Supplemental Table 1. Dosing Regimens for Double-Blind and Extension Studies

ITCH — **IMAGINE II**

Screening	Double-blind placebo-controlled		Blinded extension study with Maralixibat dosing					
Eligibility ItchRO	Dose escalation: Placebo vs 70, 140 or 280 ug/kg/d	Stable dosing	Blinded Dose Escalation: placebo escalated to 140 ug/kg/d; active remain on double-blind dose	Dose optimization based on efficacy to max dose of 280 ug/kg/d	Stable dosing	Reconsent to extension at current dose	Reconsent to optional long-term follow-up at current dose	Reconsent to additional optional long-term follow-up at current dose

IMAGO — **IMAGINE**

Screening	Double-blind placebo-controlled		Blinded extension study with Maralixibat dosing				
Eligibility ItchRO	Dose escalation: Placebo vs 140[1] or (70 or 280) ug/kg/d	Stable dosing	Blinded Dose Escalation: placebo escalated to 140 ug/kg/d; active remain on double-blind dose	Dose optimization based on efficacy to max dose of 280 ug/kg/d	Stable dosing	Reconsent to optional long-term follow-up at current dose	Reconsent to optional long-term follow-up with possibility to increase to BID dosing (560 ug/kg/d) after week 156[2]

Week	-17	-14	-13	-7	1	5	13	48	72	96	124	144	220	288[3]

[1]140 dosing completed in first 6 participants; 70 or 280 chosen based upon tolerability of first cohort

Per protocol:

The study will be opened with enrollment in Cohort A:

- Cohort A: 140 µg/kg/day LUM001 (n=6) or placebo (n=3).
- Cohort B: 70 or 280 µg/kg/day LUM001 (n=6) or placebo (n=3).

[2]Participant's start of the 560 ug/kg/d is variable

[3]There was no protocol prescribed maximum duration for IMAGINE. The study ended when study MRX-800 began that allowed enrollment of previously maralixibat-treated Alagille syndrome patients.

Supplemental Table 2A. Disease-Specific Inclusion Criteria for IMAGO and ITCH.

ITCH	IMAGO
1. Male or female subjects between the ages of 2 and 18 years inclusive	1. Male or female, 2 – 18 years of age
2. Diagnosis of ALGS based on the diagnostic criteria outlined in Section 16.3 (as published)	2. Diagnosis of ALGS based on the diagnostic criteria outlined in Section 16.3 (as published)
3. Evidence of cholestasis (one or more of the following): a. Fasting total serum bile acid > 3x ULN for age b. Direct bilirubin > 1 mg/dL c. Fat soluble vitamin deficiency otherwise unexplainable d. GGT > 3x ULN for age	3. Cholestasis as evidenced by total serum bile acid > 3x upper limit of normal (ULN) for age
	4. Intractable pruritus explainable only by liver disease
4. Average daily score ≥ 2 on the Itch Reported Outcome (ItchRO™) questionnaire	5. Average daily score ≥ 2 on the Itch Reported Outcome (ItchRO™) questionnaire
	6. Native liver

Supplemental Table 2B. Disease-Specific Exclusion Criteria for IMAGO and ITCH.

ITCH	IMAGO
1. Chronic diarrhea requiring ongoing specific intravenous fluid or nutritional intervention for the diarrhea and/or its sequelae	1. Chronic diarrhoea requiring specific intravenous fluid or nutritional intervention for the diarrhoea and/or its sequelae
2. Surgical interruption of the enterohepatic circulation	2. Surgical disruption of the enterohepatic circulation
3. Liver transplant	3. Liver transplant
4. ALT >15 x ULN	5. ALT or AST > 15 x ULN at screening
5. Decompensated cirrhosis [INR > 1.5 (unresponsive to vitamin K therapy), albumin < 3.0 gm/dL, history or presence of clinically significant ascites, variceal hemorrhage, and/or encephalopathy] with the subject participating in or completing the study	4. Decompensated cirrhosis [international normalized ratio (INR) > 1.5 albumen < 30 g/L, history or presence of clinically significant ascites, variceal hemorrhage, and/or encephalopathy]
6. History or presence of other concomitant liver disease	6. History or presence of other concomitant liver disease
7. History or presence of any other disease or condition known to interfere with the absorption, distribution, metabolism or excretion of drugs, including bile salt metabolism in the intestine (e.g., inflammatory bowel disease)	7. History or presence of any other disease or condition known to interfere with the absorption, distribution, metabolism or excretion of drugs, including bile salt metabolism in the intestine (e.g., inflammatory bowel disease)
8. Any subject whose recent medical history, or current status suggests that, in the opinion of the Investigator or Medical Monitor, the subject may be unable to complete this study without interruption for intercurrent medical problems	
9. The anticipated need for a surgical procedure within 20 weeks from randomization	

10. Administration of bile acid or lipid binding resins within 30 days prior to randomization and throughout the trial	10. Administration of bile acid or lipid binding resins within 30 days prior to randomization and throughout the trial
11. Any other conditions or abnormalities which, in the opinion of the Investigator or Medical Monitor, may compromise the safety of the subject, or interfere	11. Any other conditions or abnormalities which, in the opinion of the Investigator or Medical Monitor, may compromise the safety of the subject, or interfere with the subject participating in or completing the study

Supplemental Table 3. Enhanced Monitoring Criteria and Stopping Guidelines.

Enhanced Monitoring Criteria

Historical Baseline[1] ALT	**ALT**
≤ ULN	> 5 x ULN
> ULN	> 3 x historical baseline and > 5 x ULN

Historical Baseline[1] Total Bilirubin	**Total Bilirubin**
Total Bilirubin 1-10 mg/dL (17.10-171.04 µmol/L)	3 mg increase over historical baseline level
Total Bilirubin >10 mg/dL (> 171.04 µmol/L)	3 mg increase over historical baseline level

Stopping Guidelines

Historical Baseline Tests	**Change Observed**
ALT (any level)	ALT ≥ 20 x ULN
Total Bilirubin 1-10 mg/dL (17.10-171.04 µmol/L)	5 mg increased **and** a 2 x increase over historical baseline level
Total Bilirubin >10 mg/dL (> 171.04 µmol/L)	2 x increase over historical baseline level

[1]Historical baseline was set by the baseline values of alanine transaminase (ALT) and total bilirubin (TB) at week -13 (i.e., baseline for ITCH or IMAGO)

Supplemental Table 4. Demographic Characteristics by Double-Blind Study and Combined Studies.

