

Company Announcement – No. 9/2018

Zealand Pharma's first Phase 3 trial with dasiglucagon for treatment of severe hypoglycemia successfully meets its primary objective

- Results confirm dasiglucagon's safety profile with no treatment-induced or treatment-boosted anti-drug antibodies.
- Additional results from this Phase 3 trial will be available in Q2 2018 and results from the pivotal Phase 3 efficacy trial are expected in H2 2018.
- Dasiglucagon is a potential first-in-class stable glucagon analog to be launched in the HypoPal® rescue pen.

Copenhagen, March 20, 2018 – Zealand Pharma A/S ("Zealand") announces that the primary and key secondary objectives of the first multinational Phase 3 clinical trial of dasiglucagon for treatment of severe hypoglycemia have been met. No treatment-induced or treatment-boosted anti-drug antibodies were detected in the trial.

Dasiglucagon is a potential first-in-class stable glucagon analog invented and developed by Zealand. It has a unique stability profile in liquid formulation and is suitable for a ready-to-use rescue pen. Phase 2 clinical results showed that dasiglucagon rapidly increased plasma glucose levels after insulin-induced hypoglycemia, with a longer-lasting and more pronounced plasma glucose increase, compared to the active comparator.¹

The aim of this first Phase 3 trial was to evaluate the immunogenicity of repeated single doses of dasiglucagon (0.6 mg) following subcutaneous administration in 90 patients with type 1 diabetes. The trial also evaluated safety and tolerability. Dasiglucagon was compared to native glucagon powder that requires immediate reconstitution in an aqueous buffer before injection with a syringe. The primary and key secondary objectives in the trial were to evaluate the risk of treatment-induced and treatment-boosted anti-drug antibodies following three repeat doses of dasiglucagon or GlucaGen®. The blinded data-review of the trial demonstrates that dasiglucagon did not induce or boost anti-drug antibodies.

Adam Steensberg, Executive Vice President, Chief Medical and Development Officer of Zealand, comments: *"The positive results from the Phase 3 trial is a major step forward in the development of the HypoPal® rescue pen for the treatment of severe hypoglycemia. This remains one of the biggest fears among insulin-dependent diabetics leading to approximately 300,000 hospitalizations per year in the U.S. alone. We now look forward to completing the ongoing pivotal Phase 3 efficacy trial later this year and we remain fully committed to offering this easy-to-use solution to treat a life-threatening condition."*

Additional results from the trial are expected in Q2 2018, and the full results will be published at an appropriate scientific conference. In addition to this trial, a pivotal Phase 3 efficacy trial was initiated late 2017, and patient recruitment is progressing as planned, with results expected H2 2018.

Diabetes and severe hypoglycemia

People with type 1 diabetes suffer from insulin deficiency and inappropriate glucagon secretion. Both hormones are essential to ensure stable and healthy blood glucose levels. Consequently, patients must monitor and adjust their blood glucose levels to remain in proper glycemic control, as both high and low blood glucose may affect their health.

Severe hypoglycemia is an acute, life-threatening condition resulting from a critical drop in blood glucose levels. It is primarily associated with insulin therapy and is one of the biggest concerns for insulin-dependent patients and their relatives. Severe hypoglycemia is mainly seen in people with type 1 diabetes and also type 2 diabetes patients on insulin. Severe hypoglycemic events are characterized by confusion, seizures and often loss of consciousness, which if untreated can result in death.



Today's marketed native glucagon for treatment of severe hypoglycemia requires the powder to be dissolved in an aqueous solution and then used immediately due to the limited stability of the drug.

About dasiglucagon

Dasiglucagon is a Zealand-invented proprietary glucagon analog currently in development for three different indications:

- **Rescue treatment for severe hypoglycemia:** Ready-to-use dasiglucagon may offer diabetes patients and their families a fast treatment solution for severe hypoglycemia that is easier to use than currently marketed glucagon kits. This program is in Phase 3 development, with a positive outcome of the first Phase 3 trial reported today. A second pivotal Phase 3 trial was initiated in December 2017, with results expected in H2 2018.
- **Congenital hyperinsulinism (CHI):** CHI is an ultra-rare disease caused by inappropriately elevated levels of insulin secretion irrespective of glucose levels. This leads to frequent and often severe hypoglycemia and long-term irreversible damage to health. In 2017, the FDA in the U.S. and the Committee for Orphan Medicinal Products (COMP) in the EU issued a positive opinion on an orphan medicinal product application for Zealand's glucagon analog. In January 2018, the FDA issued a safe-to-proceed letter, and the Phase 3 program is expected to start in mid-2018.
- **Dual-hormone artificial pancreas for diabetes treatment:** Zealand has reported positive results from two Phase 2a trials during the second quarter of 2017 (Zealand Pharma company releases of 23-05-2017 and 22-06-2017), and the initiation of an outpatient Phase 2b trial of longer duration is planned for 2018 in the iLet™ dual-hormone artificial pancreas system.

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About Zealand Pharma A/S

Zealand Pharma A/S (Nasdaq Copenhagen and New York: ZEAL) ("Zealand") is a biotechnology company focused on the discovery, design and development of innovative peptide-based medicines. Zealand has a portfolio of proprietary medicines in late-stage clinical development focused on specialty gastrointestinal and metabolic diseases. In addition, Zealand has two marketed drugs under license to Sanofi and two compounds in clinical development under license to Boehringer Ingelheim.

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

¹ <https://doi.org/10.2337/dc17-1402>