T-score. Higher global scores are associated with better quality of life.</p> <p>n=2 (subjects with a baseline assessment).</p>			
Units: T-score			
arithmetic mean	39.37		
standard deviation	± 0.523	-	
Baseline (2013-003771-35) SF-12v2 Health Survey MCS Score			
<p>SF-12v2 was assessed for adults ≥ 18 years. 8 domain scores were used to generate 2 component summary scores: physical health (PCS) and mental health (MCS). Scores have mean of 50 and SD of 10. T-score based scoring method scores the data in relation to U.S. general population T-scores. Therefore, all scores obtained that are below 50 can be interpreted as below the US general population T-score. Scores above 50 can be interpreted as above the U.S. general population T-score. Higher global scores are associated with better quality of life.</p> <p>n=2 (subjects with a baseline assessment).</p>			
Units: T-score			
arithmetic mean	43.49		
standard deviation	± 4.356	-	

## End points

### End points reporting groups

Reporting group title	UX007 (Triheptanoin)
Reporting group description: UX007 dosing was targeted and/or maintained at 35% of total daily caloric intake.	

### Primary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs, Discontinuations Due to TEAEs, and Deaths

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs, Discontinuations Due to TEAEs, and Deaths <sup>[1]</sup>
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#### End point description:

An adverse event (AE) was defined as any untoward medical occurrence, whether or not considered drug related. Serious adverse events (SAEs) are AEs that at any dose, in the view of either the investigator or sponsor, results in any of the following outcomes: death; a life-threatening AE; inpatient hospitalization or prolongation of existing hospitalization; persistent or significant incapacity or disability; a congenital anomaly/birth defect; other important medical event. An AE was considered a TEAE if it occurred on or after the first dose in this study, and was not present prior to the first dose in this study, or it was present at the first dose in this study but increased in severity during the study. Severity was based on Common Terminology Criteria for Adverse Events (CTCAE): 1 = mild, 2 = moderate, 3 = severe, 4 = life threatening, and 5 = death related to AE.

End point type	Primary
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#### End point timeframe:

From first dose of study drug up to 36 months. The mean (SD) treatment duration was 667.9 (357) days.

#### 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: Descriptive statistics are presented per protocol.

End point values	UX007 (Triheptanoin)			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: subjects				
TEAEs	13			
Serious TEAEs	2			
Related TEAEs	10			
Serious and Related TEAEs	0			
Grade 3 or 4 TEAEs	1			
Gastrointestinal TEAEs	9			
TEAEs Leading to Treatment Discontinuation	0			
TEAEs Leading to Study Discontinuation	0			
TEAEs Leading to Death	0			

## Statistical analyses

**Secondary: Change From Baseline Over Time in Overall Seizure Frequency Per 4 Weeks**

End point title	Change From Baseline Over Time in Overall Seizure Frequency Per 4 Weeks
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End point description:

The number of observable seizures were recorded by the subject or caregiver via diary throughout the study. Observable seizures were defined as: generalized tonic-clonic; generalized tonic; generalized clonic; generalized atonic; partial/focal with secondary generalization; myoclonic, myoclonic (astatic) atonic, myoclonic tonic; complex partial/focal; simple partial/focal motor; absence.

End point type	Secondary
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End point timeframe:

Baseline (2013-003771-35), Month 0-3, Month 4-6, Month 7-9, Month 10-12, Month 13-18, Month 19-24, Month 25-30, Month 31-36

End point values	UX007 (Triheptanoin)			
Subject group type	Reporting group			
Number of subjects analysed	15 <sup>[2]</sup>			
Units: seizures per 4 weeks				
arithmetic mean (standard deviation)				
Change at Month 0-3; n=10	-64.22 (± 185.564)			
Change at Month 4-6; n=7	-64.19 (± 142.460)			
Change at Month 7-9; n=7	-61.81 (± 164.770)			
Change at Month 10-12; n=7	-91.93 (± 216.834)			
Change at Month 13-18; n=8	-75.56 (± 206.406)			
Change at Month 19-24; n=6	-110.12 (± 233.492)			
Change at Month 25-30; n=5	-135.60 (± 249.871)			
Change at Month 31-36; n=2	-51.88 (± 101.378)			

Notes:

[2] - n=subjects with a baseline (BL) and postbaseline (PBL) assessment at given time point.

<b>Attachments (see zip file)</b>	Statistical Analysis for Change From Baseline Over Time in
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**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change From Baseline Over Time in CNS Total Score**

End point title	Change From Baseline Over Time in CNS Total Score
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End point description:

The CNS evaluates measures of neurological function and development delay, and is the sum of scores for the following domains: Weight, Height, Head Circumference, General Medical Exam, Funduscopy Exam, Cranial Nerves, Stance & Gait, Involuntary Movements, Sensation, Cerebellar Function, Muscle



Bulk, Tone & Strength, Myotatic Reflexes, Toe Sign, Other Findings. The CNS is only scored when all domains are measured and ranges from 0 (abnormal exam) to 76 (normal exam). Higher scores are associated with higher neurological function.

