Clinical trial results:
OPEN LABEL STUDY OF THE EFFICACY AND LONG TERM SAFETY OF LUM001, AN APICAL SODIUM-DEPENDENT BILE ACID TRANSPORTER INHIBITOR (ASBTi), IN THE TREATMENT OF CHOLESTATIC LIVER DISEASE IN PEDIATRIC PATIENTS WITH PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS

Summary

EudraCT number	2013-003833-14
Trial protocol	GB PL FR
Global end of trial date	20 May 2020

Results information

Result version number	v2 (current)
This version publication date	11 December 2020
First version publication date	22 November 2020
Version creation reason	• Changes to summary attachments An change to the summary attachments is required.
Summary attachment (see zip file)	Final Clinical Study Report Synopsis (lum001-501-synopsis.pdf) Clinical Study Report Addendum Overall Conclusions (lum001-501-addend-overall conclusions.pdf)

Trial information

Trial identification

Sponsor protocol code	LUM001-501

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02057718
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Mirum Pharmaceuticals, Inc.
Sponsor organisation address	950 Tower Lane, Suite 1050, Foster City, United States, CA 94404
Public contact	Medical Information Mirum, Mirum Pharmaceuticals, Inc., 1 6506674085, medinfo@mirumpharma.com
Scientific contact	Medical Information Mirum, Mirum Pharmaceuticals, Inc., 1 6506674085, medinfo@mirumpharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001475-PIP03-17
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	20 May 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 May 2020
Global end of trial reached?	Yes
Global end of trial date	20 May 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Objectives up to/including Week 72:
- To evaluate the long-term safety/tolerability of MRX in pediatric subjects (PS) with PFIC
- To evaluate the effect of LUM001 on serum bile acids in PS with PFIC at 13 wks of treatment
- To evaluate the effect of LUM001 on biochem. markers of cholestasis and liver disease at 13 wks of treatment
- To evaluate the effect of LUM001 on pruritus in PS with PFIC at 13 wks of treatment

Objectives of Optional Follow-up Treatment Period (Post Week 72):
- To offer eligible subjects in the LUM001-501 continued study treatment beyond Week 72 until: (i) the subjects are eligible to enter another LUM001 study or (ii) LUM001 is available commercially
- To obtain safety/efficacy data in subjects treated long-term on LUM001
- To explore a BID and higher daily dosing regimen of LUM001
- To identify genetic indicators of treatment response, incl. exome sequencing
- To assess alpha-fetoprotein levels
- To assess LUM001 formulation palatability

Protection of trial subjects:

All study participants (caregivers as applicable) were required to read and sign an Informed Consent Form.

Background therapy:

none

Evidence for comparator:

none

Actual start date of recruitment	12 February 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	France: 3

Country: Number of subjects enrolled	United States: 15
Country: Number of subjects enrolled	Poland: 1
Worldwide total number of subjects	33
EEA total number of subjects	18

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	7
Children (2-11 years)	25
Adolescents (12-17 years)	1
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 33 participants were enrolled at 11 sites in 4 countries (US, UK, France, Poland). Participants included 19 females and 14 males ranging from 1 to 13 years of age. Screening, treatment and safety follow-up, was approximately 76 weeks after which participants had the option of continuing in the additional follow-up treatment period.

Pre-assignment

Screening details:

A total of 37 PFIC patients were screened for the study. Four of these patients were screen failures under the original protocol. A total of 33 participants were enrolled and subsequently had genotyping performed. Of the 33 participants, 8 were PFIC1 and 25 were PFIC2. Two pairs of siblings (all with PFIC2) from 2 families were enrolled

Period 1

Period 1 title	Baseline to Week 72
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Maralixibat

Arm description:

All subjects received maralixibat (MRX)

Arm type	Experimental
Investigational medicinal product name	Maralixibat chloride
Investigational medicinal product code	
Other name	LUM001
Pharmaceutical forms	Powder and solvent for oral solution
Routes of administration	Oral use

Dosage and administration details:

All participants received MRX, up to 280 µg/kg QD (once daily) until Protocol Amendment 4, when participants continued treatment either on QD dosing, if they met pre-defined responder criteria, or were dose escalated up to a maximum daily dose of 280 µg/kg BID (twice daily) if they did not meet the responder criteria.

