

Press Release – No. 5/2017

Dasiglucagon (pINN) presentation at the 77th Scientific Sessions of the American Diabetes Association (ADA) indicate use for treatment of severe hypoglycemia

- Elaborated results from Phase 2 trial with dasiglucagon intended for rescue treatment indicate rapid and effective increases in blood glucose in adult type 1 diabetes patients with low blood sugar
- The dasiglucagon ready-to-use pen may potentially be an effective treatment for severe hypoglycemia in insulin-dependent diabetes patients
- Phase 3 for dasiglucagon in a rescue setting is planned to be initiated within the next few months

Copenhagen, June 10, 2017 – Zealand Pharma ("Zealand") and lead scientist on the investigational side, Dr. Tim Heise of Profil Neuss, will today present elaborated data from the Phase 2 trial of dasiglucagon in patients with type 1 diabetes to treat insulin-induced hypoglycemia at the 77th Scientific Sessions of the American Diabetes Association (ADA) in San Diego, California, USA.

Dasiglucagon is a potential first-in-class glucagon analogue fully owned by Zealand. It has a unique stability profile in a liquid formulation and is suitable for a ready-to-use rescue pen to treat severe hypoglycemia.

The aim of the Phase 2 trial was to characterize the pharmacological profile of dasiglucagon and compare it to an approved glucagon rescue product (GlucaGen®). The study indicates that dasiglucagon rapidly increases plasma glucose (PG) levels after insulin-induced hypoglycemia. Times to increase PG by 20 mg/dl and to reach PG concentrations ≥ 70 mg/dl are similar for dasiglucagon and GlucaGen®, as communicated in August 2016. Dasiglucagon concentrations increased rapidly and dose-dependently. Furthermore, the increase in PG was longer lasting and more pronounced with dasiglucagon, thereby potentially presenting a favorable efficacy profile, which might prevent recurrent hypoglycemia. Post-dosing hypoglycemia events were rare, with only two events (within six hours) with dasiglucagon, compared to nine events with GlucaGen®. Dasiglucagon was observed to be safe and well tolerated in the trial and has a similar safety profile to GlucaGen®. No antidrug antibodies or severe adverse events (SAEs) were seen with either treatment.

Dr. Tim Heise, lead scientist at Profil Neuss, comments: *"The strong results from this Phase 2 trial indicate that dasiglucagon rapidly and effectively increases plasma glucose levels after insulin-induced hypoglycemia in patients with type 1 diabetes. Furthermore, they indicate the potential for a reduction in recurrent hypoglycemia as well as a much more user-friendly treatment for severe hypoglycemia than the currently available options."*

Currently available glucagon formulations for rescue treatment of severe hypoglycemia need to be reconstituted before use, which delays their use and may lead to underutilization or administration errors. Study show that a majority of parents when asked to prepare for a rescue administration are having handling difficulties resulting in potential suboptimal dosing.¹

Adam Steensberg, Executive Vice President, Chief Medical and Development Officer of Zealand, comments: *"We are excited about the data presented today, which underline the clinical potential of dasiglucagon. We see a clear need for a patient-friendly rescue treatment, and we look forward to*

¹ Harris et al. 2001, Practical Diabetes International



initiating the Phase 3 clinical development program and to getting closer to offering diabetes patients an easy-to-use rescue pen for fast rescue from severe hypoglycemia – or insulin shock.”

Type 1 diabetes and 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 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.

Severe hypoglycemia is an acute, life-threatening condition resulting from a critical drop in blood sugar levels associated primarily with insulin therapy. Severe hypoglycemia is most frequently seen in people with type 1 diabetes, since they inject themselves with insulin multiple times a day. Severe hypoglycemic events occur when blood sugar levels get critically low and are still the biggest concern for insulin-dependent patients and most feared complication of diabetes treatment. It is a condition characterized by confusion, seizures and, often, loss of consciousness which, if left untreated, can result in death.

Dasiglucagon franchise

Glucagon is used today to treat severe hypoglycemia. Current formulations on the market need to be mixed and used immediately, due to limited stability. There are a number of new glucagon formulations in development, which may impact the treatment of pancreatic diseases such as diabetes for a much wider range of patients. Dasiglucagon is being developed to offer a ready-to-use rescue treatment for severe hypoglycemia. Hypoglycemia is one of the most common endocrine emergencies and the most feared complication of having diabetes.

Dasiglucagon is also being developed to be used in a dual-hormone artificial pancreas system and it has the potential to be the first glucagon analogue for chronic use in such a system. In the U.S. alone, more than 1.25 million people living with type 1 diabetes today are facing challenges in managing hypoglycemia and overall glycemic control. A more stable glucagon could potentially be developed for use in rare pancreatic diseases such as congenital hyperinsulinism, where patients often progress to pancreatic surgery and type 1 diabetes.

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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 to reduce the risk of hypoglycemia and better 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.

**Safe Harbor/Forward-Looking Statements**

The above information contains forward-looking statements that provide our expectations or forecasts of future events such as new product introductions, product approvals and financial performance.

Such forward-looking statements are subject to risks, uncertainties and inaccurate assumptions. This may cause actual results to differ materially from expectations and it may cause any or all of our forward-looking statements here or in other publications to be wrong. Factors that may affect future results include interest rate and currency exchange rate fluctuations, delay or failure of development projects, production problems, unexpected contract breaches or terminations, government-mandated or market-driven price decreases for Zealand's products, introduction of competing products, Zealand's ability to successfully market both new and existing products, exposure to product liability and other lawsuits, changes in reimbursement rules and governmental laws and related interpretation thereof, and unexpected growth in costs and expenses.

Certain assumptions made by Zealand are required by Danish Securities Law for full disclosure of material corporate information. Some assumptions, including assumptions relating to sales associated with product that is prescribed for unapproved uses, are made taking into account past performances of other similar drugs for similar disease states or past performance of the same drug in other regions where the product is currently marketed. It is important to note that although physicians may, as part of their freedom to practice medicine in the US, prescribe approved drugs for any use they deem appropriate, including unapproved uses, at Zealand, promotion of unapproved uses is strictly prohibited.

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