Mirum Pharmaceuticals Initiates Phase 3 Clinical Trial for Pediatric Patients with Progressive Familial Intrahepatic Cholestasis

July 9, 2019

- *First patient dosed in Phase 3 trial evaluating efficacy and safety of maralixibat*
- *Topline results expected in fourth quarter of 2020*

FOSTER CITY, Calif., July 9, 2019 /PRNewswire/ -- Mirum Pharmaceuticals today announced the dosing of the first patient in the Phase 3 MARCH-PFIC clinical trial of its lead drug candidate, maralixibat, in pediatric patients with progressive familial intrahepatic cholestasis (PFIC).

"PFIC is a devastating condition that negatively affects children and their families," said Chris Peetz, president and chief executive officer of Mirum. "With no approved drug therapy, the start of the Phase 3 MARCH-PFIC clinical trial is an important milestone for Mirum and puts us one step closer to potentially offering children a new treatment option that targets bile acid overload, a primary driver of liver damage and pruritus in this progressive disease."

Maralixibat is being developed as a therapy for cholestatic liver diseases including PFIC and Alagille syndrome. These diseases result in impaired bile acid flow and accumulation of toxic levels of bile acids in the liver, leading to progressive liver damage that may ultimately result in liver failure. Severe itching, or pruritus, is generally the most debilitating manifestation in children and adults with these diseases. Maralixibat is an inhibitor of the apical sodium-dependent bile acid transporter (ASBT), which recycles bile acids from the intestine to the liver. As observed in the Phase 2 INDIGO clinical trial, blocking bile acid transport from the intestine to the liver with maralixibat resulted in profound and durable reductions in serum bile acids (sBA), clinically meaningful improvements in pruritus and acceleration of growth in some patients with PFIC2.

"There is an immediate need for effective treatment options for children with PFIC who currently suffer from the life-dominating manifestations of this disease," said Robert Squires, MD, Professor of Pediatrics, Transplant Hepatology, UPMC Children's Hospital of Pittsburgh. "The potential of maralixibat to alleviate the intense itch and control elevated bile acid levels associated with PFIC2, could represent an important new option for physicians, patients and caregivers."

About the MARCH-PFIC Phase 3 Trial
The Phase 3 MARCH-PFIC clinical trial (NCT03905330) is a global randomized, placebo-controlled clinical trial of maralixibat in PFIC. The clinical trial will evaluate maralixibat compared to placebo for six months followed by a long-term open label extension study in which all patients will receive maralixibat. The primary endpoint is a reduction in severity of pruritus as measured by the ItchRO(Obs) scale and will include up to 30 patients with residual BSEP function (PFIC2 non-truncating) aged one to 17 years. Other PFIC patients who do not meet the inclusion criteria for the primary cohort may be eligible to enroll in a supplemental cohort. Additional endpoints that will be measured include the mean change in pruritus frequency, the mean change in sBA, mean change in quality of life as measured by the PedsQL scale and the proportion of patients who experience an improvement from baseline in height and weight z-score. The MARCH-PFIC trial will be available to patients in more than 40 pediatric hepatology centers spanning the US, Canada, Europe, the Middle East, Asia and Latin America. For more information about the clinical trial, visit MirumPharma.com.

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 (ASBT), which results in more bile acids being excreted in the feces, leading to lower levels of bile acids systemically, thereby reducing bile acid mediated liver damage. More than 1,500 patients have received maralixibat with 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 subset of PFIC2 patients responded to maralixibat, which led to maralixibat receiving Breakthrough Therapy designation from the U.S. Food and Drug Administration for PFIC2. In a Phase 2b ALGS study, patients taking maralixibat had significant reductions in bile acids and pruritus compared to placebo. 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.

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