Characteristics	Baseline (Week -13)		
	ITCH	IMAGO	COMBINED STUDIES
N	37	20	57
Age, years			
mean (SD)	6.8 (4.5)	5.9 (4.9)	6.5 (4.6)
minimum, maximum	1, 17	1, 16	1, 17
Sex, Female, n (%)	16 (43.2)	10 (50.0)	26 (45.6)
Race, n (%)			
Black	5 (13.5)	1 (5.0)	6 (10.5)
White	29 (78.4)	17 (85.0)	46 (80.7)
Not Black or White (including missing)	3 (8.1)	2 (10.0)	5 (8.8)
Ethnicity, Hispanic/Latino, n (%)	7 (18.9)	0 (0.0)	7 (12.3)
Median Time on Study (weeks)[1]	16.7	16.6	16.7
# (%) of Participants with Early Termination from the Study[1]	2 (5.4)	1 (5.0)	3 (5.3)

[1]Early terminations are for any reason, not just owing to AEs. SD = Standard Deviation

Supplemental Table 5. Baseline Characteristics by Double-Blind Study and Combined Studies.

Characteristics	Statistics	Baseline (Week -13)		
		ITCH	IMAGO	COMBINED STUDIES
N		37	20	57
ItchRO(Obs)	N	37	20	57
	mean (SD)	2.9 (0.6)	2.8 (0.8)	2.9 (0.7)
	min, max	2.0, 4.0	1.6, 4.0	1.6, 4.0
Clinician Scratch Scale (CSS)	N	37 (0)	20 (0)	57
	mean (SD)	3.0 (1.1)	2.9 (0.6)	2.9 (0.9)
	min, max	0.0, 4.0	2.0, 4.0	0.0, 4.0
CSS = 0	n (%)	1 (2.7)	0 (0.0)	1 (1.8)
CSS = 1	n (%)	3 (8.1)	0 (0.0)	3 (5.3)
CSS = 2	n (%)	6 (16.2)	5 (25.0)	11 (19.3)
CSS = 3	n (%)	13 (35.1)	13 (65.0)	26 (45.6)
CSS = 4	n (%)	14 (37.8)	2 (10.0)	16 (28.1)
Serum Bile Acid (umol/L)	N	37	20	57
	median (Q1, Q3)	155.5 (57.4, 310.1)	207.3 (143.1, 348.7)	181.1 (83.4, 329.0)
	min, max	10.2, 1014.2	29.4, 899.6	10.2, 1014.2
PedsQL Total - Parent	N	36	20	56
	mean (SD)	65.0 (20.1)	58.5 (18.6)	62.7 (19.7)
	min, max	18.5, 96.7	35.9, 94.4	18.5, 96.7
Multidimensional Fatigue Scale	N	33	17	50
	mean (SD)	61.6 (21.1)	52.2 (19.4)	58.4 (20.8)
	min, max	16.7, 100.0	20.8, 91.7	16.7, 100.0
Family Impact Total Scale	N	35	19	54
	mean (SD)	63.9 (20.4)	56.2 (20.5)	61.2 (20.5)
	min, max	25.7, 98.6	13.9, 91.7	13.9, 98.6

Characteristics	Statistics	Baseline (Week -13)		
		ITCH	IMAGO	COMBINED STUDIES
Total Bilirubin (mg/dL)	N	37	20	57
	median (Q1, Q3)	2.1 (0.9, 7.2)	1.7 (0.9, 7.8)	2.1 (0.9, 7.4)
	min, max	0.3, 24.9	0.3, 16.7	0.3, 24.9
Total Cholesterol (mg/dL)	N	37	17	54
	median (Q1, Q3)	320.0 (231.0, 443.0)	302.0 (266.0, 373.0)	309.5 (234.0, 443.0)
	min, max	138.0, 1601.0	158.0, 1864.0	138.0, 1864.0
ALT (U/L)	N	37	20	57
	median (Q1, Q3)	137.0 (91.0, 214.0)	128.5 (85.0, 155.5)	130.0 (91.0, 189.0)
	min, max	40.0, 335.0	42.0, 274.0	40.0, 335.0
AST (U/L)	N	37	20	57
	median (Q1, Q3)	123.0 (76.0, 205.0)	102.5 (77.5, 163.0)	120.0 (76.0, 180.0)
	min, max	43.0, 355.0	46.0, 289.0	43.0, 355.0
GGT (U/L)	N	37	20	57
	median (Q1, Q3)	329.0 (203.0, 834.0)	398.0 (172.5, 590.5)	349.0 (196.0, 602.0)
	min, max	19.0, 1282.0	130.0, 1443.0	19.0, 1443.0
Albumin (g/dL)	N	37	20	57
	median (Q1, Q3)	4.6 (4.4, 4.7)	4.5 (4.3, 4.6)	4.5 (4.3, 4.7)
	min, max	3.1, 5.2	3.0, 5.0	3.0, 5.2
Platelet (10^3/uL)	N	37	20	57
	median (Q1, Q3)	258.0 (217.0, 342.0)	318.5 (223.5, 412.5)	267.0 (217.0, 382.0)
	min, max	151.0, 638.0	73.0, 682.0	73.0, 682.0
AST to platelet ratio index (APRI)	N	37	20	57
	median (Q1, Q3)	1.1 (0.7, 2.0)	0.7 (0.6, 1.4)	0.9 (0.6, 1.9)
	min, max	0.3, 5.0	0.4, 3.4	0.3, 5.0
Vitamin A (µg/dL)	N	36	19	55
	mean (SD)	52.5 (18.9)	50.4 (20.6)	51.7 (19.3)

