press release

Wegovy® pill demonstrated greater weight loss than orforglipron and lower odds of stopping medication due to side effects in a new indirect comparison to be presented at Obesity Medicine Association 2026

- Oral semaglutide 25 mg demonstrated significantly greater mean weight loss than orforglipron 36 mg in a population-adjusted indirect treatment comparison (ITC) using data from the OASIS 4 and ATTAIN-1 clinical trials[1]

- Treatment with orforglipron 36 mg was associated with ~14 times higher odds of stopping medication due to GI adverse events versus oral semaglutide 25 mg in the ITC[1]

- In a separate patient preference study, 84% of survey respondents favored the treatment profile similar to oral semaglutide 25 mg compared to that similar to orforglipron[2]

Plainsboro, NJ and Bagsværd, Denmark, April 2, 2026 – Novo Nordisk will present the ORION study at the upcoming Obesity Medicine Association's annual conference in San Diego showing that Wegovy® (semaglutide) tablets 25 mg was associated with significantly greater mean weight loss than orforglipron 36 mg in a population-adjusted indirect treatment comparison. It is important to note that the FDA recently approved orforglipron under the brand name Foundayo™ at doses ranging up to 17.2 mg. The approved 17.2 mg tablet is the equivalent to the orforglipron 36 mg capsules used in Phase 3 trials, and which served as the study comparator in ORION. Additionally, in a separate patient preference study, adults with overweight or obesity showed greater preference for an oral semaglutide–like profile than an orforglipron-like profile.[1,2] These findings suggest potential differentiation and provide valuable insights to inform clinical decision-making.

"These studies add to the growing body of evidence supporting the clinical strength of semaglutide and highlight attributes that patients value when choosing an obesity medicine that fits their lifestyle," said Jamey Millar, executive vice president, US Operations of Novo Nordisk. "Since its approval, we've seen strong interest in Wegovy® pill, from both healthcare professionals and people seeking obesity therapy, underscoring the importance of our continued focus on advancing obesity care through our relentless pursuit of innovation."

Novo Nordisk Inc.
US Communications

800 Scudders Mill Road
Plainsboro, NJ 08536
USA

Tel:+ 1 609-987-5800

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The ORION study was a population-adjusted indirect treatment comparison (ITC) evaluating weight loss efficacy and tolerability between oral semaglutide 25 mg and orforglipron 36 mg using data from the OASIS 4 and ATTAIN-1 phase 3 clinical trials. A simulated treatment comparison was used to assess percentage change from baseline in body weight. A two-stage matching-adjusted indirect comparison was used for tolerability outcomes (treatment discontinuation due to any adverse event and due to gastrointestinal adverse events).[1] Analyses were adjusted for baseline body weight, glycemic status, and sex.[1]

ORION results showed that oral semaglutide 25 mg demonstrated significantly greater weight loss compared with orforglipron 36 mg, with mean differences [95% CI] of -3.2 percentage points [-5.9, -0.4]* regardless of whether patients stayed on treatment and -3.0 percentage points [-5.8, -0.3]** if all patients stayed on treatment.[1] In addition, this analysis showed that when compared with oral semaglutide 25 mg, orforglipron 36 mg was associated with ~4 times higher odds of treatment discontinuation due to any adverse event (AEs) (odds ratio [OR] [95% CI]: 4.1 [1.3, 13.0]) and ~14 times higher odds of treatment discontinuation due to AEs related to gastrointestinal (GI) issues (OR [95% CI]: 13.9 [2.0, 96.0]).[1]

Although researchers adjusted for key baseline characteristics, other unaccounted factors may remain. Additionally, between-trial protocol differences may also influence comparability. While a significant difference was observed for tolerability, the magnitude of these differences should be interpreted with caution due to low adverse event counts.[1]

"People often ask how one medication compares to another when making obesity treatment management decisions," said Robert F. Kushner, MD, Northwestern Feinberg School of Medicine. "Since there are no head-to-head trials comparing oral semaglutide for obesity to orforglipron, this indirect treatment comparison from the ORION study provides important information that can be used during the shared decision-making process."

Additionally, OPTIC was an online patient preference study assessing key factors driving obesity treatment decisions conducted from October to November 2025. The study was conducted among 800 adults with either obesity or overweight and at least one obesity-related complication, with or without prior experience using obesity medicine, and included a predicted choice comparison of hypothetical treatment profiles similar to oral semaglutide 25 mg and orforglipron.[2] Results of the predicted choice comparison based on clinical trial results showed that 84% of survey respondents favored the oral semaglutide-like profile option,.[2] Additionally, a majority of all respondents (65%) agreed that taking a treatment on an empty stomach and waiting 30 minutes before eating (oral semaglutide-like dosing instructions) would not disrupt their daily lives.[2]

Key limitations include the study's observational nature, selection bias, and use of hypothetical profiles.[2] Because this survey was conducted prior to regulatory approval, treatment profiles may not exactly match the FDA-approved labeling for products.

