Research and early development
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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For an overview of some, but not all, of the risks that could adversely affect Novo Nordisk’s results or the accuracy of forward-looking statements in the Annual Report 2023, reference is made to the overview of risk factors in ‘Risk Management’ of the Annual Report 2023.

Unless required by law, Novo Nordisk has no duty and undertakes no obligation to update or revise any forward-looking statement after the distribution of the Annual Report 2023, whether as a result of new information, future events, or otherwise.

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
Strategic aspirations 2025

**Research & early development**

**Innovation and therapeutic focus**

- 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

**Purpose and sustainability (ESG)**

- Progress towards zero environmental impact
- Being respected for adding value to society
- Being recognised as a sustainable employer

**Commercial execution**

- 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 Cardiovascular & emerging therapy areas

**Financials**

- Deliver solid sales and operating profit growth
- 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

Note: The strategic aspirations are not a projection of Novo Nordisk’s financial outlook or expected growth.
Innovation starts with addressing unmet needs, improving outcomes and reaching more patients

<table>
<thead>
<tr>
<th>Diabetes care</th>
<th>Obesity care</th>
</tr>
</thead>
<tbody>
<tr>
<td>537 million people with diabetes(^1)</td>
<td>813 million people with obesity(^3)</td>
</tr>
<tr>
<td>(~15%) of people in good control(^2)</td>
<td>(~2%) of people medically treated</td>
</tr>
</tbody>
</table>

**Rare disease**

- **Haemophilia**
  - 0.6 million people with haemophilia\(^4\)
  - \(~35\%\) of people being treated

**Cardiovascular & emerging therapy areas**

- 32\% of global deaths caused by CVD\(^5\)
- \(>30\) million people affected by HFpEF\(^6\)
- \(>250\) million people affected by MASH\(^7\)
- \(>800\) million people affected by CKD\(^8\)

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\(^1\) International Diabetes Federation: Diabetes Atlas 10th edition, 2021; \(^2\) Real-world studies indicate between 30-55% of patients reach HbA\(_1c\) target \(<7\%\), e.g. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4388968/, taking 42.5% in good control of treated people; \(^3\) World Obesity Atlas, 2023; \(^4\) WFH annual survey 2020 (120 of 147 countries responded); Prevalence by calculating expected number of patients using 20.9 per 100,000 in haemophilia - Identified patients as proxy for receiving some sort of treatment; \(^5\) WHO. Cardiovascular Diseases 2023; \(^6\) Chris J Kapelios et al Cardiac Failure Review 2023; the14; \(^7\) Younossi ZM et al. Hepatology. 2023;77:1335-1347; \(^8\) Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. Kidney Int Suppl (2011). 2022 Apr;12(1):7-11

CKD: Chronic kidney disease; CVD: Cardiovascular disease; HFpEF: Heart failure with preserved ejection fraction; MASH: Metabolic dysfunction-associated steatohepatitis; WHO: World Health Organization
Research and early development focuses on continuing and expanding leadership in diabetes and obesity

<table>
<thead>
<tr>
<th>Therapy area priorities</th>
<th>Strategic research focus</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Diabetes, Obesity</td>
<td><strong>Driving leadership</strong> in diabetes and obesity with novel and disease modifying therapies</td>
</tr>
<tr>
<td>2. CVD, RBD</td>
<td><strong>Delivering next generation</strong> insulins and GLP-1 therapies</td>
</tr>
<tr>
<td>3. MASH, RED, CKD</td>
<td><strong>Improving the quality</strong> of health for people while reducing risks of co-morbidities</td>
</tr>
<tr>
<td>4. AD/PD</td>
<td><strong>Focusing on scalability and building</strong> upon core protein and peptide capabilities with siRNA, cell and gene therapies</td>
</tr>
</tbody>
</table>

AD: Alzheimer's disease; CKD: Chronic kidney disease; CVD: Cardiovascular disease; MASH: Metabolic dysfunction-associated steatohepatitis; PD: Parkinson's disease; RBD: Rare blood disorders; RED: Rare endocrine disorders; siRNA: Small interfering ribonucleic acid

Note: Research and early development comprises activities from research until phase 2.
Increased access to human data together with AI-driven analyses enables discovery of new targets

**Human data input**
- Genetics, samples, multi-omics
- **Diverse cohorts**
  - African American cohort
  - Genes & Health Industry Consortium
  - UK biobank
- **Disease cohorts**
  - Alliance Genomic Discovery (Obesity)
  - ATTRACT (CVD)
  - Cellfi (Diabetes)
- Leverage real world evidence in early discovery

**Target discovery engine**
- De-risk translation from animal models to humans
- AI driven data mining and analyses linking disease to novel targets
- In silico analyses
- Human centric in vitro assays