	min, max	16.0, 94.0	14.3, 80.2	14.3, 94.0

Characteristics	Statistics	Baseline (Week -13)		
		ITCH	IMAGO	COMBINED STUDIES
Vitamin A insufficiency: Retinol/RBP (molar ratio <0.8)	n (%)	0 (0)	0 (0)	0 (0)
Vitamin D (ng/mL)	N	36	18	54
	mean (SD)	31.1 (14.1)	26.8 (11.9)	29.7 (13.5)
	min, max	8.0, 78.0	4.6, 46.9	4.6, 78.0
Vitamin D insufficiency: 25-Hydroxyvitamin D<20 ng/mL	n (%)	8 (22.2)	5 (27.8)	5 (27.8)
Vitamin E (µg/mL)	N	36	19	55
	mean (SD)	8.1 (4.8)	8.5 (5.4)	8.3 (5.0)
	min, max	0.5, 19.7	0.2, 17.7	0.2, 19.7
Vitamin E insufficiency: Tocopherol/lipids <0.8 mg/g	n (%)	0 (0)	5 (29.4)	5 (29.4)
Vitamin K insufficiency: INR > 1.2	n (%)	0 (0)	1 (5.3)	1 (5.3)
Any Vitamin A/D/E/K Insufficiency	n (%)	17 (47.2)	8 (47.1)	25 (47.2)
Height Z-score	N	37	20	57
	mean (SD)	-1.6 (1.2)	-1.8 (1.3)	-1.7 (1.2)
	min, max	-4.4, 1.6	-4.3, 0.3	-4.4, 1.6
Weight Z-score	N	37	20	57
	mean (SD)	-1.3 (1.1)	-1.6 (1.0)	-1.4 (1.0)
	min, max	-3.2, 0.8	-4.2, -0.2	-4.2, 0.8
BMI Z-score	N	34	20	54
	mean (SD)	-0.2 (0.8)	-0.4 (1.1)	-0.3 (0.9)
	min, max	-2.1, 1.0	-2.6, 1.8	-2.6, 1.8

Supplemental Table 6. Total Follow-Up Time after Start of Study Medication by Treatment and Overall, Combined Studies.

Follow-Up Time (weeks)	MRX (N=39)	PBO (N=18)	Overall (N=57)
Median (Q1, Q3)	184.7 (88.0, 234.4)	191.4 (83.4, 264.1)	184.7 (86.4, 246.1)

Q1, Q3 = first and third quartiles, respectively.

Supplemental Table 7. Responders Analyses at Week 48, Week 72 and End of Treatment (EOT) in Major Clinical Parameters, Combined Studies.

Variable	N (%) participants with change from baseline	Week 48 Multiple Imputation[1] (N=57)	Week 72 Observed Cases (N=41)[3]	EOT Observed Cases (N=45)[4]
ItchRO(Obs)	N	57	162	45
	≤ -1	41.8 (73.3)	15 (93.8)	35 (77.8)
	≤ -2	23.2 (40.7)	8 (50.0)	25 (55.6)
	0 ≤ score ≤1 at follow-up, regardless of score at baseline[6]	24.5 (43.0)	10 (62.5)	25 (55.6)
Clinician Scratch Scale (CSS)	N	57	40	45
	≤ -1	38.9 (68.2)	28 (70.0)	36 (80.0)
	≤ -2	24.8 (43.5)	17 (42.5)	21 (46.7)
	≤ -3	16.9 (29.6)	11 (27.5)	13 (28.9)
	≤ -4	5.7 (10.0)	5 (12.5)	6 (13.3)
Serum Bile Acid (umol/L)	N	57	37	45
	≤ -25%	32 (56.1)	24 (64.9)	28 (62.2)
	≤ -50%	22.5 (39.5)	13 (35.1)	21 (46.7)
PedsQL Total - Parent	N	57	30	44
	≥ +5	33.6 (58.9)	19 (63.3)	24 (54.5)
	≥ +10	25.4 (44.6)	14 (46.7)	21 (47.7)
Multidimensional Fatigue Scale	N	57	25	39
	≥ +5	37.9 (66.5)	18 (72.0)	25 (64.1)
	≥ +10	29.7 (52.1)	15 (60.0)	19 (48.7)
Family Impact Total Scale	N	57	30	43
	≥ +5	34.4 (60.4)	19 (63.3)	26 (60.5)
	≥ +10	31.7 (55.6)	18 (60.0)	25 (58.1)
Weight Z-Score	N	57	39	45

	≥ +0.3	21.1 (37.0)	13 (33.3)	19 (42.2)
Variable	N (%) participants with change from baseline	Week 48 Multiple Imputation[1] (N=57)	Week 72 Observed Cases (N=41)[3]	EOT Observed Cases (N=45)[4]
Height Z-Score	N	57	39	45
	≥ +0.3	25.9 (45.4)	15 (38.5)	19 (42.2)

[1]10 imputed datasets were generated using the multivariate normal distribution (MVN) method for continuous measures and the fully conditional specification (FCS) method for categorical methods. The multiple imputation model included all characteristics at weeks -13, 0, 2, 4, 8, 12, 24, 36, and 48, study (ITCH/IMAGINE II or IMAGO/IMAGINE), age at baseline (years), and sex.

[2]ItchRO was not collected in IMAGINE at week 72.

[3]Week 72 is the patient's drug exposure week. That is, when a patient had a treatment gap, this period is not included.

[4]For EOT analysis, only participants who have at least 48 weeks in IMAGINE or IMAGINE II are included. The EOT data was obtained as the last value that is before the date of last treatment dose + 7 days.

[5]Vitamin A Insufficiency: Retinol/RBP (molar ratio <0.8). Vitamin D Insufficiency: 25-Hydroxyvitamin D<20 ng/mL. Vitamin E Insufficiency: Tocopherol/lipids <0.8 mg/g. Vitamin K Insufficiency: INR > 1.2.

[6]Three participants in IMAGO have ItchRO(Obs) at baseline < 2 (1.5, 1.7, 1.9).

Supplemental Table 8. Change from Baseline to Week 48 in Secondary Clinical Parameters, Combined Studies. Multiple Imputation.

Characteristics	Baseline[1]	Adjusted[2] Change from Baseline to Week 48 Multiple Imputation[3] (N=57)	p-value
Family Impact Total Scale	58.7 (47.2, 79.2)	10.06 (3.90, 16.22)	0.002
Total Cholesterol (mg/dL)	309.5 [234.0, 443.0]	-74.78 (-135.66, -13.91)	0.02
AST (U/L)	120.0 (76.0, 180.0)]	24.77 (5.62, 43.92)	0.01
GGT (U/L)	349.0 (196.0, 602.0)	-67.62, 84.53	0.83
AST to platelet ratio index (APRI)	0.9 (0.6, 1.9)	0.47 (-0.07, 1.01)	0.08
Vitamin A (µg/dL)	50.0 (38.0, 65.0)	0.91 (-4.17, 5.99)	0.72
Vitamin D (ng/mL)	30.9 (20.0, 36.5)	-1.66 (-5.76, 2.44)	0.42
Vitamin E (µg/mL)	8.4 (4.1, 12.1)	0.20 (-1.19, 1.58)	0.78
BMI Z-Score	-0.4 (-0.9, 0.4)	-0.12 (-0.33, 0.09)	0.27

[1]Median [Q1, Q3], Q1, Q3 = first and third quartiles, respectively.

