Intercept to Present New NASH and PBC Data at the Digital International Liver Congress™ 2021

June 21, 2021

New analyses from the Phase 3 REGENERATE study highlight the relationship between early reductions of aminotransferases and fibrosis improvement in patients with fibrosis due to NASH treated with obeticholic acid (OCA)

In a real-world study of patients with PBC, Ocaliva® reduced alkaline phosphatase and bilirubin after 1 and 2 years of treatment across patient subgroups

NEW YORK, June 21, 2021 (GLOBE NEWSWIRE) -- Intercept Pharmaceuticals, Inc. (Nasdaq:ICPT), a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat progressive non-viral liver diseases, today announced that multiple abstracts regarding the treatment of primary biliary cholangitis (PBC) and nonalcoholic steatohepatitis (NASH) with obeticholic acid (OCA) will be presented at the Digital International Liver Congress™ 2021, the 56th Annual Meeting of the European Association for the Study of the Liver (EASL), to be held virtually from June 23 to June 26, 2021.

“The REGENERATE data that Intercept will be presenting at this year’s International Liver Congress provide important new insight into short-term and longer-term measures of OCA treatment response in patients with fibrosis due to NASH,” said Gail Cawkwell, M.D., Ph.D., Intercept’s Senior Vice President, Medical Affairs, Safety & Pharmacovigilance. “Specifically, the early reductions in aminotransferases seen with OCA therapy show a correlation with fibrosis improvement over time. This is relevant because the early conversations between a clinician and patient about improvements in routine laboratory measures like ALT in the period after initiating therapy can help set expectations for longer term benefit.

“We are also pleased to be presenting new real-world data in PBC at this year’s Congress,” continued Dr. Cawkwell. “Using a large administrative claims database, we examined biochemical response in more than 300 patients treated with Ocaliva who had varying levels of underlying disease risk at baseline. Across groups, Ocaliva produced marked reductions in alkaline phosphatase and bilirubin after both one year and two years of treatment. It is reassuring to see that the benefits of Ocaliva from the controlled environment of clinical trials are largely consistent with these results seen with real-world use.”

The use of OCA for NASH is investigational and has not been approved by the U.S. Food and Drug Administration, the European Commission or any other health authority.

In addition to new analyses of OCA data, the International Liver Congress 2021 will also include research from Intercept and collaborators that provides new perspective on the natural history of PBC and fibrosis due to NASH, data supporting the role of noninvasive tests to risk-stratify patients with fibrosis due to NASH, and results from a multi-country survey examining patient-provider dialogue and perceptions of stigma associated with fibrosis due to NASH.

Presentations at the Digital International Liver Congress include:

**Oral Presentation**

“Incidence rates of select outcomes among patients with non-alcoholic steatohepatitis (NASH) and evidence of fibrosis or cirrhosis”  
(Abstract #1780)  
Monica L. Bertoia, Erik Ness, Thomas Capozza, Lina Titievsky, John D. Seeger

Fibrosis due to NASH Poster Presentations

“Aminotransferase level improvement in patients with non-alcoholic steatohepatitis are associated with fibrosis regression in the REGENERATE study”  
(Abstract #2290)  
Mary Rinella, Jean-François Dufour, Quentin M. Anstee, Zobair Younossi, Rohit Loomba, Arun J. Sanyal, Tom Capozza, Tanya Granston, Martin Bonacci, Aldo Trylesinski, Vlad Ratziu

“Incidence rates of hepatobiliary outcomes among patients with non-alcoholic steatohepatitis based on fibrosis-4 score severity at baseline”  
(Abstract #980)  

“Comorbidity and healthcare utilization burden of patients diagnosed with non-alcoholic steatohepatitis based on fibrosis-4 score severity”  
(Abstract #1568)  

“The unmet needs of living with NASH in Europe and Canada: results from a multicountry survey”  
(Abstract #1990)  
Jeffrey V. Lazarus, Fabienne Marcellin, Camelia Protopopescu, Aldo Trylesinski, José Luis Calleja, Patrizia Carrieri

“Disclosure of NASH Diagnosis and fear of discrimination: results from a multicountry survey”  
(Abstract #2032)  
Jeffrey V Lazarus, Fabienne Marcellin, Achim Kautz, Vanessa Heditch, Aldo Trylesinski, José Luis Calleja, Patrizia Carrieri

“NASH Dynamics – The prognosis is impaired in NAFLD patients with diabetes despite negative Fib4 <1.30”  
(Abstract #313)
PBC Poster Presentations

“Incidence of hepatic outcomes in patients with cirrhosis due to primary biliary cholangitis (PBC): A population-based epidemiology study” (Abstract #1664)
Lina Titievsky, Erik Ness, Amy Law, Ellie Goldman, Darren Wheeler, Monica Bertoia, John Seeger, Mindie Nguyen, Yuval Patel, Femi Adekunle, Chiara Bassanelli

“Effectiveness of obeticholic acid in patients with primary biliary cholangitis stratified by biochemical marker status in the real-world setting in the United States” (Abstract #254)
Robert G. Gish, Darren Wheeler, Jay Lin, Femi Adekunle, Melissa Lingohr-Smith, Chiara Bassanelli, Amy Law

A full list of sessions at the Digital International Liver Congress™ 2021 is available at https://ilc-congress.eu.

