Intercept Announces Updated U.S. Prescribing Information for Ocaliva® (obeticholic acid) to Reinforce Appropriate Dosing in PBC Patients with Advanced Cirrhosis

February 2, 2018

Company to Host Conference Call at 5:00 p.m. ET

NEW YORK, Feb. 01, 2018 (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 the Ocaliva® (obeticholic acid or OCA) Prescribing Information in the United States has been updated to reinforce appropriate dosing in primary biliary cholangitis (PBC) patients with Child-Pugh Class B or C or decompensated cirrhosis.

In the postmarketing setting, hepatic decompensation and failure have been reported in patients with advanced cirrhosis when Ocaliva was dosed more frequently than the recommended starting dosage. As a result, the Ocaliva label has been revised to include a boxed warning and a dosing table that reinforce the existing dosing schedule for such patients, who comprise two to three percent of the overall PBC population.

"Following extensive review of postmarketing data, we remain confident in Ocaliva's safety profile and the benefit it provides when used as directed in patients with PBC, a devastating disease that is one of the leading causes of liver failure in women," said Mark Pruzanski, M.D., President and CEO of Intercept. "The focus of our label update is to aid physicians in identifying and appropriately dosing Ocaliva in the most vulnerable PBC patients with advanced cirrhosis."

Intercept will be disseminating the updated Prescribing Information and a Medication Guide for patients and will continue its efforts to educate physicians on the appropriate dosing for patients with advanced cirrhosis. In addition, the U.S. Food and Drug Administration (FDA) has issued an updated Drug Safety Communication to accompany the label.

Intercept is also working with the European Medicines Agency (EMA) to update the Ocaliva European Summary of Product Characteristics (SmPC) to reinforce appropriate dosing in patients with advanced cirrhosis. In the meantime, a Direct Healthcare Professional Communication will be issued to educate physicians on the need for appropriate dosing in patients with advanced cirrhosis.

The updated label reinforces the positive benefit-risk profile of Ocaliva when used as directed. Ocaliva, the first medication approved for PBC in nearly 20 years, is the only treatment approved for people living with PBC who have an inadequate response to, or are intolerant of, the current standard of care, ursodeoxycholic acid (UDCA).

Dosing of Ocaliva

A table is included in the updated Prescribing Information to increase the prominence of the recommended Ocaliva dosage by disease stage and Child-Pugh classification.

Staging / Classification	**Non-Cirrhotic or Compensated Child-Pugh Class A**	**Child-Pugh Class B or C or Patients with a Prior Decompensation Event[a]**
Starting Ocaliva Dosage for first 3 months	5 mg once daily	5 mg once weekly
Ocaliva Dosage Titration after first 3 months, for patients who have not achieved an adequate reduction in ALP and/or total bilirubin and who are tolerating Ocaliva[b]	10 mg once daily	5 mg twice weekly (at least 3 days apart) Titrate to 10 mg twice weekly (at least 3 days apart) based on response and tolerability
Maximum Ocaliva Dosage	10 mg once daily	10 mg twice weekly (at least 3 days apart)
[a] Gastroesophageal variceal bleeding, new or worsening jaundice, spontaneous bacterial peritonitis, etc. [b] Prior to dosage adjustment, re-calculate the Child-Pugh classification		

Postmarketing Experience with Ocaliva

Intercept regularly provides pharmacovigilance information to the FDA in accordance with standard regulatory obligations and analyses of these data were shared with the Agency to inform updates to the Ocaliva label.

Because postmarketing adverse events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure, particularly in PBC patients who have progressive liver disease with advanced cirrhosis. Intercept's most recent assessment of postmarketing data did not establish a causal relationship between Ocaliva and liver decompensation and/or liver failure. A review of the currently available data shows that the pattern of events appears to be consistent with the natural history of the underlying disease. These conclusions are aligned with the assessment of an independent Hepatic Adjudication Committee of experts in drug-induced liver injury who were convened to review the postmarketing cases cited in the FDA's September 2017 Drug Safety Communication.

About Primary Biliary Cholangitis

Primary biliary cholangitis (PBC) is a rare, autoimmune cholestatic liver disease that puts patients at risk for life-threatening complications. PBC is primarily a disease of women, afflicting approximately one in 1,000 women over the age of 40. If left untreated, survival of PBC patients is significantly worse than the general population. An analysis of data from the Global PBC Study Group, the largest PBC natural history database, demonstrated that after one year, death or liver transplantation occurred in up to 41 percent of UDCA-treated PBC patients who had experienced a decompensation event.

Conference Call at 5:00 p.m. ET

Intercept will discuss the updated Ocaliva label on a conference call and webcast today at 5:00 p.m. ET. The live event will be available on the investor page of Intercept's website at http://ir.interceptpharma.com or by calling (855) 232-3919 (toll-free domestic) or (315) 625-6894 (international) five minutes prior to the start time (no passcode is required). A replay of the call will be available on Intercept's website approximately two hours after the completion of the call and will be archived for two weeks.

About Ocaliva® (obeticholic acid)

Ocaliva is indicated in the United States for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA.

This indication is approved under accelerated approval based on a reduction in alkaline phosphatase (ALP), as a surrogate endpoint which is reasonably likely to predict clinical benefit, including an improvement in liver transplant free-survival. 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. Intercept is currently enrolling COBALT, a Phase 4 clinical outcomes trial of Ocaliva in patients with PBC with the goal of confirming clinical benefit on a postmarketing basis.

In December 2016, Ocaliva received conditional marketing authorization in Europe for the treatment of PBC in combination with UDCA in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA, conditional to the company providing further data post-approval to confirm benefit. Ocaliva received conditional approval from Health Canada in May 2017.