[2]Least square mean and 95% confidence interval and p-value based on separate linear mixed models (random intercept and slope for each subject) for each characteristic with dependent variable as the change from baseline controlling for study (ITCH/IMAGINE II or IMAGO/IMAGINE), week (0, 2, 4, 8, 12, 24, 36, 48), age at baseline, and baseline level of the dependent variable as covariates.

[3]10 imputed datasets were generated using the multivariate normal distribution (MVN) method for continuous measures and the fully conditional specification (FCS) method for categorical methods. The multiple imputation model included all characteristics at weeks -13, 0, 2, 4, 8, 12, 24, 36, and 48, study (ITCH/IMAGINE II or IMAGO/IMAGINE), age at baseline (years), and sex.

Supplemental Table 9. Vitamin Status at Week 48, Week 72 and End of Treatment (EOT), Combined Studies.

Variable	N (%) participants with	Week 48 Multiple Imputation[1] (N=57)	Week 72[2] Observed Cases (N=41)	EOT[3] Observed Cases (N=45)
Vitamin A [4]	Sufficient at Baseline, N	50.4	30	37
	Sufficiency	44.7 (88.7)	28 (93.3)	29 (78.4)
	Insufficiency	5.7 (11.3)	2 (6.7)	8 (21.6)
	Insufficient at Baseline, N	6.6	1	3
	Sufficiency	4.3 (65.2)	0 (0.0)	2 (66.7)
	Insufficiency	2.3 (34.8)	1 (100.0)	1 (33.3)
Vitamin D [4]	Sufficient at Baseline, N	43.3	27	34
	Sufficiency	31.5 (72.7)	23 (85.2)	29 (85.3)
	Insufficiency	11.8 (27.3)	4 (14.8)	5 (14.7)
	Insufficient at Baseline, N	13.7	7	9
	Sufficiency	3.5 (25.5)	2 (28.6)	1 (11.1)
	Insufficiency	10.2 (74.5)	5 (71.4)	8 (88.9)
Vitamin E [4]	Sufficient at Baseline, N	33.6	25	29
	Sufficiency	30.4 (90.5)	24 (96.0)	28 (96.6)
	Insufficiency	3.2 (9.5)	1 (4.0)	1 (3.4)
	Insufficient at Baseline, N	23.4	8	13
	Sufficiency	7.7 (32.9)	4 (50.0)	4 (30.8)
	Insufficiency	15.7 (67.1)	4 (50.0)	9 (69.2)
Vitamin K [4]	Sufficient at Baseline, N	49.6	34	39
	Sufficiency	45.5 (91.7)	33 (97.1)	32 (82.1)
	Insufficiency	4.1 (8.3)	1 (2.9)	7 (17.9)
	Insufficient at Baseline, N	7.4	2	4
	Sufficiency	3.4 (45.9)	1 (50.0)	0 (0.0)
	Insufficiency	4 (54.1)	1 (50.0)	4 (100.0)

[1]Ten imputed datasets were generated using the multivariate normal distribution (MVN) method for continuous measures and the fully conditional specification (FCS) method for categorical methods. The multiple imputation model included all characteristics at weeks -13, 0, 2, 4, 8, 12, 24, 36, and 48, study (ITCH/IMAGINE II or IMAGO/IMAGINE), age at baseline (years), and sex.

[2]Week 72 is the patient's drug exposure week. That is, when a patient had a treatment gap, this period is not included.

[3]For EOT analysis, only participants who have at least 48 weeks in IMAGINE or IMAGINE II are included. The EOT data was obtained as the last value that is before the date of last treatment dose + 7 days.

[4]Vitamin A Insufficiency: Retinol/RBP (molar ratio <0.8). Vitamin D Insufficiency: 25-Hydroxyvitamin D<20 ng/mL. Vitamin E Insufficiency: Tocopherol/lipids <0.8 mg/g. Vitamin K Insufficiency: INR > 1.2.

Supplemental Table 10. Change from to Week 48, Week 72 and End of Treatment (EOT) in Secondary Clinical Parameters, Combined Studies. Observed Cases.

Characteristics	Statistics	Change from Baseline to Week 48, Unadjusted, Observed Cases (N=45)	Change from Baseline to Week 72[1], Observed Cases (N=41)	Change from Baseline to EOT[2], Observed Cases (N=45)
Family Impact Total Scale	N	41	30	43
	Mean (95% CI)	11.25 (6.77, 15.73)	14.10 (8.35, 19.85)	14.38 (8.90, 19.86)
AST (U/L)	N	44	37	45
	Mean (95% CI)	29.02 (10.49, 47.56)	33.32 (16.15, 50.50)	24.91 (3.81, 46.01)
GGT (U/L)	N	44	37	45
	Mean (95% CI)	34.36 (-21.83, 90.56)	26.19, 141.00	23.49 (-40.63, 87.61)
APRI	N	42	36	45
	Mean (95% CI)	0.41 (0.14, 0.67)	0.58 (0.31, 0.86)	0.71 (0.35, 1.06)
Vitamin A (µg/dL)	N	42	35	44
	Mean (95% CI)	1.40 (-3.27, 6.08)	3.24 (-1.29, 7.77)	-1.30 (-6.03, 3.42)
Vitamin D (ng/mL)	N	41	34	43
	Mean (95% CI)	-1.15 (-5.72, 3.42)	-0.93 (-4.03, 2.18)	-1.53 (-5.96, 2.91)
Vitamin E (µg/mL)	N	42	35	44
	Mean (95% CI)	0.07 (-0.82, 0.97)	0.87 (0.08, 1.66)	0.31 (-0.57, 1.18)
BMI Z-Score	N	44	39	45
	Mean (95% CI)	-0.08 (-0.29, 0.13)	-0.06 (-0.29, 0.17)	-0.17 (-0.42, 0.09)

[1]Week 72 is observed week

[2]For EOT analysis, only participants who have at least 48 weeks in IMAGINE or IMAGINE II are included. The EOT data was obtained as the last value that is before the date of last treatment dose + 7 days.

Supplemental Table 11. End of Treatment Effect on Various Outcomes by Stable Dosing Group after Week 48, Combined Studies.

