Research technologies and drug discovery

CMD22
CAPITAL MARKETS DAY

3 MARCH


Marcus Schindler
CSO and EVP of Research & Early development


Lars Fogh Iversen
SVP Global research technologies


Karin Conde-Knape
SVP Global drug discovery

Forward-looking statements

Novo Nordisk's reports filed with or furnished to the US Securities and Exchange Commission (SEC), including the statutory Annual Report 2021 and Form 20-F, which both were filed with the SEC in February 2022 in continuation of the publication of this Annual Report 2021, this presentation, and written information released, or oral statements made, to the public in the future by or on behalf of Novo Nordisk, may contain forward-looking statements. Words such as 'believe', 'expect, 'may', 'will', 'plan', 'strategy', 'prospect', 'foresee', 'estimate', 'project', 'anticipate', 'can', 'intend', 'target' and other words and terms of similar meaning in connection with any discussion of future operating or financial performance identify forward-looking statements. Examples of such forward-looking statements include, but are not limited to:

- 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.

These statements are based on current plans, estimates and projections. By their very nature, forward-looking statements involve inherent risks and uncertainties, both general and specific. Novo Nordisk cautions that a number of important factors, including those described in this presentation, could cause actual results to differ materially from those contemplated in any forward-looking statements.

Factors that may affect future results include, but are not limited to, global as well as local political and economic conditions, including interest rate and currency exchange rate fluctuations, delay or failure of projects related to research and/or development, unplanned loss of patents, interruptions of supplies and production, including as a result of interruptions or delays affecting supply chains on which Novo Nordisk relies, product recalls, unexpected contract breaches or terminations, government- mandated or market-driven price decreases for Novo Nordisk's products, introduction of competing products, reliance on information technology including the risk of cybersecurity breeches, Novo Nordisk's ability to successfully market current and new products, exposure to product liability and legal proceedings and investigations, changes in governmental laws and related interpretation thereof, including on reimbursement, intellectual property protection and regulatory controls on testing, approval, manufacturing and marketing, perceived or actual failure to adhere to ethical marketing practices, investments in and divestitures of domestic and foreign companies, unexpected growth in costs and expenses, failure to recruit and retain the right employees, failure to maintain a culture of compliance, epidemics, pandemics or other public health crises, and factors related to the foregoing matters and other factors not specifically identified herein.

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 this Annual Report 2021, reference is made to the overview of risk factors in 'Risk management' of this Annual Report 2021.

Unless required by law, Novo Nordisk is under no duty and undertakes no obligation to update or revise any forward-looking statement after the distribution of this Annual Report 2021, 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 in the USA and the EU 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 Other serious chronic diseases focusing on CVD, NASH and CKD**

