Rare disease

CMD22
CAPITAL MARKETS DAY

3 MARCH


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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
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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 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.

Building upon a 40-year legacy to capture the Rare disease strategic opportunity for Novo Nordisk

Rare disease at a glance – a key strategic pillar of Novo Nordisk

A significant and robust business pillar

- **14%** Share of sales
- **16%** Share of profit
- **4%** Sales growth
- **47%** Operating margin

A strategic portfolio play in specialty care

- Few patients with high unmet needs
- Specialised healthcare base
- Specialised scientific and commercial teams

A platform to spearhead new trends

From pure drug innovation to **integrated therapeutic solutions** adding diagnostics, drug, digital, device and data to new medicines

Looking ahead

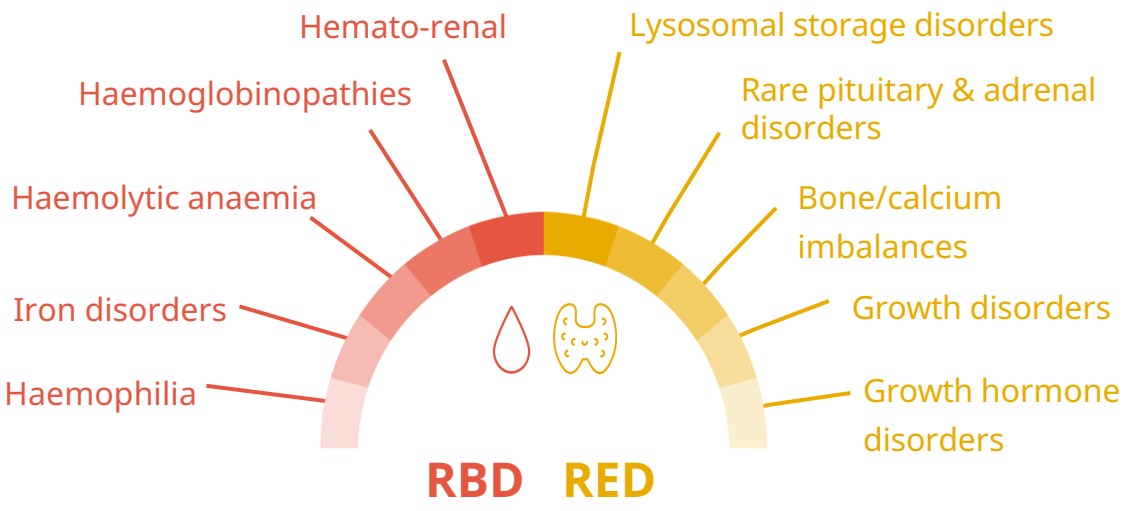
Novo Nordisk Rare disease

DARE FOR RARE

Note: Sales growth at Constant exchange rate and figures are for the financial year of 2021
Source: Company reported sales

Behind the renaming are ongoing efforts since 2019 to support the evolution and transformation of the Rare disease unit

A strategy anchored in Rare blood and endocrine disorders



Rare blood disorders **Rare endocrine disorders**

Three strategic horizons towards 2030

Today

Short-term
Maximise current portfolio

esperoct® turoctocog alfa pegol
nordiitropin® (somatropin) injection
refixia® nonacog beta pegol
NovoSeven® RT Coagulation Factor VIIa (Recombinant)

