

Company announcement – No. 21/2017

Glepaglutide meets primary endpoint in Phase 2 trial in patients with short bowel syndrome

- **Glepaglutide*** is a novel long-acting GLP-2 analogue
- **Reduction in fecal wet weight output of 30% and 23% in the two highest dose groups**
- **Increases in gastrointestinal fluid and energy absorption observed**
- **The dose response supports the further clinical development of glepaglutide**

Copenhagen, June 19, 2017 – Zealand Pharma ("Zealand") announces positive results from the Phase 2 trial of glepaglutide in adult patients with short bowel syndrome (SBS). Glepaglutide is a novel long-acting GLP-2 analogue invented and fully owned by Zealand.

The trial was initiated in 2016 at Rigshospitalet, University of Copenhagen, Denmark, one of the world's leading centers for the treatment of SBS. The aim was to assess the efficacy, safety and tolerability of different doses of glepaglutide in SBS patients. The primary trial objective was the effect of glepaglutide on patients' intestinal absorptive capacity, measured as reduction in wet weight fecal output. In addition, a number of relevant secondary endpoints were evaluated, including increase in energy uptake, change in urine output and changes in absorption of electrolytes and macronutrients.

The trial was a proof-of-concept, double-blind, cross-over, dose-finding trial investigating the effect of three different once-daily doses of glepaglutide (10 mg, 1 mg and 0.1 mg). A total of 16 SBS patients completed the trial, and each patient was treated with two different doses of glepaglutide. The first dose was administered over a three-week period, followed by a washout period of four weeks and then treatment with the second dose for a further three weeks.

Principal Investigator of the Phase 2 trial, Professor Palle Bekker Jeppesen, MD, PhD, Department of Gastroenterology, Rigshospitalet, University of Copenhagen, comments: *"This is the most comprehensive Phase 2 trial conducted to date in patients with short bowel syndrome and I am truly impressed with the clinical results seen for glepaglutide in these patients. Short bowel syndrome is a severe chronic condition where patients need better treatments to improve intestinal absorption. The results of this Phase 2 trial suggest the potential of glepaglutide to provide increases in both energy, fluid and electrolyte absorption. I look forward to contributing to the next clinical development phase."*

Glepaglutide successfully met the primary study endpoint of reducing fecal wet weight output (ostomy output or diarrhea), with 833 grams/day ($P=0.0002$) and 593 grams/day ($P=0.0021$) in the 10 mg and 1 mg dose groups, corresponding to a relative decrease of 30% and 23%, respectively. In addition, glepaglutide also appeared to increase energy absorption ($p<0.05$) for the combined 10 mg and 1 mg dose group. Pharmacokinetic data confirmed the long half-life of glepaglutide when dosed daily.

Glepaglutide was observed to be safe and well tolerated in the trial. The most frequently reported adverse events were nausea, abdominal pain, abdominal distension, vomiting, stoma complications, dizziness, polyuria, decreased appetite, peripheral edema, cough and injection site reactions. Most of these were mild to moderate.

Adam Steensberg, Executive Vice President, Chief Development and Medical Officer of Zealand, comments: *"We are very pleased with these Phase 2 findings which support the potential of glepaglutide, a novel long-acting GLP-2 analogue, for the treatment of short bowel syndrome. We believe there is a need for better treatment options for patients with this severe condition and Zealand plans to advance glepaglutide through further clinical trials as quickly as possible. We now look forward to continuing our dialogue with U.S. and EU regulatory authorities with the aim of taking glepaglutide into Phase 3 clinical development in 2018."*



Britt Meelby Jensen, President and CEO of Zealand, comments: *"It is a remarkable achievement for Zealand to have obtained these key results for glepaglutide. The successful completion of the trial reflects the strong collaboration between Professor Palle Bekker Jeppesen and his team at Rigshospitalet and Zealand. With this important milestone, Zealand has moved a major step forward to realizing our growth strategy of advancing our programs to the market and ultimately fulfilling our ambition of becoming a world leader in specialty gastrointestinal and metabolic diseases."*

Short bowel syndrome

Short bowel syndrome (SBS) is a life-threatening and complex chronic disease associated with reduced or complete loss of intestinal function. The main underlying causes of SBS are major intestinal surgery following Crohn's disease, ischemia, radiation damage and surgery in adults. In young children, congenital intestinal atresia, necrotizing enteric colitis and intestinal volvulus are the most common causes. In older children and adolescents, SBS is mainly due to volvulus or trauma.

It is estimated that 20,000-40,000 patients are affected by SBS in the U.S. and Europe. The most severely affected people are dependent on daily parenteral support. This requires them to be connected to infusion lines and pumps, which pose significant restrictions on a patient's ability to engage in daily activities.

The Phase 2 data provides guidance for dose selection in Phase 3 and supports our expectation that trials designed to measure increased nutrient uptake will show a reduction in parenteral support.

Conference call on Thursday June 22, 2017 at 3 p.m. CET

Zealand's management will be hosting a conference call on Thursday June 22, 2017 at 3 p.m. CET to discuss the trial, key results and perspectives for treatment of SBS. 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 (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). 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 as a combination product with basal insulin glargine (Lantus®) and is marketed as Soliqua® 100/33 in the U.S. and has been approved and launched as Suliqua® in Europe.

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); dasiglucagon* (ZP4207, multiple-dose version) intended for use in a dual-hormone artificial pancreas system for improved hypoglycemia control and diabetes management (Phase 2) and 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 or follow Zealand on Twitter @ZealandPharma.

Safe Harbor/Forward-Looking Statements

The above information contains forward-looking statements that provide our expectations or forecasts of future events such as new product introductions, clinical development activities and anticipated results, product approvals and financial performance. Such forward-looking statements are subject to risks, uncertainties and inaccurate assumptions. This may cause actual results to differ materially from expectations and it may cause any or all of our forward-looking statements here or in other publications to be wrong. Factors that may affect future results include interest rate and currency exchange rate fluctuations, delay or failure of clinical trials and other development activities, production problems, unexpected contract breaches or terminations, government-mandated or market-driven price decreases for Zealand's products, introduction of competing products, Zealand's ability to successfully market both new and existing products, exposure to product liability and other lawsuits, changes in reimbursement rules and governmental laws and related interpretation thereof, and unexpected growth in costs and expenses.

Certain assumptions made by Zealand are required by Danish Securities Law for full disclosure of material corporate information. Some assumptions, including assumptions relating to sales associated with a product that is prescribed for unapproved uses, are made taking into account past performances of other similar drugs for similar disease states or past performance of the same drug in other regions where the product is currently marketed. It is important to note that although physicians may, as part of their freedom to practice medicine in the US, prescribe approved drugs for any use they deem appropriate, including unapproved uses, at Zealand, promotion of unapproved uses is strictly prohibited.

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