Commercial execution

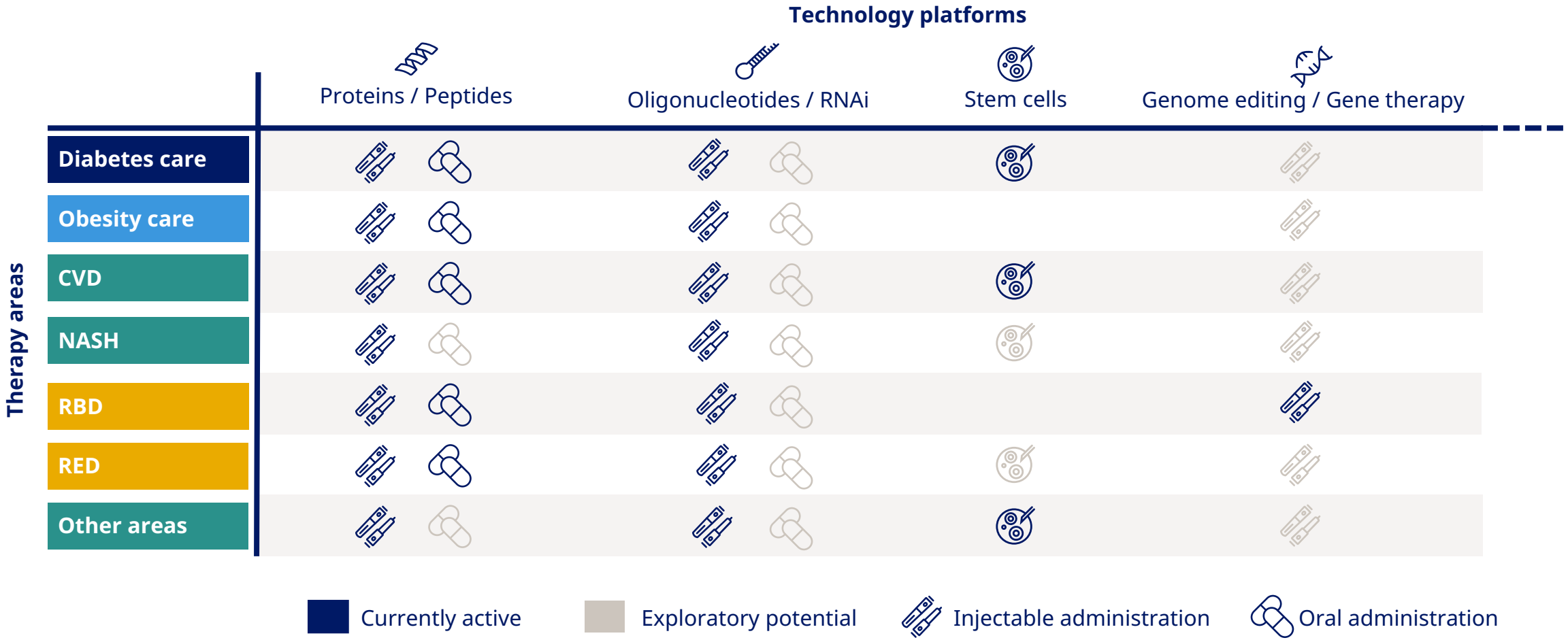
- Strengthen Diabetes leadership - aim at global value market share of more than 1/3
- More than 25 billion DKK in Obesity sales by 2025
- Secure a sustained growth outlook for Rare disease

Financials

- Deliver solid sales and operating profit growth
  - Deliver 6-10% sales growth in IO
  - Transform 70% of sales in the US[1]
- 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.

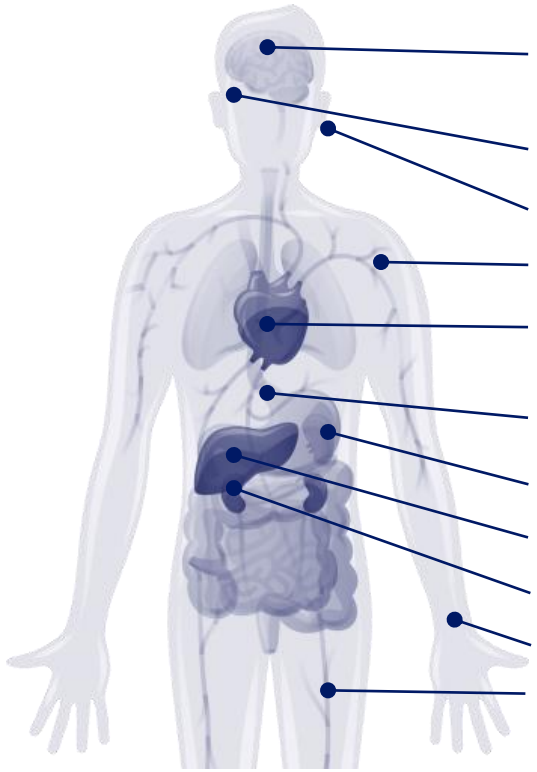
Core capabilities and additional technology platforms open up new opportunities across therapy areas



Note: Currently active means Novo Nordisk is currently pursuing research projects, while exploratory potential indicates that the platform is potentially applicable for the given disease
RBD: Rare blood disorders; RED: Rare endocrine disorders; CVD: Cardiovascular disease; NASH: Non-alcoholic steatohepatitis, RNAi: Ribonucleid acid

There is broad potential for cell therapies and Novo Nordisk has capabilities to explore the potential

