Novo Nordisk – a focused healthcare company

Novo Nordisk investor event in connection with ADA
New Orleans, 05 June 2022
Forward-looking statements

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- Statements of targets, plans, objectives or goals for future operations, including those related to Novo Nordisk's products, product research, product development, product introductions and product approvals as well as cooperation in relation thereto,
- Statements containing projections of or targets for revenues, costs, income (or loss), earnings per share, capital expenditures, dividends, capital structure, net financials and other financial measures,
- Statements regarding future economic performance, future actions and outcome of contingencies such as legal proceedings, and
- Statements regarding the assumptions underlying or relating to such statements.

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Important drug information

Victoza® and Ozempic® are approved for the management of type 2 diabetes only
Saxenda® and Wegovy® are approved for the treatment of obesity only
Today’s speakers

Karsten Munk Knudsen
Executive Vice President and Chief Financial Officer

Martin Holst Lange
Executive Vice President and Head of Development

Mads Frederik Rasmussen
Senior Vice President and Head of Clinical Drug Development
Agenda

Introduction

Obesity care  
*Post hoc analysis of STEP 1 and 4, STEP TEENS results and SELECT-LIFE*

GLP-1 Diabetes  
*Semaglutide in chronic kidney disease and peripheral artery disease*

Insulin  
*Insulin icodec hypoglycaemia frequency, results from ONWARDS 1, ONWARDS 2, and ONWARDS 6*

Q&A
# Agenda

## Introduction

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<td>All</td>
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Strategic Aspirations 2025 | Highlights first three months 2022

Progress towards zero environmental impact:
- Carbon emissions increased by 46% vs first quarter of 2021 and decreased 25% vs first quarter of 2019

Adding value to society:
- Positive scientific opinion from EMA on human insulin with more flexible storage option without refrigeration
- Two months’ supply of diabetes and haemophilia medication donated to the Ukrainian Ministry of Health

Being recognised as a sustainable employer:
- Share of females in senior leadership positions has increased to 37% from 35% in the first quarter of 2021

Diabetes value market share increased by 1.2 percentage point to 30.5%¹

Obesity care sales increased by 107% at CER to DKK 3.4 billion

Rare disease sales increased by 3% at CER to DKK 5.4 billion

Further raise innovation-bar for Diabetes treatment:
- Approval of Ozempic® 2.0 mg in the US
- Successful completion of first phase 3 trial with once-weekly insulin icodec
- Phase 1 trial with Ideal Pump insulin successfully completed
- Phase 1 initiated with a once-daily oral GLP-1/GIP agonist

Strengthen and progress Rare disease pipeline
- Concizumab phase 3 trial successfully completed in people with haemophilia A and B with inhibitors

Sales growth of 18% and Operating profit growth of 18%:
- Sales in International Operations grew by 13%
- Sales in the US grew by 23% with 67% of sales coming from products launched since 2015

Gross margin positively impacted by continued productivity gains in Product Supply

Free cash flow of DKK 21.6 billion and DKK 20 billion returned to shareholders during first quarter

¹ MAT (Moving annual total) value market share. IO: International Operations

The strategic aspirations are not a projection of Novo Nordisk’s financial outlook or expected growth.
Ozempic® is now the global GLP-1 volume market leader and the 2.0 mg dose has just been launched in the US

Global GLP-1 volume market share

<table>
<thead>
<tr>
<th></th>
<th>March 2020</th>
<th>March 2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>NN GLP-1</td>
<td>0%</td>
<td>59.4%</td>
</tr>
<tr>
<td>Ozempic®</td>
<td>12.1%</td>
<td>41.2%</td>
</tr>
<tr>
<td>Victoza®</td>
<td>38.1%</td>
<td>6.2%</td>
</tr>
</tbody>
</table>

US GLP-1 weekly NBRx prescriptions

<table>
<thead>
<tr>
<th></th>
<th>May 2020</th>
<th>May 2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ozempic® 2.0 mg launched in US</td>
<td>0%</td>
<td>40%</td>
</tr>
</tbody>
</table>

NBRx: New-to-brand prescriptions; Scripts: prescriptions; RHS: Right-hand-side, LHS: Left-hand-side
Source: LHS: IQVIA Midas applied IQVIA spot rate, monthly data. RHS: IQVIA Xponent, Weekly (ending 13 May 2022) Each data points represents a rolling four-week average
Strategic Aspirations 2025 | Today with emphasis on Innovation and therapeutic focus

**Purpose and sustainability (ESG)**
- Progress towards zero environmental impact
- Being respected for adding value to society
- Being recognised as a sustainable employer

**Innovation and therapeutic focus**
- Further raise the innovation-bar for diabetes treatment
- Develop a leading portfolio of superior treatment solutions for obesity
- Strengthen and progress the Rare disease pipeline
- Establish presence in Other serious chronic diseases focusing on CVD, NASH and CKD

**Commercial execution**
- Strengthen Diabetes leadership - aim at global value market share of more than 1/3
- More than 25 billion DKK in Obesity sales by 2025
- Secure a sustained growth outlook for Rare disease

**Financials**
- Deliver solid sales and operating profit growth
  - Deliver 6-10% sales growth in IO
  - Transform 70% of sales in the US
- Drive operational efficiencies across the value chain to enable investments in future growth assets
- Deliver free cash flow to enable attractive capital allocation to shareholders

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1 From 2015 to 2022, 70% of sales to come from products launched from 2015. IO: International Operations; CVD: Cardiovascular disease; NASH: Non-alcoholic steatohepatitis; CKD: Chronic kidney disease.

