New Phase 3 Data at AASLD Show Durable Response to Odevixibat in a Rare Pediatric Liver Disease

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- PEDFIC 1 meets both U.S. and EU primary and secondary endpoints with highly statistically significant reductions in serum bile acids and pruritus -

- Interim results from long-term extension study show sustained improvements in serum bile acids, pruritus -

- Improvements in growth measures and liver parameters observed with long-term administration suggests disease modifying potential of odevixibat -

- Treatment effect consistent across wide range of PFIC patient types 1, 2 and 3 -

- Next-generation, novel bile acid modulators for adult liver diseases unveiled, including compound A3907 -

BOSTON, Nov. 13, 2020 (GLOBE NEWSWIRE) -- Albireo Pharma, Inc. (Nasdaq: ALBO), a clinical-stage rare liver disease company developing novel bile acid modulators, today announced new data in progressive familial intrahepatic cholestasis (PFIC) confirming statistically significant reductions in serum bile acids (sBAs) and improvements in pruritus for odevixibat, a potent, once-daily, non-systemic ileal bile acid transport inhibitor (IBATi). Interim results from the extension study also showed continued treatment effect for sBAs, pruritus, growth and liver parameters across PFIC1, PFIC2 and PFIC3 patients. Data to be presented at the American Association for the Study of Liver Diseases (AASLD) Liver Meeting November 13-16.

Full results from PEDFIC 1, the first and largest, global, phase 3 study ever conducted in PFIC, confirm both U.S. and EU primary endpoints were met in the randomized, double-blind, placebo-controlled trial. Additionally, long-term data from PEDFIC 2, an open-label Phase 3 extension study, demonstrate continued and durable reductions in sBAs, improvements in pruritus assessments and encouraging markers of liver and growth function in patients treated up to 48 weeks. Across both studies, odevixibat was generally well tolerated, and treatment-emergent adverse events (TEAEs) were mostly mild or moderate. Collectively, these studies reaffirm odevixibat's potential to be the first drug treatment approved for patients living with PFIC, a devastating disease which is currently treated with surgical options including liver transplantation. The data support near-term regulatory filings in the U.S. and EU.

"The full results from the PEDFIC 1 Phase 3 trial confirm the magnitude of treatment effects seen in the topline data and reinforce the potential for odevixibat to alter the biology of PFIC disease. There were highly statistically significant reductions in both pruritus and serum bile acids in the PEDFIC 1 study," said Richard Thompson, M.D., Ph.D., Professor of Molecular Hepatology at King's College London and principal investigator of PEDFIC 1 and PEDFIC 2. "We saw durability and sustained effect in the interim results in PEDFIC 2, which are encouraging signs that IBAT inhibition with odevixibat may offer a transformative treatment and genuine alternative to surgery for patients with PFIC."

Final Results from PEDFIC 1, First and Largest Study Ever in PFIC1 and PFIC2
Full results from PEDFIC 1, the global Phase 3 clinical trial evaluating the efficacy and safety of odevixibat in children with PFIC, confirms both U.S. and EU primary endpoints were met in the placebo-controlled trial. Key findings include:

- **Significant reductions in pruritus and SBAs:** Overall, treatment with odevixibat at both doses of 40 and 120 µg/kg/day led to statistically significant reductions in pruritus symptoms and serum bile acids over 24 weeks, compared with placebo. Statistically significant improvement was seen in the proportion of positive pruritus assessments (p=0.004), which is the U.S. regulatory primary endpoint. The EU regulatory primary endpoint was also achieved, which was a 70% reduction in serum bile acids (sBAs) or reaching a level of 70 µmol/L (p=0.003).
- **Rapid, sustained effect:** Rapid onset of treatment effects, sustained through week 24.
- **Well tolerated:** Odevixibat was well tolerated, with an overall adverse event incidence not dose dependent and similar to placebo. There were no drug-related serious adverse events (SAEs) reported during the study. Diarrhea/frequent bowel movements were the most common treatment-related gastrointestinal adverse events, which occurred in 9.5% of odevixibat treated patients vs. 5.0% of placebo patients. Only one patient in the 120 µg/kg/day group discontinued treatment due to an AE of diarrhea.

	Placebo n=20	**Odevixibat n=42**	**P-value**
Proportion of positive pruritus assessments (Mean)	28.7%	53.5%	0.004
Clinically meaningful improvement in pruritus score	10.5%	42.9%	0.018
Protocol defined bile acid reduction	0%	33.3%	0.003
Absolute change in serum bile acid	13.1	-114.3	0.002
Drug-related diarrhea/frequent bowel movements	5.0%	9.5%	----

Interim Results from PEDFIC 2 Extension Study Reaffirm Odevixibat Effect in Treated and New Patients
The PEDFIC 2 interim data include results through 24 weeks of treatment (data cutoff date: July 15, 2020) from 69 patients who received 120 µg/kg/day oral dose, which is the planned commercial formulation of odevixibat.