End point type	Secondary
End point timeframe:	
Baseline (2013-003771-35), Month 0, Month 6, Month 12, Month 24, Month 36	

End point values	UX007 (Triheptanoin)			
Subject group type	Reporting group			
Number of subjects analysed	12 <sup>[3]</sup>			
Units: T-score				
arithmetic mean (standard deviation)				
Change at Month 0; n=10	11.85 (± 20.331)			
Change at Month 6; n=7	9.36 (± 18.495)			
Change at Month 12; n=7	13.64 (± 21.371)			
Change at Month 24; n=4	3.38 (± 3.092)			
Change at Month 36; n=1	0.00 (± 99999)			

Notes:

[3] - n=subjects with a BL and PBL assessment at given time point. 99999=not applicable (1 subject).

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline Over Time in SF-10 Health Survey for Children Physical Summary Score

End point title	Change From Baseline Over Time in SF-10 Health Survey for Children Physical Summary Score
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End point description:

The SF-10 Health Survey for Children was administered to caregivers of participants aged 5-17 years. Responses are used to generate 2 component summary scores: Physical Summary Score and the Psychosocial Summary Score. The T-score based scale scores were centered so that a score of 50 corresponds to the average score in a comprehensive 2006 sample (a combination of general population and supplemental disability and chronic condition samples). Higher scores are associated with better quality of life.

End point type	Secondary
End point timeframe:	
Baseline (2013-003771-35), Month 0, Month 6, Month 12, Month 18, Month 24, Month 30	

End point values	UX007 (Triheptanoin)			
Subject group type	Reporting group			
Number of subjects analysed	10 <sup>[4]</sup>			
Units: T-score				
arithmetic mean (standard deviation)				

Change at Month 0; n=9	0.25 (± 16.917)			
Change at Month 6; n=7	9.56 (± 21.522)			
Change at Month 12; n=6	-2.67 (± 9.475)			
Change at Month 18; n=5	-9.35 (± 12.702)			
Change at Month 24; n=4	-8.96 (± 20.075)			
Change at Month 30; n=2	7.74 (± 2.273)			

Notes:

[4] - n=pediatric subjects with a BL and PBL assessment at given time point.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline Over Time in SF-10 Health Survey for Children Psychosocial Summary Score

End point title	Change From Baseline Over Time in SF-10 Health Survey for Children Psychosocial Summary Score
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End point description:

The SF-10 Health Survey for Children was administered to caregivers of participants aged 5-17 years. Responses are used to generate 2 component summary scores: Physical Summary Score and the Psychosocial Summary Score. The T-score based scale scores were centered so that a score of 50 corresponds to the average score in a comprehensive 2006 sample (a combination of general population and supplemental disability and chronic condition samples). Higher scores are associated with better quality of life.

End point type	Secondary
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End point timeframe:

Baseline (2013-003771-35), Month 0, Month 6, Month 12, Month 18, Month 24, Month 30

End point values	UX007 (Triheptanoin)			
Subject group type	Reporting group			
Number of subjects analysed	10 <sup>[5]</sup>			
Units: T-score				
arithmetic mean (standard deviation)				
Change at Month 0; n=9	0.59 (± 11.049)			
Change at Month 6; n=7	-2.29 (± 12.366)			
Change at Month 12; n=6	-7.43 (± 15.514)			
Change at Month 18; n=5	-6.60 (± 14.987)			
Change at Month 24; n=4	-8.25 (± 15.316)			
Change at Month 30; n=2	8.91 (± 12.599)			

Notes:

[5] - n=pediatric subjects with a BL and PBL assessment at given time point.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline Over Time in SF-12v2 Health Survey PCS Score

End point title	Change From Baseline Over Time in SF-12v2 Health Survey PCS Score
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End point description:

SF-12v2 was assessed for adults 18 years of age and older. Eight domain scores were used to generate 2 component summary scores: physical health (PCS) and mental health (MCS). The PCS and MCS scores have mean of 50 and SD of 10. The T-score based scoring method scores the data in relation to U.S. general population T-scores. Therefore, all scores obtained that are below 50 can be interpreted as below the U.S. general population T-score and scores above 50 can be interpreted as above the U.S. general population T-score. Higher global scores are associated with better quality of life.

