Cardiovascular disease

CMD22
CAPITAL MARKETS DAY

3 MARCH

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Forward-looking statements

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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

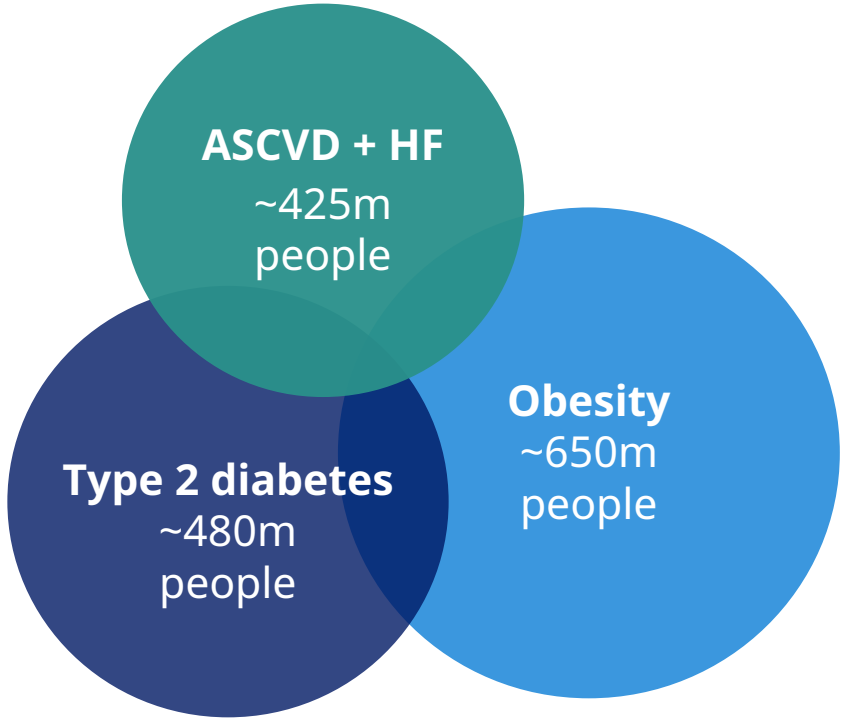
Financials

- 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

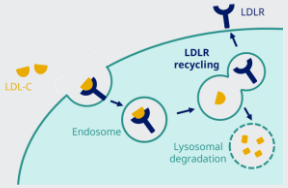
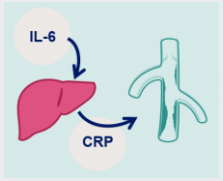
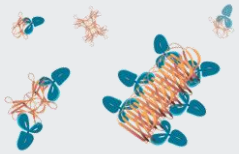
[1] From 2015 to 2022, 70% of sales to come from products launched from 2015. IO: International Operations; CVD: Cardiovascular disease; NASH: Non-alcoholic steatohepatitis; CKD: Chronic kidney disease.
Note: The strategic aspirations are not a projection of Novo Nordisk's financial outlook or expected growth.

Large patient overlaps between diabetes, obesity and CVD have guided our focused approach in CVD

Population overlap between T2D, obesity and CVD



Focused approach in CVD

Atherosclerosis		Heart failure	
High cholesterol	**Inflammation-driven pathogenesis**	**Heart failure with preserved ejection fraction** (HFpEF)	**Transthyretin amyloid cardiomyopathy** (ATTR-CM)
			
Lowering LDL-C to reduce ASCVD	hsCRP as surrogate endpoint	Improve outcomes	Amyloid-depletion through antibody-mediated phagocytosis

T2D: Type 2 diabetes, CVD: Cardiovascular disease; ASCVD: Atherosclerotic cardiovascular disease; HF: Heart failure; ATTR-CM: Transthyretin Amyloid Cardiomyopathy; LDL-C: Low-density lipoprotein cholesterol; hsCRP: High-sensitivity C-reactive protein
Sources: IDF Diabetes Atlas 2021, internal estimate based on European Cardiovascular Disease Statistics, 2017 edition, WHO obesity and overweight fact sheet, 9 June 2021

