



Albireo Announces Bylvay® (odevixibat) Now Available in Germany

September 15, 2021

– Listed on the German national price list and all pharmacy software programs –

– Bylvay is approved in U.S., EU and UK as first drug treatment for patients with PFIC –

– Only once-daily drug indicated to treat all forms of PFIC –

BOSTON, Sept. 15, 2021 (GLOBE NEWSWIRE) -- Albireo Pharma, Inc. (Nasdaq: ALBO), a rare pediatric liver disease company developing novel bile acid modulators, today announced that Bylvay (odevixibat), the first drug approved in Europe for the treatment of all types of progressive familial intrahepatic cholestasis (PFIC), is now available by prescription to patients in Germany. Bylvay is also approved in the U.S. for the treatment of pruritus in all types of PFIC. A potent, non-systemic ileal bile acid transport inhibitor (IBATI), Bylvay is administered as a once-daily capsule or opened and sprinkled onto soft foods and does not require refrigeration.

"With the availability of Bylvay in Germany, we are now able to offer the first non-surgical treatment option to the PFIC patients who are experiencing difficult developmental and physical symptoms," said Ekkehard Sturm, M.D., Ph.D., Pediatric Hepatologist and Head of Pediatric Gastroenterology-Hepatology, Liver and Intestinal Transplantation at Children's Hospital, University of Tübingen in Germany. "We are hopeful that Bylvay will help patients avoid complications associated with surgery and provide them with much needed relief from their symptoms."

Bylvay is now available through retail pharmacies. Sales promotion has already begun, with Albireo commercial staff covering the key centers to inform them of the availability of Bylvay for the treatment of PFIC and the patient support services available. Once Bylvay is prescribed, healthcare providers and families will have the option to use Albireo Assist®, which is a customized patient support program built with input from medical experts and patient advocates that aims to support patients and caregivers throughout their treatment journey.

"We are excited to bring the first drug treatment option to PFIC patients in Germany, which has the largest market potential in Europe," said Pamela Stephenson, Chief Commercial Officer of Albireo. "We have an experienced German team, including, commercial, medical and operations who are on the ground running. Based on our initial conversations with healthcare providers, we know that there is great interest in Bylvay and we are confident in the uptake."

To support payor decision-making, Albireo has submitted a value dossier to the Joint Federal Committee (G-BA) in Germany with the PEDFIC 1 and PEDFIC 2 Phase 3 data, including long-term data with patients on drug for over two years; natural history information; and a caregiver study to reflect the burden of PFIC. This submission commences the drug benefit assessment process. General national reimbursement will be granted throughout the entire process as well as thereafter.

"The PFIC patients around the world who are experiencing extreme challenges and diminished quality of life underscore our urgency to continue on our path towards global availability," said Ron Cooper, President and CEO of Albireo.

Albireo has launched Bylvay in the U.S. and is working to commercialize Bylvay in other European countries. Bylvay is currently being evaluated by a number of reimbursement agencies in Europe. Albireo is working closely with all relevant agencies to ensure access for patients in Europe as quickly as possible. Outside the U.S., access to Bylvay is available through our Managed Access Program. For more information on this program, please visit <https://www.albireopharma.com/patients-families/patient-access>.

Bylvay is currently being evaluated in the ongoing PEDFIC 2 open-label trial in patients with PFIC, ASSERT Phase 3 study for Alagille syndrome and in the BOLD Phase 3 study for patients with biliary atresia. The ASSERT and BOLD studies remain on track to report topline data in 2022 and 2024 respectively.

About Bylvay (odevixibat)

Bylvay is the first drug treatment approved in the U.S. for the treatment of pruritus in all types of progressive familial intrahepatic cholestasis (PFIC). The European Commission (EC) and UK Medicines and Healthcare Products Regulatory Agency (MHRA) have also granted marketing authorization of Bylvay in PFIC and will be available for sale in Europe following pricing and reimbursement approval. A potent, once-daily, non-systemic ileal bile acid transport inhibitor, Bylvay acts locally in the small intestine. Bylvay does not require refrigeration and can be taken as a capsule for older children, or opened and sprinkled onto food, which are factors of key importance for adherence in a pediatric patient population. The medicine can only be obtained with a prescription and treatment should be started and supervised by a doctor who has experience in the management of PFIC. For more information about using Bylvay, see the package leaflet or contact your doctor or pharmacist. For full prescribing information, visit www.bylvay.com.

In the U.S. and Europe, Bylvay has orphan exclusivity for its approved PFIC indications, and orphan designations for the treatment of Alagille syndrome, biliary atresia and primary biliary cholangitis. Bylvay is being evaluated in the ongoing PEDFIC 2 open-label trial in patients with PFIC, in the BOLD Phase 3 study for patients with biliary atresia and the ASSERT Phase 3 study for Alagille syndrome.

About Albireo

Albireo Pharma is a rare disease company focused on the development of novel bile acid modulators to treat rare pediatric and adult liver diseases. Albireo's product, Bylvay, was approved by the U.S. FDA as the first drug for the treatment of pruritus in all types of progressive familial intrahepatic cholestasis (PFIC), and it is also being developed to treat other rare pediatric cholestatic liver diseases with Phase 3 trials in Alagille syndrome and biliary atresia, as well as an Open-label Extension (OLE) study for PFIC. In Europe, Bylvay has been approved for the treatment of PFIC and has been submitted for pricing and reimbursement approval. The Company has also initiated a Phase 1 clinical trial for A3907 to advance development in adult

cholestatic liver disease, with IND-enabling studies moving ahead with A2342 for viral and cholestatic liver disease. Albireo was spun out from AstraZeneca in 2008 and is headquartered in Boston, Massachusetts, with its key operating subsidiary in Gothenburg, Sweden. The Boston Business Journal named Albireo one of the 2020 Best Places to Work in Massachusetts for the second consecutive year. For more information on Albireo, please visit www.albireopharma.com.

Forward-Looking Statements

This press release includes "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include statements, other than statements of historical fact, regarding, among other things: Albireo's commercialization plans and expectations for commercializing Bylvay in the U.S. and Europe; estimates of the number of patients impacted by PFIC; expectations about Bylvay's acceptance by healthcare practitioners to treat PFIC patients; the plans for, or progress, scope, cost, initiation, duration, enrollment, results or timing for availability of results of, development of Bylvay, A3907, A2342 or any other Albireo product candidate or program; the pivotal trial for Bylvay in biliary atresia (BOLD), and the pivotal trial for Bylvay in Alagille syndrome (ASSERT); the Phase 1 trial for A3907; the target indication(s) for development or approval, the size, design, population, location, conduct, cost, objective, enrollment, duration or endpoints of any clinical trial, or the timing for initiation or completion of or availability or reporting of results from any clinical trial, including the long-term open-label extension study for Bylvay in PFIC, and the BOLD and ASSERT trials; discussions with the FDA or EMA regarding our programs; the potential benefits or competitive position of Bylvay or any other Albireo product candidate or program or the commercial opportunity in any target indication; the potential effects of Bylvay of the treatment of PFIC patients and its potential to improve the current standard of care; the potential benefits of an orphan drug designation; the length of time for which Albireo's cash resources are expected to be sufficient, and the milestones and activities to be funded with those cash resources; or Albireo's plans, expectations or future operations, financial position, revenues, costs or expenses. Albireo often uses words such as "anticipates," "believes," "plans," "expects," "projects," "future," "intends," "may," "will," "should," "could," "estimates," "predicts," "potential," "planned," "continue," "guidance," or the negative of these terms or other similar expressions to identify forward-looking statements. Actual results, performance or experience may differ materially from those expressed or implied by any forward-looking statement as a result of various risks, uncertainties and other factors, including, but not limited to: there are no guarantees that Bylvay will be commercially successful; we may encounter issues, delays or other challenges in launching or commercializing Bylvay; whether Bylvay receives adequate reimbursement from third-party payors; the degree to which Bylvay receives acceptance from patients and physicians for its approved indication; challenges associated with execution of our sales activities, which in each case could limit the potential of our product; results achieved in Bylvay in the treatment of patients with PFIC once we have launched the product may be different than observed in clinical trials, and may vary among patients; other potential negative impacts of the COVID-19 pandemic, including on manufacturing, supply, conduct or initiation of clinical trials, or other aspects of our business; whether favorable findings from clinical trials of Bylvay to date, including findings in indications other than PFIC, will be predictive of results from other clinical trials of Bylvay; the outcome and interpretation by regulatory authorities of the ongoing third-party study pooling and analyzing of long-term PFIC patient data; the timing for initiation or completion of, or for availability of data from, clinical trials of Bylvay, including BOLD and ASSERT, and the Phase 1 clinical trial of A3907, and the outcomes of such trials; Albireo's ability to obtain coverage, pricing or reimbursement for approved products in the United States or Europe; delays or other challenges in the recruitment of patients for, or the conduct of, Company's clinical trials; and Albireo's critical accounting policies. These and other risks and uncertainties that Albireo faces are described in greater detail under the heading "Risk Factors" in Albireo's most recent Annual Report on Form 10-K or in subsequent filings that it makes with the Securities and Exchange Commission. As a result of risks and uncertainties that Albireo faces, the results or events indicated by any forward-looking statement may not occur. Albireo cautions you not to place undue reliance on any forward-looking statement. In addition, any forward-looking statement in this press release represents Albireo's views only as of the date of this press release and should not be relied upon as representing its views as of any subsequent date. Albireo disclaims any obligation to update any forward-looking statement except as required by applicable law.

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Source: Albireo Pharma, Inc.



Bylvay™ (odevixibat) FDA Approval

Hope for Children with Orphan Liver Diseases



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All forward-looking statements speak only as of the date this presentation is made and should not be relied upon as representing our views as of any date after this presentation is made. We specifically disclaim any obligation to update any forward-looking statement, except as required by applicable law. “Albireo” is a trademark of Albireo AB. All other trademarks, service marks, trade names, logos and brand names identified in this presentation are the properties of their respective owners.

Agenda

Bylvay™ (odevixibat) FDA Approval

PEDFIC 1 & 2 Dataset

Commercializing Bylvay

Q&A

Albireo Leadership Here Today



Ron Cooper

President and CEO

Former Bristol-Myers
Squibb (President
of Europe)



Pamela Stephenson

Chief Commercial Officer

Former Vertex, Pfizer



Simon Harford

Chief Financial Officer

Former Parexel,
GlaxoSmithKline, Eli Lilly



Pat Horn, MD, PhD

Chief Medical Officer

Former Orphan
Technologies, Dyax,
Tetraphase, Abbott



**First and Only Drug Treatment
Approved by the FDA for Patients
With Progressive Familial
Intrahepatic Cholestasis (PFIC)**



Bylvay™ (odevixibat)



United States



First and only drug treatment approved by the FDA for patients with PFIC



Launching immediately in the US, supply shipping in the coming days



HCPs able to write prescription now

Europe



Approved in Europe



Planned launches in EU 5, Germany to be the first in September

Bylvay™ (odevixibat) Is APPROVED



U.S. Indication

Bylvay is indicated for the treatment of pruritus in patients 3 months of age and older with progressive familial intrahepatic cholestasis (PFIC).

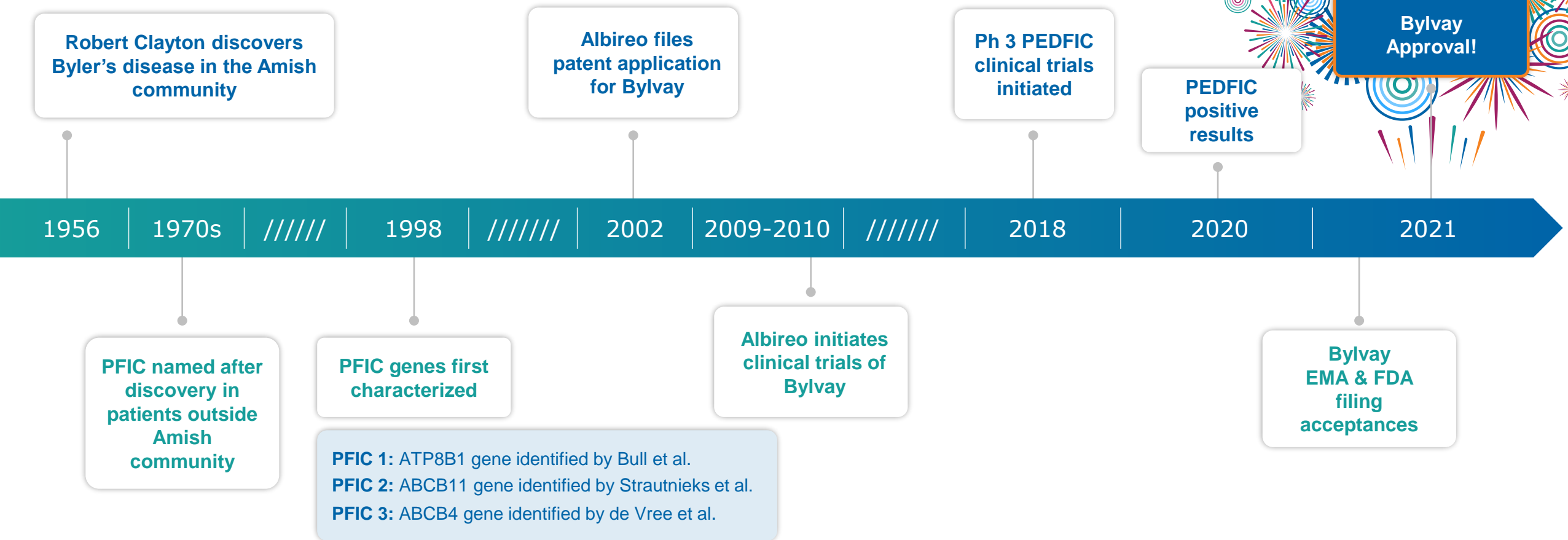
European Indication

Bylvay is indicated for the treatment of progressive familial intrahepatic cholestasis (PFIC) in patients aged 6 months or older.



For additional Important Safety Information on Bylvay, see full Prescribing Information at [Bylvay.com](https://www.bylvay.com)

Bylvay™ (odevixibat): Decades of Development



Providing Hope for Families





PEDFIC Dataset

Patrick Horn, MD, PhD
Chief Medical Officer



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Progressive Familial Intrahepatic Cholestasis (PFIC)

PFIC is a rare and devastating disorder affecting young children that causes progressive, life-threatening liver disease

Onset



Age **~1-2 years**

Patients are diagnosed young, and the majority of **patients do not** have complete response to medical therapy¹⁻⁶

Symptoms & Burden of Disease

Pruritis is widespread and often severe among patients with PFIC⁷

Parents and caregivers may devote significant time and resources to caring for patients with PFIC⁷



The burden of PFIC is not well described in the literature - Patients with PFIC have lower HRQoL compared to healthy peers⁷

Treatment & Survival

Almost no patients survive beyond **age 30 without surgical diversion or liver transplant¹**

At **18 years of age, 44%** of PFIC1 patients and **32%** of PFIC2 patients were alive with their native liver^{9, 10}



Surgical options have high morbidity necessitating lifelong care

PEBD involves routine ostomy care, supplementation of fluid and electrolytes, and may require surgical revision

Liver transplant requires lifelong immunosuppression and has a significant risk of graft rejection



“People don’t understand that the itch is from deep inside their bodies.”

