Research and early development

CMD24
CAPITAL MARKETS DAY

7 MARCH

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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
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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

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 Cardiovascular & emerging therapy areas**

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
- 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

Diabetes care

537 million people with diabetes[1]

~15% of people in good control[2]

Obesity care

813 million people with obesity[3]

~2% of people medically treated

Novo Nordisk Way

Driving change to defeat serious chronic diseases

Sustainable business

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]

[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;9:e14.; [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

Therapy area priorities

1. Diabetes, Obesity
2. CVD, RBD
3. MASH, RED, CKD
4. AD/PD

Strategic research focus

- **Driving leadership** in diabetes and obesity with novel and disease modifying therapies
- **Delivering next generation** insulins and GLP-1 therapies
- **Improving the quality** of health for people while reducing risks of co-morbidities
- **Focusing on scalability and building** upon core protein and peptide capabilities with siRNA, cell and gene therapies

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[1] 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

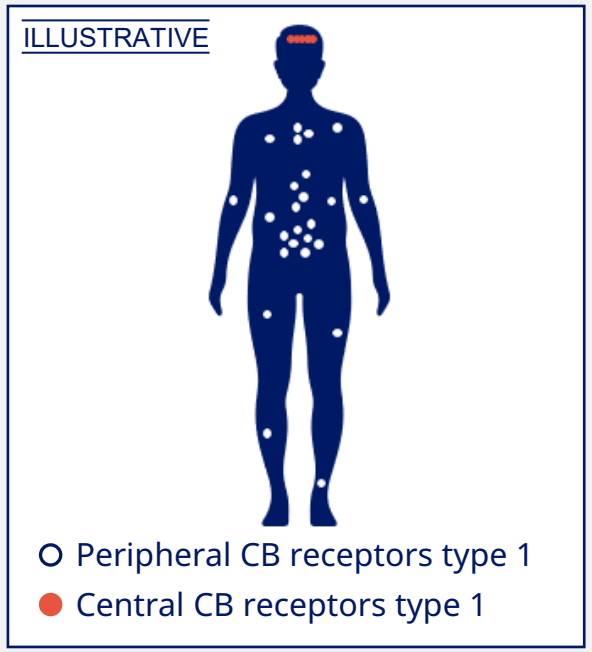
Selected key highlights of partnerships and acquisitions

Heartseed	**Heart failure** Phase 1 initiated in 2023	Cell Therapy
2seventybio	**Haemophilia A** Proof of concept in non-human primates 2023	Gene Therapy
inversago PHARMA	**Obesity** Phase 1 initiated in 2024[2]	Small Molecules
Ventus THERAPEUTICS	**Atherosclerotic cardiovascular disease** Phase 1 initiation expected in 2024	Small Molecules

[1]Partnerships include drug-enabling technology and drug-based strategic partnerships and acquisitions; [2]INV-347
MoA: Mode of action

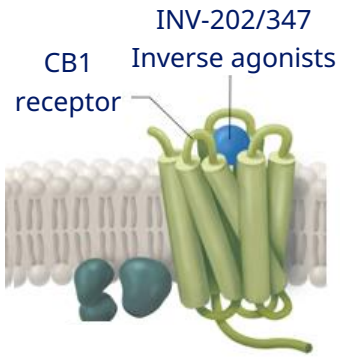
CB1R inverse agonism holds potential as a novel mechanism of action both as monotherapy and add-on treatment

CB1R are found throughout the body



- CB1 biology plays a role in regulation of energy homeostasis[1]

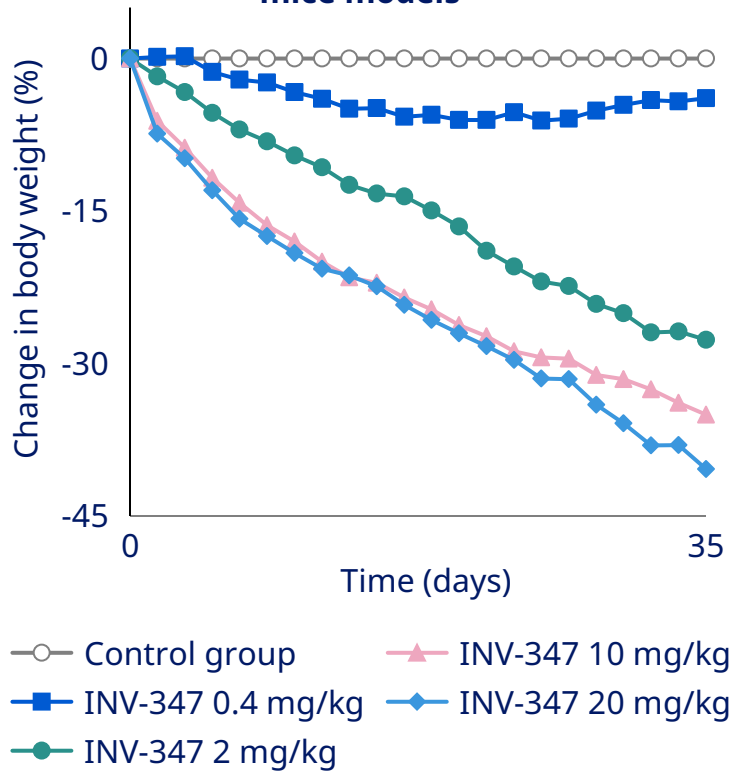
Inversago next-generation CB1R molecules



