Mirum Pharmaceuticals Presents New Data From Its Maralixibat and Volixibat Clinical Studies at AASLD Annual Meeting

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- *Maralixibat data highlights the relationship between the reduction of serum bile acids and pruritus intensity, improved growth, and other quality of life measures.*
- *Analysis of the natural variability of pruritus in children with Alagille syndrome demonstrates persistent severity.*
- *Volixibat data shows highly active dose levels selected for Phase 2 studies.*

FOSTER CITY, Calif.--(BUSINESS WIRE)--Nov. 13, 2020-- Mirum Pharmaceuticals, Inc. (Nasdaq: MIRM), a biopharmaceutical company focused on the development and commercialization of novel therapies for debilitating liver diseases, today announced new analyses from its maralixibat and volixibat clinical programs, as featured at the Annual Meeting of the American Association for the Study of Liver Diseases – The Liver Meeting Digital Experience™.

A summary of findings from each of the poster presentations is below. To view the data in full, please visit the AASLD section within the Events page on our corporate website.

“Data generated from six years of clinical evaluation of maralixibat in Alagille syndrome has offered key understandings in the severe burden of pruritus and related markers of cholestasis, helping to elucidate the potential benefit of maralixibat in this treatment setting,” said Dr. Pam Vig, chief scientific officer at Mirum. “We are also excited to begin Phase 2 studies of volixibat in adult patients with cholestatic liver disease, which will evaluate dose levels shown to be effective in increasing bile acid excretion, suggesting the potential to reduce the burden of cholestasis in these settings.”

Abstract #341: Pruritus intensity is associated with cholestasis biomarkers and quality of life measures after maralixibat treatment in children with Alagille syndrome

Alagille syndrome (ALGS)-associated pruritus is often extremely debilitating, resulting in bleeding, scarring, sleep disturbance, fatigue, and decreased quality of life, with significant impact on the patient and their family. This analysis, which utilized data from the maralixibat Phase 2b ICONIC study in pediatric patients with cholestatic pruritus associated with ALGS, evaluated how change in pruritus intensity is related to change in cholestasis markers and other clinical parameters. The study evaluated 31 patients, of which 27 were evaluated for this analysis over a 48-week period. Overall, the positive treatment effects of maralixibat in patients with ALGS demonstrate important correlations with multiple clinically relevant parameters. Pruritus, as measured by the fully validated Itch Reported Outcome Observer (ItchRO[Obs]) tool, was correlated with several parameters including the Clinician Scratch Scale, serum bile acids (sBA) and sBA subspecies, autotaxin, growth and quality of life measures, including fatigue.

Abstract #1792: Natural variability of pruritus in Alagille syndrome; an analysis from the ICONIC study utilizing the Itch Reported Outcome Observer (ItchRO[Obs]) tool

Pruritus is known to be one of the most burdensome symptoms associated with ALGS; however, the variability of its severity and frequency has not been fully established. Assessments rely on observer- or patient-reported outcomes measures. The ItchRO(Obs) and ItchRO(Pt) tools were used to assess the natural variability of pruritus in children with ALGS who were enrolled in the Phase 2b ICONIC, placebo-controlled, randomized study. The scores were assessed during the 28-day screening period of ICONIC, when no drug was administered. The results showed that both the morning and evening assessment of pruritus was persistent over time with minimal fluctuations in severity and frequency.

Abstract #1221: A Phase 1 dose-ranging study assessing fecal bile acid excretion by volixibat, an apical sodium-dependent bile acid transporter inhibitor, and coadministration with loperamide

The primary goal of this Phase 1 clinical study was to investigate the safety and efficacy of a range of dose levels and dose regimens of volixibat, to help guide dose selection for clinical trials in patients with cholestatic disease, in particular the planned Phase 2 programs in adult patients with primary sclerosing cholangitis and intrahepatic cholestasis of pregnancy. The study evaluated the effects of volixibat alone and in combination with loperamide, seeking to understand whether the addition of loperamide would reduce the mild gastrointestinal side effects that are often observed with ASBT inhibitors.

The analysis found that volixibat was well-tolerated at all dose levels and regimens evaluated. As expected for the mechanisms of action of volixibat, fecal bile acid excretion was increased across all treatment groups. Overall, twice-daily dosing was associated with greater increases in bile acid excretion compared to once-daily dosing. Use of volixibat in adult healthy volunteers was associated with meaningful increases in fecal bile acid excretion and serum 7αC4, which are markers of bile acid synthesis. In addition, standard dosing of loperamide helped to reduce the mild and transient gastrointestinal disturbance during the initial dosing of volixibat, without a drug-drug interaction. The effects on bile acid trafficking and synthesis support the further study of volixibat in patients with cholestatic liver disease.

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. The U.S. Food and Drug Administration (FDA) has granted maralixibat Breakthrough Therapy designation for 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 by the FDA 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 Volixibat

Volixibat is an oral, minimally absorbed agent designed to selectively inhibit ASBT. Volixibat may offer a novel approach in the treatment of adult cholestatic diseases by blocking recycling of bile acids, through inhibition of the apical sodium dependent bile acid transporter (ASBT), thereby reducing bile acids systemically and in the liver. Phase 1 and Phase 2 clinical trials of volixibat demonstrated on-target fecal bile acid excretion, a pharmacodynamic marker of ASBT inhibition, in addition to decreases in LDL cholesterol and increases in 7αC4 which are markers of bile acid synthesis. Volixibat has been evaluated in more than 400 subjects across multiple clinical trials. The most common adverse events reported were mild to moderate gastrointestinal events observed in the volixibat groups.

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. Follow Mirum on Twitter, Facebook and LinkedIn.

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 studies for maralixibat and volixibat, and the regulatory approval path for maralixibat and volixibat. 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," "will," "may," "expects," "goal," "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.

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