Note: The strategic aspirations are not a projection of Novo Nordisk's financial outlook or expected growth.
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Martin Holst Lange

Q&A  
All
Since the ADA 2021, progress has been made across the Novo Nordisk pipeline

- **CagriSema T2D Ph2 initiation**
- **NASH-Gilead Ph2b initiation**
- **Semaglutide Ph3 initiation in Alzheimer’s**
- **Glucose sensitive insulin Ph2 initiation**
- **IcoSema Ph3 initiation**
- **Dicerna Acquisition**
- **Wegovy® EU approval**
- **Concizumab Ph3a results (HwI)**
- **Oral GLP-1/GIP co-agonist Ph1 initiation**
- **Icodec ONWARDS 1 and 6 main phase**
- **Icodec ONWARDS 2 results**
- **Flagship Pioneering Partnership**

**Key Events:**
- **2022**
  - **Semaglutide Ph3 initiation**
  - **Icodec Sema - OW GIP Ph2 initiation**
  - **Dicerna Acquisition**
  - **Icodec Sema - OW GIP Ph2 initiation**
  - **FDC Sema - OW GIP Ph2 initiation**
  - **Ozempic® 2.0 mg EU approval**
  - **Ozempic® 2.0 mg US approval**
  - **Mim8 Ph1/2 results**
  - **Ziltivikemab Ph3 initiation**
  - **Prothena acquisition**
  - **Oral sema 50 mg Ph2 initiation**
  - **Ozempic® 2.0 mg US approval**

**Note:** Timeline non-exhaustive

T2D: Type 2 diabetes; Sema: Semaglutide; Ph: Phase; OW: Once-weekly; HwI: Haemophilia with inhibitors

T2D: Type 2 diabetes; Sema: Semaglutide; Ph: Phase; OW: Once-weekly; HwI: Haemophilia with inhibitors

Note: Timeline non-exhaustive
Research and development activity is at an all time high

Patient years in trials increasing over last four years

<table>
<thead>
<tr>
<th>Year</th>
<th>Active patient years ('000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019</td>
<td>17</td>
</tr>
<tr>
<td>2020</td>
<td>30</td>
</tr>
<tr>
<td>2021</td>
<td>39</td>
</tr>
<tr>
<td>2022E</td>
<td>48</td>
</tr>
</tbody>
</table>

Active phase 3 trials across all therapy areas

- Diabetes
- Alzheimer’s Disease
- CKD
- CVD
- Obesity
- RBD
- NASH
- RED

CKD: Chronic kidney disease; CVD: Cardiovascular disease; RBD: Rare blood disorders; RED: Rare endocrine disorders
Weight loss is associated with improvements of multiple comorbidities

**Improvements per weight loss bracket**

<table>
<thead>
<tr>
<th>Weight loss (%)</th>
<th>Improvements (examples)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5%</td>
<td>Hypertension</td>
</tr>
<tr>
<td>5-10%</td>
<td>Dislipidaemia</td>
</tr>
<tr>
<td>10-15%</td>
<td>Kidney disease – FLOW trial</td>
</tr>
<tr>
<td>&gt;15%</td>
<td>Cardiovascular disease – SELECT trial</td>
</tr>
</tbody>
</table>

**Improvements (examples)**

- **Hypertension**
- **Dislipidaemia**
- **Kidney disease – FLOW trial**
- **Cardiovascular disease – SELECT trial**
- **Prevention of T2D – STEP 1 and STEP 4**
- **NASH – ESSENCE programme**
- **CV mortality – SELECT trial**
- **NAFLD**
- **GERD**
- **HF – STEP HFpEF**
- **PCOS**
- **OSAS**
- **T2D remission**
- **Knee OA**

**Sources:**
The 10-year risk of type 2 diabetes was assessed post hoc in STEP 1 and STEP 4

STEP 1 and STEP 4 trial design

The effect of once-weekly s.c. semaglutide (sema) 2.4 mg on the risk of developing T2D in people with obesity is unknown.

Weight management with sema vs placebo plus diet and exercise was assessed\(^1\) in participants with overweight/obesity in STEP 1 and STEP 4.

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\(^1\)The 10-year T2D risk was calculated post hoc using Cardiometabolic Disease Scoring (CMDS).
T2D: Type 2 diabetes; s.c.: Subcutaneous; sema: semaglutide
Source: Garvey, et. al. Poster 2-LB presented at the 82\(^{nd}\) Scientific Sessions of the American Diabetes Association 2022, June 3-7, 2022 (New Orleans, LA, USA) meeting
Cardiometabolic Disease Scoring (CMDS) is a validated tool to assess 10-year type 2 diabetes risk

CMDS was applied post hoc to the STEP 1 and 4 trials of once-weekly s.c. semaglutide 2.4 mg

CMDS score indicates the percentage risk of developing type 2 diabetes in the next 10 years

*CMDS was developed and validated in individuals aged ≥45 years. †CMDS was developed and validated in Black and White individuals.

- Sex
- Age*
- Ethnicity†
- BMI
- Blood pressure
- Blood glucose
- Triglycerides
- HDL cholesterol

Evaluated by Bayesian logistic regression

CMDS analysis indicates that sema 2.4 mg reduces the 10-year risk of developing T2D in people with overweight/obesity by ~60%.

Absolute 10-year T2D risk scores in the overall STEP 1 and STEP 4

<table>
<thead>
<tr>
<th>Week</th>
<th>N =</th>
<th>Geometric mean risk score (% risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1,045</td>
<td>18.2</td>
</tr>
<tr>
<td></td>
<td>538</td>
<td>17.8</td>
</tr>
<tr>
<td></td>
<td>847</td>
<td>15.6</td>
</tr>
<tr>
<td>68</td>
<td>392</td>
<td>7.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Week</th>
<th>N =</th>
<th>Geometric mean risk score (% risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>772</td>
<td>20.6</td>
</tr>
<tr>
<td></td>
<td>515</td>
<td>11.4</td>
</tr>
<tr>
<td></td>
<td>261</td>
<td>10.7</td>
</tr>
<tr>
<td>20</td>
<td>467</td>
<td>7.4</td>
</tr>
<tr>
<td>68</td>
<td>224</td>
<td>15.4</td>
</tr>
</tbody>
</table>

Semaglutide 2.4 mg could help prevent T2D in people with obesity

- Semaglutide 2.4 mg treatment reduces the 10-year risk of T2D by ~60% regardless of initial glycaemic status
- Sustained treatment required to maintain this benefit
- Treatment effect similar in participants with normoglycaemia and prediabetes