About Intercept
Intercept is a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat progressive non-viral liver diseases, including primary biliary cholangitis (PBC) and nonalcoholic steatohepatitis (NASH). Founded in 2002 in New York, Intercept has operations in the United States, Europe and Canada. For more information, please visit www.interceptpharma.com or connect with the company on Twitter and LinkedIn.

About the REGENERATE Study
REGENERATE is a Phase 3, randomized, double-blind, placebo-controlled, multicenter study assessing the safety and efficacy of obeticholic acid (OCA) on clinical outcomes in patients with liver fibrosis due to NASH. A pre-specified 18-month analysis was conducted to assess the effect of OCA on liver histology comparing month 18 biopsies with baseline. REGENERATE has completed target enrollment for the clinical outcomes cohort, with 2,480 adult NASH patients randomized at over 300 qualified centers worldwide, and is expected to continue through clinical outcomes for verification and description of clinical benefit. The end-of-study analysis will evaluate the effect of OCA on all-cause mortality and liver-related clinical outcomes, as well as long-term safety.

About Ocaliva® (obeticholic acid)
OCALIVA, a farnesoid X receptor (FXR) agonist, is indicated for the treatment of adult patients with primary biliary cholangitis (PBC)

- without cirrhosis or
- with compensated cirrhosis who do not have evidence of portal hypertension,

either in combination with ursodeoxycholic acid (UDCA) with an inadequate response to UDCA or as monotherapy in patients unable to tolerate UDCA.

This indication is approved under accelerated approval based on a reduction in alkaline phosphatase (ALP). An improvement in survival or disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

IMPORTANT SAFETY INFORMATION

WARNING: HEPATIC DECOMPENSATION AND FAILURE IN PRIMARY BILIARY CHOLANGITIS PATIENTS WITH CIRRHOSIS

- Hepatic decompensation and failure, sometimes fatal or resulting in liver transplant, have been reported with OCALIVA treatment in primary biliary cholangitis (PBC) patients with either compensated or decompensated cirrhosis.
- OCALIVA is contraindicated in PBC patients with decompensated cirrhosis, a prior decompensation event, or with compensated cirrhosis who have evidence of portal hypertension.
- Permanently discontinue OCALIVA in patients who develop laboratory or clinical evidence of hepatic decompensation; have compensated cirrhosis and develop evidence of portal hypertension, or experience clinically significant hepatic adverse reactions while on treatment.

Contraindications
OCALIVA is contraindicated in patients with:

- decompensated cirrhosis (e.g., Child-Pugh Class B or C) or a prior decompensation event
- compensated cirrhosis who have evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia)
- complete biliary obstruction

Warnings and Precautions

Hepatic Decompensation and Failure in PBC Patients with Cirrhosis
Hepatic decompensation and failure, sometimes fatal or resulting in liver transplant, have been reported with OCALIVA treatment in PBC patients with cirrhosis, either compensated or decompensated. Among postmarketing cases reporting it, median time to hepatic decompensation (e.g. new onset...
ascites) was 4 months for patients with compensated cirrhosis; median time to a new decompensation event (e.g. hepatic encephalopathy) was 2.5 months for patients with decompensated cirrhosis.

Some of these cases occurred in patients with decompensated cirrhosis when they were treated with higher than the recommended dosage for that patient population; however, cases of hepatic decompensation and failure have continued to be reported in patients with decompensated cirrhosis even when they received the recommended dosage.

Hepatotoxicity was observed in the OCALIVA clinical trials. A dose-response relationship was observed for the occurrence of hepatic adverse reactions including jaundice, worsening ascites, and primary biliary cholangitis flare with dosages of OCALIVA of 10 mg once daily to 50 mg once daily (up to 5-times the highest recommended dosage), as early as one month after starting treatment with OCALIVA in two 3-month, placebo-controlled clinical trials in patients with primarily early stage PBC.

