

## Phase 2a trial results support development of dasiglucagon in the iLet™ pump system for type 1 diabetes

- Dasiglucagon\* is a potential first-in-class glucagon analog for prevention and treatment of low blood sugar in type 1 diabetes using an automated pump system
- Dasiglucagon was dosed using the iLet™ platform, a state-of-the-art dual-hormone artificial pancreas pump system, administering both glucagon and insulin
- In the Phase 2a trial, dasiglucagon together with insulin was observed to be effective in controlling blood sugar

Copenhagen, June 22, 2017 – Zealand Pharma ("Zealand") and Beta Bionics, Inc. ("Beta Bionics") announce a positive outcome from the Phase 2a clinical safety trial using dasiglucagon in the dual-hormone artificial pancreas system, developed at Boston University and licensed to Beta Bionics. The study was conducted at the Massachusetts General Hospital Diabetes Research Center in Boston, MA, USA, with Steven J. Russell, MD, as Principal Investigator.

Dasiglucagon is a glucagon analog invented and fully owned by Zealand. It has a favorable stability profile in a liquid formulation and is a potential first-in-class glucagon analog suitable for pump use. This may provide diabetes mellitus patients treated with insulin an option for more effective, safe and easy diabetes management.

The aim of the Phase 2a clinical trial was to assess the safety, efficacy and tolerability of dasiglucagon when administered automatically using the iLet™ algorithms. The trial included 10 adult patients with type 1 diabetes, and a marketed recombinant glucagon was used as comparator. The test conditions were chosen to optimize the opportunity to evaluate the ability of dasiglucagon (and comparator) to maintain blood glucose in the desired target glycemic range: subjects arrived fasting at the clinic for the 8 hour testing period, they had their first meal at lunch-time at which time they injected a standard insulin bolus. Their basal rate of insulin was up to twice their normal rate, and following the meal, they were asked to perform 30 minutes of exercise to stimulate the administration of glucagon by the system.

**Steven J. Russell, MD, Massachusetts General Hospital Diabetes Research Center in Boston, Principal Investigator, explains:** *"The results of this trial with dasiglucagon are an important step towards a new era of automated diabetes management. We now have a stable drug candidate with a potential to be used for automated prevention of hypoglycemia. We've shown over the course of several multi-day outpatient and home-use studies that the bihormonal bionic pancreas algorithms regulated sensor glucose to an average of ~140 mg/dl in adults, adolescents, and pre-adolescents with very little input from the user."*

*Until recently, the poor stability of the currently available human glucagon formulations meant that glucagon had to be freshly reconstituted every day in all of our clinical trials. Stable glucagon was the missing piece we needed to make the benefits of this technology available to the large number of people who could benefit from it. Now that we have demonstrated the feasibility of dasiglucagon as a replacement for unstable human glucagon, we can move forward with confidence towards a pivotal registration trial to support approval of the iLet™ bionic pancreas delivering both insulin and dasiglucagon."*

The automated dosing algorithms were observed to deliver both dasiglucagon and recombinant glucagon in response to falling blood glucose. During treatment, even with subjects placed under the challenging conditions of the trial, glucose levels were in the range of 70-180 mg/dl approximately 70% and 65% of the time respectively for dasiglucagon and recombinant glucagon.



Dasiglucagon infusion was observed to be safe and well tolerated in the trial, with no injection site reactions noted. No severe hypoglycemic episodes were observed and time below 60 mg/dl glucose was approximately 13% and 18% for dasiglucagon and recombinant glucagon, respectively. A few subjects experienced mild nausea with both dasiglucagon and the recombinant glucagon.

This trial, along with the pharmacodynamic data from the recently completed dasiglucagon microdose trial, provides the foundation for further clinical development of dasiglucagon in the iLet™ pump system in out-patient trials.

**Edward Damiano, President and CEO of Beta Bionics and Professor of Biomedical Engineering at Boston University, adds:** *“For the past 15 years we have been working on our bionic pancreas technology and testing our hypothesis that automated delivery of both insulin and glucagon could lead to safer, more effective, and less burdensome therapy for people with type 1 diabetes. As can be seen traced across a half-dozen manuscripts published in leading peer-reviewed medical journals over the past seven years, we have refined and optimized our insulin and glucagon dosing algorithms for a bihormonal bionic pancreas in adults, adolescents and pre-adolescents with type 1 diabetes. These algorithms have now been integrated into the iLet. All the while, we have been eagerly anticipating the development of a stable, pumpable, glucagon analog suitable for chronic use in a dual-hormone bionic pancreas.*

*The promising results of this Phase 2a study, conducted by Dr. Steven Russell’s team at the Massachusetts General Hospital, are a direct result of the hard work and resources that Zealand has invested into their remarkable glucagon analog. For Beta Bionics and the type 1 diabetes community, these results demonstrate that a realistic and practical solution for fully autonomous blood-glucose control is now within reach. The collaboration between Beta Bionics and Zealand is fueled by a commitment to a paradigm shift in diabetes management, fulfilling the promise and potential that our partnership holds for the health and well-being of people with type 1 diabetes and their families.”*

