Intercept Pharmaceuticals Announces REVERSE Phase 3 Study of Obeticholic Acid (OCA) in Compensated Cirrhosis due to NASH Did Not Meet its Primary Endpoint

September 30, 2022

Company remains on track to resubmit new drug application (NDA) for OCA in its lead indication of fibrosis due to NASH by year end based on its positive Phase 3 REGENERATE study

MORRISTOWN, N.J., Sept. 30, 2022 (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 REVERSE, a Phase 3 study evaluating the safety and efficacy of OCA in patients with compensated cirrhosis due to nonalcoholic steatohepatitis (NASH), did not meet its primary endpoint of a ≥ 1-stage histological improvement in fibrosis with no worsening of NASH following up to 18 months of therapy. No new safety signals for OCA were observed in this population of patients with cirrhosis.

REVERSE is one of Intercept's two Phase 3 studies evaluating different populations in NASH. The Company's planned NDA for its lead indication of liver fibrosis due to NASH will be supported by positive Phase 3 data from the REGENERATE study and is unaffected by the efficacy results of REVERSE. The Company is on track to resubmit its NDA in liver fibrosis due to NASH by the end of the year.

"Achieving statistical significance on a histology endpoint in compensated cirrhosis due to NASH has proven to be an extremely high bar in clinical trials and underscores the importance of treating liver fibrosis due to NASH before it progresses to cirrhosis," said M. Michelle Berrey, M.D., M.P.H., President of Research & Development and Chief Medical Officer of Intercept. "We remain confident in the potential role that OCA can play in liver fibrosis due to NASH and the Intercept team is focused on resubmitting our NDA in this indication based on the positive Phase 3 REGENERATE data."

In the REVERSE study of 919 randomized subjects with compensated cirrhosis due to NASH, 11.1% (p=NS) of subjects who were randomized to receive once-daily oral OCA 10 mg and 11.9% (p=NS) of subjects who were randomized to receive OCA 10 mg titrated to 25 mg (OCA 10-to-25 mg) after three months achieved a ≥1-stage improvement in fibrosis with no worsening of NASH after up to 18 months of treatment, compared with 9.9% of subjects who received placebo. Though the REVERSE study did not succeed on the histological evaluation of the primary endpoint, a positive impact on liver stiffness as defined by transient elastography was noted in both OCA 10 mg and OCA 10-to-25 mg arms.

Safety was evaluated in 916 subjects who took at least one dose of study drug (placebo, OCA 10 mg or OCA 10-to-25 mg). Treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs) and deaths were balanced across all treatment groups in REVERSE.

The most common TEAE was pruritus (31% in placebo, 41% in OCA 10 mg and 57% in OCA 10-to-25 mg) and pruritus was the most common reason for treatment discontinuation. Serious gallbladder-related events were balanced across arms (0.6% in placebo, 1.0% in OCA 10 mg, 1.0% in OCA 10-to-25 mg). Consistent with the known mechanism of action of FXR-agonists, the OCA 10-to-25 mg arm had a higher incidence of gallstones.

Independent experts reviewed certain categories of safety events to provide a blinded adjudication as specifically requested by FDA. These included events pertaining to hepatic safety, cardiovascular safety and renal safety. There was a numerical increase in the number of adjudicated hepatic safety events for the OCA-treated arms; most were mild in severity and related to biochemical changes. There were no severe or fatal adjudicated hepatic safety events in any treatment arm. Frequency of adjudicated kidney events and adjudicated major cardiac adverse events were balanced across treatment groups.

Intercept is grateful to the patients and clinicians who participated in the REVERSE trial. The Company will continue to work with REVERSE investigators to analyze the data from both the double-blind portion of the study as well as the open-label extension phase of REVERSE, and plans to share these data at an upcoming scientific forum.

About the REVERSE Study

REVERSE was a randomized, double-blind, placebo-controlled, multicenter Phase 3 study evaluating the safety and efficacy of OCA in NASH patients with compensated cirrhosis. The primary endpoint was the percentage of patients with histological improvement in fibrosis by at least one stage with no worsening of NASH using the NASH Clinical Research Network (CRN) scoring system after up to 18 months of treatment. Over 900 patients were randomized in a 1:1:1 ratio to the three treatment arms: once-daily placebo, OCA 10 mg, or OCA 10 mg for the first three months with titration in accordance with the study protocol up to OCA 25 mg for the remaining study period. Patients who successfully completed the double-blind phase of REVERSE were eligible to enroll in an open-label extension phase of the study for up to 12 additional months.

About Liver Fibrosis and Cirrhosis due to Nonalcoholic Steatohepatitis (NASH)

Nonalcoholic steatohepatitis (NASH) is a serious progressive liver disease caused by excessive fat accumulation in the liver that induces chronic inflammation, resulting in progressive fibrosis (scarring) that can lead to cirrhosis, eventual liver failure, cancer or death. There are currently no medications approved for the treatment of NASH.

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). For more information, please visit www.interceptpharma.com or connect with the Company on Twitter and LinkedIn.

Forward-Looking Statements

This press release contains forward-looking statements (FLS), including regarding resubmission and timing of Intercept's new drug application for OCA for treatment of liver fibrosis due to NASH. Important factors could cause actual results to differ materially from the FLS. For example, our resubmission could be delayed or be unsuccessful because of efficacy, safety, or tolerability concerns, problems with our clinical studies and their data or methods, or our inability to address to the satisfaction of the FDA the issues raised in their complete response letter of June 2020 responding to our

earlier submission.

Contact

For more information about Intercept, please contact:

For investors:
Nareg Sagherian, Executive Director, Global Investor Relations
Investors@interceptpharma.com

For media:
Karen Preble, Executive Director, Global Corporate Communications
Media@interceptpharma.com

Source: Intercept Pharmaceuticals, Inc.