- 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

INV-347 shows weight loss in DIO mice models



[1]Dörnyei G, et al. Biomedicines. 2023 Jan 21;11(2):306. doi: 10.3390/biomedicines11020306
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

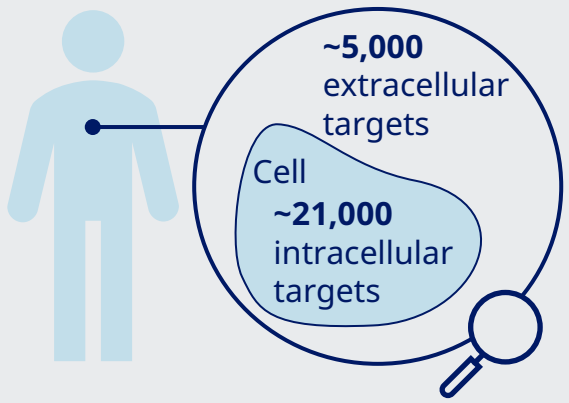
siRNA platform is deployed across all therapy areas

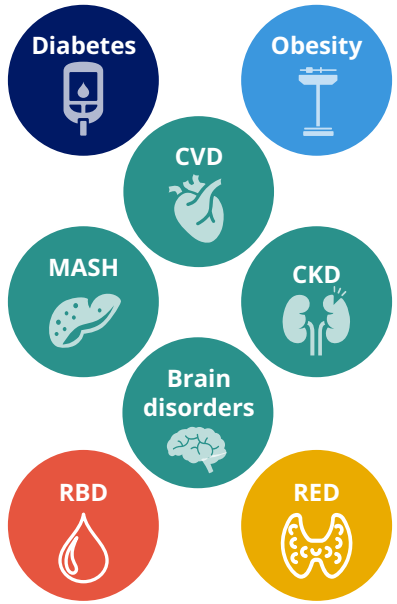
GalXC™
Enables RNA silencing in hepatic cells

+

GalXC-Plus™
Enables RNA silencing in extra-hepatic cells

Disease targets
(expressed genes)





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™ (nedosiran) injection 80mg, 128mg, 160mg

