NorthSea Therapeutics Initiates Phase 2A Trial of Orziloben (NST-6179) in Intestinal Failure-Associated Liver Disease (IFALD)

- Phase 2a study evaluating the safety, tolerability, PK, and PD of Orziloben in IFALD
- The study will enrol up to 36 adult subjects at multiple sites in North America
- Study strengthens NST's position as a multi-asset, clinical stage company

Amsterdam, The Netherlands, 21 February 2024 – NorthSea Therapeutics B.V. ('NST', or the 'Company'), a biotech company developing novel and innovative strategies for the treatment of non-alcoholic steatohepatitis (NASH) and other liver-associated metabolic diseases, today announced the dosing of the first patient in its Phase 2a clinical trial of Orziloben (NST-6179) in intestinal failure-associated liver disease (IFALD), an orphan liver disease affecting individuals on prolonged intravenous (parenteral) nutrition (PN).

The trial is a randomized, double-blind, Phase 2a, placebo-controlled study, which will be conducted at multiple sites across North America. It is designed to evaluate the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of Orziloben in adult subjects with IFALD. The readout of the trial is anticipated in H2 2025.

For more information on the study, see ClinicalTrials.gov (NCT05919680).

Commenting on the milestone, Rob de Ree, NST's CEO, said: *"Dosing the first patient in our Phase 2a trial for Orziloben in IFALD is a significant achievement for NorthSea Therapeutics, and is a testament to our commitment to advance innovative treatments for liver diseases. There is a critical need for effective therapies in IFALD as, to date, there are no drug therapies approved to treat this orphan indication. We believe Orziloben has the potential to make a substantial impact in addressing this unmet medical need."*

IFALD is a complex condition, characterized by the development of hepatic inflammation, cholestasis and steatosis, in patients with intestinal failure and/or short bowel syndrome. It is known to be associated with prolonged administration of PN. One major concern for patients with the condition is the development of hepatic fibrosis, which can progress to cirrhosis and liver failure.

Preclinical studies have demonstrated the efficacy of Orziloben in preventing severe cholestasis, fibrosis, and other key markers of liver damage in models where PN was administered. In one pre-clinical model of PN-induced liver injury, Orziloben treatment completely prevented severe

cholestasis and the development of fibrosis. Orziloben was also shown to prevent the pronounced increase in markers of liver damage in another in vivo model of PN in combination with an inflammatory stimulus (endotoxin). Furthermore, Orziloben significantly reduced the number of myofibroblasts, the main collagen producing cell in the liver, in addition to hepatic inflammation and steatosis in a model of established fibrosis. The unique ability of Orziloben to target multiple pathogenic components of IFALD, and its potential for oral dosing, make it a promising candidate for the treatment of PN-induced liver disease, as well as other liver disease indications.

Professor Palle Bekker Jeppesen, Head of the Department of Intestinal Failure and Liver Diseases at Rigshospitalet in Copenhagen, added: *"Orziloben has shown consistently robust efficacy in several pre-clinical models, and has demonstrated a strong preventative effect on important disease pathophysiology components, such as cholestasis and fibrosis. If these impressive pre-clinical effects translate to clinical effects, Orziloben has the potential to become an effective therapeutic for intestinal failure patients who currently have limited treatment options."*

If you are interested in learning more about Orziloben, the NorthSea Therapeutics team will be attending the ASPEN 2024 Nutrition Science & Practice Conference (2-5 March, Tampa, Florida). Please contact: carine.beysen@northseatherapeutics.com

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Notes to Editors

About Intestinal failure-associated liver disease (IFALD)

IFALD is a multifactorial condition in patients with intestinal failure and/or significant resection. It is characterized by the development of hepatic inflammation, cholestasis, and steatosis. It has been shown to be associated with prolonged administration of parenteral nutrition (PN). Patients with IFALD are often asymptomatic in the early stages but progress with signs of liver damage such as increases in liver chemistry tests, steatosis, and fibrosis. If left untreated, the live damage can eventually lead to liver failure, transplant, and death. There is a clear medical need for treatment options for patients and there is currently no approved therapy for IFALD.

About Orziloben

Orziloben is a novel, orally administered, highly potent, synthetic, medium chain fatty acid analogue (MCFA). MCFAs are rapidly absorbed via passive diffusion, rather than receptor-mediated transport, but are rapidly metabolised. Orziloben was designed to maintain the ease of transport to the liver and into cells that is characteristic of unmodified MCFAs, whilst offering enhanced pharmacological effects by avoiding rapid metabolism.

In one pre-clinical model of intravenous PN-induced liver injury, Orziloben treatment completely prevented severe cholestasis and the development of fibrosis. Orziloben was also shown to prevent the pronounced increase in markers of liver damage in a model of PN in combination with an inflammatory stimulus (endotoxin). Furthermore, Orziloben significantly reduced the number of myofibroblasts, the main collagen producing cell in the liver, in addition to hepatic inflammation and steatosis in a model of established fibrosis.

The ability of Orziloben to target multiple pathogenic components of IFALD, in addition to its potential for oral dosing, highlight its potential to become a highly efficacious drug for the treatment of PN-induced liver disease as well as potentially other liver disease indications.

About NorthSea Therapeutics

NorthSea Therapeutics B.V.(NST) is a Dutch biotech company focused on developing structurally engineered fatty acids ('SEFAs') for the treatment of NASH and other metabolic disorders. NST licensed the rights to its lead compound icosabutate and a library of SEFAs from BASF Norge AS (formerly known as Pronova BioPharma Norge AS), who developed Lovaza® (US brand, branded Omacor® in Europe), a blockbuster cardiometabolic drug.

Icosabutate has been found safe and well tolerated in two prior Phase 2 clinical studies for treatment of hypertriglyceridemia and mixed dyslipidemia and is currently in clinical development for NASH. The results of the icosabutate Phase 2b ICONA NASH trial were announced in November 2023.

Two additional SEFAs are also in clinical development: NST-1024, which is being developed for SHTG, has entered Phase 2a; and Orziloben, which is being developed for the orphan indication IFALD (Intestinal Failure Associated Liver Disease), initiated a Phase 2a study in Q1-2024.

NST is headquartered in the Netherlands with a presence in Norway and the US and is supported by Forbion Growth, Forbion Ventures, Novo Holdings, venBio Partners and Sofinnova investments, Ysios Capital, BGV and NSV.

Find out more about us online at: www.northseatherapeutics.com

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