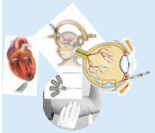
Broad potential for clinical use of cell therapies



Parkinson's disease
Stroke
Alzheimer's disease
Dry AMD
Blindness
Hearing loss
Congenital bone disorders
Chronic heart failure
Spinal cord injury
Chronic kidney disease
NASH
Diabetes
Osteoarthritis
Muscular dystrophy

Multiple sites: Cancers and wound healing

Maturing the platform to enable development of competitive cell therapies

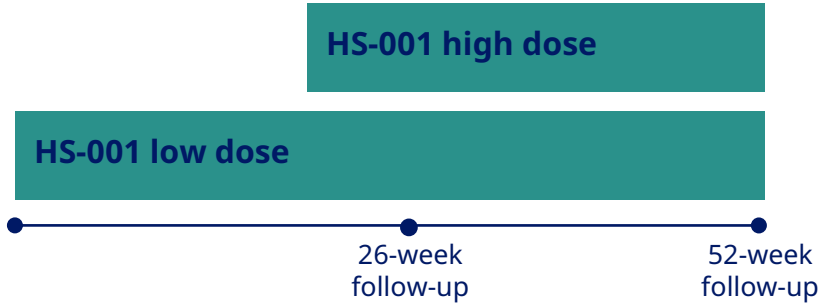
	Focus area	Novo Nordisk capabilities
	Pluripotent stem cell	In-depth know-how on embryonic pluripotent stem cells
	Bank of several undifferentiated stem cells	Exploitation of quality controlled stem cells
	Differentiated to specific cell types	IP-protected protocols for differentiation
	Upscaling, manufacturing and delivery/devices	GMP-grade cell manufacturing and development of cell delivery devices[1]
	Clinical development and regulatory affairs	Early interactions with regulators Clinical trial experience

[1]In collaboration with academia and industrial partners
Dry AMD: Dry age-related macular degeneration; NASH: Non-alcoholic steatohepatitis; IP: Intellectual property; GMP: Good manufacturing practices

First efforts to combine Novo Nordisk and partner competencies in cell therapies start with heart failure and Parkinson's disease

Heartseed: Phase 1/2 trial in patients with severe heart failure

10 patients with
- Resting LVEF ≤40%
- NYHA cardiac function classification grade ≥II

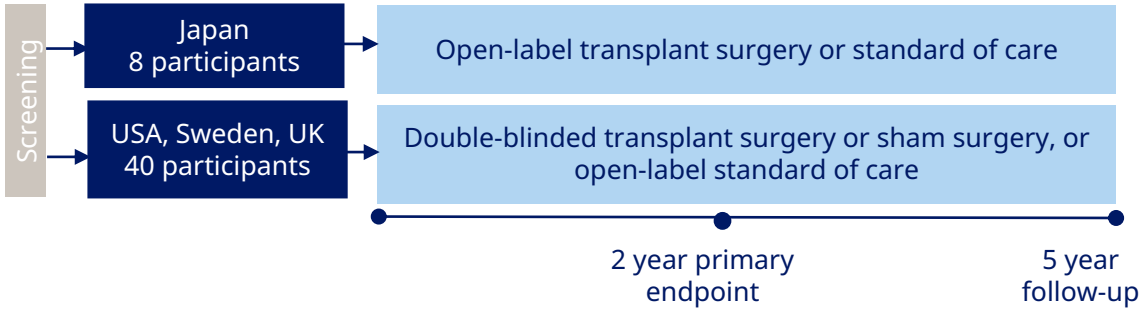


Objectives to evaluate:
- Safety of cardiomyocytes spheroids
- Efficacy and dose-response
- Feasibility of transplantation procedures

Estimated start date: First half of 2022

A **follow-up phase 2 trial** is planned to investigate further dose increase and catheter delivery as route of administration

TRANSCEND 1 and 2 trials to evaluate stem cells impact on quality of life for people with moderate Parkinson's disease



TRANSCEND 1: observational study of patients with moderate PD aiming at identifying potential candidates to the interventional TRANSCEND 2 trial