Variable		Stable Dosing Group			
	Statistics	All	140 mcg/kg/d	280 mcg/kg/d	560 mcg/kg/d
ItchRO (Obs)	N	45	6	34	5
	Median (Q1, Q3)	-2.0 (-2.7, -1.1)	-2.5 (-2.6, -1.7)	-2.2 (-2.7, -1.1)	-1.3 (-1.4, -0.4)
	Min, Max	-3.6, 0.0	-3.1, -0.3	-3.6, 0.0	-2.0, 0.0
ItchRO (Obs) Responder, n (%) participants with change from baseline	≤ -1	35 (77.8%)	5 (83.3%)	27 (79.4%)	3 (60.0%)
	≤ -2	25 (55.6%)	4 (66.7%)	20 (58.8%)	1 (20.0%)
CSS	N	45	6	34	5
	Median (Q1, Q3)	-1.0 (-3.0, -1.0)	-1.0 (-2.0, -1.0)	-1.0 (-3.0, -1.0)	-2.0 (-3.0, -1.0)
	Min, Max	-4.0, 2.0	-4.0, 0.0	-4.0, 2.0	-3.0, -1.0
CSS Responder, n (%) participants with change from baseline	≤ -1	36 (80.0%)	5 (83.3%)	26 (76.5%)	5 (100.0%)
	≤ -2	21 (46.7%)	2 (33.3%)	16 (47.1%)	3 (60.0%)
	≤ -3	13 (28.9%)	1 (16.7%)	10 (29.4%)	2 (40.0%)
	≤ -4	6 (13.3%)	1 (16.7%)	5 (14.7%)	0 (0.0%)
Serum Bile Acid (umol/L)	N	45	6	34	5
	Median (Q1, Q3)	-52.9 (-126.9, -	-12.4 (-40.4, 15.9)	-51.6 (-121.5, -15.0)	-145.3 (-297.2, -126.9)
	Min, Max	-304.4, 192.6	-163.8, 60.2	-260.2, 192.6	-304.4, -98.2
Serum Bile Acid Responder, n (%) participants with change from baseline	≤ -25%	28 (62.2%)	2 (33.3%)	21 (61.8%)	5 (100.0%)
	≤ -50%	21 (46.7%)	1 (16.7%)	16 (47.1%)	4 (80.0%)
PedsQL Parent	N	44	6	33	5
	Median (Q1, Q3)	7.2 (-1.7, 22.8)	3.4 (-8.7, 26.6)	12.0 (1.1, 22.8)	0.6 (-6.4, 3.3)
	Min, Max	-41.9, 40.2	-19.6, 40.2	-17.9, 34.4	-41.9, 22.8
PedsQL Parent Responder, n (%) participants with change from baseline	≥ +5	24 (54.5%)	3 (50.0%)	20 (60.6%)	1 (20.0%)
	≥ +10	21 (47.7%)	2 (33.3%)	18 (54.5%)	1 (20.0%)
Multidimensional Fatigue	N	39	6	28	5

Variable		Stable Dosing Group			
	Statistics	All	140 mcg/kg/d	280 mcg/kg/d	560 mcg/kg/d
	Median (Q1, Q3)	9.7 (1.4, 26.4)	5.6 (0.0, 30.6)	14.3 (3.5, 26.4)	-15.3 (-16.7, 8.3)
	Min, Max	-45.8, 45.8	-8.3, 45.8	-22.2, 43.1	-45.8, 30.6
Multidimensional Fatigue Responder, n (%) participants with change from baseline	≥ +5	25 (64.1%)	3 (50.0%)	20 (71.4%)	2 (40.0%)
	≥ +10	19 (48.7%)	2 (33.3%)	16 (57.1%)	1 (20.0%)
Family Impact	N	43	6	32	5
	Median (Q1, Q3)	11.2 (0.0, 24.3)	12.5 (-7.6, 16.7)	12.6 (0.0, 25.3)	2.1 (0.0, 24.3)
	Min, Max	-18.8, 67.4	-11.8, 67.4	-18.8, 52.1	0.0, 43.1
Family Impact Responder, n (%) participants with change from baseline	≥ +5	26 (60.5%)	4 (66.7%)	20 (62.5%)	2 (40.0%)
	≥ +10	25 (58.1%)	4 (66.7%)	19 (59.4%)	2 (40.0%)
Total Bilirubin (mg/dL)	N	45	6	34	5
	Median (Q1, Q3)	0.1 (-0.5, 0.3)	-0.0 (-3.2, 0.1)	0.1 (-0.5, 0.3)	0.0 (-0.1, 0.2)
	Min, Max	-9.7, 13.9	-5.1, 0.2	-4.1, 7.9	-9.7, 13.9
Total Cholesterol (mg/dL)	N	43	6	33	4
	Median (Q1, Q3)	-26.0 (-91.0, 3.0)	-46.0 (-111.0,	-26.0 (-88.0, 2.0)	-29.0 (-90.5, -1.5)
	Min, Max	-538.0, 111.0	-538.0, 27.0	-427.0, 111.0	-137.0, 11.0
ALT (U/L)	N	45	6	34	5
	Median (Q1, Q3)	26.0 (-1.0, 58.0)	6.0 (-15.0, 15.0)	26.5 (5.0, 44.0)	59.0 (58.0, 60.0)
	Min, Max	-160.0, 396.0	-109.0, 58.0	-74.0, 396.0	-160.0, 244.0
AST (U/L)	N	45	6	34	5
	Median (Q1, Q3)	12.0 (-10.0, 36.0)	-2.0 (-38.0, 14.0)	10.0 (-8.0, 45.0)	29.0 (19.0, 36.0)
	Min, Max	-141.0, 201.0	-106.0, 85.0	-74.0, 201.0	-141.0, 113.0
GGT (U/L)	N	45	6	34	5
	Median (Q1, Q3)	31.0 (-89.0, 172.0)	-34.0 (-180.0,	36.5 (-62.0, 194.0)	57.0 (-333.0, 95.0)
	Min, Max	-421.0, 666.0	-313.0, 219.0	-421.0, 666.0	-356.0, 345.0
Albumin (g/dL)	N	45	6	34	5
	Median (Q1, Q3)	0.0 (-0.4, 0.2)	-0.3 (-0.7, 0.1)	0.0 (-0.2, 0.2)	0.0 (-0.7, 0.2)