– Emily K, mother of Kennedy⁸

Bylvay™ (odevixibat) Studied in Two Phase 3 Efficacy & Safety Studies

96 WEEKS COLLECTIVE

PEDFIC 1

24 WEEKS

Randomized, double-blind, placebo-controlled, global, multicenter 24-week Phase 3 clinical trial of Bylvay in 62 patients, ages 6 months to 15.9 years, with PFIC type 1 or type 2

PEDFIC 2

72 WEEKS

Open-label, single-arm, 72-week long-term extension trial in PFIC patients using Bylvay 120 mcg/kg/day

Patients enrolled in PEDFIC 1 could enter PEDFIC 2 cohort 1 (n=53), and other PFIC patients could enter PEDFIC 2 cohort 2 (n=31)

Statistically significant improvement in pruritus assessment $p=0.004$

Statistically significant reduction in serum bile acid response $p=0.003$

Both Bylvay doses statistically significant for both endpoints

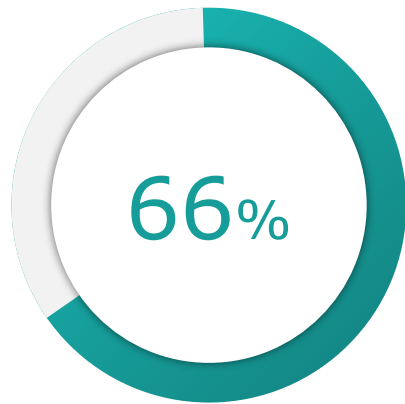
Sustained efficacy; response across PFIC1, PFIC2, PFIC3

Well-tolerated with low diarrhea rate

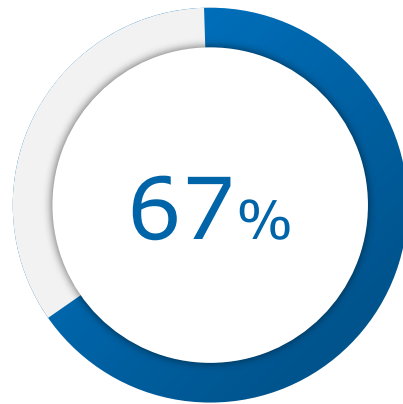
Rapid & Durable Effect

Patients had rapid reductions in serum bile acid (sBA) levels and improvements in pruritus severity, with durable clinical benefits sustained through 48 weeks of treatment

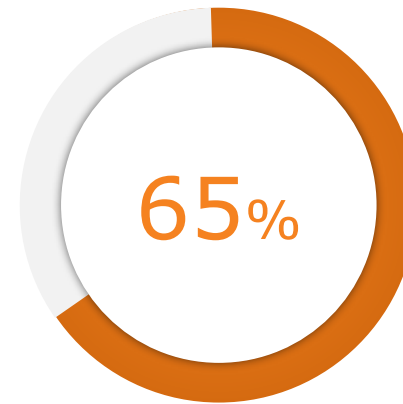
Bylvay™ (odevixibat) patient responder data show sustained improvements in cholestasis markers vs. non-responders



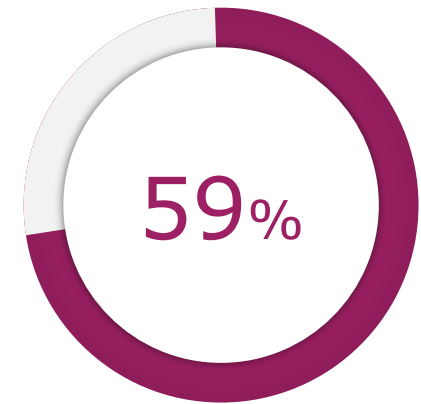
Proportion of positive pruritus assessments with Bylvay treatment



Patients who were serum bile acid responders at weeks 46-48



Rate of pruritus responders

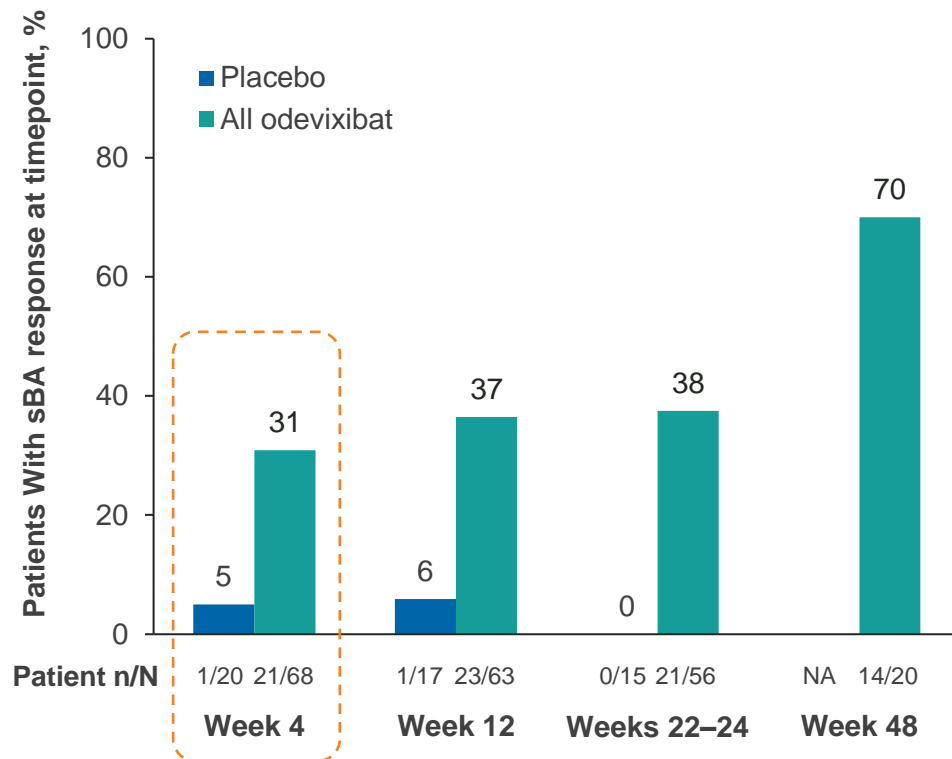


Rate of serum bile acid responders

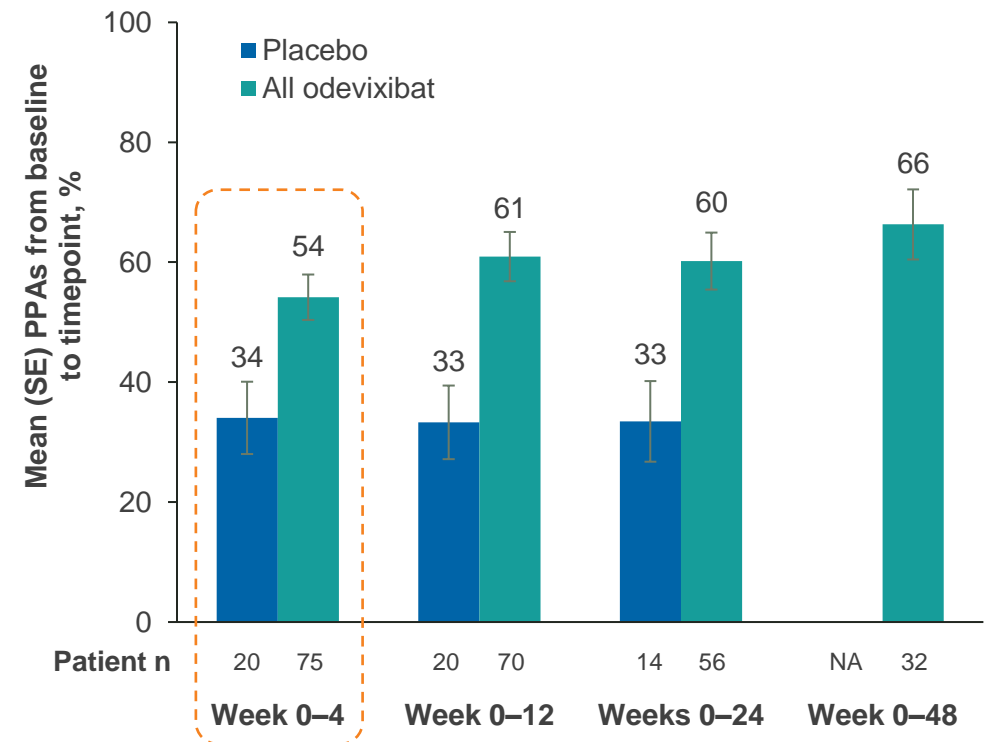
Bylvay (odevixibat)TM Works Rapidly

As early as Week 4, significant serum bile acid reductions and improvements in pruritus were observed

Serum Bile Acid Responders



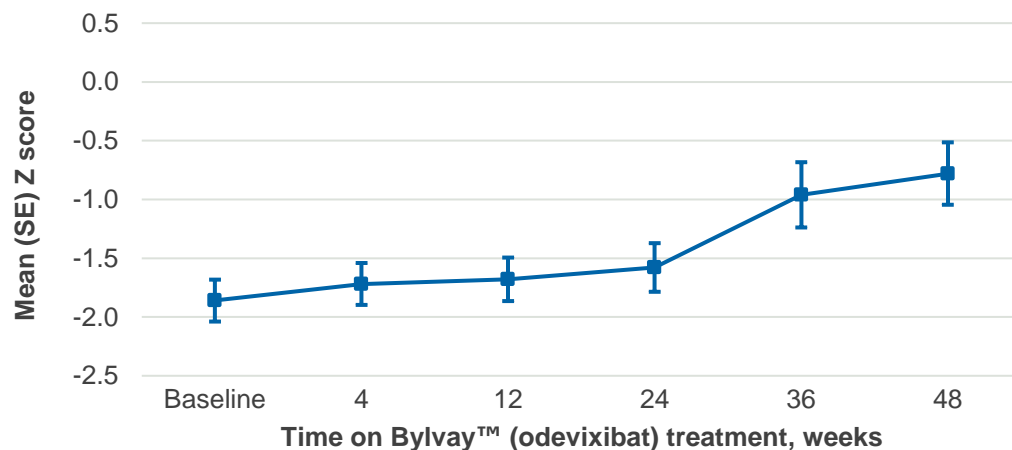
Positive Pruritus Assessments



Improvements in Key Health Measures

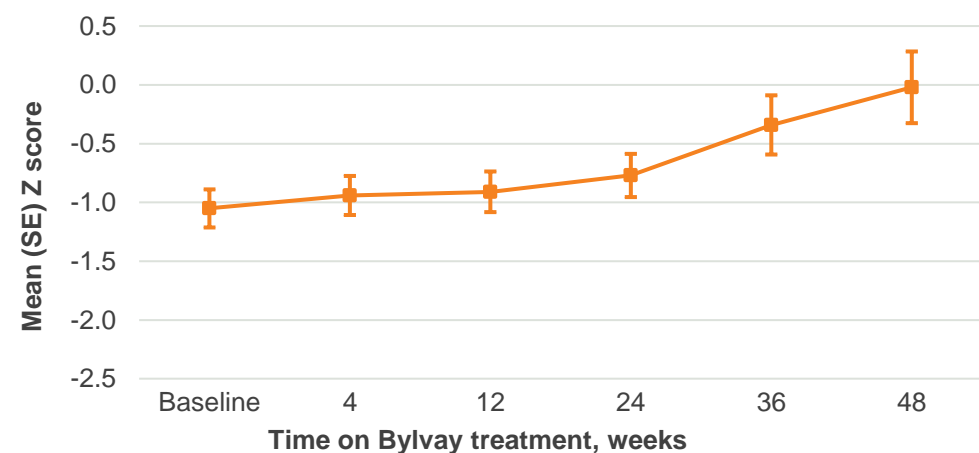
Improvements in growth & weight gain through 48 weeks

Height Z Score Over Time



✓ Height Z scores increased from baseline -1.9 to -0.8

Weight Z Score Over Time



✓ Weight Z scores increase from baseline -1.1 to -0.0

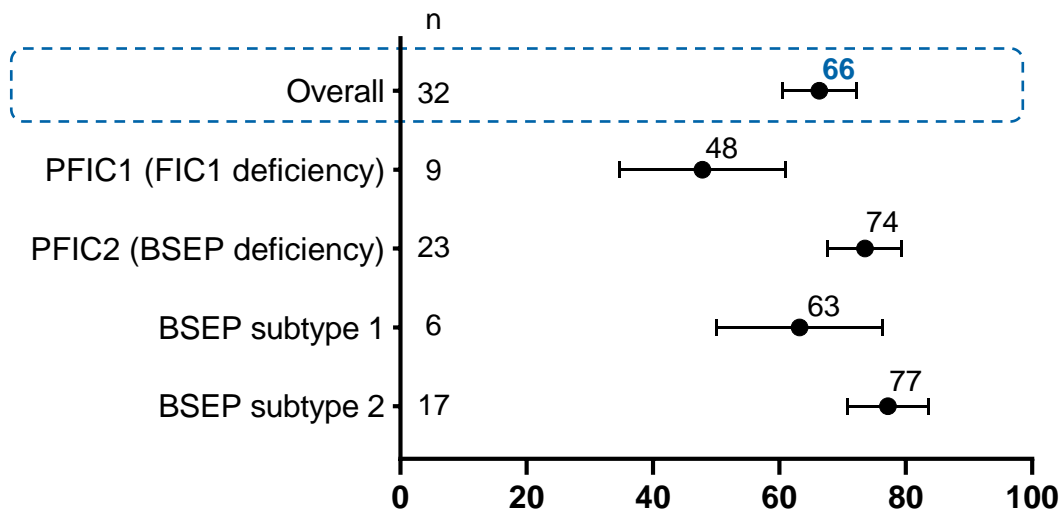
Improvement in multiple sleep parameters

Clinicians and caregivers reported that $\geq 88\%$ of responders had moderately or very much better sleep

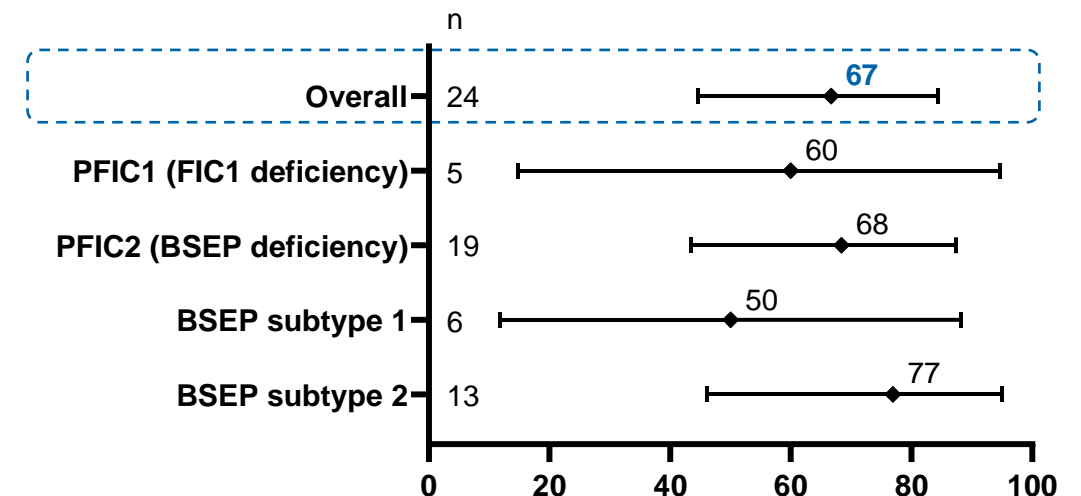
Pruritus Improvement Demonstrated Across PFIC Subtypes

Patients had substantial benefits with Bylvay™ (odevixibat), including reductions in serum bile acids and improvement in pruritus symptoms

Mean (SE) PPAs at the Patient Level



Proportion of Patients with sBA Response (95% CI)



Overall AE Profile Similar to Placebo With Low Diarrhea Rate

Long-term treatment with Bylvay™ (odevixibat) was well tolerated through Week 48, regardless of PFIC classification or BSEP subtype

Good Safety Profile & Well-Tolerated

The observed safety and tolerability profile of Bylvay was consistent across studies, treatment groups and doses.