**Increasing probability for clinical success**
- 80% more targets screened in 2023 compared to 2022.
- Capacity increasing in 2024
- Significant number of new targets expected to enter phase 1

AI: Artificial intelligence; CVD: Cardiovascular disease
SELECT trial provides a unique opportunity to identify new targets and biomarkers for future projects

**SELECT trial data set**
- Samples from >17,000 people
- Collected over 5 years and 1,270 events
- CVD, obesity, pre-diabetes, and CKD endpoints
- Proteomics for 3 time points from ~11,000 people
- Genetic data from ~11,000 people

**Fuels future research**
- Human data for drug discovery
- Identify and validate new biomarkers
- Linking novel targets to disease

**Enhanced by digital and AI capabilities**

**Potential outcomes**
- New drug targets and molecular mechanisms
- Responder subtype profiles enabling precision medicine
- Prediction of disease progression and treatment response

**SELECT**

semaglutide | effects on cardiovascular outcomes in people with overweight or obesity

AI: Artificial intelligence; CKD: Chronic kidney disease; CVD: Cardiovascular disease
Accelerating innovation through partnerships and acquisitions to grow and advance pipeline

**Number of partnerships and acquired assets to date**

- **60+** active partnerships (including 7 acquisitions)
- **37** partnerships focused on cardiometabolic diseases and obesity
- **21** partnerships exploring new MoAs
- **~50%** of partnerships have resulted in projects entering the pipeline as of today

**Selected key highlights of partnerships and acquisitions**

1. **Heart failure**
   - Phase 1 initiated in 2023
   - **Heartseed**
   - Cell Therapy

2. **Haemophilia A**
   - Proof of concept in non-human primates 2023
   - **2seventybio**
   - Gene Therapy

3. **Obesity**
   - Phase 1 initiated in 2024
   - **inversago PHARMA**
   - Small Molecules

4. **Atherosclerotic cardiovascular disease**
   - Phase 1 initiation expected in 2024
   - **Ventus THERAPEUTICS**
   - Small Molecules

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1 Partnerships include drug-enabling technology and drug-based strategic partnerships and acquisitions; 2 INV-347
MoA: Mode of action
CB1R inverse agonism holds potential as a novel mechanism of action both as monotherapy and add-on treatment

- CB1R are found throughout the body
  - Peripheral CB receptors type 1
  - Central CB receptors type 1

- CB1 biology plays a role in regulation of energy homeostasis

- Novel design minimising brain penetration

**MONLUNABANT** (INV-202) appeared to have a **safe and well-tolerated profile** with no serious or severe treatment-emergent adverse events in a phase 1 trial.

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**Inversago next-generation CB1R molecules**

**INV-347 shows weight loss in DIO mice models**

- **INV-347 0.4 mg/kg**
- **INV-347 2 mg/kg**
- **INV-347 10 mg/kg**
- **INV-347 20 mg/kg**
- **INV-347 20 mg/kg**

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CB: Cannabinoid; CB1R: Cannabinoid receptor type 1; DIO: Diet induced obesity
Integrating siRNA technology into Novo Nordisk adds capabilities to access intracellular targets across therapy areas

**Integration of Dicerna**
- Dicerna partnership since 2019, acquired in 2021 and now Global Nucleic Acid Therapies
- Allows Novo Nordisk to access patented siRNA research technology platform
- Investments made in CMC capabilities to deliver industrial scale siRNA therapeutics across therapy areas
- Boston presence enables Novo Nordisk to tap into surrounding life science ecosystem

**siRNA platform is deployed across all therapy areas**
- **GalXC™** Enables RNA silencing in hepatic cells
- **GalXC-Plus™** Enables RNA silencing in extra-hepatic cells

**Disease targets**
- (~5,000) extracellular targets
- (~21,000) intracellular targets

**Targets**
- Diabetes
- Obesity
- CVD
- MASH
- CKD
- Brain disorders
- RBD
- RED

CKD: Chronic kidney disease; CMC: Chemistry manufacturing and controls; CVD: Cardiovascular disease; MASH: Metabolic dysfunction-associated steatohepatitis; RBD: Rare blood disorders; RED: Rare endocrine disorders; RNA: Ribonucleic acid; siRNA: Small interfering ribonucleic acid
siRNA platform expected to deliver and mature across therapy areas in alignment with corporate strategy

**Progress with the siRNA platform**

- 11 phase 1 trial initiations with GalXC™ since 2017
- Rivfloza™ the first Novo Nordisk siRNA drug, approved in 2023
- First extra-hepatic phase 1 trial with GalXC-Plus™ in 2023
- 50% of upcoming phase 1 trials expected to be with GalXC-Plus™

