Selective Somatostatin Subtype 5 (sst5) Agonists for the Treatment of Hyperinsulinism: Orally-Bioavailable Small Molecules Suppress Insulin and Rescue Glyburide-Induced Hypoglycemia.

Stacy Markison, Ana Karin Kusnetzow, Rick Shin, Emmanuel Sturchler, Jian Zhao, Yun Fei Zhu, R. Scott Struthers, Stephen F. Betz

Cinetics Pharmaceuticals, San Diego, CA.

MON-193, #6731

Hypothesis: An Oral Drug Selectively Targeting sst5 is the Optimal Strategy for Treating HI

Discovery of Selective Nonpeptide sst5 Agonists

CRN02481 Pharmacokinetic Profile in Dog and Rat

CRN02481 dose dependently reverses glyburide-induced hypoglycemia in rat

CRN02481 increases blood glucose, decreases insulin, and has no effect on glucagon in rat

Hyperinsulinemic State

Conclusions

CRN02481 is a novel sst5-selective agonist being developed for the treatment of congenital hyperinsulinemia:

- Potent agonist at sst5 and selective over other sst receptor subtypes
- Exhibits good PK in both the rat and the dog
- Increases basal blood glucose and rescues hypoglycemia induced by treatment with glyburide
- Suppresses insulin while having no effect on glucagon

Preclinical safety and toxicology studies are underway to determine if CRN02481 is suitable for human clinical trials.