Press Release
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Zealand presented danegaptide as a case study on an innovative novel peptide therapeutic at the 9th Annual Peptide Therapeutics Symposium in the U.S.

- **Danegaptide is being evaluated in a Zealand-designed clinical Phase II PoC trial as a potential first-ever medicine against ischemic reperfusion injuries. More than 50% of the planned 600 patients with acute myocardial infarction are now enrolled and treated in the trial, running on schedule**

Copenhagen, 29 October 2014 – Zealand Pharma A/S ("Zealand") (Nasdaq Copenhagen: ZEAL) informs that the company presented a case study on danegaptide as a novel and innovative peptide therapeutic and potential first-in-class gap junction modifier at the 9th Annual Peptide Therapeutics Symposium, which recently took place in La Jolla, California, the U.S.

The Symposium is an annual scientific meeting that brings together world leaders in peptide research from academia and the biopharmaceutical industries, focusing on core advances in peptide-based drug discovery and therapeutic candidate development.

In the presentation, entitled "*Danegaptide - Potential First and Best in Class Peptide Medicine for Prevention of Myocardial Reperfusion Injury*", Rie Schultz Hansen, Principal Scientist at Zealand, outlined that danegaptide has both anti-arrhythmic and cell-protective properties, and that this novel peptide has been shown to protect cardiac tissue in preclinical models of ischemic reperfusion injuries, causing significant reductions in infarct sizes in both dogs and pigs. Further, she presented the design and status of the ongoing clinical Phase II Proof-of-concept trial on danegaptide, conducted by Zealand in collaboration with Rigshospitalet in Denmark, one of Europe's leading cardiac centres with key expertise in Acute Myocardial Infarction (AMI). To date, more than 50% of the targeted 600 patients with an AMI have been enrolled and treated, and the study is on track to complete and report results in H2 2015.

Danegaptide was invented by Zealand and has been shown to be both very safe and well-tolerated in three clinical Phase I trials. In October 2013, Zealand started the Phase II Proof-of-Concept study to evaluate the efficacy and safety of danegaptide in the protection against cardiac tissue damage from ischemic reperfusion injuries in patients with an AMI, who are undergoing percutaneous coronary intervention (PCI). The study is designed as a randomized, double-blind, placebo-controlled trial evaluating two different doses of danegaptide against placebo with a three months primary endpoint of change in myocardial salvage index as a validated measure of cardiac infarct size.

Commenting on the presentation, **Dr. Torsten Hoffmann, Executive Vice President and Chief Scientific Officer of Zealand, said:**

"*Zealand's invitation to this prestigious event is a recognition of the company's competences and position in the field of innovative peptide R&D. It also reflects the attention that danegaptide attracts, and we are thrilled to have been given this opportunity to show-case the ground-breaking work we have done so far and the potential of danegaptide as a first-ever therapeutic for the protection of cardiac damage in patients with an AMI. There are estimated to be 750,000 incidents of AMI annually in the seven major markets by 2020, and reperfusion injuries represent an area of large unmet medical need for these patients*."

In collaboration with the Copenhagen University, Zealand also has a project ongoing to investigate the full therapeutic potential of danegaptide as a novel approach in the protection of tissue from ischemic reperfusion injuries. The project was selected by the Danish Innovation Fund (InnovationsFonden) to receive a DKK 1 million grant.

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About danegaptide

Danegaptide is a therapeutic peptide invented by Zealand, exerting effect via activation of gap junction communication channels between cells, and demonstrating both anti-arrhythmic and cell protective properties. In a pre-clinical model of acute myocardial infarction (AMI), i.e. an acute blood clot in the heart, danegaptide has shown dose-dependent significant reductions in infarct size after reperfusion. In another relevant translational model of reperfusion injury associated with an AMI, danegaptide significantly reduced infarct size compared to immediate full reperfusion1. Results from an extensive Phase I program, including three (3) individual studies with a total of 153 subjects, showed that danegaptide was safe and well tolerated.

Reference
1 Journal of the American College of Cardiology: Volume 61, Issue 10, Supplement, Page E67, 12 March 2013

About Ischemic Reperfusion Injury

In case of an acute myocardial infarction (AMI), or a heart attack, a blood clot blocks the blood flow to important parts of the heart for a longer period of time (ST segment elevation myocardial infarction, STEMI). The standard treatment of AMI today is different types of interventions aimed at re-establishing blood flow to the ischemic myocardium, thereby limiting the size of the infarct. Percutaneous coronary intervention (PCI), also called balloon

dilatation, is the most common. In 2020, the incidence for STEMI is predicted to be 756.700 in US, EU and Japan combined, and approximately 80% of STEMI patients undergo PCI procedure.

Interventional treatment is the most effective method to restore blood flow or re-perfuse the heart, thereby reducing the infarct size and improving the outcome for patients with a STEMI. The process of myocardial reperfusion however, can paradoxically itself induce further cardiac tissue damage, a phenomenon known as myocardial reperfusion injury.

To date there are no marketed pharmacological treatments for the prevention of reperfusion injury. Both mechanical pre- and post-conditioning (series of repetitive interruptions of the coronary blood flow during the PCI procedure) seem to protect cardiomyocytes during reperfusion. Reducing infarct size by 15% corresponds to a reduction in six month absolute mortality of 1% making this a meaningful marker for long term outcomes for patients.

About Zealand Pharma

Zealand Pharma A/S ("Zealand") (Nasdaq Copenhagen: ZEAL) is a biotechnology company based in Copenhagen, Denmark. Zealand has leading expertise in the discovery, design and development of novel peptide medicines, in-house competences in clinical trial design and management and a therapeutic focus on cardio-metabolic diseases. The company has a broad portfolio of therapeutic products – proprietary and partnered.

Zealand's first invented medicine, lixisenatide, a once-daily prandial GLP-1 agonist for the treatment of Type 2 diabetes, is marketed world-wide ex-US as Lyxumia® and in Phase III development as a single-injection combination with Lantus® (LixiLan), both under a global license agreement with Sanofi. US regulatory filing for both products is planned for 2015 ─ summer for Lyxumia® and as early as end 2015 for LixiLan.

Zealand is advancing a pipeline of proprietary, next-generation therapies, including danegaptide (prevention of Ischemic Reperfusion Injury) in addition to several preclinical programs. Partnering represents an important component of strategy to share development risk in large clinical trials, to provide funding and to commercialize the company's products. Zealand currently has global license agreements and partnerships with Sanofi, Boehringer Ingelheim, Eli Lilly and Helsinn Healthcare.

For further information: **www.zealandpharma.com** Follow us on Twitter @ZealandPharma