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Icosabutate latest data shows direct and potent anti-fibrotic effect in both differentiated rodent NASH models and human stellate cells.

Results to be presented at the AASLD congress 2018, 9-13 November

- In a biopsy-confirmed fibrotic *ob/ob* NASH mouse model, icosabutate reduced hepatic fibrosis in association with a 45% decrease in myofibroblast content in pre- versus post-treatment liver biopsies
- In a CDAA NASH mouse model, icosabutate reduced fibrosis levels to baseline despite delayed onset of treatment in association with a >50% reduction in collagen fiber number
- Highly significant anti-proliferative effects of icosabutate demonstrated in human stellate cells *in vitro*
- Extensive changes in the hepatic concentrations of multiple lipotoxic NASH-associated lipid species
- Superior anti-fibrotic and anti-inflammatory efficacy versus other late-stage NASH drugs under development
- Strong impetus for phase 2b NASH trial initiation in 2019 Q2

Naarden, The Netherlands, Xx November 2018 – NorthSea Therapeutics B.V., ('NST') a newly established Dutch biotech company developing novel and innovative strategies for the treatment of NASH and other metabolic, inflammatory and fibrotic diseases, today announces the publication of two posters to be presented at the AASLD The Liver Meeting™ 2018 in San Francisco on 9-13 November. The posters will outline the Company's latest research data of its lead product's anti-fibrotic effect in both differentiated rodent NASH models and human stellate cells.

NorthSea Therapeutics' lead product, icosabutate, is a structurally designed fatty acid that regulates pivotal lipid signalling pathways involved in hepatic inflammation and fibrosis.

Commenting on the newest data, Dr. David A. Fraser, NorthSea's CSO, stated,"Icosabutate exhibits consistent anti-fibrotic effects in multiple NASH models, but it was unclear whether these effects were indirect. The new data in proliferating human stellate cells suggest these effects are not dependent on paracrine signals from other cell types. These findings are of considerable relevance to given the association between degree of fibrosis and clinical outcomes and the complexity of indirect targeting of fibrosis in a highly heterogenous patient population."

All experiments were carried out in the laboratories of Professor Detlef Schuppan, Professor Scott Friedman and with Gubra (CRO), where pre- and post-treatment liver biopsies allowed longitudinal comparisons to be assessed in a well-established NASH ob/ob mouse model.

Both posters highlight the superior efficacy of icosabutate versus other late-stage NASH drugs on multiple fibrosis endpoints in rodent models. Data collected utilising an advanced optical imaging technique showing that the reduction in fibrosis after icosabutate treatment is associated with a >50% reduction in collagen fiber number, with no significant change after treatment with a GLP-1R agonist used as control.

Professor Scott Friedman, Scientific Advisory Board member and expert in stellate cell biology, liver fibrosis and NASH, added, “Proliferation of myofibroblasts is a key driver of fibrogenesis and thus represents an attractive target for novel anti-fibrotic therapies. Icosabutate’s ability to inhibit proliferative responses without reducing cell viability is a promising attribute of the compound and, while the mechanism is being explored, could translate into a potential benefit of reducing hepatic fibrosis in NASH.”

Commenting on the combined preclinical and clinical results, Professor John J. Kastelein, Scientific and Advisory Board member, added: “We frequently see that the improved efficacy of a drug is offset by a worsening in the safety profile. On the contrary, icosabutate demonstrates superior efficacy versus other NASH drugs under development and, based on its clinical profile in hyperlipidemic subjects, should also prove superior on both safety and treatment of comorbidities.”

Previous phase 1b and two phase 2 clinical studies on icosabutate in hyperlipidemic subjects have demonstrated significant improvements in atherogenic lipids/lipoproteins and glycemic control along with excellent safety. Icosabutate is on course to be phase 2b ready by Q2 2019 .

For more information please visit the NorthSea team in the poster area of the conference.

Poster 1

Icosabutate, a novel structurally engineered fatty-acid, exhibits potent anti-inflammatory and anti-fibrotic effects in a dietary mouse model resembling progressive human NASH

Session Date and Time: Saturday, November 10, 2018, 2:00 PM
Presentation Type: Poster Presentation
Location: Moscone Center North/South Building, Hall C

Poster 2

A liver-targeted structurally engineered fatty acid, icosabutate, potently reduces hepatic pro-fibrotic gene expression and improves glycemic control in an obese diet-induced mouse model of NASH

Session Date and Time: Sunday, November 11, 2018, 8:00 AM
Presentation Type: Poster Presentation
Location: Moscone Center North/South Building, Hall C

The two posters will also be available to view on the Northsea Therapeutics website once the congress has started: http://www.northseatherapeutics.com/AASLD

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Notes to Editors

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 inflammatory, metabolic and liver diseases. NST licensed the rights to its lead compound icosabutate and a library of discovery- and pre-clinical-stage SEFAs from Pronova BioPharma Norge AS, who developed Omacor®, a blockbuster cardiovascular drug. Icosabutate has been found safe and effective in two prior phase 2 clinical studies for treatment of hypertriglyceridemia and is currently in clinical development for NASH, aiming to start a phase 2b study by Q2 of 2019. NST is a Dutch company, backed by Forbion Capital, Novo Seeds, BGV and NSV. Its employees are also based in the UK and Norway.

www.northseatherapeutics.com

About NASH

NASH is liver inflammation and damage often preceded by a build-up of fat in the liver and represents a more advanced stage of non-alcoholic fatty liver disease (NAFLD). Although a similar condition can occur in people who abuse alcohol, NASH occurs in those who drink little to no alcohol. It is frequently associated with certain metabolic disorders such as diabetes, obesity and insulin resistance. An estimated 15–30% of the adult population in developed countries have NAFLD, 10-15% of whom may advance to NASH representing at least ~15–30 million patients in the 6 major markets. Further disease progression in 15-20% of NASH patients leads to advanced liver fibrosis and cirrhosis with a high risk of liver failure, hepatocellular cancer and the need for liver transplantation.

About icosabutate

Fatty-acids and their metabolites function as signalling molecules in a broad array of pathways in the liver regulating metabolic, inflammatory and fibrotic responses.

Icosabutate is an orally administered, structurally engineered, liver-targeted eicosapentaenoic acid derivative designed to directly target the liver via the portal vein, avoid β-oxidation and minimize esterification into complex lipids. The structural modifications result in high hepatic concentrations of non-esterfied icosabutate and its metabolites that in turn regulate multiple metabolic, inflammatory and fibrotic pathways of relevance to NASH. In addition to improving components of the metabolic syndrome, such as insulin resistance and dyslipidemia, these pleiotropic actions, coupled with an excellent safety profile, suggest that icosabutate could offer a highly efficacious treatment option for NASH.