Docket #: S17-244

Formulation for single injection insulin/amylin analogues to treat diabetes

Disease indication - Type 1 and Type 2 Diabetes

Drug format - Peptide hormones (combination of amylin analogues and insulin analogues)

Drug class - Novel formulation with designer excipient for improved/simplified delivery

Research stage and Preliminary data
In vitro: The inventors have demonstrated that their designer excipient stabilizes a co-formulation of aspart (insulin analogue) and pramlintide (amylin analogue) for several days under stressed conditions (compared to 3 hours of stability without the excipient)

In vivo: The inventors tested the formulation with subcutaneous administration in fasted healthy C57BL/6 mice and found that it reduced blood glucose significantly faster than the standard aspart formulation. The inventors are pursuing further studies to validate and optimize the formulations in animal models of diabetes.

Background - Patients with diabetes can regulate their glucose levels with injections of insulin and amylin analogues. Currently, it is impossible to combine these two molecules in a single formulation because amylin is formulated at pH 4 while insulin is formulated at pH 7.4. This means that patients taking both drugs require two separate injections after each meal and have the burden of calculating the appropriate dosage for each. Moreover, the pharmacokinetics of insulin and amylin are very different, making their therapeutic action difficult to predict. This invention solves those problems by enabling a highly stable co-formulation of amylin and insulin to simplify administration into a single injection. This could provide

powerful new strategy for glycemic control that closely mimics natural pancreatic behavior, benefiting all patients taking insulin, including those with Type 1 and Type 2 diabetes. These advancements could make the production and distribution of the co-formulation significantly less expensive and make their administration significantly less burdensome on patients.

Mode of action - Amylin complements the action of insulin to regulate blood glucose levels. When taken together, patients with diabetes have better glycemic control and reduced weight. This technology is a designer excipient that specifically binds to the terminal tyrosine residue on amylin analogues to stabilize the molecule and enable co-formulation with insulin analogues. The excipient can be mixed with amylin analogues and insulin for supramolecular PEGylation of both proteins, without modifying either protein.

Patent status - Patent application filed

Advantages

- **Single injection** - compared with two separate injections a single injection formulation of amylin and insulin analogues:
  - is simpler/easier for patients to administer
  - can optimize the therapeutic ratio of the two molecules in the formulation (instead of requiring the patient to calculate the proper dosages separately)
  - is expected to reduce production and distribution costs
- **Improved bioavailability and pharmacokinetics** - when they are co-formulated, the bioavailability and pharmacokinetics of amylin and insulin analogues are expected to be similar to each other, improving safety and efficacy

Patents

- Published Application: WO2020168003
- Published Application: 20220125886

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