No drug-related serious adverse events were reported in either PEDFIC 1 or PEDFIC 2.

One patient in PEDFIC 1 and 3 patients in PEDFIC 2 treated with Bylvay withdrew due to an adverse event.

There were low numbers of gastrointestinal adverse events.

Treatment-related diarrhea/frequent bowel movements reported in **9.5%** of Bylvay treated patients in PEDFIC 1 and **5%** of placebo-treated patients.



Commercializing Bylvay™ (odevixibat)

Pamela Stephenson
Chief Commercial Officer



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Commercial Execution Plan Ready to Launch in PFIC

United States



Targeting
~60 Key U.S. Centers

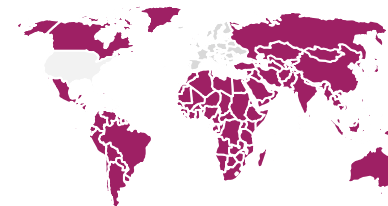
- ✓ Immediate product launch
- ✓ Sales, payer and medical teams trained, out in the field
- ✓ AlbireoAssist™ is live
- ✓ Supply shipping in the coming days
- ✓ Specialty pharmacies in place
- ✓ Meetings planned with major insurers

Europe



- ✓ Approved/Waiting
- ✓ Launch first in EU 5
- ✓ September launch in Germany

ROW

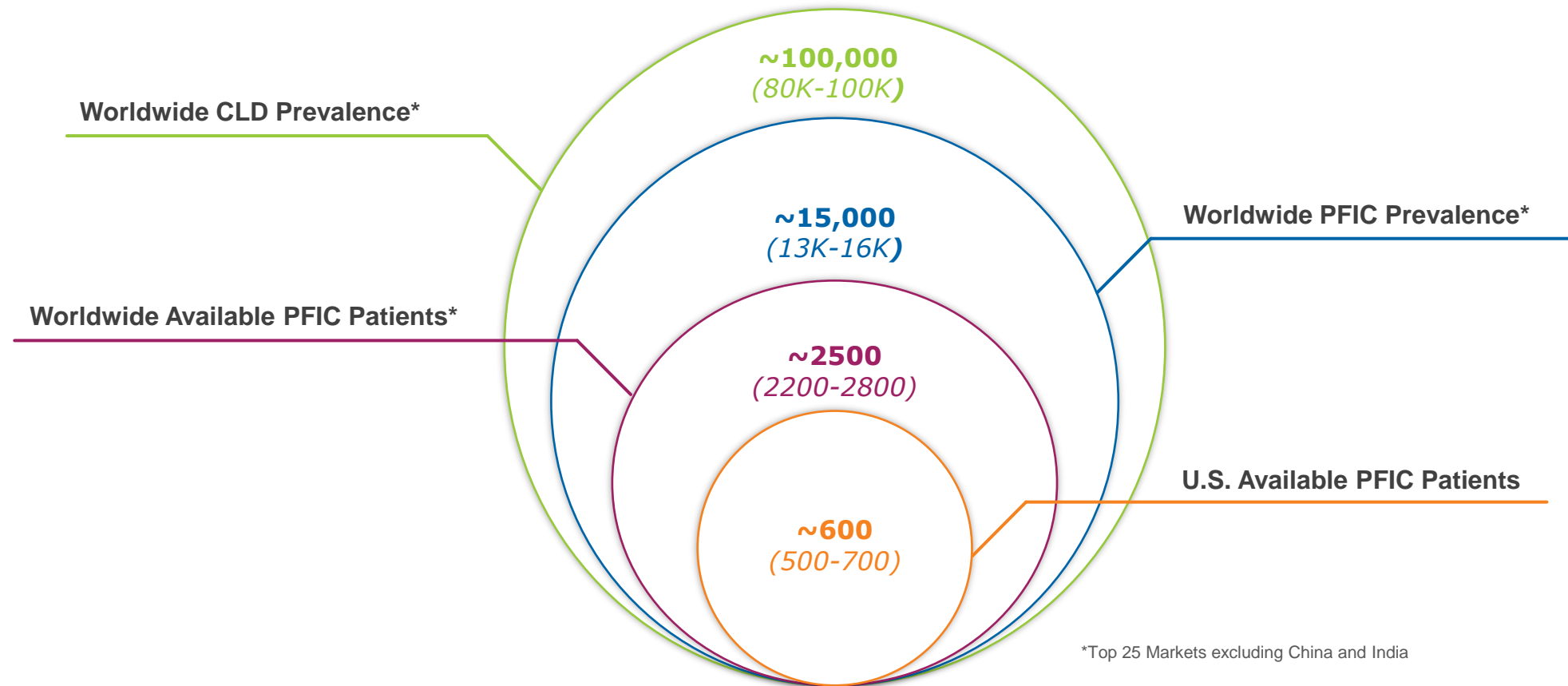


Local distributorship
agreements in place, further
deal exploration ongoing

- ✓ Medison
- ✓ GEN
- ✓ Genpharm Services

PFIC Is a Rare Life-Threatening Disease

Global market opportunity size: **~100,000** patients with pediatric cholestatic liver disease in top 25 countries



Evidence Supports Orphan Pricing Model for Bylvay™ (odevixibat)

Rare Value Pricing Factors

Severe Disease

High Unmet Need

Robust Clinical Evidence

Low Budget Impact

Commitment to Patient Access



Demonstrated Bylvay Value Proposition



Progressive, fatal liver diseases affecting children



No approved medical treatments, only surgery



Randomized, placebo-controlled Phase 3 with 62 pts



Natural history data support long-term outcomes



Early Access Program



Patient Support



Average U.S. annual price:
\$385,000

Before mandatory government rebates

U.S. Patient Journey: From Prescription to Treatment

Albireo is committed to providing reimbursement assistance and will work closely with HCPs to share information on anticipated documentation and requirements



**Commercial
Co-pay Assistance**



Free Drug Program
Patient Assistance Program (PAP)

First FDA Approved Drug for the Treatment of Pruritus in Patients with PFIC



Favorable Profile

- ✓ Once-Daily dosing
- ✓ Oral capsule or oral pellets
- ✓ No refrigeration required
- ✓ Minimal systemic exposure
- ✓ Favorable tolerability profile

Quality Design & Data

- ✓ Gold standard randomized, placebo-controlled trials
- ✓ Largest PFIC study with 62 patients
- ✓ Demonstrated short- and long-term improvements
- ✓ All PFIC types
- ✓ AE profile similar to placebo with low diarrhea rate

Access

- ✓ Rare progressive, fatal liver diseases affecting children
- ✓ Data strength supports value proposition with payors
- ✓ Caregiver Burden Study demonstrates humanistic value
- ✓ Natural history data support long-term outcomes
- ✓ Albireo Assist to take the lead in patient benefits and financial support



Bylvay™ (odevixibat) FDA Approval

Hope for Children with Orphan Liver Diseases



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Albireo Receives European Marketing Authorization of Bylvay™ (odevixibat), the First Drug Treatment for Progressive Familial Intrahepatic Cholestasis (PFIC)

July 19, 2021

- First approval in the world of Bylvay for the treatment of PFIC –*
- Only once-daily drug indicated to treat all forms of PFIC –*
- European Commission (EC) decision based on data from the largest Phase 3 PFIC trial to date –*
- German price listing followed by commercial launch expected in September –*
- U.S. FDA has set an action date of July 20, 2021, under the Prescription Drug User Fee Act (PDUFA) –*

BOSTON, July 19, 2021 (GLOBE NEWSWIRE) -- Albireo Pharma, Inc. (Nasdaq: ALBO), a rare liver disease company developing novel bile acid modulators, today announced European Commission (EC) authorization of Bylvay (odevixibat), the first drug approved for the treatment of all subtypes of progressive familial intrahepatic cholestasis (PFIC). Bylvay is a potent, non-systemic ileal bile acid transport inhibitor (IBATI), which does not require refrigeration and is easily administered as a once-daily capsule or opened and sprinkled onto soft foods.

"In 1998 one of the genes causing PFIC was discovered in our laboratory. Bylvay is the first approved pharmacological therapy available to children after over 20 years of research," said Richard Thompson, Professor of Molecular Hepatology at King's College London and principal investigator of PEDFIC 1 and PEDFIC 2. "Until now the standard of care for PFIC patients was limited to invasive surgeries including liver transplants. As the first non-surgical treatment option, Bylvay represents a fundamental shift in the way PFIC is treated."

PFIC is a rare and devastating disorder affecting young children that causes progressive, life-threatening liver disease. In many cases, PFIC leads to cirrhosis and liver failure within the first 10 years of life. The most prominent and problematic ongoing manifestation of PFIC is pruritus, or intense itching, which often results in a severely diminished quality of life. Until now, there have been no approved drugs for PFIC; only surgical options that include biliary diversion surgery (BDS) and liver transplantation, and without them most PFIC patients do not survive past the age of 30. Of the estimated 100,000 patients with cholestatic liver disease worldwide without an approved drug treatment, there are approximately 15,000 PFIC patients, excluding China and India.

"The suffering and quality of life for children with PFIC is terrible. The approval of Bylvay gives parents tremendous hope as the first drug treatment now available," said Alison Taylor, Chief Executive of Children's Liver Disease Foundation (CLDF). "The decisions we have to make as parents are hard enough, but for PFIC parents they might have to consider surgery and liver transplantation for children, while managing an immense disease burden that affects the entire family."

The EC authorization was based on data from PEDFIC 1 and PEDFIC 2, the largest, global, Phase 3 trials ever conducted in PFIC. In [PEDFIC 1](#), a randomized, double-blind, placebo-controlled study, Bylvay met both its pruritus ($p=0.004$) and serum bile acid ($p=0.003$) primary endpoints and was well tolerated with very low incidence of drug-related diarrhea/frequent bowel movements (9.5% of treated patients vs. 5.0% of placebo patients). PEDFIC 2, a long-term, open-label Phase 3 extension study, affirmed Bylvay delivered sustained reductions in serum bile acid as well as improvements in pruritus assessments, growth and other markers of liver function in patients treated up to 48 weeks in an interim analysis. Across both studies, Bylvay was well tolerated with diarrhea/frequent stools being the most common treatment-related gastrointestinal adverse events. There were no serious treatment-related adverse events reported in any clinical study with Bylvay.

"The approval of Bylvay in Europe marks the first drug ever approved in multiple countries in the world for a pediatric cholestatic liver disease and Albireo's evolution to a commercial-stage, rare liver disease company," said Ron Cooper, President and Chief Executive Officer of Albireo. "We are grateful to the children, families, investigators, advocates, and employees whose contributions turned hope into the first ever drug option for the PFIC community. We are hopeful that Bylvay will soon be available in the U.S. and other countries around the world to ensure access for this rare disease population."

Albireo plans to directly commercialize Bylvay in the European Union (EU) and is prepared for a global launch with commercial, market access and medical affairs personnel already on the ground. This includes Germany, which has the largest EU market potential, with launch planned for September 2021, following price listing. Pricing and reimbursement dossiers have been submitted to many member states to provide access to Bylvay treatment as soon as possible. Albireo has developed a compelling value package with the PEDFIC gold standard Phase 3 data, natural history information and data from a recent study reflecting the burden of PFIC on caregivers and families.

The Company also anticipates an upcoming regulatory decision by the U.S. FDA on Bylvay for the treatment of pruritus in patients with PFIC. The FDA has granted a Priority Review for the NDA and has set an action date of July 20, 2021 under the Prescription Drug User Fee Act (PDUFA). Albireo is also studying the use of Bylvay in other rare pediatric cholestatic diseases with the BOLD Phase 3 clinical trial in patients with biliary atresia and the ASSERT Phase 3 clinical trial in Alagille syndrome. Topline data from the ASSERT trial is expected in 2022, and data from the BOLD trial is expected in 2024.

About Bylvay (odevixibat)

Bylvay is the first drug treatment approved in the world for the treatment of all subtypes of progressive familial intrahepatic cholestasis (PFIC). A potent, once-daily, non-systemic ileal bile acid transport inhibitor, Bylvay acts locally in the small intestine. Bylvay does not require refrigeration and can be taken as a capsule for older children, or opened and sprinkled onto food, which are factors of key importance for adherence in a pediatric

patient population.

Bylvay has an Orphan Designation for the treatment of PFIC. The EMA's Pediatric Committee has agreed to Albireo's Bylvay Pediatric Investigation Plans for PFIC, biliary atresia, and Alagille syndrome. In addition to PFIC, Bylvay has Orphan Designations for the treatment of Alagille syndrome, biliary atresia and primary biliary cholangitis.

Bylvay is available as capsules. The recommended dose is 40 microgram per kilogram body weight. The capsules should be taken once a day in the morning. They can be taken whole, or they can be opened and sprinkled on food. If the clinical response is inadequate after three months, the dose may be increased up to 120 microgram per kilogram body weight. The medicine can only be obtained with a prescription and treatment should be started and supervised by a doctor, who has experience in the management of PFIC. For more information about using Bylvay, see the package leaflet or contact your doctor or pharmacist.

For full EU product information: <https://albiropharma.com/programs/bylvay>.

