Novo Nordisk
- a focused healthcare company

Conference call on decision to enter phase 3 development in early Alzheimer’s disease and GLP-1 R&D strategy update
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® is approved for the management of type 2 diabetes only
- Saxenda® is approved in the USA and the EU for the treatment of obesity only
Strategic aspirations for 2025 – focus point today is Innovation and therapeutic focus

<table>
<thead>
<tr>
<th>Purpose and sustainability</th>
<th>Innovation and therapeutic focus</th>
<th>Commercial execution</th>
<th>Financials</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Being respected for adding value to society</td>
<td>• Further raise the innovation-bar for diabetes treatment</td>
<td>• Strengthen Diabetes leadership - aim at global value market share of more than 1/3</td>
<td>• Deliver solid sales and operating profit growth</td>
</tr>
<tr>
<td>• Progress towards zero environmental impact</td>
<td>• Develop a leading portfolio of superior treatment solutions for obesity</td>
<td>• Strengthen Obesity leadership and double current sales(^1)</td>
<td>• Deliver 6-10% sales growth in IO</td>
</tr>
<tr>
<td>• Ensure distinct core capabilities and evolve culture</td>
<td>• Strengthen and progress the Biopharm pipeline</td>
<td>• Secure a sustained growth outlook for Biopharm</td>
<td>• Transform 70% of sales in the USA(^2)</td>
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<td>• Establish presence in Other serious chronic diseases focusing on CVD, NASH and CKD</td>
<td></td>
<td>• Drive operational efficiencies across the value chain to enable investments in future growth assets</td>
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<td>• Deliver free cash flow to enable attractive capital allocation to shareholders</td>
<td></td>
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</tbody>
</table>

\(^1\) Based on reported sales in 2019, \(^2\) From 2015 to 2022. IO: International Operations; CVD: Cardiovascular disease; NASH: Non-alcoholic steatohepatitis; CKD: Chronic kidney disease.
Full ownership of the oral delivery technology Eligen® SNAC

The acquisition is completed

- The total acquisition price is USD 1.8 billion, which will be financed through debt
- Acquisition eliminates future SNAC royalty payments and provides full access to the technology platform for future pipeline projects

2020 financial impact from acquisition:
- No impact on operating profit
- Tax rate expected to be in the middle of the range
- Free cash flow expected to be lowered by the acquisition price

2021: Expected impact on operating profit from the acquisition is less than 1%, driven by amortisations partly offset by eliminated royalty payments

Medium term: Acquisition expected to have a neutral to positive net impact on operating profit
- Usage of the technology platform for future pipeline projects

Expectations 30 October 2020

- Operating profit: 5-8%
- Effective tax rate: 20-22%
- Free cash flow: DKK 34 to 39 billion

Notes and references are included on slide 15
Novo Nordisk has decided to initiate phase 3 trials in early Alzheimer’s disease with oral semaglutide

Novo Nordisk aspires to address a high unmet medical need within Alzheimer’s disease using GLP-1

- Alzheimer’s disease is a serious chronic disease with devastating consequences for patients and their families as well as a burden for societies
- Novo Nordisk expects to initiate a phase 3 programme in early Alzheimer’s disease during H1 2021 with oral semaglutide
- The decision is based on GLP-1 data from randomised clinical trials, real world evidence, preclinical models and discussions with regulatory agencies
Large unmet need within Alzheimer’s disease with ~85 million people living with mild cognitive impairment and dementia

~50 million people live with dementia across the world

Alzheimer’s is the leading cause of dementia

- ~55 million people have mild cognitive impairment due to Alzheimer’s disease
- ~30 million people have Alzheimer’s dementia
- Currently no approved disease modifying medical treatments for Alzheimer’s disease
- Historic failure rate within Alzheimer’s clinical development programmes >99%
Alzheimer’s disease has different clinical disease stages defined by the impairment of cognition

