



Intercept Reports Additional Positive Data from REGENERATE, the First Successful Phase 3 Study in NASH

April 11, 2019

OCA significantly improved fibrosis in patients with liver fibrosis due to NASH and demonstrated consistent efficacy across multiple histologic and biochemical parameters

REGENERATE data to be presented during the Opening Ceremony of EASL

NEW YORK, April 11, 2019 (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 additional supportive data from its pivotal Phase 3 REGENERATE study of obeticholic acid (OCA) in patients with liver fibrosis due to nonalcoholic steatohepatitis (NASH). The new data based on additional analyses show that OCA demonstrated robust efficacy across a range of additional histologic and biochemical parameters. These data from REGENERATE are being presented today at the International Liver Congress™ 2019, the 54th Annual Meeting of the European Association for the Study of the Liver (EASL), in Vienna, Austria.

"Halting or reversing fibrosis is a central therapeutic objective for patients with NASH, so the results from the 18-month interim analysis of REGENERATE are highly meaningful and clinically important," said Zobair M. Younossi, M.D., PhD, Professor and Chairman of the Department of Medicine at Inova Fairfax Medical Campus, Professor of Medicine at Virginia Commonwealth University, Inova Campus and the Chair of the REGENERATE Steering Committee. "The new REGENERATE data indicate that OCA also improves other important measures of liver health, including the key underlying drivers of NASH and biochemical tests that clinicians routinely monitor when managing patients in the real world."

REGENERATE is the largest Phase 3 trial in patients with fibrosis due to NASH and the study remains ongoing with more than 2,000 patients enrolled to confirm benefit on clinical outcomes.

Primary Efficacy Analysis

The primary efficacy analysis (Intent-to-Treat or ITT) assessed efficacy at 18 months in 931 patients with stage 2 or 3 liver fibrosis due to NASH. Patients with biopsy proven NASH with fibrosis were randomized 1:1:1 to receive placebo, OCA 10 mg or OCA 25 mg once daily. A repeat biopsy was conducted after 18 months for histologic endpoint assessment. Overall, study discontinuations in the primary efficacy analysis population were balanced across treatment groups.

As previously reported, in the primary efficacy analysis, once-daily OCA 25 mg met the primary endpoint of fibrosis improvement (≥ 1 stage) with no worsening of NASH⁽¹⁾ in 23.1% of patients compared to 11.9% of placebo patients at the planned 18-month interim analysis ($p=0.0002$ vs. placebo). In the primary efficacy analysis, a numerically greater proportion of patients in both OCA treatment groups compared to placebo achieved the primary endpoint of NASH resolution⁽²⁾ with no worsening of liver fibrosis; however, this did not reach statistical significance. As agreed with the U.S. Food and Drug Administration (FDA), in order for the primary objective to be met, the study was required to achieve one of the two primary endpoints.

Additional Supportive Efficacy Data

Additional supportive efficacy analyses were conducted using the per protocol population. The per protocol population ($n=668$) is defined as a subset of the ITT population and included all patients who completed ≥ 15 months of treatment, had a month 18/end of treatment biopsy, were on investigational product for at least 30 days immediately preceding the biopsy, and did not have any major protocol deviations. All p-values presented for the per protocol population are nominal. Of note:

- Approximately three-fold more patients in the OCA 25 mg group achieved an improvement of fibrosis by ≥ 2 stages compared to placebo (13.3% vs 4.5%; $p=0.0008$).
- In an analysis of changes in fibrosis by ≥ 1 stage, approximately three-fold more patients in the OCA 25 mg group improved versus worsened (38.0% vs 13.1%); in contrast, in the placebo group, a similar proportion of patients improved versus worsened (23.2% vs 20.9%).⁽³⁾
- Substantially more patients in the OCA 25 mg group achieved improvements in the key underlying features of NASH, including hepatocellular ballooning (where an improvement of ≥ 1 point was seen in 43.6% of patients receiving OCA 25 mg, as compared to 28.6% of patients receiving placebo [$p=0.0008$]) and lobular inflammation (where an improvement of ≥ 1 point was seen in 52.3% of patients receiving OCA 25 mg, as compared to 42.0% of patients receiving placebo [$p=0.03$]).
- Rapid and sustained reductions in key liver biochemistry parameters, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were observed in the OCA treatment groups.
 - In the OCA 25 mg group, 65.6% of patients with elevated ALT⁽⁴⁾ at baseline achieved normalization of ALT, compared to 37.3% of patients in the placebo group.
 - In the OCA 25 mg group, 54.7% of patients with elevated AST⁽⁴⁾ at baseline achieved normalization of AST, compared to 29.3% of patients in the placebo group.

Safety and Tolerability

The safety population included 1,968 randomized patients who received at least one dose of investigational product (OCA or placebo) with exposures up to 37 months. Adverse events were generally mild to moderate in severity and the most common were consistent with the known profile of OCA. The frequency of serious adverse events was similar across treatment groups (11% in placebo, 11% in OCA 10 mg, and 14% in OCA 25 mg), and no serious adverse event occurred in >1% of patients in any treatment group. There were 3 deaths in the study (2 in placebo: bone cancer and cardiac arrest and 1 in OCA 25 mg: glioblastoma) and none were considered related to treatment.