About PFIC

Progressive familial intrahepatic cholestasis (PFIC) is a rare disorder that causes progressive, life-threatening liver disease. Patients have impaired bile flow, or cholestasis, caused by genetic mutations. The resulting bile build-up in liver cells causes liver disease and symptoms. The most prominent and problematic ongoing manifestation of the disease is pruritus, or intense itching, which often results in a severely diminished quality of life. Other symptoms include jaundice, poor weight gain and slowed growth. In many cases, PFIC leads to cirrhosis and liver failure within the first 10 years of life, and nearly all people with PFIC require treatment before age 30. There are no drugs currently approved for PFIC, only surgical options that include partial external biliary diversion (PEBD) and liver transplantation. For information on patient advocacy and disease education, check out resources from the PFIC Advocacy and Resource Network at [PFIC.org](https://pfic.org) and Children's Liver Disease Foundation (CLDF) at childliverdisease.org.

About Albireo

Albireo Pharma is a rare disease liver company focused on the development of novel bile acid modulators to treat rare pediatric and adult liver diseases. Albireo's lead product, Bylvay, received European Commission (EC) authorization as the first drug approved for the treatment of all subtypes of progressive familial intrahepatic cholestasis (PFIC), while also being developed to treat other rare pediatric cholestatic liver diseases with Phase 3 trials in Alagille syndrome and biliary atresia, as well as an Open-label Extension (OLE) study for PFIC. The Company has also initiated a Phase 1 clinical trial for A3907 to advance development in adult cholestatic liver disease, with IND-enabling studies moving ahead with A2342 for viral and cholestatic liver disease. Albireo was spun out from AstraZeneca in 2008 and is headquartered in Boston, Massachusetts, with its key operating subsidiary in Gothenburg, Sweden. The Boston Business Journal named Albireo one of the 2020 Best Places to Work in Massachusetts for the second consecutive year. For more information on Albireo, please visit www.albiropharma.com.

Forward-Looking Statements

This press release includes "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include statements, other than statements of historical fact, regarding, among other things: Albireo's commercialization plans and expectations for commercializing Bylvay in the U.S. and the E.U., including the timing for commercial launch and related activities; estimates of the number of patients impacted by PFIC; the potential future approval of Bylvay by the FDA and, if approved, Albireo's plans to commercialize Bylvay in the U.S., expectations about Bylvay's acceptance by healthcare practitioners to treat PFIC patients; the plans for, or progress, scope, cost, initiation, duration, enrollment, results or timing for availability of results of, development of Bylvay or any other Albireo product candidate or program; the pivotal trial for Bylvay in biliary atresia (BOLD), and the pivotal trial for Bylvay in Alagille syndrome (ASSERT); the target indication(s) for development or approval, the size, design, population, location, conduct, cost, objective, enrollment, duration or endpoints of any clinical trial, or the timing for initiation or completion of or availability or reporting of results from any clinical trial, including the long-term open-label extension study for Bylvay in PFIC, and the BOLD and ASSERT trials; discussions with the FDA or EMA regarding our programs; the potential benefits or competitive position of Bylvay or any other Albireo product candidate or program or the commercial opportunity in any target indication; the potential effects of Bylvay of the treatment of PFIC patients and its potential to improve the current standard of care; the potential benefits of an orphan drug designation; or Albireo's plans, expectations or future operations, financial position, revenues, costs or expenses. Albireo often uses words such as "anticipates," "believes," "plans," "expects," "projects," "future," "intends," "may," "will," "should," "could," "estimates," "predicts," "potential," "planned," "continue," "guidance," or the negative of these terms or other similar expressions to identify forward-looking statements. Actual results, performance or experience may differ materially from those expressed or implied by any forward-looking statement as a result of various risks, uncertainties and other factors, including, but not limited to: there are no guarantees that Bylvay will be commercially successful; we may encounter issues, delays or other challenges in launching or commercializing Bylvay; whether Bylvay receives adequate reimbursement from third-party payors; the degree to which Bylvay receives acceptance from patients and physicians for its approved indication; challenges associated with execution of our sales activities, which in each case could limit the potential of our product; results achieved in Bylvay in the treatment of patients with PFIC once we have launched the product may be different than observed in clinical trials, and may vary among patients; whether the NDA for Bylvay for pruritus in PFIC will be approved by the FDA; whether the FDA will complete their review within the target timeline, as a potential result of the impact of the COVID-19 pandemic or otherwise; whether the FDA will require additional information, whether we will be able to provide in a timely manner any additional information that the FDA requests, and whether such additional information will be satisfactory to the FDA; other potential negative impacts of the COVID-19 pandemic, including on manufacturing, supply, conduct or initiation of clinical trials, or other aspects of our business; whether favorable findings from clinical trials of Bylvay to date, including findings in indications other than PFIC, will be predictive of results from other clinical trials of Bylvay; whether the FDA will determine that the primary endpoint for its evaluation and treatment duration of the double-blind Phase 3 trial in patients with PFIC are sufficient to support approval of Bylvay in the U.S., to treat pruritus in PFIC, or otherwise; the outcome and interpretation by regulatory authorities of the ongoing third-party study pooling and analyzing of long-term PFIC patient data; the timing for initiation or completion of, or for availability of data from, clinical trials of Bylvay, including BOLD and ASSERT, and the outcomes of such trials; Albireo's ability to obtain coverage, pricing or reimbursement for approved products in the United States or European Union; delays or other challenges in the recruitment of patients for, or the conduct of, company's clinical trials; and Albireo's critical accounting policies. These and other risks and uncertainties that Albireo faces are described in greater detail under the heading "Risk Factors" in Albireo's most recent Annual Report on Form 10-K or in subsequent filings that it makes with the Securities and Exchange Commission. As a result of risks and uncertainties that Albireo faces, the results or events indicated by any forward-looking statement may not occur. Albireo cautions you not to place undue reliance on any forward-looking statement. In addition, any forward-looking statement in this press release represents Albireo's views only as of the date of this press release and should not be relied upon as representing its views as of any subsequent date. Albireo disclaims any obligation to update any forward-looking statement except as required by applicable law.

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Source: Albireo Pharma, Inc.



Albireo Receives UK MHRA Approval of Bylvay® (odevixibat)

September 8, 2021

– Bylvay now approved in U.S., EU and UK as first drug treatment for patients with PFIC –

– Only once-daily drug indicated to treat all forms of PFIC –

– MHRA decision based on data from the largest Phase 3 PFIC trial to date –

BOSTON, Sept. 08, 2021 (GLOBE NEWSWIRE) -- Albireo Pharma, Inc. (Nasdaq: ALBO), a rare pediatric liver disease company developing novel bile acid modulators, today announced that the UK Medicines and Healthcare Products Regulatory Agency (MHRA) has granted marketing authorization for Bylvay (odevixibat) for the treatment of all types of progressive familial intrahepatic cholestasis (PFIC). Bylvay is a potent, non-systemic ileal bile acid transport inhibitor (IBATi), administered as a once-daily capsule or opened and sprinkled onto soft foods and which does not require refrigeration. The MHRA authorization follows the European Commission (EC) authorization of Bylvay in July 2021.

"The approval of Bylvay gives parents tremendous hope as the first drug treatment specifically for PFIC to be deemed safe and effective," said Alison Taylor, Chief Executive of Children's Liver Disease Foundation (CLDF). "The suffering and quality of life for children with PFIC is terrible, which is why we are so glad that Bylvay now has broad approval across Europe, and we are optimistic that it will be made available to patients in the UK."

The MHRA authorization was based on data from PEDFIC 1 and PEDFIC 2, the largest, global, Phase 3 trials ever conducted in PFIC. In PEDFIC 1, a randomized, double-blind, placebo-controlled study, Bylvay met both its pruritus ($p=0.004$) and serum bile acid ($p=0.003$) primary endpoints and was well tolerated with low incidence of drug-related diarrhea/frequent bowel movements (9.5% of treated patients vs. 5.0% of placebo patients). PEDFIC 2, a long-term, open-label Phase 3 extension study, affirmed Bylvay delivered sustained reductions in serum bile acid as well as improvements in pruritus assessments, growth and markers of liver function in patients treated up to 48 weeks in an interim analysis. Across both studies, Bylvay was well tolerated with diarrhea/frequent stools being the most common treatment-related gastrointestinal adverse events. There were no serious treatment-related adverse events reported in any clinical study with Bylvay.

"The approval of Bylvay in the UK marks an important milestone to provide global access to the first approved drug for children with PFIC who desperately need it," said Ron Cooper, President and Chief Executive Officer of Albireo. "We are excited that we now have broad approval across Europe so that we can continue our global launch efforts to make Bylvay available in over 30 countries worldwide."

Albireo has launched Bylvay in the U.S. and is working to commercialize Bylvay in Europe. Bylvay is currently being evaluated by NICE under the Highly Specialised Technologies (HST) pathway, and Albireo is working closely with NICE and NHS England to ensure access for patients in England and Wales as quickly as possible. The Company is also actively engaging with the Scottish Medicines Consortium (SMC). Albireo has developed a compelling value package with the PEDFIC gold standard Phase 3 data, natural history information and data from a recent study reflecting the burden of PFIC on caregivers and families.

Bylvay is currently being evaluated in the ongoing PEDFIC 2 open-label trial in patients with PFIC, ASSERT Phase 3 study for Alagille syndrome and in the BOLD Phase 3 study for patients with biliary atresia. The ASSERT and BOLD studies remain on track to report topline data in 2022 and 2024 respectively.

About Bylvay (odevixibat)

Bylvay is the first drug treatment approved in the U.S. for the treatment of pruritus in all types of progressive familial intrahepatic cholestasis (PFIC). The European Commission (EC) and UK Medicines and Healthcare Products Regulatory Agency (MHRA) have also granted marketing authorization of Bylvay for the treatment of PFIC and will be available for sale in Europe following pricing and reimbursement approval. A potent, once-daily, non-systemic ileal bile acid transport inhibitor, Bylvay acts locally in the small intestine. Bylvay does not require refrigeration and can be taken as a capsule for older children, or opened and sprinkled onto food, which are factors of key importance for adherence in a pediatric patient population. The medicine can only be obtained with a prescription and treatment should be started and supervised by a doctor who has experience in the management of PFIC. For more information about using Bylvay, see the package leaflet or contact your doctor or pharmacist. For full prescribing information, visit www.bylvay.com.

In the U.S. and Europe, Bylvay has orphan exclusivity for its approved PFIC indications, and orphan designations for the treatment of Alagille syndrome, biliary atresia and primary biliary cholangitis. Bylvay is being evaluated in the ongoing PEDFIC 2 open-label trial in patients with PFIC, in the BOLD Phase 3 study for patients with biliary atresia and the ASSERT Phase 3 study for Alagille syndrome.

About Albireo

Albireo Pharma is a rare disease company focused on the development of novel bile acid modulators to treat rare pediatric and adult liver diseases. Albireo's product, Bylvay, was approved by the U.S. FDA as the first drug for the treatment of pruritus in all types of progressive familial intrahepatic cholestasis (PFIC), and it is also being developed to treat other rare pediatric cholestatic liver diseases with Phase 3 trials in Alagille syndrome and biliary atresia, as well as an Open-label Extension (OLE) study for PFIC. In Europe, Bylvay has been approved for the treatment of PFIC and has been submitted for pricing and reimbursement approval. The Company has also initiated a Phase 1 clinical trial for A3907 to advance development in adult cholestatic liver disease, with IND-enabling studies moving ahead with A2342 for viral and cholestatic liver disease. Albireo was spun out from AstraZeneca in 2008 and is headquartered in Boston, Massachusetts, with its key operating subsidiary in Gothenburg, Sweden. The Boston Business Journal named Albireo one of the 2020 Best Places to Work in Massachusetts for the second consecutive year. For more information on Albireo, please visit www.albireopharma.com.

Forward-Looking Statements

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Source: Albireo Pharma, Inc.



MULTIMEDIA UPDATE - Albireo Announces FDA Approval of Bylvay™ (odevixibat), the First Drug Treatment for Patients With Progressive Familial Intrahepatic Cholestasis (PFIC)

July 20, 2021

– Only once-daily drug indicated for the treatment of pruritus in PFIC –

– Commercial launch of Bylvay immediate; available for prescription in the coming days –

– Rare Pediatric Disease Priority Review Voucher issued to Albireo by the FDA –

– Company to host investor conference call on July 21 at 8:30 a.m. ET –

BOSTON, July 20, 2021 (GLOBE NEWSWIRE) -- Albireo Pharma, Inc. (Nasdaq: ALBO), a rare liver disease company developing novel bile acid modulators, today announced U.S. Food & Drug Administration (FDA) approval of Bylvay (odevixibat), the first drug approved for the treatment of pruritus in all subtypes of progressive familial intrahepatic cholestasis (PFIC). Bylvay is a potent, non-systemic ileal bile acid transport inhibitor (IBATi), which does not require refrigeration and is easily administered as a once-daily capsule or opened and sprinkled onto soft foods. Albireo is launching Bylvay immediately to accelerate availability for the patients and families impacted by PFIC.

"Treating children with PFIC can be difficult and frustrating given the current treatment options. Bylvay gives us a non-surgical option and will change how we treat PFIC," said Richard Thompson, Professor of Molecular Hepatology at King's College London and principal investigator of PEDFIC 1 and PEDFIC 2. "With this approval, my colleagues and I now have the opportunity to revisit how PFIC patients are being managed and we are hopeful for better outcomes for these children."

PFIC is a rare and devastating disorder affecting young children that causes progressive, life-threatening liver disease. In many cases, PFIC leads to cirrhosis and liver failure within the first 10 years of life. The most prominent and problematic ongoing manifestation of PFIC is pruritus, or intense itching, which often results in a severely diminished quality of life. Until now, there have been no approved drugs for PFIC. Only surgical options that include biliary diversion surgery (BDS) and liver transplantation have been available, and without them, most PFIC patients do not survive past the age of 30. There are an estimated 100,000 patients with cholestatic liver disease without an approved drug treatment. Of those patients, there are approximately 15,000 with PFIC (excluding China and India).

"Until now invasive surgery was the only approved treatment option. With the approval of Bylvay, parents may find hope in having a less invasive treatment option available," said Emily Ventura, leader of PFIC Advocacy and Resource Network (www.pfic.org) and mother to a PFIC patient. "As a community, we experience extreme challenges and diminished quality of life for children and families with PFIC. Managing the symptoms can be extremely difficult -- the burden is unimaginable with our kids suffering physically, emotionally and developmentally."

The approval of Bylvay was supported by data from PEDFIC 1 and PEDFIC 2, the largest, global, Phase 3 trials ever conducted in PFIC. In [PEDFIC 1](#), a randomized, double-blind, placebo-controlled study, Bylvay met both its pruritus ($p=0.004$) and serum bile acid ($p=0.003$) primary endpoints and was well tolerated with very low incidence of diarrhea/frequent bowel movements (9.5% of treated patients vs. 5.0% of placebo patients). PEDFIC 2, a long-term, open-label Phase 3 extension study, reaffirmed Bylvay delivered sustained reductions in serum bile acids as well as improvements in pruritus assessments, growth and other markers of liver function in patients treated up to 48 weeks. Across both studies, Bylvay was well tolerated with diarrhea/frequent stools being the most common treatment-related gastrointestinal adverse events. There were no serious treatment-related adverse events.

