Mirum Pharmaceuticals Announces Data Presented During AASLD Highlighting Durable Improvements in Pruritus and Quality of Life in Children with Alagille Syndrome Treated with Maralixibat

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- Results of long-term treatment from the ITCH and IMAGINE II studies presented in late-breaking oral presentation at AASLD

- Data demonstrates significant and durable improvements in pruritus in children with Alagille syndrome through 220 weeks of maralixibat treatment

- Results have been included as supportive data in ongoing rolling NDA submission for treatment of cholestatic pruritus in patients with Alagille syndrome

FOSTER CITY, Calif.--(BUSINESS WIRE)--Nov. 15, 2020-- Mirum Pharmaceuticals, Inc. (Nasdaq: MIRM), a biopharmaceutical company focused on the development and commercialization of novel therapies for debilitating liver diseases, announced data presented at the Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) - The Liver Meeting Digital Experience™. The data were presented by DrBenjamin Shneider of Baylor College of Medicine and Texas Children's Hospital presenting on behalf of the Childhood Liver Disease Research Network (ChiLDReN) in a late-breaking oral presentation titled "Preliminary Analysis of ITCH and IMAGINE II – Outcome of Long-term Administration of Maralixibat in Children with Alagille Syndrome."

The objective of the studies was to assess pruritus and other markers of cholestasis in patients with Alagille syndrome (ALGS) with up to 220 weeks of treatment with maralixibat. Maralixibat, an apical sodium bile acid transporter (ASBT) inhibitor, has previously been shown to interrupt the enterohepatic circulation of bile acids, reducing pruritus.

Of the children enrolled in the ITCH and IMAGINE II studies, 28 of the 37 patients were on study at 48 weeks with 80% of those experiencing clinically meaningful reductions in pruritus (ItchRO[Obs] reduction ≥1.0 point) which were durable beyond four years (Week 220), with 90% of patients who continued on study experiencing a pruritus response at the end of treatment. The mean reduction in ItchRO(Obs) at week 48 was -1.9 points and deepened to -2.3 points at the end of treatment. Maralixibat treatment improved quality of life and led to improved growth parameters. The long-term data suggest that maralixibat has the potential to be an effective treatment and could serve as an alternative to surgery for ALGS patients, if approved.

"Maralixibat has the potential to address the severe pruritus experienced by children with Alagille syndrome, resulting in meaningful improvement in quality of life, meeting a major unmet need for this patient population," said Benjamin L. Shneider, M.D., principal study investigator and member of the Childhood Liver Disease Research Network, funded largely by the National Institute of Diabetes and Digestive and Kidney Diseases. "Alagille syndrome often leads to progressive liver disease frequently complicated by severe pruritus, often disrupting sleep, interfering with school, and impacting the quality of life for children and their families so greatly that surgical intervention via external biliary diversion or liver transplant are required. These data show that with maralixibat, we have the potential to positively impact children's health across multiple clinical measures, without resorting to invasive surgeries which can be associated with significant complications and potential mortality."

To view the presentation and the complete data, please visit the AASLD section within the Events page on Mirum's website.

"These results from the study confirm the potential for maralixibat to address the consequences of cholestasis in Alagille syndrome, supporting the effects seen in the long term analysis of the pivotal ICONIC study," said Chris Peetz, president and chief executive officer of Mirum. "As we progress toward completion of our rolling NDA submission, maralixibat is being offered to eligible patients with Alagille syndrome through an expanded access program until it is available for prescribing."

About the ITCH and IMAGINE II study

The ITCH study is a randomized, placebo-controlled study of maralixibat in children with ALGS. The IMAGINE II study is an open-label study for participants who completed the ITCH study. ITCH and IMAGINE II were conducted by ChiLDReN in the context of a Cooperative Research and Development Agreement between Mirum Pharmaceuticals and the NIDDK. Thirty-seven children were enrolled into the ITCH study. Children receiving maralixibat in the studies also demonstrated improvements in biomarkers of disease, including reductions in cholesterol and bile acid levels. After over 4 years of treatment, maralixibat continues to be generally well tolerated. There were two serious adverse events possibly related to administration of maralixibat leading to drug withdrawal in both patients (hematochezia/anemia and autoimmune hepatitis).