Variable		Stable Dosing Group			
	Statistics	All	140 mcg/kg/d	280 mcg/kg/d	560 mcg/kg/d
	Min, Max	-1.3, 0.5	-1.2, 0.2	-0.6, 0.5	-1.3, 0.3
Platelet (10^3/uL)	N	45	6	34	5
	Median (Q1, Q3)	-38.0 (-99.0, -4.0)	-14.0 (-55.0, 14.0)	-40.0 (-99.0, -18.0)	-22.0 (-210.0, -4.0)
	Min, Max	-336.0, 83.0	-326.0, 24.0	-253.0, 83.0	-336.0, 71.0
AST to Platelet Ratio Index (APRI)	N	45	6	34	5
	Median (Q1, Q3)	0.3 (0.1, 0.9)	-0.1 (-0.6, 0.7)	0.3 (0.1, 0.9)	0.3 (0.1, 1.1)
	Min, Max	-0.8, 4.7	-0.8, 2.7	-0.6, 4.7	-0.0, 3.0
Vitamin A (ug/dL)	N	44	6	33	5
	Median (Q1, Q3)	-2.9 (-8.3, 8.8)	-1.0 (-27.0, 9.0)	-3.0 (-8.0, 5.0)	8.9 (7.2, 15.5)
	Min, Max	-42.0, 34.4	-42.0, 17.0	-33.0, 34.4	-18.9, 28.3
Vitamin A Insufficiency2, n (%) participants with	Sufficient at Baseline, N	37	4	28	5
	Sufficiency	29 (78.4%)	2 (50.0%)	22 (78.6%)	5 (100.0%)
	Insufficiency	8 (21.6%)	2 (50.0%)	6 (21.4%)	0 (0.0%)
	Insufficient at Baseline, N	3	0	3	0
	Sufficiency	2 (66.7%)	0	2 (66.7%)	0
	Insufficiency	1 (33.3%)	0	1 (33.3%)	0
Vitamin D (ng/mL)	N	43	6	33	4
	Median (Q1, Q3)	-5.0 (-10.8, 5.0)	-10.5 (-13.5, 3.0)	-2.0 (-9.0, 6.9)	-7.8 (-13.6, -5.0)
	Min, Max	-26.4, 52.0	-18.0, 14.0	-26.4, 52.0	-19.2, -2.4
Vitamin D Insufficiency2, n (%) participants with	Sufficient at Baseline, N	34	4	26	4
	Sufficiency	29 (85.3%)	4 (100.0%)	22 (84.6%)	3 (75.0%)
	Insufficiency	5 (14.7%)	0 (0.0%)	4 (15.4%)	1 (25.0%)
	Insufficient at Baseline, N	9	2	7	0

Variable		Stable Dosing Group			
	Statistics	All	140 mcg/kg/d	280 mcg/kg/d	560 mcg/kg/d
	Sufficiency	1 (11.1%)	0 (0.0%)	1 (14.3%)	0
	Insufficiency	8 (88.9%)	2 (100.0%)	6 (85.7%)	0
Vitamin E (mg/L)	N	44	6	33	5
	Median (Q1, Q3)	0.8 (-1.3, 2.4)	1.5 (0.0, 2.4)	0.8 (-0.7, 1.3)	3.4 (-3.9, 4.0)
	Min, Max	-7.1, 6.8	-4.2, 2.5	-7.1, 6.8	-4.0, 5.1
Vitamin E Insufficiency2, n (%) participants with	Sufficient at Baseline, N	29	3	23	3
	Sufficiency	28 (96.6%)	3 (100.0%)	22 (95.7%)	3 (100.0%)
	Insufficiency	1 (3.4%)	0 (0.0%)	1 (4.3%)	0 (0.0%)
	Insufficient at Baseline, N	13	3	9	1
	Sufficiency	4 (30.8%)	1 (33.3%)	2 (22.2%)	1 (100.0%)
	Insufficiency	9 (69.2%)	2 (66.7%)	7 (77.8%)	0 (0.0%)
Vitamin K Insufficiency2, n (%) participants with	Sufficient at Baseline, N	39	5	30	4
	Sufficiency	32 (82.1%)	3 (60.0%)	25 (83.3%)	4 (100.0%)
	Insufficiency	7 (17.9%)	2 (40.0%)	5 (16.7%)	0 (0.0%)
	Insufficient at Baseline, N	4	1	2	1
	Sufficiency	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Insufficiency	4 (100.0%)	1 (100.0%)	2 (100.0%)	1 (100.0%)
Any Vitamin Insufficiency, n (%) participants with	Sufficient at Baseline, N	25	3	19	3
	Sufficiency	15 (60.0%)	2 (66.7%)	11 (57.9%)	2 (66.7%)
	Insufficiency	10 (40.0%)	1 (33.3%)	8 (42.1%)	1 (33.3%)
	Insufficient at Baseline, N	17	3	13	1
	Sufficiency	2 (11.8%)	0 (0.0%)	2 (15.4%)	0 (0.0%)
	Insufficiency	15 (88.2%)	3 (100.0%)	11 (84.6%)	1 (100.0%)

Variable		Stable Dosing Group			
	Statistics	All	140 mcg/kg/d	280 mcg/kg/d	560 mcg/kg/d
Height Z-score	N	45	6	34	5
	Median (Q1, Q3)	0.2 (-0.1, 0.7)	0.2 (-0.4, 0.4)	0.2 (-0.1, 0.8)	0.5 (0.5, 1.1)
	Min, Max	-1.1, 1.9	-0.5, 0.6	-0.7, 1.9	-1.1, 1.8
Height Z-score Responder, n (%) participants with change from baseline	≥ +0.3	19 (42.2%)	2 (33.3%)	13 (38.2%)	4 (80.0%)
Weight Z-score	N	45	6	34	5
	Median (Q1, Q3)	0.1 (-0.6, 0.5)	-0.2 (-1.2, 0.5)	0.0 (-0.4, 0.8)	0.5 (0.3, 1.4)
	Min, Max	-1.5, 1.7	-1.2, 0.5	-1.3, 1.7	-1.5, 1.5
Weight Z-score Responder, n (%) participants with change from baseline	≥ +0.3	19 (42.2%)	3 (50.0%)	12 (35.3%)	4 (80.0%)
BMI Z-score	N	45	6	34	5
	Median (Q1, Q3)	-0.2 (-0.8, 0.4)	-0.2 (-1.2, 0.3)	-0.3 (-0.8, 0.4)	0.4 (-0.3, 0.5)
	Min, Max	-2.1, 2.2	-2.1, 0.3	-1.4, 2.2	-1.3, 0.7
BMI Z-score Responder, n (%) participants with change from baseline	≥ +0.3	13 (28.9%)	1 (16.7%)	9 (26.5%)	3 (60.0%)

[1]IMAGINE subject 001005 had stable dose switching between 420 mcg/kg/d and 560 mcg/kg/d. This subject was combined into group 560 mcg/kg/d.

