

Company announcement – No. 23/2017

## Zealand initiates first Phase 3 trial with dasiglucagon for the treatment of severe hypoglycemia in diabetes

- First patients enrolled in a multinational Phase 3 clinical trial of dasiglucagon
- Dasiglucagon is a potential first-in-class glucagon analog suitable for a ready-to-use rescue pen to treat severe hypoglycemia

*Copenhagen, July 3, 2017* – Zealand Pharma A/S ("Zealand") announces the initiation of a multinational Phase 3 clinical trial of dasiglucagon in four countries (Austria, Germany, Canada and the U.S.).

Dasiglucagon is a potential first-in-class 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 to treat severe hypoglycemia. Phase 2 clinical results indicated that dasiglucagon rapidly increases plasma glucose (PG) levels after insulin-induced hypoglycemia, with a longer lasting and more pronounced PG increase with dasiglucagon compared to the active comparator, GlucaGen®. This potentially leads to a favorable efficacy profile of preventing recurrent hypoglycemia. Post-dosing hypoglycemia events were rare, with only two events (within six hours) with dasiglucagon, compared to nine events with GlucaGen®.

The aim of this first Phase 3 trial is to evaluate the immunogenicity of repeated single doses of dasiglucagon (0.6 mg) following subcutaneous administration to patients with type 1 diabetes, as well as effect, safety, tolerability. Dasiglucagon will be compared with GlucaGen®, a glucagon analog marketed in powder form for reconstitution. The trial will be conducted over 15 weeks, during which 90 patients will be exposed to either dasiglucagon or GlucaGen® in a parallel randomized double-blind design. An additional Phase 3 trial is planned for initiation in the fourth quarter of 2017.

**Britt Meeby Jensen, President and CEO of Zealand, comments:** "The initiation of Phase 3 clinical development of dasiglucagon, a glucagon analog stable in liquid formulation, demonstrates Zealand's leadership and expertise in the development of peptide drugs. We are excited about bringing Zealand significantly closer to making the ready-to-use pen available to diabetes patients for the treatment of severe hypoglycemia. Millions of people with diabetes live with a daily fear of hypoglycemia, and a user-friendly solution to address severe hypoglycemia, or insulin shock, would be a significant help in living with diabetes."

### 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 become critically low and are still the biggest concern for insulin-dependent patients and the 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.

Currently marketed formulations of glucagon for the treatment of severe hypoglycemia need to be mixed and used immediately, due to limited stability. Dasiglucagon is being developed to offer a ready-to-use rescue treatment for severe hypoglycemia.

## Zealand is developing dasiglucagon in multiple indications

In addition to the formulation of dasiglucagon being evaluated for the treatment of severe hypoglycemia, Zealand is developing another formulation for use in a future dual-hormone artificial pancreas, where it has potential to be the first glucagon analog for chronic use. This formulation is also being evaluated for use as a treatment of congenital hyperinsulinism, for which it has received an orphan drug designation in the European Union.

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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 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 3) as well as for the treatment of congenital hyperinsulinism, 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](http://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 a 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 U.S., 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).