Dosing Periods:
•4-week dose escalation [Dose Level 1-4]
•4-week stable dosing at 140 µg/kg QD
•5-week stable dosing at 280 µg/kg QD (participants who tolerated Dose Level 4)
•59-week long-term exposure (up to maximum 280 µg/kg BID)

Number of subjects in period 1	Maralixibat
Started	33
Week 72	22
Completed	22
Not completed	11
Physician decision	1

Consent withdrawn by subject	1
Adverse event, non-fatal	3
Liver Transplant	1
Non-compliance with study drug	1
Consent withdrawn by caregiver	2
Progressive disease	2

Period 2

Period 2 title	Optional follow-up treatment period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Maralixibat

Arm description:

All subjects received maralixibat (MRX)

Arm type	Experimental
Investigational medicinal product name	Maralixibat chloride
Investigational medicinal product code	
Other name	LUM001
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

All participants received MRX, up to 280 µg/kg QD until Protocol Amendment 4, when participants continued treatment either on QD dosing, if they met pre-defined responder criteria, or were dose escalated up to a maximum daily dose of 280 µg/kg BID if they did not meet the responder criteria.

Subjects may be eligible for BID dosing based on efficacy as measured by sBA level and ItchRO score.

Number of subjects in period 2	Maralixibat
Started	22
Completed	12
Not completed	10
Adverse event, non-fatal	3
Liver Transplant	2
Did not consent to protocol amendment	4
Progressive disease	1

Baseline characteristics

Reporting groups	
Reporting group title	Baseline to Week 72

Reporting group description:

A total of 37 PFIC patients were screened for the study. Four of these patients were screen failures under the original protocol. A total of 33 participants were enrolled in the study and subsequently had genotyping performed. Of the 33 participants, 8 were PFIC1 and 25 were PFIC2.

Reporting group values	Baseline to Week 72	Total	
Number of subjects	33	33	
Age categorical			
The mean (SE) overall age was 4.2 (0.56) years, and participants ranged from 1 to 13 years of age.			
Units: Subjects			
<2 years	7	7	
2 to 4 years	15	15	
5 to 8 years	6	6	
9 to 12 years	4	4	
13 to 18 years	1	1	
Gender categorical			
Overall, there were slightly more females than males (19 females [57.6%] and 14 males [42.4%]).			
Units: Subjects			
Female	19	19	
Male	14	14	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	3	3	
Black or African American	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
White	26	26	
More than 1 race	1	1	
Not reported	3	3	
Ethnicity Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	29	29	
Not Reported	3	3	
Country Units: Subjects			
France	3	3	
Britain	14	14	
Poland	1	1	
United States	15	15	
Height z-score Units: z-score			
median	-1.653		
full range (min-max)	-6.06 to 0.77	-	
Weight z-score			

Units: z-score			
median	-0.844		
full range (min-max)	-9.14 to 0.60	-	

Subject analysis sets	
Subject analysis set title	PFIC1
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Enrolled subjects with PFIC1 subtype	
Subject analysis set title	nt-PFIC2
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Enrolled with PFIC2 phenotype: non-truncating (mild to moderate phenotype with residual BSEP [liver-specific transporter] function)	
Subject analysis set title	t-PFIC2
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Enrolled with PFIC2 phenotype: truncating (severe phenotype without residual BSEP function or complete absence of BSEP)	
Subject analysis set title	PFIC2 (overall)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Overall PFIC2 subtype to include PFIC2 phenotype: - non-truncating (mild to moderate phenotype with residual BSEP [liver-specific transporter] function) - truncating (severe phenotype without residual BSEP function or complete absence of BSEP)	