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

Phase 1 initiation ambition with siRNA

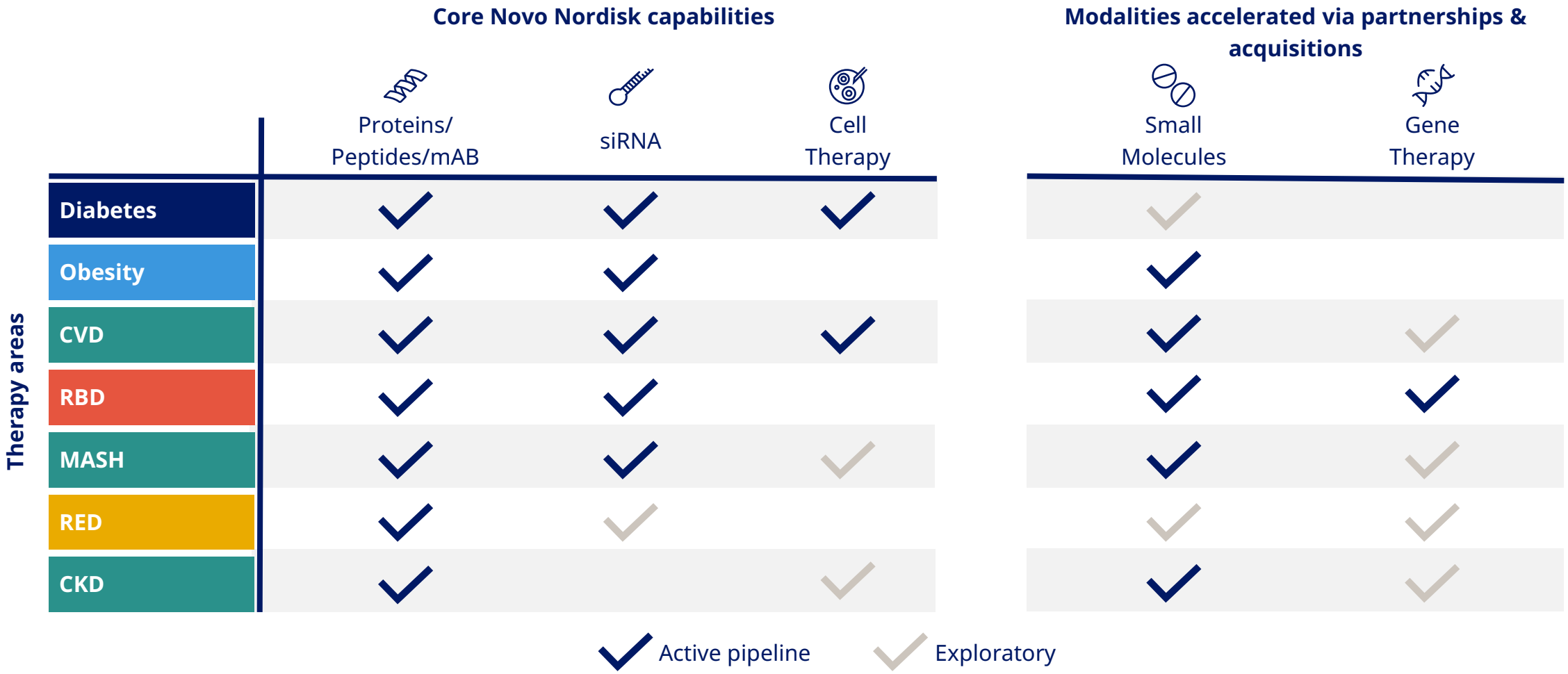
3

… phase 1 initiations on average per year across disease areas with the siRNA platform is

on track

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 ask for resources to evaluate proof of concept

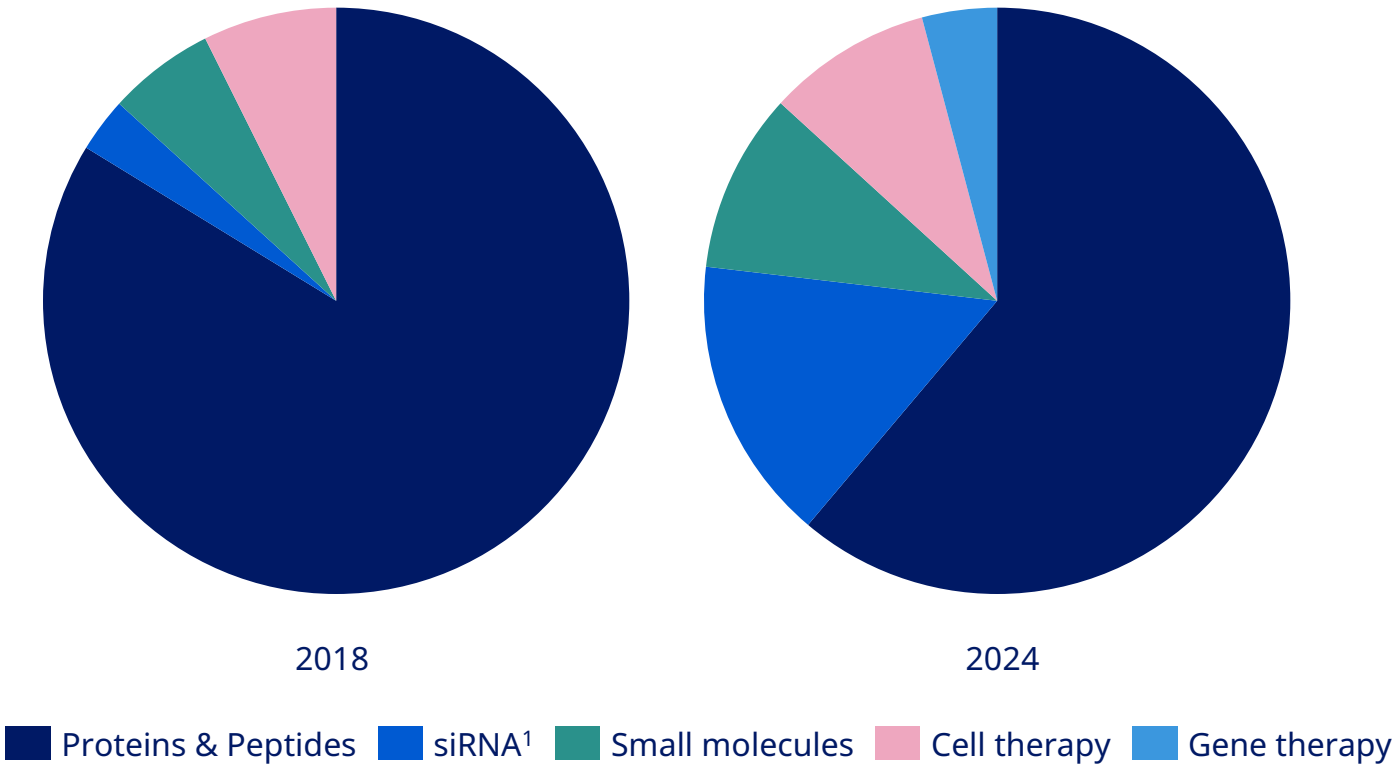
Core capabilities together with additional drug modalities open up new opportunities across therapy areas