Cohort 1 consists of PFIC1 and PFIC2 patients from PEDFIC 1 who rolled into PEDFIC 2. This includes patients treated with odevixibat (patient group P1O), as well as patients treated with placebo (patient group P1P).

Cohort 2 consists of newly enrolled patients who did not participate in the PEDFIC 1 trial, including patients with PFIC 1, PFIC 2, PFIC3 and MYO5B deficiency.

Key findings include:

- **Affirmation of efficacy:** Mean reductions in sBAs and improvements in pruritus assessments, height and weight with odevixibat exposure were observed in all PEDFIC 2 patient groups.
- **Sustained effect:** Patients with 48 weeks of cumulative odevixibat exposure (P10 group) achieved a mean reduction in sBAs from 251.8 µmol/L to 85.1 µmol//L ($p<0.0001$) and a mean monthly improvement in the pruritus score, defined as a drop from baseline of 1.0 point or more on the 0-4 point scale, from 3.0 to 1.4 ($p<0.0001$). Cohort 2 confirms the 24-week data from PEDFIC 1, reinforcing the decline in sBA and pruritus seen in the PEDFIC 1 study.
- **Encouraging change in height & weight observed:** In patients exposed to odevixibat for 48 weeks (P10), mean height Z scores also improved from –1.6 to –0.5 ($p=0.02$) from baseline to PEDFIC 2 week 24, and mean weight Z scores normalized over 48 weeks (–0.9 to 0.2; $p=0.03$).
- **Patients remain on treatment:** 93% of treated patients are on ongoing treatment with odevixibat.
- **Improvement across PFIC types 1, 2 and 3:** Subgroup analyses showed rapid effect and improvements in patients across multiple PFIC subtypes. For example, patients with PFIC 1, PFIC 2 and PFIC 3 in P1P and cohort 2 had mean reductions vs. baseline in sBAs of -31.7 umol/L, -120.8umol/L and 126.8 umol/L, respectively, through week 12.
- **Well tolerated:** Odevixibat was generally well tolerated in PEDFIC 2. Most TEAEs were mild or moderate. No drug-related serious TEAEs occurred. The incidence of diarrhea was low (10.1% overall), and no patient experienced severe diarrhea. No clinically significant changes or safety signals were noted in laboratory assessments.

“PEDFIC 1 & 2 demonstrated how odevixibat has profound and durable improvements in multiple parameters, including serum bile acids, pruritus, height, growth, sleep and liver parameters. Even more important is we saw a sustained treatment effect across a wide range of PFIC patients,” said Ron Cooper, President and Chief Executive Officer of Albireo. “These results give us confidence in the potential for IBAT inhibition in our pivotal studies in biliary atresia and Alagille syndrome.”

The PEDFIC 1 (#LO4) and PEDFIC 2 (#LP19) results will be shared in late-breaking presentations at the American Association for the Study of Liver Diseases (AASLD) The Liver Meeting Digital Experience™ (TLMdX®).

Novel Bile Acid Modulator Approaches
Albireo will present the latest preclinical data on multiple new approaches to modulating bile acids in adult liver diseases (#P348) by targeting certain bile acid transporters: the apical sodium-dependent bile acid transporter (ASBT) and the sodium-taurocholate co-transporting peptide (NTCP). This has the potential to significantly change the bile acid transporter approach in adult liver diseases by diverting bile acids (BAs) from the liver through several pathways.

Data from the first preclinical study will be presented on Albireo’s ASBT inhibitor A3907 (#P509) as a novel intervention for adult liver diseases. A3907 is a selective ASBT inhibitor being developed for adult liver diseases, including primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC). Due to oral bioavailability, A3907 can inhibit ASBT in the intestine and kidney, with the potential to increase elimination of bile acids by both fecal and urinary excretion. By using dual pathway diversion of sBAs, next generation modulators like A3907 seek to improve efficacy while reducing side effects such as diarrhea, which can be common with bile acid transport inhibitors today.

Results from the preclinical studies of A3907:

- Demonstrated ability to increase urinary excretion of bile acids in mice
- Reduced the NAFLD activity score by ≥2 points in >50% and >40 % of animals at 30 and 45 mg/kg, respectively ($p<0.001$ and $p<0.05$ vs. pretreatment)
- Prevented fibrosis stage progression in >50% of animals at 10, 30 and 45 mg/kg ($p<0.001$, $p<0.001$, and $p<0.01$ vs. pretreatment) in a diet-induced mouse model of biopsy confirmed NASH
- Significantly reduced plasma levels of transaminases, total cholesterol, and markers for cell damage and fibrosis, as well as liver weight and liver total cholesterol levels

“In addition to the exciting results of our work with odevixibat in PFIC, we are progressing multiple approaches for modulating bile acids with new compounds like A3907, with the goal of finding new ways to maximize the approach to increase efficacy without sacrificing tolerability for patients,” added Cooper. “Our current work in adult liver diseases represent important pipeline developments for Albireo and reinforce our scientific leadership in bile acid modulation.”

