

Summary of supportive clinical data presented on Lyxumia[®] and LixiLan at EASD, new large-scale Lyxumia[®] observational study, INTENSE, initiated by Sanofi and other pipeline updates

- *Results presented from an 8-week clinical study of Lyxumia[®] versus liraglutide as add-on to basal insulin showed Lyxumia[®] delayed gastric emptying significantly more than liraglutide, an effect correlated with a decrease in meal related blood sugar levels*
- *Results presented on LixiLan show robust HbA1c reductions to 6.3% with weight loss, no increased hypoglycaemia vs Lantus[®] and very low gastrointestinal adverse events*
- *Sanofi has launched a new, large-scale initiative on Lyxumia[®]; a post-approval observational study, INTENSE, to gain valuable insight into the safety and effectiveness of different therapeutic approaches to insulin intensification, including add-on of Lyxumia[®]. Interim study results expected 2015*

Copenhagen, 19 September 2014 – Zealand Pharma A/S (“Zealand”) (NASDAQ OMX Copenhagen: ZEAL) provides a summary of new clinical data presented on Lyxumia[®] and Lixilan at the 50th Annual Meeting of the European Association for the Study of Diabetes (EASD), which has taken place in Vienna, Austria on September 15-19, 2014 and of a new observational real-world study of Lyxumia[®], recently launched by Sanofi. Further, the company gives a few additional updates on its pipeline of partnered and proprietary products.

Additional supportive clinical results presented on Lyxumia[®] at EASD

Sanofi presented six abstracts on Lyxumia[®] (lixisenatide) at EASD, a once-daily prandial GLP-1 agonist, invented by Zealand and approved and marketed in several countries ex-US by Sanofi.

The presentations on Lyxumia[®] included an oral presentation entitled “*Impact of baseline gastric emptying on effects of lixisenatide and liraglutide in type 2 diabetes mellitus (T2DM) as an add-on to insulin glargine.*” (Menge et al.).

The presentation was on results of a further analysis from an 8-week head-to-head pharmacodynamic study of Lyxumia[®] versus liraglutide in patients optimally titrated with Lantus[®] (insulin glargine). The analysis showed that treatment with Lyxumia[®] delayed gastric emptying significantly more than treatment with liraglutide and that the effect correlated with a decrease in



post-prandial (after-meal) blood glucose (PPG). Previously reported results from this study^[1] demonstrated a significantly greater reduction in PPG from baseline with Lyxumia[®] than with liraglutide.

The new analysis also showed a less pronounced delay in gastric emptying within the Lyxumia[®] treatment group for patients who had slower gastric emptying at the start of treatment (baseline), suggesting a limited risk of aggravating pre-existing gastric emptying disturbances.

Phase IIb results presented on LixiLan at EASD

On LixiLan, the fixed-ratio combination of Lyxumia[®] and Lantus[®], currently in Phase III development by Sanofi, new data from the completed Phase IIb trial (323 patients) was presented orally today by Dr. Julio Rosenstock (Abstract # 241) under the headline “*Benefits of a fixed-ratio formulation of once-daily insulin glargine/lixisenatide (LixiLan) vs glargine in type 2 diabetes inadequately controlled on metformin.*” (J. Rosenstock et al.).

The results presented show that LixiLan achieved robust HbA1c reductions to 6.3% with weight loss (-1.0 kg from baseline and -1.4 kg vs Lantus[®]) and no increased hypoglycaemia vs Lantus[®], with very low gastrointestinal adverse events in Type 2 diabetes patients inadequately controlled on metformin.

Sanofi has previously confirmed the planned completion of Phase III development of LixiLan in H2 2015 and with a subsequent US regulatory filing expected as early as end 2015.

Copies of the Lyxumia[®] and LixiLan abstracts as well as replays of the Oral Presentations are available as webcasts via the EASD Annual Meeting App and the EASD website, <http://www.easd.org/images/easdwebfiles/annualmeeting/50thmeeting/index.html>.

New real-world observational study of Lyxumia[®] initiated in Europe

Sanofi also announced the recent initiation of the INTENSE (Intensifying iNsulin Therapy in type 2 diabetes: lixisENatide or Standard of carE) trial, a new patient-centric non-interventional study of Lyxumia[®] compared to other forms of injectable insulin intensification therapies, including short acting insulin. INTENSE, which is being initiated in several European countries, has a prospective recruitment of 2,400 adults with Type 2 diabetes, and will assess the safety and efficacy of adding injectable therapies to basal insulin, as well as the factors predicting the effectiveness of this intensification of treatment in a real-world standard of care setting.

INTENSE will follow patients to also examine the ways real-life circumstances can impact patients' perceptions, their ability to manage diabetes and their adherence to treatment. The first participant in this large-scale, post-approval observational study was enrolled at the end of July 2014 at Hospital Universitario de Gran Canaria Doctor Negrín, Las Palmas, Gran Canaria, Spain. Interim results will be available in 2015.

1. Meier et al. 'Effect of Lixisenatide vs Liraglutide on Glycemic Control, Gastric Emptying, and Safety Parameters in Optimized Insulin Glargine T2DM ± Metformin', 74th Scientific Sessions of the American Diabetes Association, San Francisco, CA, U.S., Poster presentation #1017-P, June 14, 2014.



Other Zealand pipeline updates

ZP1480 (ABT-719) removed from the pipeline after discontinuation by AbbVie

Zealand's license partner, AbbVie, has decided to discontinue the development of ABT-719 (ZP1480) based on results from a Phase II study on its use to treat acute kidney injury associated with cardiac surgery and other indications.

AbbVie's decision has no financial impact on Zealand and the program has been removed from Zealand's pipeline.

New Zealand publication of preclinical data on novel GLP-1-gastrin dual agonist

Antidiabetic treatments aiming to preserve or increase β -cell mass are currently gaining increased interest. Newly published data from a study of Zealand's novel GLP-1-gastrin dual agonist, ZP3022, in a diabetes model (db/db mice) demonstrate that the compound causes a sustained improvement in glycemic control accompanied by an increase in β -cell mass, increased proliferation, and increased mean islet mass. The results demonstrate that dual GLP-1-gastrin agonists could potentially be developed into a new class of anti-diabetic treatment with preventive and curative aspects.

The results have been published online in the Journal of Pharmacology and Experimental Therapeutics under the title "*The novel GLP-1-gastrin dual agonist ZP3022 improves glucose homeostasis and increases β -cell mass without affecting islet number in db/db mice*", [Dalbøge LS et al. \(<http://www.ncbi.nlm.nih.gov/pubmed/24902584>\)](#).

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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, both proprietary and partnered. The company's focus lies in the field of cardio-metabolic diseases, diabetes and obesity in particular, and it has its first product, 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[®] and Lantus[®] (LixiLan) is in Phase III development by Sanofi with planned first regulatory filing as early as at the end of 2015.



Zealand has a partnering strategy to leverage its activities and competences, while ensuring funding and sharing risk. In addition to the license agreement with Sanofi in Type 2 diabetes, the company has two collaborations with Boehringer Ingelheim in diabetes/obesity and cardio-metabolic diseases, one with Lilly in diabetes and obesity, and one with Helsinn Healthcare in chemotherapy induced diarrhea.

For further information: www.zealandpharma.com

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