"Bylvay is the first ever approval by the FDA of a drug developed for a pediatric cholestatic liver disease and provides a non-surgical treatment for patients living with the burden of PFIC," said Ron Cooper, President and CEO of Albireo. "We're humbled by the children, families and investigators whose commitment to our clinical trials will bring hope and treatment benefit for so many future patients."

Ready for Bylvay Launch

Bylvay is expected to be packaged and shipped within the coming days. With the immediate Bylvay launch, Albireo is ready with a focus on access and reimbursement, sales promotion, and patient support. To support payor decision-making, Albireo is submitting a compelling value package with the PEDFIC, gold standard, Phase 3 data, which includes long-term data with patients on drug for over two years; natural history information; and a caregiver study to reflect the burden of PFIC.

Sales promotion will begin immediately. The Albireo and Travele Therapeutics sales representatives will rapidly cover the 60 key centers to inform them of the availability of Bylvay for the treatment of pruritus in PFIC and patient access services.

Once Bylvay is prescribed, HCPs and families will have the option to use Albireo Assist™, which is a customized patient support program built with input from patient advocates. The program features dedicated, US-based regional Care Coordinators employed by Albireo who will investigate benefits and review financial assistance options to help ensure optimal patient access. They will also proactively assist with facilitating dosing changes, lab work, refill reminders, reauthorization and other activities.

Bylvay is the first commercially available drug for Albireo in the United States. With the U.S. approval, the FDA issued a Rare Pediatric Disease Priority Review Voucher (PRV), which the Company plans to monetize. The Company had cash and cash equivalents of \$186.3 million as of June 30, 2021 (unaudited) and anticipates the 2021 operating cash burn will be between \$130-\$135 million. Excluding any proceeds from the planned sale of the PRV, the Company believes that its cash and cash equivalents will fund its operating expenses and capital expenditure requirements into 2023, which should be sufficient to launch Bylvay and expansion beyond PFIC.

Albireo is also studying the use of Bylvay in other rare pediatric cholestatic liver diseases with the BOLD Phase 3 clinical trial in patients with biliary atresia and the ASSERT Phase 3 clinical trial in Alagille syndrome. Topline data from the ASSERT trial is expected in 2022 and the BOLD trial expected in 2024.

Conference Call

Albireo will host a conference call and webcast tomorrow, July 21, 2021 at 8:30 a.m. ET. To access the live conference call by phone, dial 877-407-0792 (domestic) or 201-689-8263 (international), and provide the access code 13720443. Live audio webcast will be accessible from the Albireo Media & Investors page ir.albireopharma.com/. To ensure a timely connection to the webcast, it is recommended that participants register at least 15 minutes prior to the scheduled start time. An archived version of the webcast will be available for replay on the Events & Presentations section of the Albireo Media & Investors page for three months following the event.

About Bylvay (odevixibat)

Bylvay is the first drug treatment approved in the U.S. for the treatment of pruritus in all subtypes of progressive familial intrahepatic cholestasis (PFIC). A potent, once-daily, non-systemic ileal bile acid transport inhibitor, Bylvay acts locally in the small intestine. Bylvay does not require refrigeration and can be taken as a capsule for older children, or opened and sprinkled onto food, which are factors of key importance for adherence in a pediatric patient population.

The recommended dosage of Bylvay is 40 mcg/kg once-daily in the morning with a meal. If there is an inadequate clinical response after three months, the dosage may be increased in 40 mcg/kg increments up to 120 mcg/kg once-daily not to exceed a total daily dose of 6 mg. The medicine can only be obtained with a prescription and treatment should be started and supervised by a doctor who has experience in the management of PFIC. For more information about using Bylvay, see the package leaflet or contact your doctor or pharmacist. For full prescribing information, visit www.bylvay.com.

The European Commission (EC) has granted marketing authorization of Bylvay in PFIC and will be available for sale in Europe following pricing and reimbursement approval. Bylvay has Orphan Designations for the treatment of Alagille syndrome, biliary atresia and primary biliary cholangitis. Bylvay is being evaluated in the ongoing PEDFIC 2 open-label trial in patients with PFIC, in the BOLD Phase 3 study for patients with biliary atresia and the ASSERT Phase 3 study for Alagille syndrome.

About PFIC

Progressive familial intrahepatic cholestasis (PFIC) is a rare disorder that causes progressive, life-threatening liver disease. Patients have impaired bile flow, or cholestasis, caused by genetic mutations. The resulting bile build-up in liver cells causes liver disease and symptoms. The most prominent and problematic ongoing manifestation of the disease is pruritus, or intense itching, which often results in a severely diminished quality of life. Other symptoms include jaundice, poor weight gain and slowed growth. In many cases, PFIC leads to cirrhosis and liver failure within the first 10 years of life, and nearly all people with PFIC require treatment before age 30. Until now, there were no drugs currently approved for PFIC, only surgical options that include partial external biliary diversion (PEBD) and liver transplantation. For information on patient advocacy and disease education, check out resources from the PFIC Advocacy and Resource Network at PFIC.org and Children's Liver Disease Foundation (CLDF) at childliverdisease.org.

About AlbireoAssist™

AlbireoAssist is designed to help patients and families access treatment with Bylvay. The program features dedicated, regional Care Coordinators to proactively assist with dosing changes, lab work, refill reminders, reauthorization and other activities. Care Coordinators will also help investigate benefits and review financial assistance options. Families with questions about AlbireoAssist and Albireo's patient support programs should contact AlbireoAssist at albireoassist.com | 855-ALBIREO (855-252-4736) 8am-6pm ET. Families outside the U.S. should call contact medinfo@albireopharma.com | 857-378-2035.

About Albireo

Albireo Pharma is a rare disease liver company focused on the development of novel bile acid modulators to treat rare pediatric and adult liver diseases. Albireo's lead product candidate, Bylvay, was approved by the U.S. FDA as the first for the treatment of pruritus in patients with all sub-types of progressive familial intrahepatic cholestasis (PFIC), while also being developed to treat other rare pediatric cholestatic liver diseases with Phase 3 trials in Alagille syndrome and biliary atresia, as well as an Open-label Extension (OLE) study for PFIC. In Europe, Bylvay has been approved for the treatment of PFIC and has been submitted for pricing and reimbursement approval. The Company has also initiated a Phase 1 clinical trial for A3907 to advance development in adult cholestatic liver disease, with IND-enabling studies moving ahead with A2342 for viral and cholestatic liver disease. Albireo was spun out from AstraZeneca in 2008 and is headquartered in Boston, Massachusetts, with its key operating subsidiary in Gothenburg, Sweden. The Boston Business Journal named Albireo one of the 2020 Best Places to Work in Massachusetts for the second consecutive year. For more information on Albireo, please visit www.albireopharma.com.

Forward-Looking Statements

This press release includes "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include statements, other than statements of historical fact, regarding, among other things: Albireo's commercialization plans and expectations for commercializing Bylvay in the U.S. and Europe; estimates of the number of patients impacted by PFIC; expectations about Bylvay's acceptance by healthcare practitioners to treat PFIC patients; Albireo's plans to monetize its Rare Pediatric Disease Priority Review Voucher; the plans for, or progress, scope, cost, initiation, duration, enrollment, results or timing for availability of results of, development of Bylvay or any other Albireo product candidate or program; the pivotal trial for Bylvay in biliary atresia (BOLD), and the pivotal trial for Bylvay in Alagille syndrome (ASSERT); the target indication(s) for development or approval, the size, design, population, location, conduct, cost, objective, enrollment, duration or endpoints of any clinical trial, or the timing for initiation or completion of or availability or reporting of results from any clinical trial, including the long-term open-label extension study for Bylvay in PFIC, and the BOLD and ASSERT trials; discussions with the FDA or EMA regarding our programs; the potential benefits or competitive position of Bylvay or any other Albireo product candidate or program or the commercial opportunity in any target indication; the potential effects of Bylvay of the treatment of PFIC patients and its potential to improve the current standard of care; the potential benefits of an orphan drug designation; the length of time for which Albireo's cash resources are expected to be sufficient, and the milestones and activities to be funded with those cash resources; or Albireo's plans, expectations or future operations, financial position, revenues, costs or expenses. Albireo often uses words such as "anticipates," "believes," "plans," "expects," "projects," "future," "intends," "may," "will," "should," "could," "estimates," "predicts," "potential," "planned," "continue," "guidance," or the negative of these terms or other similar expressions to identify forward-looking statements. Actual results, performance or experience may differ materially from those expressed or implied by any forward-looking statement as a

result of various risks, uncertainties and other factors, including, but not limited to: there are no guarantees that Bylvay will be commercially successful; we may encounter issues, delays or other challenges in launching or commercializing Bylvay; whether Bylvay receives adequate reimbursement from third-party payors; the degree to which Bylvay receives acceptance from patients and physicians for its approved indication; challenges associated with execution of our sales activities, which in each case could limit the potential of our product; results achieved in Bylvay in the treatment of patients with PFIC once we have launched the product may be different than observed in clinical trials, and may vary among patients; other potential negative impacts of the COVID-19 pandemic, including on manufacturing, supply, conduct or initiation of clinical trials, or other aspects of our business; whether favorable findings from clinical trials of Bylvay to date, including findings in indications other than PFIC, will be predictive of results from other clinical trials of Bylvay; the outcome and interpretation by regulatory authorities of the ongoing third-party study pooling and analyzing of long-term PFIC patient data; the timing for initiation or completion of, or for availability of data from, clinical trials of Bylvay, including BOLD and ASSERT, and the outcomes of such trials; Albireo's ability to obtain coverage, pricing or reimbursement for approved products in the United States or Europe; delays or other challenges in the recruitment of patients for, or the conduct of, company's clinical trials; and Albireo's critical accounting policies. These and other risks and uncertainties that Albireo faces are described in greater detail under the heading "Risk Factors" in Albireo's most recent Annual Report on Form 10-K or in subsequent filings that it makes with the Securities and Exchange Commission. As a result of risks and uncertainties that Albireo faces, the results or events indicated by any forward-looking statement may not occur. Albireo cautions you not to place undue reliance on any forward-looking statement. In addition, any forward-looking statement in this press release represents Albireo's views only as of the date of this press release and should not be relied upon as representing its views as of any subsequent date. Albireo disclaims any obligation to update any forward-looking statement except as required by applicable law.

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Photos accompanying this announcement are available at

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Source: Albireo Pharma, Inc.

Bylvay(TM) (odevixibat) - Product Photo



Bylvay(TM) is a once-daily drug indicated for the treatment of pruritus in PFIC

Pamela Stephenson



Pamela Stephenson, Chief Commercial Officer at Albireo

Patrick Horn, MD, Ph.D.



Patrick Horn, MD, Ph.D., Chief Medical Officer at Albireo

Ron Cooper



Ron Cooper, President and Chief Executive Officer at Albireo



NICE Recommends Albireo's Bylvay® (odevixibat) for All PFIC Types

February 22, 2022

– Decision provides access to the first drug treatment approved in PFIC for patients in England, Wales and Northern Ireland

– Positive NICE review completed in less than six months post MHRA approval

– NICE review is first successful clinical & economic benefit assessment of Bylvay completed in Europe

– Bylvay already submitted for reimbursement in multiple European countries

BOSTON, Feb. 22, 2022 (GLOBE NEWSWIRE) -- Albireo Pharma, Inc. (Nasdaq: ALBO), a rare liver disease company developing novel bile acid modulators, today announced that the National Institute for Health and Care Excellence (NICE) has issued guidance that recommends Bylvay (odevixibat) for the treatment of all types of progressive familial intrahepatic cholestasis (PFIC) in people aged six months and older. Bylvay is a potent, non-systemic ileal bile acid transport inhibitor (IBATI), administered as a once-daily treatment. With this final recommendation under the Highly Specialised Technologies (HST) pathway, Bylvay will be funded for use within 90 days in the National Health Service in England, Wales and Northern Ireland.

"It's incredibly gratifying to see children with PFIC gain access to the first ever non-surgical treatment option for a disease that causes tremendous suffering, in many cases leading to cirrhosis and liver failure within the first 10 years of life," said Richard Thompson, Professor of Molecular Hepatology at King's College London and principal investigator of PEDFIC 1 & PEDFIC 2 studies. "Odevixibat represents an important advance for patients, allowing us to respond to urgent treatment needs with a drug option that can provide clinically meaningful benefits and the ability to reduce the disease burden for patients and families who otherwise face PEBD surgery or liver transplant."

"Children living with PFIC have an incurable devastating disease that causes pruritus which was treated with liver transplantation. Until the recommendation from NICE, we've had no approved drug options to address this devastating disease," said Professor Deirdre Kelly, Consultant Paediatric Hepatologist, Liver Unit, Birmingham Women's and Children's Hospital and University of Birmingham. "My colleagues and I are delighted that we now have an effective non-surgical treatment option to reduce the burden of this disease on children and families and improve the quality of their lives."

The final NICE recommendation is aligned to the European Marketing Authorization (EMA) and UK Medicines and Healthcare Products Regulatory Agency (MHRA) approval as the first medicine for the treatment of PFIC, a rare and devastating disorder affecting young children that causes progressive, life-threatening liver disease. Patients with PFIC have impaired bile flow, or cholestasis, the resulting bile build-up in liver cells causes liver disease and symptoms such as intense itching, poor sleep, delayed growth and diminished quality of life. The harmful impacts of the disease extend beyond the individuals with PFIC to those caring for them as shown by the 2022 multinational PICTURE study, which revealed PFIC negatively affects caregivers' quality of life, relationships and career prospects.

"Bylvay is a ground-breaking drug that has the potential to transform the lives of children and young people living with PFIC and the families that care for them who experience terrible suffering and quality of life," said Alison Taylor, patient advocate and outgoing Chief Executive of Children's Liver Disease Foundation (CLDF). "We are delighted that Bylvay will be available to patients in the UK and commend NICE for their review and recommendation."

The NICE recommendation is based on data from PEDFIC 1 and PEDFIC 2, the largest, global, Phase 3 trials ever conducted in PFIC. In PEDFIC 1, a randomized, double-blind, placebo-controlled study, Bylvay met both its pruritus ($p=0.004$) and serum bile acid ($p=0.003$) primary endpoints and was well tolerated with low incidence of drug-related diarrhea/frequent bowel movements (9.5% of treated patients vs. 5.0% of placebo patients). PEDFIC 2, a long-term, open-label Phase 3 extension study, affirmed Bylvay delivered sustained reductions in serum bile acid as well as improvements in pruritus assessments, growth and sleep and markers of liver function in patients treated up to 48 weeks in an interim analysis. Across both studies, Bylvay was well tolerated. The most common adverse reactions for Bylvay were diarrhea, liver test abnormalities, vomiting, abdominal pain, and fat-soluble vitamin deficiency. There were no serious treatment-related adverse events reported in any clinical study with Bylvay.