1The 10-year T2D risk was calculated post hoc using Cardiometabolic Disease Scoring (CMDS).
220 weeks of semaglutide followed by 48 weeks of placebo
T2D: Type 2 diabetes; s.c.: Subcutaneous; sema: semaglutide
Source: Garvey, et. al. Poster 2-1B presented at the 82nd Scientific Sessions of the American Diabetes Association 2022, June 3-7, 2022 (New Orleans, LA, USA)
Semaglutide 2.4 mg was investigated in an adolescent population in the STEP TEENS phase 3 trial

**STEP TEENS comparing the effects and safety and tolerability of sema 2.4 mg vs placebo**

**STEP TEENS trial with 200 adolescents with obesity**

**Characteristics:**
- Increasing rapidly
- Associated with multiple obesity-related complications
- Independent risk factor for obesity in adulthood
- Predisposing to both reduced life expectancy and quality of life

**Besides Saxenda®, very few pharmacotherapies approved for use in adolescents with obesity**

**Endpoints**
- Primary: Change in BMI (%)  
- Confirmatory secondary: ≥5% body weight reduction  
- Supporting secondary endpoints include: IWQOL-Kids, lipids, etc.

**Key inclusion criteria**
- 12 to <18 years  
- Tanner stage 2-5  
- BMI ≥95th percentile* or BMI ≥85th percentile* with ≥1 weight-related comorbidity*

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*On sex-specific BMI-for-age Growth Charts (cdc.gov).† Hypertension, dyslipidaemia, obstructive sleep apnoea or Type 2 diabetes
MTD: Maximum tolerated dose; s.c.: Subcutaneous; Sema: Semaglutide; BMI: Body Mass Index; IWQOL: Impact of Weight on Quality of Life
Source: Atlas of Childhood Obesity, October 2019 (estimating +250m children living with obesity in 2025)
BMI reduction of 16% in adolescents treated with semaglutide 2.4 mg in the STEP TEENS trial

STEP TEENS showed greater than 16% reduction in BMI

Time since randomisation (weeks)

Data from STEP TEENS

- Average age 15.4 years
- 62% female
- Average BMI of 37.0 kg/m²

Semaglutide 2.4 mg was superior to placebo on %-change in BMI and 5% body weight responders

- BMI: 16.7% ETD, 5% body weight responders: 72.5%
- Improvements seen in all other weight-related parameters as well as also CV risk factors and glucose metabolism

Semaglutide 2.4 mg appeared well-tolerated

- Safety and tolerability were consistent phase 3 data in adults and the GLP-1 RA class in general

* Lines are based on observed mean data where the value denoted after 68 weeks is the estimated mean value

Note: Treatment policy estimand
IWQOL-Kids: Impact of Weight on Quality of Life-Kids; ETD: Estimated treatment difference; CV: Cardiovascular
First anti-obesity medication showing weight-related quality of life benefit in a study of an adolescent population

Sema 2.4 mg showed a statistically significant treatment difference versus placebo in the IWQOL-Kids

<table>
<thead>
<tr>
<th>IWQOL-Kids scores</th>
<th>ETD [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body esteem</td>
<td>3.92 [-1.94 : 9.77]</td>
</tr>
<tr>
<td>Family relation</td>
<td>3.42 [-0.26 : 7.11]</td>
</tr>
<tr>
<td>Physical comfort</td>
<td>6.60 [1.99 : 11.21]</td>
</tr>
<tr>
<td>Social life</td>
<td>3.08 [-1.76 : 7.92]</td>
</tr>
<tr>
<td>Total</td>
<td>4.27 [0.23 : 8.32]</td>
</tr>
</tbody>
</table>

Exploratory endpoint: Impact of Weight on Quality of Life-Kids

Semaglutide 2.4 mg improved weight-related quality of life as measured by IWQOL-kids

Results suggest a benefit of semaglutide 2.4mg vs placebo across all domains giving a statistically significant benefit on total score

Strongest benefit of semaglutide 2.4mg vs placebo was seen in the physical comfort score (statistically significant)
The interim analysis for the SELECT trial is expected to be conducted in the third quarter of 2022.

**SELECT trial with 17,500 people with obesity**

- **Semaglutide 2.4 mg**
- **Placebo**

1:1

Event driven

5 weeks follow-up

**Objective**
Demonstrate that semaglutide 2.4 mg lowers the incidence of MACE vs placebo

**Primary endpoint**
Time from randomisation to first occurrence of MACE

**Secondary endpoints**
CV death, all-cause death, 5-point MACE composite, composite HF, composite nephropathy, glucose metabolism, other metabolic parameters

**Stopping at interim**
A decision to stop the trial based on the interim analysis follows assessment of the totality of the data

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1 MACE includes non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death.
MACE: Major adverse cardiovascular events; HF: Heart failure; CV: Cardiovascular
SELECT-LIFE is a 10-year observational follow-up study with twice-yearly collection of self-reported patient data

**SELECT trial with 17,500 people with obesity**

- Semaglutide 2.4 mg
- Placebo

**SELECT-LIFE extension 10-year extension**

- All patients completing the SELECT study\(^1\) will be invited to take part in SELECT-LIFE
- Expected to enrol 5,000-10,000 people with obesity

**Purpose of SELECT-LIFE**

Improve understanding of obesity and its complications, positively impact future treatment guidelines and contribute to improved clinical care in people living with obesity and CVD

Regular data publications are expected

**Examples of endpoint focus areas**

- Survival
- Cardiovascular events
- Type 2 diabetes
- Obesity-related complications

\(^1\) Within countries participating in SELECT-LIFE

CVD: Cardiovascular Disease
**Obesity: Key take-aways**

A post hoc analysis of STEP 1 and 4 indicates a ~60% reduction in the 10-year risk of developing type 2 diabetes

STEP TEENS in adolescents reads out with around 16% reduction in BMI

SELECT interim analysis expected to be conducted in the third quarter of 2022

SELECT-LIFE, a 10-year observation follow-up study, to improve understanding of obesity and its complications long-term
# Agenda

