Novo Nordisk successfully completes the first phase 3a trial, PIONEER 1, with oral semaglutide

Bagsværd, Denmark, 22 February 2018 - Novo Nordisk today announced the headline results from PIONEER 1, the first phase 3a trial with oral semaglutide for treatment of adults with type 2 diabetes. Oral semaglutide is a new GLP-1 analogue taken once daily as a tablet. The global 26-week trial investigated the efficacy and safety of 3, 7 and 14 mg oral semaglutide compared with placebo in 703 people with type 2 diabetes.

Two distinct approaches to evaluating the effect of oral semaglutide were applied in the PIONEER 1 trial; a primary statistical principle\(^1\) required by recent regulatory guidelines evaluating the effect regardless of treatment adherence and a secondary statistical principle\(^2\) describing the effect if people had adhered to treatment and did not initiate rescue medication.

The trial achieved its primary objective according to the primary statistical principle by demonstrating significant and superior improvements in HbA\(_{1c}\) (long-term blood sugar) for all three doses of oral semaglutide compared to placebo. Moreover, the 14 mg dose of oral semaglutide demonstrated significant and superior weight loss versus placebo, weight loss was observed for the 7 mg and 3 mg doses but did not reach statistical significance.

Applying the secondary statistical principle, people treated with 3, 7 and 14 mg oral semaglutide achieved reductions in HbA\(_{1c}\) of 0.8\%, 1.3\% and 1.5\%, respectively, compared to a reduction of 0.1\% in people treated with placebo from a mean baseline of 8.0\%. The American Diabetes Association (ADA) treatment target of HbA\(_{1c}\) below 7.0\% was achieved by 59\%, 72\% and 80\% of people on treatment with 3, 7 and 14 mg oral semaglutide, respectively, compared to 34\% of the people treated with placebo.

\(^1\) Treatment policy estimand approach: treatment effect regardless of treatment adherence or initiation of rescue medication (analysed by Pattern mixture model using multiple imputations to handle missing week 26 data).

\(^2\) Hypothetical estimand approach: treatment effect if all people adhered to treatment and did not initiate rescue medication (analysed by Mixed Models for Repeated Measurements (MMRM)). Similar statistical methodology as applied in the SUSTAIN programme for subcutaneous semaglutide.
addition, from a mean baseline body weight of 88 kg and a BMI of 31.8 kg/m², people treated with 3, 7 and 14 mg oral semaglutide experienced a weight loss of 1.7 kg, 2.5 kg and 4.1 kg, respectively, compared to a weight loss of 1.5 kg in people treated with placebo.

In the trial, oral semaglutide appeared to have a safe and well-tolerated clinical profile. The most common adverse event for all three oral semaglutide doses was mild to moderate nausea, which diminished over time. Between 5% and 16% of people treated with oral semaglutide experienced nausea, compared to 6% of people treated with placebo. Premature 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.

“We are very encouraged by the results of the PIONEER 1 trial, which confirm the unprecedented oral efficacy of semaglutide that was reported in the phase 2 clinical trial in type 2 diabetes,” said Mads Krogsgaard Thomsen, executive vice president and chief science officer of Novo Nordisk. “We look forward to providing data from the remaining nine PIONEER trials throughout this year and an expected regulatory submission in 2019.”

About PIONEER 1 and the PIONEER clinical 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 people with type 2 diabetes treated with diet and exercise only. 703 people were enrolled in PIONEER 1 and randomised 1:1:1:1 to receive either a dose of oral semaglutide (3, 7 or 14 mg) or placebo once daily. The primary endpoint was change in HbA1c from baseline at week 26.

The PIONEER phase 3a clinical development programme for oral semaglutide is a global development programme with an expected enrolment of more than 9,000 people with type 2 diabetes across 10 clinical trials, which all are expected to complete in 2018.
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 42,100 people in 79 countries and markets its products in more than 170 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.

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