Medium-term
Succeed with next-generation launches

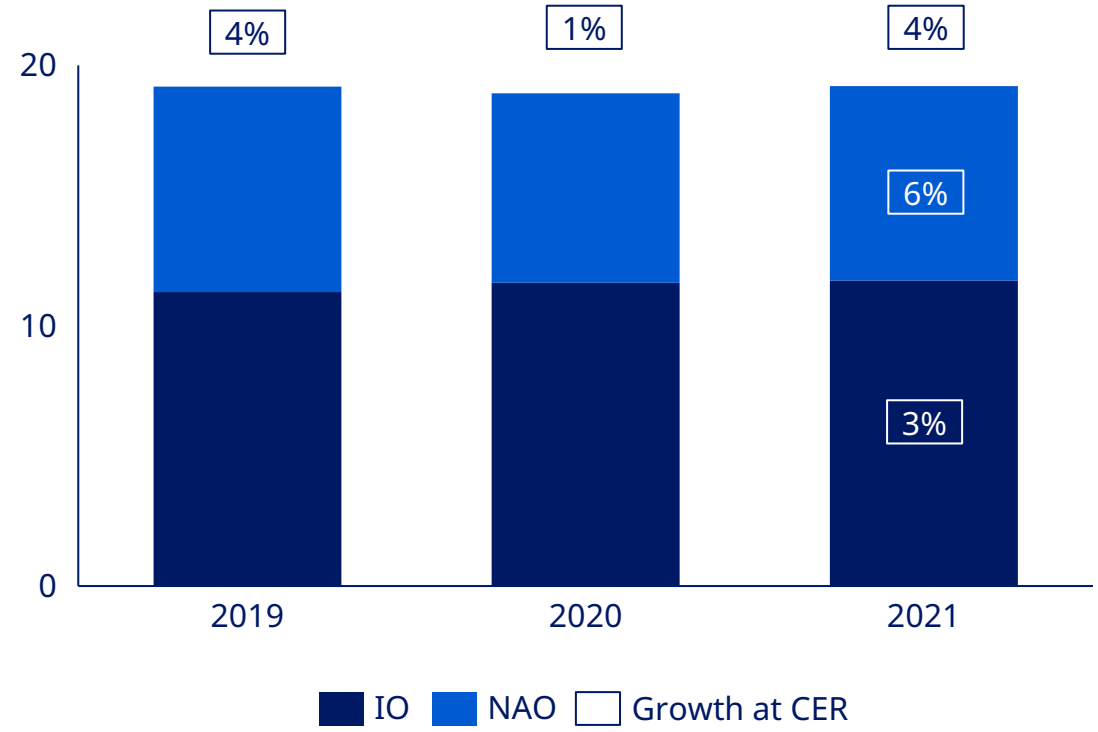
SOGROYA® somapacitan
Concizumab & Mim8
Nedosiran

Long-term
Expand from core

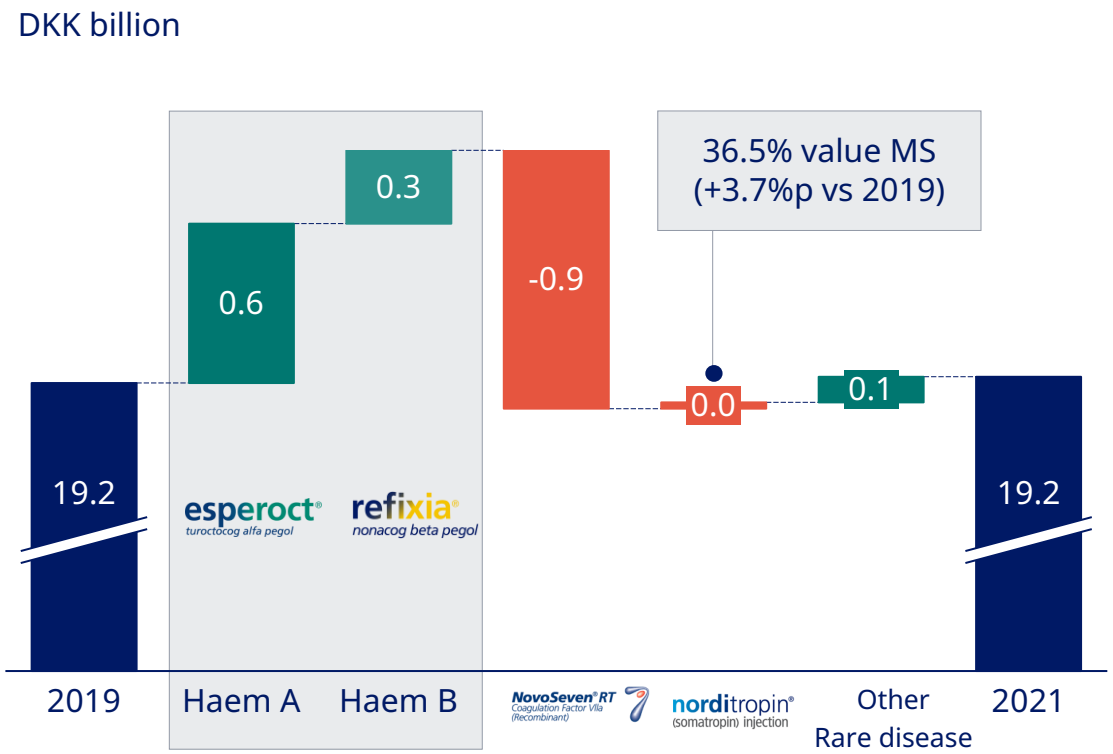
New disease areas via accelerated internal and external innovation