Conference Call
Albireo will host a post-AASLD conference call and live audio webcast on November 17, at 10 a.m. EST. To access the live conference call by phone, please dial 877-407-0792 (domestic) or 201-689-8263 (international) and provide the access code 13709929. The live audio webcast will be accessible from the Albireo Media & Investors page: http://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 in the Events & Presentations section of the Media & Investors page of Albireo’s website for two weeks following the event.

About Odevixibat
Odevixibat is an investigational product candidate being developed to treat rare pediatric cholestatic liver diseases, including progressive familial

intrahepatic cholestasis (PFIC), biliary atresia and Alagille syndrome. A highly potent, once-daily, non-systemic ileal bile acid transport inhibitor (IBATi), odevixibat acts locally in the small intestine. Odevixibat 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. Odevixibat is currently being evaluated in the ongoing PEDFIC 2 open-label trial (NCT03659916) and the BOLD Phase 3 trial in patients with biliary atresia (NCT04336722). Initiation of a pivotal Phase 3 trial of odevixibat for Alagille syndrome is also anticipated by the end of 2020.

Odevixibat has received Fast Track, Rare Pediatric Disease and Orphan Drug Designations in the United States. In addition, the FDA has granted Orphan Drug Designation to odevixibat for the treatment of Alagille syndrome, biliary atresia and primary biliary cholangitis. The EMA has granted odevixibat Orphan Designation, as well as access to the PRIority MEdicines (PRIME) scheme for the treatment of PFIC. Its Pediatric Committee has agreed to Albireo's odevixibat Pediatric Investigation Plan for PFIC and biliary atresia. EMA has also granted Orphan Designation to odevixibat for the treatment of Alagille syndrome, biliary atresia and primary biliary cholangitis. Odevixibat has the potential to become the first approved drug treatment for patients with PFIC. The company intends to complete regulatory filings in the EU and U.S. for odevixibat in PFIC no later than early 2021, in anticipation of potential regulatory approval, issuance of a rare pediatric disease priority review voucher and launch in the second half of 2021.

About PFIC
Progressive familial intrahepatic cholestasis (PFIC) is a rare genetic disorder that causes progressive, life-threatening liver disease. People diagnosed with PFIC 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. PFIC is also characterized by jaundice, and poor weight gain and 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, including a procedure known as partial external biliary diversion (PEBD) and liver transplantation. These options carry substantial risks. Additional information on PFIC is available at https://www.pficvoices.com.

About A3907
A3907 is a selective inhibitor of the apical sodium-dependent bile acid transporter (ASBT) with a dual mechanism of action. Due to oral bioavailability, A3907 acts on both renal and ileal transporters to increase elimination of bile acids by both fecal and urinary excretion. This dual inhibition approach may yield greater dosing flexibility, greater efficacy and lower rates of adverse events associated with the category, such as diarrhea. We expect to complete investigational new drug enabling studies for A3907 this year and plan to advance development in adult liver disease.

About Albireo
Albireo Pharma is a clinical-stage biopharmaceutical company focused on the development of novel bile acid modulators to treat rare pediatric and adult liver diseases, and other adult liver diseases and disorders. Albireo's lead product candidate, odevixibat, is being developed to treat rare pediatric cholestatic liver diseases and is in Phase 3 development in progressive familial intrahepatic cholestasis (PFIC) and biliary atresia, with a third Phase 3 trial being planned in Alagille syndrome. The Company expects to complete IND-enabling studies for new preclinical candidate A3907 this year and plans to advance development in adult 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: the plans for, or progress, scope, cost, initiation, duration, enrollment, results or timing for availability of results of, development of odevixibat or any other Albireo product candidate or program, including regarding expectations regarding the impact of COVID-19 on our business and our ability to adapt our approach as appropriate; the Phase 3 clinical program for odevixibat in patients with PFIC, the pivotal trial for odevixibat in biliary atresia (BOLD), and the planned pivotal trial for odevixibat in Alagille syndrome; 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 odevixibat in PFIC, the pivotal trial for odevixibat in biliary atresia, the planned pivotal trial for odevixibat in Alagille syndrome; the potential approval and commercialization of odevixibat; discussions with the FDA or EMA regarding our programs; the potential benefits or competitive position of odevixibat, A3907, or any other Albireo product candidate or program or the commercial opportunity in any target indication; the potential effects of odevixibat 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 potential issuance of a rare pediatric disease priority review voucher; 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," and 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: 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 odevixibat to date, including findings in indications other than PFIC, will be predictive of results from other clinical trials of odevixibat; whether either or both of the FDA and EMA will determine that the primary endpoint for their respective evaluations and treatment duration of the double-blind Phase 3 trial in patients with PFIC are sufficient to support approval of odevixibat in the United States or the European Union, to treat PFIC, a symptom of PFIC, a specific PFIC subtype(s) 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 odevixibat, including the pivotal program in biliary atresia or the planned pivotal program in Alagille syndrome, 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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