Discovery and Identification of Late Stage, Selective Nonpeptide Somatostatin Subtype 5 (SST5) Agonists for the Treatment of Hyperinsulinemic Hypoglycemia


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SST5 Agonist Assay Cascade

SST5 Agonists Have Drug-like Characteristics and Are Orally Bioavailable

Effects of Doses of SST5 Agonists Are Sustained Over Seven Days

Figure 5. Effect of repeated oral administration of SST5 agonists on oral glucose tolerance. Male Sprague Dawley rats were orally administered vehicle or SST5 agonist (15, 30, or 60 mg/kg) for 7 days. An oral glucose tolerance test measuring blood glucose and insulin in response to an oral glucose load (1.5 g/kg) was performed on fasted rats on Day 1 and Day 7.

Conclusions

Cerineos has discovered potent, selective, and drug-like SST5 agonists. We describe several agonists that:

- are potent and selective for SST5 over other SST subtypes
- have desirable drug-like characteristics
- show good oral exposure at oral doses
- reverse hypoglycemic hyperinsulinemia in rats
- show sustained efficacy in increasing blood glucose and decreasing insulin after repeated administration in rats

We have nominated one agonist for development and are pursuing first-in-human clinical trial GPL toxicity studies enabling studies.

This work was supported in part by an SBIR grant from the NIH awarded to Dr. Betz (R44DK088351).