Rare disease is delivering on the sustained growth aspiration

Rare disease franchise is back to growth



With key products in current portfolio as growth drivers



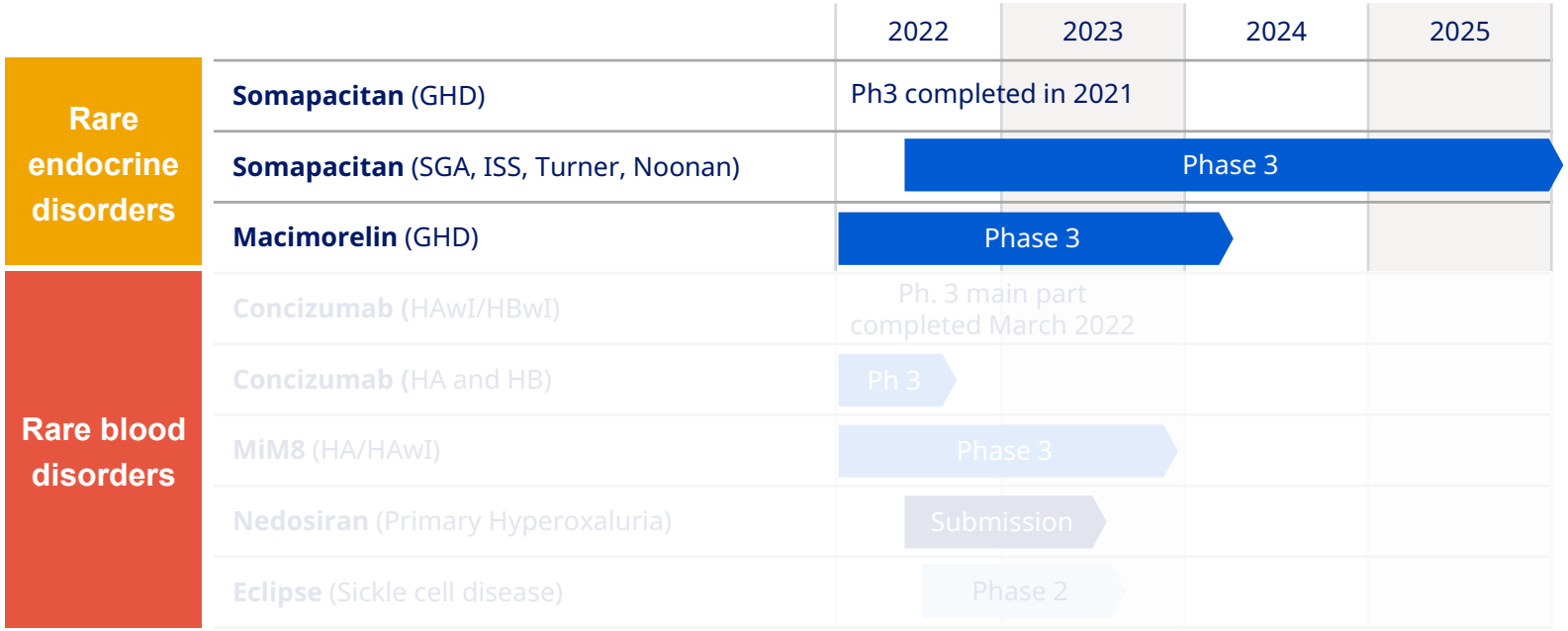
Note: Other Biopharm includes Vagifem® and Activelle®. Global Norditropin® value market share as of December 2021 vs December 2019
CER: Constant exchange rate, MS: Market share; Haem A: Haemophilia A; Haem B: Haemophilia B; IO: International Operations; NAO: North America Operations
Source: Company reported sales, IQVIA, MAT Dec 2021

