



Dr. Falk Pharma and Zedira announce successful completion of the phase 2a proof-of-concept study of ZED1227 for the treatment of Celiac Disease

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Dr. Falk Pharma GmbH and Zedira announce successful completion of the phase 2a clinical trial of ZED1227, a direct-acting and specific inhibitor of tissue transglutaminase, in patients with Celiac Disease. The proof-of-concept study enrolled patients in 7 European countries including Germany, Finland, and Norway. The clinical trial demonstrated a substantial protective effect of the first-in-class drug candidate ZED1227 on the duodenal mucosa during a 6-week gluten challenge. The placebo-controlled dose-finding 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, difference in duodenal mucosal injury reached statistical significance for all three doses. 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](https://doi.org/10.1056/NEJMoa2032441)). The trial coordinating investigator Professor (emeritus) Markku Mäki, MD, PhD from Tampere, Finland comments “On behalf of the CEC3/CEL research team I thank celiac disease patients around Europe volunteering to our clinical drug trial using the proof-of-concept gluten challenge study design. You are the beneficiaries of our research results. Industry, academia and patients have to work together. This time our efforts led to powerful results. With your help ZED1227 got green light for further development towards a pill for celiac disease.” Markku Mäki shares first authorship with Professor Detlef Schuppan, MD, PhD, from University Medical Center Mainz, Germany, stating: “I am thankful to our patients who underwent in this gluten challenge and to the participating clinicians and scientists. I am very happy about the success of our therapeutic approach that addresses a mechanism that is highly disease specific and based on our prior research. An oral drug for celiac disease is urgently needed, since many patients do not heal despite the gluten free diet.”

Dr. Falk Pharma currently initiates a phase 2b study in Europe.

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.

Already in 2011, 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 specializes in the development and marketing of pharmaceuticals used in hepatology and gastroenterology. Falk is one of the leading European companies in the field marketing its products by means of subsidiaries in selected countries and a network of sales partners. Further, the Falk Foundation, an independent organization associated with Dr. Falk Pharma, is well-known for its international symposia, forums and educational literature supporting medical doctors, patients, and their families.

The press release is published by:

Zedira GmbH

Dr. Martin Hils,
Dr. Ralf Pasternack

Roesslerstr. 83
64293 Darmstadt
Germany

Phone: +49 6151 3251-00
Fax: +49 6151 3251-19
E-mail: contact@zedira.com
Web: www.zedira.com

Dr. Falk Pharma GmbH

Dr. Roland Greinwald

Leinenweberstr. 5
79108 Freiburg
Germany

Phone: +49 761 1514-0
Fax: +49 761 1514-377
E-mail: zentrale@drfalkpharma.de
Web: www.drfalkpharma.de