The novel glucagon analogue ZP-GA-1 has superior physicochemical properties while maintaining the pharmacokinetic and pharmacodynamic profile of native glucagon

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Glucagon is used in diabetic patients for treatment of severe episodes of hypoglycemia. Pharmacologically, however, native glucagon possesses poor physicochemical properties, making convenient dosing in a ready-to-use rescue pen or the development of an artificial pancreas difficult. Accordingly the development of novel glucagon analogues such as ZP-GA-1 is pursued.

The solubility of ZP-GA-1 at physiological pH was shown to be >25 mg/mL and thus highly superior to that of native glucagon ~0.2 mg/mL. In addition, the stability data suggest that ZP-GA-1 is suitable for long term storage as a liquid formulation. The pharmacokinetic (PK) and pharmacodynamic (PD) properties of ZP-GA-1 and native human glucagon were investigated in dogs. Animals were administered either subcutaneously (SC, 20 and 120 nmol/kg) or intravenously (IV, 75 nmol/kg). Our data demonstrated overall similar PK profiles as well as blood glucose (BG) profiles of ZP-GA-1 and glucagon. Further, the SC effect of ZP-GA-1 on BG in a rat model of hypoglycemia was investigated (Figure). Both ZP-GA-1 and glucagon restored BG to baseline levels or above in a dose-dependent manner during insulin-induced hypoglycemia.

In conclusion, ZP-GA-1 displays improved physicochemical properties while maintaining similar PK and PD profiles compared to native glucagon.