"The positive NICE recommendation was rapidly obtained, within six months of MHRA approval, and it reinforces the significant benefit Bylvay offers to patients. We are pleased that more children will now have access to Bylvay," said Ron Cooper, President and Chief Executive Officer of Albireo. "Additional pricing and reimbursement discussions for Bylvay are ongoing across Europe and are being accelerated wherever possible. The early response has been encouraging, for example, in France Bylvay has received an SMR 'Important' and ASMR III from the HAS Transparency Committee."

About Bylvay (odevixibat)

Bylvay is the first drug approved in the U.S. for the treatment of pruritus in patients 3 months of age and older in all types of progressive familial intrahepatic cholestasis (PFIC). The European Commission (EC) and UK Medicines and Healthcare Products Regulatory Agency (MHRA) have also granted marketing authorization of Bylvay for the treatment of PFIC in patients aged 6 months or older. Bylvay is available in Germany and the UK and will be available for sale in other European countries following pricing and reimbursement approval. With the final NICE recommendation under the HST pathway, and the Company providing Bylvay according to commercial arrangement, Bylvay will be funded for use within 90 days in the National Health Service in England, Wales and Northern Ireland. Bylvay is a potent, once-daily, non-systemic ileal bile acid transport inhibitor. Bylvay acts locally in the small intestine. Bylvay can be taken as a capsule for patients that are able to swallow capsules, or opened and sprinkled onto food, which is a factor of key importance for adherence in a pediatric patient population. The most common adverse reactions for Bylvay are diarrhea, liver test

abnormalities, vomiting, abdominal pain, and fat-soluble vitamin deficiency. The medicine can only be obtained with a prescription. For more information about using Bylvay, see the package leaflet or contact your doctor or pharmacist. For full prescribing information, visit www.bylvay.com.

In the U.S. and Europe, Bylvay has orphan exclusivity for its approved PFIC indications, and orphan designations for the treatment of Alagille syndrome, biliary atresia and primary biliary cholangitis. Bylvay is being evaluated in the ongoing PEDFIC 2 open-label trial in patients with PFIC, in the BOLD Phase 3 study for patients with biliary atresia and the ASSERT Phase 3 study for Alagille syndrome.

About Albireo

Albireo Pharma is a rare disease company focused on the development of novel bile acid modulators to treat rare pediatric and adult liver diseases. Albireo's lead product, Bylvay, was approved by the U.S. FDA as the first drug for the treatment of pruritus in all types of progressive familial intrahepatic cholestasis (PFIC), and it is also being developed to treat other rare pediatric cholestatic liver diseases with Phase 3 trials in Alagille syndrome and biliary atresia, as well as an Open-label Extension (OLE) study for PFIC. In Europe, Bylvay has been approved for the treatment of PFIC with pricing listing in Germany and guidance from the National Institute for Health and Care Excellence (NICE) recommending Bylvay for use in the National Health Service in the England, Wales and Northern Ireland UK. The Company has also completed a Phase 1 clinical trial for A3907 to advance development in adult cholestatic liver disease, with IND-enabling studies progressing with A2342 for viral and cholestatic liver disease. Albireo was spun out from AstraZeneca in 2008 and is headquartered in Boston, Massachusetts, with its key operating subsidiary in Gothenburg, Sweden. The Boston Business Journal named Albireo one of the 2019 and 2020 Best Places to Work in Massachusetts. For more information on Albireo, please visit www.albireopharma.com.

Forward-Looking Statements

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Source: Albireo Pharma, Inc.

Efficacy and safety of odeixibat over 72 weeks of treatment in patients with progressive familial intrahepatic cholestasis

Richard J. Thompson¹, Emmanuel Gonzalès², Reha Artan³, Winita Hardikar⁴, Florence Lacaille⁵, Alain Lachaux⁶, Bertrand Roquelaure⁷, Ulrich Baumann⁸, Ekkehard Sturm⁹, Eyal Shteyer¹⁰, Pier Luigi Calvo¹¹, Henkjan J. Verkade¹², Mohammad Shagrani^{13,14}, Janis M. Stoll¹⁵, Piotr Czubkowski¹⁶, Buket Dalgic¹⁷, Girish Gupta¹⁸, Tassos Grammatikopoulos^{19,20}, Patrick McKiernan²¹, Qifeng Yu²², Lise Kjems²², Patrick Horn²²

¹Institute of Liver Studies, King's College London, London, UK; ²Hépatologie et Transplantation Hépatique Pédiatriques, Centre de Référence de l'Atrésie des Voies Biliaires et des Cholestases Génétiques, FSMR FILFOIE, ERN RARE LIVER, Hôpital Bicêtre, AP-HP, Université Paris-Saclay, Hépatinov, Inserm U 1193, Paris, France; ³Akdeniz University, Antalya, Turkey; ⁴Royal Children's Hospital, Melbourne, Australia; ⁵Paediatric Gastroenterology-Hepatology-Nutrition Unit, Hôpital Universitaire Necker-Enfants Malades, Paris, France; ⁶Hospices Civils de Lyon, Hôpital Femme-Mère-Enfant, Service D'hépatogastroentérologie et Nutrition Pédiatrique, Lyon, France; ⁷CHU, Hospital de la Timone, Marseille, France; ⁸Paediatric Gastroenterology and Hepatology, Hannover Medical School, Hannover, Germany; ⁹Paediatric Gastroenterology and Hepatology, University Children's Hospital Tübingen, Tübingen, Germany; ¹⁰Faculty of Medicine, Hebrew University of Jerusalem, Juliet Keidan Department of Paediatric Gastroenterology, Shaare Zedek Medical Centre, Jerusalem, Israel; ¹¹Paediatric Gastroenterology Unit, Regina Margherita Children's Hospital, Azienda Ospedaliera Città della Salute e della Scienza di Torino, Turin, Italy; ¹²Department of Paediatrics, University of Groningen, Beatrix Children's Hospital/University Medical Centre Groningen, Groningen, the Netherlands; ¹³King Faisal Specialist Hospital and Research Centre–Organ Transplant Centre, Riyadh, Saudi Arabia; ¹⁴College Of Medicine-Alfaisal University, Riyadh, Saudi Arabia; ¹⁵Department of Paediatrics, Washington University School of Medicine, St. Louis, Missouri, USA; ¹⁶Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, The Children's Memorial Health Institute, Warsaw, Poland; ¹⁷Department of Paediatric Gastroenterology, Gazi University

Faculty of Medicine, Ankara, Turkey; ¹⁸Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey; ¹⁹Liver Unit and Small Bowel Transplantation, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK; ²⁰Institute of Liver Studies, King's College London, London, UK; ²¹Division of Gastroenterology/Hepatology/Nutrition, UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA, USA; ²²Albireo Pharma, Inc., Boston, MA, USA

Background and Aims: Progressive familial intrahepatic cholestasis (PFIC) is a group of paediatric cholestatic liver diseases characterised by disruption of bile production and transport, pruritus, and progressive liver disease. Here, using pooled data from two phase 3 studies in patients with PFIC (PEDFIC 1 and PEDFIC 2), we describe key long-term outcomes with odevixibat, an ileal bile acid transporter inhibitor, in the subgroup of patients treated with odevixibat for ≥ 72 weeks.

Method: PEDFIC 1 was a 24-week, placebo-controlled, double-blind study of odevixibat in children with PFIC1 or PFIC2. PEDFIC 2 is an ongoing, 72-week extension study in patients of any age with any type of PFIC. This pooled analysis spans from patients' first dose of odevixibat in PEDFIC 1 or PEDFIC 2 to a cut-off of December 4, 2020. The following outcomes are described over time in the subgroup of patients who had ≥ 72 weeks of exposure to odevixibat: serum bile acids (sBAs), caregiver-reported pruritus score (range, 0–4; higher scores indicate worse symptoms), laboratory parameters, growth, and safety.

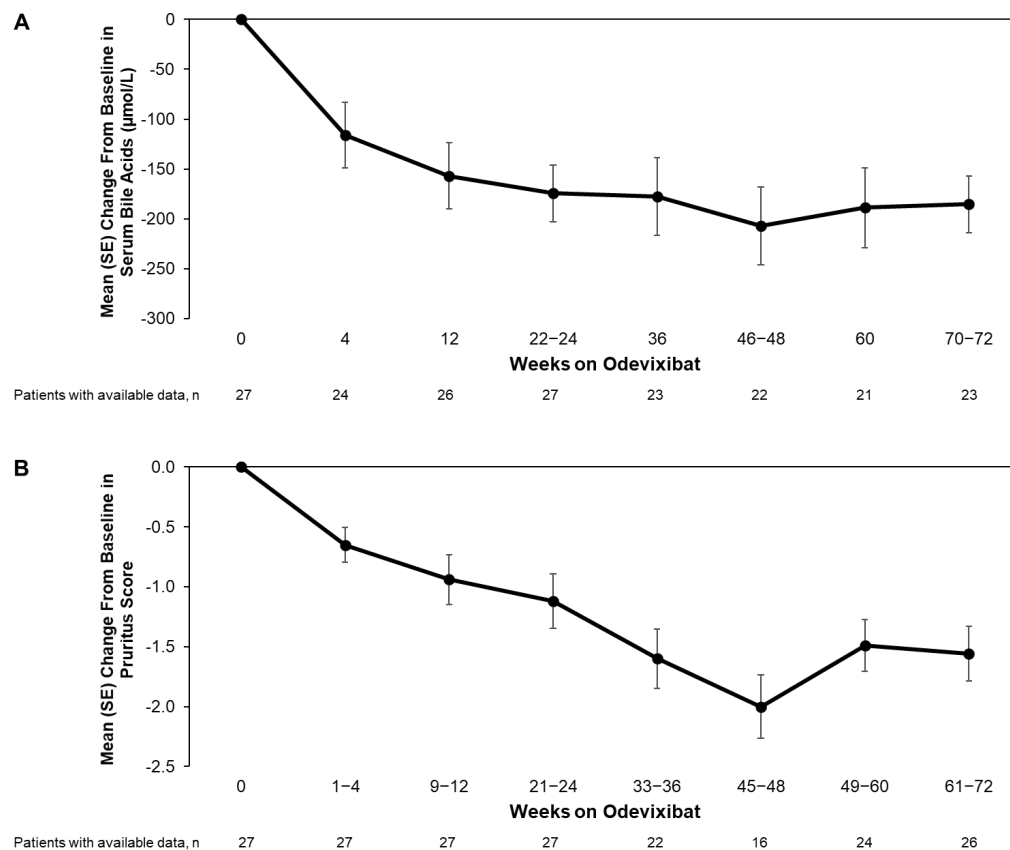
Results: Of 84 patients in the pooled population, 27 were treated with odevixibat for ≥ 72 weeks (median [range], 92 [76–128] weeks). Of these 27 patients (mean age, 3 years), 52% were male, 70% had PFIC2, and 30% had PFIC1. At baseline, 82% of these 27 patients were using ursodeoxycholic acid (UDCA), 56% were using

rifampicin, and 89% were using UDCA and/or rifampicin. Mean (SE) sBA levels at baseline were 291 (26) $\mu\text{mol/L}$, which decreased by -185 (28) at weeks 70–72 of odevixibat treatment (**Figure**). Mean (SE) pruritus score at baseline was 2.9 (0.1), which decreased by -1.56 (0.2) at weeks 61–72 (**Figure**). At week 72 of odevixibat treatment, decreases in alanine aminotransferase (-64.9 U/L), aspartate aminotransferase (-18.8 U/L), and total bilirubin (-5.4 $\mu\text{mol/L}$) were also observed; mean (SE) height and weight Z scores increased by 0.8 (0.1) and 0.5 (0.2), respectively. In this group of patients with ≥ 72 weeks of odevixibat treatment, 26 (96%) patients experienced any treatment-emergent adverse event (TEAE) and 52% experienced drug-related TEAEs. There were no TEAEs leading to discontinuation.

Conclusion: Odevixibat was well tolerated and demonstrated durable clinical treatment benefits for up to 72 weeks in improving sBA levels, pruritus scores, hepatic parameters, and growth in patients with PFIC who were treated for at least 72 weeks.

Figure

Change From Baseline in sBA Levels (A) and Pruritus (B) in Patients Treated With Odevixibat for ≥ 72 Weeks



Conflicts of Interest

Richard J. Thompson is a consultant for Albireo, Alnylam, EVOX Therapeutics, Generation Bio, Mirum, Rectify Therapeutics, Retrophin, Qing Therapeutics, and Sana Biotechnology.

Emmanuel Gonzales is a consultant for Laboratoires C.T.R.S., Mirum, and Albireo.

Reha Artan has nothing to disclose.

Winita Hardikar has nothing to disclose.

Florence Lacaille is a consultant for Alexion.

Alain Lachaux is a consultant for GMP-Orphan and CSL Behring.

Bertrand Roquelaure has nothing to disclose.

Ulrich Baumann is a consultant for Albireo, Mirum, Alnylam, Vivet and Nestlé.

Ekkehard Sturm is a consultant for and/or received travel support from Albireo, Mirum, and Astellas.

Eyal Shteyer has nothing to disclose.

Pier Luigi Calvo has nothing to disclose.

Henkjan J. Verkade is a consultant for Ausnutria BV, Albireo, Danone/Nutricia Research, Intercept, Mirum, Orphalan, and Vivet.

Mohammad Shagrani has nothing to disclose.

Janis M. Stoll has nothing to disclose.

Piotr Czubkowski has nothing to disclose.

Buket Dalgic has nothing to disclose.

Girish Gupte has nothing to disclose.

Tassos Grammatikopoulos is a consultant for Albireo.

Patrick McKiernan is a consultant for SOBI AB and Albireo.

Qifeng Yu is an employee of Albireo.

Lise Kjems was an employee of Albireo. at the time of the study.

Patrick Horn is an employee of Albireo.

Changes in hepatic parameters, growth, sleep, and biochemical markers with odevixibat treatment across patients with various types of progressive familial intrahepatic cholestasis

Lorenzo D'Antiga¹, Girish Gupte², Richard J. Thompson³, Ekkehard Sturm⁴, Pier Luigi Calvo⁵, Mohammad Shagrani^{6,7}, Janis M. Stoll⁸, Reha Artan⁹, Buket Dalgic¹⁰, Hasan Özen¹¹, Kathleen M. Loomes¹², Jennifer M. Vittorio¹³, Saul J. Karpen¹⁴, Angelo Di Giorgio¹⁵, Quanhong Ni¹⁶, Lise Kjems¹⁶, Patrick Horn¹⁶

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Background and Aims: PEDFIC 1 and PEDFIC 2 evaluated the safety and efficacy of odevixibat, an ileal bile acid transporter inhibitor, in patients with progressive familial intrahepatic cholestasis (PFIC). Using pooled data from these studies, we

analysed secondary and exploratory endpoints in patients with PFIC type 1 (PFIC1), 2 (PFIC2), 3 (PFIC3), and 6 (PFIC6).

