

Press release No. 2/2014

## Presentation of several Zealand peptide therapeutics at the American Diabetes Association's (ADA) 74<sup>th</sup> Scientific Sessions

- New data to be presented on Lyxumia® (lixisenatide) and on LixiLan, including results from an 8-week head-to-head pharmacodynamic study of Lyxumia® versus liraglutide and a Phase IIb study of the fixed-ratio combination of lixisenatide with Lantus® (insulin glargine)
- Zealand presents two novel diabetes therapeutics from its proprietary preclinical pipeline; a glucagon analogue for liquid formulation and a GLP-1/GLP-2 dualacting agonist

Copenhagen, 10 June 2014 – Zealand Pharma A/S ("Zealand") (NASDAQ OMX Copenhagen: ZEAL) informs that new data will be presented on four products from the company's portfolio of novel diabetes peptide therapeutics at the upcoming 74<sup>th</sup> Scientific Sessions of the American Diabetes Association (ADA) to be held in San Francisco, 13-17 June 2014.

Zealand's own-invented product, lixisenatide, a once-daily prandial GLP-1 agonist for the treatment of Type 2 diabetes, developed and marketed as Lyxumia® under a global license agreement with Sanofi, will feature in 11 abstracts. These include the presentation of results from an 8-wk clinical study of lixisenatide versus liraglutide (Victoza®) under the title:

"Effect of lixisenatide vs liraglutide on glycemic control, gastric emptying, and safety parameters in optimized insulin glargine T2DM  $\pm$  metformin"

Abstract # 1017 – POSTER PRESENTATION

Two abstracts will also be presented on LixiLan, the fixed-ratio combination of lixisenatide with Lantus<sup>®</sup>, including results from a Phase IIb trial under the title:

"The benefits of a fixed-ratio formulation of once-daily insulin glargine/lixisenatide (LixiLan) versus glargine in Type 2 Diabetes (T2DM) inadequately controlled on Metformin - Abstract # 332 – ORAL PRESENTATION.



From Zealand's proprietary pipeline of novel peptide therapeutics for the treatment of diabetes and obesity, two preclinical products will be presented as follows:

# (1) "The novel glucagon analogue ZP-GA-1 has superior physicochemical properties while maintaining the pharmacokinetic and pharmacodynamic profile of native glucagon" – POSTER PRESENTATION

When: Monday, June 16, 12:00 – 1:00 pm CDT (Guided Audio Poster Tour: *Predictors*,

Morbidity, and Mortality)

Presenter: Pia Noerregaard, Scientist, Zealand, Denmark

Location: Poster Hall (Hall D, North Building)

### Introduction and conclusion

Glucagon is used in diabetic patients for the treatment of severe episodes of hypoglycemia. Pharmaceutically, however, native glucagon possesses poor physicochemical properties, making convenient dosing in a ready-to-use rescue pen or the development of an artificial pancreas difficult.

Accordingly, Zealand has developed novel glucagon analogues, including ZP-GA-1, showing a highly superior solubility to that of native glucagon. In addition, the stability data suggest that ZP-GA-1 is suitable for long term storage as a liquid formulation. Both ZP-GA-1 and native glucagon restored blood glucose to baseline levels or above in a dose-dependent manner during insulin-induced hypoglycemia in rats. Further, ZP-GA-1 and glucagon showed overall similar PK profiles as well as blood glucose profiles in dogs.

In conclusion, ZP-GA-1 displays improved physicochemical properties while maintaining similar pharmacokinetic and pharmacodynamic profiles compared to native glucagon.

### (2) "The novel GLP-1/GLP-2 dual agonist ZP-GG-72 increases intestinal growth and improves insulin sensitivity in DIO mice" – ORAL PRESENTATION

When: Monday, June 16, 4:30 PM - 6:30 PM

Presenter: Rasmus Just, Principal scientist, Zealand, Denmark

Location: IP-OR03 - Glucose Regulation by Enteric Peptides - W-2016 (West Building)

### Introduction and conclusion

Low grade inflammation associated with obesity and diabetes is thought to arise from leakage of bacterial wall components across the intestinal barrier and to contribute to the diseases by reducing insulin sensitivity.



Zealand has tested the hypothesis that adding GLP-2 agonism, promoting intestinal barrier function and thereby reducing inflammation, to the established beneficial effects of GLP-1 agonism on glycemic control, may represent a novel strategy for treating diabetes. Thus, a novel GLP-1/GLP-2 dual agonist, ZP-GG-72 has been evaluated for potency on GLP-1 and GLP-2 receptors and its pharmacological effects were investigated in DIO (Diet Induced Obese) mice versus teduglutide (a GLP-2 analogue) and exendin-4 (a GLP-1 analogue). Data showed that treatment with ZP-GG-72 caused an increase in intestinal weight and improved glycemic control.

In conclusion, the technical feasibility of engineering a GLP-1/GLP-2 dual agonist, which displays pharmacological effects in obese mice, was demonstrated. GLP-1/GLP-2 dual agonists may represent a novel paradigm addressing diabetes and obesity associated low grade inflammation.

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#### **About Zealand**

Zealand Pharma A/S ("Zealand") (NASDAQ OMX 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 a mature portfolio of therapeutic products, which are all based on internal inventions. The company's focus lies in the field of cardio-metabolic diseases, diabetes and obesity in particular, and its lead product is lixisenatide, a once-daily prandial GLP-1 agonist for the treatment of Type 2 diabetes, marketed as Lyxumia® under a license agreement with Sanofi. Lyxumia® is approved in several countries globally, including Europe and Japan. In the US, submission of an NDA is expected in 2015, after completion of a cardiovascular outcome study, ELIXA. A once-daily single injection combination of Lyxumia® with Lantus® (LixiLan) is in Phase III development with planned first regulatory filing end 2015.

Zealand has a partnering strategy for the development and commercialization of its products and in addition to the license agreement with Sanofi in Type 2 diabetes, the company has partnerships with Boehringer Ingelheim in diabetes/obesity, Lilly in diabetes and obesity, Helsinn Healthcare in chemotherapy induced diarrhea and AbbVie in acute kidney injury.

For further information: www.zealandpharma.com

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