# 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 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
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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

## Purpose and sustainability

- Being respected for adding value to society
- Progress towards zero environmental impact
- Ensure distinct core capabilities and evolve culture

## 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 Biopharm 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
- Strengthen Obesity leadership and double current sales[1]
- Secure a sustained growth outlook for Biopharm

## Financials

- Deliver solid sales and operating profit growth
  - Deliver 6-10% sales growth in IO
  - Transform 70% of sales in the USA[2]
- 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] 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

| | Expectations 30 October 2020[1] |
|---|---|
| Operating profit | 5-8% |
| Effective tax rate | 20-22% |
| Free cash flow | DKK 34 to 39 billion |

## 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[2]
- **Medium term:** Acquisition expected to have a neutral to positive net impact on operating profit[2]
- Usage of the technology platform for future pipeline projects

Notes and references are included on slide 15

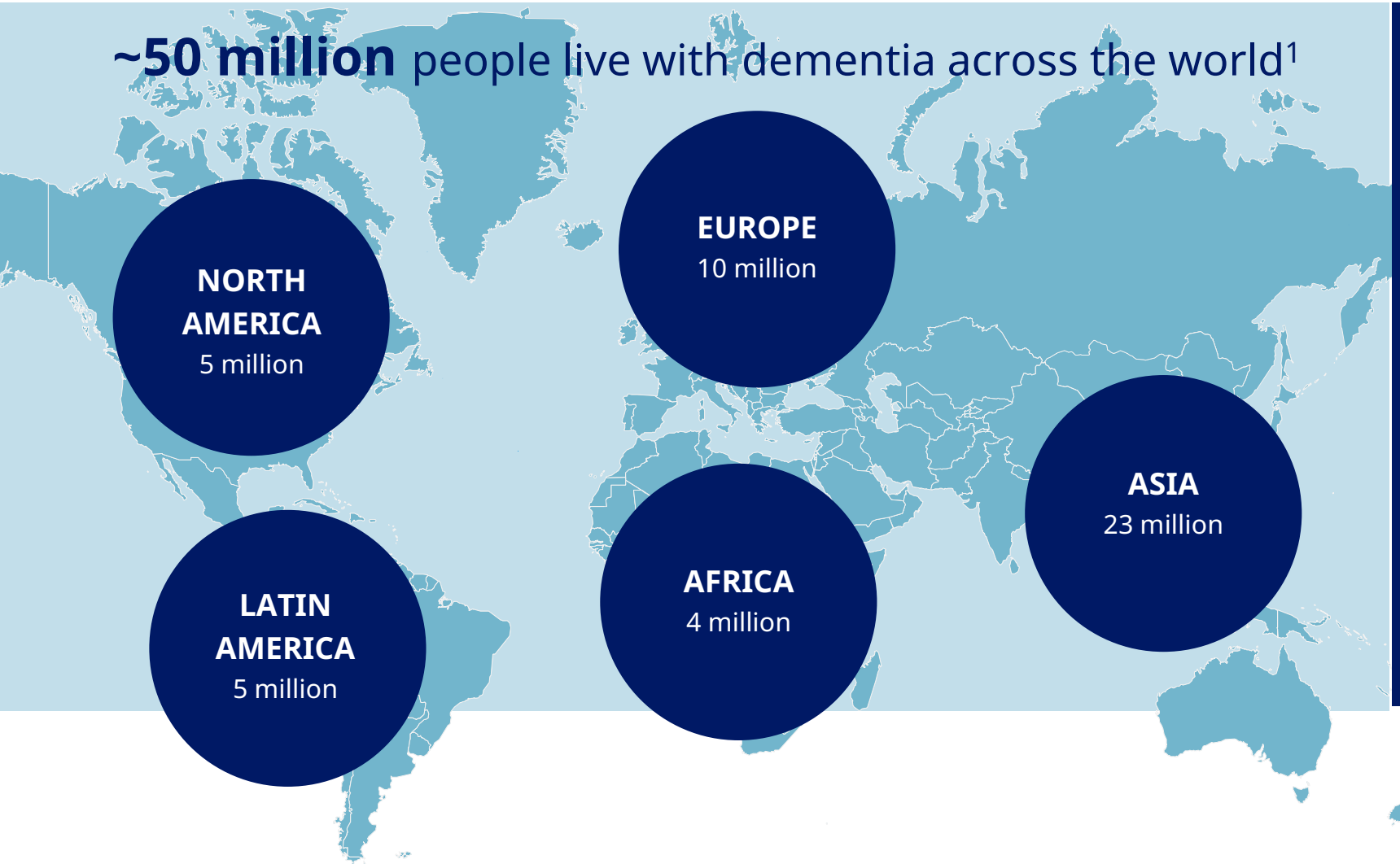
# Novo Nordisk has decided to initiate phase 3 trials in early Alzheimer’s disease with oral semaglutide