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Investigating semaglutide effects beyond glucose lowering in people with type 2 diabetes

**FOCUS**
Diabetic retinopathy outcomes trial
Semaglutide 1.0 mg, injectable + standard of care
- ~1,500 patients with T2D for 10 or more years
- Primary endpoint: Presence of ≥3 steps ETDRS patient level progression
- Estimated completion in 2027

**SOUL**
Cardiovascular outcomes trial
Semaglutide 14 mg, oral
- ~9,600 patients with T2D, established CVD or CKD
- Primary endpoint: Time to first major adverse cardiovascular event \(^1\)
- Estimated completion in 2024

**FLOW**
Chronic kidney disease outcomes trial
Semaglutide 1.0 mg, injectable
- ~3,500 patients with T2D, moderate to severe CKD
- Primary endpoint: Time to first occurrence of a composite outcome event \(^2\)
- Estimated completion in 2024

**STRIDE**
Peripheral arterial disease
Semaglutide 1.0 mg, injectable
- ~800 patients with type 2 diabetes and PAD
- Primary endpoint: Change in maximum walking distance
- Estimated completion in 2024

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\(^1\) Major adverse cardiovascular event defined as CV death, non-fatal stroke or non-fatal myocardial infarction; \(^2\) Defined as persistent eGFR decline of ≥50% from trial start, reaching end stage renal disease, death from kidney disease or death from cardiovascular disease

T2D: Type 2 diabetes; CVD: Cardiovascular disease; PAD: Peripheral arteries disease; ETDRS: Early treatment diabetic retinopathy study; CKD: Chronic kidney disease
Investigating semaglutide effects beyond glucose lowering in people with type 2 diabetes

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T2D: Type 2 diabetes; CVD: Cardiovascular disease; PAD: Peripheral arteries disease; ETDRS: Early treatment diabetic retinopathy study; CKD: Chronic kidney disease
Chronic kidney disease is common in patients with diabetes and remains a large unmet need

Chronic kidney disease (CKD) is common in patients with diabetes

Diabetes is directly correlated with ~50% of all ESKD cases

10 in 1001 patients with diabetic kidney disease progress to ESKD

14-17% at 20 years

CKD: Chronic Kidney Disease; ESKD: End Stage Kidney Disease; T1D: Type 1 diabetes; T2D: type 2 diabetes

Attenuated loss of kidney function observed across SUSTAIN 6 and LEADER

CI: confidence interval; eGFR: estimated glomerular filtration rate; HR: hazard ratio; ETD: Estimated treatment difference; eGFR: estimated glomerular filtration rate; Sema: Semaglutide; Lira: Liraglutide; NS: Non-significant

Source: Presented at the 56th European Renal Association - European Dialysis and Transplant Association (ERA-EDTA) Congress, 13–16 June 2019; Budapest, Hungary, Poster F482
Semaglutide 1.0 mg is investigated in people with diabetes and chronic kidney disease in the ongoing phase 3b trial FLOW

Phase 3b trial for semaglutide 1.0 mg in ~3,500 people with type 2 diabetes and chronic kidney disease

Inclusion
- T2D, HbA1c ≤10%
- eGFR ≤75 to ≥50\(^1\) and UACR >300 to <5,000 mg/g or eGFR <50 to ≥25\(^1\) and UACR >100 to <5,000 mg/g
- RAAS blocker

Primary end-points
- Time to first occurrence of a composite endpoint:
  - Onset of persistent ≥50% reduction in eGFR
  - Onset of persistent eGFR <15 mL/min/1.73 m\(^2\)
  - Initiation of chronic renal replacement therapy (dialysis or kidney transplantation)
  - Renal death
  - CV death

Secondary end-points
- Change in eGFR (total eGFR slope)
- 3-point MACE
- All-cause death

Trial objective
- Demonstrate that semaglutide delays the progression of renal impairment and lowers risk of renal - and CV mortality

Treatment period: Expected up to 5 years or more
Estimated completion: 2024

1 mL/min/1.73 m\(^2\)
T2D: Type 2 diabetes; UACR: Urine albumin-creatinine ratio; RAAS: Renin-angiotensin-aldosterone system; CV: Cardiovascular; MACE: Major adverse cardiovascular events; eGFR: estimated glomerular filtration rate; Sc: Subcutaneous
FLOW is investigating kidney outcomes and the role of GLP-1 in a trial population with multiple risk factors and comorbidities

### Trial baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Trial population, N=3,535</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years mean (SD)</td>
<td>66.6 (9.0)</td>
</tr>
<tr>
<td>HbA1c, % mean (SD)</td>
<td>7.8 (1.3)</td>
</tr>
<tr>
<td>Diabetes duration, years mean (SD)</td>
<td>17.4 (9.3)</td>
</tr>
<tr>
<td>eGFR, mL/min/1.73m² mean (SD)</td>
<td>47.0 (15.1)</td>
</tr>
<tr>
<td>UACR, mg/g, median (min.-max.)</td>
<td>567 (1-11,852)</td>
</tr>
</tbody>
</table>

### Diabetic comorbidities

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Count (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic neuropathy(^1)</td>
<td>1,519 (43.0)</td>
</tr>
<tr>
<td>Diabetic retinopathy in at least one eye(^2)</td>
<td>1,578 (44.6)</td>
</tr>
<tr>
<td>Diabetic macular edema in at least one eye(^2)</td>
<td>241 (6.8)</td>
</tr>
<tr>
<td>Very high CKD progression risk, n (%)</td>
<td>2,414 (68.2%)</td>
</tr>
</tbody>
</table>

### Key take-aways

- First and only kidney outcomes trial specifically designed and powered to assess whether treatment with a GLP-1 can reduce risk of kidney failure and loss of kidney function
- Patients with high risk of CKD progression with long diabetes duration, high medication use and prevalent comorbidities
- No observed association of HbA1c or diabetes duration with KDIGO risk category
- FLOW, alongside SOUL, SELECT and REMODEL trials, will assess the effect of semaglutide in the interconnected disease areas of CKD, T2D, obesity and CVD