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It is important to note that semaglutide tablets 25 mg contains a Boxed Warning for possible thyroid tumors, including cancer and should not be used in those with a personal or family history of medullary thyroid carcinoma (MTC) or Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). The most common side effects include nausea, diarrhea, vomiting, constipation, stomach (abdomen) pain, changes in skin sensations, headache, tiredness (fatigue), upset stomach, dizziness, feeling bloated, belching, low blood sugar in people with type 2 diabetes, gas, stomach flu, heartburn, and hair loss.[3]

*Based on the treatment regimen estimand: treatment effect regardless of whether patients stayed on treatment or took other weight loss therapies.
** Based on the efficacy estimand: estimated efficacy in an idealized scenario in which all patients stayed on treatment and took no other weight loss therapies.

About ORION
The ORION study was a population-adjusted indirect treatment comparison (ITC) that evaluated the efficacy and tolerability of oral semaglutide 25 mg (OASIS 4 trial data) versus orforglipron 36 mg (ATTAIN-1 trial data) in adults with obesity or overweight without diabetes. A simulated treatment comparison (STC) was used to compare percentage change from baseline in body weight, while a two-stage matching-adjusted indirect comparison (2SMAIC) was used to assess tolerability outcomes, including treatment discontinuations due to any adverse event (AEs) and gastrointestinal AEs. The analyses were adjusted for differences between trial populations, including sex, glycemic status (blood sugar levels), and baseline body weight however, residual differences may remain.[1]

About OPTIC
OPTIC was a noninterventional, cross-sectional online survey study of 800 US adults with obesity or overweight and at least one obesity-related complication conducted between October-November 2025. Out of 800 survey respondents, half (n=400) had never used an obesity medicine and half (n=400) had used an obesity medicine. The survey included a discrete choice experiment which presented respondents with a series of questions to choose between two hypothetical oral obesity medicine profiles with 7 attributes such as efficacy, CV risk reduction, administration, and dosing instructions. Using a statistical model, researchers calculated preference weights, which were used to predict the probability an average respondent would choose a given treatment profile. Additionally, a predicted-choice comparison asked respondents to choose between an oral semaglutide-like and orforglipron-like treatment profile.[2]

About obesity
Obesity is a serious, chronic, progressive, and complex disease that requires long-term management.[4-6] One key misunderstanding is that this is a disease of just lack of willpower, when in fact there is underlying biology that may impede people with obesity from losing

weight and keeping it off.[4,6] Obesity is influenced by a variety of factors, including genetics, social determinants of health, and the environment.[7,8]

About Novo Nordisk

Novo Nordisk is a leading global healthcare company with a heritage of more than 100 years in diabetes care. Building on this foundation, our purpose is to drive change to defeat serious chronic diseases — from diabetes and obesity to rare blood and endocrine disorders — by pioneering scientific breakthroughs, expanding access to medicines, and working to prevent and ultimately cure disease. We are committed to long-term, responsible business practices that deliver financial, social and environmental value. Headquartered in Denmark and operating in around 80 countries, Novo Nordisk employs approximately 68,800 people and markets products in roughly 170 countries. In the United States, Novo Nordisk has a 40-year presence, is headquartered in New Jersey and employs approximately 10,000 people across more than 10 manufacturing, R&D, and corporate locations in seven states plus Washington, D.C. For more information, visit novonordisk-us.com, Facebook, Instagram, and X.

Contacts for further information

Media:

Liz Skrbkova (US)
+1 609 917 0632
USMediaRelations@novonordisk.com

Ambre James-Brown (Global)
+45 3079 9289
Globalmedia@novonordisk.com

Investors:

Frederik Taylor Pitter (US)
+1 609 613 0568
fptr@novonordisk.com

Michael Novod (Global)
+45 3075 6050
nvno@novonordisk.com

Jacob Martin Wiborg Rode (Global)
+45 3075 5956
jrde@novonordisk.com

Sina Meyer (Global)
+45 3079 6656
azey@novonordisk.com

Max Ung (Global)
+45 3077 6414
mxun@novonordisk.com

Christoffer Sho Togo Tullin (Global)
+45 3079 1471
cftu@novonordisk.com

Alex Bruce (Global)
+45 3444 2613
axeu@novonordisk.com

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