U.S. IMPORTANT SAFETY INFORMATION

WARNING: HEPATIC DECOMPENSATION AND FAILURE IN INCORRECTLY DOSED PBC PATIENTS WITH CHILD-PUGH CLASS B OR C OR DECOMPENSATED CIRRHOSIS

- **In postmarketing reports, hepatic decompensation and failure, in some cases fatal, have been reported in patients with Primary Biliary Cholangitis (PBC) with decompensated cirrhosis or Child-Pugh Class B or C hepatic impairment when OCALIVA was dosed more frequently than recommended.**
- **The recommended starting dosage of OCALIVA is 5 mg once weekly for patients with Child-Pugh Class B or C hepatic impairment or a prior decompensation event.**

Contraindications
OCALIVA is contraindicated in patients with complete biliary obstruction.

Warnings and Precautions

Hepatic Decompensation and Failure in Incorrectly-Dosed PBC Patients with Child-Pugh Class B or C or Decompensated Cirrhosis
In postmarketing reports, hepatic decompensation and failure, in some cases fatal, have been reported in patients with decompensated cirrhosis or Child-Pugh B or C hepatic impairment when OCALIVA was dosed more frequently than the recommended starting dosage of 5 mg once weekly. Reported cases typically occurred within 2 to 5 weeks after starting OCALIVA and were characterized by an acute increase in total bilirubin and/or ALP concentrations in association with clinical signs and symptoms of hepatic decompensation (e.g., ascites, jaundice, gastrointestinal bleeding, worsening of hepatic encephalopathy).

Routinely monitor patients for progression of PBC disease, including liver-related complications, with laboratory and clinical assessments. Dosage adjustment, interruption or discontinuation may be required. Close monitoring is recommended for patients at an increased risk of hepatic decompensation. Severe intercurrent illnesses that may worsen renal function or cause dehydration (e.g., gastroenteritis), may exacerbate the risk of hepatic decompensation. Interrupt treatment with OCALIVA in patients with laboratory or clinical evidence of worsening liver function indicating risk of decompensation, and monitor the patient's liver function. Consider discontinuing OCALIVA in patients who have experienced clinically significant liver-related adverse reactions. Discontinue OCALIVA in patients who develop complete biliary obstruction.

Liver-Related Adverse Reactions
Dose-related, liver-related adverse reactions including jaundice, worsening ascites and primary biliary cholangitis flare have been observed in clinical trials, as early as one month after starting treatment with OCALIVA 10 mg once daily up to 50 mg once daily (up to 5-times the highest recommended dosage). Monitor patients during treatment with OCALIVA for elevations in liver biochemical tests and for the development of liver-related adverse reactions.

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 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 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 from subjects taking OCALIVA were 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 colesevelam 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 coadministering OCALIVA and warfarin.

- CYP1A2 Substrates with Narrow Therapeutic Index
  Obeticholic acid, the active ingredient in OCALIVA, 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 coadministered 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 see **Full Prescribing Information, including Boxed WARNING** and **Medication Guide** for OCALIVA.

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.

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), nonalcoholic steatohepatitis (NASH), primary sclerosing cholangitis (PSC) and biliary atresia. Founded in 2002 in New York, Intercept now 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.

Safe Harbor Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements on the safety, benefits and efficacy of Ocaliva, the commercial potential of Ocaliva, any future events that may be experienced by patients who use Ocaliva and the association of such events with its use, the results of Intercept's educational efforts with healthcare providers and other planned and ongoing initiatives, the dosing of Ocaliva, and our strategic directives under the caption "About Intercept." These "forward-looking statements" are based on management's current expectations of future events and are subject to a number of important risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: the effect of label changes on prescriptions and sales of Ocaliva, the potential benefit and commercial potential of Ocaliva in PBC, and Intercept's ability to maintain its regulatory approval in jurisdictions in which Ocaliva is approved for use in PBC; the initiation, cost, timing, progress and results of Intercept's development activities, preclinical studies and clinical trials; the timing of and Intercept's ability to obtain and maintain regulatory approval of OCA in PBC in countries outside the ones in which it is approved and in indications other than PBC and any other product candidates it may develop such as INT-767; conditions that may be imposed by regulatory authorities on Intercept's marketing approvals for its products and product candidates such as the need for clinical outcomes data (and not just results based on achievement of a surrogate endpoint), and any related restrictions, limitations, and/or warnings in the label of any approved products and product candidates; Intercept's plans to research, develop and commercialize its product candidates; Intercept's ability to obtain and maintain intellectual property protection for its products and product candidates; Intercept's ability to successfully commercialize its products and product candidates; the size and growth of the markets for Intercept's products and product candidates and its ability to serve those markets; the rate and degree of market acceptance of any of Intercept's products, which may be affected by the reimbursement received from payors; the success of competing drugs that are or become available; regulatory developments in the United States and other countries; the performance of third-party suppliers and manufacturers; the election by Intercept's collaborators to pursue research, development and commercialization activities; Intercept's ability to attract collaborators with development, regulatory and commercialization expertise; Intercept's need for and ability to obtain additional financing; Intercept's estimates regarding expenses, revenues and capital requirements and the accuracy thereof; Intercept's use of cash and short-term investments; Intercept's ability to attract and retain key scientific or management personnel; and other factors discussed under the heading "Risk Factors" contained in our annual report on Form 10-K for the year ended December 31, 2016 filed on March 1, 2017 as well as any updates to these risk factors filed from time to time in our other filings with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and Intercept undertakes no duty to update this information unless required by law.

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