Cardiovascular and emerging therapy areas

CMD24
CAPITAL MARKETS DAY

7 MARCH


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BILL RITCHIE
Bill lives with cardiovascular disease
USA

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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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

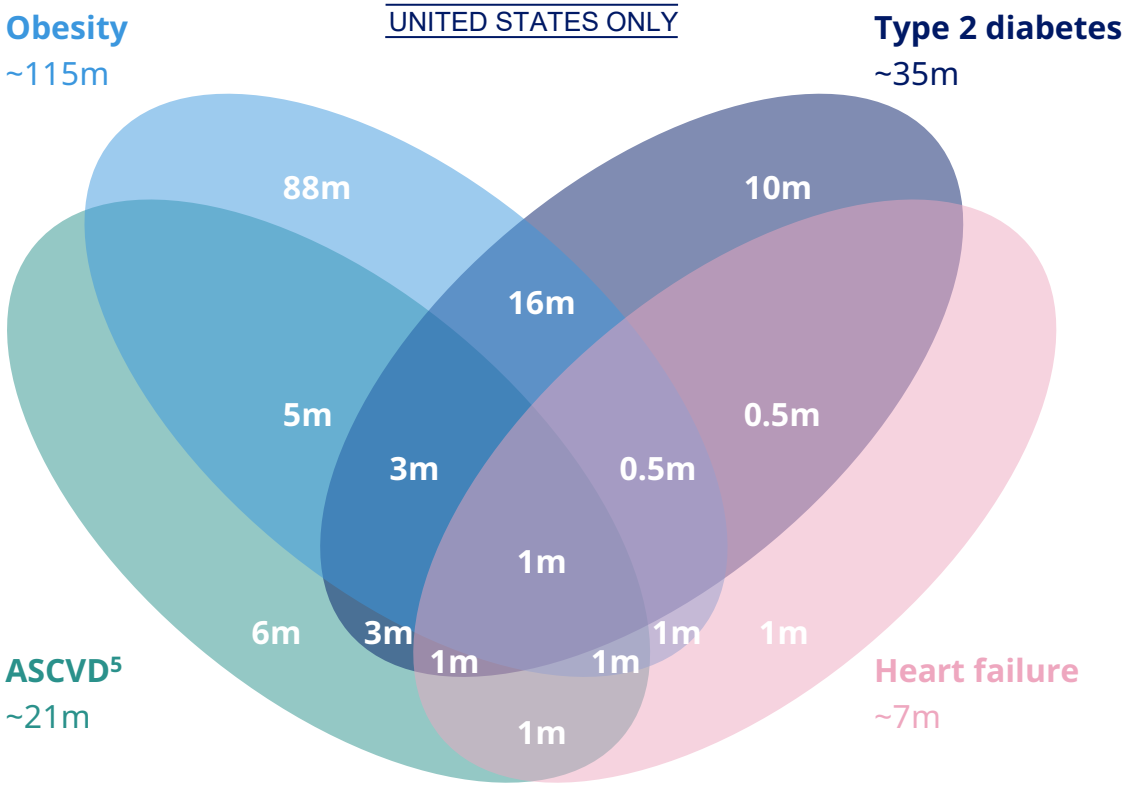
Note: The strategic aspirations are not a projection of Novo Nordisk's financial outlook or expected growth

Novo Nordisk is expanding into Cardiovascular and emerging therapy areas

New therapeutic areas have unmet medical needs

Therapy area	Unmet need
1 CVD	**32% of global deaths caused by CVD[1]**
2 MASH	**>250 million people affected by MASH[2]**
3 CKD	**>800 million people affected by CKD[3]**
4 AD/PD	**~70 million people are living with AD worldwide[4]**

Patient overlaps between Novo Nordisk core therapy areas



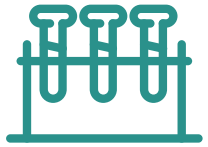
[1]WHO: Cardiovascular Diseases 2023; [2]Csaba P. Kovesdy et al.Kidney International Supplements. 2022; 12: 7-11; [3]WHO: Dementia key facts 2021; [4]Alzheimer's Association report: 2020 Alzheimer's disease facts and figures, 2020 (16:391-460); [5]Myocardial infarction, stroke and coronary heart disease
AD: Alzheimer's disease; ASCVD: Atherosclerotic cardiovascular disease; CKD: Chronic kidney disease; CVD: Cardiovascular disease; MASH: Metabolic dysfunction-associated steatohepatitis; PD: Parkinson's disease; WHO: World Health Organization
Note: Prevalence overlaps have been estimated on patient-level data from NHANES. Post-estimation adjustments have been undertaken to match certain key metrics as reported by publicly available sources. Numbers are rounded
Source: NHANES (waves 2003-2004, 2013-2014, 2015-2016 and 2017-2020); UN World Population Prospects 2022; International Diabetes Federation: Diabetes Atlas 10th edition, 2021; World Obesity Atlas 2023

Novo Nordisk has a focused approach in cardiovascular disease

Focus areas within cardiovascular disease

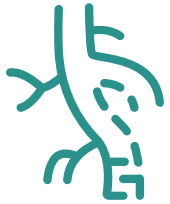
Atherosclerotic cardiovascular disease

Dyslipidaemia



Globally, one third of ischemic heart disease is attributable to high cholesterol[1]

Systemic inflammation



Around half of ASCVD patients estimated to have residual inflammatory risk[2]

Uncontrolled and resistant hypertension

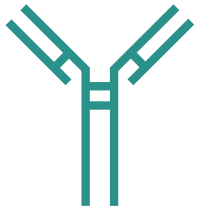
Hypertension is a leading risk factor for CVD, HF, CKD and premature death[3]

Heart failure

Heart failure with preserved ejection fraction

HFpEF is associated with high morbidity and mortality[4]

Transthyretin amyloid cardiomyopathy



ATTR-CM is a progressive, life-threatening disease[5]

[1]WHO: Cardiovascular Diseases (Cholestorol); [2]Ridker et. al, J Am Coll 2018;72:3320-3333; [3]WHO: Cardiovascular Diseases (Hypertension); [4]Chioncel O et al. Eur J Heart Fail 2017; 19; 1574; [5]Singh A. et al. J Am Coll Cardiol 2017; 69:750-759
ASCVD: Atherosclerotic disease; ATTR-CM: Transthyretin amyloid cardiomyopathy; CKD: Chronic kidney disease; CVD: Cardiovascular disease; HF: Heart Failure; HFpEF: Heart failure with preserved ejection fraction; WHO: World Health Organization