Reporting group values	PFIC1	nt-PFIC2	t-PFIC2
Number of subjects	8	19	6
Age categorical			
The mean (SE) overall age was 4.2 (0.56) years, and participants ranged from 1 to 13 years of age.			
Units: Subjects			
<2 years	1	5	1
2 to 4 years	5	9	1
5 to 8 years	2	2	2
9 to 12 years	0	2	2
13 to 18 years	0	1	0
Gender categorical			
Overall, there were slightly more females than males (19 females [57.6%] and 14 males [42.4%]).			
Units: Subjects			
Female	2	13	4
Male	6	6	2
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	0	1
Black or African American	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
White	6	18	2
More than 1 race	0	1	0
Not reported	0	0	3

Ethnicity Units: Subjects			
Hispanic or Latino	0	1	0
Not Hispanic or Latino	8	18	3
Not Reported	0	0	3
Country Units: Subjects			
France	0	0	3
Britain	3	9	2
Poland	0	1	0
United States	5	9	1
Height z-score Units: z-score			
median	-2.500	-1.356	-1.901
full range (min-max)	-6.06 to -1.62	-2.73 to 0.77	-2.81 to -1.34
Weight z-score Units: z-score			
median	-1.775	-0.216	-1.267
full range (min-max)	-9.14 to -0.29	-1.83 to 0.60	-2.73 to -0.20

Reporting group values	PFIC2 (overall)		
Number of subjects	25		
Age categorical			
The mean (SE) overall age was 4.2 (0.56) years, and participants ranged from 1 to 13 years of age.			
Units: Subjects			
<2 years	6		
2 to 4 years	10		
5 to 8 years	4		
9 to 12 years	4		
13 to 18 years	1		
Gender categorical			
Overall, there were slightly more females than males (19 females [57.6%] and 14 males [42.4%]).			
Units: Subjects			
Female	17		
Male	8		
Race Units: Subjects			
American Indian or Alaska Native	0		
Asian	1		
Black or African American	0		
Native Hawaiian or Other Pacific Islander	0		
White	20		
More than 1 race	1		
Not reported	3		
Ethnicity Units: Subjects			
Hispanic or Latino	1		
Not Hispanic or Latino	21		
Not Reported	3		
Country Units: Subjects			

France	3		
Britain	11		
Poland	1		
United States	10		
Height z-score			
Units: z-score			
median	-1.493		
full range (min-max)	-2.81 to 0.77		
Weight z-score			
Units: z-score			
median	-0.342		
full range (min-max)	-2.73 to 0.60		

End points

End points reporting groups

Reporting group title	Maralixibat
Reporting group description:	
All subjects received maralixibat (MRX)	
Reporting group title	Maralixibat
Reporting group description:	
All subjects received maralixibat (MRX)	
Subject analysis set title	PFIC1
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Enrolled subjects with PFIC1 subtype	
Subject analysis set title	nt-PFIC2
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Enrolled with PFIC2 phenotype: non-truncating (mild to moderate phenotype with residual BSEP [liver-specific transporter] function)	
Subject analysis set title	t-PFIC2
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Enrolled with PFIC2 phenotype: truncating (severe phenotype without residual BSEP function or complete absence of BSEP)	
Subject analysis set title	PFIC2 (overall)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Overall PFIC2 subtype to include PFIC2 phenotype: - non-truncating (mild to moderate phenotype with residual BSEP [liver-specific transporter] function) - truncating (severe phenotype without residual BSEP function or complete absence of BSEP)	

Primary: Change from baseline to endpoint (Week 13) in fasting sBA level

End point title	Change from baseline to endpoint (Week 13) in fasting sBA level
End point description:	
End point type	Primary
End point timeframe:	
Baseline (Day 0) to Week 13	

End point values	Maralixibat	PFIC1	PFIC2 (overall)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	31	8	23	
Units: umol/L				
arithmetic mean (full range (min-max))	-23 (-463 to 279)	18 (-117 to 149)	-38 (-463 to 279)	

Statistical analyses

Statistical analysis title	Change from baseline to Week 13 in sBA levels

Statistical analysis description:

This analysis shows the change from baseline to Week 13 in sBA levels for the overall Modified Intent-to-treat Population. Even though a comparison of PFIC1 vs PFIC2 (overall) is noted, the results are the change from baseline for all participants and is not comparative.

