Company Announcement
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Zealand starts clinical development of a multiple-dose version of its stable glucagon analogue, ZP4207 for the treatment of mild to moderate hypoglycemia, targeting use also in an artificial pancreas

Supported by USD 1.8 million grant from The Leona M. and Harry B. Helmsley Charitable Trust

- **Grant from the Helmsley Charitable Trust to fund initial clinical and pre-clinical activities for the multiple-dose version of ZP4207 with the ultimate aim of offering better treatment to patients with Type 1 diabetes**
- **Results of a Phase Ib multiple-dose study of ZP4207 are expected in H2 2015**
- **The ongoing clinical development program with ZP4207 as a single-use rescue pen for the treatment of severe hypoglycemia events in diabetes patients on insulin treatment continues on track**

Copenhagen, 20 May 2015 - Zealand Pharma A/S (Nasdaq Copenhagen: ZEAL) ("Zealand") informs that it has advanced a multiple-dose version of its novel stable glucagon analogue, ZP4207, into clinical development. The ZP4207 multiple-dose version is for the treatment of mild to moderate hypoglycemia in diabetes patients, and could also be an essential component in a dual-hormone artificial pancreas system.

To support preclinical and initial clinical activities related to the multiple-dose version of ZP4207, Zealand has been granted USD 1,833,000 from the Helmsley Charitable Trust. The grant will be paid in three installments with USD 600,000 to be received upfront and the rest in the first half (H1) of 2016.

In a comment to the decision to grant support to ZP4207 as a potential new treatment for Type 1 diabetes patients, **Eliot Brenner, Program Director at the Helmsley Charitable Trust** said: "*We are excited to fund this project because having a stable liquid form of glucagon could change the way a rescue dose for severe hypoglycemia is given. In addition, glucagon that has a stable formulation and is safe for chronic use could enable bi-hormonal automated glucose control systems*."

ZP4207 is invented and wholly owned by Zealand. The new clinical development program with the multiple-dose version of ZP4207 will run in parallel with Zealand's ongoing clinical development program with ZP4207 as a single-use rescue pen for the treatment of severe hypoglycemia events in diabetes patients on insulin treatment.

Adam Steensberg, Senior Vice President for Development and Chief Medical Officer at Zealand said: "*We are very pleased to have advanced our multiple-dose version of ZP4207 into clinical development,*

thereby adding a new program to our pipeline of wholly-owned products. The support from the Helmsley Charitable Trust is an important recognition of the broad potential for this Zealand invented product to offer better hypoglycemia treatments to diabetes patients."

Speaking about the importance of a stable glucagon analogue to offer better treatment to patients with Type 1 diabetes, **Finn Kristensen, CEO and founder of the Juvenile Diabetes Research Foundation (JDRF) Denmark**, noted: "*We believe that a stable liquid glucagon like ZP4207 from Zealand can help prevent and remedy hypoglycemia, which remains one of the most feared conditions associated with Type 1 diabetes."*

"In addition, the product might play a key role in future generation artificial pancreas systems, which represent an advanced form of therapy for type 1 diabetes patients and is driven forward by JDRF through our Artificial Pancreas Project. I am also excited to note that Zealand's efforts help place Denmark at the forefront in this area."

The new Phase Ib clinical trial initiated with ZP4207 is a randomized, double blind and placebo-controlled study to evaluate primarily the safety and tolerability of the compound after multiple dosing. Secondary endpoints will measure the pharmacokinetics and pharmacodynamics (blood sugar levels) of ZP4207 after multiple dosing. The trial is conducted at a clinical diabetes center in Germany and is planned to enroll 24 healthy volunteers, who will receive three different cohorts of daily doses of ZP4207, each over 5 days. Results from this study is expected in the second half (H2) of 2015. For further information, see ClinicalTrials.gov Identifier: NCT02390141

The grant from the Helmsley Charitable Trust and the initiation of clinical development of ZP4207 as a multiple-dose version to benefit people with Type 1 diabetes do not change Zealand's financial guidance for 2015.

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About ZP4207

ZP4207 is a novel analogue of human glucagon, invented by Zealand. Glucagon is a peptide hormone, produced by alpha cells of the pancreas and secreted to prevent blood glucose levels dropping too low, thus playing an essential role for a well-functioning metabolic system. The therapeutic use of native glucagon is made difficult by the peptide's very poor solubility and low stability in liquid solution.

ZP4207 has shown a high solubility and a strong physical and chemical stability profile in liquid solution, while data from preclinical studies suggest that it is comparable to native glucagon in releasing glucose stores into the blood stream. Following insulin-induced hypoglycemia in rats, ZP4207 demonstrated its ability to rapidly and dose-

dependently restore blood glucose to baseline levels or above. Furthermore, this novel glucagon analogue has shown both a pharmacokinetic profile and an effect on blood glucose overall similar to native glucagon in dogs.

The features of ZP4207 support its potential use as a ready-to-use rescue pen for the treatment of severe hypoglycemia as well as for the treatment of mild to severe hypoglycemia in the form of a multiple-dosing pen and as an essential component in an insulin-glucagon dual hormone pump, (the 'artificial pancreas'), which would represent an important advancement in the treatment of patients with Type 1 diabetes..

About the Helmsley Charitable Trust

The Leona M. and Harry B. Helmsley Charitable Trust aspires to improve lives by supporting exceptional nonprofits and other mission-aligned organizations in health, selected place-based initiatives, and education and human services. Since 2008, when the Trust began its active grant making, it has committed more than $1 billion. The Helmsley Type 1 Diabetes Program is the largest private foundation funder of T1D in the United States focused on understanding the disease, developing better treatments and improving care and access. For more information, visit helmsleytrust.org.

About Zealand Pharma

Zealand Pharma A/S ("Zealand") (Nasdaq Copenhagen: ZEAL) is a biotechnology company based in Copenhagen, Denmark. Zealand has leading expertise in the discovery, design and development of novel peptide medicines and possesses in-house competences also in clinical trial design and management with a therapeutic focus on metabolic diseases and acute care indications. The company is advancing a pipeline of novel wholly-owned medicines in development alongside a partnered product and development portfolio.

Zealand's first invented medicine, lixisenatide, a once-daily prandial GLP-1 agonist for the treatment of Type 2 diabetes, is marketed globally (ex-US) as Lyxumia® and in Phase III development as a single-injection combination with Lantus® (LixiLan), both under a global license agreement with Sanofi. US regulatory submission of Lyxumia® is planned for Q3 2015 with US and EU regulatory submissions of LixiLan expected in Q4 2015 and Q1 2016, respectively.

Zealand's wholly-owned products include danegaptide (prevention of Ischemic Reperfusion Injury) in Phase II and the stable glucagon product, ZP4207 (treatment of severe hypoglycemia) in Phase I as well as several preclinical peptide therapeutics. Partnering represents an important component of strategy to leverage in-house expertise, share development risk in large clinical trials, provide funding and commercialize the company's products. Zealand currently has global license agreements and partnerships with Sanofi, Helsinn Healthcare, Boehringer Ingelheim and Eli Lilly.

For further information: www.zealandpharma.com Follow us on Twitter @ZealandPharma