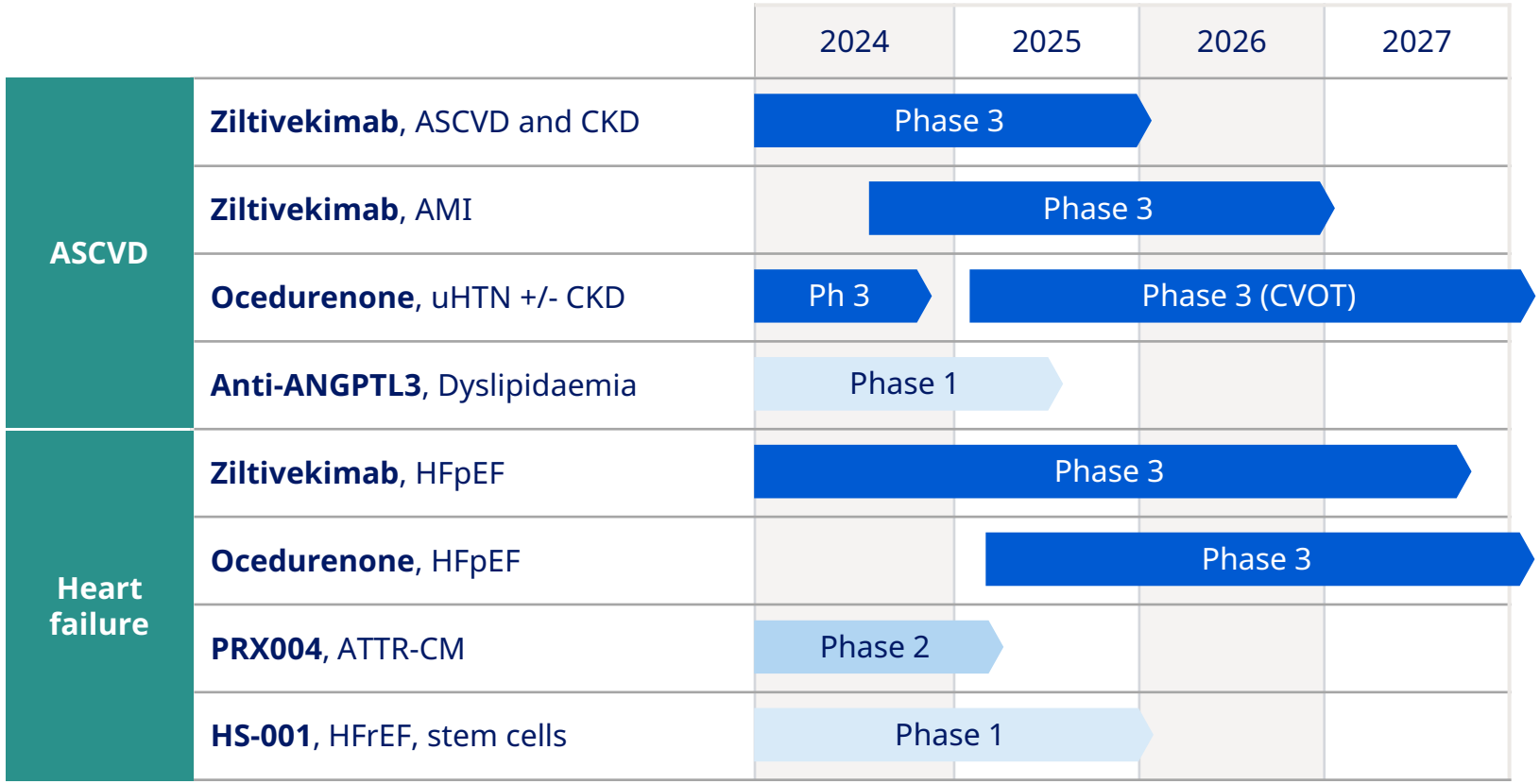
Cardiovascular disease clinical pipeline has expanded, leveraging internal and external innovation and synergies

Establishing a presence in CVD

Our key focus areas:

- Address significant unmet needs
- Pursue innovative mechanisms of action
- Combine internal and external innovation

Development pipeline



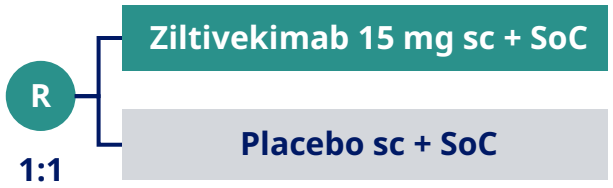
AMI: Acute myocardial infarction; ASCVD: Atherosclerotic cardiovascular disease; ATTR-CM: Transthyretin Amyloid Cardiomyopathy; CKD: Chronic kidney disease; CVD: Cardiovascular disease; HFpEF: Heart failure with preserved ejection fraction; HFrEF: Heart failure with reduced ejection fraction; uHTN: Uncontrolled Hypertension

Ziltivekimab phase 3 development programme targets high unmet need populations within CVD

ZEUS
ziltivekimab cardiovascular outcomes trial

Atherosclerosis and chronic kidney disease

n = 6,200



2021 — **~2026**

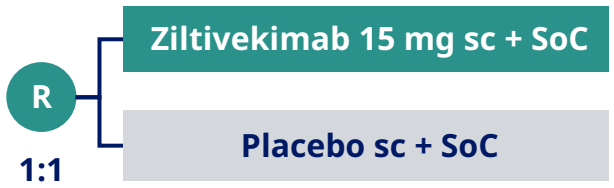
Event driven
~ 3.5 years

Primary Endpoint:
Time to the first occurrence of 3-point MACE
- Cardiovascular death
- Non-fatal myocardial infarction
- Non-fatal stroke

HERMES
ziltivekimab in patients with heart failure with mildly reduced or preserved ejection fraction and systemic inflammation

HFmrEF and HFpEF

n = 5,600



2023 — **~2027**

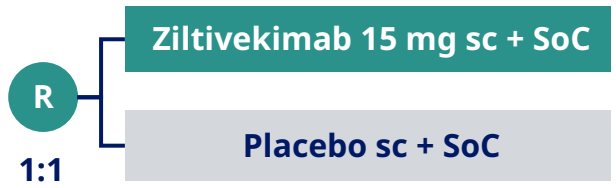
Event driven
~ 4 years

Primary Endpoint:
Time to the first occurrence of
- Cardiovascular death
- Hospitalisation for heart failure
- Urgent heart failure visit

ARTEMIS
ziltivekimab in patients with acute myocardial infarction

Acute myocardial infarction

n = 10,000



2024 — **~2027**

Event driven
~ 2.5 years

Primary Endpoint:
Time to the first occurrence of 3-point MACE
- Cardiovascular death
- Non-fatal myocardial infarction
- Non-fatal stroke

CVD: Cardiovascular disease; HF: Heart failure; MACE: Major adverse cardiovascular event; sc: Subcutaneous; SoC: Standard of care; HFmrEF: Heart failure with mildly reduced ejection fraction; HFpEF: Heart failure with preserved ejection fraction