Routinely monitor patients for progression of PBC, including hepatic adverse reactions, with laboratory and clinical assessments to determine whether drug discontinuation is needed. Closely monitor patients with compensated cirrhosis, concomitant hepatic disease (e.g., autoimmune hepatitis, alcoholic liver disease), and/or with severe intercurrent illness for new evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia), or increases above the upper limit of normal in total bilirubin, direct bilirubin, or prothrombin time to determine whether drug discontinuation is needed. Permanently discontinue OCALIVA in patients who develop laboratory or clinical evidence of hepatic decompensation (e.g., ascites, jaundice, variceal bleeding, hepatic encephalopathy), have compensated cirrhosis and develop evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia), experience clinically significant hepatic adverse reactions, or develop complete biliary obstruction. If severe intercurrent illness occurs, interrupt treatment with OCALIVA and monitor the patient’s liver function. After resolution of the intercurrent illness, consider the potential risks and benefits of restarting OCALIVA treatment.

Severe Pruritus
Severe pruritus was reported in 23% of patients in the OCALIVA 10 mg arm, 19% of patients in the OCALIVA titration arm, and 7% of patients in the placebo arm in a 12-month double-blind randomized controlled clinical trial of 216 patients. Severe pruritus was defined as intense or widespread itching, interfering with activities of daily living, or causing severe sleep disturbance, or intolerable discomfort, and typically requiring medical interventions. Consider clinical evaluation of patients with new onset or worsening severe pruritus. Management strategies include the addition of bile acid binding resins or antihistamines, OCALIVA dosage reduction, and/or temporary interruption of OCALIVA dosing.

Reduction in HDL-C
Patients with PBC generally exhibit hyperlipidemia characterized by a significant elevation in total cholesterol primarily due to increased levels of high-density lipoprotein-cholesterol (HDL-C). Dose-dependent reductions from baseline in mean HDL-C levels were observed at 2 weeks in OCALIVA-treated patients, 20% and 9% in the 10 mg and titration arms, respectively, compared to 2% in the placebo arm. Monitor patients for changes in serum lipid levels during treatment. For patients who do not respond to OCALIVA after 1 year at the highest recommended dosage that can be tolerated (maximum of 10 mg once daily), and who experience a reduction in HDL-C, weigh the potential risks against the benefits of continuing treatment.

Adverse Reactions
The most common adverse reactions (≥5%) are: pruritus, fatigue, abdominal pain and discomfort, rash, oropharyngeal pain, dizziness, constipation, arthralgia, thyroid function abnormality, and eczema.

Drug Interactions

- **Bile Acid Binding Resins**
  Bile acid binding resins such as cholestyramine, colestipol, or colesvelam adsorb and reduce bile acid absorption and may reduce the absorption, systemic exposure, and efficacy of OCALIVA. If taking a bile acid binding resin, take OCALIVA at least 4 hours before or 4 hours after taking the bile acid binding resin, or at as great an interval as possible.

- **Warfarin**
  The International Normalized Ratio (INR) decreased following coadministration of warfarin and OCALIVA. Monitor INR and adjust the dose of warfarin, as needed, to maintain the target INR range when co-administering OCALIVA and warfarin.

- **CYP1A2 Substrates with Narrow Therapeutic Index**
  Obeticholic acid may increase the exposure to concomitant drugs that are CYP1A2 substrates. Therapeutic monitoring of CYP1A2 substrates with a narrow therapeutic index (e.g., theophylline and tizanidine) is recommended when co-administered with OCALIVA.

- **Inhibitors of Bile Salt Efflux Pump**
  Avoid concomitant use of inhibitors of the bile salt efflux pump (BSEP) such as cyclosporine. Concomitant medications that inhibit canalicular membrane bile acid transporters such as the BSEP may exacerbate accumulation of conjugated bile salts including taurine conjugate of obeticholic acid in the liver and result in clinical symptoms. If concomitant use is deemed necessary, monitor serum transaminases and bilirubin.

Please click here for Full Prescribing Information, including Boxed WARNING.

To report SUSPECTED ADVERSE REACTIONS, contact Intercept Pharmaceuticals, Inc. at 1-844-782-ICPT or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements, including, but not limited to, statements regarding the progress, timing and results of our clinical trials, including our clinical trials for the treatment of nonalcoholic steatohepatitis ("NASH"), the safety and efficacy of our approved product, Ocaliva (obeticholic acid or "OCA") for primary biliary cholangitis ("PBC"), and our product candidates, including OCA for liver fibrosis due to NASH, the timing and acceptance of our regulatory filings and the potential approval of OCA for liver fibrosis due to NASH, the review of our New Drug Application for OCA for the treatment of liver fibrosis due to NASH by the U.S. Food and Drug Administration ("FDA"), our intent to work with the FDA to address the issues raised in a complete response letter ("CRL"), the potential commercial success of OCA, as well as our strategy, future operations, future financial position, future revenue, projected costs, financial guidance, prospects, plans and objectives.

These statements constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "possible," "continue" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this release, and we undertake no obligation to update any forward-looking statement except as required by law. These forward-looking statements are based on estimates and assumptions by our management that, although believed to be reasonable, are inherently uncertain and subject to a number of risks.

