

Company Announcement  
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## **Zealand Pharma announces pipeline update**

- First European sales of Lyxumia® (lixisenatide):  
Zealand-invented peptide medicine now available for adult diabetes patients***
- Elsiglutide for chemotherapy induced diarrhea:  
Patient enrolment completed in Phase IIa study, top-line results expected later in H1 2013***
- In accordance with its strategy, Zealand Pharma has decided  
to advance danegaptide into a single site clinical efficacy study to further profile  
this promising novel peptide drug in cardio-protection, and  
to only advance ZP1848 for inflammatory bowel disease with a partner***

*Copenhagen, 8 March 2013* – Zealand Pharma A/S (NASDAQ OMX Copenhagen: ZEAL) announces updates to its portfolio of partnered and proprietary peptide medicines and drug candidates including commercial and development progress, and clinical decisions.

### **Lyxumia® (lixisenatide) for Type 2 diabetes – Licensed to Sanofi**

Lixisenatide (European product name Lyxumia®) is a new, once-daily prandial GLP-1 peptide agonist invented by Zealand Pharma. Global rights to the product are licensed to Sanofi (SANF.PA) for the treatment of Type 2 diabetes in combination with basal insulin, including Lantus® (insulin glargine), the world's most prescribed basal insulin, and/or oral anti-diabetic medicines.

In February, the European Commission granted a Marketing Authorisation for Lyxumia®, approving the product in all 27 EU member countries as well as Norway, Iceland and Liechtenstein for the treatment of adults with Type 2 diabetes. Recently, this was followed by an important commercial milestone in the form of Sanofi's first sales of Lyxumia®, which happened in the United Kingdom, the first country to make this Zealand-invented medicine available for patients. Lyxumia® has received approval also in Mexico.

Further in February, the FDA accepted the New Drug Application filed by Sanofi in December 2012 for lixisenatide in the US and the product is now under regulatory review in a large number of countries globally.

Regulatory filings and approvals of Lyxumia® (lixisenatide) are based on results from the global GetGoal clinical Phase III program, establishing the product as the first once-daily prandial GLP-1 receptor agonist, characterized by a pronounced lowering effect on post-prandial glucose (PPG) contributing to HbA1c reduction, a beneficial effect on body weight, and a limited risk of hypoglycemia. The PPG-lowering effect of lixisenatide complements the predominantly fasting plasma glucose (FPG)-lowering effect of basal insulin, making Lyxumia® particularly relevant as an add-on therapy to basal insulins, including Lantus®, to better control blood sugar.

To further advance the therapeutic rationale for lixisenatide in combination with Lantus®, Sanofi is evaluating a Fix-Flex single product to allow for full flexible dosing of Lantus® combined with a fixed dose of Lyxumia®, and in parallel evaluating a Fixed-Ratio combination product in a Phase IIb study. Given a recent technical issue encountered during the last development steps of the Fix-Flex product, Sanofi is currently reassessing timelines for the start of Phase III studies of the Lantus®/lixisenatide single combination product and an update is expected in due course. The enrolment of up to 323 patients has been completed for the Phase IIb study evaluating the Fixed-Ratio combination product.

#### **ZP2929 for diabetes and/or obesity – In partnership with Boehringer Ingelheim**

ZP2929 is a novel, dual acting glucagon/GLP-1 peptide agonist invented by Zealand Pharma. The drug candidate is being developed as a potential new treatment for diabetes and/or obesity under a global licence and research collaboration agreement with Boehringer Ingelheim.

Under the agreement, Zealand Pharma advanced ZP2929 into a Phase I clinical study in September 2012 in the United States under an Investigational New Drug (IND) Application with the FDA.

Zealand Pharma may receive up to EUR 376 million in total projected milestone payments for ZP2929 and is also entitled to tiered royalties ranging from high single to low double digits on global sales of the product. Boehringer Ingelheim finances all development costs. Based on current expected timelines in the development of ZP2929, Zealand Pharma has revised expectations for payments to be received in 2013 under the agreement to EUR 4 million (EUR 14 million).

#### **Elsiglutide for chemotherapy induced diarrhea – In partnership with Helsinn**

Elsiglutide is a novel, potent and selective GLP-2 peptide agonist invented by Zealand Pharma. The drug candidate has been shown to stimulate small-intestinal growth and repair with potential therapeutic use in gastro-intestinal disorders. Global development and commercial rights for the use of elsiglutide in cancer supportive care are licensed to Helsinn Healthcare, which is developing the drug candidate for the prevention of chemotherapy induced diarrhea. Diarrhea is one of the most common and very severe side effects of chemotherapy today.

In February 2012, Helsinn initiated a randomized, double-blind, placebo-controlled Phase IIa proof-of-concept study of elsiglutide to evaluate its efficacy in preventing diarrhea in patients with colorectal cancer receiving 5-FU based chemotherapy (FOLFOX4 or FOLFIRI regimen). This is a multi-centre study, conducted in the US under an IND with the FDA, and planned to include 138 patients. Enrolment has been completed and top-line study results are expected later in H1 2013.