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



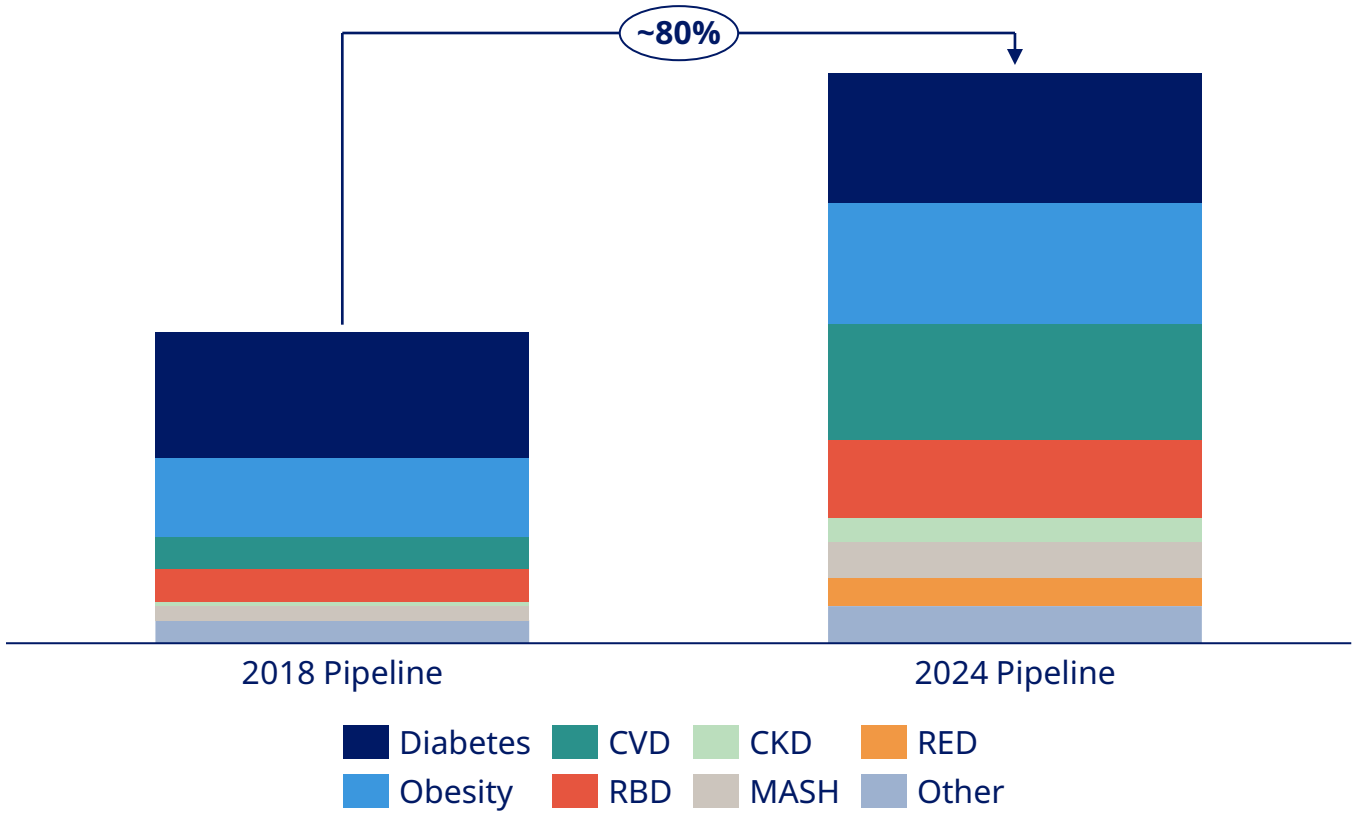
Strategic changes made since 2018

- Build upon core capabilities with new modalities
- 1+ More than one modality per target biology
- Focus on automation and scalability
- Building in silico capabilities to better predict
- Increased investments

[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



Strategic changes made 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

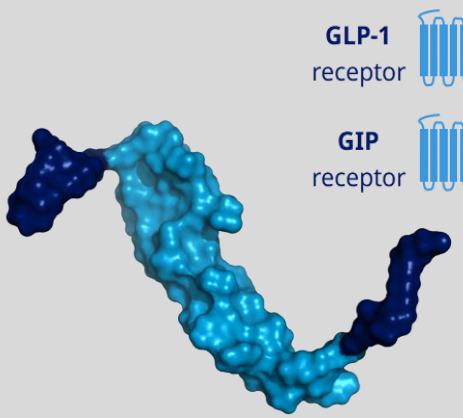
Next-generation innovation drives the phase 1 pipeline within diabetes

Diabetes phase 1 pipeline

Diabetes

- 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



NN9650
(OM GLP-1/GIP)

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

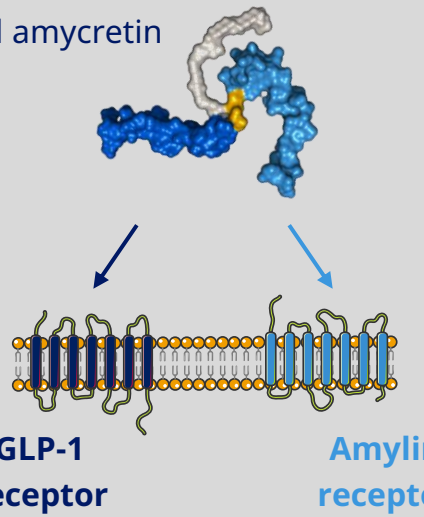
Obesity phase 1 pipeline

Obesity

- 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

NN9487
Oral amycretin



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; OW: Once-weekly; Sc: Subcutaneous

Amylin shows potential for additional and complementary benefits to GLP-1 in metabolic diseases

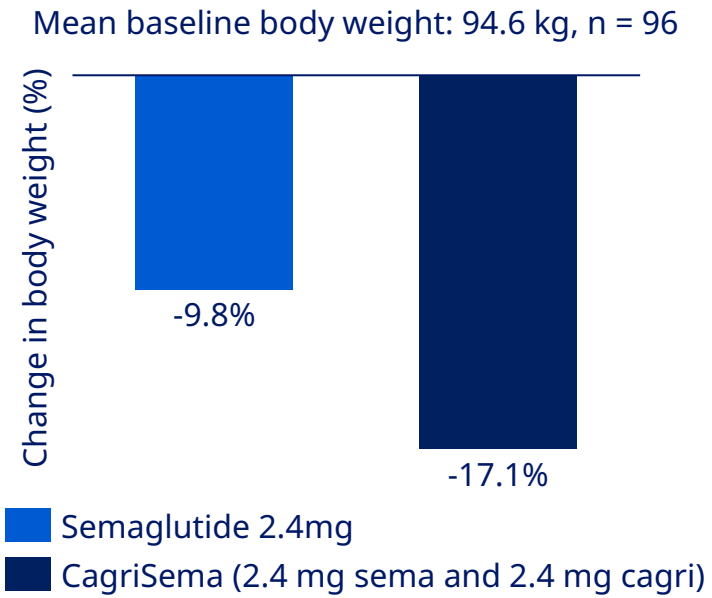
Amylin and GLP-1 are endocrine peptide hormones