**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[1]

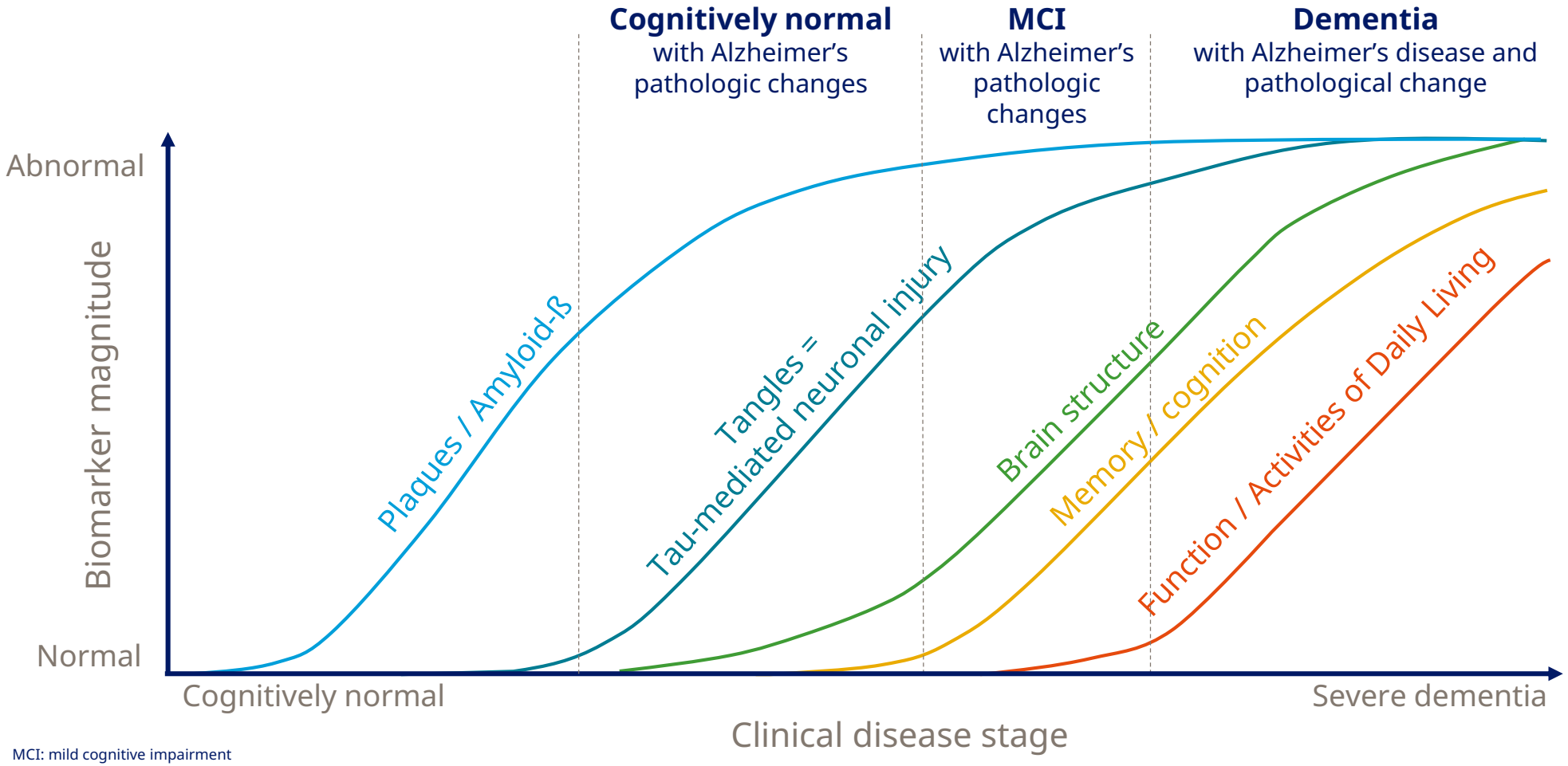



**Alzheimer's is the leading cause of dementia**

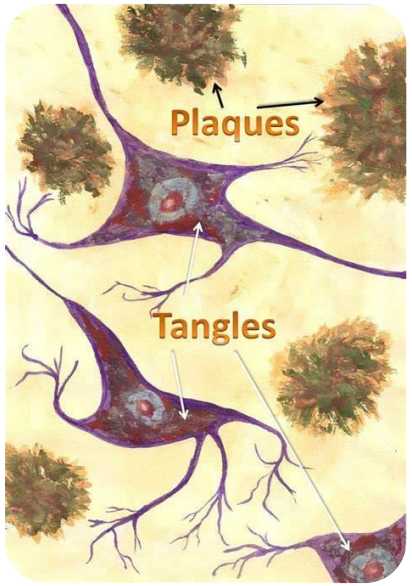
- **~55 million** people have mild cognitive impairment due to Alzheimer's disease[2,3]
- **~30 million** people have Alzheimer's dementia[2]
- Currently **no approved disease modifying medical treatments** for Alzheimer's disease
- Historic failure rate within Alzheimer's clinical development programmes >99%[4]

Notes and references are included on slide 15

# Alzheimer's disease has different clinical disease stages defined by the impairment of cognition




Alzheimer pathology




MCI: mild cognitive impairment