TRANSCEND 2: in combination with **Lund University** trial, a phase 1/2 trial investigating the treatment of Parkinson's disease

Primary endpoint: Number of treatment-emergent adverse events 2 years after dosing

Estimated start date: First half of 2022

PD: Parkinson's disease; LVEF: Left ventricular ejection fraction; NYHA: New York Heart Association

Combining deeply rooted protein engineering know-how with AI paves the way forward to the new drug formats

Next-generation protein engineering is AI based and automated

‘Super-charged molecular design’: AI/ML Centre of Excellence

Seattle

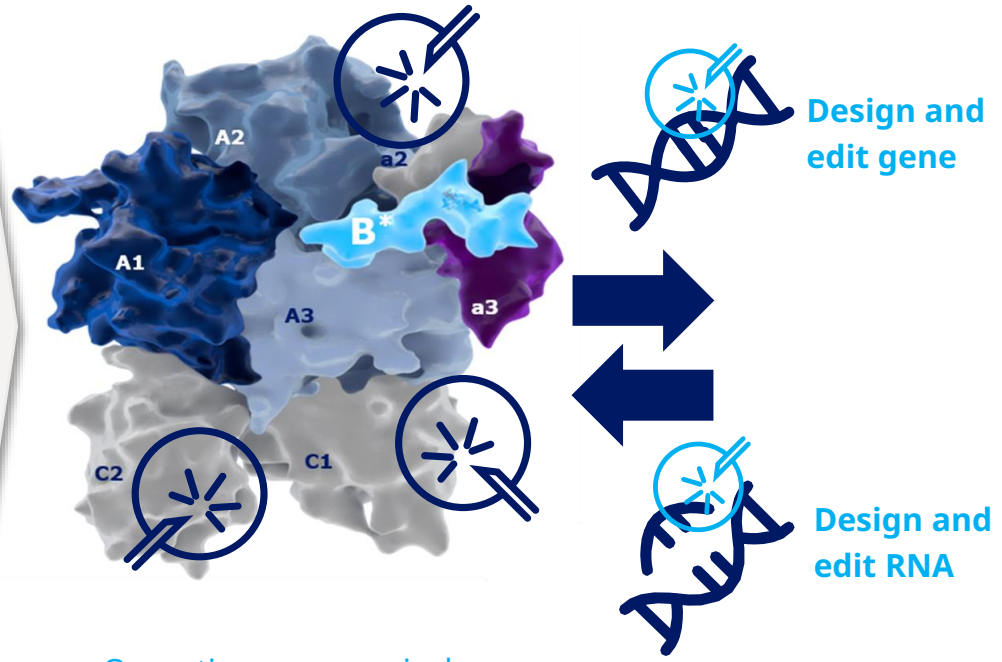
Labdroid-automation centre in Måløv

Måløv

Testing thousands of hypotheses in parallel

Understanding of the protein is key for the design of genes and RNAs

Same deeply rooted protein engineering know-how enables precision engineering of the new drug formats



Operating very precisely on complex proteins allows for designing and editing proteins

AI: Artificial intelligence; ML: Machine learning

Novo Nordisk and 2seventy bio extend partnership in next-generation genome editing for people with haemophilia A