End point type	Secondary
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End point timeframe:

Baseline (2013-003771-35), Month 0, Month 6, Month 12, Month 18

End point values	UX007 (Triheptanoin)			
Subject group type	Reporting group			
Number of subjects analysed	2 <sup>[6]</sup>			
Units: T-score				
arithmetic mean (standard deviation)				
Change at Month 0; n=2	10.25 (± 5.077)			
Change at Month 6; n=2	12.37 (± 5.367)			
Change at Month 12; n=2	5.09 (± 1.619)			
Change at Month 18; n=1	-0.35 (± 99999)			

Notes:

[6] - n=adult subjects with a BL and PBL assessment at given time point. 99999=not applicable (1 subject).

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline Over Time in SF-12v2 Health Survey MCS Score

End point title	Change From Baseline Over Time in SF-12v2 Health Survey MCS Score
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End point description:

SF-12v2 was assessed for adults 18 years of age and older. Eight domain scores were used to generate 2 component summary scores: physical health (PCS) and mental health (MCS). The PCS and MCS scores have mean of 50 and SD of 10. The T-score based scoring method scores the data in relation to U.S. general population T-scores. Therefore, all scores obtained that are below 50 can be interpreted as below the U.S. general population T-score and scores above 50 can be interpreted as above the U.S. general population T-score. Higher global scores are associated with better quality of life.

End point type	Secondary
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End point timeframe:

Baseline (2013-003771-35), Month 0, Month 6, Month 12, Month 18

<b>End point values</b>	UX007 (Triheptanoin)			
Subject group type	Reporting group			
Number of subjects analysed	2 <sup>[7]</sup>			
Units: T-score				
arithmetic mean (standard deviation)				
Change at Month 0; n=2	8.63 (± 2.249)			
Change at Month 6; n=2	5.84 (± 3.316)			
Change at Month 12; n=2	6.90 (± 5.706)			
Change at Month 18; n=1	16.96 (± 99999)			

Notes:

[7] - n=adult subjects with a BL and PBL assessment at given time point. 99999=not applicable (1 subject).

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to 36 months. The mean (SD) treatment duration was 667.9 (357) days.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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### Reporting groups

Reporting group title	UX007 (Triheptanoin)
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Reporting group description:

UX007 dosing was targeted and/or maintained at 35% of total daily caloric intake.

Serious adverse events	UX007 (Triheptanoin)		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 15 (13.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Intestinal Obstruction			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Croup Infectious			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear Infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Otitis Media			

subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Otitis Media Acute			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	UX007 (Triheptanoin)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 15 (86.67%)		
Vascular disorders			
Hot Flush			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Thirst			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Immune system disorders			
Seasonal Allergy			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		

Vulvovaginal Pruritus subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)  Nasal Congestion subjects affected / exposed occurrences (all)  Oropharyngeal Pain subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1  1 / 15 (6.67%) 1  1 / 15 (6.67%) 1		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 2		
Investigations Alanine Aminotransferase Increased subjects affected / exposed occurrences (all)  Blood Glucose Increased subjects affected / exposed occurrences (all)  Weight Increased subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1  1 / 15 (6.67%) 1  1 / 15 (6.67%) 1		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)  Head Injury subjects affected / exposed occurrences (all)  Ligament Sprain	1 / 15 (6.67%) 1  1 / 15 (6.67%) 3		

subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Procedural Pain subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Nervous system disorders Disturbance In Attention subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Dysarthria subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Head Titubation subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 2		
Headache subjects affected / exposed occurrences (all)	4 / 15 (26.67%) 79		
Lethargy subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 3		
Petit Mal Epilepsy subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 3		
Seizure subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Tremor subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Gastrointestinal disorders			



Abdominal Pain			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	5		
Abdominal Pain Upper			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	26		
Breath Odour			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	7 / 15 (46.67%)		
occurrences (all)	13		
Dysphagia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Flatulence			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Haematochezia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	12		
Vomiting			
subjects affected / exposed	5 / 15 (33.33%)		
occurrences (all)	16		
Skin and subcutaneous tissue disorders			
Hair Growth Abnormal			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			

Back Pain			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Muscle Spasms			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Muscular Weakness			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Musculoskeletal Pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Pain In Extremity			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Infections and infestations			
Ear Infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	3		
Influenza			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Otitis Media			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Otitis Media Acute			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Pharyngitis Streptococcal			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Upper Respiratory Tract Infection			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	9		
Viral Upper Respiratory Tract Infection			

subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 4		
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	5		
Hyponatraemia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 June 2016	<ul style="list-style-type: none"><li>• The number of study sites was changed from 'approximately 12' to 'up to 16.' The number of subjects planned was approximated at 40 subjects from the UX007 CL201 study and additional subjects who participated in qualified ISTs.</li><li>• Updated inclusion criteria to state that all subjects at least 1 year of age at time of informed consent are eligible for participation in this study.</li><li>• Modified inclusion criteria to remove the 3 month window following completion of the feeder study, to allow more flexibility.</li><li>• The inclusion criterion regarding pregnancy testing and contraception was split into 2 separate inclusion criteria for clarity.</li><li>• The exclusion criterion regarding serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels was removed, as it was not considered a likely safety concern.</li><li>• Removed specific requirements regarding percent of daily fat intake from the exclusion criteria, to allow investigators to manage subject diet.</li><li>• Removed diabetes mellitus as an exclusionary condition.</li><li>• The first secondary objective was changed to 'Evaluate the long-term effect of UX007 efficacy on seizures associated with Glut1 DS'. This change affects multiple sections of the protocol related to statistical evaluations and analyses.</li><li>• Stopping rules were modified to correct notification procedures should unexpected and study drug-related SAEs occur, or if the study was restarted.</li><li>• The Investigational Product section was modified to specify UX007 should be mixed with food; the requirement to never administer directly as the oil was removed. In addition, the language around dose level was modified to recognize and allow the subject to remain on current dose, which may be different (ie, lower or higher) than 35% of total daily caloric intake.</li></ul>
02 June 2016	<p>(continued)</p> <ul style="list-style-type: none"><li>• Study Duration section was modified to state "The planned duration of treatment in this study is 3 years, or until one of the following occurs: the subject withdraws consent or is discontinued from the study at the discretion of the Investigator or Ultragenyx; the study is terminated, or until commercial availability of study drug in a subject's region, whichever occurs first.". Due to this change, specific references to a "3-year Treatment Extension" were changed to "Treatment Extension Period" throughout the protocol.</li><li>• Updated Prohibited Medications section to remove valproate, MCT oil, KetoCal, or other KD supplements, or other prescribed diet plan as prohibited medications; pancreatic lipase inhibitors was added to the list of prohibited medications.</li><li>• The frequency of overnight EEG assessments was increased. Interictal epileptiform discharges will not be examined as an efficacy variable.</li><li>• Efficacy assessments including Cambridge Neuropsychological Test Automated Battery Six Minute Walk Test and associated paroxysmal exertional dyskinesia (6MWT/PED), the Clinical Global Impression Scales (CGI), and the Pediatric Evaluation of Disability Inventory – Computer Adaptive Test (PEDI-CAT) were removed from the study. Study objectives and endpoints were updated to reflect this change. The Short Form Health Surveys (SF-10 and SF-12v2) will not be performed if no pre-treatment baseline data was available from feeder study.</li><li>• Beta-ketopentanoic acid (BKP) will no longer be assayed.</li><li>• Physical examination of the genitourinary system was no longer specified.</li><li>• Dietitian Consultation and Diet Assessment Section was modified to remove the requirement for a 3-day diet diary prior to the Baseline Visit. Daily caloric intake and UX007 dose determined by interview with the dietitian at the Baseline Visit.</li></ul>

02 June 2016	(continued) <ul style="list-style-type: none"> <li>• Separate safety analysis and intent-to-treat populations were replaced with 1 analysis set to include all subjects who receive at least 1 dose of UX007 during the study.</li> <li>• Reduction in frequency of seizures was removed as an efficacy analysis and replaced with a list of efficacy measures to be assessed.</li> <li>• A coordinating investigator will be named for this multicenter study.</li> <li>• The Record Retention section was updated to state that all study records must be retained for at least 25 years after the end of the clinical trial or in accordance with national law.</li> <li>• The Adverse Event Reporting section was updated to match Sponsor's current safety reporting procedures.</li> </ul>
28 July 2016	The main purpose of Amendment 2 was to update the list of examples of highly effective contraception methods, to add a Safety Follow-up Phone Call to standardize how AE information was collected 30 days following the last dose of UX007, and to clarify that the end of study was the last subject's Safety Follow-up Phone Call, per Regulatory Authorities' request for end of study clarification.
20 September 2017	<ul style="list-style-type: none"> <li>• Phone calls were added 3 months between study site visits during Years 2 and 3.</li> <li>• Optional study site visits were added 3 months between study site visits during Years 2 and 3.</li> <li>• Additional language was added throughout the protocol and within the Study Schema to specify that, at the discretion of the Sponsor, additional subjects who participated in other clinical studies, ISTs, or expanded access/compassionate use treatment programs may be eligible for inclusion in UX007G-CL202.</li> <li>• The window of time to draw blood for UX007 metabolites was expanded from 90 min (<math>\pm</math> 5 min) to 90 min (<math>\pm</math> 10 min) following consumption of food and study drug, as specified within Footnote 6 in the Schedule of Events.</li> </ul>

Notes:

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## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported