Development of Novel Succinyl CoA:3-Ketoacid CoA Transferase (SCOT) Inhibitors with Reduced Brain Penetration for the Treatment of Type 2 Diabetes

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HIGHLIGHTS

- Novel glucose-lowering small molecules.
- Brain-impermeable SCOT inhibitors offer a targeted approach to treating type 2 diabetes (T2D) while minimizing side effects associated with previous SCOT inhibitors that have CNS related side effects.
- As ketones are a major fuel source for the brain, brain-impermeable SCOT inhibitors will preserve the brain's ability to use ketones as a fuel.

OPPORTUNITY

University of Alberta researchers have developed novel SCOT inhibitors with peripheral selectivity and reduced brain penetration. These new chemical entities are designed to specifically block SCOT activity in peripheral tissues rather than in the brain, while still maintaining the glucose-lowering effects seen in obesity with diphenylbutylpiperidines (DPBPs). In T2D obesity models, these new agents inhibit ketone oxidation and improve glycemia, with reduced accumulation in the brain compared to the DPBP, pimozide

Inhibiting SCOT, a key enzyme in ketone oxidation, can reduce hyperglycemia in obesity and T2D. While this effect has been previously demonstrated with antipsychotics like pimozide, these drugs are associated with undesirable effects on the brain. In this context, this invention offers a promising solution to effectively address these previous challenges while maintaining efficacy.

COMPETITIVE ADVANTAGE

- Effective glucose-lowering in experimental obesity.
- Exhibits minimal brain penetration and minimizes adverse effects associated with DPBPs.
- Allow the brain to continue using ketones as a fuel source unlike the DPBPs.

STATUS

- Patent pending.

INVENTORS

- Dr. John Ussher and his team

MORE INFORMATION

Quang Tran
Associate Director, Licensing
Technology Transfer Services, University of Alberta
T: 780.492.6254
qmtran@ualberta.ca