Notes and references are included on slide 15

# 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[1]
- Systemic anti-inflammatory effects with semaglutide[3,4]
- **Less decline** in cerebral glucose metabolism (FDG-PET) with liraglutide in AD[2]
- 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[6]
- Short-term memory improvement with liraglutide in people with obesity[5]


## Real world evidence

- Two studies show significantly lower risk of dementia after GLP-1 exposure[7,8]
- 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

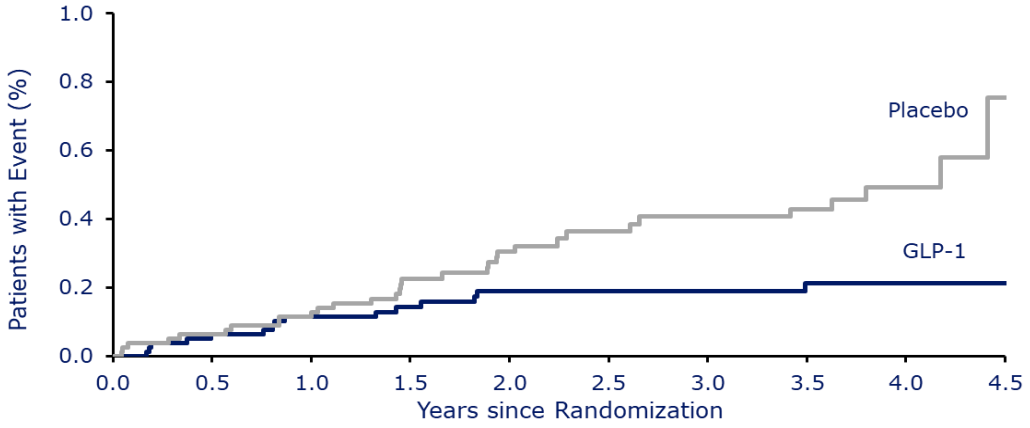
- Improved memory function with GLP-1[9] incl. semaglutide[13]
- Reduced phospho-tau accumulation[10]
- Reduced neuroinflammation with GLP-1[11,12] incl. semaglutide[13]