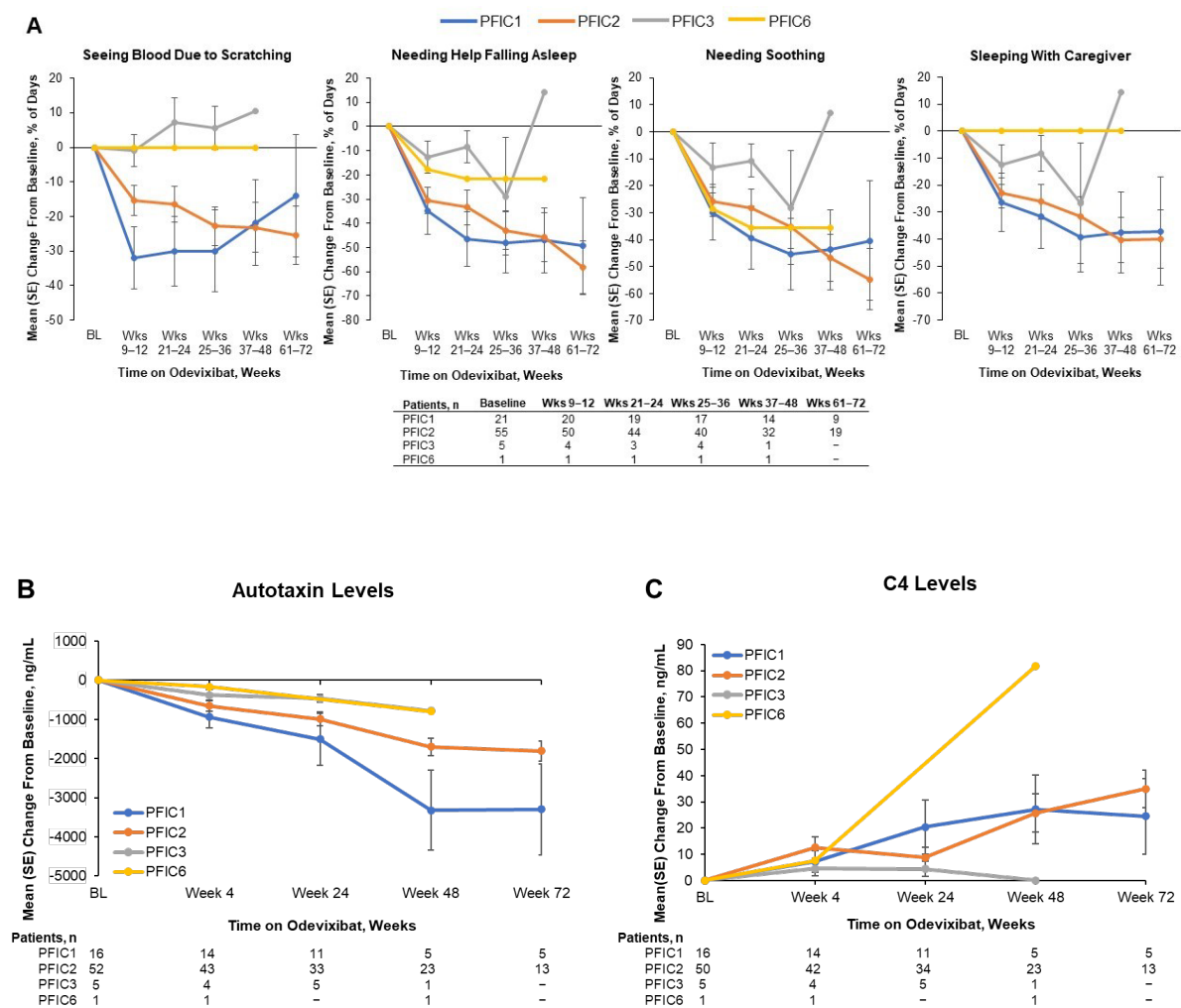
Method: PEDFIC 1 was a 24-week, randomised, placebo-controlled study in children with PFIC1 and PFIC2. PEDFIC 2 is an ongoing 72-week extension study in patients with any PFIC type. This pooled analysis spans from patients' first dose of odevixibat to a cut-off of 4 December 2020. Assessments included changes from baseline (BL) in alanine aminotransferase (ALT), total bilirubin, growth, caregiver-reported sleep parameters, autotaxin, and 7 α -hydroxy-4-cholesten-3-one (C4); data are presented to wk72 of odevixibat treatment for patients with PFIC1 and PFIC2 and to wk36 or wk48 for patients with PFIC3 and PFIC6 (who have less time on treatment vs patients with PFIC1 or PFIC2, who could have participated in PEDFIC 1).

Results: Of 84 patients in the pooled population (mean age, 5.0 years), 26% had PFIC1 (n = 22), 67% PFIC2 (n = 56), 6% PFIC3 (n = 5), and 1% PFIC6 (n = 1). With odevixibat, mean changes in ALT levels to wk72 in patients with PFIC1 (n = 6) and PFIC2 (n = 15) who reached this timepoint as of the data cut-off were –14 U/L and –85 U/L, respectively; mean changes in ALT levels to wk36 in patients with PFIC3 (n = 4) and PFIC6 (n = 1) were 67 U/L and 89 U/L. Patients with PFIC1 and PFIC2 with available data at wk72 had mean changes in total bilirubin of –6 μ mol/L and –5 μ mol/L, respectively; for patients with PFIC3 and PFIC6, mean changes to wk36 were 18 μ mol/L and –83 μ mol/L. Mean height and weight Z scores increased with odevixibat treatment across the various types of PFIC. Sleep parameters, C4, and autotaxin improved over time in almost all PFIC types (**Figure**). Across PFIC types, most treatment-emergent adverse events with odevixibat were mild or moderate in severity.

Conclusion: In patients with PFIC treated with odevixibat assessed to date, growth improved, autotaxin levels decreased, and C4 levels increased over time; changes in hepatic and sleep parameters in some PFIC types were more variable (eg, PFIC3, PFIC6), but these conclusions may be limited by the small size of these subgroups, particularly at later timepoints. Odevixibat was generally well tolerated.

Figure

Changes From BL in Sleep Parameters (A), Autotaxin Levels (B), and C4 Levels (C) Over Time With Odevixibat Treatment by PFIC Type



Conflicts of Interest

L. D'Antiga: Albireo, Alexion, Mirum, Selecta, Vivet, and Spark – Consultant

G. Gupte, P.L. Calvo, M. Shagrani, R. Artan, B. Dalgic , H. Özen, J.M. Stoll, and

A. Di Giorgio: Nothing to disclose

R.J. Thompson: Albireo, Alnylam, Evox Therapeutics, Generation Bio, Mirum, Rectify Therapeutics, Retrophin, Qing Therapeutics, and Sana Biotechnology – Consultant

E. Sturm: Albireo, Mirum, and Astellas – Consultant and/or received travel support

K.M. Loomes: Albireo, Mirum and Traverre Therapeutics – Consultant

J.M. Vittorio: Mirum – Consultant

S.J. Karpen: Albireo, Intercept, Mirum, and Vertex – Consultant

Q. Ni, P. Horn, and L. Kjems: Albireo – Current or former employment

Changes in Hepatic Parameters, Growth, Sleep, and Biochemical Markers With Odevixibat Treatment Across Patients With Various Types of Progressive Familial Intrahepatic Cholestasis

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Objectives and Study: PEDFIC 1 and PEDFIC 2 evaluated the safety and efficacy of odevixibat, an ileal bile acid transporter inhibitor, in patients with progressive familial intrahepatic cholestasis (PFIC). Using pooled data from these studies, we analysed secondary and exploratory endpoints in patients with PFIC type 1 (PFIC1), 2 (PFIC2), 3 (PFIC3), and 6 (PFIC6).

Methods: PEDFIC 1 was a 24-week, randomised, placebo-controlled study in children with PFIC1 and PFIC2. PEDFIC 2 is an ongoing 72-week extension study in patients with any PFIC type. This pooled analysis spans from patients' first dose of odevixibat to a cut-off of 4 December 2020. Assessments included changes from baseline in alanine aminotransferase (ALT), total bilirubin, growth, caregiver-reported sleep parameters, autotaxin, and 7 α -hydroxy-4-cholesten-3-one (C4); data are presented to week 72 of odevixibat treatment for patients with PFIC1 and PFIC2 and to week 36 or week 48 for patients with PFIC3 and PFIC6 (who have less time on treatment vs patients with PFIC1 or PFIC2, who could have participated in PEDFIC 1).

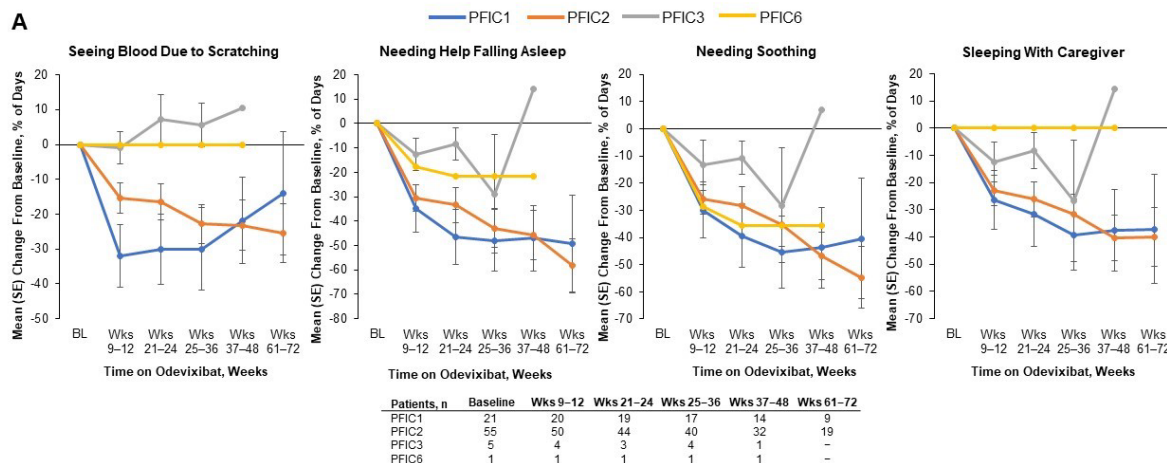
Results: Of 84 patients in the pooled population (mean age, 5.0 years), 26% had PFIC1 (n=22), 67% PFIC2 (n=56), 6% PFIC3 (n=5), and 1% PFIC6 (n=1). With odevixibat, mean changes in ALT levels to week 72 in patients with PFIC1 (n=6) and PFIC2 (n=15) who reached this time point as of the data cut-off were -14 U/L and -85 U/L, respectively; mean changes in ALT levels to week 36 in patients with PFIC3 (n=4) and PFIC6 (n=1) were 67 U/L and 89 U/L. Patients with PFIC1 and PFIC2 with available data at week 72 had mean changes in total bilirubin of -6 μ mol/L and -5 μ mol/L, respectively; for patients with PFIC3 and PFIC6, mean changes to week 36 were 18 μ mol/L and -83 μ mol/L. Mean height and weight Z scores increased with odevixibat treatment across the various types of PFIC. Sleep parameters, C4, and autotaxin

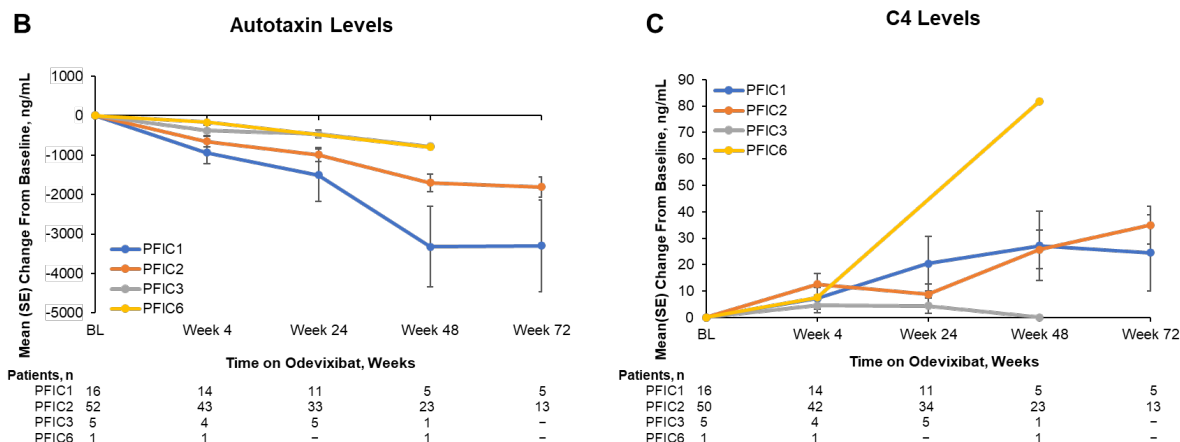
improved over time in almost all PFIC types (**Figure**). Across PFIC types, most treatment-emergent adverse events with odeixibat were mild or moderate in severity.

Conclusion: In patients with PFIC treated with odeixibat assessed to date, growth improved, autotaxin levels decreased, and C4 levels increased over time; changes in hepatic and sleep parameters in some PFIC types were more variable (eg, PFIC3, PFIC6), but these conclusions may be limited by the small size of these subgroups, particularly at later time points. Odeixibat was generally well tolerated.

Figure

Changes From BL in Sleep Parameters (A), Autotaxin Levels (B), and C4 Levels (C) Over Time With Odeixibat Treatment by PFIC Type





Conflict of interest disclosure

L. D'Antiga: Albireo, Alexion, Mirum, Selecta, Vivet, and Spark – Consultant

G. Gupte, P.L. Calvo, M. Shagrani, R. Artan, B. Dalgic, H. Özen, J.M. Stoll, and A.

Di Giorgio: Nothing to disclose

R.J. Thompson: Albireo, Alnylam, Evox Therapeutics, Generation Bio, Mirum, Rectify Therapeutics, Retrophin, Qing Therapeutics, and Sana Biotechnology – Consultant

E. Sturm: Albireo, Mirum, and Astellas – Consultant and/or received travel support

K.M. Loomes: Albireo, Mirum, and Traveo Therapeutics – Consultant

J.M. Vittorio: Mirum – Consultant

S.J. Karpen: Albireo, Intercept, Mirum, and Vertex – Consultant

Q. Ni, L. Kjems, and P. Horn: Albireo – Current or former employment

Abstract topic: HEPATOLOGY; General Hepatology

Efficacy and Safety Outcomes in Patients With Progressive Familial Intrahepatic Cholestasis Who Had an Odevixibat Dose Escalation: Pooled Results From the PEDFIC 1 and PEDFIC 2 Studies

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Objectives and Study: Using pooled data from the phase 3 PEDFIC 1 and PEDFIC 2 studies of the ileal bile acid transporter inhibitor odevixibat in patients with progressive familial intrahepatic cholestasis (PFIC), we report efficacy and safety outcomes in a subset of patients who escalated odevixibat dose from 40 (O-40) to 120 µg/kg/day (O-120).