Lifelong correction via a unique modality

Potentially lifelong correction of FVIII deficiency

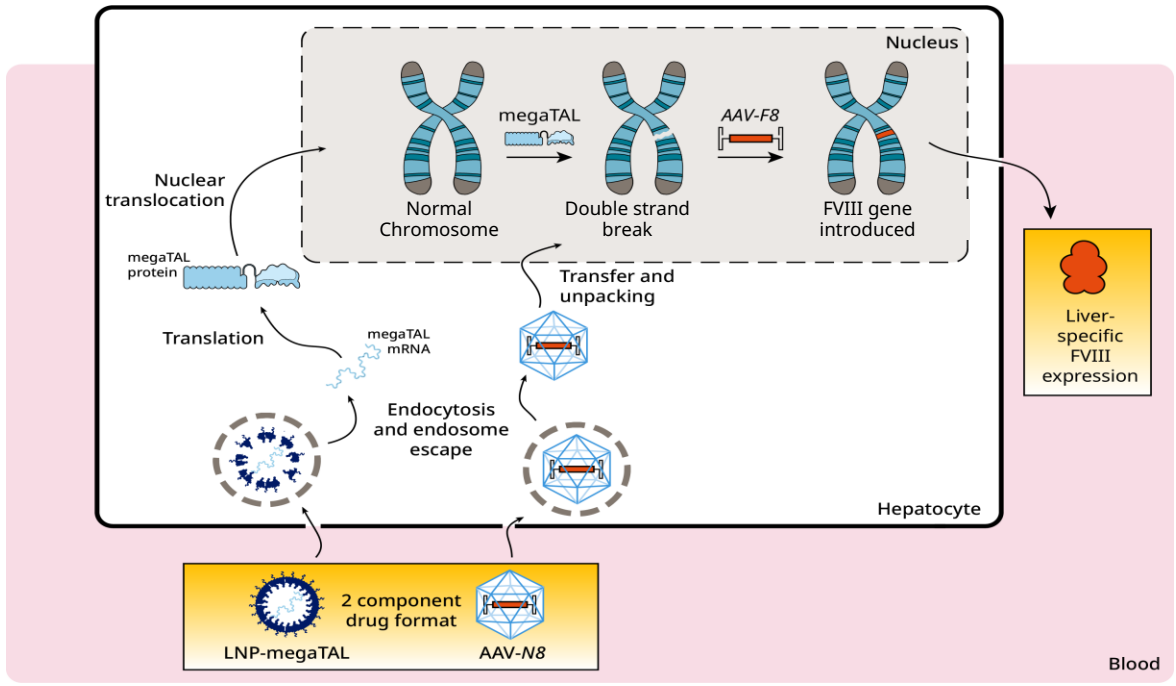
FVIII gene engineered and packed in an AAV vehicle

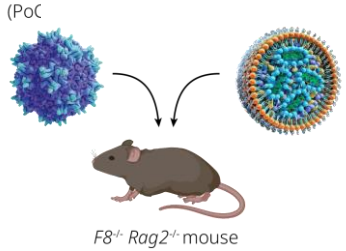
Utilising the skills of both 2seventy bio and Novo Nordisk

Utilisation of **megaTAL™** technology, in-vivo mRNA manufacturing/purification platform, and gene editing know-how

Haemophilia A understanding and protein and molecular engineering capabilities

Mode of action





AAV vector with N8 gene (PoC design)

LNP-formulated surrogate megaTAL targeting site specific locus

PoC: Proof-of-Concept; AAV: Adeno-associated virus; Rag2: recombination-activating gene; F8: Factor 8

Preclinical mouse proof-of-concept achieved for the FVIII gene editing project between 2seventy bio and Novo Nordisk