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

## 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

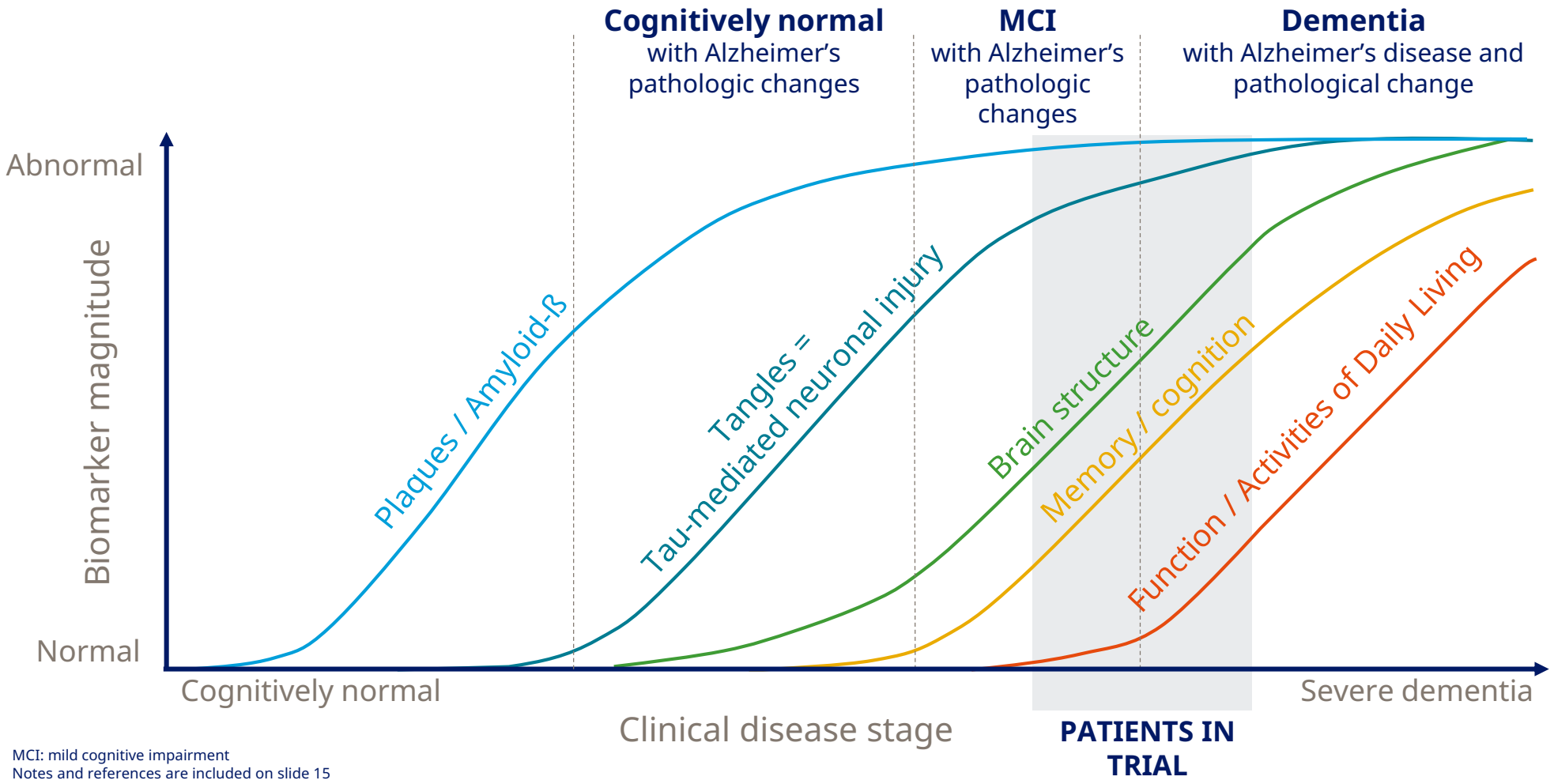
- **11%** lower risk of dementia per year of GLP-1 exposure. Hazard ratio: 0.89 [0.84; 0.93]$_{95\%CI}$
- 25% lower risk of dementia after 2.5 years of GLP-1 exposure
- n= ~470,000

