Oral semaglutide demonstrated significant reduction in blood sugar vs placebo in PIONEER 1 trial

Orlando, US, 23 June 2018 – Oral semaglutide, an investigational GLP-1 analogue taken as a once-daily tablet, achieved significant reductions in blood sugar versus placebo in adults with type 2 diabetes, according to findings from the PIONEER 1 phase 3a trial. The trial evaluated the efficacy and safety of 3, 7 and 14 mg oral semaglutide compared with placebo as monotherapy over 26 weeks in adults with type 2 diabetes. The new data will be presented tomorrow, 24 June, 2018 at the American Diabetes Association’s 78th Scientific Sessions (ADA) in Orlando, FL, US.

Two distinct approaches to evaluating the effects of oral semaglutide were applied in the PIONEER 1 trial; a primary approach utilising an intention-to-treat principle required by recent regulatory guidance, evaluating the treatment effect including the effect of rescue medication and regardless of premature trial product discontinuation; a secondary approach utilising an on-treatment principle evaluated the treatment effect while on trial product and without use of rescue medication.

Applying the intention-to-treat principle, the trial achieved its primary objective by demonstrating that people treated with any of the three doses of oral semaglutide achieved significant HbA1c reductions compared to placebo (p<0.001 for all estimated treatment differences in HbA1c for oral semaglutide vs placebo). Furthermore, people treated with 14 mg oral semaglutide achieved significant reductions (p<0.001) in weight vs placebo while weight reductions with 7 mg and 3 mg doses did not reach statistical significance.1

“Despite advancements in the diabetes treatment landscape, many people with type 2 diabetes still struggle to reach their HbA1c target,” said Vanita Aroda, MD, associate director, diabetes clinical research, Brigham and Women’s Hospital, Boston, MA, U.S. “Based on the first results of PIONEER, I am optimistic about the potential of having an oral GLP-1 receptor agonist that may help patients achieve their HbA1c and blood sugar goals.”

When applying the on-treatment principle, from a mean baseline HbA1c of 8.0%, people treated with 3, 7 and 14 mg oral semaglutide achieved HbA1c reductions of 0.8%, 1.3%...
and 1.5%, respectively, compared to 0.1% with placebo.\(^1\) In addition, 59%, 72% and 80% of people, respectively, treated with oral semaglutide achieved the ADA treatment target of HbA\(_{1c}\) below 7% compared to 34% treated with placebo.\(^1\)

Furthermore, when applying the on-treatment principle, people treated with 3, 7 and 14 mg oral semaglutide experienced a weight reduction of 1.7 kg, 2.5 kg and 4.1 kg, respectively, compared to 1.5 kg with placebo.\(^1\) Moreover, 21%, 29% and 44% of people treated with oral semaglutide achieved a weight reduction of 5% or more compared to 16% with placebo.\(^1\)

The most common adverse events (>5%) were mild or moderate nausea, which occurred in 5–16% of people treated with oral semaglutide and diminished over time, compared with 6% in those treated with placebo. Overall, adverse events were reported by 58%, 53% and 57% of people treated with 3, 7 and 14 mg oral semaglutide, respectively, and in 56% of people treated with placebo. Treatment discontinuation due to adverse events ranged from 2% to 7% for people treated with oral semaglutide, compared to 2% for people treated with placebo.\(^1\)

**About oral semaglutide**

Semaglutide is an analogue of human glucagon-like peptide-1 (GLP-1) that is provided in tablet formulation with an absorption enhancer SNAC (sodium N-(8-[2-hydroxybenzoyl] amino) caprylate).\(^2\) SNAC increases the bioavailability of semaglutide, facilitating absorption of semaglutide from the stomach, thereby enabling oral dosing.\(^3\) Oral semaglutide is in phase 3 development for blood sugar control in adults with type 2 diabetes.

**About PIONEER 1 and the PIONEER clinical trial programme**

PIONEER 1 was a 26-week, randomised, double-blinded, placebo-controlled, four-armed, parallel-group, multicentre, multinational trial comparing the efficacy and safety of three dose levels of once-daily oral semaglutide vs placebo in adults with type 2 diabetes treated with diet and exercise only. PIONEER 1 randomized 703 people in a randomised 1:1:1:1 manner to receive either a dose of oral semaglutide (3, 7 or 14 mg) or placebo once daily. The primary endpoint was change in HbA\(_{1c}\) from baseline at week 26. The proportion of patients achieving HbA\(_{1c}\) of <7% and change in body weight were secondary endpoints.

The PIONEER phase 3a clinical development programme for oral semaglutide is a global development programme with enrollment of 8,845 adults with type 2 diabetes across 10 clinical trials, which are all expected to complete in 2018.

**About Novo Nordisk**

*Novo Nordisk is a global healthcare company with 95 years of innovation and leadership in diabetes care. This heritage has given us experience and capabilities that also enable us to help people defeat obesity, haemophilia, growth disorders and other serious chronic diseases. Headquartered in Denmark, Novo Nordisk employs approximately 42,700 people in 79 countries and markets its products in more than 170 countries.*
countries. Novo Nordisk's B shares are listed on Nasdaq Copenhagen (Novo-B). Its ADRs are listed on the New York Stock Exchange (NVO). For more information, visit novonordisk.com, Facebook, Twitter, LinkedIn, YouTube.

Further information

Media:
Katrine Sperling +45 4442 6718 krsp@novonordisk.com
Åsa Josefsson +45 3079 7708 aajf@novonordisk.com
Michael Bachner (US) +1 609 664 7308 mzyb@novonordisk.com

Investors:
Peter Hugreff Ankersen +45 3075 9085 phak@novonordisk.com
Anders Mikkelsen +45 3079 4461 armk@novonordisk.com
Christina Kjær +45 3079 3009 cnje@novonordisk.com

References