Amylin	GLP-1
β-cells in pancreas	L-cells in intestines

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

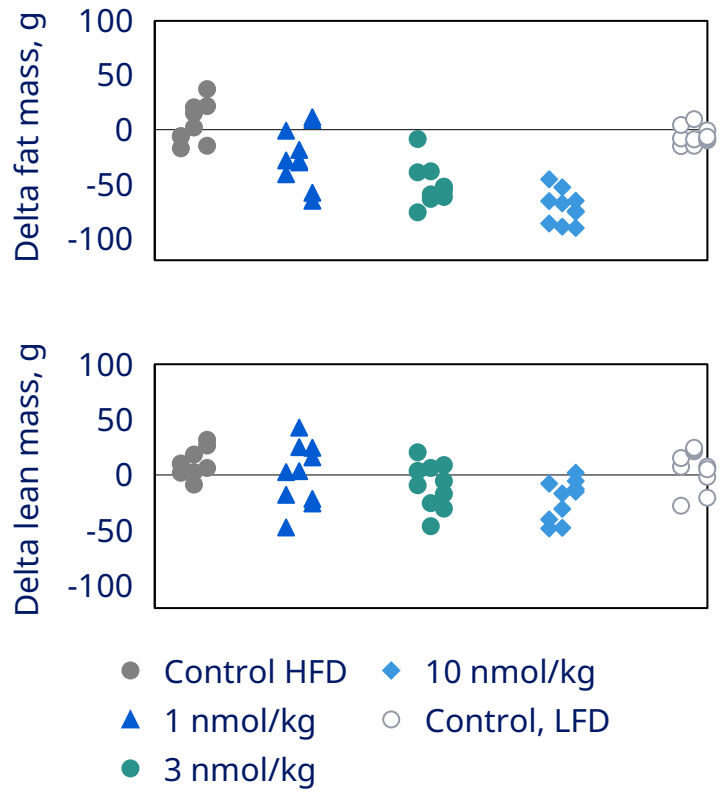
Amylin is also involved in[2,3]:
- Bone homeostasis
- Body composition

Weight loss in a 20-week phase 1 obesity trial



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

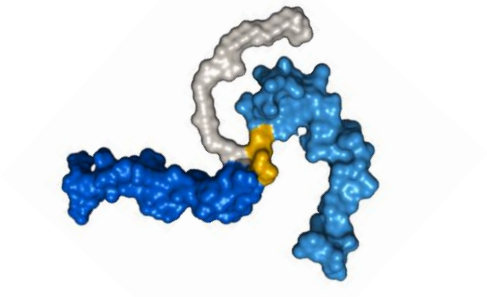
Cagrilintide improves body composition in obesity DIO rat model[3]



[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

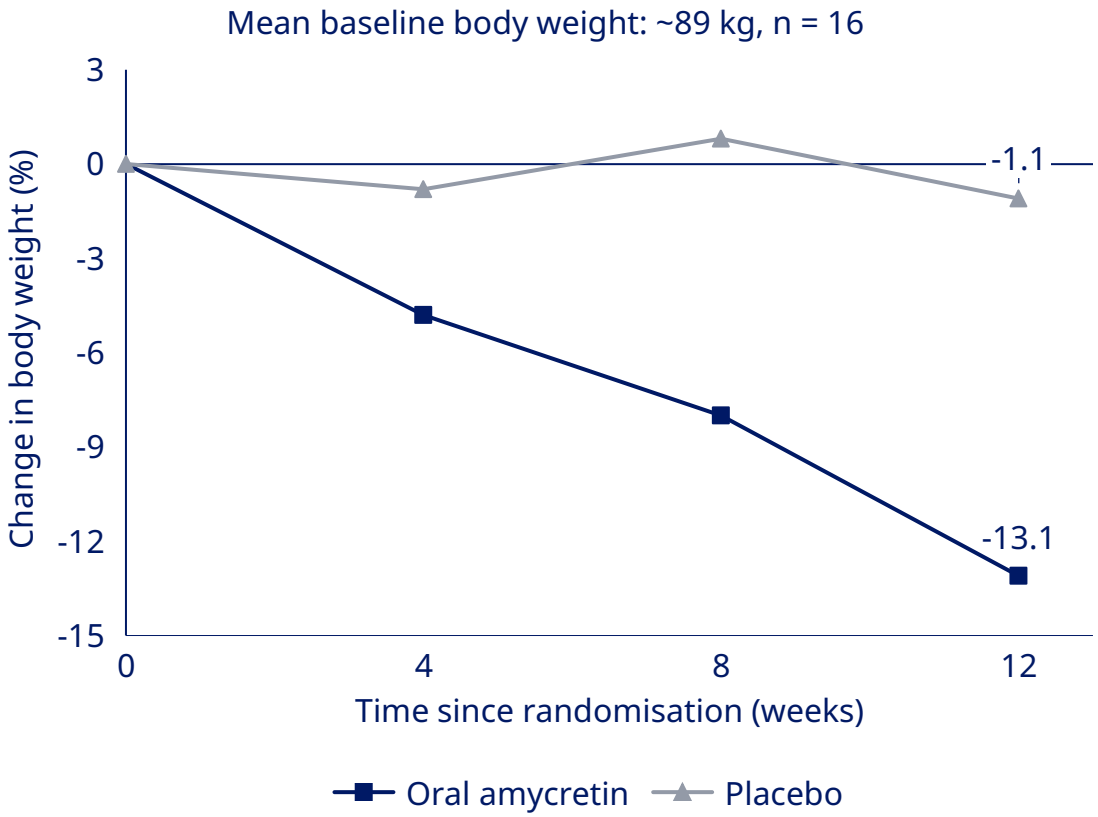
Oral amycretin phase 1 trial in obesity was successfully completed



