

Zedira Press Release

Reversibly acting transglutaminase 2 inhibitors: drug candidates for the treatment of fibrosis

Darmstadt, July 1st, 2020

Zedira successfully completed the development of novel reversibly acting tissue transglutaminase (TG2) inhibitors as drug candidates for the treatment of fibrotic disorders.

Zedira is a clinical stage biotech company located in Darmstadt, Germany. The company is specializing in targeting the family of crosslinking enzymes called transglutaminases. ZED1227 developed by Zedira is a first-in-class tissue transglutaminase inhibitor. This irreversible enzyme blocker is now in advanced clinical trials for the treatment of celiac disease (gluten-induced autoimmune disorder).

The aim of the present project supported by the Federal Ministry of Education and Research (BMBF) was to develop a novel class of proprietary, reversibly acting transglutaminase inhibitors to target kidney fibrosis, e.g. diabetic nephropathy.

Zedira scientists discovered that ketoamides are suitable warheads that mimic the carboxamide group of the glutamine sidechain when presented in an appropriate peptidomimetic backbone. The extensive lead structure optimization program over more than 3 years focused on improvement of small molecules with respect to potency, selectivity, and permeability. This medicinal chemistry approach was also strongly supported by structural biology, cell biology and biochemistry. Formidable challenges were overcome to develop the present candidate drug molecules with highly optimized in vivo oral bioavailability and favorable pharmacokinetic profiles. Patent applications were filed for global protection of the novel drug class.

Eventually the outcome of the project exceeded expectations. Zedira successfully developed highly potent and selective reversible TG2 inhibitors. Furthermore, the scope of possible indications has widened during the project. Not only kidney fibrosis, but also lung and liver fibrosis shall be addressed in appropriately designed future preclinical and clinical trials. In summary, Zedira developed tailor-made compounds for each of these indications.

Zedira intends to bring these compounds into the clinic. The company is open to engage in partnerships for clinical development of these molecules, in analogy to Zedira’s current program for TG2-inhibitor ZED1227 which is being developed for celiac disease and has been licensed to Dr. Falk Pharma in
Europe. Zedira is planning to expand its global leadership position in the transglutaminase field by investing into follow-up drug discovery projects.