November 6, 2014

FLINT Trial in NASH Published in The Lancet

-OCA meets primary endpoint with high statistical significance of p=0.0002

-First therapeutic NASH trial to show significant improvement in liver fibrosis

- Investor conference call and webcast on Friday, November 7 at 8:00 a.m. ET

- Analyst event and webcast on Monday, November 10 at 6:30 p.m. ET

NEW YORK, Nov. 6, 2014 (GLOBE NEWSWIRE) -- Intercept Pharmaceuticals, Inc. (Nasdaq:ICPT) (Intercept), announced today that results from the FLINT trial evaluating obeticholic acid (OCA) for the treatment of nonalcoholic steatohepatitis (NASH) were published today in *The Lancet.*

In FLINT, OCA was superior to placebo for the primary outcome of improved liver histology (p = 0.0002) as described below, as well as the secondary endpoint of fibrosis improvement by at least one stage (p=0.004). Additionally, significant OCA treatment effects were demonstrated on the major histological features of NASH, including steatosis (p=0.001), lobular inflammation (p=0.006) and hepatocellular ballooning (p=0.03). Notably, post-hoc subgroup analyses found that the histological improvements were consistently greater in patients with more advanced disease and at greatest risk of progressing to liver failure and death. OCA was generally well tolerated in the FLINT trial, with pruritus occurring more frequently and at a higher grade in the OCA treatment group. The number of severe or life threatening events was not different compared to placebo.

NASH is a chronic, progressive form of fatty liver disease, marked by inflammation and scarring (fibrosis) of the liver. NASH is the most prevalent chronic liver disease, affecting more than 10% of the adult population of the United States [Williams 2011, Minervini 2009], greater than chronic hepatitis C viral infection and alcoholic liver disease. Obesity and type 2 diabetes, which afflict a large proportion of NASH patients, are important clinical risk factors associated with more progressive NASH-associated liver disease [Adams 2005].

FLINT was sponsored by the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK) and conducted by the NASH clinical research network (CRN), the same cooperative group that conducted the PIVENS trial [Sanyal 2011]. More than half of the NASH patients in the FLINT trial had co-morbid type 2 diabetes and, importantly, one third of the OCA-treated patients had advanced fibrosis (i.e., F3 bridging fibrosis). Therefore, the NASH population studied in FLINT had markedly more advanced disease than the non-diabetic NASH patients studied in PIVENS.

"The results of this landmark trial are exciting in light of the serious unmet need for new therapies for NASH," said Vlad Ratziu, M.D., Professor of Hepatology at the Institute for Cardiometabolism and Nutrition, Université Pierre et Marie Curie, Paris, France, and author of an accompanying editorial in *The Lancet*. "The results show that OCA has a clear improvement in all histologic features of NASH, fibrosis and markers of hepatic damage. Importantly, these benefits were observed in a difficult to treat patient population, which included a large proportion of diabetics and vitamin E non-responders. If the FLINT results are confirmed in phase 3, OCA could become an important new therapy for NASH patients who currently have no effective pharmacologic options."

"The readout from FLINT marks the first time that a therapy has been shown to meaningfully improve both liver fibrosis and other important histologic features of NASH in a significant proportion of patients," said Mark Pruzanski, M.D., CEO of Intercept. "After more detailed review of the data provided in the publication, we are pleased to see that the benefits observed with OCA therapy are consistent across key subpopulations of NASH patients, including those at most risk of progression to liver failure. FLINT provides us with a rich set of results in a 'real world' NASH population that will inform the design of our upcoming pivotal Phase 3 program that we plan to initiate in the first half of 2015."

Primary Endpoint

The proportion of patients meeting the FLINT primary histological endpoint, defined as a decrease in the NAFLD Activity Score (NAS) of at least two points with no worsening of fibrosis, was 45% in the OCA treatment group and 21% in the placebo group (p = 0.0002, n=219). Post-hoc subgroup analyses showed significant response rates in the OCA treatment group in patients with risk factors for disease progression, including baseline fibrosis stage, co-morbid type 2 diabetes, insulin resistance and severe obesity (each factor $p < 0.05$ for OCA compared to placebo based on 95% confidence interval of published odds ratios).

Secondary Endpoint: Fibrosis Stage Improvement

In FLINT, the NASH CRN fibrosis staging system was used to categorize the pattern of fibrosis and architectural remodeling of the liver: no fibrosis (F0), perisinusoidal or periportal fibrosis (F1), perisinusoidal and periportal fibrosis (F2), bridging fibrosis (F3) and cirrhosis (F4). Fibrosis sub-stages 1a, 1b and 1c were considered F1 for the analysis. A significantly greater proportion of OCA patients achieved an improvement of at least one fibrosis stage (35% vs 19%, p=0.004), with OCA showing greater response rates as compared to placebo across all stages of fibrosis. Detailed patient data grouped by fibrosis stage can be found in the Supplementary Appendix (Table S4A) of *The Lancet*, and show favorable OCA-mediated results in a subset of patients achieving fibrosis resolution, as well as reduced fibrosis progression to bridging fibrosis or cirrhosis, in each case as compared to placebo.