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



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

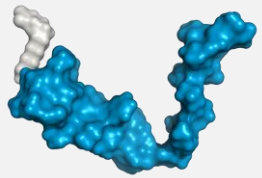
MoA: Mechanism of action; GIP: Gastric inhibitory polypeptide

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

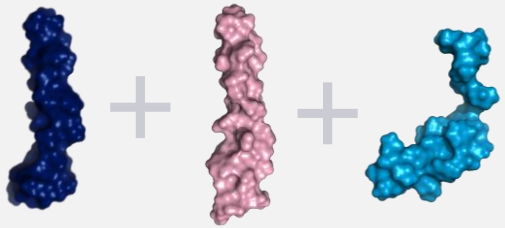
New amylin

- 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



ILLUSTRATIVE

Focus areas for upcoming projects

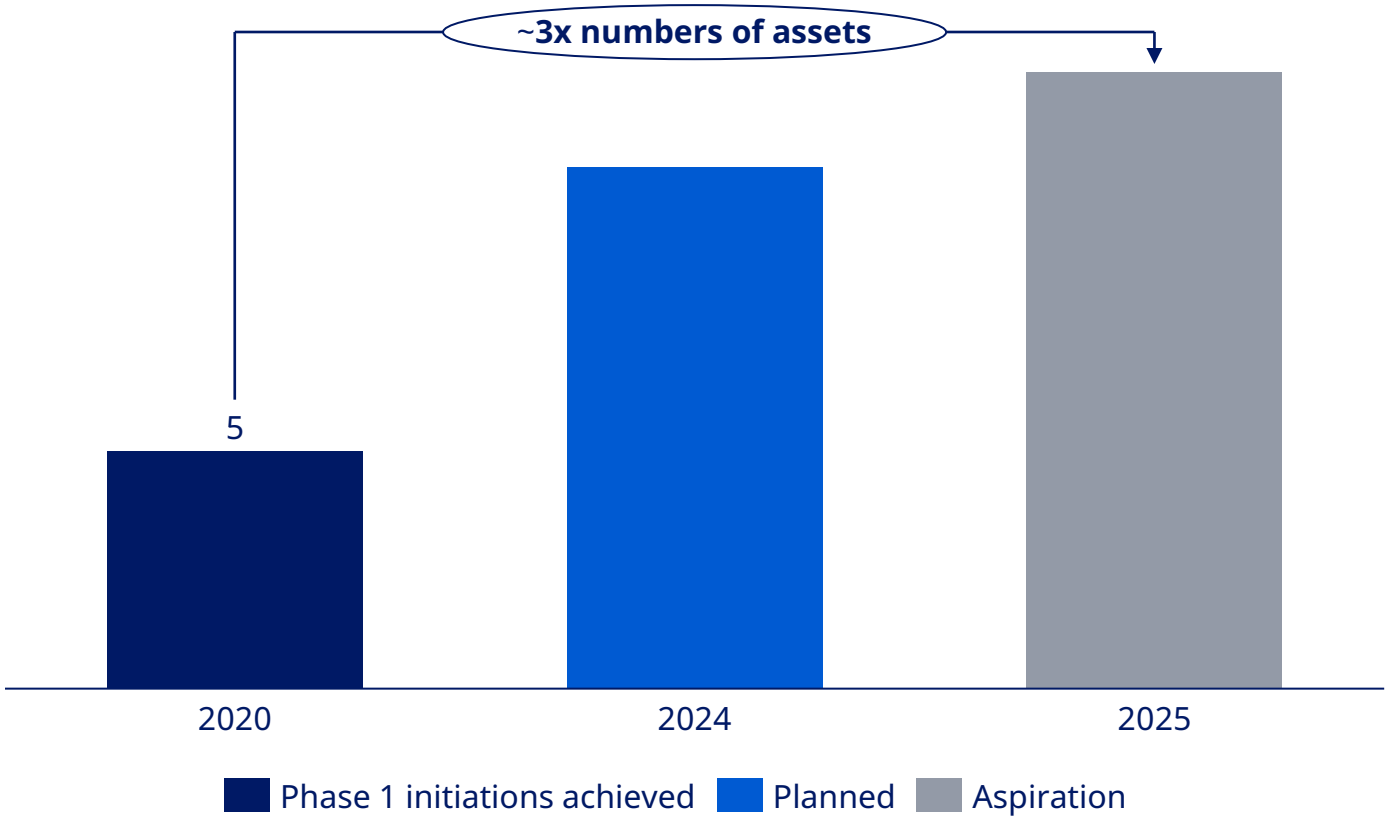
- Regulating appetite and energy expenditure
- Weight maintenance
- Lean body mass preservation
- Sustained release