Novo Nordisk will leverage experiences within diabetes and obesity with the aim to build a presence within CVD

Current indications

T2D

Type 2 diabetes

LEADER – Liraglutide Effect and Action in Diabetes: Evaluation of cardiovascular outcome Results	13%*
SUSTAIN 6 – SEMAGLUTIDE UNABATED SUSTAINABILITY IN TREATMENT OF TYPE 2 DIABETES	26%*
PIONEER 6 – Peptide InnOvatioN for Early diabEtes tReatment	21%*

Near-term indications

Broader indications (towards 2025)

SELECT – semaglutide | effects on cardiovascular outcomes in people with overweight or obesity	Semaglutide 2.4 mg in people with overweight or obesity[1]
SOUL – semaglutide | cardiovascular outcomes trial	Oral semaglutide 14 mg in people with T2D (CVOT)
FLOW – semaglutide | renal outcomes trial	Sema 1.0 mg on renal outcomes in people with T2D and CKD
STEP HFpEF	Sema 2.4 mg on HF in people with obesity and chronic HFpEF[1]
STRIDE – Effects of semaglutide on functional capacity in patients with type 2 diabetes and peripheral arterial disease	Sema 1.0 mg tested on PAD in people with T2D and PAD

Future indications

Stand-alone CVD (beyond 2025)

ZEUS – ziltivekimab cardiovascular outcomes trial	CVOT for ziltivekimab
Oral PCSK-9i	Dose-finding trial with oral PCSK-9i to treat dyslipeidaemia and reduce the risk of ASCVD
ATTR CM	Proof-of-principle trial of NNC6019-0001[2] in patients with ATTR-CM (HF)

* 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

[1] Incomplete inclusion criteria as e.g. established CVD is also a requirement; [2] Formerly noted as PRX004; CVD: Cardiovascular disease; CKD: Chronic kidney disease; T2D: Type 2 diabetes; Sema: semaglutide; PAD: peripheral arterial disease; ATTR-CM: Transthyretin amyloid cardiomyopathy, CVOT: Cardiovascular outcome trial; ASCVD: Atherosclerotic cardiovascular disease; HFpEF: Heart failure with preserved ejection fraction; HF: Heart failure

