

company announcement

Oral semaglutide 25 mg and 50 mg demonstrate superior reductions in HbA_{1c} and body weight versus 14 mg in people with type 2 diabetes in the PIONEER PLUS phase 3 trial

Bagsværd, Denmark, 24 March 2023 – Novo Nordisk today announced headline results from the PIONEER PLUS trial, a phase 3b, 68-week, efficacy and safety trial with once-daily oral semaglutide 25 mg and 50 mg versus 14 mg as add-on to a stable dose of 1–3 oral antidiabetic medicines in people with type 2 diabetes in need of treatment intensification. The trial achieved its primary endpoint by demonstrating a statistically significant and superior reduction in HbA_{1c} at week 52 with both the 25 mg and 50 mg doses versus the 14 mg dose of oral semaglutide.

When evaluating the effects of treatment taken as intended¹ and from a mean baseline HbA_{1c} of 9.0 %, people treated with 25 mg and 50 mg oral semaglutide achieved a statistically significant higher HbA_{1c} reduction of 1.9 percentage points and 2.2 percentage points, respectively, compared with a reduction of 1.5 percentage points with oral semaglutide 14 mg.

From a mean baseline body weight of 96.4 kg, people treated with oral semaglutide 25 mg and 50 mg experienced a statistically significant higher weight loss of 7.0 kg and 9.2 kg, respectively, compared with a reduction of 4.5 kg with oral semaglutide 14 mg.

When applying the treatment policy estimand², people treated with 25 mg and 50 mg oral semaglutide achieved a superior HbA_{1c} reduction of 1.8 percentage points and 2.0 percentage points, respectively, compared with a reduction of 1.5 percentage points with oral semaglutide 14 mg. People treated with oral semaglutide 25 mg and 50 mg experienced a superior weight loss of 6.7 kg and 8.0 kg, respectively, compared with a reduction of 4.4 kg with oral semaglutide 14 mg.

¹ Based on the trial product estimand: treatment effect if all people adhered to treatment and did not initiate other type 2 diabetes therapies

² Based on the treatment policy estimand: treatment effect regardless of treatment adherence or initiation of other type 2 diabetes therapies

	Trial product estimand			Treatment policy		
	14 mg	25 mg	50 mg	14 mg	25 mg	50 mg
Oral semaglutide	14 mg	25 mg	50 mg	14 mg	25 mg	50 mg
HbA _{1c} reduction (%-points)	1.5	1.9 [†]	2.2 [†]	1.5	1.8 [†]	2.0 [†]
Body weight reduction (kg)	4.5	7.0 [†]	9.2 [†]	4.4	6.7 [†]	8.0 [†]

[†]Statistically significant/superior vs oral semaglutide 14 mg

In the trial, all doses of oral semaglutide appeared to have a safe and well-tolerated profile. The most common adverse events were gastrointestinal, the vast majority were mild to moderate and diminished over time and were consistent with the GLP-1 receptor agonist class. Gastrointestinal adverse events were most prominent during dose escalation and more frequent with oral semaglutide 25 mg and 50 mg than with oral semaglutide 14 mg.

“We are pleased to see the results from the PIONEER PLUS trial which add further evidence of the benefits of oral semaglutide for people living with type 2 diabetes,” said Martin Holst Lange, executive vice president for Development at Novo Nordisk. “The higher efficacy from 25 mg and 50 mg doses provides the option to progress to higher doses if additional glycemic control or weight loss are needed”.

Novo Nordisk expects to file for regulatory approvals in the US and the EU in 2023. The global roll-out of the 25 mg and 50 mg doses is contingent on portfolio prioritisations and manufacturing capacity.

About the PIONEER clinical programme

The PIONEER clinical development programme for oral semaglutide currently comprises nine phase 3 global clinical trials, including a cardiovascular outcomes trial, involving more than 10,000 adults with type 2 diabetes in total. Oral semaglutide 3 mg, 7 mg and 14 mg are approved under the brand name Rybelsus[®], indicated for type 2 diabetes.

Novo Nordisk is a leading global healthcare company, founded in 1923 and headquartered in Denmark. Our purpose is to drive change to defeat diabetes and other serious chronic diseases such as obesity and rare blood and endocrine disorders. We do so by pioneering scientific breakthroughs, expanding access to our medicines, and working to prevent and ultimately cure disease. Novo Nordisk employs about 54,400 people in 80 countries and markets its products in around 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](#) and [YouTube](#).

Contact for further information

Media:

Ambre Brown Morley

+45 3079 9289

abmo@novonordisk.com

Natalia Salomao Abrahao (US)

+1 848 304 1027

niaa@novonordisk.com

Investors:

Daniel Muusmann Bohsen

+45 3075 2175

dabo@novonordisk.com

Jacob Martin Wiborg Rode

+45 3075 5956

jrde@novonordisk.com

David Heiberg Landsted

+45 3077 6915

dhel@novonordisk.com

Mark Joseph Root (US)

+1 848 213 3219

mjhr@novonordisk.com