As previously disclosed, the most common adverse event reported was dose-related pruritus (19% in placebo, 28% in OCA 10 mg and 51% in OCA 25 mg). The incidence of pruritus across all three treatment groups was highest in the first three months and decreased thereafter. Of patients who experienced pruritus in the OCA 25 mg group, the vast majority of these events were mild to moderate in severity. A higher incidence of pruritus-associated treatment discontinuation was observed for OCA 25 mg (<1% in placebo, <1% in OCA 10 mg, and 9% in OCA 25 mg).

Consistent with observations from previous NASH studies, OCA treatment was associated with an increase in LDL cholesterol, with a peak increase of 22.6 mg/dL at 4 weeks and subsequently reversing and approaching baseline at month 18 (4.0 mg/dL increase from baseline). Triglycerides rapidly and continually decreased in the OCA treatment groups through month 18. There were few and varied serious cardiovascular events and incidence was balanced across the three treatment groups (2% in placebo, 1% in OCA 10 mg and 2% in OCA 25 mg).

With respect to hepatobiliary events, more patients (3%) on OCA 25 mg experienced gallstones or cholecystitis compared to <1% on placebo and 1% on OCA 10 mg. While hepatic serious adverse events were rare (<1% incidence in each of the three treatment groups), more occurred in the OCA 25 mg group with no pattern attributable to OCA.

About Liver Fibrosis due to 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 and death. Advanced fibrosis is associated with a substantially higher risk of liver-related morbidity and mortality in patients with NASH, and as early as 2020, the disease is projected to become the leading cause of liver transplants in the United States. There are currently no medications approved for the treatment of NASH.

About the REGENERATE Study

The Phase 3 REGENERATE study is a randomized, double-blind, placebo-controlled, multicenter study assessing the safety and efficacy of obeticholic acid (OCA) on liver-related clinical outcomes in patients with liver fibrosis due to NASH. An 18-month analysis was conducted to assess the effect of OCA in liver histology comparing month 18 biopsy with baseline. REGENERATE is targeted to enroll more than 2,000 adult NASH patients with stage 2 and 3 fibrosis across 339 qualified centers worldwide. A smaller exploratory cohort of 287 patients with high-risk early fibrosis (defined as stage 1 fibrosis and metabolic syndrome) were also enrolled in REGENERATE, but were not included in the primary efficacy analysis or per protocol analysis. These patients were included in the safety analysis. REGENERATE is planned to continue through clinical outcomes in order to confirm clinical benefit. The end-of-study analysis will evaluate the effect of OCA on mortality and liver-related clinical outcomes, as well as its long-term safety.

Conference Call at 5:45 p.m. CEST

Intercept will hold an investor event and conference call today at 5:45 p.m. CEST to discuss the REGENERATE data presented at EASL. The live event will be available on the investor page of Intercept's website at <http://ir.interceptpharma.com> or by calling (866) 312-3937 (toll-free domestic) or (574) 990-1191 (international) five minutes prior to the start time (Conference ID 3191358). 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 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](#).

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 development candidates, including OCA for NASH, the timing and acceptance of our potential regulatory filings and potential approval of OCA for NASH or any other indications in addition to PBC, the timing and potential commercial success of OCA and any other product candidates we may develop and our strategy, future operations, future financial position, future revenue, projected costs, financial guidance, prospects, plans, objectives of management and expected market growth.

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; 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, 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; our ability to timely and cost-effectively file for and obtain regulatory approval of our product candidates, including OCA for NASH, in the United States, Europe and our other target markets; conditions that may be imposed by regulatory

authorities on our marketing approvals for our 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 contained in the label of any of our products or product candidates; any potential side effects associated with Ocaliva for PBC, OCA for 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; 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 NASH, and our clinical trial activities; our ability to identify, develop and successfully commercialize our products and product candidates, including our ability to timely and successfully launch OCA for 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 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 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 prevent system failures, data breaches or violations of data protection laws; costs and outcomes relating to any disputes, governmental inquiries or investigations, 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 and short-term investments; our ability to acquire, license and invest in businesses, technologies, product candidates and products; our ability to attract and retain key personnel to manage our business effectively; our ability to manage the growth of our operations, infrastructure, personnel, systems and controls; our ability to obtain and maintain adequate insurance coverage; the impact of general U.S. and foreign economic, industry, market, regulatory or political conditions, including the potential 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, 2018.

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- (1) Defined as no worsening of hepatocellular ballooning, no worsening of lobular inflammation and no worsening of steatosis.
- (2) Defined as the overall histopathologic interpretation of (i) no fatty liver disease or (ii) fatty liver disease (simple or isolated steatosis) without steatohepatitis AND a nonalcoholic fatty liver disease (NAFLD) activity score of 0 for ballooning and 0-1 for inflammation.
- (3) Percentages for improvement or worsening are calculated based on per protocol population with available biopsy at Month 18 / end of treatment, which excluded 12 patients with missing or inadequate biopsies across the 3 treatment arms (n=656).
- (4) Upper Limit of Normal (ULN) as established by central laboratories is 55 U/L (ALT) and 34 U/L (AST).



Source: Intercept Pharmaceuticals, Inc.