Broad pipeline leveraging internal and external innovation

Establishing a presence in CVD

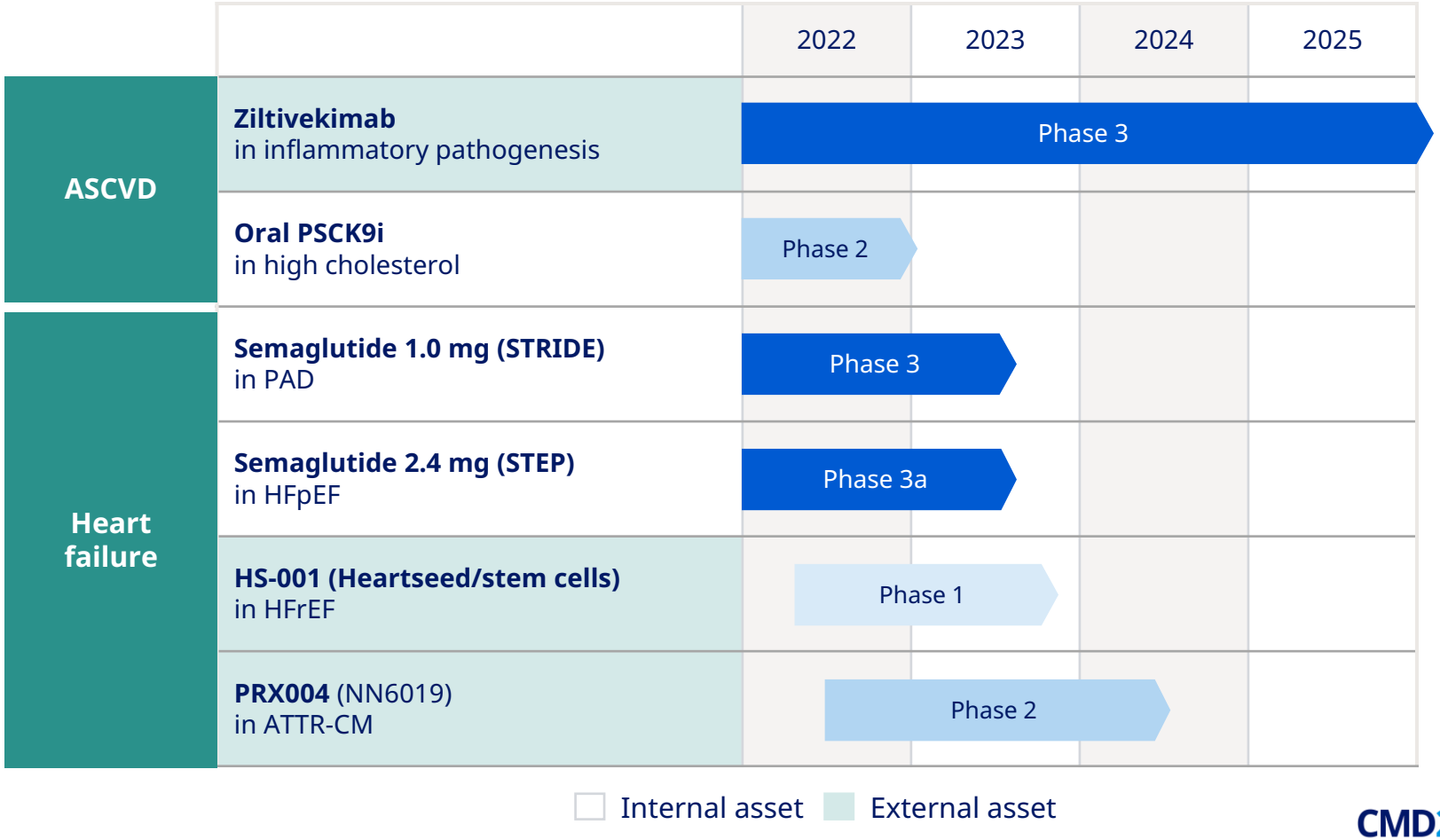
Ambition:

At least one product launched between 2024-2028 targeting ASCVD or heart failure

Priorities:

- Be first-to-market addressing a significant unmet need
- Pursue highly innovative MoAs
- Combine internal and external innovation

