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Positive Topline Data Announced from Mirum's LIVMARLI Phase 3 MARCH Study in Progressive Familial Intrahepatic Cholestasis (PFIC)

- Met primary endpoint (p=0.0098); highly statistically significant effects in all PFIC subtypes.
- Significant improvements in total bilirubin and growth versus placebo at six months.
- Mirum plans to submit these data to regulatory agencies.
- Mirum to host conference call to discuss data today, October 24, at 9:00 a.m. ET/6:00 a.m. PT.

October 24, 2022 08:30 AM Eastern Daylight Time

FOSTER CITY, Calif.--(BUSINESS WIRE)--Mirum Pharmaceuticals, Inc. (Nasdaq: MIRM) today announced positive topline results from its pivotal Phase 3 MARCH study evaluating LIVMARLI® (maralixibat) oral solution in 93 patients with progressive familial intrahepatic cholestasis (PFIC) in a broad range of subtypes, age one to 17 years. The primary endpoint of improvement in pruritus severity in PFIC2 was statistically significant (p=0.0098).

"The LIVMARLI data observed in the MARCH study showcase an unprecedented reduction in pruritus and serum bile acids. These data confirm our thesis that higher doses can result in improved efficacy and better outcomes for these patients," said Chris Peetz, president and chief executive officer at Mirum. "We are grateful to the patients, caregivers, and healthcare providers who participated in this study and who helped make these groundbreaking results possible."

The primary analysis was conducted in PFIC2 patients (n=31). The secondary analyses were evaluated in the All-PFIC cohort, which included PFIC2 as well as additional PFIC subtypes (n=64). The Full-Study population included All-PFIC as well as supplemental patients who had previously undergone surgery, had truncating mutations and other patients (n=93).

Topline results

PFIC2 (n=31)

Endpoint	Absolute Change		Effect Size*	P-value
	LIVMARLI	Placebo		
Primary: Change from baseline in ItchRO(Obs) severity	-1.7	-0.6	-1.0	0.0098
Secondary: Change from baseline in serum bile acid	-176	11	-187	0.0013

**Effect size compared the difference between LIVMARLI and placebo, averaged over the last 3 time periods using a repeated measures mixed effect model. Placebo adjusted. Numbers in tables may not sum due to rounding.*

All-PFIC (n=64) [PFIC1, PFIC2, PFIC3, PFIC4, PFIC6]

Endpoint	Absolute Change		Effect Size*	P-value
	LIVMARLI	Placebo		
Secondary: Change from baseline in ItchRO(Obs) severity	-1.8	-0.6	-1.2	<0.0001
Secondary: Change from baseline in serum bile acid	-157	3	-160	<0.0001

**Effect size compared the difference between LIVMARLI and placebo, averaged over the last 3 time periods using a repeated measures mixed effect model. Placebo adjusted.*

LIVMARLI's safety and tolerability profile was comparable to previously published data and no new safety signals emerged in the MARCH study. The most common treatment emergent adverse event was diarrhea, which was predominantly mild, with no severe cases, and transient with a median duration of 5.5 days. One patient had a treatment emergent adverse event of mild diarrhea that led to discontinuation.

Full-Study (n=93)

Treatment Emergent Adverse Event (TEAE)	LIVMARLI (n=47)	Placebo (n=46)
Any TEAE, n (%)	47 (100%)	43 (93.5%)
Severe TEAE, n (%)	3 (6.4%)	3 (6.5%)
Serious TEAE, n (%)	5 (10.6%)	3 (6.5%)
TEAE leading to discontinuation, n (%)	1 (2.1%)	0
TEAE leading to death, n (%)	0	0
Most common TEAE Diarrhea, n (%)	27 (57.4%)	9 (19.6%)

Further data from the MARCH study will be presented at an upcoming scientific conference.