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



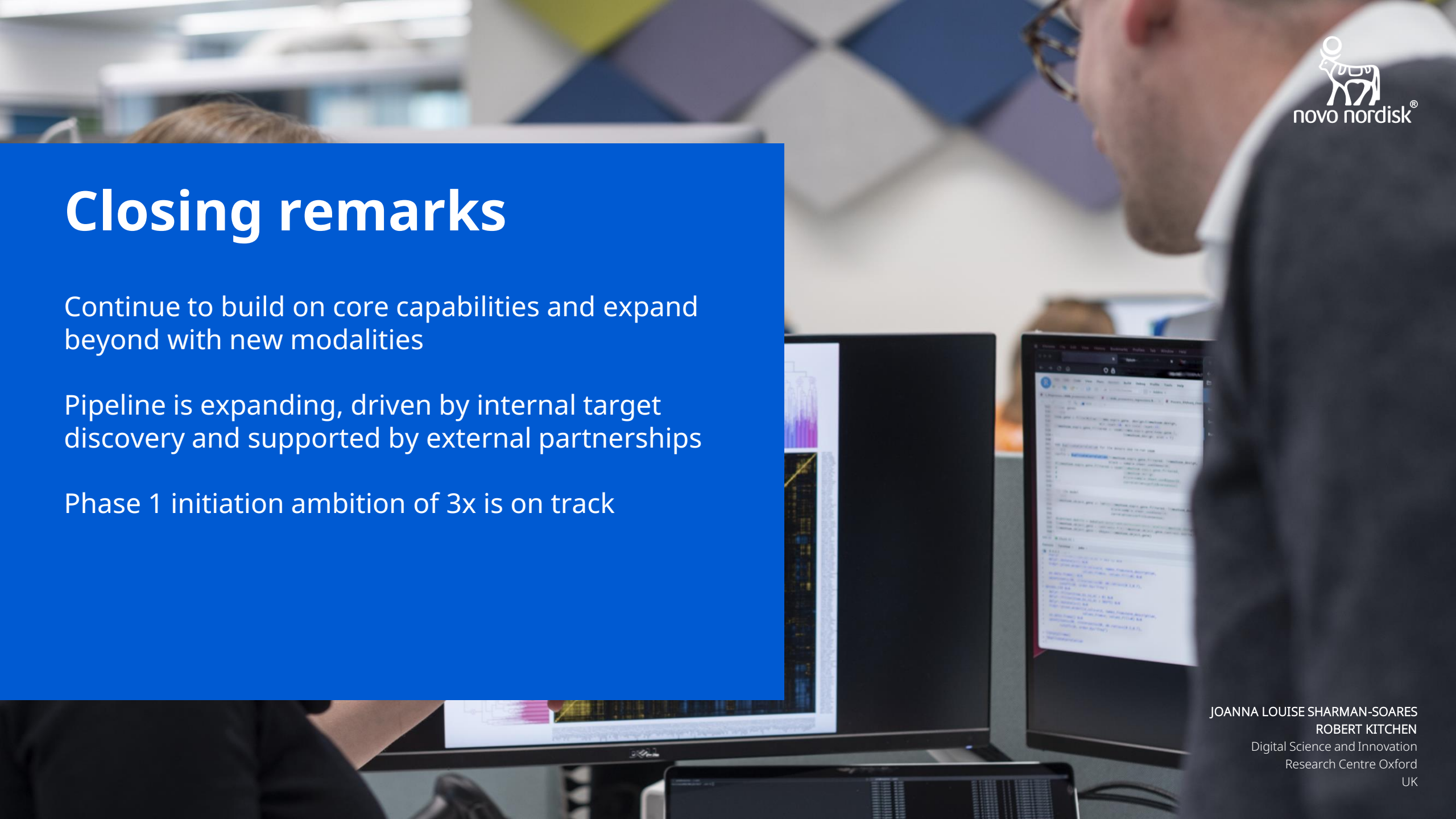
AI: Artificial intelligence

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



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