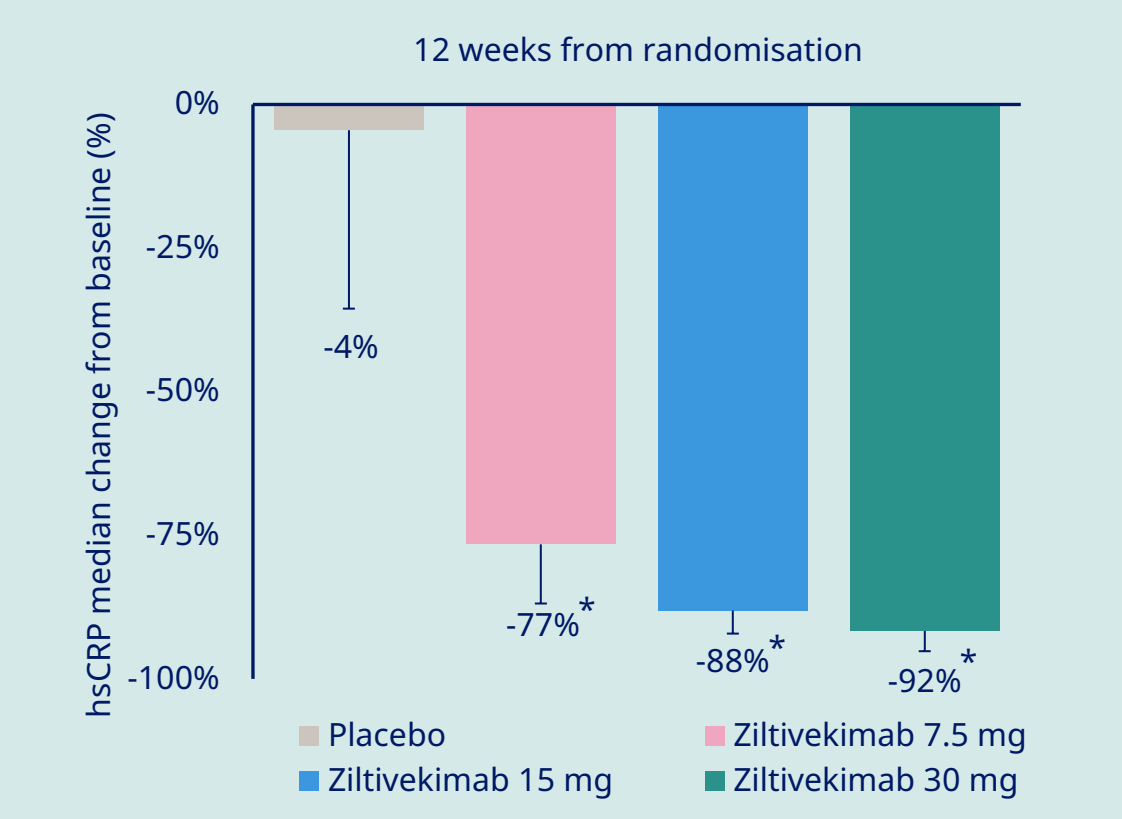
Cardiovascular disease pipeline overview



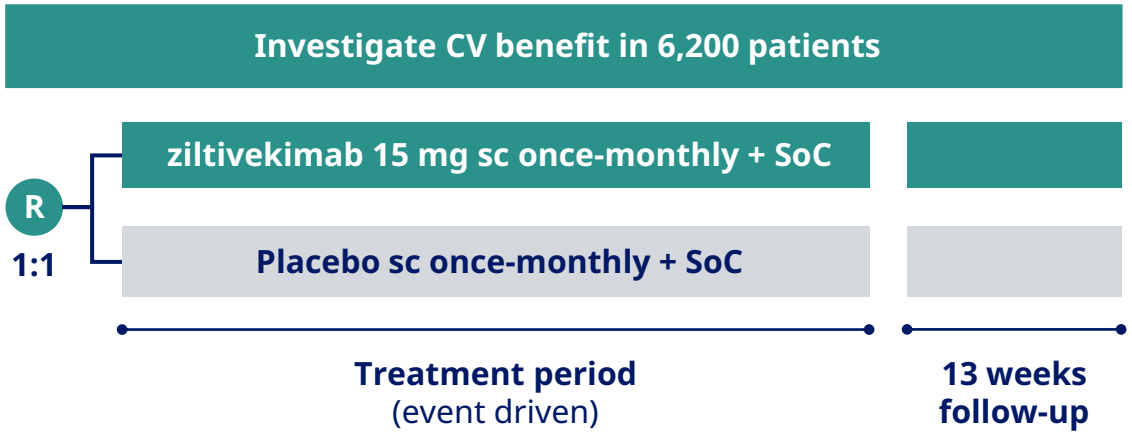
CVD: Cardiovascular Disease; ASCVD: Atherosclerotic cardiovascular disease; MoA: Mode of Action; HFpEF: Heart failure with preserved ejection fraction; PAD: Peripheral arterial disease; ATTR-CM: Transthyretin Amyloid Cardiomyopathy

ZEUS trial with ziltivekimab aims to validate the link between hsCRP and major adverse cardiovascular events

