press release

Rybelsus® (oral semaglutide 14 mg) demonstrates superior reduction in cardiovascular events in the SOUL trial at ACC 2025

- Rybelsus® reduced major adverse cardiovascular events by 14% vs placebo in adults with type 2 diabetes and cardiovascular and/or chronic kidney disease in the SOUL cardiovascular outcomes trial[1].
- Data were presented at the American College of Cardiology's (ACC) Annual Scientific Session and Expo in Chicago, US, while simultaneously published today in *New England Journal of Medicine*[2].
- Rybelsus®, the only approved oral GLP-1 medicine, demonstrated this risk reduction on top of standards of cardiovascular and diabetes care.
- Based on SOUL findings, Novo Nordisk submitted a label extension application for Rybelsus® for CV event risk reduction to the US FDA and EMA.

Bagsværd, Denmark, 29 March 2025 – Novo Nordisk today presented the full results from the SOUL cardiovascular outcomes trial, demonstrating that Rybelsus® (oral semaglutide) significantly reduced the risk of major adverse cardiovascular events in adults with type 2 diabetes and cardiovascular disease (CVD) and/or chronic kidney disease (CKD)[1]. These new data from the phase 3b trial were featured during a late-breaking clinical trial session at the American College of Cardiology's (ACC) Annual Scientific Session and Expo in Chicago, US and simultaneously published today in *New England Journal of Medicine*[2].

The SOUL trial achieved its primary endpoint, demonstrating a 14% reduction in risk of major adverse cardiovascular events (MACE) in adults with type 2 diabetes and CVD and/or CKD when treated with Rybelsus® compared to placebo. Each component of MACE, being CV death, nonfatal myocardial infarction and nonfatal stroke, contributed to the risk reduction[1].

“Heart attacks and strokes are the leading causes of disability and death for people with type 2 diabetes, and there is a need for new, patient-centric treatments to help manage this risk,” said Darren McGuire, MD, Distinguished Chair in Cardiovascular Science and Teaching Professor of Medicine at UT Southwestern, US, and SOUL steering committee co-chair. “The SOUL trial in adults with type 2 diabetes and atherosclerotic cardiovascular disease (ASCVD) and/or CKD demonstrated significant reductions in the risk of major cardiovascular events including heart attack, stroke and CV death in those treated with oral semaglutide vs placebo. The proven

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cardiovascular benefit reflects a profound clinical impact for our patients who now have an oral option to improve health outcomes."

Cardiometabolic diseases span a wide range of conditions, including cardiovascular and peripheral artery disease, type 2 diabetes and chronic kidney disease[3]. When combined, these conditions represent the leading cause of death globally[4]. Having type 2 diabetes directly increases the risk of developing interconnected cardiometabolic diseases, while also contributing to the progression of other cardiovascular risk factors[5]. Nearly one in three adults with type 2 diabetes have CVD[6].

"Novo Nordisk continues to evolve its focus beyond diabetes and obesity towards a broader spectrum of metabolic and cardiovascular health," said Martin Holst Lange, executive vice president for Development at Novo Nordisk. "These data, alongside our other data being presented at ACC, reinforce the comprehensive set of health benefits of semaglutide, making it a strong option for healthcare professionals addressing the spectrum of metabolic and cardiovascular health – and our continued leadership in the space."

The overall safety profile of oral semaglutide in SOUL was consistent with that seen in previous semaglutide trials, and no new safety signals were observed. The incidence of serious adverse events (SAEs) was lower in participants receiving Rybelsus® than those receiving placebo, mostly due to the higher rate of cardiovascular events and infections in the placebo group. The most common SAEs were cardiac disorders (17.8% and 19.8%, respectively) and infections/infestations (15.0% and 16.5%, respectively) in the Rybelsus® and placebo arms[1].

In a key secondary analysis from SOUL published simultaneously, oral semaglutide reduced risk of MACE independently of baseline use of SGLT2i and suggests similar benefits in participants with and without concomitant SGLT2i use during trial[7].

SOUL confirmed the well-established safety and tolerability profile of semaglutide supported by long-term safety data with more than 33 million patient years[8].

Based on data from the SOUL clinical trial, Novo Nordisk submitted a label extension application for Rybelsus®, which has been accepted for review by the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA. A decision is anticipated in 2025.

About SOUL

SOUL was a multicentre, international, randomised, double-blind, parallel-group, placebo-controlled, phase 3 cardiovascular outcomes trial with 9,650 people enrolled. It was conducted to assess the effect of oral semaglutide vs placebo on cardiovascular outcomes in people with type 2 diabetes and established CVD and/or CKD. The SOUL trial was initiated in 2019. The key

objective of SOUL was to demonstrate that oral semaglutide lowers the risk of major adverse cardiovascular events (a composite endpoint consisting of cardiovascular death, non-fatal myocardial infarction and non-fatal stroke) compared to placebo, both added to standard of care in patients with type 2 diabetes and established CVD and/or CKD[9,10].

About Rybelsus®

Rybelsus® (oral semaglutide) is a GLP-1 receptor agonist indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus to improve glycaemic control as an adjunct to diet and exercise[11,12]. Rybelsus® is administered once daily and is approved for use in three therapeutic dosages: 3 mg, 7 mg and 14 mg[13,14]. Rybelsus® offers superior blood glucose lowering vs Januvia® and Jardiance®[13,14], together with consistent weight reduction[13-15] and reduction in cardiometabolic risk factors[15]. Rybelsus® is currently commercially marketed in 45 countries. More than 2.1 million people with type 2 diabetes are currently being treated with Rybelsus® worldwide[16].

About Novo Nordisk

Novo Nordisk is a leading global healthcare company founded in 1923 and headquartered in Denmark. Our purpose is to drive change to defeat serious chronic diseases built upon our heritage in diabetes. We do so by pioneering scientific breakthroughs, expanding access to our medicines and working to prevent and ultimately cure disease. Novo Nordisk employs about 76,300 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, Instagram, X, LinkedIn and YouTube.

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