Company announcement – No. 16/2017

Positive Phase 2a results with microdoses of dasiglucagon support use in a dual-hormone artificial pancreas system

- **Dasiglucagon is a potential first-in-class glucagon analogue for pump use in the management of type 1 diabetes**
- **Data from this first Phase 2a trials indicate that dasiglucagon increases blood sugar levels across all tested dose levels**
- **Dasiglucagon was observed to be safe and well tolerated in the trial**
- **Results from the second Phase 2a trial on the use of dasiglucagon in the dual-hormone artificial pancreas system, iLet™, are expected at the end of June 2017**

Copenhagen, May 23, 2017 – Zealand Pharma ("Zealand") announces positive results from a Phase 2a trial following administration of the multiple-dose version of dasiglucagon in adult patients with type 1 diabetes. Dasiglucagon is a glucagon analogue fully owned by Zealand with a unique stability profile in liquid formulation and a potential first-in-class glucagon analogue suitable for pump use.

The Phase 2a trial was initiated in December 2016 to assess the efficacy, safety and tolerability of different doses of the concentrated formulation of dasiglucagon for pump use. The primary objective was to characterize the pharmacokinetic and pharmacodynamic properties of dasiglucagon 4 mg/ml formulated with preservatives.

The trial was a double-blind, randomized, four-period, sequential complete crossover trial in patients with type 1 diabetes. Four different doses of dasiglucagon were tested under normal blood glucose level (euglycemia) and low blood glucose level (hypoglycemia) conditions and with reference to responses observed with freshly reconstituted glucagon (NCT02916251).

A clear dose-response with increases in blood glucose levels was observed across the broad dose range tested, allowing for titration of dasiglucagon to counteract present or incumbent hypoglycemia. All dasiglucagon doses provided clinically relevant mean increases in blood glucose (mean plasma glucose increases of 20 mg/dl or more) under both euglycemic and hypoglycemic conditions.

Dasiglucagon and Glucagon were observed to be safe and well-tolerated in the trial, with no injection site reactions observed with dasiglucagon. Nausea and vomiting were the most frequent side effects observed, predominantly at the higher dose-levels, with both dasiglucagon and Glucagon.

Adam Steensberg, Chief Development and Medical Officer of Zealand, comments:

"We are very pleased with the Phase 2a results. Dasiglucagon in a dual-hormone artificial pancreas system holds the potential for patients to live more spontaneously with tight glucose control, without the constant fear of hypoglycemia and worry about their disease. Such systems can potentially transform type 1 diabetes management. We look forward to the results of the next Phase 2a study with dasiglucagon in the Beta Bionics iLet™ system at the end of June and to progressing this opportunity further into development for the future benefit of patients."

Type 1 diabetes dual hormone artificial pancreas system

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 sugar levels to remain in proper glycemic control, as both high and low blood glucose may affect their health, both in the short and long term.

As glucagon is not yet available in a liquid formulation, no pumps capable of mimicking a healthy pancreas are available today. Dasiglucagon is a potential first-in-class glucagon analogue with a unique stability profile in liquid formulation suitable for pump use. Zealand is working with a dual-hormone pump containing insulin and dasiglucagon that can decrease and increase blood sugar levels, guided by an algorithm to control blood glucose levels without patient intervention. In June 2016 Zealand and Boston based Beta Bionics announced a partnership to progress the clinical development of iLet™, a state-of-the-art dual-hormone artificial pancreas device.

Zealand expects to report top-line results from a second Phase 2a trial, which is conducted under this partnership, by the end of June 2017, after which we will decide on the next clinical development steps.

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About Zealand Pharma A/S

Zealand Pharma A/S (Nasdaq Copenhagen: ZEAL) ("Zealand") is a biotechnology company focused on the discovery, design and development of innovative peptide-based medicines. Zealand has a portfolio of medicines and product candidates under license collaborations with Sanofi, Boehringer Ingelheim and Helsinn, and a pipeline of internal product candidates focusing on specialty gastrointestinal and metabolic diseases.

Zealand's first invented medicine, lixisenatide, a once-daily prandial GLP-1 receptor agonist for the treatment of type 2 diabetes, is licensed to Sanofi. Lixisenatide is marketed as Adlyxin® in the U.S. and as Lyxumia® in the rest of the world. Lixisenatide has been developed in a combination with basal insulin glargine (Lantus®) and is marketed as Soliqua®100/33 in the U.S. and has been approved as Suliqua® in Europe and launched in the Netherlands.

Zealand's clinical pipeline includes: dasiglucagon* (ZP4207, single-dose rescue treatment) for acute, severe hypoglycemia (Phase 2); glepaglutide* (ZP1848) for short bowel syndrome (Phase 2); dasiglucagon* (ZP4207, multiple-dose version) intended for use in a dual-hormone artificial pancreas system for improved hypoglycemia control and diabetes management (Phase 2) and other earlier-stage clinical and preclinical peptide therapeutics.

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 Twitter @ZealandPharma.

* Dasiglucagon and glepaglutide are proposed International Nonproprietary Names (pINN).