With the acquisition of ocedurenone, Novo Nordisk moves into uncontrolled hypertension

Uncontrolled hypertension

Unmet need: Hypertension is leading risk factor for cardiovascular events, heart failure and chronic kidney disease[1] despite current standard of care

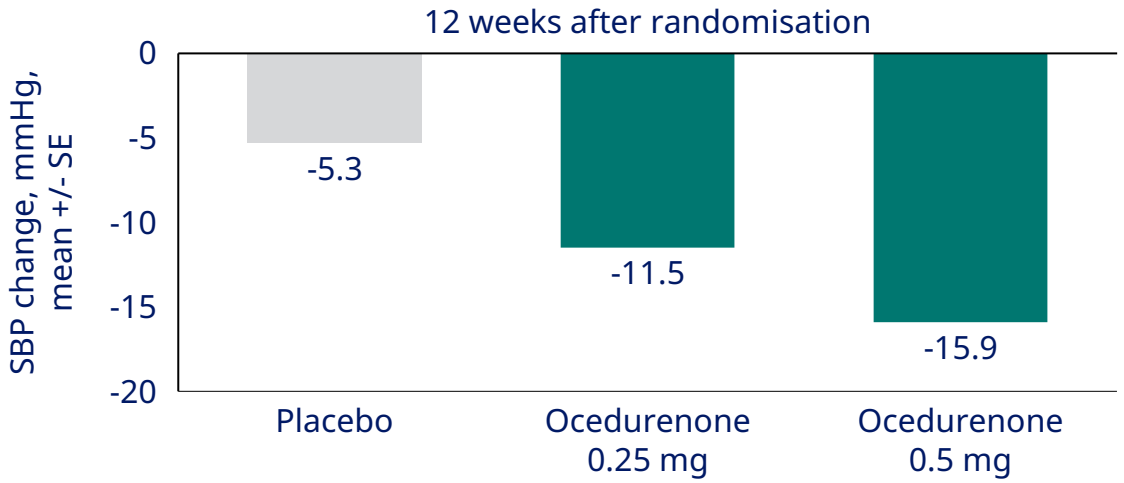
Therapy: Ocedurenone is an oral, once daily, small molecule antagonist directed against the mineralocorticoid receptor

Target: Ocedurenone's potent blood-pressure lowering effect is expected to reduce the risk of poor outcomes in heart failure and chronic kidney disease

Next Steps:

- Ongoing phase 3 trial: CLARION-CKD
- Planned phase 3 trials: uHTN +/-CKD and HFpEF CVOT

BLOCK-CKD Phase 2 Results



Differentiator efficacy

- Ocedurenone has potent sustained blood pressure lowering effect
- High affinity for the MR and long half-life ~50 hours

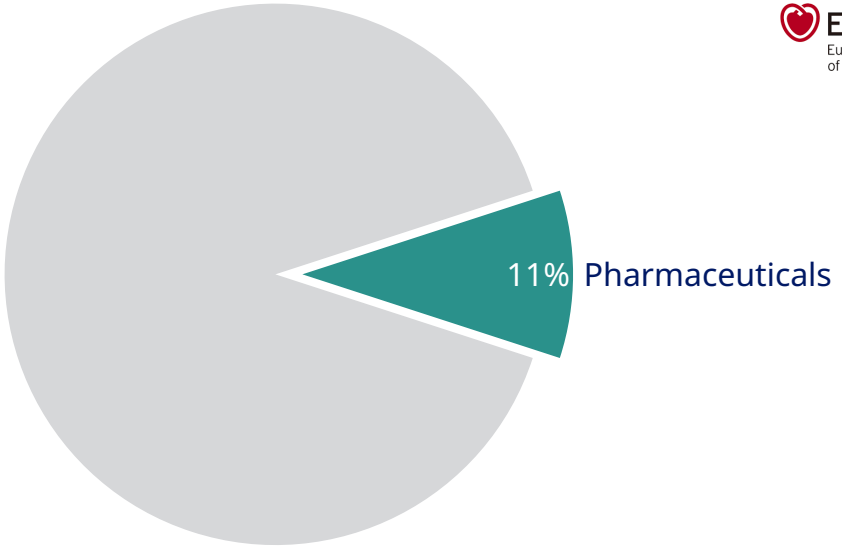
Differentiator safety

- Low risk of hyperkalemia (<1%), also in stage 3b-4 CKD
- No steroidal side effects

[1]WHO: Cardiovascular Diseases (Hypertension)
CKD: Chronic kidney disease; CVOT: Cardiovascular outcomes trial; HFpEF: Heart failure with preserved ejection fraction; MoA: Mechanism of action; MR: Mineralocorticoid receptor; SBP: Systolic blood pressure; SE: Standard error; uHTN: Uncontrolled hypertension; WHO: World Health Organization
Note: Hypertension is defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or taking medication for hypertension. Uncontrolled hypertension is defined as SBP >140mmHg and maximally tolerated dose of ≥2 anti-hypertensives or history of documented intolerance or lack of efficacy. Block-CKD Baseline SBP 155.3 mmHg, DBP 87.7 mmHg.
Source: Bakris et al. Effect of KBP-5074 on Blood Pressure in Advanced Chronic Kidney Disease: Results of the BLOCK-CKD Study. Hypertension. 2021;78:74–81

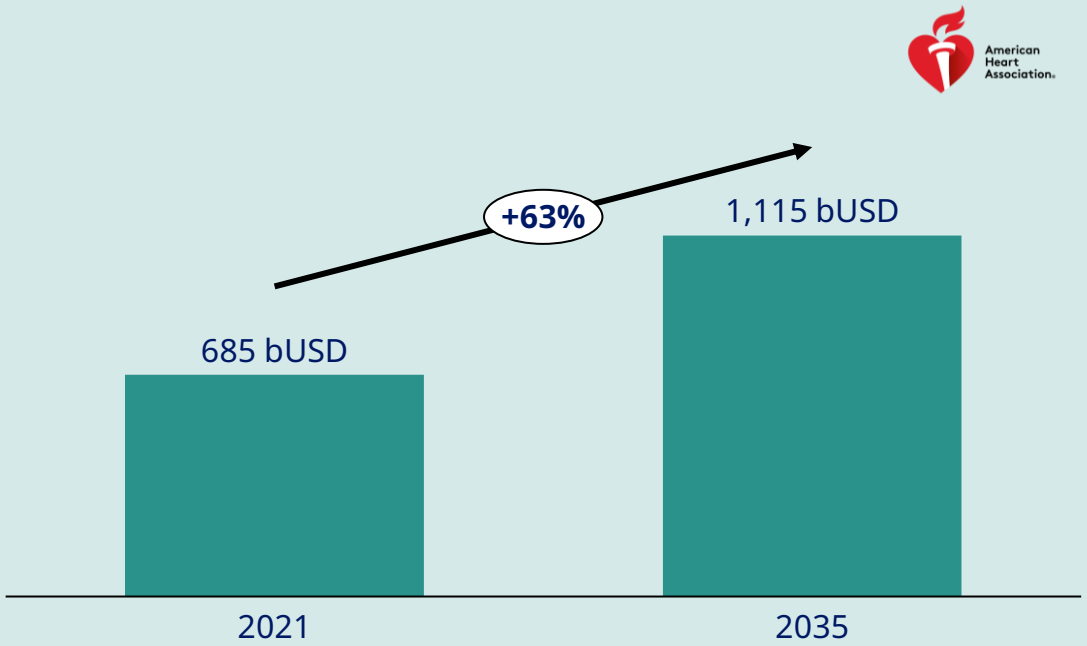
The cardiovascular market is well established with significant and growing healthcare burden

