The Lancet Publishes Data From Mirum Pharmaceuticals' ICONIC Pivotal Study of Maralixibat (LIVMARLI) Treatment in Alagille Syndrome

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- Maralixibat data demonstrate four-year durable and clinically meaningful improvements across multiple cholestasis parameters including pruritus.

FOSTER CITY, Calif.--(BUSINESS WIRE)--Nov. 1, 2021-- Mirum Pharmaceuticals, Inc. (Nasdaq: MIRM), a leader in rare liver disease, today announced that *The Lancet* has published four-year data highlighting the safety and efficacy of maralixibat in patients with Alagille syndrome (ALGS), a rare liver disease affecting one in 30,000 children. Maralixibat is an ileal bile acid transporter (IBAT) inhibitor that interrupts enterohepatic bile acid recirculation and has recently been approved by the U.S. FDA under the name of LIVMARLI. Data published in *The Lancet* demonstrate that maralixibat provides durable and clinically meaningful improvements across multiple disease parameters and has the potential to provide a new treatment paradigm for patients with ALGS.

“Maralixibat is the first medication shown to deliver durable and clinically meaningful improvements in cholestasis for patients treated through the course of the four-year clinical study,” said Professor Emmanuel Gonzales, MD, Hépatologie Pédiatrique, Hôpital Bicêtre, AP-HP, Université Paris-Saclay, Le Kremlin-Bicêtre, France and lead author of the publication in *The Lancet*. “These data are important as they signal a meaningful treatment opportunity to address chronic cholestasis and to potentially extend transplant-free survival for patients with ALGS.”

ALGS is a rare, life-threatening multisystem disease that first occurs in childhood with a range of clinical manifestations, including pruritus, jaundice, failure to thrive, xanthomas, and progressive liver disease, which can lead to liver transplantation. In an analysis of children with ALGS conducted by the Global Alagille Alliance (GALA) study, 10 and 18-year native liver survival in 911 ALGS patients presenting with neonatal cholestasis was only 57% and 41%, respectively, representing a previously underappreciated burden of liver disease in ALGS.

The Lancet publication presents data from the pivotal Phase 2b ICONIC study (n=31) of maralixibat for patients with ALGS. ICONIC demonstrates a significant multi-parameter clinical response including pruritus, serum bile acid (sBA), xanthomas, improved quality of life, and growth. By inhibiting the enterohepatic circulation, maralixibat 380 µg/kg once daily demonstrated improved pruritus response in >80% of participants at Week 48. Responses were durable across the 204-week period analyzed, demonstrating long-term treatment effect. Maralixibat was generally well-tolerated throughout the study. The most common adverse events were diarrhea and abdominal pain; most cases were mild to moderate and transient in nature, and no cases resulted in discontinuation.

The full publication including an overview of the Phase 2b ICONIC study can be accessed through *The Lancet* website.

“Maralixibat is the first medication to have been rigorously studied in ALGS and we believe that the robustness of the data collected from the ICONIC study provides evidence that maralixibat is an effective treatment for patients with this rare liver disease,” said Pam Vig, Ph.D., chief scientific officer at Mirum. “The publication of these data in *The Lancet* speaks to the significance of these results and the important role they may play in making a meaningful impact on the way Alagille syndrome is treated.”

Maralixibat (now commercially available as LIVMARLI (maralixibat) oral solution) was recently approved by the U.S. Food and Drug Administration for the treatment of cholestatic pruritus in patients with Alagille syndrome one year of age and older. Mirum has also submitted a Marketing Authorization Application to the European Medicines Agency for maralixibat for the treatment cholestatic liver disease in patients with Alagille syndrome. To support patients outside of the U.S., the company’s Expanded Access Program for maralixibat is available to eligible patients with Alagille syndrome in Canada, Australia, the United Kingdom, and regions throughout Europe.

About LIVMARLI™ (maralixibat) oral solution

LIVMARLI™ (maralixibat) oral solution is an orally administered, once-daily, ileal bile acid transporter (IBAT) inhibitor approved by the U.S. Food and Drug Administration for the treatment of cholestatic pruritus in patients with Alagille syndrome one year of age and older. For more information, please visit LIVMARLI.com.

LIVMARLI is the only FDA-approved medication to treat cholestatic pruritus associated with Alagille syndrome.

LIVMARLI is currently being evaluated in late-stage clinical studies in other rare cholestatic liver diseases including progressive familial intrahepatic cholestasis and biliary atresia, of which both have received Breakthrough Therapy designation and Orphan Drug designation. To learn more about ongoing clinical trials with LIVMARLI, please visit Mirum’s clinical trials section on the company’s website.

About Alagille syndrome

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 ALGS 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]

IMPORTANT SAFETY INFORMATION

LIVMARLI can cause serious side effects, including:

Changes in liver tests. Changes in certain liver tests are common in patients with Alagille syndrome and can worsen during treatment with LIVMARLI. These changes may be a sign of liver injury and can be serious. Your healthcare provider should do blood tests before starting and during treatment to check your liver function. Tell your healthcare provider right away if you get any signs or symptoms of liver problems, including nausea or vomiting, skin or the white part of the eye turns yellow, dark or brown urine, pain on the right side of the stomach (abdomen) or loss of appetite.

Stomach and intestinal (gastrointestinal) problems. LIVMARLI can cause stomach and intestinal problems, including diarrhea, stomach pain, and vomiting during treatment. Tell your healthcare provider right away if you have any of these symptoms more often or more severely than normal for you.

A condition called **Fat Soluble Vitamin (FSV) Deficiency** caused by low levels of certain vitamins (vitamin A, D, E, and K) stored in body fat. FSV deficiency is common in patients with Alagille syndrome but may worsen during treatment. Your healthcare provider should do blood tests before starting and during treatment.

Other common side effects reported during treatment were bone fractures and gastrointestinal bleeding.

Prescribing information

About Mirum Pharmaceuticals, Inc.

Mirum Pharmaceuticals, Inc. is a biopharmaceutical company dedicated to transforming the treatment of rare liver diseases. Mirum's approved medication is LIVMARLI™ (maralixibat) oral solution which is approved in the U.S. for the treatment of cholestatic pruritus in patients with Alagille syndrome one year of age and older.

Mirum's late-stage pipeline includes two investigational treatments for debilitating liver diseases affecting children and adults. Maralixibat (LIVMARLI), an oral ileal bile acid transporter (IBAT) inhibitor, is currently being evaluated in clinical trials for pediatric liver diseases and includes the MARCH Phase 3 study for progressive familial intrahepatic cholestasis (PFIC) and the EMBARK Phase 2b study for patients with biliary atresia. In addition, Mirum has an expanded access program open in Canada, Australia, the UK and several countries in Europe for eligible patients with Alagille syndrome.

Mirum has submitted a Marketing Authorization Application to the European Medicines Agency for maralixibat for the treatment of cholestatic liver disease in patients with Alagille syndrome.

Mirum's second investigational treatment, volixibat, also an oral IBAT inhibitor, is being evaluated in two registrational studies including the OHANA Phase 2b study for pregnant women with intrahepatic cholestasis of pregnancy and the VISTAS Phase 2b study for adults with primary sclerosing cholangitis. Mirum is planning to launch a Phase 2b study in primary biliary cholangitis later this year.

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. 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.

References

[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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