### TRUVEN claims database (US)

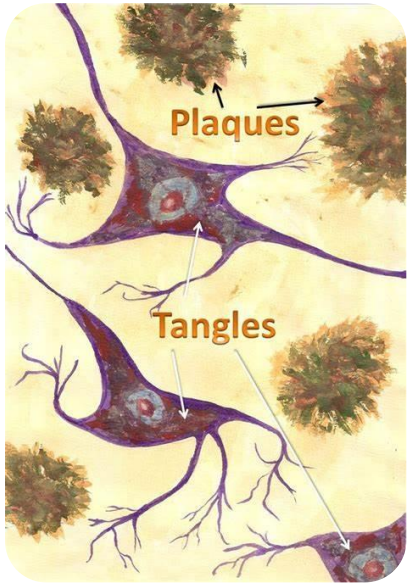
- **31%** lower risk of dementia after >2 years of GLP-1 exposure. Hazard ratio: 0.69 [0.57; 0.82]$_{95\%CI}$
- n= >300,000

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

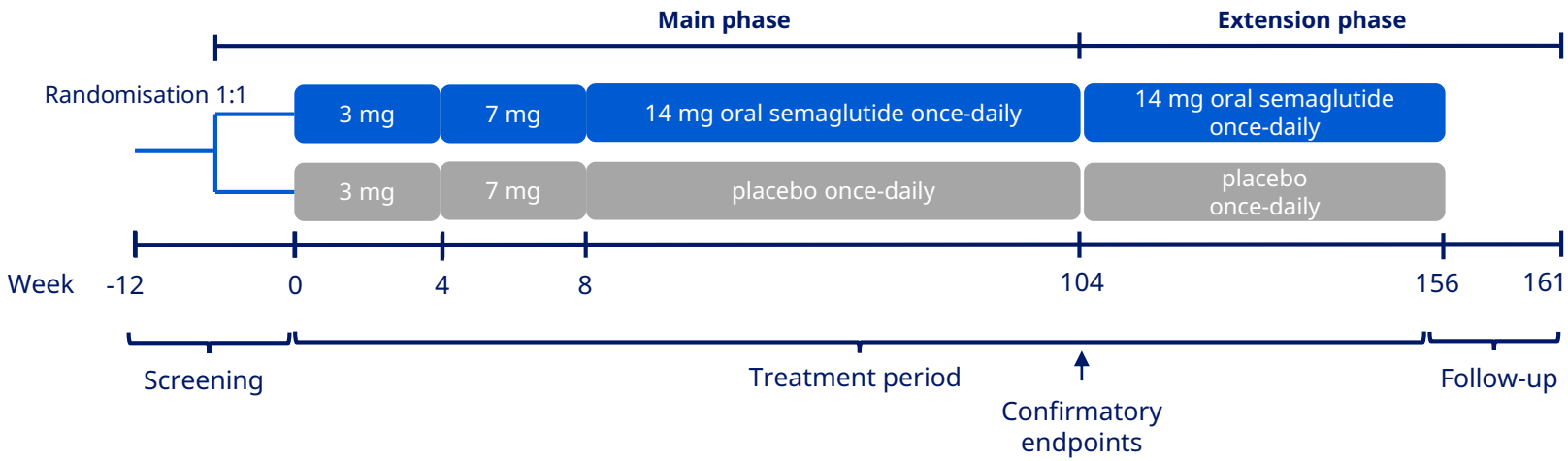



Alzheimer pathology




MCI: mild cognitive impairment