"The landmark MARCH study represents a significant step forward in the evaluation of therapies for PFIC. Knowing of the impact of itching on the quality of life for children with PFIC, the sustained and clinically significant reduction in itching scores in the LIVMARLI treatment arm is an important topline result," said Alexander G. Miethke, MD, associate professor of pediatrics from the PFIC Research Center at Cincinnati Children's Medical Center. "Lowered serum bile acids are a

prognostic marker for native liver survival, and it is encouraging to see such an impressive response. These data improved upon the compelling results seen in the LIVMARLI Phase 2 study and underscore the strong effect that this IBAT inhibitor can have on patients with all PFIC subtypes when optimally dosed."

"The advancement of new medications, particularly for rare diseases like PFIC, is incredibly important and provides hope to families who are in need of a treatment option that can effectively address itch, the most burdensome aspect of the disease," said Emily Ventura, executive director, PFIC Network. "The itch experienced with PFIC can have lasting and devastating consequences for patients and their families, and we are excited that LIVMARLI, backed by such promising data, may be a new option on the horizon for the PFIC community."

Data Review Conference Call

Mirum will be hosting a conference call to discuss the topline data from the MARCH study today, Monday, October 24, 2022, at 9:00 a.m. ET/6:00 a.m. PT. Join the call by dialing 1-646-904-5544 (US) or 1-844-200-6205 (toll-free), call ID: 200410. You may also access the webcast through Mirum's Investor Relations site.

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 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 (ALGS) one year of age and older and is the only FDA-approved medication to treat cholestatic pruritus associated with Alagille syndrome. For more information, please visit LIVMARLI.com.

LIVMARLI is currently being evaluated in late-stage clinical studies in other rare cholestatic liver diseases including an open-label extension study in progressive familial intrahepatic cholestasis (PFIC), and in biliary atresia. LIVMARLI has received Breakthrough Therapy designation for ALGS and PFIC type 2 and orphan designation for ALGS, PFIC and biliary atresia. To learn more about ongoing clinical trials with LIVMARLI, please visit Mirum's clinical trials section on the company's website.

IMPORTANT SAFETY INFORMATION

LIVMARLI can cause 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

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. In Europe, the European Committee for Medicinal Products for Human Use (CHMP) has issued a positive opinion for LIVMARLI for the treatment of cholestatic pruritus in patients with Alagille syndrome two months of age and older. A decision by the European Commission is expected by year-end 2022.

Mirum's late-stage pipeline includes two investigational treatments for debilitating liver diseases affecting children and adults. 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 clinical trial for progressive familial intrahepatic cholestasis (PFIC) and the EMBARK Phase 2b clinical trial for patients with biliary atresia. In addition, Mirum has an expanded access program open across multiple countries for eligible patients with ALGS and PFIC.

Mirum's second investigational treatment, volixibat, an oral IBAT inhibitor, is being evaluated in three potentially registrational studies including the VISTAS Phase 2b clinical trial for adults with primary sclerosing cholangitis, the OHANA Phase 2b clinical trial for pregnant women with intrahepatic cholestasis of pregnancy, and the VANTAGE Phase 2b clinical trial for adults with primary biliary cholangitis.

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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, Mirum's plans with respect to the regulatory approval process of LIVMARLI in PFIC and LIVMARLI's effect on patients with all PFIC subtypes when optimally dosed. 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," "can," "may" 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 geopolitical and macroeconomic events, 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.

Contacts

Media Contact:
Erin Murphy
media@mirumpharma.com

Investor Contacts:
Ian Clements, Ph.D.
ir@mirumpharma.com

Sam Martin
Argot Partners
ir@mirumpharma.com

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Replying to @mirumpharma

(2/2) Follow along as these groups share information about #PSC and ways to get involved.

#PSCAware #PSC #PSCAwarenessDay

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Today is international PSC Awareness Day, and the second year that global organizations, including @EuropeLiver, @PSCPartners, @PSCPartnersCa, @PSCSupportUK, @Hetz_liver, and others, are coming together to educate the public about Primary Sclerosing Cholangitis or #PSC. (1/2)

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Mirum Pharmaceuticals @mirumpharma · Oct 24

In honor of #Diwali our Foster City team came together to enjoy delicious Indian food, made by a generous employee, and a quick dance lesson. We had a wonderful celebration together. Wishing everyone a joyous #Diwali celebration filled with

friends and family.

#Hashtags

#raredisease #alagillesyndrome #algs

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