NorthSea Therapeutics Announces Positive Phase 2 Topline Data in First-ever Randomized Placebo-controlled Study of an Oral Therapy in Intestinal Failure-Associated Liver Disease

Orziloben-treated patients saw rapid and sustained improvements in cholestatic liver injury.

Orziloben's differentiated multi-modal mechanism of action addresses three key biological drivers of IFALD: cholestasis, inflammation, and fibrosis.

Amsterdam, The Netherlands, November 9, 2026 – NorthSea Therapeutics B.V. ("NorthSea" or the "Company"), a private, late-stage clinical biotechnology company leveraging its proprietary SEFA™ platform to develop novel drugs addressing the multiple pathways implicated in rare heterogeneous liver diseases, today announced positive topline data from its Phase 2 study of orziloben (NST-6179) in adults with intestinal failure-associated liver disease (IFALD). The data, which was presented in a late-breaking oral presentation at AASLD The Liver Meeting® 2026, showed that orziloben rapidly reduced the three, key biological markers of IFALD with greater than 38% reduction in both alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT) and an approximately 30% reduction in bilirubin by week 12 of treatment.

IFALD is a serious heterogeneous rare liver disease, characterized by progressive hepatic dysfunction, manifesting as persistent cholestasis, hepatic inflammation, fibrosis, and ultimately biliary cirrhosis. It occurs in patients with intestinal failure who are receiving parenteral nutrition. There are currently no approved treatment options for IFALD.

"We are excited by the results from the Phase 2 study in IFALD, and what it means for people currently living with this life-threatening condition. Orziloben has the potential to be a truly transformative treatment option to address the unmet medical need," said Sophie Jeannin, M.D., Chief Medical Officer of NorthSea Therapeutics. "Orziloben is a highly differentiated potential therapy, with a multi-modal mechanism that addresses three key biological drivers of IFALD: cholestasis, through the targeting of PPAR-α, liver inflammation by targeting GPR84, and fibrosis by targeting PPAR-γ. The data presented at The Liver Meeting is key as we move ahead to Phase 3."

"IFALD is recognized by the FDA as a life-threatening and chronically debilitating disease with progression to end-stage liver disease, which can lead to the need for a liver transplant. As a practitioner, I have seen firsthand how devastating this disease can be. The robust data from this study showing rapid and sustainable reductions in multiple liver biomarkers, as well as a good safety profile, are very encouraging as a treatment option for IFALD patients," said Manpreet Mundi, M.D., Medical Director at the Home Parenteral and Enteral Nutrition Program, and Principal Investigator in the trial. "These findings provide a rationale for continued clinical development to further evaluate its clinical benefit in adults with IFALD."

Orziloben has been granted Orphan Drug Designation by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency's (EMA) Committee for Orphan Medicinal Products (COMP). It has also been granted Rare Pediatric Disease designation by the FDA.

The Phase 2 Study of Orziloben in IFALD

The Phase 2 study (NCT05919680) was a randomized, double-blind, placebo-controlled study, that evaluated safety, tolerability, pharmacokinetics, and pharmacodynamic effect of orziloben 800 mg once daily versus placebo for four weeks of treatment (Part A), and orziloben 1200 mg once daily for 12 weeks (Part B) in patients with IFALD. The study evaluated reductions from baseline in ALP, GGT, aspartate transaminase (AST), alanine transaminase (ALT), and bilirubin.

The Phase 2 trial enrolled a total 33 patients, with IFALD defined by persistent (≥6 months) elevation of at least one of the five key diagnostic criteria: ALP, GGT, ALT, or AST ≥1.5× upper limit of normal, and/or total bilirubin >1x upper limit of normal. Patients were categorized into subgroups according to the number of IFALD diagnostic criteria met at screening. Among the enrolled patients, 75% met ≥2 IFALD diagnostic criteria and 45% met ≥3 criteria. Those meeting multiple criteria demonstrated greater elevations in cholestatic and hepatocellular injury biomarker concentrations.

Safety and tolerability were similar across treatment groups, and no serious safety signals were detected.

About Orziloben
Orziloben is a novel, highly bioavailable and potent, oral drug candidate that is administered once daily for the treatment of intestinal failure associated liver disease (IFALD). Orziloben is a fully synthetic small molecule that is passively absorbed from the gut and directly targets the liver. Orziloben's differentiated multi-modal mechanism addresses three key biological drivers of IFALD: cholestasis (PPAR-α), inflammation (GPR84), and fibrosis (PPAR-γ).

About Intestinal Failure Associated Liver Disease (IFALD)
Intestinal failure-associated liver disease (IFALD) represents one of the most serious and life-threatening conditions in patients with intestinal failure (IF) receiving parenteral nutrition (PN). IFALD is a heterogeneous liver disease, characterized by progressive hepatic dysfunction, manifesting as persistent cholestasis, hepatic inflammation, fibrosis, and ultimately biliary cirrhosis.[1] There are an estimated 53,000[2] patients in the United States with chronic intestinal failure. Of these, approximately 15-40% of adults and approximately 40-60% of children develop IFALD.[3]

About our Phase 2
The Phase 2 trial was a randomized, double-blind, placebo-controlled study, evaluating safety, tolerability, pharmacokinetics, and pharmacodynamic effect of orziloben 800 mg oral administration once daily in adult patients with IFALD versus placebo for four weeks of treatment, and orziloben 1200 mg oral administration once daily for 12 weeks. The trial has evaluated reductions from baseline in alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), bilirubin, aspartate transaminase (AST), and alanine transaminase (ALT).

About NorthSea Therapeutics

NorthSea Therapeutics B.V. is a private, late-stage clinical biotechnology company that leverages its SEFA™ platform to develop novel drugs that target cholestatic, inflammatory, and fibrotic pathways to treat rare heterogeneous liver diseases that require a multi-modal mechanism of action. Its proprietary SEFAs are designed to target each of these key disease pathways simultaneously in a single, oral dose, offering potential first-in-class treatments. NorthSea's lead program is orziloben, a Phase 2 program for the treatment of intestinal failure associated liver disease (IFALD). NorthSea's investors include Forbion, Ysios Capital, venBio, Novo Seeds, Sofinnova, BGV, and New Science Ventures. Headquartered in the Netherlands, NorthSea also has a presence in the U.S. and Norway. To learn more, visit https://northseatherapeutics.com/en/.

[1]Pironi et al. 2023; Cuerda et al. 2021; Di Dato et al. 2022
[2] Komodo Claim Data Analysis; April 2026
[3]Zafirovska, M.; Zafirovski, A.; Rotovnik Kozjek, N. Current Insights Regarding Intestinal Failure-Associated Liver Disease (IFALD): A Narrative Review. Nutrients 2023, 15, 3169. https://doi.org/10.3390/nu15143169

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