Driving change and addressing the unmet need within Rare disease with a competitive late-stage pipeline

Strengthening and progressing the Rare disease pipeline

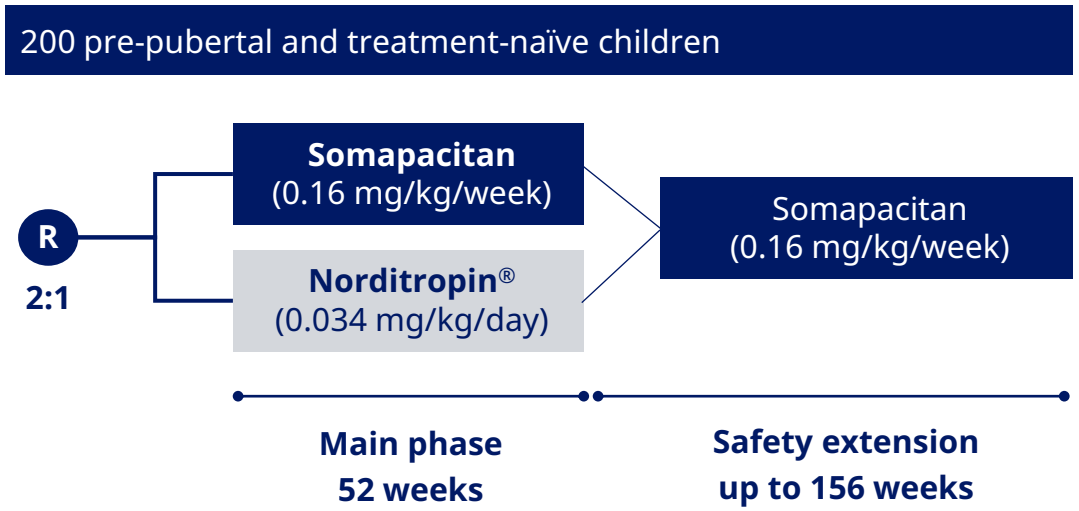
- Better individual patient outcomes with improved safety and efficacy across RBD and RED
- Accelerate innovation and speed of trial execution
- Develop integrated solutions (drug, data, diagnostics, digital, device)
- Maximise lifetime value of therapeutic solutions and develop full portfolio

Rare disease development pipeline



RBD: Rare blood disorders; RED: Rare endocrine disorders; Ph: Phase; HA/HB: Haemophilia A and Haemophilia B; HAwI/HBwI: Haemophilia A and B with inhibitors; GHD: Growth hormone deficiency; SGA: Small for gestational age; ISS: Idiopathic short stature

Once-weekly Sogroya® was investigated in children with growth hormone deficiency in the phase 3 trial, REAL



Objective

- To compare the efficacy and safety of once-weekly somapacitan vs Norditropin® on longitudinal growth in children with growth hormone deficiency

Inclusion criteria

- Treatment-naïve pre-pubertal patients with a confirmed diagnosis of growth hormone deficiency with impaired height and height velocity