Lifelong correction via a unique modality

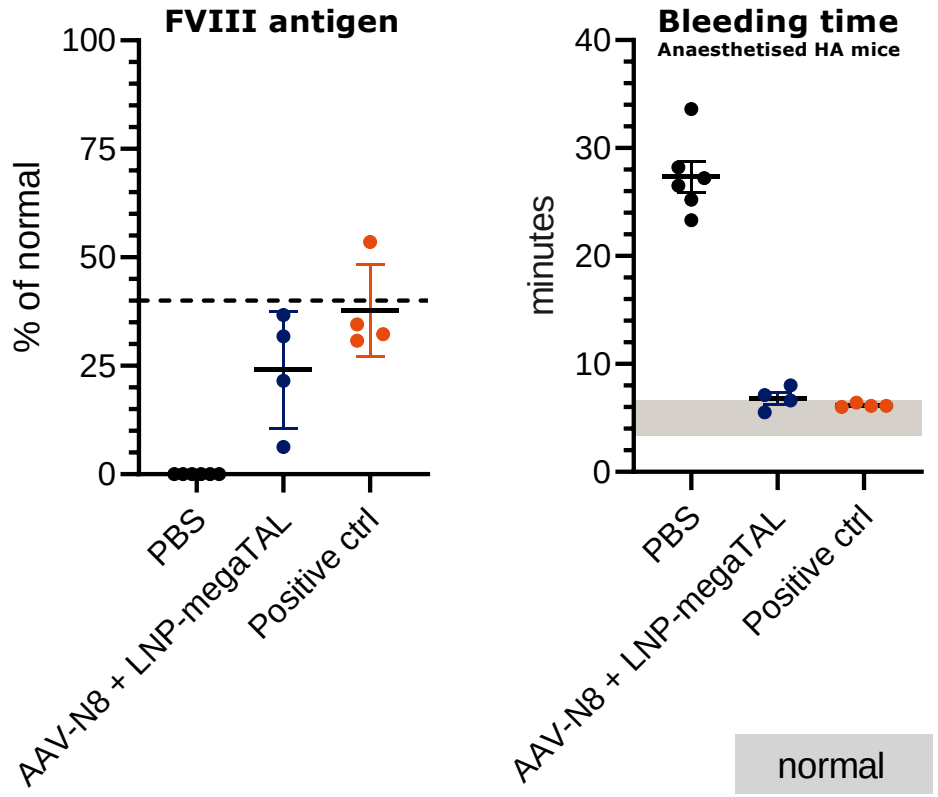
Potentially lifelong correction of FVIII deficiency

FVIII gene engineered and packed in an AAV vehicle

Key characteristics of the preclinical study

- AAV-N8 + LNP-megaTAL leads to integration of N8 gene in surrogate mouse alleles
- Duration of effect is not addressed in this study
- 1st generation mouse model-specific megaTAL reagent

Preclinical PoC for FVIII expression after *in vivo* gene editing

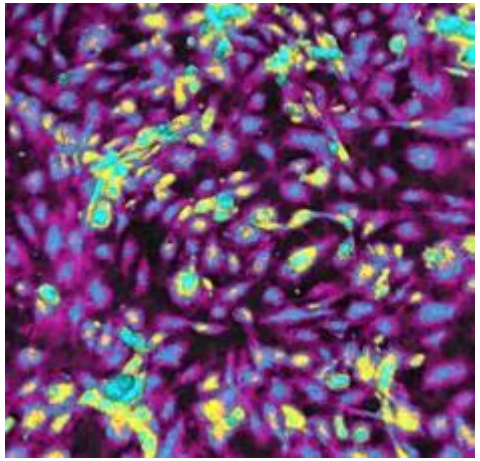


Note: Positive ctrl: promoter-driven FVIII sequence anticipated from literature, packaged in AAV8 capsids
PoC: Proof-of-Concept; ctrl: control; PBS: phosphate-buffered saline

Driving human-centric novel target identification in the cardiometabolic space to address residual risk