Comparison groups	PFIC1 v PFIC2 (overall)
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	Mean difference (net)
Point estimate	-23.304
Confidence interval	
level	95 %
sides	2-sided
lower limit	-82.35
upper limit	35.742
Variability estimate	Standard deviation
Dispersion value	160.9748

Notes:

[1] - Null hypothesis (H0): mean change from baseline to Week 13 is zero. The null hypothesis was tested for each of the 2 PFIC subgroups and overall; the change in the overall population is presented here.

Secondary: Change from baseline to Week 13/ET in ALT

End point title	Change from baseline to Week 13/ET in ALT

End point description:

End point type	Secondary

End point timeframe:

Baseline (Day 0) to Week 13

End point values	Maralixibat	PFIC1	PFIC2 (overall)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	31	8	23	
Units: U/L				
arithmetic mean (standard deviation)	-9 (± 61.8)	-2 (± 29.1)	-11 (± 70.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 13/ET in total bilirubin

End point title	Change from baseline to Week 13/ET in total bilirubin

End point description:

End point type	Secondary

End point timeframe:
Baseline (Day 0) to Week 13

End point values	Maralixibat	PFIC1	PFIC2 (overall)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	31	8	23	
Units: mg/dL				
arithmetic mean (standard deviation)	-0.2 (± 1.65)	-0.8 (± 2.95)	-0.0 (± 0.90)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 13/ET in direct bilirubin

End point title	Change from baseline to Week 13/ET in direct bilirubin

End point description:

End point type	Secondary

End point timeframe:
Baseline (Day 0) to Week 13

End point values	Maralixibat	PFIC1	PFIC2 (overall)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	31	8	23	
Units: mg/dL				
arithmetic mean (standard deviation)	-0.1 (± 1.12)	-0.3 (± 1.93)	-0.0 (± 0.72)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 13/ET in pruritus as measured by ItchRO(Obs)

End point title	Change from baseline to Week 13/ET in pruritus as measured by ItchRO(Obs)

End point description:
ItchRO(Obs) (4-week average morning scores)

End point type	Secondary

End point timeframe:
Baseline (Day 0) to Week 13

End point values	Maralixibat	PFIC1	PFIC2 (overall)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	31	8	23	
Units: Points (0-4)				
arithmetic mean (standard deviation)	-0.7 (± 0.65)	-0.8 (± 0.83)	-0.7 (± 0.59)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 13/ET in pruritus as measured by ItchRO(Pt)

End point title	Change from baseline to Week 13/ET in pruritus as measured by ItchRO(Pt)
End point description:	
ItchRO(Pt) (4-week average morning scores)	
End point type	Secondary
End point timeframe:	
Baseline (Day 0) to Week 13	

End point values	Maralixibat	PFIC1	PFIC2 (overall)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	9	2	7	
Units: Points (0-4)				
arithmetic mean (standard deviation)	-0.6 (± 0.57)	-0.4 (± 0.65)	-0.7 (± 0.57)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to EOT

Adverse event reporting additional description:

All treatment-emergent AEs, whether observed by the Investigator, reported by the subject, the subject’s caregiver, from laboratory findings, or other means, were recorded on the AE eCRF and medical record. 'Occurrences' relates to the number of events; 'subjects affected' relates to the number of subjects who experienced the AE.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Safety population

Reporting group description:

The safety population is defined as all subjects who were assigned and received at least one dose of the study drug.

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 33 (45.45%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
International normalised ratio increased			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Ulna fracture			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Enteral nutrition			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal tube insertion			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			

subjects affected / exposed	1 / 33 (3.03%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Melaena				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholelithiasis				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Pruritus				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Electrolyte imbalance			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 33 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Spider vein			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Surgical and medical procedures			
biliary-tract operation			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	20 / 33 (60.61%)		
occurrences (all)	83		
Fatigue			
subjects affected / exposed	4 / 33 (12.12%)		
occurrences (all)	4		
Influenza like illness			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences (all)	3		
Malaise			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences (all)	4		
Chest pain			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	4		
Disease progression			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Pain			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Calcinosis			

subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Feeling hot			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Injection site discomfort			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	2		
Injection site mass			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	2		
Injection site pain			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	5		
Injection site rash			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Peripheral swelling			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences (all)	7		
Reproductive system and breast disorders			
Scrotal disorder			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	18 / 33 (54.55%)		
occurrences (all)	39		
Oropharyngeal pain			
subjects affected / exposed	13 / 33 (39.39%)		
occurrences (all)	22		
Epistaxis			

subjects affected / exposed	9 / 33 (27.27%)			
occurrences (all)	20			
Rhinorrhoea				
subjects affected / exposed	8 / 33 (24.24%)			
occurrences (all)	12			
Nasal congestion				
subjects affected / exposed	4 / 33 (12.12%)			
occurrences (all)	7			
Sleep apnoea syndrome				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	2			
Sneezing				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	2			
Upper-airway cough syndrome				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	3			
Dry throat				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Paranasal sinus discomfort				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Pharyngeal inflammation				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Respiratory disorder				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Rhinitis allergic				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Sinus disorder				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Upper respiratory tract congestion				

subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Psychiatric disorders			
Irritability			
subjects affected / exposed	5 / 33 (15.15%)		
occurrences (all)	7		
Anxiety			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Attention deficit hyperactivity disorder			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Encopresis			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Executive dysfunction			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Initial insomnia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Mood altered			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Sleep disorder			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Sleep terror			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Investigations			
International normalised ratio increased			
subjects affected / exposed	7 / 33 (21.21%)		
occurrences (all)	18		
Blood bilirubin increased			

subjects affected / exposed	5 / 33 (15.15%)			
occurrences (all)	6			
Alanine aminotransferase increased				
subjects affected / exposed	3 / 33 (9.09%)			
occurrences (all)	3			
Aspartate aminotransferase increased				
subjects affected / exposed	3 / 33 (9.09%)			
occurrences (all)	3			
International normalised ratio abnormal				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	4			
Vitamin E decreased				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	3			
Bilirubin conjugated increased				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Blood bicarbonate decreased				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Blood phosphorus decreased				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Blood urine present				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Haemoglobin decreased				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	2			
Human rhinovirus test positive				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	2			
Platelet count decreased				

subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Prothrombin time prolonged			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Vitamin D decreased			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences (all)	3		
Traumatic haemorrhage			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences (all)	3		
Contusion			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Scratch			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Skin laceration			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	3		
Upper limb fracture			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	2		
Arthropod bite			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	2		
Ear injury			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Fall			

subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Femur fracture			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Head injury			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Humerus fracture			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Ligament injury			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Ligament sprain			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Limb injury			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Skin abrasion			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Sunburn			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Vaccination complication			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Wound haemorrhage			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Congenital, familial and genetic disorders			
Protein C deficiency			

subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 33 (21.21%)		
occurrences (all)	15		
Encephalopathy			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Lethargy			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	2		
Migraine			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	4		
Paraesthesia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Poor quality sleep			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	3		
Seizure			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Increased tendency to bruise			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Iron deficiency anaemia			

subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Lymphadenitis			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Lymphadenopathy			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	5 / 33 (15.15%)		
occurrences (all)	9		
Cerumen impaction			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Ear disorder			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Ear haemorrhage			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	2		
Excessive cerumen production			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Eye disorders			
Dry eye			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Eye pain			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	3		
Gastrointestinal disorders			

Diarrhoea				
subjects affected / exposed	19 / 33 (57.58%)			
occurrences (all)	70			
Abdominal pain				
subjects affected / exposed	15 / 33 (45.45%)			
occurrences (all)	34			
Abdominal pain upper				
subjects affected / exposed	8 / 33 (24.24%)			
occurrences (all)	37			
Faeces pale				
subjects affected / exposed	6 / 33 (18.18%)			
occurrences (all)	7			
Constipation				
subjects affected / exposed	5 / 33 (15.15%)			
occurrences (all)	6			
Toothache				
subjects affected / exposed	4 / 33 (12.12%)			
occurrences (all)	7			
Nausea				
subjects affected / exposed	3 / 33 (9.09%)			
occurrences (all)	3			
Vomiting				
subjects affected / exposed	17 / 33 (51.52%)			
occurrences (all)	38			
Frequent bowel movements				
subjects affected / exposed	4 / 33 (12.12%)			
occurrences (all)	5			
Abdominal discomfort				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	2			
Dyspepsia				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	3			
Gastrointestinal pain				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	2			

