TITLE PAGE

Study Title:	**ICONIC**: Long-Term, Open-Label Study with a Double-Blind, Placebo-Controlled, Randomized Drug Withdrawal Period of LUM001, an Apical Sodium-Dependent Bile Acid Transporter Inhibitor (ASBTi), in Patients with Alagille Syndrome
Short Title:	**ICONIC**: Maralixibat (LUM001), an Apical Sodium-Dependent Bile Acid Transporter Inhibitor (ASBTi), in the Treatment of Patients with Alagille Syndrome
Study Intervention:	Maralixibat (or maralixibat chloride; formerly LUM001)
Indication:	Treatment of patients with Alagille Syndrome
Study Sponsor:	Mirum Pharmaceuticals, Inc. 950 Tower Lane, Suite 1050 Foster City, CA 94404
Study Number:	LUM001-304
Study Phase:	2
Study Initiation Date:	28 October 2014
Study Completion Date:	28 May 2020
Regulatory Agency Identifier Number:	EudraCT No: 2013-005373-43

Report Date:

Document Version	Date
Interim V1.0	13 Oct 2020
Final V2.0	11 Nov 2020

OVERALL CONCLUSIONS

This final CSR represents the final data (as of database lock date of 21 Aug 2020) after all enrolled participants had completed their final (or ET) study visit.

At the time of the previous data cutoff date (01 Dec 2019), 14 participants were ongoing in Study LUM001-304. All 14 participants completed the study.

The mean (SD) treatment duration increased from 944.3 (587.07) days to 1029.6 (667.99) days between the data cuts of the interim CSR and this final CSR. The last week of follow-up was Week 288 for 2 participants.

The interim CSR reported statistically significant mean decreases from baseline in sBA at each time point, except for Week 108 and Weeks ≥240. The final data demonstrate statistically significant mean decreases from baseline in sBA at Week 240 (n=10; p=0.0157) and Week 252 (n=9; p=0.0146). The reduction in sBA was not statistically significant at Week 264 (n=4) and only 1 participant reached Week 276.

The interim CSR reported statistically significant mean decreases from baseline in ItchRO(Obs) weekly aver morning score at each visit up to Week 240, with the exception of Week 132, which only included data from 5 participants. The final data demonstrate statistically significant mean decreases from baseline in ItchRO(Obs) weekly average morning severity score at Week 240 (n=10; p=0.0003) and Week 252 (n=4; p=0.0067). The reduction in ItchRO(Obs) weekly average morning severity score was not statistically significant at Week 264 (n=2) and only 1 participant reached Week 276.

Overall, 13 (41.9%) participants experienced an SAE. None of the SAEs were considered potentially related to study medication. Events from the SOCs of Infections and infestations (reported for 7 participants) and GI disorders (reported for 3 participants) were the most frequently reported types of SAEs. A total of 6 participants experienced TEAEs that led to study drug discontinuation. No deaths occurred during the study.

The most frequently reported TEAEs (>40% overall) were abdominal pain (58.1%), diarrhea (54.8%), vomiting and pyrexia (51.6% each), and cough and nasopharyngitis (41.9% each).

Most of the TEAEs reported were mild or moderate in severity. No events of Grade 5 (fatal) severity were reported. A total of 5 participants (16.1%) had a Grade 4 event, which included aplasia pure red cell, extradural hematoma, subdural hemorrhage, alanine aminotransferase increased, acute kidney injury, and marrow hyperplasia in maralixibat-treated participants.

There was only 1 additional SAE since the interim CSR (Grade 3 influenza). There were no additional TEAEs that led to study drug discontinuation since the interim CSR. Additional AESIs since the interim CSR include diarrhoea (1 participant).

Overall, maralixibat was well tolerated and demonstrated an acceptable long-term safety profile.