Novel therapeutics for cardiovascular complications in diabetes and aging

“Turning an overactive and harmful enzyme into an ally to improve the vascular health of patients”

Despite current treatments 68% of diabetic patients age 65 or older die from cardiovascular diseases. To meet this therapeutic need, Tissue Transglutaminase (TG2) has emerged as a promising new target.

Current approaches:
- Targeted to active site
- Inhibit transamidase activity
- Lock TG2 open
- Reduce sensitivity to NO

Our solution: ESTUS-001
- Targeted to GTP-related site
- Inhibit transamidase activity
- Promote closed-TG2
- ↑ endothelial function

Vessel stiffness • Endothelial dysfunction • Cardiac fibrosis • Hypertension •

TRANSAMIDASE ACTIVITY (Pro-fibrotic)

MEMBRANE SIGNALING • Vasodilation • ↑ NO sensitivity

Technology Description
Tissue Transglutaminase (TG2) is an enzyme with two faces: its open conformation has pro-fibrotic effects, being overactive in diabetes and aging, and participating in several harmful processes in the cardiovascular system, while in its closed conformation it increases cell survival and facilitates vasodilation. We have observed that the molecule ESTUS-001 can induce the closed conformation of the enzyme, preventing the deleterious effects of the open conformation while increasing the sensitivity of the vasculature to natural vasodilatory signals, particularly in aging and diabetes.

Intellectual Property Rights
PCT application filed August 6, 2019

Team
- MD. and PhD, Ulf Simonsen
  Inventor and Scientific Development, Professor
- Cand Pharm, Estéfano Pinilla
  Inventor and Scientific Development
- PhD, Dan Peters
  Chemical Development
- PhD, Claus E. Olesen
  Commercial Development

Current State
Proof of concept with known molecule ESTUS-001 using different bioassays that cover the cellular, the tissue and the organism levels, additionally we have preliminary data confirming the translation of these findings to human tissue. Optimization of the drug candidate and characterisation of it is currently ongoing. 

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Call to action
We are looking for partners to join us in validating our approach for other important endpoints in addition to endothelial function and blood pressure lowering, like anti-fibrotic effect and kidney function. This will help us move forward to Toxicology, PK/PD, etc. in order to get ready for clinical trials. The current goal is to form a spin-out company by 2021.

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