TITLE PAGE

Study Title:	**INDIGO STUDY:** 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
Short Title:	**INDIGO**: Apical Sodium-Dependent Bile Acid Transporter Inhibitor (ASBTi) in the Treatment of Cholestatic Liver Disease in Pediatric Patients with Progressive Familial Intrahepatic Cholestasis
Study Intervention:	Maralixibat chloride (formerly LUM001)
Indication:	Treatment of patients with progressive familial intrahepatic cholestasis (PFIC)
Study Sponsor:	Mirum Pharmaceuticals, Inc. 950 Tower Lane, Suite 1050 Foster City, California 94404
Chief Medical Officer:	Ed Tucker, MD, MBA Mirum Pharmaceuticals, Inc. 950 Tower Lane, Suite 1050 Foster City, California 94404
Study Number:	LUM001-501
Study Phase:	2
Study Initiation Date:	12 February 2014 (first participant first visit)
Data Report Date:	20 May 2020 (last participant last visit)
Regulatory Agency Identifier Number:	EuDRA CT No: 2013-003833-14
Final CSR Report Date:	07-May-2020
CSR Addendum Date:	13-Oct-2020

This study was performed in compliance with Good Clinical Practices and applicable regulatory requirements, including the archiving of essential documents.

OVERALL CONCLUSIONS

This CSR addendum focuses on data collected after participants' Week 72 visit, and only addresses objectives of the optional follow-up treatment period (after Week 72).

- Improvements in pruritus previously reported at 48 weeks of treatment with MRX, continued throughout the study. Numerical improvement was observed in participants with PFIC2 and PFIC1 in ItchRO(Obs) weekly morning average, weekly average, and weekly evening average scores. Improvements were greater in participants with PFIC2 than those with PFIC1, and generally, participants with nt-PFIC2 showed a better response than those with t-PFIC2.
- Previously reported numerical reductions in sBA observed at 13 weeks and 72 weeks of treatment with MRX in participants with PFIC2 continued throughout the study. These improvements in sBA levels were not evident in participants with PFIC1.
- The numerical improvement in ALT described for participants with PFIC2 in the LUM001-501 Final CSR continued throughout the study. A numerical improvement in AST was also observed. These improvements were not observed in participants with PFIC1.
- Previously reported numerical increases of treatment in total bilirubin, and direct bilirubin, in participants with PFIC2 and PFIC1 from baseline to Week 72 were not sustained long term; by Week 204 total bilirubin levels had returned to close to baseline (participants with nt-PFIC2) or showed a reduction (improvement) (participants with PFIC1), and by Week 204 direct bilirubin levels showed a reduction (improvement) from baseline (participants with nt-PFIC2 and PFIC1).
- The change from baseline in height, weight, and BMI z-scores was not statistically significant regardless of analysis visit, in participants with PFIC1, PFIC2, or in the overall study population, with the exception of the BMI z-scores at 2 analysis visits (for participants with PFIC2 at Week 2 and Week 252, and participants with PFIC1 at Week 252).
- In post hoc analyses, 7/19 participants with nt-PFIC2 experienced control of the sBA levels to below 102 µmol/L or a 75% reduction from baseline resulting in clinically meaningful reductions in pruritus ($\geq$1.0 reduction in ItchRO(Obs) or score below 1.0), normalization of bilirubin, ALT, and AST if elevated, and improvement in height z-score. These responses happened at both 280 µg/kg once daily and 280 µg/kg twice daily dosing of MRX. All 7 of these participants demonstrating this response to maralixibat treatment remained on the study for over 5 years.
- Serious AEs were experienced by 15 participants (45.5%) during the study. The only SAEs reported for more than 1 participant were abdominal pain, diarrhea, and gastroenteritis, each experienced by 2 participants (6.1%). Treatment-related SAEs wereexperienced by 5 participants (15.2%). The treatment-related SAEs were reported for 1 participant each and included abdominal pain, abdominal pain upper, diarrhea, pancreatitis, blood bilirubin increased, and INR increased. No SAEs were experienced by participants on a dose of MRX of 280 µg/kg BID.

- Overall, reported TEAEs were generally mild or moderate in severity.
- Fourteen participants (42.4%) experienced CTCAE Grade 3 or CTCAE Grade 4 TEAEs during the study. A total of 12 participants (36.4%) experienced TEAEs of maximum severity Grade 3. A Grade 4 event of hyperbilirubinemia (considered potentially related to study drug) was experienced by 1 participant while Grade 4 events of ALT increased and AST increased (both considered unlikely related to study drug) were experienced by another participant.
- Treatment-emergent AEs potentially related to study drug were experienced by 26 participants (78.8%) overall.
- The most common TEAEs reported included the following: pyrexia (20 participants [60.6%]), diarrhea (19 participants [57.6%]), cough (18 participants [54.5%]), and vomiting (17 participants [51.5%]).
- A total of 10 participants (30.3%) experienced TEAEs that led to permanent treatment discontinuation. Treatment-emergent AEs leading to permanent treatment discontinuation in more than 1 participant were reported as blood bilirubin increased and disease progression.
- No deaths were reported in the study.
- Long-term safety data presented here were consistent with those reported in the LUM001-501 Final CSR, during the first 72 weeks of treatment with MRX.
- Overall, MRX was safe and well tolerated.