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[2]Vitamin A Insufficiency: Retinol/RBP (molar ratio <0.8). Vitamin D Insufficiency: 25-Hydroxyvitamin D<20 ng/mL. Vitamin E Insufficiency: Tocopherol/lipids <0.8 mg/g. Vitamin K Insufficiency: INR > 1.2.

Supplemental Table 12. Treatment-Emergent Gastrointestinal Adverse Events by Treatment, Combined Studies.

Characteristic	ITCH/IMAGO		IMAGINE/IMAGINE II		Combined IMAGINE/ IMAGINE II
	MRX	PBO	MRX-MRX	PBO-MRX	MRX
N	39	18	37	16	53
# of AEs	60	26	165	66	231
Mean # of AEs per subject	1.5	1.4	4.5	4.1	4.4
AE Rate (per person-year of treatment follow-up)	5.4	5.4	1.6	1.5	1.6
# (%) of Participants with > 1 AE[1]	26 (66.7)	11 (61.1)	29 (78.4)	13 (81.3)	42 (80.8)
# (%) of AEs By Severity					
Mild	53 (88.3)	17 (65.4)	155 (93.9)	54 (81.8)	209 (90.5)
Moderate	6 (10)	8 (30.8)	6 (3.6)	10 (15.2)	16 (6.9)
Severe	1 (1.7)	1 (3.8)	4 (2.4)	2 (3)	6 (2.6)

[1]If a participant started an AE in ITCH or IMAGO that continued during the extension period, the AE is counted in the ITCH or IMAGO study only. All AEs in extension studies are included, even those after 48 weeks.

Treatment-emergent adverse events are AEs where the start of the event is (a) on or after the first dose date, and (b) within 14 days of the last dose date.

Gastrointestinal AEs are defined by MedDRA Preferred Term = "Gastrointestinal disorders".

Treatment follow-up is no. of days from from first tx date to (last dose date + 14 days) or end of participation whichever is earlier, excluding days on drug holiday (treatment gap).

None of the GI AEs started during the drug holiday (treatment gap).

Supplemental Table 13. Listing of Treatment-Emergent SAEs, Combined Studies.

Treatment[1]	Dose at time of SAE Onset	ID #	SAE Description (Verbatim Term)	Days from Start of Study Medication*	SAE Duration (days)	Severity Grade[2]	Study Drug Action Taken
MRX-MRX	70	13	Vomiting	68	4	Severe	Drug Interrupted
MRX-MRX	280	3	Prolongation Of Hospitalization Due To Bleeding From Ears	555	2	Mild	Dose Not Changed
MRX-MRX	280	6	Hospital Admission For Reinsertion Of Cholecystostomy Button	175	3	Mild	Dose Not Changed
MRX-MRX	280	6	Hospital Admission For Reinsertion Of Cholecystostomy Button	208	2	Mild	Dose Not Changed
MRX-MRX	280	6	Hospital Admission For Fracture Of Right Forearm	463	2	Moderate	Dose Not Changed
MRX-MRX	280	10	Hospital Admission For Dental Procedure Complicated By Prolonged Bleeding	265	2	Mild	Dose Not Changed
MRX-MRX	280	18	Reduced Gastrointestinal Stoma Output Hospital Admission	88	196	Moderate	Not Applicable
MRX-MRX		18	Vomiting	158	3	Mild	Dose Not Changed
MRX-MRX		18	Dehydration	158	3	Mild	Dose Not Changed
MRX-MRX	280	14	Nose Bleed	1309	2	Severe	Dose Not Changed

Treatment[1]	Dose at time of SAE Onset	ID #	SAE Description (Verbatim Term)	Days from Start of Study Medication*	SAE Duration (days)	Severity Grade[2]	Study Drug Action Taken
MRX-MRX		40	End Stage Liver Disease	1273	1	Severe	Dose Not Changed
MRX-MRX	140	52	Nutrition And Vitamin Deficiencies	813	7	Moderate	Dose Not Changed
MRX-MRX	140	52	Fungal Infection	866	19	Moderate	Dose Not Changed
MRX-MRX	280	54	Hepatobiliary Disorders - Other, Specify (Hepatitis-Autoimmune)	939		Severe	Drug Withdrawn
PBO-MRX	70	1	Hypoxia	114	4	Severe	Dose Not Changed
PBO-MRX	280	1	Postoperative Pericardial Effusion	292	9	Moderate	Dose Not Changed
PBO-MRX	280	1	Febrile Episode	344	2	Mild	Dose Not Changed
PBO-MRX	280	1	Hypoxia	344	2	Mild	Dose Not Changed
PBO-MRX	280	1	High INR	292	9	Moderate	Dose Not Changed
PBO-MRX	280	1	Hospital Admission For Flare Up Of Bronchitis	1494	4	Mild	Dose Not Changed
PBO-MRX	560	1	Gastrointestinal Bleeding	1781	4	Moderate	Drug Interrupted
PBO-MRX	560	1	Gastrointestinal Infection	1899	3	Moderate	Dose Not Changed
PBO-MRX	560	1	Fracture Of Left Proximal Humerus	2162	60	Moderate	Dose Not Changed

PBO-MRX	560	1	Pathological Fracture Of Right Femur (While Walking)	2169	53	Moderate	Dose Not Changed
Treatment[1]	Dose at time of SAE Onset	ID #	SAE Description (Verbatim Term)	Days from Start of Study Medication*	SAE Duration (days)	Severity Grade[2]	Study Drug Action Taken
PBO-MRX	560	1	Post Procedure Complication – Pulmonary Hemorrhage	1771	1	Severe	Dose Not Changed
PBO-MRX	560	1	Post Procedure Complication Bradycardia	1771	1	Moderate	Dose Not Changed
PBO-MRX	560	1	Post Procedure Complication – Hypotension	1771	1	Severe	Dose Not Changed
PBO-MRX	560	1	Hospital Admission For Chest Infection	2343	5	Mild	Dose Not Changed
PBO-MRX	560	1	Hospital Admission For Chest Infection	2355	13	Moderate	Dose Not Changed
PBO-MRX	560	1	Hospital Admission For Right Heart Failure	2355	13	Moderate	Dose Not Changed
PBO-MRX	280	5	Raised ALT	497	.	Moderate	Drug Withdrawn
PBO-MRX	70	23	Hematochezia	178	4	Severe	Drug Withdrawn
PBO-MRX	70	23	Anemia	178	4	Severe	Drug Withdrawn

PBO-MRX	140	49	Hematemesis	1787	3	Moderate	Dose Not Changed

Note: Adverse events coded using MedDRA version 16.0 (March 2013). In determining treatment-emergent AEs and study day, partial dates were imputed based on the SAP. Treatment-emergent adverse events are AEs where the start of the event is (a) on or after the first dose date, and (b) within 14 days of the last dose date.