**Britt Meelby Jensen, President & CEO of Zealand, comments:** *“We are very pleased with the Phase 2a results, which marks an important step forward in our collaboration with Beta Bionics. The clinical results with dasiglucagon in the iLet™ dual-hormone artificial pancreas system support that the algorithms used can effectively administer dasiglucagon to prevent and treat falling blood glucose levels. We believe this combined solution of cutting-edge technology and the world’s first stable glucagon analog, our dasiglucagon, is a major innovation. This may allow diabetes patients to be less concerned about their disease, eliminating the fear of hypoglycemia while gaining more effective, continuous glucose control. We look forward to initiating the Phase 2b trial with dasiglucagon in the iLet™ pump system.”*

### **Type 1 diabetes dual-hormone artificial pancreas system**

People with type 1 diabetes suffers from insulin deficiency and inappropriate glucagon secretion. Both hormones are essential to ensure stable and healthy blood glucose levels. 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.

As glucagon is not yet available in a liquid formulation, no pump systems capable of mimicking a healthy pancreas are available today. Dasiglucagon has the potential to be the first glucagon analog for chronic use in a future dual-hormone artificial pancreas. Globally, more than 20 million people have type 1 diabetes (IDF) and are facing challenges in managing hypoglycemia and achieving good glycemic control.

### **The collaboration between Zealand and Beta Bionics**

In 2016, Zealand and Beta Bionics, a medical technology company, entered into a collaboration, the objective of which is to combine product rights from each party to advance a new dual-hormonal artificial, or bionic, pancreas system. Such a system has the potential to offer people with diabetes on insulin therapy more efficacious, safer and easier blood sugar control for better long-term disease management and outcomes.



The system under the collaboration is based on an advanced bionic pancreas platform technology, developed at Boston University, which has been integrated into a pocket-sized wearable medical device, called the iLet™. Boston University has granted an exclusive worldwide license of the iLet™ technology to Beta Bionics. The bionic pancreas technology in the iLet™ is designed for automated delivery of both insulin and glucagon and has been tested and refined for nearly 10 years in clinical trials.

#### Conference call today at 3 p.m. CET

Zealand's management will be hosting a conference call today at 3 p.m. CET to discuss the glepaglutide results announced Monday 19 June and the dasiglucagon results announced today. Participating in the call will be Britt Meelby Jensen (President and Chief Executive Officer), Adam Steensberg (Executive Vice President and Chief Medical and Development Officer) and Professor Palle Bekker Jeppesen, MD, PhD, Principal Investigator of the Phase 2 trial on glepaglutide (Department of Gastroenterology, Rigshospitalet, University of Copenhagen). The presentation will be followed by a Q&A session.

The conference call will be conducted in English, and the dial-in numbers are:

DK standard access	+45 32 71 16 58
UK and international	+44 (0) 20 3427 1900
U.S. (free dial-in)	+1 212 444 0481
Passcode	5677547

A live audio webcast of the call, including an accompanying slide presentation, will be available via the following link, <http://edge.media-server.com/m/p/36e7nbi5>, also accessible on the Investor section of Zealand's website ([www.zealandpharma.com](http://www.zealandpharma.com)). Participants are advised to register for the webcast approximately 10 minutes before the start. A recording of the event will be made available on the Investor section of Zealand's website after the call.

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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 and 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); and 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 2) and other indications, as well as 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.

\* Dasiglucagon and glepaglutide are proposed International Nonproprietary Names (pINN).

#### About Beta Bionics, Inc.

Beta Bionics is a Massachusetts public benefit corporation founded in 2015 to license, seek regulatory approval, and commercialize the bionic pancreas closed-loop automated glucose control system known as the iLet. The iLet is an externally worn, dual chamber pumping platform that autonomously administers insulin and glucagon analogs via algorithmically controlled subcutaneous continuous infusion to fully automate glucose control. In 2015, Boston University granted Beta Bionics licenses to the bionic pancreas technology developed in the Damiano Lab and integrated into the iLet. The iLet is currently in clinical trials for purposes of gaining regulatory approval and is an investigational device and is not yet commercially available.

Beta Bionics is also a Certified B Corporation® by B Lab®. B Corporations are leaders of the global movement of people using business as a Force for Good™.

For more information about Beta Bionics please visit [www.betabionics.org](http://www.betabionics.org) or follow the company on all social media platforms @BetaBionics.

#### Forward looking statement:

This press release contains forward-looking statements about the collaboration between Zealand Pharma and Beta Bionics related to the potential use of dasiglucagon in a dual-hormone artificial pancreas system and reflects the current beliefs of the respective companies. There remains substantial risks and uncertainties in the process of drug and medical device research, development, and commercialization. There is no guarantee that the research collaboration will yield successful results or that either company will achieve the anticipated benefits, or that the iLet or dasiglucagon will achieve additional positive study results or regulatory approval. For further discussion of these risks and uncertainties and more generally of the risks related to the businesses of Beta Bionics please see Beta Bionics' filings in the United States with the United States Securities and Exchange Commission (SEC) and Zealand Pharma's filings in Denmark with the Danish Financial Supervisory Authority (DFSA) (Finanstilsynet). Neither Beta Bionics nor Zealand undertake any duty to update such forward-looking statements.