Results from the phase 2 trial RESCUE with ziltivekimab



Phase 3 CVOT trial ZEUS with ziltivekimab

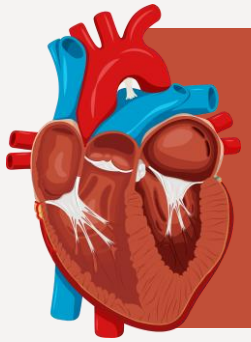


Primary endpoint	• Time to the first occurrence of 3-point MACE[1]
Secondary endpoints	• Time to first occurrence of expanded MACE[1] • Number of hospitalisations for HF or urgent HF visit • Time to occurrence of all-cause mortality • Time to first occurrence of a composite CKD endpoint

* Statistically significant; [1] Inclusion criteria: Age ≥18 years, History of ASCVD, eGFR ≥15 and <60 mL/min/1.73 m2, Serum hsCRP ≥2 mg/L
[1] MACE includes CV death, non-fatal MI or non-fatal stroke, Expanded MACE includes: (CV death, non-fatal MI, non-fatal stroke or hospitalisation for unstable angina pectoris requiring urgent coronary revascularisation)
hsCRP: High-sensitivity C-reactive protein; CVOT: Cardiovascular outcome trial; CV: Cardiovascular; sc: Subcutaneous; SoC: Standard of care; HF: Heart failure; CKD: Chronic kidney disease
Source: Ridker PM, et al., IL-6 inhibition with ziltivekimab in patients at high atherosclerotic risk (RESCUE): a double-blind, randomised, placebo-controlled, phase 2 trial, 17 May 2021

For patients with heart failure, the goal is to bring disease modifying and curative treatments to the market

Heart failure at a glance



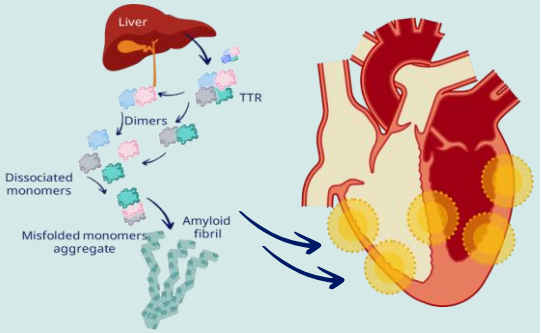
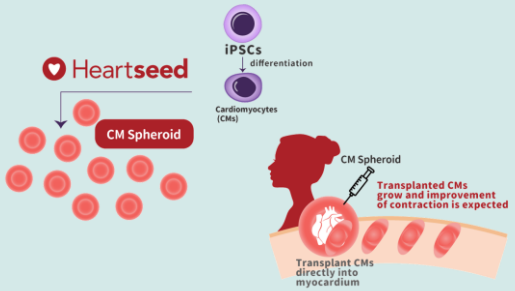
Diastolic dysfunction (HFpEF)

- Impaired filling capacity
- Stiff and thick ventricle

Systolic dysfunction (HFrEF)