---

\(^1\) Based on medical history; \(^2\) Based on eye examination at baseline

UACR: Urine albumin-creatinine ratio; CKD: Chronic kidney disease; SD: Standard deviation; eGFR: estimated glomerular filtration rate; T2D: Type 2 diabetes; CVD: Cardiovascular disease; KDIGO: Kidney Disease: Improving Global Outcomes

Source: ADA 2022 poster 747-P: Baseline characteristics of subjects in the once-weekly semaglutide FLOW kidney outcomes trial (diabetes status)
Limited treatment options for the millions of people with type 2 diabetes and peripheral artery disease (PAD)

20-30% of people with PAD have diabetes

Million people

>200

Approximately 40-60

PAD

Diabetes and PAD

People with type 2 diabetes are at higher risk of suffering from PAD

Factors increasing risk of PAD in people with type 2 diabetes

- Duration of diabetes
- Age
- Presence of peripheral neuropathy
- Poor glycaemic control

Low diagnosis rates and limited treatment options

Difficult to diagnose due to peripheral neuropathy

Treatment is

- diet, exercise, secondary prevention medicine
- endovascular treatment and surgical thromboendarterectomy
- open surgical revascularisation or amputation

Unmet need: Limited treatment options for people with type 2 diabetes and PAD

PAD: Peripheral artery disease; MACE: Major adverse cardiovascular events.
The ongoing STRIDE phase 3a trial investigates semaglutide for the treatment of peripheral artery disease in people with T2D

**Phase 3a trial (STRIDE) for semaglutide 1.0 mg in type 2 diabetes for treatment of PAD expected to read out in 2024**

**Inclusion criteria**
- Adults with T2D and PAD
- Intermittent claudication stage Fontaine IIa ≥ 3 months
- Max walking distance ≤600m

**Primary end-point**
Change in maximum walking distance on a constant load treadmill test

**Secondary end-points**
- Change in pain-free walking distance on a constant load treadmill test
- Change in Vascular Quality of Life Questionnaire-6 (VascuQoL-6) score

**Next steps**
Estimated completion is during 2024

R: Randomisation; PAD: Peripheral artery disease; T2D: Type 2 Diabetes; S.c.: Subcutaneous
Source: ClinicalTrials.gov identifier: NCT04560998
GLP-1: Key take-aways

Chronic kidney disease and peripheral artery disease have large overlaps with diabetes, with a large population affected and a high unmet need.

Evidence from previous GLP-1 trials forms the basis for the decision for Novo Nordisk to address new disease areas.

Novo Nordisk continues to investigate opportunities to expand the label of semaglutide through eg FLOW, SOUL, FOCUS and STRIDE.
Agenda

Introduction

Obesity care
Post hoc analysis of STEP 1 and 4, STEP TEENS results and SELECT-LIFE
Martin Holst Lange

GLP-1 Diabetes
Semaglutide in chronic kidney disease and peripheral artery disease
Mads Frederik Rasmussen

Insulin
Insulin icodec hypoglycaemia frequency, results from ONWARDS 1, ONWARDS 2, and ONWARDS 6
Martin Holst Lange

Q&A
All
Hypoglycaemia frequency and physiological response to double or triple doses of insulin icodec vs insulin glargine U100

**Objective**

To compare between once-weekly insulin icodec and once-daily insulin glargine U100 in people with type 2 diabetes

Specifically:
- **Hypoglycaemia frequency** after double or triple doses
- **Physiological response to hypoglycaemia** after a triple dose in patients with plasma glucose <54 mg/dL and/or hypoglycaemia symptoms

**Inclusion criteria**

- **43 people with T2D** on basal insulin ± OAD
- **Age:** 18-72 years
- **HbA1c:** ≤9.0%
- **BMI:** 18.5-37.9 kg/m²

T2D: Type 2 diabetes; OAD: Oral anti-diabetic; BMI: Body mass index
Comparable clinically significant hypoglycaemia for insulin icodec vs insulin glargine U100 in the trial

Individuals who experienced clinically significant hypoglycaemia

**Double dose**
- Insulin icodec: 40%
- Insulin glargine U100: 36%

**Triple dose**
- PG<sub>nadir</sub> >54 mg/dL: 53%
- PG<sub>nadir</sub> ≤54 mg/dL: 70%

Key findings

**Hypoglycaemia frequency**
Comparable proportions of individuals experienced clinically significant hypoglycaemia with once-weekly insulin icodec vs once-daily insulin glargine U100 after double and triple doses.

**Physiological response to hypoglycaemia after 3x dose**
During hypoglycaemia, a comparable symptomatic response and a moderately greater endocrine response were seen for insulin icodec.

**Overall safety**
No severe hypoglycaemic episodes during the treatment periods and no serious AEs following the induced hypoglycaemic episodes or during the trial overall.

AE: Adverse events; PG: Plasma glucose
The first three trials of the ONWARDS programme have read out

<table>
<thead>
<tr>
<th>Trial</th>
<th>Read out available</th>
</tr>
</thead>
<tbody>
<tr>
<td>ONWARDS 1</td>
<td>984 people insulin-naïve, 78-week, vs insulin glargine U100</td>
</tr>
<tr>
<td>ONWARDS 2</td>
<td>526 people on basal, 26-week, vs insulin degludec</td>
</tr>
<tr>
<td>ONWARDS 3</td>
<td>580 people insulin-naïve, 26-week, vs insulin degludec</td>
</tr>
<tr>
<td>ONWARDS 4</td>
<td>580 people on both basal and bolus, 26-week, vs insulin degludec</td>
</tr>
<tr>
<td>ONWARDS 5</td>
<td>1,100 people, insulin-naïve using app-based dosing recommendations, 52-week</td>
</tr>
<tr>
<td>ONWARDS 6</td>
<td>582 people, type 1 diabetes using bolus insulin, 52-week, vs insulin degludec</td>
</tr>
</tbody>
</table>