<table>
<thead>
<tr>
<th>Clinical disease stage</th>
<th>Biomarker magnitude</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitively normal</td>
<td>Normal</td>
</tr>
<tr>
<td>MCI with Alzheimer's pathologic changes</td>
<td>Abnormal</td>
</tr>
<tr>
<td>Dementia with Alzheimer's disease and pathological change</td>
<td>Abnormal</td>
</tr>
</tbody>
</table>

Notes and references are included on slide 15

MCI: mild cognitive impairment

Plaques / Amyloid β
Tangles = Tau-mediated neuronal injury
Brain structure
Memory / cognition
Function / Activities of Daily Living

Alzheimer pathology

Plaques
Tangles
The decision to go into phase 3 is based on data from clinical trials, real world evidence and animal studies

### Randomised controlled trials
- **53%** lower risk of dementia with liraglutide/semaglutide in NN CVOTs in T2D
- Systemic anti-inflammatory effects with semaglutide
- **Less decline** in cerebral glucose metabolism (FDG-PET) with liraglutide in AD
- No improvement in cerebral glucose metabolism, but less decline in temporal lobe volume and total grey matter volume for liraglutide vs placebo in the ELAD phase 2 study
- Short-term memory improvement with liraglutide in people with obesity

### Real world evidence
- Two studies show significantly lower risk of dementia after GLP-1 exposure
- Analysis of Danish nationwide registry showed 11% lower risk of dementia per year of GLP-1 exposure
- Analysis of US TRUVEN claims database showed 31% lower risk of dementia after >2 years of GLP-1 exposure

### Animal studies
- Improved memory function with GLP-1 incl. semaglutide
- Reduced phospho-tau accumulation
- Reduced neuroinflammation with GLP-1 incl. semaglutide

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AD: Alzheimer’s disease; FDG-PET: Positron emission tomography (PET) using a [18F]fluorodeoxyglucose (FDG); T2D: type 2 diabetes; CV: Cardiovascular; CVOT: Cardiovascular outcome trial; ELAD: Evaluating Liraglutide in Alzheimer’s Disease.

Notes and references are included on slide 15
The analysed data indicate reduced risk of dementia with GLP-1 treatment.

### Lower risk for dementia with GLP-1 treatment in Novo Nordisk CVOT trials
- LEADER, SUSTAIN 6 and PIONEER 6 pooled data including 15,820 people with T2D
- 53% lower risk of dementia in post-hoc analysis with liraglutide, s.c. or oral semaglutide vs placebo (n=47). Hazard ratio: 0.47 [0.25; 0.86]$_{95\%CI}$

### Real-world evidence shows lower risk of dementia in GLP-1 treated type 2 diabetes patients
#### Danish nationwide registry
- 11% lower risk of dementia per year of GLP-1 exposure. Hazard ratio: 0.89 [0.84; 0.93]$_{95\%CI}$
- 25% lower risk of dementia after 2.5 years of GLP-1 exposure
- n= ~470,000

#### TRUVEN claims database (US)
- 31% lower risk of dementia after >2 years of GLP-1 exposure. Hazard ratio: 0.69 [0.57; 0.82]$_{95\%CI}$
- n= >300,000

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CI: confidence interval; HR: hazard ratio; s.c.: subcutaneous; CVOT: Cardiovascular outcome trial
Notes and references are included on slide 15
The phase 3 trial will enrol early Alzheimer’s patients in the continuum of mild cognitive impairment and mild AD dementia.
Two phase 3 trials with a total of ~3,700 early Alzheimer’s patients testing oral semaglutide 14 mg vs placebo

Objectives: To confirm superiority of oral semaglutide vs placebo on the change in cognition and function in people with early Alzheimer’s disease

Primary endpoint: Change in the Clinical Dementia Rating – Sum of Boxes (CDR-SB) score from baseline to end of 104 weeks of treatment

Key inclusion criteria: Early Alzheimer’s disease (mild cognitive impairment or mild dementia), Mini-Mental State Examination ≥ 22/30, and age between 55-85 years. One of the trials will have around 20% with small vessel pathology

Trial timeline: Expected to be initiated during H1 2021 and complete 3-4 years from initiation