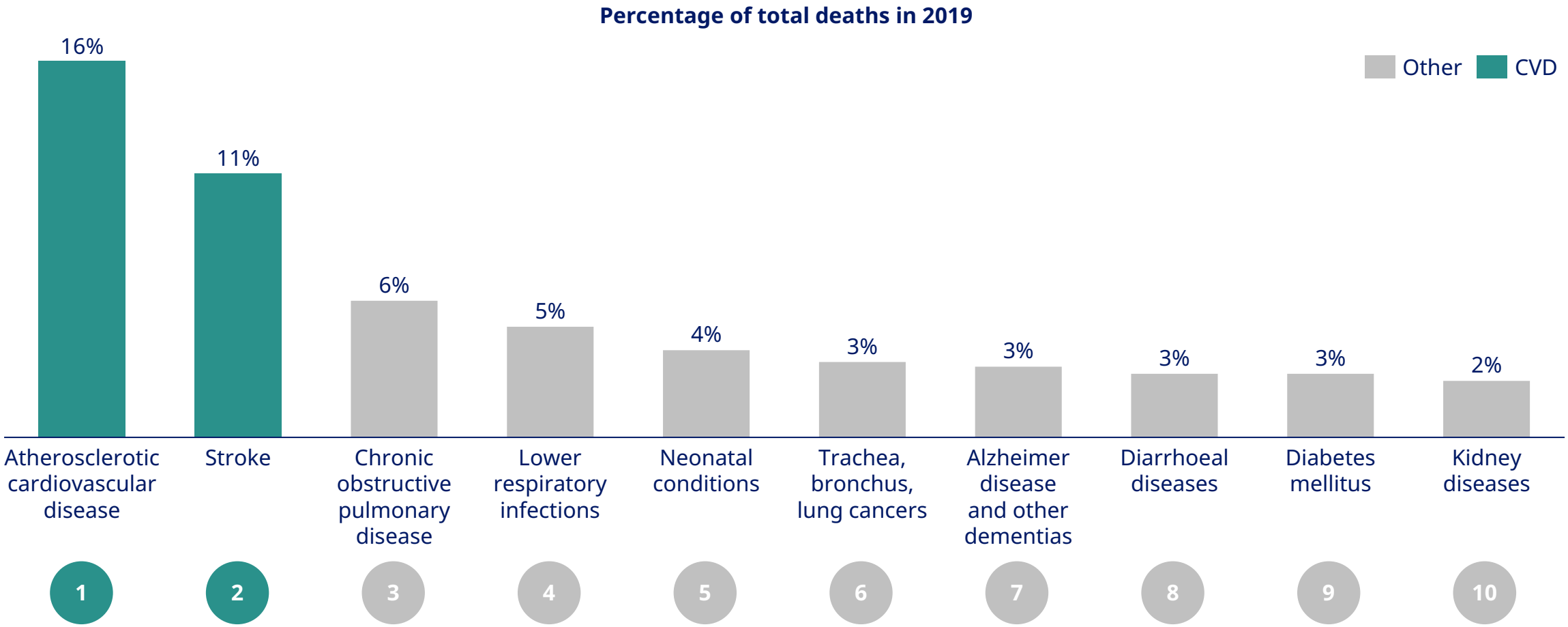
- Impaired contractility
- Stretched and thin ventricle

Pipeline includes potential disease modifying and curative treatments

Symptom relief	Disease modifying	Curative
Today's marketed treatments	**Prothena** (PRX004)	**Heartseed** (HS-001)
		
	A monoclonal antibody designed to deplete the amyloid placks associated with ATTR–CM in a niche population	• HS-001 use iPSC-derived cardiomyocytes to treat HF • The cells are treated in a solution to enhance survival and/or engrafment

ATTR-CM: Transthyretin Amyloid Cardiomyopathy, iPSC: Induced pluripotent stem cells; HF: Heart failure

There is still room for innovation with a high unmet need in CVD



CVD: Cardiovascular disease
Source: "The top 10 causes of death", WHO, 9 December 2020 (ASCVD denoted as ischaemic heart disease)

An innovative late-stage CVD pipeline provides opportunities to make a difference for many patients

Focus areas

Near-term

Leverage broader CV indications to establish presence with Cardiologists and build an adequate PCP footprint for entry of stand-alone CVD product

Medium-term

Utilise leading scientific and commercial capabilities to launch first CVD stand-alone product

Long-term

Expand pipeline with differentiated MoAs through leading discovery and translational capabilities

Examples of unmet needs in CVD pipeline

Category	Broader indications		Stand-alone CVD
Study Current phase	**HFpEF** Phase 3 Sema 2.4mg	**PAD** Phase 3 Sema 1.0mg	**ATTR-CM** Phase 2 to be initiated in 2022 PRX004 (NN6019)
Global unmet need (people)	~13m	~200m	No consensus (estimated 0.1-2.8 cases per 10,000 in EU)
Potential differentiators	1st in class indication[1]	First and only for T2D	Reverse disease pathology
Potential launch year	2023/24	2023/24	2028

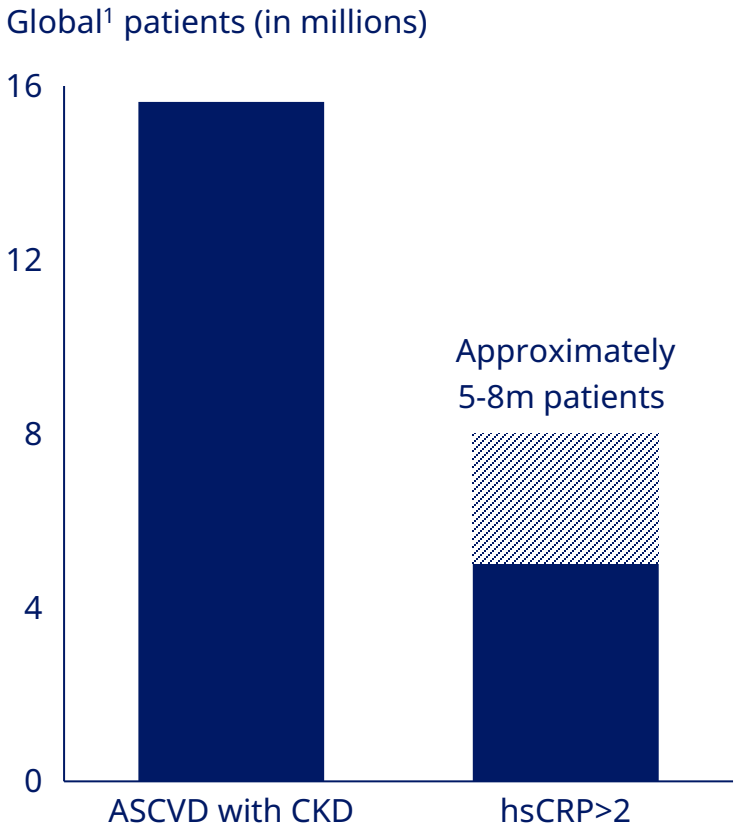
1 Specifically for a functional outcomes trial in an obese patient population

PCP: Primary Care Physician; CV(D): Cardiovascular Disease; MoA: Mode of Action; HFpEF: Heart failure with preserved ejection fraction; PAD: Peripheral arterial disease; ATTR-CM: Transthyretin Amyloid Cardiomyopathy; T2D: Type 2 Diabetes

Sources: HFpEF: Savarese G, Lund LH. Global Public Health Burden of Heart Failure, 3 April 2017; PAD: Shu J, Santulli G. Update on peripheral artery disease: Epidemiology and evidence-based facts, 22 May 2018; ATTR-CM: Orphan Maintenance Assessment Report for tafamidis, EMA, 17 February 2020

Ziltivekimab aspires to address an unmet need in more than 5 million people

Ziltivekimab aspires to reduce MACE in people with ASCVD and CKD



Critical success factors to commercialise ziltivekimab

Market building	Focus areas	Investment levels
Targeted HCP outreach and relationship building	• Increase presence with key prescriber base being cardiologists and PCPs • Enhance awareness of inflammatory burden in CVD with KOLs and HCP associations	●
Successful payer engagement	• Utilise ZEUS read-out to quantify anti-inflammatory clinical benefit in ASCVD patients with CKD vs Standard of Care	◑
Integrated evidence generation	• Understand hsCRP and inflammation, epidemiology of disease and socio-economic burden of disease	◑

○ Low ● High

[1] Includes US, EU5 (Germany, France, Spain, Italy, United Kingdom) and Japan
MACE or major adverse cardiovascular events includes CV death, non-fatal MI or non-fatal stroke; ASCVD: Atherosclerotic cardiovascular disease; CKD: Chronic kidney disease; HCP: Healthcare professional; PCP: Primary care physician
KOL: Key opinion leader; hsCRP: High-sensitivity C-reactive protein

Closing remarks

Entering a growing market with a clear strategy and focus to build a presence in CVD

High unmet needs and new innovations are required to help improve treatment outcomes

Pre-launch activities are initiated and ongoing to ensure successful commercialisation of CVD pipeline