Notes and references are included on slide 15

# 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

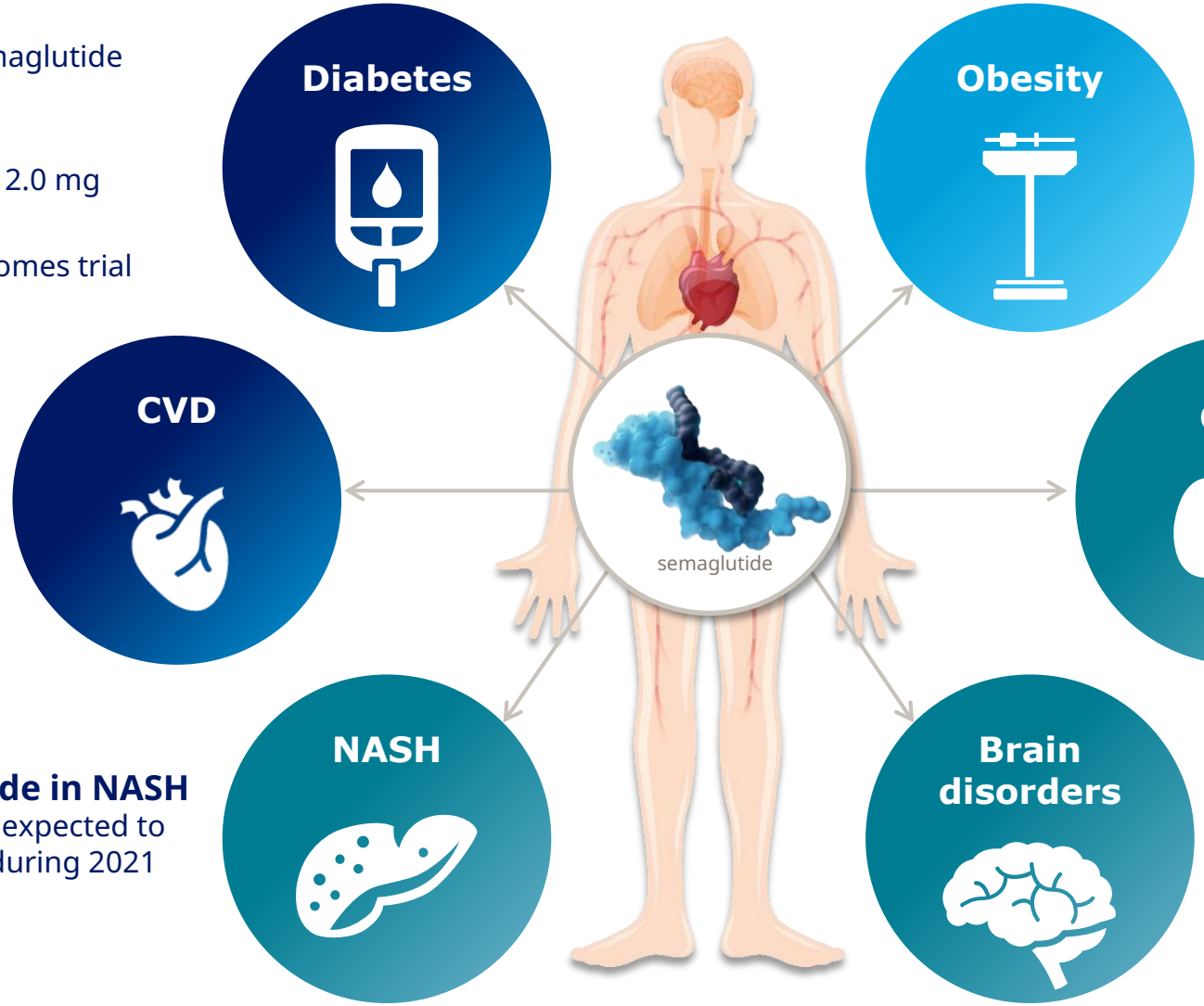
AD: Alzheimer's disease; ADCS-ADL-MCI: Alzheimer's Disease Cooperative Study-Activities of Daily Living adapted for patients with mild cognitive impairment; MCI: mild cognitive impairment; CDR-SoB: Clinical Dementia Rating Scale – Sum of Boxes