About Alagille Syndrome

ALGS is a rare genetic disorder in which bile ducts are abnormally narrow, malformed and reduced in number, which leads to bile accumulation in the liver and ultimately progressive liver disease. The estimated incidence of ALGS is one in every 30,000 people.[1] In patients with ALGS, multiple organ systems may be affected by the mutation, including the liver, heart, kidneys and central nervous system.[2] The accumulation of bile acids prevents the liver from working properly to eliminate waste from the bloodstream and, according to recent reports, 60% to 75% of patients with Alagille syndrome have a liver transplant before reaching adulthood.[3] Signs and symptoms arising from liver damage in ALGS may include jaundice (yellowing of the skin), xanthomas (disfiguring cholesterol deposits under the skin), and pruritus (itch)[2]. The pruritus experienced by patients with ALGS is among the most severe in any chronic liver disease and is present in most affected children by the third year of life.[4]

About Maralixibat

Maralixibat is a novel, minimally absorbed, orally administered investigational drug being evaluated in several rare cholestatic liver diseases. Maralixibat inhibits the apical sodium dependent bile acid transporter (ASBT), resulting in more bile acids being excreted in the feces, leading to lower levels of bile acids systemically, thereby potentially reducing bile acid mediated liver damage and related effects and complications. More than 1,600 individuals have received maralixibat, including more than 120 children who have received maralixibat as an investigational treatment for Alagille syndrome (ALGS) and progressive familial intrahepatic cholestasis (PFIC). In the ICONIC Phase 2b ALGS clinical trial, patients taking maralixibat had significant reductions in bile acids and pruritus compared to placebo, as well as reduction in xanthomas and accelerated growth long-term. In a Phase 2 PFIC study, a genetically defined subset of BSEP deficient (PFIC2), patients responded to maralixibat with an increase in transplant-free survival. The U.S. Food and Drug Administration has granted maralixibat Breakthrough Therapy designation for the treatment of pruritus associated with ALGS in patients one year of age and older and for PFIC2. Maralixibat was generally well-tolerated throughout the studies. The most frequent treatment-related adverse events were diarrhea and abdominal pain. Until maralixibat is approved and available for prescribing, the medication is available to patients with ALGS through Mirum's expanded access program. For more information, please visit ALGSEAP.com. For more information about the Phase 3 study for maralixibat in pediatric patients with PFIC, visit PFICtrial.com.

About Mirum Pharmaceuticals

Mirum Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company focused on the development and commercialization of a late-stage pipeline of novel therapies for debilitating liver diseases. The company's lead product candidate, maralixibat, is an investigational oral drug in development for Alagille syndrome (ALGS), progressive familial intrahepatic cholestasis (PFIC), and biliary atresia. The company has initiated a rolling NDA submission for maralixibat in the treatment of patients with cholestatic pruritus associated with ALGS and expects to complete the submission in the first quarter of 2021. Additionally, the company plans to submit a marketing authorization application to the European Medicines Agency for maralixibat in the treatment of patients with PFIC2 in the fourth quarter 2020.

The company is also developing volixibat, also an oral ASBT-inhibitor, in primary sclerosing cholangitis and intrahepatic cholestasis of pregnancy. For more information, visit MirumPharma.com.

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Forward-Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements include statements regarding, among other things, the results, conduct and progress of Mirum's ongoing and planned clinical studies for maralixibat and volixibat, the regulatory approval path for maralixibat, and the potential launch of maralixibat, if approved. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Words such as "plans," "expects," "potential" and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Mirum's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, risks and uncertainties associated with Mirum's business in general, the impact of the COVID-19 pandemic, and the other risks described in Mirum's filings with the Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made and are based on management's assumptions and estimates as of such date. Mirum undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by law.

The content in this release is the sole responsibility of the authors and does not necessarily represent the official views or imply endorsement of the National Institutes of Health.

[1]Danks, et al. Archives of Disease in Childhood 1977

[2]Johns Hopkins Medicine. hopkinsmedicine.org/health/conditions-and-diseases/Alagille-syndrome

[3]Vandriel, et al. GALA EASL 2020; Kamath, et al. Hepatology Communications 2020

[4]Elisofon, et al. Journal of Pediatric Gastroenterology and Nutrition 2010

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