Mirum Pharmaceuticals Presents Analyses From Its Rare Liver Disease Programs at the EASL International Liver Congress 2021

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- Data from five years of treatment with maralixibat reinforces safety and tolerability in patients with Alagille syndrome.

- Intrahepatic cholestasis of pregnancy patient-reported data demonstrates significant burden of disease and underscores urgent need for new treatment options.

FOSTER CITY, Calif.--(BUSINESS WIRE)--Jun. 23, 2021-- Mirum Pharmaceuticals, Inc. (Nasdaq: MIRM) today announced the presentation of analyses from its rare liver disease programs during the EASL International Liver Congress™. The posters being presented feature an integrated safety analysis of maralixibat in patients with Alagille syndrome (ALGS) and the unveiling of a multi-national survey of patient reported outcomes from pregnant women with intrahepatic cholestasis of pregnancy (ICP). The posters are now available on the congress website.

Abstract PO-1285: An integrated analysis of long-term clinical safety in maralixibat-treated participants with Alagille syndrome

Data from more than five years of maralixibat treatment across three Phase 2 clinical studies (and their extension studies) were analyzed to assess the overall clinical safety of maralixibat in patients with ALGS (n=86). The analysis evaluated treatment-emergent adverse events (TEAEs) and laboratory parameters including reported rates, severity and seriousness, actions taken with maralixibat (i.e., dose reductions and discontinuations), time to onset and potential dose-response relationships. A sub-analysis of safety data was also conducted evaluating data from 13-week placebo-controlled studies.

The analysis concluded:

- Maralixibat was well-tolerated for more than five years.
- The most common TEAEs were diarrhea and abdominal pain.
- Mild to moderate gastrointestinal events (GI events) were observed in the first weeks of treatment, were transient, and lasted less than one week in duration.
    - In placebo-controlled studies, GI events occurred at similar rates between maralixibat and placebo in the background of ALGS.
    - There were no discontinuations of maralixibat due to diarrhea or abdominal pain.
- No clinically significant trends or patterns in laboratory measures were observed.
    - ALT levels were consistent with natural history comparisons of ALGS.

Abstract PO-2657: Patient perspectives on pruritus in intrahepatic cholestasis of pregnancy: a multinational survey

The multinational survey was conducted in collaboration with ICP Support, a leading patient advocacy group focused on ICP and based in the United Kingdom.

The survey evaluated the burden of cholestatic pruritus, the impact on quality of life, and the effectiveness of available treatments as reported by women who have or have had ICP (n=688). Participants in the survey were asked to assess severity of their itch, sleep disturbance, and impact of medications received, using a numerical rating scale (NRS) of 0-10, with 0 representing none and 10 representing the worst imaginable, for each symptom.

Responses from the survey demonstrated that pruritus has debilitating effects on patients living with ICP, including a substantial impact on sleep and quality of life. The results found that:

- The median worst itch reported was a 9 out of 10 on the NRS.
- 94% of women reported itch-related sleep disturbances, which were associated with degree of itch severity.
- Itch was associated with mood changes and often led to a disruption of day-to-day responsibilities and routines.
- 71% of women reported that they were not asked about itch by their healthcare provider.
- A majority of women reported taking ≥2 medications; however, most reported either only partial or no resolution of ICP-related pruritus.

These responses underscore the significant impact pruritus can have on women with ICP as well as the high unmet need for the development of safe and effective therapies to treat this rare liver disease.

“This integrated safety analysis of maralixibat with more than five years of evaluation across 86 patients with ALGS continues to underscore the safety and tolerability profile of maralixibat for use in this chronic disease setting,” said Pam Vig, Ph.D., chief scientific officer at Mirum. “We are also excited to showcase the ICP survey data which demonstrates the significant burden that pruritus can have on these women, and the tremendous need for new therapies. As we continue to enroll patients in our OHANA study, we remain hopeful that volixibat’s potential to reduce cholestasis and pruritus associated with ICP may improve quality of life.”

“Understanding the severity of pruritus and the impact on a woman’s quality of life whilst pregnant is of critical importance to advancing research and identifying a new treatment option for ICP,” said Jenny Chambers, chief executive officer, ICP Support. “We surveyed nearly 700 women globally to assess the scale of how debilitating this condition can be and to champion research that will help us better understand the effects of the condition. We hope this in turn will lead to improved outcomes for women with this uncommon and unrelenting 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 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. Maralixibat has been studied extensively and its safety database represents the largest database for an ASBT inhibitor.

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 further information about maralixibat’s ongoing studies in pediatric liver disease, please visit the study websites: Phase 3 MARCH study for PFIC and Phase 2b EMBARK study for biliary atresia.

About Volixibat

Volixibat is an oral, minimally absorbed agent designed to selectively inhibit the apical sodium dependent bile acid transporter (ASBT). Volixibat may offer a novel approach in the treatment of adult cholestatic diseases by blocking the recycling of bile acids, through inhibition of ASBT, thereby reducing bile acids systemically and in the liver. Phase 1 and Phase 2 studies 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 individuals across multiple clinical trials. The most common adverse events reported were mild to moderate gastrointestinal events observed in the volixibat groups.

Volixibat is currently being evaluated in Phase 2b studies for primary sclerosing cholangitis (VISTAS study) and intrahepatic cholestasis of pregnancy (OHANA study). Mirum plans to initiate a Phase 2b study for primary biliary cholangitis later this year.

About Mirum Pharmaceuticals, Inc.

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. Mirum’s lead product candidate, maralixibat, is an investigational oral drug in development for Alagille syndrome (ALGS), progressive familial intrahepatic cholestasis (PFIC), and biliary atresia. Mirum has submitted an NDA for maralixibat in the treatment of cholestatic pruritus in patients with ALGS. The NDA has been accepted for priority review by the FDA with a PDUFA action date of September 29, 2021. Additionally, Mirum’s marketing authorization application for the treatment of pediatric patients with PFIC2 has been accepted for review (validated) by the European Medicines Agency. Mirum is also developing volixibat, also an oral ASBT-inhibitor, in primary sclerosing cholangitis, intrahepatic cholestasis of pregnancy, and primary biliary cholangitis. For more information, visit MirumPharma.com.

To augment its pipeline in cholestatic liver disease, Mirum has acquired the exclusive option to develop and commercialize gene therapy programs VTX-803 and VTX-802 for PFIC3 and PFIC2, respectively, from Vivet Therapeutics SAS, following preclinical evaluation and investigational new drug-enabling studies.

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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 potential benefits and an assessment on the severity of side effects of 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 “will,” “could,” “would,” “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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