Methods: In the 24-week PEDFIC 1 study, children could receive O-40 or O-120. PEDFIC 2 is an ongoing 72-week extension study that enrolled patients from PEDFIC 1 or new patients; all receive O-120. This pooled analysis spans from patients' first dose of odevixibat to a cut-off date of 4 December 2020. Efficacy outcomes evaluated in patients who escalated from O-40 in PEDFIC 1 to O-120 in PEDFIC 2 included changes in pruritus and serum bile acids (sBAs) in pruritus responders (Rs; ≥1-point drop in pruritus score) and in sBA Rs (sBAs reduced by ≥70% or levels ≤70 µmol/L) and nonresponders (NRs). Caregivers scored pruritus (range: 0–4). Treatment-emergent adverse events (TEAEs) were monitored.

Results: In the pooled analysis population (N=84), 21 patients had an odevixibat dose escalation (mean age, 3.4 y; median exposure, 24 wk [O-40] and 64 wk [O-120]). While receiving O-40 during PEDFIC 1, 12 patients were pruritus Rs and 9 were NRs. Of these 9 NRs, 4 (44%) became pruritus Rs with O-120 treatment by week 12 of PEDFIC 2 (**Table**). While receiving O-40 during PEDFIC 1, 11 patients were sBA Rs and 10 were NRs. Of the 6 sBA NRs with available data at PEDFIC 2 weeks 22/24, 1 patient (17%) became an sBA R (**Table**). Most O-40 Rs remained Rs with dose escalation to O-120 (**Table**). In patients with dose escalation, 15/21 experienced any gastrointestinal TEAEs, but no serious TEAEs or TEAEs leading to treatment discontinuation occurred.

Conclusion: Among odeixibat-treated patients with PFIC who had a dose escalation from O-40 to O-120, additional patients became pruritus Rs. Odeixibat was generally well tolerated throughout dose escalation.

Table. Pruritus and sBA Responses in Patients With Odeixibat Dose Escalation in PEDFIC 2

		PEDFIC 1 Rs on 40 µg/kg/day		PEDFIC 1 NRs on 40 µg/kg/day	
		R on 120 µg/kg/day n/N (%)	NR on 120 µg/kg/day n/N (%)	R on 120 µg/kg/day n/N (%)	NR on 120 µg/kg/day n/N (%)
Pruritus response	Wk 9–12	12/12 (100)	0/12 (0)	4/9 (44)	5/9 (56)
	Wk 21–24	9/9 (100)	0/9 (0)	4/9 (44)	5/9 (56)
sBA response	Wk 12	8/10 (80)	2/10 (20)	0/10 (0)	10/10 (100)
	Wk 22/24	9/10 (90)	1/10 (10)	1/6 (17)	5/6 (83)

Conflict of interest disclosure

T. Grammatikopoulos: Albireo – Consultant

B. Dalgic, G. Gupte, B. Roquelaure, P. L. Calvo, R. Artan, H. Özen, and S. R. Rajwal: Nothing to disclose

F. Lacaille: Alexion – Consultant

A. Lachaux: GMP-Orphan and CSL Behring – Consultant

U. Baumann: Albireo, Mirum, Alnylam, Vivet, and Nestlé – Consultant

E. Sturm: Albireo, Mirum, and Astellas – Consultant and/or received travel support

C. L. Mack: Albireo – Consultant

Q. Ni, L. Kjems, and P. Horn: Albireo – Current or former employment

Abstract topic: HEPATOLOGY; General Hepatology

Total, Primary, and Secondary Serum Bile Acid Concentrations in Patients With Progressive Familial Intrahepatic Cholestasis With Serum Bile Acid Response or Not With Odevixibat Treatment: Assessing the Contribution of Ursodeoxycholic Acid Concentration

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Objectives and Study: Children with progressive familial intrahepatic cholestasis (PFIC) who received odevixibat in the 24-week PEDFIC 1 study had significant reductions in total serum bile acids (sBAs) vs placebo-treated patients. These study data supported odevixibat approval in the European Union for the treatment of PFIC in patients aged 6 months or older. Here, we evaluated the effect of concomitant ursodeoxycholic acid (UDCA) on sBA concentrations in odevixibat-treated patients from PEDFIC 1 (n=42) who met sBA response (R) criteria or not; we also assessed whether excluding UDCA concentrations from total sBA measurements altered the proportion of patients with sBA R.

Methods: Patients eligible for PEDFIC 1 had elevated sBAs at screening. Concomitant UDCA was allowed provided the patient's dose was stable. In PEDFIC 1, sBA concentrations were evaluated via a colorimetric enzymatic assay. The PEDFIC 1

per-protocol definition of sBA R was sBAs ≤ 70 $\mu\text{mol/L}$ or sBA levels reduced $\geq 70\%$ from baseline (BL) based on the average of sBA measurements taken at weeks 22 and 24; those not meeting this criteria, including early-exit patients (ie, patients who prematurely discontinued treatment or who rolled over early to the extension study), were considered nonresponders (NRs). Using this per-protocol definition of sBA R and sBA concentrations evaluated via mass spectrometry (described subsequently), the rate of sBA R excluding the contribution of UDCA was also analysed. Finally, the proportion of patients who met sBA R was re-evaluated using the following updated definition: sBAs ≤ 70 $\mu\text{mol/L}$ or sBA levels reduced $\geq 70\%$ from BL based on the average of sBA measurements taken at weeks 22 and 24 for treatment completers and based on the last available sBA assessment for early-exit patients (using colorimetric assay-derived data). sBA concentration and composition (ie, total, primary, and secondary sBAs, with UDCA concentration included as a secondary BA) were evaluated at BL and at the end of treatment (EOT) using liquid chromatography–tandem mass spectrometry. Secondary sBA concentrations (and therefore, total sBAs) were evaluated with and without UDCA concentration included.

Results: In the primary analysis of PEDFIC 1 study data, 14/42 patients met criteria for sBA R at EOT. When using the same per-protocol definition but with the contribution of UDCA excluded, 13/42 of patients met sBA R criteria. In addition, when an updated R definition was used, 17/42 patients had an sBA R (3 early-exit patients were now counted as having an sBA R). Median concentrations of total and primary sBAs decreased considerably from BL to EOT in these Rs both with and without UDCA; however, these parameters remained largely unchanged in NRs regardless of whether UDCA concentration was considered (**Table**). In all odeixibat-treated patients

regardless of sBA R status, median values for secondary sBAs without UDCA at BL and at EOT were near 0 (**Table**).

Conclusion: The proportion of patients with sBA R to odeixibat in PEDFIC 1 did not change appreciably when serum UDCA concentrations were excluded from total sBA levels. In addition, in those with sBA R per an updated definition, large reductions in sBAs occurred whether or not UDCA concentration was included.

Table: Summary of Median sBA Concentrations in sBA Responders^a and Nonresponders With and Without UDCA Concentration Included: Data From Odeixibat-Treated Patients in the PEDFIC 1 Study

		Total sBAs, μmol/L		Primary sBAs, μmol/L		Secondary sBAs, μmol/L	
		R	NR	R	NR	R	NR
With UDCA	Baseline	185	261	134	195	54	36
	EOT	8.5	260	4.7	201	2.4	57
Without UDCA	Baseline	135	197	134	195	0.3	0.3
	EOT	4.7	202	4.7	201	0.0	0.2

^aR defined as ≥70% reduction in fasting sBA concentration from baseline to EOT or sBA levels ≤70 μmol/L at EOT; EOT was the average of sBA measurements taken at weeks 22 and 24 for treatment completers and the last available sBA assessment for early-exit patients. EOT, end of treatment; NR, responder; R, responder; sBA, serum bile acid; UDCA, ursodeoxycholic acid.

Conflict of interest disclosure

H.J. Verkade: Ausnutria BV, Albireo, Danone/Nutricia Research, Intercept, Mirum, Orphalan, and Vivet – Consultant

F. Kuipers: Albireo – Consultant

Q. Ni and V. Valcheva: Albireo – Employment

Abstract topic: HEPATOLOGY; General Hepatology

Analysis of quality of life, hepatic biochemical markers, and sleep in patients with progressive familial intrahepatic cholestasis who had a pruritus response with odevixibat treatment

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Background and Aims: Patients with progressive familial intrahepatic cholestasis (PFIC), a group of rare paediatric cholestatic liver diseases, have debilitating symptoms including severe pruritus that can impact sleep and quality of life (QoL). In the phase 3 PEDFIC 1 and PEDFIC 2 studies, the ileal bile acid transporter inhibitor odevixibat reduced serum bile acids (sBAs) and improved pruritus and sleep in children with PFIC. Using pooled data from these studies, we examined secondary and exploratory efficacy endpoints and safety outcomes in patients who met criteria for a pruritus response with odevixibat treatment.

Method: PEDFIC 1 was a 24-week, randomised, placebo-controlled study in children with PFIC1 or PFIC2. PEDFIC 2 is an ongoing 72-week extension study in patients of with any PFIC type. Pruritus was rated using the Albireo observer-reported outcome instrument (range: 0–4). This pooled analysis spans from patients' first dose of odevixibat to a cut-off of 4 December 2020. We analysed sBAs, QoL (Pediatric QoL Inventory [PedsQL] and PedsQL family impact [FI] questionnaire; higher scores indicate improved QoL), alanine aminotransferase (ALT), total bilirubin, sleep parameters, and treatment-emergent adverse events (TEAEs) in patients with a pruritus response (ie, ≥ 1 -point drop in pruritus score from baseline) following odevixibat treatment.

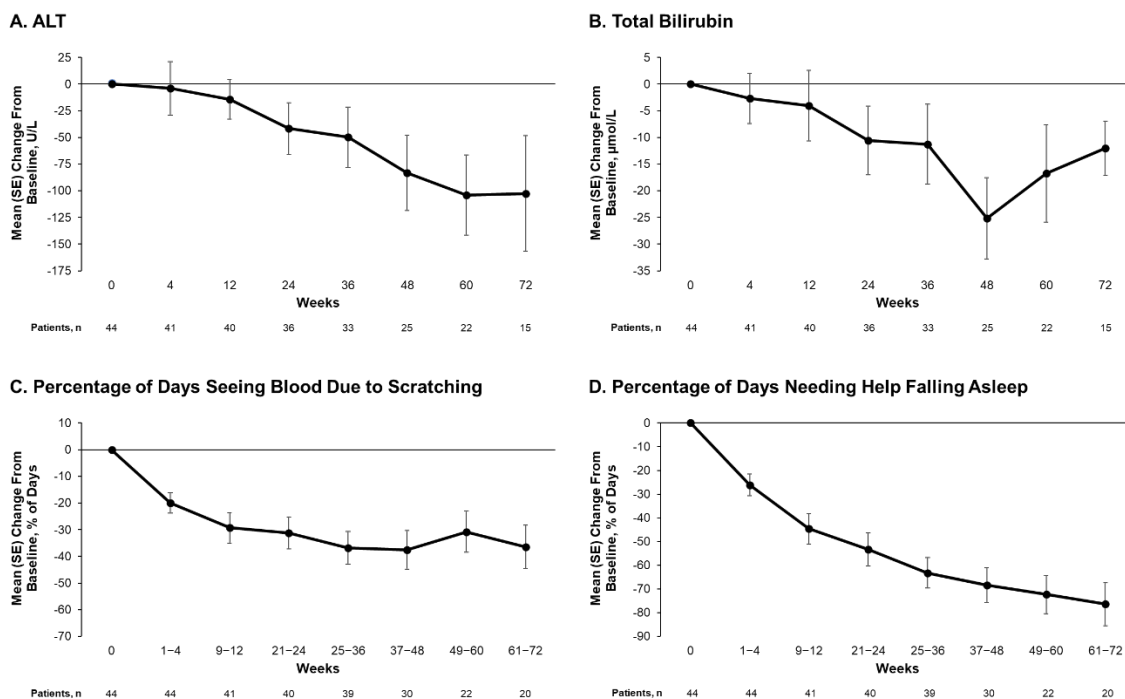
Results: Of 82 patients in the pooled population (of whom, 49% were female), 44 (54%) were pruritus responders. Of these 44 pruritus responders (mean age, 4.6 years), 24 (55%) were female; 23%, 68%, and 7% had PFIC 1, 2, and 3, respectively. Mean sBA levels were 247 $\mu\text{mol/L}$ at baseline ($n = 44$) and decreased

over time by 77% at weeks 70–72 in pruritus responders who reached this timepoint (n = 18). Mean PedsQL and FI total scores were 56 (n = 30) and 50 (n = 42) at baseline and increased by 11 (n = 8) and 24 (n = 14) at week 72, respectively, in pruritus responders. Mean ALT and total bilirubin levels decreased over time from 109 U/L and 40 $\mu\text{mol/L}$ at baseline to 40 U/L and 18 $\mu\text{mol/L}$ (n = 15) (**Figure 1A, B**), and sleep parameters improved over time in these patients (**Figure 1C, D**). There were no drug-related serious TEAEs.

Conclusion: Overall, patients with PFIC with a pruritus response following treatment with odevixibat experienced improvements in sBAs, QoL, hepatic biochemical markers, and sleep parameters that were sustained over time. Odevixibat was generally well tolerated.

Figure

Mean Changes From Baseline in ALT, Bilirubin, and Sleep Parameters With Odevixibat in Pruritus Responders



Conflicts of Interest

G. Gupte, B. Roquelaure, E. Lainka, E. Shteyer, P. Czubkowski, R. Artan, B. Dalgic, H. Özen, and A. Di Giorgio:

Nothing to disclose

R. J. Thompson: Albireo, Alnylam, EVOX Therapeutics, Generation Bio, Mirum, Rectify Therapeutics, Retrophin, Qing Therapeutics, and Sana Biotechnology – Consultant

L. D’Antiga: Albireo, Alexion, Mirum, Selecta, Vivet, and Spark – Consultant

T. Grammatikopoulos: Albireo – Consultant

B. M. Kamath: Albireo, Mirum, and Audentes – Consultant; Albireo and Mirum – Unrestricted educational grants

E. Gonzales: Laboratoires C.T.R.S., Mirum, and Albireo – Consultant

F. Lacaille: Alexion – Consultant

A. Lachaux: GMP-Orphan and CSL Behring – Consultant

U. Baumann: Albireo, Mirum, Alnylam, Vivet, and Nestlé – Consultant

E. Sturm: Albireo, Mirum, and Astellas– Consultant and/or travel support

K. M. Loomes: Albireo, Mirum, and Traverre Therapeutics – Consultant

J. M. Vittorio: Mirum – Consultant

S. J. Karpen: Albireo, Intercept, LogicBio, Mirum, and Spruce Biosciences – Consultant

P. McKiernan: SOBI AB and Albireo – Consultant

C. L. Mack: Albireo – Consultant

Q. Yu, L. Kjems, P. Horn: Albireo – Current or former employment