Clinical dementia rating - sum of boxes (CDR-SB) explanation
- Ratings in six domains are summed to provide a clinical measure = sum of boxes (SoB)
- Six domains (boxes):
  - Memory
  - Orientation
  - Judgment and problem solving
  - Community affairs
  - Home and hobbies
  - Personal care
- CDR-SB Scores range from 0 to 18

AD: Alzheimer's disease; ADCS-ADL-MCI: Alzheimer's Disease Cooperative Study-Activities of Daily Living adapted for patients with mild cognitive impairment; MCI: mild cognitive impairment; CDR-SoB: Clinical Dementia Rating Scale – Sum of Boxes
Novo Nordisk continues to explore opportunities with GLP-1 and utilise the oral technology platform

PIioneer plus
Phase 3 trial with oral semaglutide
25 mg and 50 mg

Sustain forte
Phase 3 with semaglutide 2.0 mg

Focus
Diabetic retinopathy outcomes trial

SOUL
CVOT in T2D patients with established CVD or CKD
~9,600 patients

Select
CVOT in people with obesity without diabetes
~17,500 patients

Flow
Chronic kidney disease outcomes trial in T2D patients with moderate to severe CKD
~3,200 patients

NASH
Semaglutide in NASH
Phase 3 trial expected to be initiated during 2021

Alzheimer's disease
Phase 3 programme in early Alzheimer's disease
~3,700 patients

Diabetes
Obesity
CVD
CKD
Brain disorders
NASH
Phase 3 trial with oral semaglutide 25 mg and 50 mg in T2D will assess efficacy for patients in need for improved outcomes

Randomisation 1:1:1

- Semaglutide 50 mg
- Semaglutide 25 mg
- Semaglutide 14 mg

Dose escalation
Maintenance
Primary endpoint after 52 weeks
5-weeks Follow-up
68 weeks in total

**Trial design:** One trial with a total of ~1,200 patients with type 2 diabetes

**Primary endpoint:** Change in \( \text{HbA}_{1c} \) from baseline to week 52

**Confirmatory secondary endpoint:** Change in body weight from baseline to week 52

**Key inclusion criteria:** Type 2 diabetes; \( \text{HbA}_{1c} \): 8.0-10.5%; \( \text{BMI} \): ≥25.0 kg/m\(^2\) and stable dose of 1-3 oral antidiabetics

**Higher doses of oral semaglutide phase 3 programme in T2D**

- Objective is to confirm superiority of oral semaglutide 25 mg and 50 mg once daily versus oral semaglutide 14 mg once daily on \( \text{HbA}_{1c} \) reduction
- Phase 3 expected to be initiated during H1 2021
- Trial expected to complete in around 2.5 years from initiation

T2D: Type 2 diabetes
Two phase 3 trials with oral semaglutide 14 mg vs placebo in early Alzheimer’s disease will be initiated during H1 2021
• Alzheimer’s is an area with a large unmet need
• Data from modes of action of GLP-1 indicates a potential effect
• High risk trial due to historic failure rate within Alzheimer’s clinical development

A phase 3 trial with oral semaglutide 25 mg and 50 mg vs oral semaglutide 14 mg in patients with type 2 diabetes will be initiated during H1 2021
• Phase 3 trial with oral semaglutide 25 mg and 50 mg in T2D will assess efficacy for patients in need for improved outcomes
Notes and sources

**Slide 4:** 1. Novo Nordisk Q3 2020 Company Announcement; 2. Press release 5. November - Novo Nordisk to acquire Emisphere Technologies and obtain ownership of the Eligen® SNAC oral delivery technology


**Slide 9:** Danish register: Dementia cases based on diagnosis (ICD10) or treatment (anticholinesterases, memantine) codes; TRUVEN: Dementia cases based on SNOMED ids for all diagnoses (ICD-10) or treatment (anticholinesterases, memantine). Data from cardiovascular outcomes trials, LEADER, SUSTAIN 6 and PIONEER 6 are included in the post-hoc analysis.