The EU annual economic burden of CVD was estimated to 282 billion EUR in 2021[1]



- Despite current treatments, 11% of EU spend from healthcare and social care budgets is on CVD
- Innovative treatments are needed to improve outcomes and limit the expected increase in CVD economic burden

The US annual economic burden of CVD is estimated to exceed 1 trillion USD in the 2030's[2]



[1]Economic burden of cardiovascular diseases in the European Union: a population-based cost study, European Heart Journal, 2023; [2]Cardiovascular disease: A costly burden for America – Projections through 2035 American Heart Association, 2016
AHA: American Heart Association; CVD: Cardiovascular disease; ESC: European Society of Cardiology; EU: European Union; US: United States

Novo Nordisk will leverage expertise within diabetes and obesity to build presence within cardiovascular disease

Cardiovascular outcomes trials in Type 2 diabetes and obesity

LEADER – Liraglutide Effect and Action in Diabetes: Evaluation of cardiovascular outcome Results	13%[1]
SUSTAIN 6 – SEMAGLUTIDE UNABATED SUSTAINABILITY IN TREATMENT OF TYPE 2 DIABETES	26%[1]
PIONEER 6 – Peptide InnOvatioN for Early diabEtes tReatment	21%[1]
SELECT – semaglutide | effects on cardiovascular outcomes in people with overweight or obesity	20%[1]
STEP-HFpEF – semaglutide | treatment effect in people with obesity; heart failure with preserved ejection fraction	Superior[2]
FLOW – semaglutide | renal outcomes trial	24%[3]

SOUL – semaglutide | cardiovascular outcomes trial	Oral semaglutide 14 mg in T2D (CVOT)
STRIDE – Effects of semaglutide on functional capacity in patients with type 2 diabetes and peripheral arterial disease	Semaglutide 1.0 mg in T2D and PAD
REDEFINE 3 – cagrilintide and semaglutide combination | assessing cardiovascular outcomes and safety	CagriSema in T2D or Obesity, with CVD

Clinical trials in stand-alone CVD

ZEUS – ziltivekimab cardiovascular outcomes trial	Ziltivekimab in ASCVD and CKD
HERMES – ziltivekimab in patients with heart failure with mildly reduced or preserved ejection fraction and systemic inflammation	Ziltivekimab in HFpEF/HFmrEF
ATHENA – ziltivekimab functional outcomes in patients with heart failure with mildly reduced or preserved ejection fraction	Ziltivekimab in HFpEF/HFmrEF
ARTEMIS – ziltivekimab in patients with acute myocardial infarction	Ziltivekimab in AMI
Hypertension -HFpEF	CVOT with ocedurenone expected to be initiated
ATTR-CM	PRX004 in ATTR-CM (HF) proof-of-principle

[1]indicates statistically significant risk reduction of 3-point major adverse cardiovascular events (MACE) defined as a composite of non-fatal stroke, non-fata myocardial infarction (MI), and cardiovascular death;
[2] Not Published. [3]FLOW was a kidney outcomes trial. 24% based on treatment policy estimand
AMI: Acute myocardial infarction; ASCVD: Atherosclerotic cardiovascular disease; ATTR-CM: Transthyretin amyloid cardiomyopathy; CKD: Chronic kidney disease; CVD: Cardiovascular disease; CVOT: Cardiovascular outcome trial; HF: Heart failure; HFrEF: Heart failure with reduced ejection fraction; HFpEF: Heart failure with preserved ejection fraction; PAD: Peripheral arterial disease

Commercialisation of late-stage assets will build upon existing commercial efforts with semaglutide

2024 2027 2030

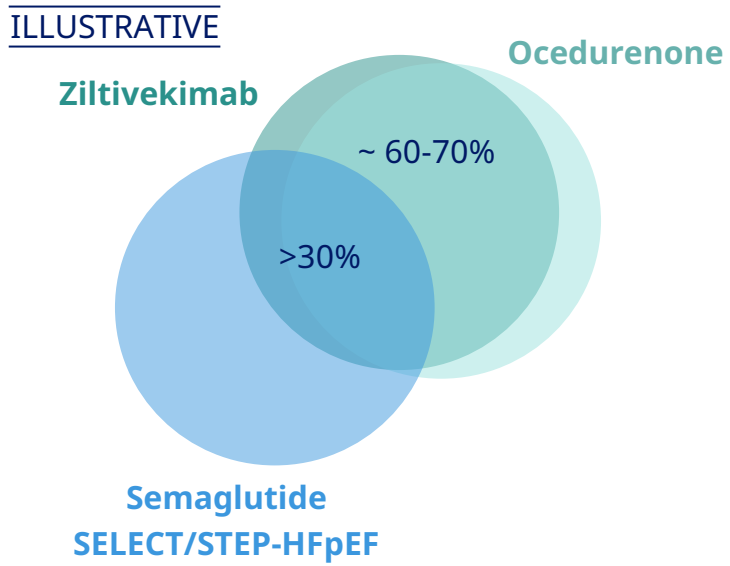
Ocedurenone

Ziltivekimab

Semaglutide cardiovascular indications

Near-term	Mid-term	Long-term
Leverage semaglutide CV indications to establish presence with cardiologists and PCPs for entry of stand-alone CVD product	Utilise scientific and commercial foundation to launch first CVD stand-alone product	Expand pipeline with differentiated MoAs through discovery and translational capabilities

Commercial synergies among cardiologist prescribers



Expected cardiologist prescriber overlap for semaglutide CV indications, and stand-alone CV assets ziltivekimab and ocedurenone

CV(D): Cardiovascular (disease); HFpEF: Heart failure with preserved ejection fraction; MoA: Mode of action; PCP: Primary care physician

Strategy is backed up by an innovative late-stage cardiovascular disease pipeline to address unmet needs for patients