Under the agreement with Helsinn, Zealand Pharma is eligible to receive milestone payments of up to EUR 140 million, of which EUR 14 million have been received to date, plus royalties on global sales of elsiglutide.

#### **Danegaptide for ischemic reperfusion injury**

Danegaptide is a small dipeptide invented by Zealand Pharma. The drug candidate works as a gap junction modifier with cardio protective properties. Zealand retains global rights to the product.

A substantial Phase I safety data package has been established, including three studies in 153 subjects, demonstrating that danegaptide is safe and well tolerated.

In accordance with the company's strategy, Zealand Pharma will advance danegaptide into a clinical efficacy study to further profile and build evidence for the potential of this drug candidate as a novel approach in the prevention and treatment of ischemic reperfusion injury following a heart attack (Acute Myocardial Infarction). Ischemic reperfusion injury represents an area of high unmet medical needs, and Zealand Pharma's decision is based on a careful evaluation of value creation, commercial prospects and investment requirements.

The study is planned as a randomized, placebo-controlled Phase IIa proof-of-concept study of danegaptide to be conducted at a single site with renowned experience in heart attack studies. The study is expected to include several hundred patients with a heart attack, and has as primary objective to measure reduction of cardiac infarct size as a validated surrogate marker for mortality and morbidity outcomes following a cardiac event. The study is expected to start in Q4 2013.

**ZP1480 (ABT-719) for acute kidney injury – In partnership with AbbVie**

ZP1480 is a first-in-class, melanocortin (alpha-MSH) peptide analogue partially invented with one of Zealand Pharma's peptide modification technologies. ZP1480 is in Phase II development for the prevention of acute kidney injury under a license agreement with AbbVie (formerly Abbott), which owns all rights to the compound, and is referred to as ABT-719 in AbbVie's pipeline.

In a Phase II clinical study, ZP1480 has shown positive effects in the prevention of kidney injury in patients undergoing cardiac surgery. In a 2013 Pipeline Outlook release from 30 January 2013, AbbVie confirmed plans to start a Phase IIb study of ZP1480 for the prevention of acute kidney injury associated with major cardiac and other surgeries in 2013.

Under the license agreement with AbbVie, Zealand Pharma is entitled to single digit royalties on global sales of ZP1480.

**ZP1848 for inflammatory bowel disease**

ZP1848 is a GLP-2 peptide agonist invented by Zealand Pharma for the treatment of inflammatory bowel disease.

Zealand Pharma has conducted Phase Ia and Ib studies showing that multiple doses of ZP1848 were safe and tolerable in patients with Crohn's disease and, using a surrogate biomarker, showed the possibility of efficacy. Several development and commercial options have been evaluated for the compound resulting in the decision to advance ZP1848 into clinical Phase II development only in collaboration with a partner.

**David H. Solomon, President and CEO of Zealand Pharma, commented:**

*"We are delighted that the first Zealand invented peptide medicine, Lyxumia® (lixisenatide), is now available to diabetes patients in the UK. This follows the European approval in February and marks a transforming milestone for our company. We look forward to additional market launches in the coming months."*

*"The progress made for several of our pipeline assets, in partnerships as well as proprietary, is also greatly encouraging, underscoring our competence in peptide drug innovation. Our decision to advance danegaptide into a single centre clinical proof-of-concept study, while taking ZP1848 forward only in collaboration with a partner are reflections of our development strategy to carefully balance value creation with risk and investment requirements."*

**Financial guidance for 2013**

Zealand Pharma will provide financial guidance for 2013 in connection with the release of its 2012 full-year announcement on 14 March 2013.

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**For further information, please contact:**

David H. Solomon, President and Chief Executive Officer  
Tel: +45 2220 6300

Hanne Leth Hillman, Vice President and Head of IR & Corporate Communication  
Tel: +45 5060 3689, email: hlh@zealandpharma.com

**About Zealand Pharma**

Zealand Pharma A/S (NASDAQ OMX Copenhagen: ZEAL) is a biotechnology company based in Copenhagen, Denmark. Zealand Pharma specializes in the discovery, optimization and development of novel peptide drugs and has a broad and mature pipeline of drug candidates identified through its own drug discovery activities. The company's focus lies in the field of diabetes/metabolic diseases, and its lead drug invention is lixisenatide, a once-daily prandial GLP-1 agonist, which is licensed to Sanofi for the treatment of Type 2 diabetes. Lixisenatide is approved in Europe (February 2013) under the name of Lyxumia®, and under regulatory review in a large number of other countries globally, including in the US (NDA filed in Dec 2012) and Japan (NDA filed in June 2013).

Zealand Pharma has a partnering strategy for the development and commercialization of its products and in addition to the collaboration with Sanofi in Type 2 diabetes, the company has partnerships with Boehringer Ingelheim in diabetes/obesity, Helsinn Healthcare in chemotherapy induced diarrhea and AbbVie in acute kidney injury. For further information: [www.zealandpharma.com](http://www.zealandpharma.com)