Press release

Dr. Falk Pharma and Zedira announce start of the phase 2b real-life study of ZED1227 for the treatment of Celiac Disease

Freiburg and Darmstadt, November 2nd, 2021

Dr. Falk Pharma GmbH and Zedira announce start of the phase 2b clinical trial of ZED1227, a direct-acting and specific inhibitor of tissue transglutaminase, in patients with Celiac Disease. The real-life study enrolls 400 patients in several European countries including Germany, Finland, and Norway. The placebo-controlled dose-finding study will evaluate the efficacy and tolerability of the new pharmacological agent in Celiac Disease subjects experiencing symptoms and having mucosal damage despite gluten-free diet.

Efficacy, safety, and tolerability of ZED1227 have already been shown in earlier successful clinical trials. Especially the encouraging results of the phase 2a proof-of-concept gluten-challenge study revealed that each of the three active dose groups met the primary endpoint: ZED1227 attenuated the gluten-induced mucosal damage as indicated by the villous height to crypt depth ratio. Compared to placebo, all three doses provided statistically significant protection from duodenal mucosal injury. Moreover, ZED1227 protected from inflammation and yielded significantly improved patient reported outcome. Further, the oral compound was found to be safe and well tolerated. The results of the study were published on July 1st, 2021, in the *New England Journal of Medicine* (N Engl J Med 2021;385:35-45. DOI: 10.1056/NEJMoa2032441).

Celiac Disease is the most common chronic inflammation of the small intestine. The autoimmune disease affects up to 2% of most populations and is caused by nutritional gluten in genetically predisposed individuals. A key step in Celiac Disease pathogenesis is gluten-deamidation and immunogenic potentiation catalyzed by the patient's own tissue transglutaminase in the gut. The small molecule ZED1227 designed by Zedira scientists targets the dysregulated transglutaminase within the small intestine, to prevent the immune response to transglutaminase-modified gluten which drives the disease process. Blocking tissue transglutaminase has the potential to offer patients additional safety when used in conjunction with a 'largely' gluten-free diet thereby improving the quality-of-life of millions of people.

Dr. Falk Pharma licensed the rights for ZED1227 in Europe and took responsibility of preclinical and clinical development of the new chemical entity towards a pharmacological agent. The license agreement secured Zedira an upfront payment and further milestone payments as well as royalties. The rights outside Europe are jointly owned by the partners.

The early phase of the development of ZED1227 was accompanied by a joint research project of Zedira, Prof. Schuppan and Dr. Falk Pharma GmbH as part of the "Ci3-Cluster for Individualized

Immune Intervention”. The project was financially supported by the German Federal Ministry of Education and Research.

About Zedira GmbH:

The Darmstadt-based biotech company has a focus on Celiac Disease and other transglutaminase-linked conditions in the arena of autoimmunity, fibrotic diseases, and thrombosis. The company develops, produces, and markets specialty reagents and kits for research and development as well as for clinical diagnostics. Zedira established a pipeline of drug candidates adapted to specific indications based on a series of patented low-molecular transglutaminase blockers. ZED1227 is the first direct-acting transglutaminase inhibitor in clinical development. Zedira is a portfolio company of the German High-Tech Gründerfonds.

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 and Switzerland. Dr. Falk Pharma GmbH employs approximately 990 individuals globally, of those 214 in Freiburg.

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