2022
ONWARDS 2 was completed as the first of six trials in the phase 3 programme for once-weekly insulin icodex

The ONWARDS 2 phase 3a trial has been completed

- Insulin icodex ± non-insulin anti-diabetic drugs
- Insulin degludec ± non-insulin anti-diabetic drugs

26 weeks

Objective
To confirm the efficacy (non-inferiority on HbA1c) and safety of once-weekly insulin icodex in patients with type 2 diabetes treated with basal only insulin

Primary endpoint
- Change in HbA1c from baseline to week 26

Inclusion criteria
- T2D treated with basal insulin ± OADs* ± GLP-1 s.c.
- Age ≥ 18 years
- HbA1c 7-10%
- BMI ≤ 40 kg/m2

*Pre-trial all OADs including oral GLP-1s are allowed but SU and glinides are to be discontinued at randomisation
T2D: Type 2 diabetes; OAD: Oral Anti Diabetics; s.c.: subcutaneous; BMI: Body mass index, SU: Sulfonylurea
Simple and easy titration for insulin icodec in the ONWARDS programme

<table>
<thead>
<tr>
<th>Pre-breakfast SMPG</th>
<th>mmol/L</th>
<th>mg/dL</th>
<th>Dose adjustment insulin icodec</th>
<th>Dose adjustment comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowest of the SMPG values</td>
<td>&lt;4.4</td>
<td>&lt;80</td>
<td>-20</td>
<td>-3</td>
</tr>
<tr>
<td>Mean of the SMPG values</td>
<td>4.4–7.2</td>
<td>80–130</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt;7.2</td>
<td>&gt;130</td>
<td>+20</td>
<td>+3</td>
</tr>
</tbody>
</table>

SMPG: Self-measured plasma glucose; mmol/L: Millimoles per litre
Note: Starting dose: 70U weekly (Ico) and 10U daily (IGlar). Dose adjustment based on the three pre-breakfast SMPG values measured on two days prior to titration and on the day of the titration.
ONWARDS 2 met its primary endpoint and demonstrated superiority on HbA$_{1c}$ reduction compared to insulin degludec

**Primary endpoint:**
- From an overall baseline HbA$_{1c}$ of 8.13%, once-weekly insulin icodec achieved a superior reduction in estimated HbA$_{1c}$ compared to insulin degludec.
- Estimated treatment difference: -0.22%

* Lines are based on observed data where the value denoted after 26 weeks is estimated mean value derived based on multiple imputation.
No statistically significant difference in hypoglycaemic events in ONWARDS 2

### Overall hypoglycaemic episodes in the trial

<table>
<thead>
<tr>
<th>Level 2: Clinically significant hypo</th>
<th>Insulin icodex</th>
<th></th>
<th>Insulin degludec</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>E</td>
<td>R</td>
<td>N (%)</td>
<td>E</td>
</tr>
<tr>
<td>37 (14.1)</td>
<td>1.13</td>
<td>0.73</td>
<td>19 (7.2)</td>
<td>0.41</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level 3: Severe hypo</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1 (0.4)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level 3 or 2: Severe or clinically significant hypo</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>37 (14.1)</td>
<td>1.13</td>
<td>0.73</td>
</tr>
</tbody>
</table>

### Key highlights

- No statistically significant difference in estimated rates of severe or clinically significant hypoglycaemia events
  - 0.73 events\(^1\) for insulin icodex and 0.27 events for insulin glargine
- In the trial, once-weekly insulin icodex appeared to have a safe and well-tolerated profile

---

\(^1\) Events measured as per patient year

Hypo: hypoglycaemia; N: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events, R: Rate (number of events per patient year of exposure), hypoglycaemia alert value (level 1): Plasma glucose value of < 3.9 mmol/L (70 mg/dL) and >= 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Clinically significant hypoglycaemia (level 2): Plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by blood glucose meter. Severe hypoglycaemia (level 3): Hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. Note: Lines in graph 1 are based on observed data where the value denoted after 26-week is estimated mean value
ONWARDS 2 showed a statistically significant improvement in quality of life compared to insulin degludec

**ONWARDS 2 quality of life assessment**

<table>
<thead>
<tr>
<th>Treatment satisfaction score</th>
<th>Treatment difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Once-weekly insulin icodec</td>
<td>4.22</td>
</tr>
<tr>
<td>Once-daily insulin degludec</td>
<td>2.96</td>
</tr>
</tbody>
</table>

**ONWARDS 2 treatment satisfaction**

Patient reported clinical outcome assessments via a Diabetes Treatment Satisfaction Questionnaire (DTSQ) without assistance of site personnel. The DTSQs were measured at baseline and end of treatment and the treatment satisfaction is evaluated across six dimensions including:

- Convenience
- Flexibility
- Satisfaction
- Recommend treatment

**Conclusion**

- Statistically significant improvement of treatment satisfaction score in favour of insulin icodec

* Treatment difference = 1.25 (0.41;2.10) 95% CI, P value: 0.0036
ONWARDS 1 comparing insulin icodec in insulin-naïve patients with insulin glargine U100

**ONWARDS 1 trial design**

1:1

- **Insulin icodec** ± non-insulin anti-diabetic drugs
- **Insulin glargine U100** ± non-insulin anti-diabetic drugs

78 weeks

**Objective**

To confirm the efficacy (non-inferiority on HbA1c) and safety of once-weekly insulin icodec in insulin-naïve patients with type 2 diabetes

**Primary endpoint**

- Change in HbA1c from baseline to week 52

**Inclusion criteria**

- T2D treated with OADs* ± GLP-1 s.c.
- Age ≥ 18 years
- HbA1c 7.0-11.0%
- BMI ≤ 40 kg/m²

*Pre-trial all OADs including oral GLP-1s are allowed but SU and glinides are to be discontinued at randomisation.

