Liver Biopsy Data from POISE Phase 3 Substudy Supports Obeticholic Acid's Ability to Reverse or Stabilize Fibrosis and Cirrhosis in Primary Biliary Cholangitis (PBC) Patients

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11 of 13 patients improved or maintained histological fibrosis stage after three years of treatment with obeticholic acid (OCA)

NEW YORK, April 13, 2018 (GLOBE NEWSWIRE) -- Intercept Pharmaceuticals, Inc. (Nasdaq:ICPT) (Intercept), a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat progressive non-viral liver diseases, today announced clinical data from a liver biopsy-based substudy from the POISE Phase 3 trial suggesting that long-term OCA treatment in patients with PBC was associated with reversal or stabilization of fibrosis and cirrhosis. The data are being presented at the International Liver Congress™ 2018, the 53rd Annual Meeting of the European Association for the Study of the Liver (EASL), in Paris, France, from April 11-15, 2018.

"In this small but important study, some patients treated with OCA had regression of fibrosis and even cirrhosis. This is a significant finding because it further supports the clinical relevance of the biochemical improvements that predict the medication's impact on disease progression and clinical outcomes," said lead author Christopher Bowlus, M.D., University of California, Davis. "We look forward to the results of the Phase 4 COBALT study to further evaluate OCA's effects on fibrosis regression and clinical outcomes in patients with PBC."

OCA is not currently indicated for the reversal of fibrosis or cirrhosis in patients with PBC.

Prior longitudinal biopsy studies have shown that patients who are not treated with, or have an inadequate response to, ursodeoxycholic acid (UDCA), the current standard of care, are at significantly higher risk of fibrosis progression, liver failure, transplant and death. Liver biopsy is not the standard of care in PBC and difficult to obtain in clinical trials. In this voluntary substudy of the POISE Phase 3 trial, paired biopsies adequate for analysis were obtained for 13 patients, all of whom had liver fibrosis or cirrhosis at baseline.

After three years of treatment with OCA, the majority of patients improved (n=6, 46%) or maintained (n=5, 38%) histological fibrosis stage, while two patients (15%) experienced one stage progression. Of the four patients with cirrhosis at baseline, all showed reversal by at least one stage, and three (75%) improved to fibrosis without cirrhosis.

Pruritus is the most common symptom in patients with PBC and was also the most common adverse event in the POISE Phase 3 substudy. Nine (69%) patients experienced pruritus in the substudy, an incidence consistent with the rate observed in the broader study population. A total of five serious adverse events in five patients were reported. All serious adverse events were considered unlikely to be related, or not related, to OCA.

Additional Data Presentations

A separate poster, "Durable Response in the Markers of Cholestasis through 36 Months of Open-Label Extension Study of Obeticholic Acid in Primary Biliary Cholangitis," presented at the International Liver Congress provided additional results from the open-label extension of the POISE trial. Sustained improvements in ALP were observed through three years of OCA therapy, with similar improvements seen for GGT, ALT and AST. Mean total bilirubin remained below baseline throughout the three-year open-label period. The most common adverse event observed with OCA therapy was pruritus, resulting in the discontinuation of seven patients (4%) during the open-label extension treatment phase.

An additional poster, "Change in Bilirubin with Obeticholic Acid Treatment in Primary Biliary Cholangitis Patients with High Baseline Bilirubin: A Retrospective Analysis of POISE, 201, and 202," assessed changes in total bilirubin observed in the POISE Phase 3 trial and two Phase 2 trials. The analysis, which included patients with total bilirubin ≥0.67 times the upper limit of normal at baseline, found that total bilirubin increased after 12 months of placebo treatment and decreased after 12 months of treatment with OCA. In the double-blind phase of POISE, 14% of placebo-treated and 78% of OCA-treated patients with abnormal total bilirubin at baseline attained normal levels after 12 months. Further, of 10 placebo-treated and 20 OCA-treated patients with normal total bilirubin at baseline, 60% of placebo-treated and 15% of OCA-treated patients worsened to abnormal total bilirubin after 12 months. Per EASL clinical guidelines, increasing bilirubin levels – even within the normal range – indicate progressive disease and are strongly associated with adverse clinical outcomes.