Category	Stand-alone cardiovascular assets				
	ASCVD		Heart failure		
Study Current phase	**ASCVD** Phase 3 Ziltivekimab	**uHTN** Phase 3 Ocedurenone	**HFpEF** Phase 3 Ziltivekimab	**ATTR-CM** Phase 2 PRX004	**HFpEF** Phase 3 Ocedurenone
Estimated global target population[1] (million people)	~75	~15	~15	~1.5	~30
Potential differentiators	Superior product profile	Superior product profile	1st in class indication	Disease modifying	Superior product profile

[1]Chronic HF: Groenewegen A et al. Eur J Heart Fail 2020;22:1342–1356; HFpEF: Chris J Kapelios et al Cardiac Failure Review 2023;9:e14; ATTR-CM: Orphan Maintenance Assessment Report for tafamidis, EMA, 17 February 2020. Vos T et al. Lancet. 2020; 396:1204–1222. Ramachandran S. Vasan et al. Temporal Trends in the Remaining Lifetime Risk of Cardiovascular Disease Among Middle-Aged Adults Across 6 Decades: The Framingham Study, Circulation. 2022;145:1324–1338; Michael et. al Prevalence and Characteristics of Systemic Inflammation in Adults With Atherosclerotic Cardiovascular Disease and Chronic Kidney Disease, Circulation. 2022;146:A11398

ASCVD: Atherosclerotic cardiovascular disease; ATTR-CM: Transthyretin Amyloid Cardiomyopathy; CVD: Cardiovascular disease; HFpEF: Heart failure with preserved ejection fraction; MoA: Mode of Action; uHTN: Uncontrolled hypertension

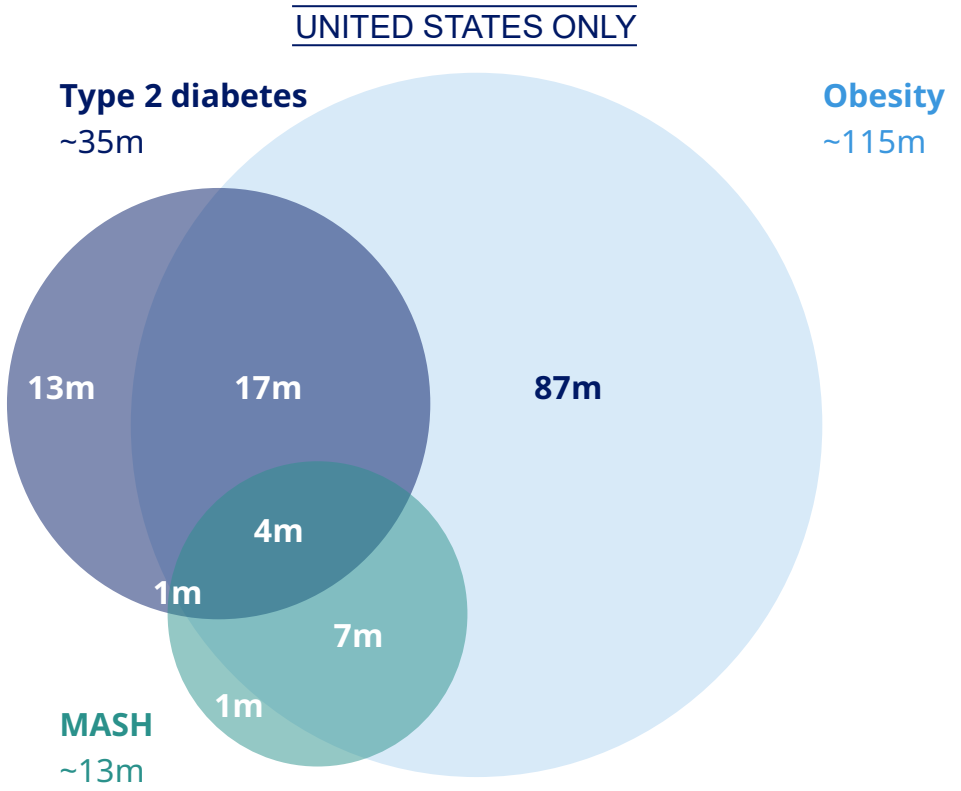
Note: Target population defined as global unmet need according to respective trial population

Metabolic dysfunction-associated steatohepatitis shares a large patient population with Novo Nordisk's core therapy areas

New therapeutic areas have high unmet medical needs

Therapy area	Unmet need
1 CVD	32% of global deaths caused by CVD[1]
2 MASH	>250 million people affected by MASH[2]
3 CKD	>800 million people affected by CKD[3]
4 AD/PD	~70 million people are living with AD worldwide[4]

Patient overlap between Novo Nordisk core therapy areas and MASH



[1]WHO: Cardiovascular Diseases 2023; [2]Csaba P. Kovesdy et al.Kidney International Supplements. 2022; 12: 7-11; [3]WHO Dementia key facts 2021; [4]Alzheimer's Association report: 2020 Alzheimer's disease facts and figures, 2020 (16:391-460)
AD: Alzheimer's disease; CKD: Chronic Kidney disease; CVD: Cardiovascular disease; MASH: Metabolic dysfunction-associated steatohepatitis; PD: Parkinson's disease; WHO: World Health Organization
Note: Prevalence overlaps have been estimated on patient-level data from NHANES. Post-estimation adjustments have been undertaken to match certain key metrics as reported by publicly available sources. Numbers are rounded
Source: NHANES (waves 2003-2004, 2013-2014, 2015-2016 and 2017-2020); UN World Population Prospects 2022; International Diabetes Federation: Diabetes Atlas 10th edition, 2021; World Obesity Atlas 2023