Additional Secondary Endpoints

More patients in the OCA treatment group experienced significant improvements in the major histological features of NASH, including steatosis (61% vs. 38%, p=0.001), lobular inflammation (53% vs 35%, p=0.006) and hepatocellular ballooning (46% vs 31%, p=0.03). The secondary endpoint of NASH resolution, based on a global histological assessment, also showed improvement, although not statistically significant (22% vs. 13%, p=0.08). Detailed patient data grouped by steatohepatitis category can be found in the Supplementary Appendix (Table S4B) of *The Lancet* and show more favorable OCA-mediated results on NASH resolution when excluding patients found not to have had NASH at baseline.

The histological improvements observed in OCA-treated patients versus placebo were accompanied by significant reductions in relevant biochemical parameters, including the serum liver enzymes alanine aminotransferase (ALT, $p < 0.0001$ at 72 weeks), aspartate aminotransferase (AST, p=0.0001 at 72 weeks), gamma-glutamyl transferase (GGT, $p < 0.0001$ at 72 weeks), each of which were above generally accepted normal limits at baseline, and total bilirubin (p=0.002 at 72 weeks). A modest but statistically significant increase in alkaline phosphatase (ALP, $p < 0.0001$ at 72 weeks) in the OCA treatment group was also observed, but levels remained within typical normal limits.

Consistent with earlier reported results, OCA treatment was associated with cholesterol changes that developed within 12 weeks of treatment initiation, then began reversing through the end of treatment and returned to baseline during the 24-week post-treatment follow-up phase. Based on these observations, lipid management was emphasized partway into the trial, using generally accepted guidelines. At 72 weeks as compared to baseline, the following effects were observed in the OCA treatment group: an increase in mean total cholesterol (0.16 mmol/L or 6 mg/dL increase OCA vs 0.19 mmol/L or 7mg/dL decrease placebo, $p < 0.0009$), an increase in mean LDL-cholesterol (0.22 mmol/L or 9 mg/dL increase OCA vs 0.22 mmol/L or 8 mg/dL decrease placebo, $p < 0.0001$), a decrease in mean HDL-cholesterol (0.02 mmol/L or 1 mg/dL decrease OCA vs 0.03 mmol/L or 1 mg/dL increase placebo, p=0.01) and a decrease in triglycerides (0.22 mmol/L or 20 mg/dL decrease OCA vs 0.08 mmol/L or 7 mg/dL decrease placebo, p=0.88).

In FLINT, statistically significant weight loss of an average of 2.3 kilograms was observed in OCA patients compared to no weight loss in the placebo group (p=0.008), and this weight loss reverted towards baseline during the 24-week follow-up phase. A pre-specified sensitivity analysis conducted by the investigators showed that weight loss was not a driver of the primary endpoint. An increase in a marker of hepatic insulin resistance, HOMA-IR (calculated as the product of fasting plasma insulin and glucose divided by 22.5) was observed at 72 weeks in the OCA treatment group (p=0.01). However, it should be noted that there was an imbalance in baseline plasma insulin levels (201 pmol/L OCA vs 138 pmol/L placebo), and an even larger relative and absolute increase in HOMA-IR was observed in the placebo group at the conclusion of the 24-week follow-up phase. This is potentially attributable to the inherent variability in HOMA-IR measurements, particularly in patients with type 2 diabetes, that make single time-point to time-point changes of this magnitude clinically uninterpretable [Jayagopal 2002]. There were virtually no changes in mean hemoglobin A1c, a measure of average blood sugar control over a period of approximately three months, in either OCA or placebo groups at 72 weeks. A previous study of OCA in diabetic NAFLD patients employed the hyperinsulinemic-euglycemic insulin clamp, the gold standard for detecting changes in insulin resistance, and demonstrated that OCA improved glucose disposal rate consistent with reduced insulin resistance [Mudaliar 2013].

Safety and Tolerability

OCA was generally well tolerated. Adverse events were generally mild to moderate in severity and the incidence in the OCA and placebo treatment groups was similar for all symptoms except pruritus. Pruritus in the OCA treatment group occurred more frequently (23% vs 6%, $p < 0.0001$), at a higher grade (predominantly moderate pruritus) and resulted in one patient discontinuation. The incidence of severe or life threatening events was not different between the two treatment groups and most of the events in both groups were deemed to be unrelated to treatment, including all severe or life threatening cardiovascular events. As previously disclosed, two deaths occurred in the OCA treatment group, but neither were considered related to OCA treatment.

Investor Conference Call and Analyst Details

Intercept will hold a conference call and webcast on Friday, November 7, 2014 at 8:00 a.m. ET to discuss today's publication.