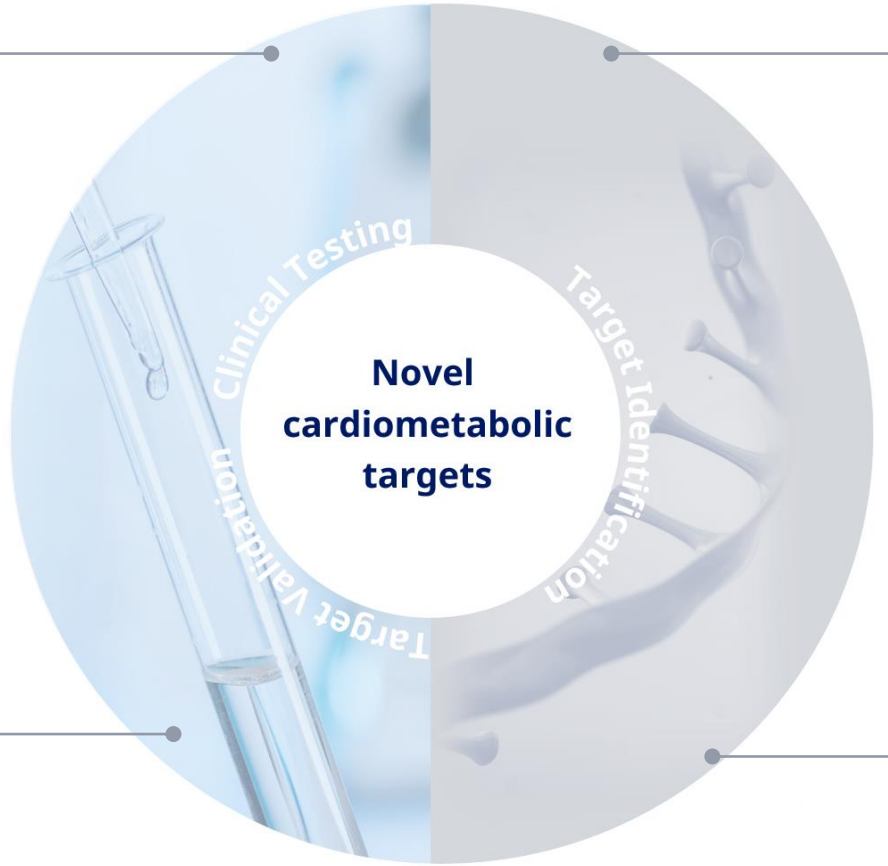
Functional assays

- Biomarker strategy
- Patient selection



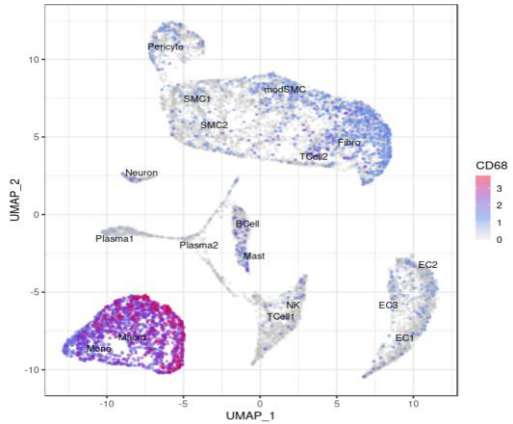
Identified cell phenotypes

- In vitro
- Ex vivo
- In vivo



Genetics

- Genetics (+PheWAS)
- Tissue/plasma expression
- Clinical data



scRNAseq, snRNAseq

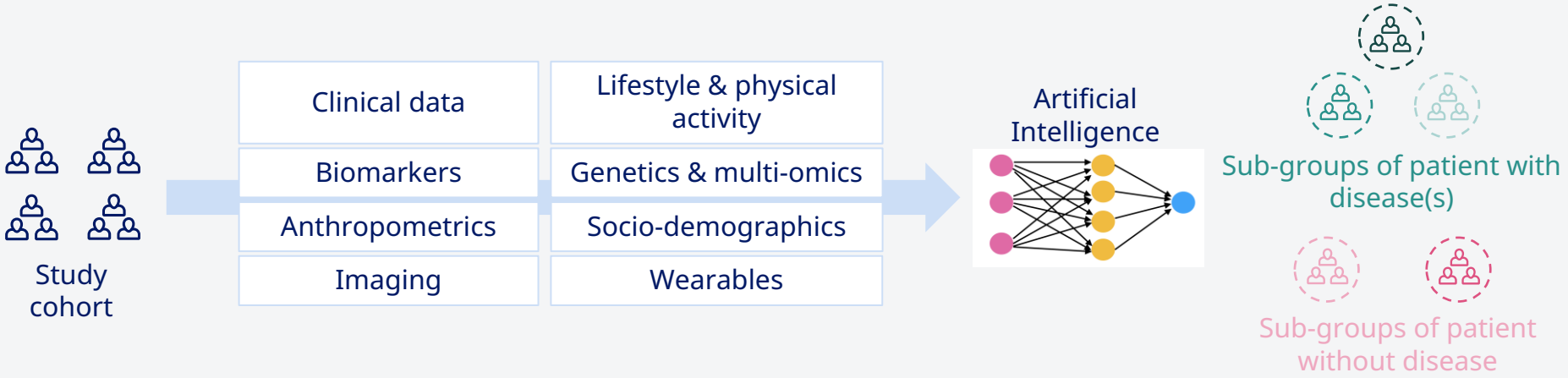
- Real world evidence
- Mechanism independent of lipids and blood pressure