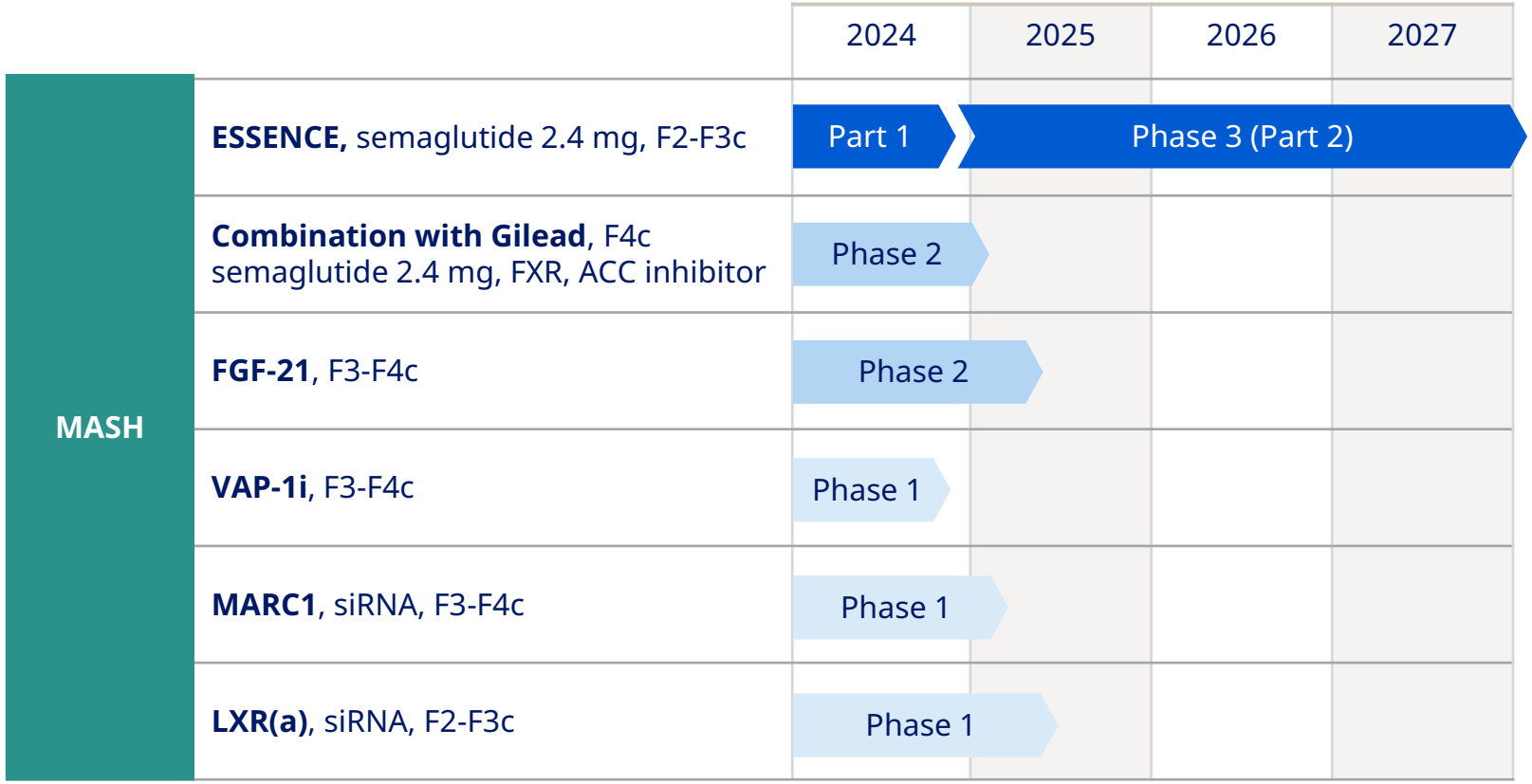
MASH pipeline development across F2-F4c segments

Establishing a presence in MASH

Our key focus areas

- Address the unmet need within MASH
- Aim for effect on resolution of MASH and improvement or no worsening of fibrosis
- Prioritise multi-MoA anti-fibrotics in F3-F4c to secure a best-in-class profile