The following represent some, but not necessarily all, of the factors that could cause actual results to differ materially from historical results or those anticipated or predicted by our forward-looking statements: our ability to successfully commercialize Ocaliva for PBC; our ability to maintain our regulatory approval of Ocaliva for PBC in the United States, Europe, Canada, Israel, Australia and other jurisdictions in which we have or may receive marketing authorization; our ability to timely and cost-effectively file for and obtain regulatory approval of our product candidates on an accelerated basis or at all, including OCA for liver fibrosis due to NASH following the issuance of the CRL by the FDA; any advisory committee recommendation or disapproval resolution determination that our product candidates, including OCA for liver fibrosis due to NASH, should not be approved or approved only under certain conditions; any future determination that the regulatory applications and subsequent information we submit for our product candidates, including OCA for liver fibrosis due to NASH, do not contain adequate clinical or other data or meet applicable regulatory requirements for approval; conditions that may be imposed by regulatory authorities on our marketing approvals for our products and product candidates, including OCA for liver fibrosis due to NASH, such as the need for clinical outcomes data (and not just results based on achievement of a surrogate endpoint), any risk mitigation programs such as a REMS, and any related restrictions, limitations and/or warnings contained in the label of any of our products or product candidates; any potential side effects associated with Ocaliva for PBC; OCA for liver fibrosis due to NASH or our other product candidates that could delay or prevent approval, require that an approved product be taken off the market, require the inclusion of safety warnings or precautions, or otherwise limit the sale of such product or product candidate, including in connection with the newly identified safety signal relating to Ocaliva identified by the FDA in May 2020 and with respect to patients with PBC with decompensated cirrhosis, a prior decompensation event or with compensated cirrhosis who have evidence of portal hypertension; the initiation, timing, cost, conduct, progress and results of our research and development activities, preclinical studies and clinical trials, including any issues, delays or failures in identifying patients, enrolling patients, treating patients, retaining patients, meeting specific endpoints in the jurisdictions in which we intend to seek approval or completing and timely reporting the results of our NASH or PBC clinical trials; the outcomes of ongoing discussions with the FDA and European Medicines Agency regarding the feasibility of the COBALT and 401 trials; our ability to establish and maintain relationships with, and the performance of, third-party manufacturers, contract research organizations and other vendors upon whom we are substantially dependent for, among other things, the manufacture and supply of our products, including Ocaliva for PBC and, if approved, OCA for liver fibrosis due to NASH; and our clinical trial activities; our ability to identify, develop and successfully commercialize our products and product candidates, including our ability to successfully launch OCA for liver fibrosis due to NASH, if approved; our ability to obtain and maintain intellectual property protection for our products and product candidates, including our ability to cost-effectively file, prosecute, defend and enforce any patent claims or other intellectual property rights; the size and growth of the markets for our products and product candidates and our ability to serve those markets; the degree of market acceptance of Ocaliva for PBC and, if approved, OCA for liver fibrosis due to NASH or our other product candidates among physicians, patients and healthcare payors; the availability of adequate coverage and reimbursement from governmental and private healthcare payors for our products, including Ocaliva for PBC and, if approved, OCA for liver fibrosis due to NASH, and our ability to obtain adequate pricing for such products; our ability to establish and maintain effective sales, marketing and distribution capabilities, either directly or through collaborations with third parties; competition from existing drugs or new drugs that become available; our ability to attract and retain key personnel to manage our business effectively; our ability to prevent system failures, data breaches or violations of data protection laws; costs and outcomes relating to any disputes, governmental inquiries or investigations, regulatory proceedings, legal proceedings or litigation, including any securities, intellectual property, employment, product liability or other litigation; our collaborators' election to pursue research, development and commercialization activities; our ability to establish and maintain relationships with collaborators with development, regulatory and commercialization expertise; our need for and ability to generate or obtain additional financing; our estimates regarding future expenses, revenues and capital requirements and the accuracy thereof; our use of cash, cash equivalents and short-term investments; our ability to acquire, license and invest in businesses, technologies, product candidates and products; our ability to manage the growth of our operations, infrastructure, personnel, systems and controls; our ability to obtain and maintain adequate insurance coverage; continuing threats from COVID-19, including additional waves of infections, and their impacts including quarantines and other government actions, delays relating to our regulatory applications, disruptions relating to our ongoing clinical trials or involving our contract research organizations, study sites or other clinical partners, disruptions relating to our supply chain or involving our third-party manufacturers, distributors or other distribution partners and facility closures or other restrictions, and the impact of the foregoing on our results of operations and financial position; the impact of general U.S. and foreign economic, industry, market, regulatory or political conditions, including the impact of Brexit; and the other risks and uncertainties identified in our periodic filings filed with the U.S. Securities and Exchange Commission, including our Annual Report on Form 10-K for the year ended December 31, 2020.

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