**Distribution of siRNA portfolio projects**

- **Diabetes and Obesity**
- **CVD and MASH**
- **RBD and RED**
- **Other projects**

**Phase 1 initiation ambition with siRNA**

3 phase 1 initiations on average per year across disease areas with the siRNA platform is **on track**

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CVD: Cardiovascular disease; MASH: Metabolic dysfunction-associated steatohepatitis; RBD: Rare blood disorders; RED: Rare endocrine disorders; siRNA: Small interfering ribonucleic acid

Note: A project is defined when a target is identified and assigned team asks for resources to evaluate proof of concept.
Core capabilities together with additional drug modalities open up new opportunities across therapy areas

### Core Novo Nordisk capabilities

<table>
<thead>
<tr>
<th>Therapy areas</th>
<th>Proteins/Peptides/mAB</th>
<th>siRNA</th>
<th>Cell Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Obesity</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>CVD</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>RBD</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>MASH</td>
<td>✔</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>RED</td>
<td>✔</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>CKD</td>
<td>✔</td>
<td>✔</td>
<td></td>
</tr>
</tbody>
</table>

### Modalities accelerated via partnerships & acquisitions

<table>
<thead>
<tr>
<th>Therapy areas</th>
<th>Small Molecules</th>
<th>Gene Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Obesity</td>
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<td>✔</td>
</tr>
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<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>RBD</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>MASH</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>RED</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>CKD</td>
<td></td>
<td>✔</td>
</tr>
</tbody>
</table>

✔ Active pipeline  ✔ Exploratory

CKD: Chronic kidney disease; CVD: Cardiovascular disease; mAB: Monoclonal antibody; MASH: Metabolic dysfunction-associated steatohepatitis; RBD: Rare blood disorders; RED: Rare endocrine disorders; siRNA: Small interfering ribonucleic acid

Note: Currently active means Novo Nordisk is currently pursuing research projects, while exploratory indicates active early exploration activities and/or partnerships initiated.
Novo Nordisk's modality portfolio has expanded since 2018 with more projects using newer platforms

Distribution of research and phase 1 projects across modalities

- **Proteins & Peptides**
- **siRNA**
- **Small molecules**
- **Cell therapy**
- **Gene therapy**

<table>
<thead>
<tr>
<th>Strategic changes made since 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Build upon core capabilities with new modalities</td>
</tr>
<tr>
<td>More than one modality per target biology</td>
</tr>
<tr>
<td>Focus on automation and scalability</td>
</tr>
<tr>
<td>Building in silico capabilities to better predict</td>
</tr>
<tr>
<td>Increased investments</td>
</tr>
</tbody>
</table>

1 primarily siRNA projects
siRNA: Small interfering ribonucleic acid
The research and early development pipeline is broad and has increased across therapy areas since 2018.

Growing research and phase 1 pipeline since 2018

- Continued key focus on diabetes and obesity
- Broadening and advancing CVD pipeline
- Increased commitment in Rare blood disorders
- Increased investments

CKD: Chronic kidney disease; CVD: Cardiovascular disease; MASH: Metabolic dysfunction-associated steatohepatitis; RBD: Rare blood disorders; RED: Rare endocrine disorders
Next-generation innovation drives the phase 1 pipeline within diabetes

**Diabetes phase 1 pipeline**

- NN1845 – GSI
- NN1471 – Pumpsulin
- NN9041 – DNA Immunotherapy
- NN9904 – OW oral semaglutide
- NN9650 – OM GIP/GLP-1 co-agonist
- NN9541 – OW GIP/GLP-1 co-agonist

**Once monthly GIP/GLP-1 co-agonist**

- **Mode of action**: Co-agonist to GIP and GLP-1 receptors
- **Differentiation**: Improved convenience; 12 injections yearly
- **Dosing**: Once monthly sc injection
- **Next steps**: Phase 1 results expected in 2025

**DNA**: Deoxyribonucleic acid; **GIP**: Gastric inhibitory polypeptide; **GSI**: Glucose sensitive insulin; **OM**: Once-monthly; **OW**: Once-weekly; **sc**: Subcutaneous
Oral amycretin is a novel, unimolecular co-agonist of both GLP-1 and amylin receptors that successfully completed phase 1 trial.

