press release

Semaglutide 2.4 mg shows large reductions in heart failure-related symptoms and physical limitations in people with heart failure with preserved ejection fraction and obesity

Amsterdam, Netherlands, 25 August 2023 – Novo Nordisk today announced results from the phase 3 STEP HFpEF trial showing that compared with placebo, once-weekly semaglutide 2.4 mg led to large reductions in heart failure-related symptoms, physical limitations and improvements in exercise function, and resulted in greater weight loss in adults with heart failure with preserved ejection fraction (HFpEF) and obesity.[1]

HFpEF comprises roughly half of all heart failure cases[2] and is associated with a high burden of symptoms and physical limitations affecting daily life,[3] including fatigue, shortness of breath, reduced ability to exercise, and swelling of extremities. The majority (80%) of people with HFpEF also live with overweight or obesity, which is linked to a higher burden of symptoms, worse physical function and lower quality of life.[4-6]

The findings, presented today at the European Society of Cardiology (ESC) Congress in Amsterdam, Netherlands and published simultaneously in the *New England Journal of Medicine,* show large improvement in patient-reported Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS), measuring the symptoms and physical limitations of HFpEF.

“As clinicians, we have limited treatment options to offer our patients living with HFpEF and obesity. Yet this is a condition that seriously impacts patients’ day-to-day experience, due to debilitating symptoms and functional limitations,” said Dr Mikhail Kosiborod, lead study investigator and cardiologist at Saint Luke’s Mid America Heart Institute, Kansas City, USA. “Today’s news heralds a possible fundamental paradigm shift in how cardiologists approach HFpEF in people with obesity. It’s gratifying to be able to share important evidence that has a potential to change the future clinical management of this vulnerable patient population.”

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The mean change in the KCCQ-CSS was a 16.6-point increase at 52 weeks with semaglutide 2.4 mg vs 8.7 points with placebo, leading to an estimated treatment difference of 7.8 points ($p<0.001$). Mean change in body weight was 13.3% reduction with semaglutide 2.4 mg vs. 2.6% reduction with placebo, leading to an estimated treatment difference of 10.7% weight reduction ($p<0.001$).[1]

STEP HFpEF also demonstrated a mean increase in 6-Minute Walking Distance (6MWD) of 21.5 metres at 52 weeks with semaglutide vs. 1.2 metres with placebo leading to an estimated treatment difference of 20.3 meters ($p<0.001$).[1] Semaglutide also reduced inflammation, as measured by high-sensitivity C-reactive protein (hsCRP).[1]

The safety profile of semaglutide 2.4 mg was consistent with previous studies; fewer serious adverse events were observed with semaglutide 2.4 mg compared with placebo.[1]

"We are delighted with the results from STEP HFpEF, which show that semaglutide 2.4 mg is able to ease the disease burden for people with HFpEF and obesity in a substantial way," said Martin Lange, executive vice president and head of Development at Novo Nordisk. "These results come just weeks after the topline findings of our semaglutide 2.4 mg and cardiovascular outcomes trial were announced and reinforce the potential of semaglutide 2.4 mg to enhance cardiovascular care, beyond weight management. We look forward to working closely with the clinical community and regulators to help realise this potential over the coming months."

About heart failure with preserved ejection fraction (HFpEF) and obesity

There are 64 million people living with heart failure worldwide.[7] HFpEF is now the most common form of heart failure, comprising approximately 50% of all cases.[2,8] Importantly, 80% of people with HFpEF also live with overweight or obesity.[4]

Obesity is rapidly increasing and is considered a key driver in the development and progression of HFpEF.[2,5] Despite therapeutic advances in HFpEF, significant unmet needs persist, and it has been hypothesised that phenotype-specific treatments may provide clinical benefits.[5] People with HFpEF and obesity have a high mortality rate, high risk of hospitalisation, and high burden of debilitating symptoms, physical and social limitations and poor quality of life.[2,6]

About STEP HFpEF and STEP HFpEF-DM

The primary objective of STEP HFpEF trial was to investigate the effects of semaglutide 2.4 mg subcutaneous once-weekly on symptoms, physical function, and body weight compared with placebo in patients with HFpEF and obesity. STEP HFpEF included 529 people with symptomatic HFpEF (ejection fraction ≥45%) and obesity (BMI ≥30 kg/m2). Dual primary endpoints were change in KCCQ-CSS from baseline to week 52 and change in body weight from baseline to week 52; with key secondary endpoints of change in 6MWD from baseline to week 52, hierarchical

composite endpoint (all cause death, heart failure events, difference in KCCQ-CSS change and difference in 6MWD change from baseline to week 52), and change in C-reactive protein from baseline (screening) to week 52.

The ongoing STEP HFpEF-DM trial – another study of HFpEF and obesity in people with type 2 diabetes – is to be included in the regulatory submission. STEP HFpEF-DM is expected to complete in Q4 2023, and subject to positive outcomes Novo Nordisk expects to file for approval of Wegovy® label update in the US and EU in the first half of 2024.

About Wegovy® (semaglutide 2.4 mg)

Wegovy® (once-weekly subcutaneous semaglutide 2.4 mg) is a GLP-1 receptor agonist indicated as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management in adults with a BMI of 30 kg/m2 or greater (obesity), adults with a BMI of 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition, and pediatric patients aged 12 years and older with an initial BMI at the 95th percentile or greater for age and gender (obesity). Wegovy® is launched in the US, Denmark, Norway and Germany.

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 59,000 people in 80 countries and markets its products in around 170 countries. For more information, visit novonordisk.com, Facebook, Instagram, X, LinkedIn and YouTube.

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