RNA: ribonucleic acid; scRNA: Small conditional RNA, snRNS: Small nuclear RNA, PheWAS: Phenome-wide association study

Understanding the multiple factors playing a role in the development of obesity

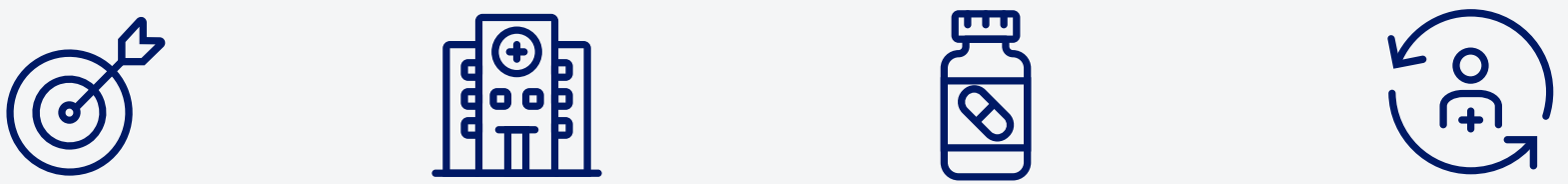
Discovery

Discovery of novel obesity targets for patient sub-groups



Artificial intelligence

Integration of AI-driven precision medicine and patient stratification to promote target discovery in big diseases



Targeted therapeutic development

Evidence-based patient selection for trials

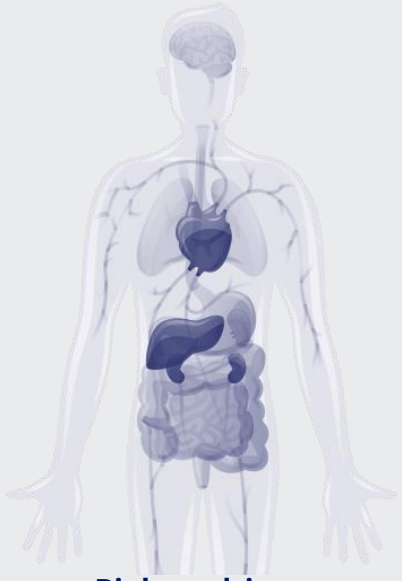
Precision reimbursement models

Real-world insights to response and adherence

AI: Artificial intelligence

A human-centric approach to drug discovery combined with core competencies and technology platforms drive future innovation

Explore biology

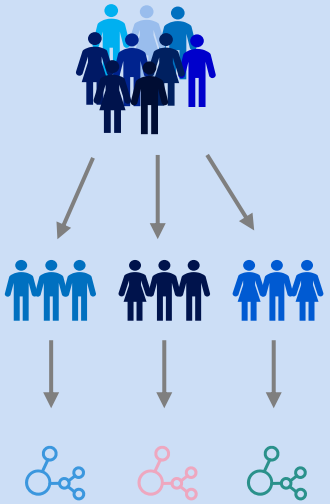


Biology-driven projects within core and adjacent areas

Human-centric approach

Finding the biological targets to address

Precision medicine



Drive better outcomes for a specific patient population powered by digitalisation

Core competencies and technology platforms

Technology platforms

Therapy areas	Proteins / peptides	Oligonucle-otides / RNAi	Stem cells	Genome editing / Gene therapy
Diabetes care	●	●	●	
Obesity care	●	●		
CVD	●	●	●	
NASH	●	●	●	
RBD	●	●		●
RED	●	●	●	
Other areas	●	●	●	

RNA: Ribonucleic acid; RBD: Rare blood disorders; RED: Rare endocrine disorders; NASH: Non-alcoholic steatohepatitis; CVD: Cardiovascular disease

Closing remarks

Proteins and peptides remain a key investment and development area

New technology platforms are synergistic extension of the proteins and peptides stronghold

Driving novel target identification within major cardiometabolic diseases