Primary endpoints

- Height velocity at week 52

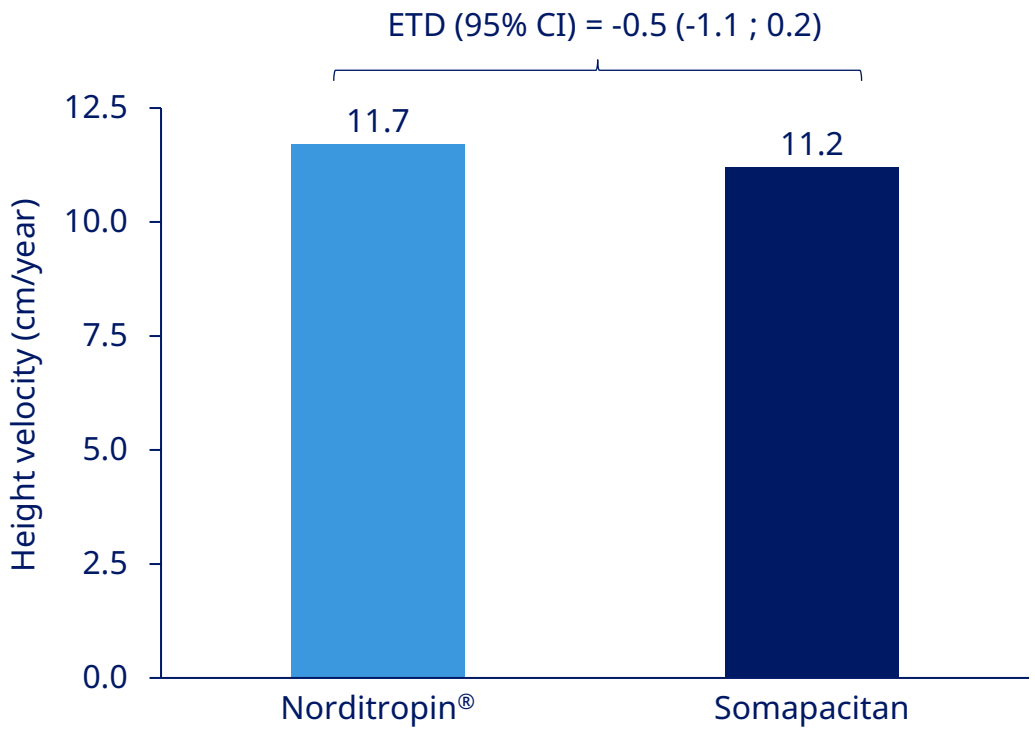
Secondary endpoints

- Height velocity SD score and height SDS
- IGF-I SDS, bone age, fasting plasma glucose and HbA_{1c}

GHD: Growth hormone deficiency; AGHD: Adult growth hormone deficiency; R: Randomisation; SDS: Standard deviation score; IGF-I SDS: Insulin growth factor-1 standard deviation score; HbA1c: haemoglobin A1c,

Sogroya® phase 3 trial successfully completed with aspirational target product profile achieved

Phase 3a trial results in children with GHD



Key highlights

Efficacy

- Non-inferiority versus Norditropin® for the primary endpoint, height velocity, at week 52 was confirmed
- IGF-I SDS, bone age and glucose metabolism were all similar between somapacitan and Norditropin®

Safety and tolerability

- Overall the safety profile of somapacitan appeared to be similar to the well-known safety profile of daily GHD treatment
- No local tolerability issues were identified

