Press release

Dr. Falk Pharma announces positive results from its pivotal phase 3 trial on norucholic acid in primary sclerosing cholangitis

Freiburg, May 7th, 2025

Study results demonstrate superiority of norucholic acid (NCA) over placebo in the combined primary endpoint. There is currently no approved medicine to treat primary sclerosing cholangitis. The results of the 96-week analysis of the NUC-5 trial will be presented at 2025 EASL Congress in Amsterdam.

Dr. Falk Pharma, a research-based pharmaceutical company specializing in digestive and metabolic medicine, today announced positive results from its pivotal, phase 3 trial (NUC-5) on norucholic acid (NCA) in primary sclerosing cholangitis (PSC).

NUC-5 (NCT03872921) is a double-blind, placebo-controlled trial enrolling 301 patients with PSC, who receive either 1,500 mg NCA or placebo for a total of 192 weeks. At the primary data analysis after 96 weeks of treatment, the primary endpoint of combined partial normalization of blood levels of a liver enzyme linked to PSC (alkaline phosphatase) and no worsening of disease stage on histology was achieved by a statistically significantly greater proportion of patients receiving NCA than placebo. Significant superiority of NCA was also observed in multiple secondary endpoints. The safety results revealed similar rates of study patients with adverse events and serious adverse events between the NCA and placebo groups.

The topline results from NUC-5 will be presented during the Late Breaker session on Saturday, May 10, 2025 at the EASL Congress in Amsterdam.

PSC is a rare, progressive disease in which the immune system attacks the bile ducts in the liver, which leads to fibrosis, or the formation of scar tissue. A considerable proportion of patients develop bile duct, liver, or colorectal cancer, while many others eventually progress to cirrhosis of the liver. No approved pharmaceutical treatment is currently available, and the most effective treatment option is liver transplantation.

“Finding a medicine that effectively treats PSC has been a challenge in the field of hepatology for decades” said Prof. Michael Trauner, Head of the Division of Gastroenterology and Hepatology at the Medical University of Vienna, Austria and principal investigator of the trial. “After so many disappointments in this space, the first positive results from a phase 3 study on PSC is a watershed moment for people with PSC, their families, physicians and the entire PSC community. The results of this study will not only advance patient care but will also give researchers new insights into the disease itself”.

“We are very excited about the positive results of the NUC-5 trial, which was the largest clinical trial on PSC to date which compared biopsies from patients before and after treatment” said Dr. Kai Pinkernell, Managing Director Science and Innovation for Dr. Falk Pharma. “A trial of this duration and involvement is a major undertaking, and we thank all of the participating patients, investigators, and trial staff for their dedication to this trial”.

About norucholic acid

Norucholic acid is an engineered bile acid derivative. Unlike endogenous bile acids, it undergoes no meaningful amidation with glycine or taurine, allowing NCA to be absorbed from bile by cholangiocytes and subsequently re-secreted into bile by hepatocytes in a process called cholehepatic shunting. This together with putative direct anti-inflammatory and anti-fibrotic mechanisms are thought to confer protective effects in PSC. In a previous phase 2 trial, 12 weeks of treatment with NCA was shown to significantly reduce levels of alkaline phosphatase (ALP).

About NUC-5

NUC-5 is a randomized, double-blind, placebo-controlled trial enrolling 301 patients with biopsy-confirmed PSC and levels of ALP at least 1.5-fold greater than the upper limit of normal (ULN). The combined primary endpoint was partial normalization of ALP to <1.5-fold ULN and no worsening of disease stage by histology (Ludwig classification). The key secondary endpoint was partial normalization of ALP to <1.5-fold ULN and no worsening of disease stage by histology (modified Nakanuma staging).

At week 96, 15.1% of patients receiving NCA achieved the primary endpoint compared to 4.2% of placebo patients ($p = 0.0048$). Similarly, 15.1% of NCA patients versus 5.1% of placebo patients achieved the key secondary endpoint ($p = 0.0086$). NCA treatment led to improvement by at least 1 Ludwig stage for 25.2% of NCA patients compared to 10.5% of placebo patients ($p = 0.0217$). Furthermore, worsening by at least one Ludwig stage was observed in 40.4% of placebo patients compared to 20.3% of NCA patients ($p = 0.0069$). Blood levels of multiple liver enzymes improved under NCA but not placebo. NCA was well tolerated, with similar rates of serious adverse events between the two arms.

NUC-5 is still ongoing, with patients receiving continuous double-blind treatment with either NCA or placebo for an additional 96 weeks. Additional results will be reported after the conclusion of all 192 weeks of double-blind treatment. Patients completing all 192 weeks of double-blind treatment will have the option of receiving open-label treatment with NCA for up to 72 weeks.

Read the abstract here (LBO-001)

About Dr. Falk Pharma GmbH

Dr. Falk Pharma GmbH has been developing and marketing innovative medicines to treat a wide range of gastrointestinal disorders like inflammatory bowel disease or eosinophilic esophagitis as well as hepatobiliary disorders such as primary biliary cholangitis for over 60 years. As the international experts in digestive and metabolic medicine, the company brings together physicians, scientists, and patients to devise new and powerful approaches to patient care. Dr. Falk Pharma engages in pre-clinical and clinical stage research that aims to meaningfully improve therapeutic practice as well as patient health and well-being. A family-owned business with a global presence, Dr. Falk Pharma has ten affiliates in Europe and Australia and is continuously growing. The company has its headquarters and R&D facilities

in Freiburg, Germany, its pharmaceutical products are manufactured in Europe, mainly at sites in Germany, France, Italy and Switzerland. Dr. Falk Pharma GmbH employs approximately 1400 individuals globally and 340 in Freiburg.

Further information on Dr. Falk Pharma can be found online: https://drfalkpharma.com

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