Mirum Pharmaceuticals Presents Data Demonstrating Long-term Durability of Treatment Effect of Maralixibat in Children With Cholestatic Liver Diseases

November 8, 2019

Statistically and clinically significant effects on pruritus, xanthomas and growth maintained for up to four years of treatment in Alagille syndrome

Durable multi-parameter treatment response and correlation of response with increased bile acid synthesis in progressive familial intrahepatic cholestasis

FOSTER CITY, Calif.--(BUSINESS WIRE)--Nov. 8, 2019-- Mirum Pharmaceuticals, Inc. (Nasdaq: MIRM), a biopharmaceutical company focused on the development and commercialization of novel therapies for debilitating liver diseases, today announced that results from the long-term extension of the Phase 2b ICONIC study demonstrate the durability of treatment effect and disease-modifying potential of maralixibat in children with Alagille syndrome (ALGS). The data will be presented on Monday in a late breaking oral presentation at the annual meeting of the American Association of the Study of Liver Diseases (the Liver Meeting®) in Boston. The company will also present data from the long-term extension of the Phase 2 INDIGO study of maralixibat in children with progressive familial intrahepatic cholestasis (PFIC) demonstrating the durability of multi-parameter treatment response in children with PFIC2, as well as correlation of treatment response to non-truncating bile salt export pump mutations and increased bile acid synthesis as a result of ASBT inhibition.

“The new analyses of years of treatment with maralixibat supports the disease-modifying potential of the medicine in children with Alagille syndrome and PFIC2,” said Chris Peetz, president and CEO of Mirum. “Our commitment at Mirum is to work tirelessly to bring maralixibat as quickly as possible to the families who are seeking to reclaim their lives from severe pruritus, sleepless nights, xanthomas and the suppressed growth which their children experience as a result of these diseases.”

Long-Term Extension of ICONIC Study in ALGS

At the conclusion of the 48-week treatment period of the placebo-controlled Phase 2b ICONIC study of maralixibat in children with ALGS, 23 participants entered into the long-term extension. At the time of this new analysis, 15 remained on study with a duration of up to 4 years. Consistent with results reported after 48 weeks of treatment with maralixibat, reductions in serum bile acids (sBA) and pruritus (itching), were statistically significant and further improved in the participants who remained on maralixibat through 191 weeks of treatment compared to baseline ($p<0.005$ and $p<0.0001$, respectively).

In addition, clinician scratch scale scores continued to improve ($p<0.0001$) and xanthomas continued to diminish ($p<0.05$) with long-term treatment. Improvements were also seen in the PedsQL Multidimensional Fatigue Scale score ($p<0.01$). Children taking maralixibat exhibited a clinically meaningful and statistically significant acceleration in height growth as measured by height z-score ($p\leq0.01$). The growth acceleration continued in those children who took 400 µg/kg maralixibat twice daily. Maralixibat was generally well tolerated at doses of up to 800 µg/kg day. During the extension phase, four patients withdrew consent, two had liver transplants, one had renal failure unrelated to maralixibat and one had ALT elevation as of the week 191 data cutoff.

Maralixibat has been granted Breakthrough Therapy Designation for the treatment of pruritus associated with Alagille syndrome in patients one year of age and older by the U.S. Food and Drug Administration (FDA).

Long-Term Extension of INDIGO Study in PFIC

An analysis of the long-term extension of the Phase 2 INDIGO study demonstrating that response to maralixibat in children with bile salt export pump (BSEP) deficiency, or PFIC2, is maintained and is correlated to the non-truncating mutations. Of the 25 children with BSEP deficiency, 19 had non-truncating mutations (mild and moderate) and 6 children had truncating mutations (severe).

Half of the children with moderate mutations experienced clinically meaningful long-term multi-parameter responses, as defined by a greater than 70% reduction or normalization in sBA and a greater than 1.0 reduction in ItchRO(Obs) score, a measure of pruritus. The data are summarized in the table below. Increased bile acid synthesis was shown to correlate with maralixibat treatment response, offering physiologic and mechanism-based elucidation in responders vs. non-responders.

Genotype Status	**Multi-parameter Responders**
Non-truncating BSEP (n=19)	7/19 (36.8%)
Mild (n=7)	1/7 (14.3%)
Moderate (n=12)	6/12 (50%)

Truncating BSEP (n=6)	0/6 (0%)

Upcoming Investor Events

Mirum management will be participating in a conference call hosted by Whitney Ijem from Guggenheim Securities on Monday November 11, 2019 at 11:30 a.m. ET.

Call Details: Live from AASLD with Mirum Pharmaceuticals
Date and Time: Monday November 11, 2019; 11:30 a.m. ET
Format: Q&A with Mirum management, hosted by Whitney Ijem, Equity Research Analyst, Guggenheim Securities
Dial-in: 1 (888) 771-4371

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 to 50,000 births in the United States and Europe. In patients with ALGS, multiple organ systems may be affected by the mutation, including the liver, heart, kidneys and central nervous system. The accumulation of bile acids prevents the liver from working properly to eliminate waste from the bloodstream and leads to progressive liver disease that ultimately requires liver transplantation in 15% to 47% of patients. Signs and symptoms arising from liver damage in ALGS may include jaundice, pruritus and xanthomas, which are disfiguring cholesterol deposits under the skin. 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.

About PFIC

Progressive familial intrahepatic cholestasis (PFIC) is a rare genetic disorder that causes progressive liver disease typically leading to liver failure. In people with PFIC, liver cells are less able to secrete bile. The resulting buildup of bile causes liver disease in affected individuals. Signs and symptoms of PFIC typically begin in infancy. Patients experience severe itching, jaundice, failure to grow at the expected rate (failure to thrive), and an increasing inability of the liver to function (liver failure). The disease is estimated to affect one in every 50,000 to 100,000 births in the United States and Europe. Six types of PFIC have been genetically identified, all of which are similarly characterized by impaired bile flow and progressive liver disease The PFIC2 patient population accounts for approximately 60% of the PFIC patient population. PFIC2 is caused by a mutation in the ABCB11 gene, which normally encodes a bile salt export pump protein that moves bile acids out of the liver.

About Maralixibat

Maralixibat is a novel, minimally-absorbed, orally administered investigational drug being evaluated in several rare cholestatic liver diseases for pediatric populations. Maralixibat inhibits the apical sodium dependent bile acid transporter, which results 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 1,500 individuals have received maralixibat, including more than 100 children who have received maralixibat as an investigational treatment for Alagille syndrome (ALGS) and progressive familial intrahepatic cholestasis (PFIC). In a Phase 2 PFIC study, a genetically defined subset of BSEP (bile salt export pump) deficient (PFIC2), patients responded to maralixibat, which led to maralixibat receiving Breakthrough Therapy designation from the FDA for PFIC2. In the ICONIC Phase 2b ALGS clinical trial, patients taking maralixibat had significant reductions in bile acids and pruritus compared to placebo. The FDA has granted maralixibat breakthrough therapy designation for pruritus associated with Alagille syndrome in patients one year of age and older. Maralixibat was generally well-tolerated throughout the studies. The most frequent adverse events were diarrhea, abdominal pain and vomiting.

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 progressive familial intrahepatic cholestasis (PFIC) and Alagille syndrome (ALGS). 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, progress and timing of Mirum's clinical trials, and the regulatory approval path for 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 "plans," "will," "believes," "anticipates," "expects," "intends," "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, and the other risks described in Mirum's filings with the Securities and Exchange Commission, including without limitation in its Quarterly Report on Form 10-Q for the quarter ended September 30, 2019. All forward-looking statements contained in this press release speak only as of the date on which they were made. 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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