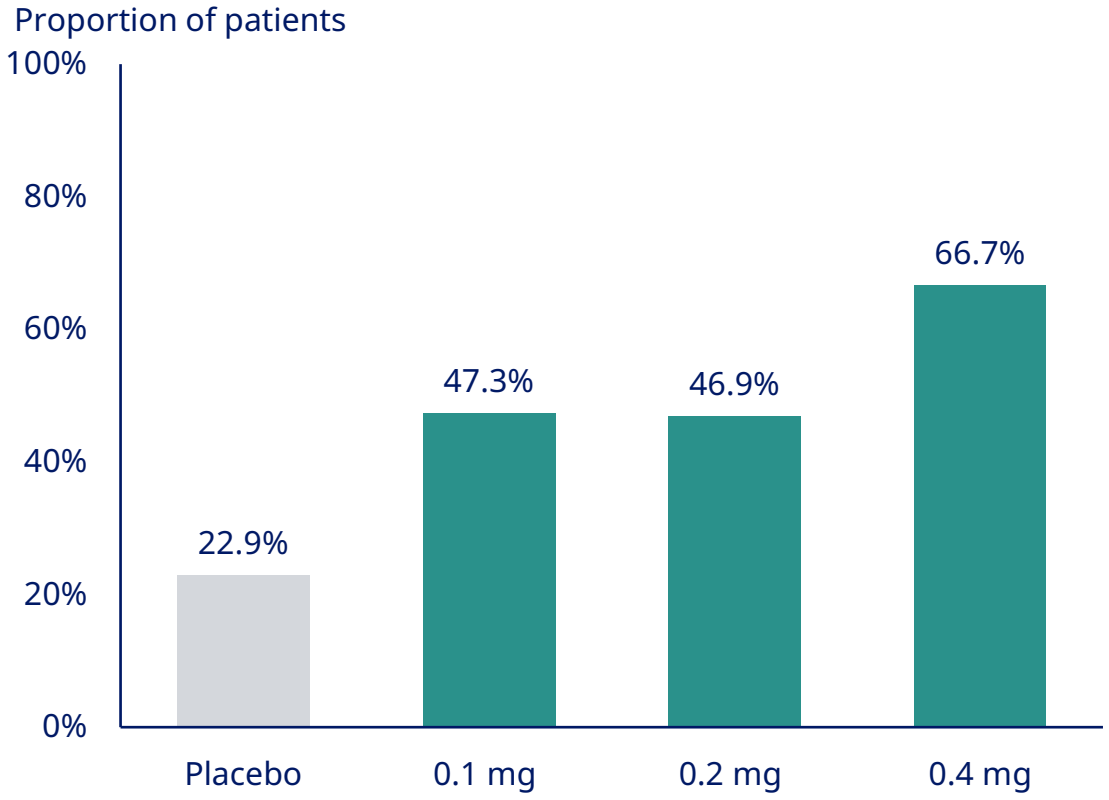
Development pipeline



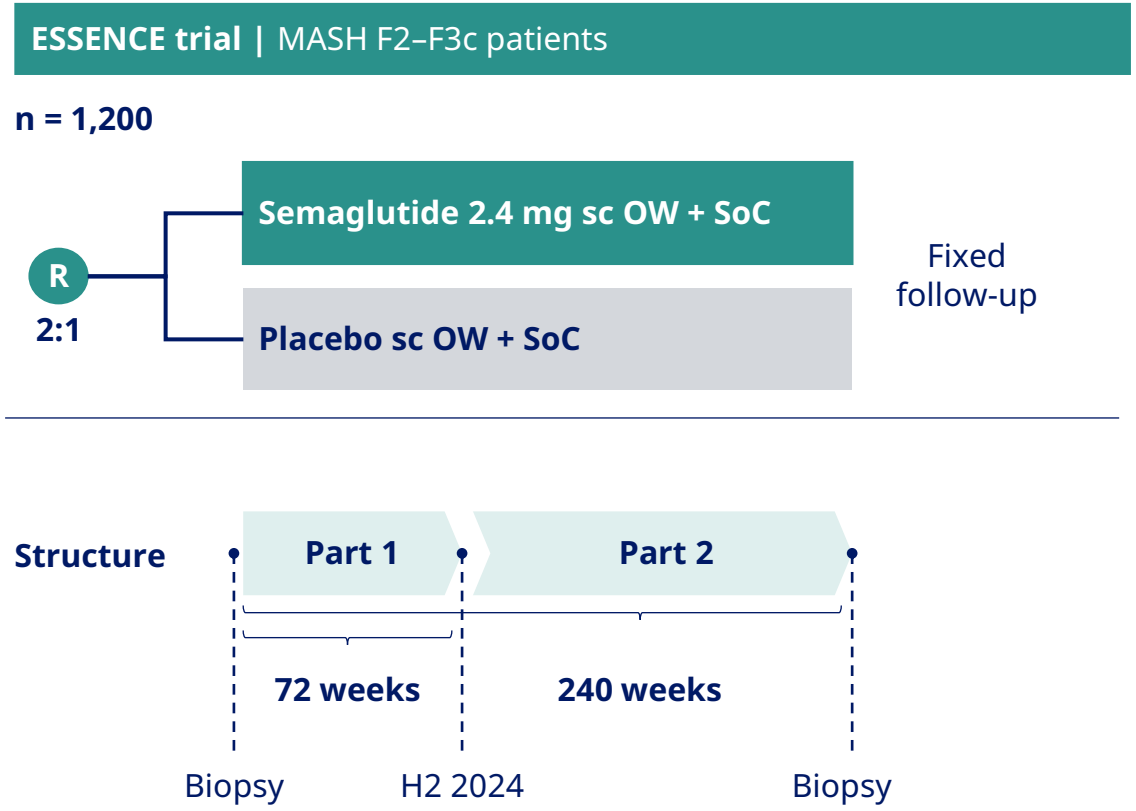
ACC: firsocostat; AD: Alzheimer's Disease; F: Fibrosis stage; F4c: Compensated cirrhosis; FXR: Cilofexor Farnesoid X inhibitor; LXR(a): Liver X receptor alpha; MARC1: Mitochondrial amidoxime reducing component 1; MASH: Metabolic dysfunction-associated steatohepatitis; MoA: Mode of action; VAP-1i: Vascular adhesion protein-1 inhibitor; siRNA: Small interfering ribonucleic acid

MASH is a progressive disease and semaglutide could be the therapeutic foundation

Semaglutide showed resolution of MASH with no worsening of fibrosis versus placebo in the phase 2 trial



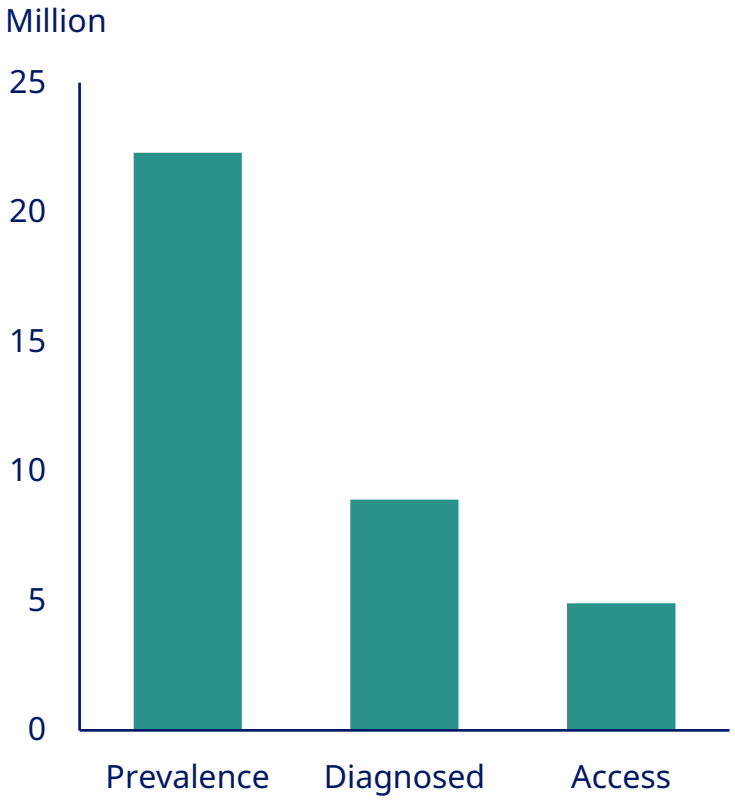
Phase 3a ESSENCE trial in MASH



F: Fibrosis stage; MASH: Metabolic-dysfunction associated steatohepatitis; OW: Once-weekly; Sc: Subcutaneous; SoC: Standard of care
Source: Based on a complete case analysis, using people with an evaluable biopsy at end of trial. Analysis included patients with fibrosis stage 1, 2, or 3 at baseline. Data is from the semaglutide in NASH phase 2 trial

Novo Nordisk will focus on F2-F4c with commercial efforts related to awareness, referrals and diagnosis

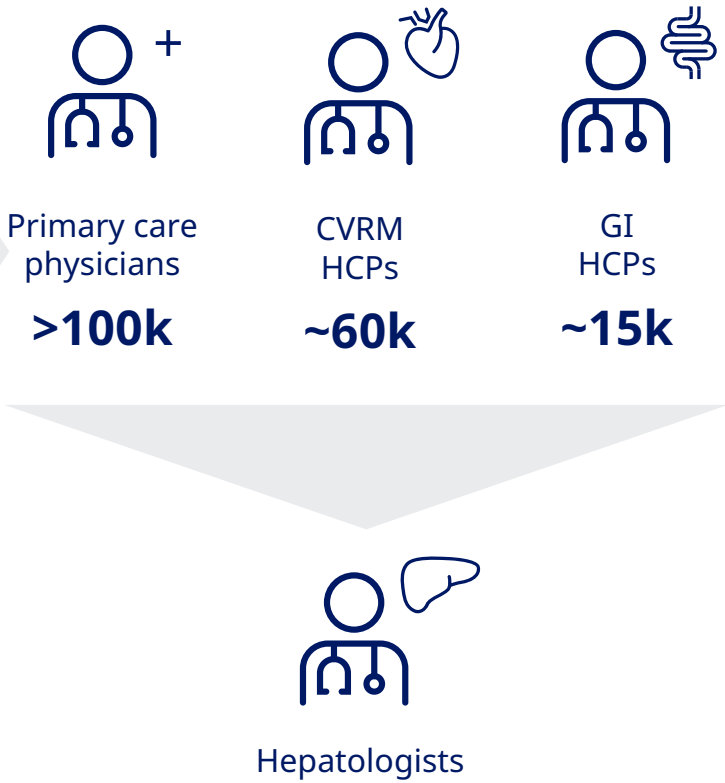
~22 million people are expected to live with MASH F2-F4c by 2030[1]