Intercept will also webcast an analyst event on Monday, November 10, 2014 starting at 6:30 p.m. ET. During this webcast, management and key opinion leaders, including Dr. Scott Friedman (Icahn School of Medicine at Mt. Sinai), Dr. Gideon Hirschfield (University of Birmingham), and Dr. Vlad Ratziu (Université Pierre et Marie Curie) will review Intercept's development programs for PBC and NASH and the FLINT trial results.

Both events 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 required. A replay of the call will be available on our website approximately two hours after the completion of the call and will be archived for two weeks.

About FLINT

The Farnesoid X Receptor Ligand Obeticholic Acid in Nonalcoholic Steatohepatitis Treatment (FLINT) trial has been sponsored by the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK). FLINT enrolled 283 adult NASH patients at eight US centers comprising the NIDDK's NASH clinical research network (CRN). Patients were randomized to receive either a 25 mg dose of OCA or placebo for 72 weeks. Patients enrolled in the trial were qualified based on a diagnosis determined by liver biopsy at the start of the trial with a NAFLD Activity Score (NAS) of four or greater and with a score of at least one in each component of the NAS eight point scale (steatosis 0-3, lobular inflammation 0-3, ballooning 0-2). End of trial biopsies were conducted in patients after the 72-week treatment period, with all biopsies centrally scored in a blinded fashion. Further details can be found at http://clinicaltrial.gov/ct2/show/NCT01265498.

About NASH

NASH is a serious chronic liver disease caused by excessive fat accumulation in the liver that induces chronic inflammation which leads to progressive fibrosis (scarring) that can lead to cirrhosis, eventual liver failure and death. There are currently no drugs approved for the treatment of NASH. Studies have shown that 21-26% of NASH patients will develop cirrhosis over 8.2 years of follow-up [Matteoni 1999] and that liver-related mortality due to this disease is ten-fold that of the general population. According to recent epidemiological studies, it is estimated that more than 10% of the U.S. adult population has NASH, while 2.7% (potentially more than six million patients) are believed to have advanced liver fibrosis or cirrhosis due to progression of the disease [Williams 2011, Minervini 2009]. The proportion of liver transplants attributable to NASH has increased rapidly in past years and over the next decade the disease is projected to become the leading indication for liver transplant ahead of chronic hepatitis C and alcoholic liver disease. Diabetes is associated with a 23-fold higher risk of liver-related mortality [Younoussi 2004] in NASH patients. Patients with nonalcoholic fatty liver disease and diabetes are more likely to have advanced fibrosis (57% vs 19%) and NASH (84% vs. 57%)[Sanyal 2014]. NASH patients with advanced fibrosis and diabetes are at greater risk of progressing to cirrhosis, liver failure and cancer [Bhala 2011].

About Intercept

Intercept is a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat orphan and more prevalent chronic liver and intestinal diseases utilizing its expertise in bile acid chemistry. The company's lead product candidate, obeticholic acid (OCA), is a bile acid analog and first-in-class agonist of the farnesoid X receptor (FXR). OCA is being developed for a variety of chronic liver diseases including primary biliary cirrhosis (PBC), nonalcoholic steatohepatitis (NASH), and primary sclerosing cholangitis (PSC). OCA has received Fast Track Designation in the United States and orphan drug designation in both the United States and Europe for the treatment of PBC and PSC. Several large, randomized, controlled trials of OCA in the treatment of chronic liver disease have been completed. These include Intercept's Phase 3 POISE trial for the treatment of patients with PBC and the FLINT trial for the treatment of patients with NASH. Intercept owns worldwide rights to OCA outside of Japan, China and Korea, where it has out-licensed the product candidate to Sumitomo Dainippon Pharma. For more information about Intercept, please visit the company's website at: www.interceptpharma.com.

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 regarding the potential utility of the histological primary and secondary endpoints used in FLINT in designing future trials for regulatory approval; the potential acceptance by regulatory authorities of the endpoints used in FLINT; the anticipated clinical and regulatory milestones for OCA in NASH, including the potential timeframe for the commencement of our Phase 3 program in NASH; the anticipated prevalence of NASH and the potential increase thereof; 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 initiation, cost, timing, progress and results of our development activities, preclinical studies and clinical trials; the timing of and our ability to obtain and maintain regulatory approval of OCA and any other product candidates we may develop, particularly the possibility that regulatory authorities may require clinical outcomes data (and not just results based on achievement of a surrogate endpoint) as a condition to any marketing approval

for OCA, and any related restrictions, limitations, and/or warnings in the label of any approved product candidates; our plans to research, develop and commercialize our product candidates; the election by our collaborators to pursue research, development and commercialization activities; our ability to attract collaborators with development, regulatory and commercialization expertise; our ability to obtain and maintain intellectual property protection for its product candidates; our ability to successfully commercialize our product candidates; the size and growth of the markets for our product candidates and our ability to serve those markets; the rate and degree of market acceptance of any future products; 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; our need for and ability to obtain additional financing; our estimates regarding expenses, future revenues and capital requirements and the accuracy thereof; our ability to 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, 2013 filed on March 14, 2014 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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