T2D: Type 2 diabetes; OAD: Oral Anti-Diabetics; s.c.: Subcutaneous; BMI: Body mass index; SU: Sulfonylurea
ONWARDS 1 met its primary endpoint and demonstrated superior HbA$_{1c}$ reduction compared to insulin glargine U100

**Key highlights from main phase**

**Primary endpoint:**
- From an overall baseline HbA$_{1c}$ of 8.5%, once-weekly insulin icodec achieved a superior reduction in estimated HbA$_{1c}$ of -1.55% compared to -1.35% for insulin glargine U100
- Estimated treatment difference: -0.19%

*Lines are based on observed data where the value denoted after 52 weeks is estimated mean value derived based on multiple imputation*
With insulin icodec, more patients reached HBA$_{1c}$ target without hypoglycemia and achieved superior time in range

Achievement of HBA$_{1c}$ target after 52 weeks without hypoglycemia$^1$

- More participants achieved the HBA$_{1c}$ target without any severe or clinically significant hypoglycaemia when treated with insulin icodec compared to insulin glargine U100

Superior time in range for insulin icodec vs insulin glargine U100

- 3.9–10.0 mmol/L from week 48 to week 52 was 71.94% with insulin icodec and 66.90% with insulin glargine U100, confirming superiority of insulin icodec vs insulin glargine U100
- Broadly equal to one additional hour in range per day

---

$^1$ Specifically an HBA$_{1c}$ <7% without level 2 or 3 hypoglycaemic episodes; * Statistically significant difference in favour of insulin icodec.

CI: Confidence interval, No correction for multiplicity. HBA$_{1c}$: Haemoglobin A$_{1c}$. The binary response after 52 weeks is analysed using a binary logistic regression model (logit link) with treatment and region as fixed factors, and the baseline HBA$_{1c}$ value as covariate. Missing HBA$_{1c}$ measurements are imputed using the same method as specified for the primary analysis before the target achievement criterion is applied; EOR: Estimated odds ratio
No statistically significant difference in hypoglycaemic events in ONWARDS 1

Overall hypoglycaemic episodes in the trial

| On treatment | Insulin icodec | | | Insulin glargine U100 | | |
|--------------|---------------|-------------|-------------|-----------------|-------------|
|              | N (%) | E | R | N (%) | E | R |
| **Level 2:** Clinically significant hypo | 48 (9.8) | 1.43 | 0.29 | 49 (10.0) | 0.75 | 0.15 |
| **Level 3:** Severe hypo | 1 (0.2) | 0.01 | 0.00 | 3 (0.6) | 0.03 | 0.01 |
| **Level 3 or 2:** Severe or clinically significant hypo | 48 (9.8) | 1.44 | 0.30 | 52 (10.6) | 0.78 | 0.16 |

Key highlights from main phase

**Safety**
- No statistically significant difference in estimated rates of severe or clinically significant hypoglycaemia events
  - 0.30 events\(^1\) for insulin icodec and 0.16 events for insulin glargine U100
  - Insulin icodec appeared to have a safe and well-tolerated profile

---

\(^1\) Events measured per patient year

Hypo: hypoglycaemia; N: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events, R: Rate (number of events per patient year of exposure), hypoglycaemia alert value (level 1): Plasma glucose value of < 3.9 mmol/L (70 mg/dL) and >= 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Clinically significant hypoglycaemia (level 2): Plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by blood glucose meter. Severe hypoglycaemia (level 3): Hypoglycaemia with severe cognitive impairment requiring external assistance for recovery.
ONWARDS 6 in type 1 diabetes patients on bolus insulin and insulin icodex or insulin degludec

ONWARDS 6 trial design

1:1

Insulin icodex
+ insulin aspart

Insulin degludec
+ insulin aspart

52 weeks

Included 582 people with type 1 diabetes

Objective
To confirm the efficacy (non-inferiority on HbA1c) and safety of once-weekly insulin icodex + bolus insulin in patients with type 1 diabetes

Primary endpoint
- Change in HbA1c from baseline to week 26

Inclusion criteria
- T1D treated with basal-bolus insulin
- Age ≥ 18 years
- HbA1c < 10%

*Pre-trial all OADs including oral GLP-1s are allowed but SU and glinides are to be discontinued at randomisation

T1D: Type 1 diabetes
ONWARDS 6 met its primary endpoint of demonstrating non-inferiority in reducing HbA$_{1c}$ compared to insulin degludec.

**Non-inferior change in HbA$_{1c}$ from baseline over 26 weeks**

**Primary endpoint:**
- From an overall baseline HbA$_{1c}$ of 7.6%, once-weekly insulin icodec achieved a reduction in estimated HbA$_{1c}$ of -0.47% compared to -0.51% for insulin degludec in a T1D population.
- Estimated treatment difference: 0.05%.

* Lines are based on observed data where the value denoted after 26-week is estimated mean value derived based on multiple imputation.

T1D: Type 1 diabetes.
Statistically significant difference in hypoglycaemic events in people with type 1 diabetes in ONWARDS 6 trial

### Overall hypoglycaemic episodes in the trial

<table>
<thead>
<tr>
<th>On treatment</th>
<th>Insulin icodec</th>
<th>Insulin degludec</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N  (%)</td>
<td>E</td>
</tr>
<tr>
<td><strong>Level 2: Clinically significant hypo</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>246 (84.8)</td>
<td>27.89</td>
</tr>
<tr>
<td><strong>Level 3: Severe hypo</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9 (3.1)</td>
<td>0.47</td>
</tr>
<tr>
<td><strong>Level 3 or 2: Severe or clinically significant hypo</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>247 (85.2)</td>
<td>28.36</td>
</tr>
</tbody>
</table>

### Key highlights

- A statistical difference in the estimated rates of severe or clinically hypoglycaemia events\(^1\)
  - 19.93 events for insulin icodec vs 10.37 events for insulin degludec
- Insulin icodec appeared to have a safe and well-tolerated profile

---

\(^1\) Events measured as per patient year

Hypo: hypoglycaemia; N: Number of subjects with one or more events, %: Percentage of subjects with one or more events, E: Number of events, R: Rate (number of events per patient year of exposure), hypoglycaemia alert value (level 1): Plasma glucose value of < 3.9 mmol/L (70 mg/dL) and >= 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Clinically significant hypoglycaemia (level 2): Plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by blood glucose meter. Severe hypoglycaemia (level 3): Hypoglycaemia with severe cognitive impairment requiring external assistance for recovery.
Insulin: Key take-aways