**Obesity phase 1 pipeline**

- NN9542 – OW GIP/GLP-1 co-agonist
- NN9441 – INV-347
- NN9487 – Oral amycretin
- NN9490 – Sc amycretin

**Amycretin combines several beneficial effects of GLP-1 and amylin**

- **Mode of action**: Co-agonist to the GLP-1 and amylin receptor
- **Differentiation**: Complementary biologies for additive effect
- **Dosing**: Once daily oral
- **Next steps**: Further clinical development

GIP: Gastric inhibitory polypeptide; DW: Once-weekly; Sc: Subcutaneous
Amylin shows potential for additional and complementary benefits to GLP-1 in metabolic diseases

Amylin and GLP-1 are endocrine peptide hormones

<table>
<thead>
<tr>
<th>Amylin</th>
<th>GLP-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-cells in pancreas</td>
<td>L-cells in intestines</td>
</tr>
</tbody>
</table>

Amylin and GLP-1 both have a role in\(^1,2\):  
- Appetite regulation (hunger and satiety)  
- Glucose control

Amylin is also involved in\(^2,3\):  
- Bone homeostasis  
- Body composition

Weight loss in a 20-week phase 1 obesity trial

Mean baseline body weight: 94.6 kg, n = 96

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Change in body weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>-9.8%</td>
</tr>
<tr>
<td>1 nmol/kg</td>
<td>-17.1%</td>
</tr>
<tr>
<td>3 nmol/kg</td>
<td>-17.1%</td>
</tr>
<tr>
<td>10 nmol/kg</td>
<td>0%</td>
</tr>
</tbody>
</table>

Cagrilintide improves body composition in obesity DIO rat model\(^3\)

CagriSema (2.4 mg sema and 2.4 mg cagri)

Novo Nordisk amylin analogues have appeared to have safe and well-tolerated profiles in clinical trials

\(^1\)Campbell et al. Cell Metabolism 2013 (17):819-837; \(^2\)Hay et al. Pharmacological reviews 2015 (67) 564-600; \(^3\)Daquin et al. 2004 164(4):509-14

Cagri: Cagrilintide; DIO: Diet induced obesity; g: gram; HFD: High-fat diet; LFD: Low-fat diet; nmol: nanomole; Sema: semaglutide
Phase 1 results in obesity allows further clinical development of amycretin

Oral amycretin phase 1 trial in obesity was successfully completed

Phase 1 key findings

- Pharmacokinetic profile allows for further clinical development
- 13.1% weight loss after 12 weeks
- Amycretin appeared to have a safe and well-tolerated profile
- Adverse effects in line with previous Novo Nordisk GLP-1 and CagriSema trials

Results from exploratory endpoint on body weight change

Mean baseline body weight: ~89 kg, n = 16

Change in body weight (%) vs. Time since randomisation (weeks)

- Oral amycretin
- Placebo
Drug development in diabetes and obesity is built around core Novo Nordisk capabilities

**Core Novo Nordisk capabilities**

- Deep biology understanding
- Protein/peptide development and engineering
- Efficient large-scale production of proteins

**Innovation through different approaches**

Maximise GLP-1 franchise

- GLP-1

Maximise value in incretin/amylin biology

- GLP-1
- Amylin
- GIP
- Novel

Building a broad pipeline

- GLP-1
- Amylin
- GIP
- Novel
- Novel

**Key drivers for innovation**

- Speed
- Differentiation parameters
- Scalability

MoA: Mechanism of action; GIP: Gastric inhibitory polypeptide
New standalone and tri-agonist molecule to enter phase 1 within the next 12 months, with new concepts to follow

**Expected phase 1 initiations within the next 12 months**

**New amylin**
- Phase 1 initiation expected in 2024
- New molecule for mono-therapy provides opportunity for weight management
- Potential for combination therapy

**New tri-agonist**
- Phase 1 initiation expected within next 12 months
- Potential for improved weight loss efficacy
- Potential for improved effect on obesity related comorbidities

**Focus areas for upcoming projects**

- Regulating appetite and energy expenditure
- Weight maintenance
- Lean body mass preservation
- Sustained release
Phase 1 aspiration of bringing more targets from research to development faster is on track for 2025

Key drivers increasing number of phase 1 initiations

- Increased investments across portfolio
- Target discovery engine delivers targets that are relevant to human disease
- Leverage AI/digital capabilities throughout drug discovery process
- Early pipeline growth delivers more phase 1 opportunities

Number of phase 1 initiations in 2020 and aspirations towards 2025

- 3x numbers of assets

<table>
<thead>
<tr>
<th>Year</th>
<th>Phase 1 initiations achieved</th>
<th>Planned</th>
<th>Aspiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020</td>
<td>5</td>
<td></td>
<td></td>
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<tr>
<td>2024</td>
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<tr>
<td>2025</td>
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Closing remarks

Continue to build on core capabilities and expand beyond with new modalities

Pipeline is expanding, driven by internal target discovery and supported by external partnerships

Phase 1 initiation ambition of 3x is on track