About the POISE Trial
The POISE trial studied the safety and efficacy of once-daily treatment with OCA in PBC patients with an inadequate therapeutic response to, or who are unable to tolerate UDCA, the current standard of care. Of 216 patients randomized to three treatment arms—placebo, OCA 5 mg titrated to 10 mg or OCA 10 mg—93% continued receiving UDCA. The OCA 5-10 mg titration group received OCA 5 mg for six months, after which dosing was increased to 10 mg based on tolerability and biochemical response. The trial's primary endpoint was a reduction in ALP to below a threshold of 1.67 times the upper limit of normal, with a minimum of 15% reduction in ALP level from baseline and a normal bilirubin level after 12 months of therapy. The majority (97%) of the patients who completed the double-blind phase of the POISE trial entered an open-label extension.

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.

About Ocaliva® (obeticholic acid)
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.

EU IMPORTANT SAFETY INFORMATION

Contraindications
Hypersensitivity to the active substance or to any of the excipients and complete biliary obstruction.

Warnings and Precautions
Elevations in alanine amino transferase (ALT) and aspartate aminotransferase (AST) have been observed in patients taking obeticholic acid. Clinical signs and symptoms of hepatic decompensation have also been observed. These events have occurred as early as within the first month of treatment. Liver-related adverse events have primarily been observed at doses higher than the maximum recommended dose of 10 mg once daily. In the post marketing setting, serious liver injury and death have been reported with more frequent dosing of obeticholic acid than recommended in patients with moderate to severe decreases in liver function.

After initiation of therapy, all patients should be monitored for progression of PBC disease with laboratory and clinical assessment to determine whether dosage adjustment is needed. Patients at an increased risk of hepatic decompensation, including those with laboratory evidence of worsening liver function and/or progression to cirrhosis, should be monitored more closely. Dosing frequency should be reduced for patients who progress to advanced disease (i.e. from Child-Pugh Class A to Child-Pugh Class B or C).

Severe pruritus was reported in 23% of patients treated in the Ocaliva 10 mg arm, 19% of patients in the Ocaliva titration arm and 7% of patients in the placebo arm. The median time to onset of severe pruritus was 11, 158 and 75 days for patients in the Ocaliva 10 mg, Ocaliva titration and placebo arms, respectively. Management strategies include the addition of bile acid binding resins or antihistamines, dose reduction, reduced dosing frequency and/or temporary dose interruption.

Adverse Reactions
The most commonly reported adverse reactions were pruritus (63%) and fatigue (22%). Other common adverse reactions observed in clinical trials (> 5%) were abdominal pain and discomfort, rash, oropharyngeal pain, dizziness, constipation, arthralgia, thyroid function abnormality and eczema.

Drug Interaction
Bile acid binding resins such as cholestyramine, colestipol or colesevelam adsorb and reduce bile acid absorption and may reduce efficacy of obeticholic acid. When concomitant bile acid binding resins are administered, obeticholic acid should be taken at least 4-6 hours before or 4-6 hours after taking a bile acid binding resin, or at as great an interval as possible.

For detailed safety information for Ocaliva (obeticholic acid) 5 mg and 10 mg tablets including posology and method of administration, special warnings, drug interactions and adverse drug reactions, please see the European Summary of Product Characteristics.

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 about Intercept, please visit www.interceptpharma.com or connect with the company on Twitter and LinkedIn.

Forward-Looking Statements

This press release contains forward-looking statements, including, but not limited to, statements regarding the progress, timing and results of Intercept's clinical trials, including its clinical trials for the treatment of nonalcoholic steatohepatitis ("NASH"), the safety and efficacy of Intercept's approved product, Ocaliva (obeticholic acid or "OCA"), the potential approval of OCA in indications other than primary biliary cholangitis ("PBC") and the timing and potential commercial success of OCA and any other product candidates Intercept may develop.

These statements constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "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 Intercept undertakes no obligation to update any forward-looking statement except as required by law. These forward-looking statements are based on estimates and assumptions by Intercept's 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 Intercept's forward-looking statements: Intercept's ability to successfully commercialize Ocaliva in PBC; Intercept's ability to maintain its regulatory approval of Ocaliva in PBC in the United States, Europe, Canada and other jurisdictions in which it has or may receive marketing authorization; the initiation, cost, timing, progress and results of Intercept's development activities, preclinical studies and clinical trials, including its clinical trials for the treatment of NASH; the timing of and Intercept's ability to obtain regulatory approval of OCA in indications other than PBC and regulatory approval of any other product candidates it may develop; 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 products or product candidates; Intercept's plans to research, develop and commercialize its products and 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 Intercept's third-party suppliers and manufacturers; Intercept's collaborators' election 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 the other risks and uncertainties identified in Intercept's periodic filings, including Intercept's Annual Report on Form 10-K for the year ended December 31, 2017.

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