In a dedicated hypoglycemia study, no difference in hypoglaecemic events for insulin icodec vs insulin glargine U100 at double or triple dose

ONWARDS 1 and ONWARDS 2 met primary endpoints and demonstrated superior HbA$_{1c}$ reductions compared to insulin glargine U100 and insulin degludec, respectively

ONWARDS 6 met its primary endpoint of demonstrating non-inferiority in HbA$_{1c}$ reduction compared to insulin degludec

Once-weekly insulin icodec has the potential to be the ideal starting insulin for people with type 2 diabetes
## R&D milestones for 2022

### Innovation and therapeutic focus

<table>
<thead>
<tr>
<th>Project</th>
<th>Q1 2022</th>
<th>Q2 2022</th>
<th>Q3 2022</th>
<th>Q4 2022</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diabetes care</strong></td>
<td></td>
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</tr>
<tr>
<td>Ozempic® 2.0 mg</td>
<td></td>
<td>US decision (✓)</td>
<td></td>
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<tr>
<td>FDC Sema – OW GIP</td>
<td></td>
<td></td>
<td>Phase 1 results</td>
<td></td>
</tr>
<tr>
<td>CagriSema T2DM</td>
<td></td>
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<td>Phase 2 results</td>
<td></td>
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<tr>
<td>Higher doses inj. sema</td>
<td></td>
<td></td>
<td>Phase 2 initiation</td>
<td></td>
</tr>
<tr>
<td>Rybelsus®</td>
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<td>CN submission</td>
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<td></td>
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<tr>
<td>Icodec</td>
<td>Phase 1 results (✓)</td>
<td></td>
<td>Phase 3a results</td>
<td>Phase 1 results</td>
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<tr>
<td>Ideal Pump insulin</td>
<td>Phase 1 initiation (✓)</td>
<td></td>
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<tr>
<td>Oral GLP-1/GIP co-agonist</td>
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<tr>
<td><strong>Obesity care</strong></td>
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<tr>
<td>SELECT CVOT</td>
<td></td>
<td></td>
<td>Potential interim analysis</td>
<td>Phase 3 initiation</td>
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<tr>
<td>CagriSema</td>
<td></td>
<td></td>
<td>Phase 1 results</td>
<td></td>
</tr>
<tr>
<td>LA-GDF15</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Rare disease</strong></td>
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<td></td>
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<td></td>
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<tr>
<td>Sogroya® (somapacitan)</td>
<td></td>
<td>US/EU/JP submission (GHD)</td>
<td></td>
<td>Phase 3 treatment (✓)</td>
</tr>
<tr>
<td>Mim8</td>
<td>Phase 1/2 results (✓)</td>
<td></td>
<td>Phase 3a results (HwI)</td>
<td>Phase 3a results (HA/HB)</td>
</tr>
<tr>
<td>Concizumab</td>
<td>Phase 3a results (HwI)</td>
<td></td>
<td>US submission (HwI)</td>
<td></td>
</tr>
<tr>
<td>Eclipse/Ndec</td>
<td></td>
<td></td>
<td>Phase 2 initiation</td>
<td></td>
</tr>
<tr>
<td>PRX004 (ATTR-CM)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 Expected to be published in the given quarter or in the subsequent quarterly company announcement. 2 First patient first visit in Q4 2021, which is solely for baselining purposes.

Note: Trial initiations could be impacted by COVID-19; GHD: Growth Hormone Deficiency; sema: semaglutide; HwI: Haemophilia with inhibitors; ATTR-CM: Transthyretin Amyloid Cardiomyopathy; CVOT: Cardiovascular Outcomes Trial; Inj.: Injectable; Sema: Semaglutide.
Strategic aspirations 2025

**Purpose and sustainability (E,S,G)**
- Progress towards zero environmental impact
- Being respected for adding value to society
- Being recognised as a sustainable employer

**Innovation and therapeutic focus**
- Further raise the innovation-bar for diabetes treatment
- Develop a leading portfolio of superior treatment solutions for obesity
- Strengthen and progress the Rare disease pipeline
- Establish presence in Other serious chronic diseases focusing on CVD, NASH and CKD

**Commercial execution**
- Strengthen Diabetes leadership - aim at global value market share of more than 1/3
- More than 25 billion DKK in Obesity sales by 2025
- Secure a sustained growth outlook for Rare disease

**Financials**
- Deliver solid sales and operating profit growth
  - Deliver 6-10% sales growth in IO
  - Transform 70% of sales in the US¹
- Drive operational efficiencies across the value chain to enable investments in future growth assets
- Deliver free cash flow to enable attractive capital allocation to shareholders

¹ From 2015 to 2022, 70% of sales to come from products launched from 2015. IO: International Operations; CVD: Cardiovascular disease; NASH: Non-alcoholic steatohepatitis; CKD: Chronic kidney disease.

Note: The strategic aspirations are not a projection of Novo Nordisk's financial outlook or expected growth.
# Agenda

## Introduction
- **Obesity care**
  - Post hoc analysis of STEP 1 and 4, STEP TEENS results and SELECT-LIFE
- **GLP-1 Diabetes**
  - Semaglutide in chronic kidney disease and peripheral artery disease
- **Insulin**
  - Insulin icodect hypoglycaemia frequency, results from ONWARDS 1, ONWARDS 2, and ONWARDS 6

## Q&A
- All
Investor contact information

Share information

Novo Nordisk's B shares are listed on the stock exchange in Copenhagen under the symbol ‘NOVO B’. Its ADRs are listed on the New York Stock Exchange under the symbol ‘NVO’.

For further company information, visit Novo Nordisk on: www.novonordisk.com

Upcoming events

04 August 2022   Financial statement for the first six months of 2022
02 November 2022   Financial statement for the first nine months of 2022
01 February 2023   Financial statement 2022

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