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Zealand initiates dosing of patients in Phase 2 with its stable glucagon analogue, ZP4207, for hypoglycemia in diabetes

- **The Phase 2 trial is an important step in the dual product development of ZP4207: both as a rescue pen to treat severe hypoglycemia and as an essential component in an artificial pancreas device for better diabetes control**
- **Advancing ZP4207 into Phase 2 development is in line with Zealand's strategic focus on growing its pipeline of proprietary peptide medicines for accelerated value creation**
- **Trial completion and results are expected in H2 2016**

Copenhagen, 4 February 2016 – Zealand informs that the first patients have successfully been dosed in a Phase 2 trial with ZP4207 for the treatment and control of hypoglycemia associated with diabetes. ZP4207 is a novel stable glucagon analogue for liquid formulation, invented and fully owned by Zealand.

The Phase 2 trial is a single-center, randomized, double-blind trial, which will enroll 56 patients with Type 1 diabetes. The primary trial objective is to evaluate the pharmacokinetics and pharmacodynamics of ZP4207 to be able to fully compare its effect to that of a marketed native glucagon product. Patients in the trial will be randomized to one of four groups and four different single doses of ZP4207 administered subcutaneously after an insulin-induced hypoglycemia event. In the lowest dose group, a parallel design is applied, and in dosing groups 2-4, patients will be dosed with both ZP4207 and a marketed glucagon in a crossover design. For further details, see ClinicalTrials.gov - Identifier: NCT02660008.

Completion of the Phase 2 trial is planned for H2 2016 with top-line results expected to be available before year-end.

In a comment to this release, Britt Meelby Jensen, CEO and President of Zealand, said:
"*ZP4207 is a very important product in our growing pipeline of proprietary peptide medicines. We have been successful in developing a novel glucagon analogue with a unique stability profile in liquid formulation, and we see potential for ZP4207 both in a single-dose auto-injector rescue pen for severe hypoglycemia and as a key component in the development of an artificial pancreas device. In particular, the latter field is gaining significant traction, as closed loop dual-hormone pumps have the potential to transform glucose control in diabetes patients on insulin.*

The advancement of ZP4207 into Phase II supports our strategic focus of growing the value of our proprietary pipeline."

In Phase 1 and 1b trials, ZP4207 has shown to be safe and well-tolerated with the ability to provide a clinically relevant blood glucose response after both single and repeat daily dosing in healthy

volunteers. In addition, single-dosing of ZP4207 demonstrated effects in raising blood glucose levels in Type 1 diabetes patients after an insulin-induced hypoglycemia event.

Zealand has two parallel clinical development programs ongoing for ZP4207: 1) For single-dose use in an auto-injector rescue-pen to treat severe hypoglycemia in diabetes patients on insulin treatment and 2) For multiple dose use in a dual-hormone pump, referred to as an artificial pancreas, for better glucose control in diabetes patients. Zealand expects to advance into next development phase with the multiple dose version of ZP4207 in H2 2016.

For further information, please contact:

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About severe hypoglycemia

Severe hypoglycemia is an acute, life threatening condition resulting from a serious drop in blood sugar levels associated with insulin therapy in Type 1 and Type 2 diabetes patients. Hypoglycemia is also an issue to some extent for patients on sulfonylurea drugs. All patients with Type-1 diabetes and approximately 20% of Type-2 diabetes patients in the US are treated with insulin (Decision Resource, 2012). Type-1 diabetes patients are the most likely to experience episodes of hypoglycemia since they inject themselves with insulin several times per day or use an insulin pump.

Despite the availability of improved insulin products with reduced risk of severe hypoglycemia, the condition remains a major concern for patients. The American Diabetes Association (ADA) recommends that all patients with Type 1 diabetes and patients with Type 2 diabetes on insulin therapy carry a glucagon kit with them at all times (Center for Disease Control and Prevention 2011).

About glucagon and existing glucagon rescue treatments

Glucagon is a native peptide, which plays an important role in the control of blood sugar levels. The effects of glucagon are opposite to those of insulin – it helps to release stored glucose into the blood stream to increase blood sugar levels. The therapeutic use of native glucagon in cases of hypoglycemia is challenging due to the peptide's low solubility and very poor stability in liquid solution. Current glucagon treatments are therefore solely available in the form of a lyophilized powder, which requires reconstitution with sterile water in a multi-step process before use. In the case of an acute and severe hypoglycemia event, this can lead to handling errors, delay administration of glucagon and result in sub-optimal treatment.

About Zealand Pharma

Zealand Pharma A/S (Nasdaq Copenhagen: ZEAL) ("Zealand") is a biotech company with leading-edge scientific expertise in turning peptides into medicines. Zealand has a growing proprietary pipeline of novel specialty drug candidates and a mature portfolio of products and projects under license collaborations with Sanofi, Helsinn Healthcare and Boehringer Ingelheim.

Zealand's first invented medicine, lixisenatide, a once-daily prandial GLP-1 analogue for the treatment of Type 2 diabetes, is marketed globally (ex-US) as Lyxumia® by Sanofi and under regulatory review in the US. The license

agreement with Sanofi covers also LixiLan, which is a single-product combination of lixisenatide and insulin glargine (Lantus®). LixiLan has been submitted for regulatory priority review in the US and regulatory submission is expected in the EU in Q1 2016.

The proprietary pipeline includes; *danegaptide* for ischemic reperfusion Injuries (Phase 2); *ZP1848* for Short Bowel Syndrome (Phase 2); and the *stable glucagon analogue, ZP4207* for single-dose use in a rescue pen for severe hypoglycemia (Phase 2) and for multiple-dose use to improve glucose control in diabetes (Phase 1); *ZP2929* for diabetes/obesity (Phase 1); and several preclinical peptide therapeutics.

The company is based in Copenhagen (Glostrup), Denmark. For further information about Zealand's business and activities, please visit: www.zealandpharma.com or follow us on Twitter @ZealandPharma