[1]Treatment group is designated according to the randomized treatment group into which the participant was randomized in the ITCH or IMAGO study and if the SAE occurred in the extension study, -MRX, is appended.

[2]Adverse event severity grades are reported according to the Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0. If the CTCAE does not have a grading for a particular adverse event, the severity of the event is reported by the investigator as mild, moderate, or severe.

*Time since start of study medication includes any study drug interruption due to Amendment #4 implementation delays and adverse events; subjects designated with an asterisk had an interruption due to Amendment #4 implementation delays.

Supplemental Table 14. Proportion of Subjects with Treatment-Emergent Adverse Events Causing Discontinuation by Treatment, Combined Studies.

Characteristic	ITCH/IMAGO		IMAGINE II/IMAGINE	
	MRX	PBO	MRX-MRX	PBO-MRX
N	39	18	37	16
# of AEs	1	1	5	3
Total Participants With Events Causing Discontinuation	1	1	5	2
System Organ Class				
Preferred Term				
Blood and lymphatic system disorders				
Anemias nonhemolytic and marrow depression, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (6.2)
Hepatobiliary disorders				
Hepatic and hepatobiliary disorders, n (%)	0 (0.0)	0 (0.0)	1 (2.7)	0 (0.0)
Gastrointestinal disorders				
Gastrointestinal hemorrhages NEC, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (6.2)
Investigations				
Hepatobiliary investigations, n (%)	1 (2.5)	0 (0.0)	4 (10.8)	1 (6.2)
Psychiatric disorders				
Psychiatric and behavioral symptoms NEC, n (%)	0 (0.0)	1 (5.6)	0 (0.0)	0 (0.0)
% = n/N*100				
NEC = not elsewhere classified				

Supplemental Table 15. Listing of Treatment-Emergent Adverse Events Causing Discontinuation by Treatment, Combined Studies.

Treatment[1]	Dose at time of AE Onset	ID #	AE Description (Verbatim Term)	Days from Start of Study Medication*	AE Duration (days)	Serious Event?	Severity Grade[2]
MRX		21	Increased ALT	3		N	Moderate
PBO-MRX	70	23	Hematochezia	178	4	Y	Severe
PBO-MRX	70	23	Anemia	178	4	Y	Severe
MRX-MRX	140	31	Increased ALT	164	15	N	Severe
MRX-MRX	280	40	Elevated Bilirubin	1224	50	N	Mild
MRX-MRX	280	45	Increased ALT	890		N	Severe
MRX-MRX	280	47	Increased ALT	266	28	N	Moderate
MRX-MRX	280	54	Hepatitis Autoimmune	939		Y	Severe
PBO-MRX	280	5	Increased ALT	497		Y	Moderate
PBO	70	16	Behavioral Changes	18	16	N	Moderate

Note: Adverse events coded using MedDRA version 16.0 (March 2013). In determining treatment- emergent AEs and study day, partial dates were imputed based on the SAP.

Treatment-emergent adverse events are AEs where the start of the event is (a) on or after the first dose date, and (b) within 14 days of the last dose date.

[1]Treatment group is designated according to the randomized treatment group into which the participant was randomized in the ITCH or IMAGO study and if the AE occurred in the extension study, -MRX, is appended.

[2]Adverse event severity grades are reported according to the Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0. If the CTCAE does not have a grading for a particular adverse event, the severity of the event is reported by the investigator as mild, moderate, or severe.

Supplemental Table 16. Listing of Peak ALT/Peak TB and corresponding TB/ALT, CSS, and ItchRO(Obs) for Subjects with Treatment-Emergent Adverse Events Causing Discontinuation, Combined Studies.

Treatment	ID #	AE Description	Days from start of medication	hDISH Peak ALT					hDISH Peak TB				
				Baseline/ peak ALT	study week	corresp TB	change in CSS	change in ItchRO(Obs)	Baseline/ peak TB	study week	corresp ALT	change in CSS	change in ItchRO(Obs)
PBO	16	Behavioral	18	65/NA	NA	NA	NA	NA	0/3/NA	NA	NA	NA	NA
MRX	21	Increased ALT	3	105/NA	NA	NA	NA	NA	0.6/NA	NA	NA	NA	NA
PBO-MRX	23	Hematochezia	178	322/203	2	19.1	0	-1	20.1/19.1	2	203	0	-1
		Anemia	178	322/203	2	19.1	0	-1	20.1/19.1	2	203	0	-1
PBO-MRX	5	Increased ALT	497	78/316	48	2.2	-2	-2.7	2.1/2.5	36	234	-2	-2.7
MRX-MRX	31	Increased ALT	164	66/263	-5	0.7	-2	-0.3	1.6/1.1	-11	119	0	0
MRX-MRX	40	Increased TB	1224	189/246	-11	8	-1	-1.3	7.2/15.1	156	216	-1	-2.9
MRX-MRX	45	Increased ALT	890	150/546	108	1.2	-1	-2.3	0.9/1.3	-11	128	-2	-0.3
MRX-MRX	47	Increased ALT	266	122/275	24	1.3	0	-2	2.5/2	-11	234	-2	-0.9
MRX-MRX	54	Autoimmune hepatitis	939	40/219	36	0.9	-4	-3.3	0.9/1.1	-11 48	44 82	-1 -4	-0.4 -2

Supplemental Table 17. Incidence of Enhanced Monitoring and Stopping Guidelines for ALT and Total Bilirubin (TB), Combined Studies.

Cumulative incidence through each time point	Week 48	Week 72	EOT1
	N=57	N=57	N=57
Number and % of participants who met enhanced monitoring criteria for ALT	7 (12.3)	9 (15.8)	15 (26.3)
Number and % of participants who met enhanced monitoring criteria for TB	8 (14.0)	9 (15.8)	9 (15.8)
Number and % of participants who met enhanced monitoring criteria for ALT or TB	15 (26.3)	18 (31.6)	24 (42.1)
Number and % of participants who met EARLY STOPPING criteria for ALT	1 (1.8)	1 (1.8)	1 (1.8)
Number and % of participants who met EARLY STOPPING criteria for TB	1 (1.8)	1 (1.8)	2 (3.5)
Number and % of participants who met EARLY STOPPING criteria for ALT or TB	2 (3.5)	2 (3.5)	3 (5.3)

[1]The EOT data was obtained as the last value that is on or before the date of last treatment dose + 7 days.