Gastrooesophageal reflux disease				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	2			
Haematochezia				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	3			
Teething				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	3			
Anal haemorrhage				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	2			
Defaecation urgency				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Diarrhoea haemorrhagic				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Faeces discoloured				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Flatulence				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Gingival bleeding				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Haematemesis				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Oral pain				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Pancreatic failure				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			

Pancreatitis subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Perianal erythema subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Rectal tenesmus subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Varices oesophageal subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Rectal haemorrhage subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 2		
Hepatobiliary disorders			
Hyperbilirubinaemia subjects affected / exposed occurrences (all)	3 / 33 (9.09%) 6		
Jaundice subjects affected / exposed occurrences (all)	3 / 33 (9.09%) 4		
hepatic mass subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2		
Cholangitis subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Ocular icterus subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Portal hypertension subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Skin and subcutaneous tissue disorders			

Pruritus				
subjects affected / exposed	10 / 33 (30.30%)			
occurrences (all)	19			
Rash				
subjects affected / exposed	5 / 33 (15.15%)			
occurrences (all)	8			
Alopecia				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	2			
Dermatitis diaper				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	2			
Cold sweat				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Dry skin				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Eczema				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Erythema				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Miliaria				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Petechiae				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Spider naevus				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Telangiectasia				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			

Urticaria subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 2		
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all) Chromaturia subjects affected / exposed occurrences (all) Pollakiuria subjects affected / exposed occurrences (all) Urinary tract pain subjects affected / exposed occurrences (all)	 2 / 33 (6.06%) 3 1 / 33 (3.03%) 1 1 / 33 (3.03%) 1 1 / 33 (3.03%) 1		
Endocrine disorders Delayed puberty subjects affected / exposed occurrences (all) Growth hormone deficiency subjects affected / exposed occurrences (all)	 1 / 33 (3.03%) 1 1 / 33 (3.03%) 1		
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Clubbing subjects affected / exposed occurrences (all)	 6 / 33 (18.18%) 8 1 / 33 (3.03%) 1 1 / 33 (3.03%) 1 1 / 33 (3.03%) 1		

Muscle spasms subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Myalgia subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Neck pain subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	15 / 33 (45.45%) 49		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	11 / 33 (33.33%) 35		
Gastroenteritis subjects affected / exposed occurrences (all)	4 / 33 (12.12%) 4		
Varicella subjects affected / exposed occurrences (all)	5 / 33 (15.15%) 5		
Conjunctivitis subjects affected / exposed occurrences (all)	4 / 33 (12.12%) 5		
Ear infection subjects affected / exposed occurrences (all)	4 / 33 (12.12%) 4		
Influenza subjects affected / exposed occurrences (all)	4 / 33 (12.12%) 4		
Pharyngitis streptococcal subjects affected / exposed occurrences (all)	4 / 33 (12.12%) 7		
Viral infection			

subjects affected / exposed	4 / 33 (12.12%)			
occurrences (all)	7			
Gastroenteritis viral				
subjects affected / exposed	3 / 33 (9.09%)			
occurrences (all)	3			
Rhinitis				
subjects affected / exposed	3 / 33 (9.09%)			
occurrences (all)	4			
Tooth abscess				
subjects affected / exposed	3 / 33 (9.09%)			
occurrences (all)	3			
Urinary tract infection				
subjects affected / exposed	3 / 33 (9.09%)			
occurrences (all)	9			
Body tinea				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	2			
Epstein-Barr virus infection				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	2			
Eye infection				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	3			
Fungal skin infection				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	3			
Hand-foot-and-mouth disease				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	2			
Lower respiratory tract infection				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	2			
Otitis media				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	3			
Pharyngitis				

subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	2			
Respiratory tract infection				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Tonsillitis				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	2			
Viral upper respiratory tract infection				
subjects affected / exposed	2 / 33 (6.06%)			
occurrences (all)	3			
Bronchitis				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	8			
Candida infection				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	2			
Cellulitis				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Conjunctivitis viral				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Coxsackie viral infection				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Gastroenteritis norovirus				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Genital infection fungal				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Gingivitis				
subjects affected / exposed	1 / 33 (3.03%)			
occurrences (all)	1			
Laryngitis				

subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Lice infestation			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Oropharyngeal candidiasis			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Otitis externa			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	2		
Viral pharyngitis			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Ear infection viral			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	4 / 33 (12.12%)		
occurrences (all)	4		
Decreased appetite			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences (all)	3		
Hypocalcaemia			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Electrolyte imbalance			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Hypoglycaemia			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		

Acidosis			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Hypertriglyceridaemia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Iron deficiency			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Malnutrition			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Vitamin E deficiency			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Vitamin K deficiency			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 May 2014	Protocol amendment 1: (UK and EU) Substantial changes made to the protocol were to: limit propylene glycol exposure to within the recommended limits; modify testing requirements for monitoring the liver chemistry test; and add evaluations in the event of a confirmed elevation in ALT or total bilirubin level. (US) In addition to the changes noted for the UK and EU amendment, substantial changes were made to clarify the frequency for the evaluation of MRX plasma levels.
05 November 2014	Protocol amendment 2: Substantial changes made to the protocol were to: modify inclusion and exclusion criteria regarding serum bile acid levels, surgical procedures, and prohibited medications; increase the number of evaluable participants; increase the number of clinic visits and duration of treatment from 48 weeks to 72 weeks. A second interim analysis was added when all enrolled subjects reached the 48-week visit.
02 November 2015	Protocol amendment 3: Substantial changes made to the protocol were to: add an Optional Follow-up Treatment Period (After Week 72) that allowed eligible participants treated in the LUM001-501 study to continue on treatment after Week 72 until the first of the following occurred: (i) up to 52 weeks of additional treatment (Week 124), or (ii) in the event that a new study opened to enrollment; and added an objective to obtain safety and efficacy data in participants treated long term on MRX including genotyping characteristics
20 December 2016	Protocol amendment 4: Substantial changes made to the protocol were to: - allow continued participation in the Optional Follow-Up Treatment Period - clarify that study treatment in the Optional Follow-up Treatment Period could continue until the first of the following occurred: (i) the participants were eligible to enter another MRX study or (ii) MRX was available commercially - clarify that eligible participants who had previously discontinued from the study could re-enter and receive study treatment in the Optional Follow-up Treatment Period (after Week 72) - describe objectives and assessments of the Optional Follow-up Treatment Period, including the following: exploration of a BID dosing regimen and higher daily dosing of MRX; identification of genetic indicators of treatment response, including use of exome sequencing; assessment of AFP levels; assessment of the palatability of the MRX formulation in all patients; addition of an exploratory objective to allow the possibility of analysis of serum markers of treatment response using metabolomic and proteomic analysis on previously collected serum samples. A higher maximum dosing level was selected for the Optional Follow-up Treatment Period because of the findings in healthy volunteers (Study SHP625-101) of higher fecal bile acid (fBA) excretion on higher maralixibat doses and BID dosing regimen up to 100 mg QD and 50 mg BID with a comparable safety profile across the tested dose range. During the BID dosing regimen, the dose was to be taken at least 30 minutes prior to the main morning and evening meal in order to cover the luminal bile acid release associated with meals. Participants with sBA levels above the ULN and/or ItchRO score ≥1.5 were eligible to start BID dosing. If a participant experienced intolerance at any time during the study, the physician Investigator in consultation with the Medical Monitor may have lowered the dose for the remainder of the study.

08 February 2019	Protocol amendment 4.1: Substantial changes made to the protocol were to reflect the change of sponsorship from Lumena Pharmaceuticals LLC to Mirum Pharmaceuticals, Inc; document the change in Medical Monitor; and reduce the interval that new medications used to treat pruritus were prohibited to between Baseline until Week 13 (time point for primary analysis).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported