

# News Release

February 19, 2019  
EA Pharma Co., Ltd.

## EA Pharma Signs A License Agreement with Dr. Falk Pharma GmbH for A Novel Liver Disease Treatment “nor-Ursodeoxycholic Acid” for Japan Market

EA Pharma Co., Ltd. (President, Yuji Matsue; Headquarters, Tokyo, Japan) (hereinafter “EA Pharma”) has signed a license agreement with Dr. Falk Pharma GmbH (Managing Directors, Roland Greinwald, Philipp Argast and Susanne Höppner; Headquarters, Freiburg, Germany) (hereinafter “Dr. Falk Pharma”) to grant EA Pharma the rights to develop, manufacture and commercialize nor-Ursodeoxycholic Acid (norUDCA), Dr. Falk Pharma’s developing new liver disease treatment, in Japan.

Under the license agreement, EA Pharma develops norUDCA for treatment of primary sclerosing cholangitis (PSC) and non-alcoholic steatohepatitis (NASH) in Japan. Once the marketing approval is obtained, EA Pharma will exclusively commercialize norUDCA in Japan. EA Pharma pays an upfront payment, milestone payments and royalties to Dr. Falk Pharma under the license agreement.

norUDCA is a novel liver disease treatment that Dr. Falk Pharma has been developing for treatment of PSC and non-alcoholic fatty liver disease (NAFLD). In Phase II clinical trial in patients with PSC conducted in European countries, improvements in liver function parameters including alkaline phosphatase were demonstrated. PSC is one of the designated intractable diseases in Japan. PSC can progress to non-compensated liver cirrhosis, but there exists no effective medicine indicated for PSC at this moment. Development of new treatment to suppress disease progression of PSC has been awaited. Further, in Phase II clinical trial in patients with NAFLD conducted in European countries, improvements in liver fat content and liver stiffness in addition to alanine aminotransferase, which is a liver damage parameter, were confirmed. The results suggest that norUDCA can be available as a treatment of NASH. EA Pharma and Dr. Falk Pharma will collaborate under the license agreement to quickly obtain the marketing approval of norUDCA in Japan.

As a gastrointestinal specialty pharma, EA Pharma positions “inflammatory bowel disease”, “liver and pancreatic diseases”, “gastrointestinal function and symptoms improvement”, and “gastrointestinal mucosal protection” and “supports for gastrointestinal endoscopy/surgery” as its key areas to provide new solutions for unmet medical needs. EA Pharma expects that development of norUDCA as a new treatment of liver disease can contribute to fulfilment of unmet medical needs of patients with liver diseases for which no effective treatment exist at this moment.

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## More Information

### 1. About nor-Ursodeoxycholic Acid (norUDCA)

norUDCA is a homologue of Ursodeoxycholic acid (UDCA), with a shorter side chain than that of UDCA. norUDCA is an artificially synthesized bile acid. As compared to UDCA, norUDCA has a relative resistance to taurine and glycine conjugation, and, once the nonconjugated acid form is secreted into the bile, it can be reabsorbed by cholangiocytes and return to hepatocytes (this process is called cholehepatic shunting). This process increases bicarbonate ion secretion in the bile duct as well as bile acid production, which can protect the bile duct and the liver.

### 2. About Primary Sclerosing Cholangitis (PSC)

PSC is a progressive chronic inflammatory disease with fibrous stenosis of the intra- and extra-hepatic bile ducts. PSC is one of the designated intractable diseases by the Ministry of Health, Labour and Welfare (MHLW) of Japan. Based on the epidemiological survey conducted in 2007, it is estimated that the total number of patients in Japan is approximately 1,200<sup>1)</sup>. Although its etiology is unknown, autoimmunity is thought to relate, like autoimmune hepatitis and primary biliary cholangitis. According to a nation-wide questionnaire survey conducted in Japan in 2012, the prevalence was relatively high in male and showed bimodal peaks in the ages of 20s and 60s. The survey report also says that most patients had lesions in both intra- and extra-hepatic bile ducts and disease complications of cholangiocarcinoma in 7.3% and ulcerative colitis in 34%<sup>2)</sup>. At this point in time, however, there exists no medicine indicated for PSC available in the market.

### 3. About Non-Alcoholic Fatty Liver Disease (NAFLD) and Non-Alcoholic Steatohepatitis (NASH)

If diagnosed with fatty liver by histology or diagnostic imaging regardless of no alcohol drinking habit, the condition is called non-alcoholic fatty liver disease (NAFLD). In 80-90% of patients with NAFLD, the disease remains a simple fatty liver for long years. But, in 10-20%, the disease gradually progresses to involve liver cirrhosis or liver cancer. Among the fatty liver disease of non-alcohol cause, if the fatty liver disease involves inflammation and fibrosis, the condition is called NASH, which can progress to liver cirrhosis or liver cancer. It is reported that the disease prevalence of NAFLD is 9-30% and the total number of patients for NAFLD in Japan is more than 10,000,000, many in the middle age in male and the elderly in female. In addition, the disease prevalence of NASH is estimated to be 3-5%<sup>3)</sup>. With increase of patients with obesity or metabolic syndrome, the patient number of NAFLD and NASH can increase. At this point in time, however, there exists no medicine indicated for NAFLD and NASH available in the market.

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## 4. About EA Pharma Co., Ltd.

EA Pharma, a subsidiary of Eisai Co., Ltd. for gastrointestinal disease area, was established in April 2016 by integration of the gastrointestinal business unit with more than 60 years' history of the Eisai Group and the gastrointestinal business unit of the Ajinomoto Group having amino acid as its business core. EA Pharma is a gastrointestinal specialty pharma with a full value chain covering R&D, logistics and sales & marketing.

For more information on EA Pharma Co., Ltd., please see <http://www.eapharma.co.jp/en/>

## 5. About Dr. Falk Pharma GmbH

Dr. Falk Pharma GmbH is one of the leading companies worldwide in gastroenterology with its products being sold in more than 60 countries. Its pharmaceuticals are used successfully to treat inflammatory bowel disease, cholestatic liver disease, irritable bowel syndrome, constipation, and for colon cleansing prior to colonoscopies. The Falk Foundation, which is associated with the company, provides medical information via international symposia, forums, postgraduate courses and literature services. Over the past 45 years the Falk Foundation has sponsored more than 200 international Falk symposia and workshops in which over 100,000 researchers and physicians from 110 countries have come together to advance knowledge in gastroenterology and hepatology.

Rectabul® 2 mg Rectal Foam 14 Doses (budesonide rectal foam), for which EA Pharma obtained marketing approval in Japan in November 2017, is an ulcerative colitis treatment in-licensed from Dr. Falk Pharma.

For more information on Dr. Falk Pharma GmbH, please see <https://www.dralkpharma.de>

1) Japan Intractable Disease Information Primary Sclerosing Cholangitis (Designated intractable disease 94) :

<http://www.nanbyou.or.jp/entry/3967>

2) Japan Intractable Disease Information Primary Sclerosing Cholangitis (Designated intractable disease 94) :

<http://www.nanbyou.or.jp/entry/3968>

3) THE JAPANESE SOCIETY OF GASTROENTEROLOGYGUIDELINE NAFLD/NASH GUIDE :

<https://www.jsge.or.jp/guideline/disease/naflid.html>