# Novo Nordisk continues to explore opportunities with GLP-1 and utilise the oral technology platform

**PIONEER 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




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

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

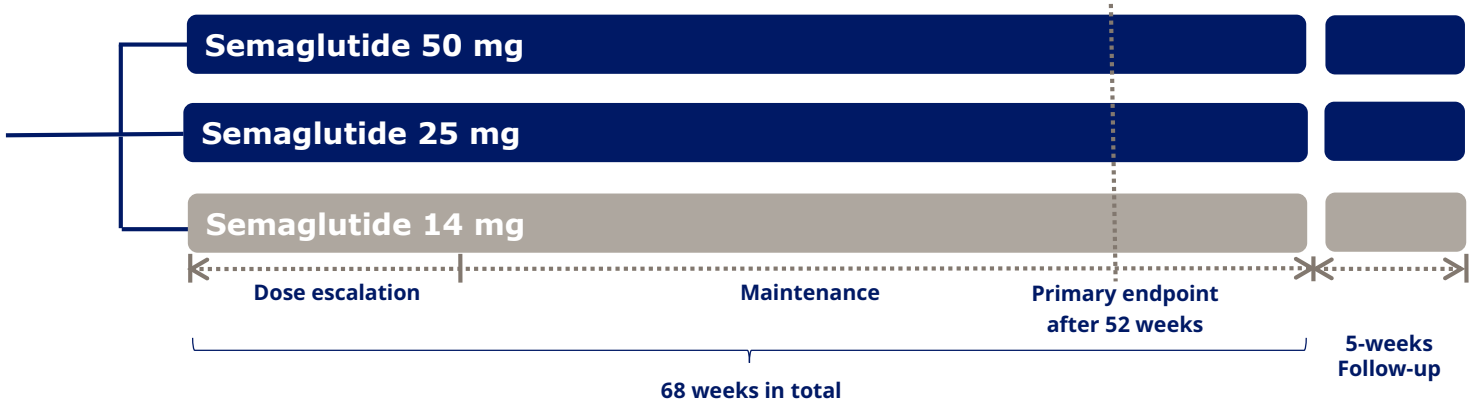
**FLOW**
Chronic kidney disease outcomes trial in T2D patients with moderate to severe CKD
~3,200 patients

**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

# 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




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

**Primary endpoint:** Change in $HbA_{1c}$ from baseline to week 52

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

**Key inclusion criteria:** Type 2 diabetes; $HbA_{1c}$: 8.0-10.5%; 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 $HbA_{1c}$ 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

# Key takeaways

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 6:** Note: Numbers for Latin America includes the Caribbean and Europe includes Russia; 1.The World Alzheimer Report 2015, The Global Impact of Dementia, Alzheimer's Disease International (ADI), London. 2. Number based on 60% of people with dementia having AD (Dementia UK Update 2nd edition, 2014, Alzheimer's society); 3. Petersen RC. Continuum (Minneap Minn). 2016 Apr;22(2 Dementia):404-18), ~1,000 million people >60 years in world by 2020 (Source: United Nations) and Busse A. Br J Psychiatry. 2006 Nov;189:399-404. [Population based study]; 4. Jeffrey Cummings Clin Transl Sci. 2018 Mar; 11(2): 147–152)

**Slide 7 and 10:** Schematic illustration based on Aisen P et al. Alzheimers Res Ther. 2017 Aug 9;9(1):60.

**Slide 8:** 1. Ballard C et al. Poster #42909. Alzheimer's Association International Conference (AAIC); 2020; 2. Gejl M et al. Front Aging Neurosci. 2016 24;8:108; 3. Aroda VR, et al. Diabetes Care 2019;42:1724–32; 4. Rodbard HW, et al. Diabetes Care 2019;42:2272–2281; 5. Vadini F et al Int J Obes (Lond). 2020 21; 6, Presented at the 13 th Clinical trals on Alzheimer's disease; 7. Wium-Andersen IK et al. Eur J Endocrinol. 2019;181(5):499-507; 8. Akimoto H et al. Am J Alzheimers Dis Other Demen. 2020;35:1-11; 9. Hansen HH et al. J Alzheimers Dis. 2015;46:877; 10. Hansen HH et al. Brain Research 2016;1634:158; 11. Brundin L et al. Nature Med. 2018;24:900; 12. Yun SP et al. Nature Med. 2018;24,931; 13. Preliminary data in NN ongoing studies.

**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.