Focus areas to establish presence in MASH

- **Awareness**
  Recognise liver health as additional risk factor and increase patient screening at scale
- **Referrals**
  Ensure high risk patient referral and support guideline changes
- **Diagnosis**
  Ensure sequential NITs are used in diagnosis
- **Treatment**
  Semaglutide as foundation; Liver-specific MoAs as add-on in F2-F3c; Multi-MoA anti-fibrotics in F3-F4c

MASH referrals to hepatologists in the US



[1]Estes C, Modelling the epidemic of non-alcoholic fatty liver disease demonstrates an exponential increase in burden of disease, Hepatology, 2018
CVRM: Cardiovascular, renal, metabolic; F: Fibrosis stage; (F0-F1: no or mild fibrosis; F2 significant fibrosis; F3-4 advanced fibrosis); GI: Gastrointestinal; HCPs: Healthcare professionals; MASH: Metabolic dysfunction-associated steatohepatitis; MoA: Mode of action; NIT: Non-invasive tests
Note: Advanced fibrosis (F3-4) defined as per Kleiner DE. Hepatology. 2005;41:1313–21 and Brunt EM. Hepatology. 2011;53: 810–20.

Novo Nordisk enters partnerships to enhance diagnosis in MASH

Partnerships across relevant non-invasive tests

Blood test		
Pro-C3	ELF test	OW Liver

Blood test score		
NIS4	FIB-4	Fibro Sure

Scan			
SWE	MRE/MRI-PDFF	Liver MultiScan	TE FibroScan

Novo Nordisk supports NIT for MASH screening and diagnosis

- Clinical guideline development recommending screening for MASH in type 2 diabetes
- Disease education activities to enable screening, diagnosis and evidence generation
- Engaging in consortia (Litmus, Nimble, Liver Forum)
- Engaging with larger diagnostic companies to ensure NIT capacity

AACE: American Association of Clinical Endocrinologists; ADA: American Diabetes Association; ELF: Enhanced liver fibrosis; FDA: The US Food and Drug Administration; FIB-4: Fibrosis-4; MASH: Metabolic dysfunction-associated steatohepatitis; MRI-PDFF: Magnetic resonance imaging proton density fat fraction; MRE: Magnetic resonance elastography; NITs: Non-invasive tests; NIS4: Non-invasive biomarker panel; OW: Once-weekly; SWE: Shear wave elastography; TE: Transient elastography

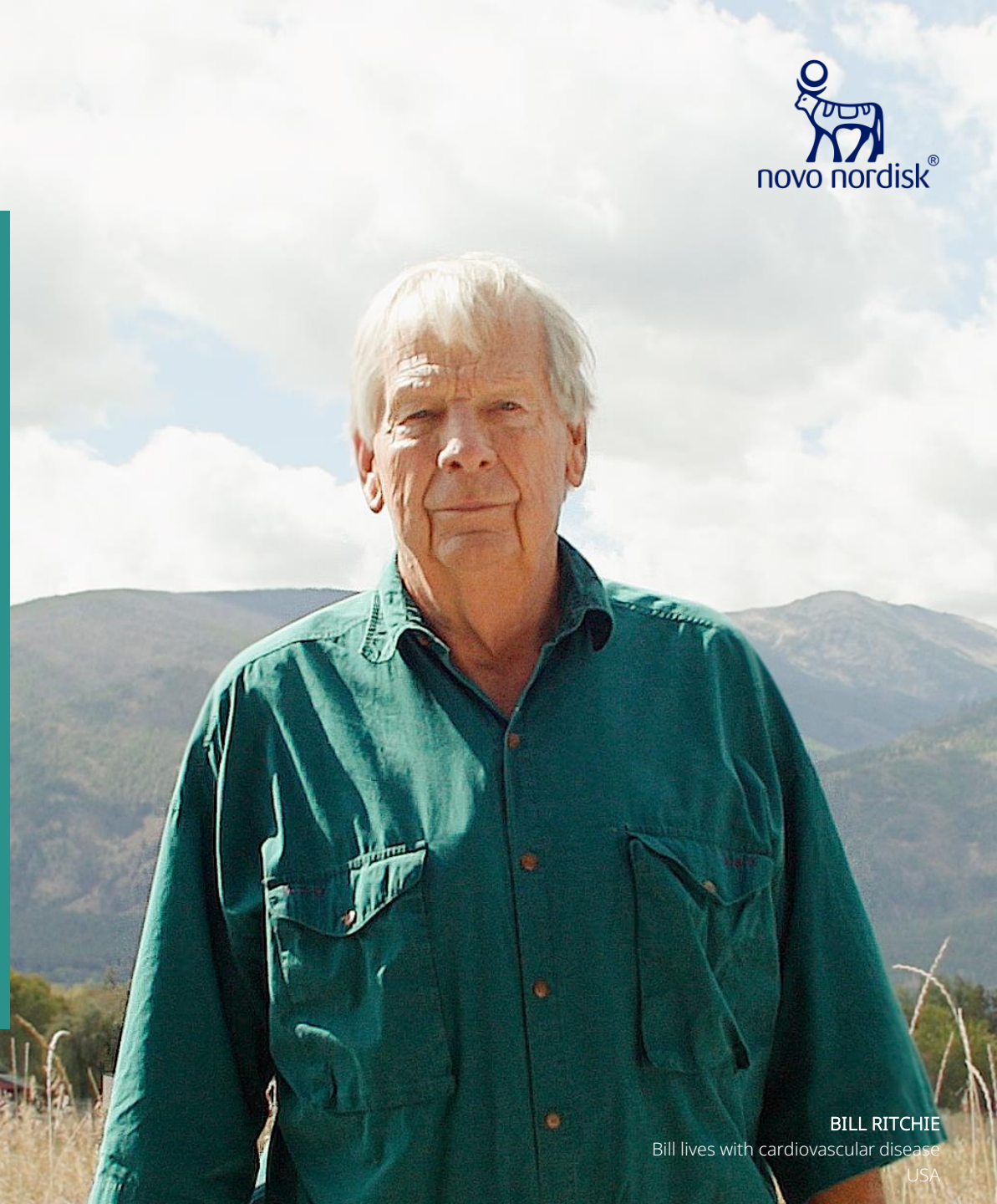
Closing remarks

A significant unmet need remains in cardiovascular disease

Novo Nordisk has cardiometabolic competencies and is growing a late-stage pipeline in CVD

Significant unmet need in MASH

Phase 3 results for semaglutide 2.4 mg in MASH expected end 2024



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Bill lives with cardiovascular disease
USA