Other treatment parameters

- Significantly reduced treatment burden[1] compared to Norditropin®

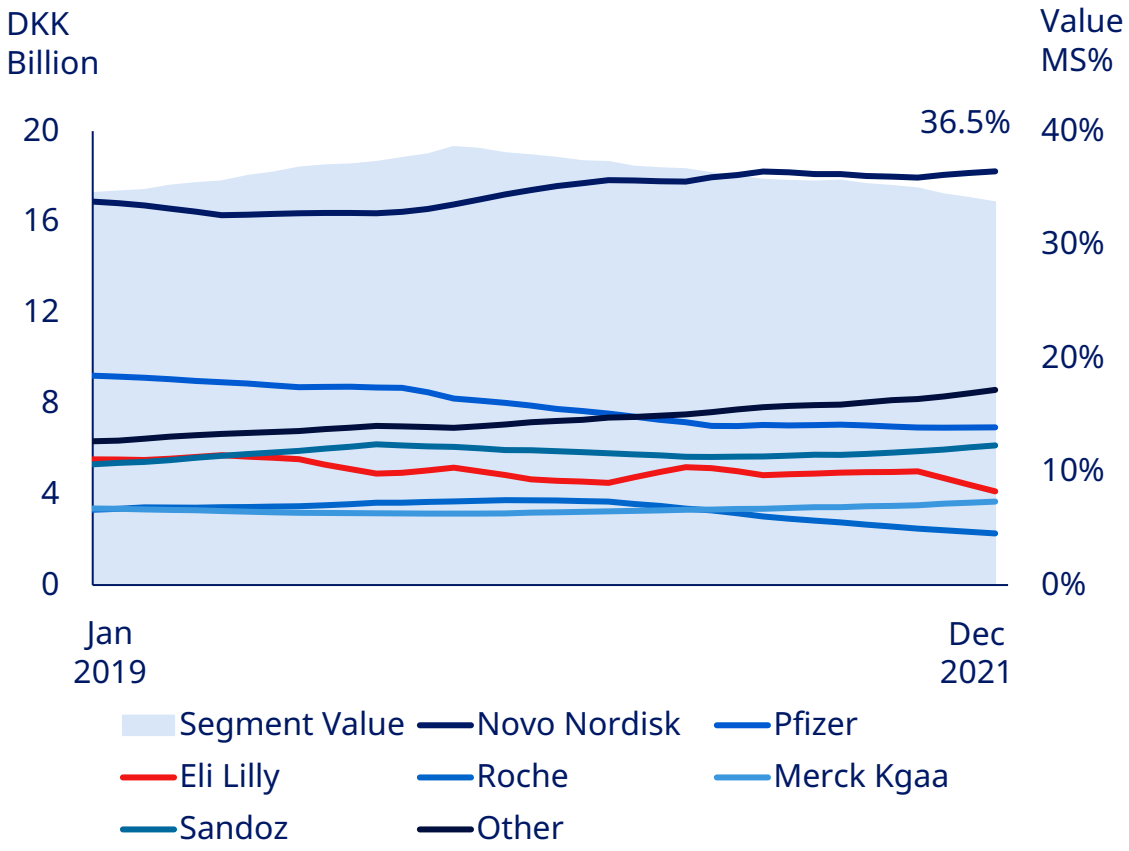
Next steps

- Submission expected in Q2 2022

[1] Measured using patient reported outcome TB-CGHD-P (Treatment burden measure - child growth hormone deficiency – parent)
ETD: Estimated treatment difference; IGF-I SDS: Insulin growth factor-1 standard deviation score; GHD: Growth hormone deficiency; IGF-I SDS: Insulin growth factor-1 standard deviation score

Within Rare endocrine disorders, Sogroya® would be an opportunity for patients with growth disorders

Novo Nordisk leadership in competitive hGH market



A portfolio offering across markets

SOGROYA® somapacitan

Sogroya® launches

- Once-weekly efficacious treatment on par with Norditropin®
- Appears to have safe profile and no injection site reactions
- Simple and easy-to-use device
- Phase 3 trial towards broad range of indications (e.g. SGA, Turner, Noonan, ISS) to expand the market

norditropin® (somatropin) injection

Norditropin® strategy

- Accompany markets slower to transition and specific patient groups
- Apply broad label across eight indications

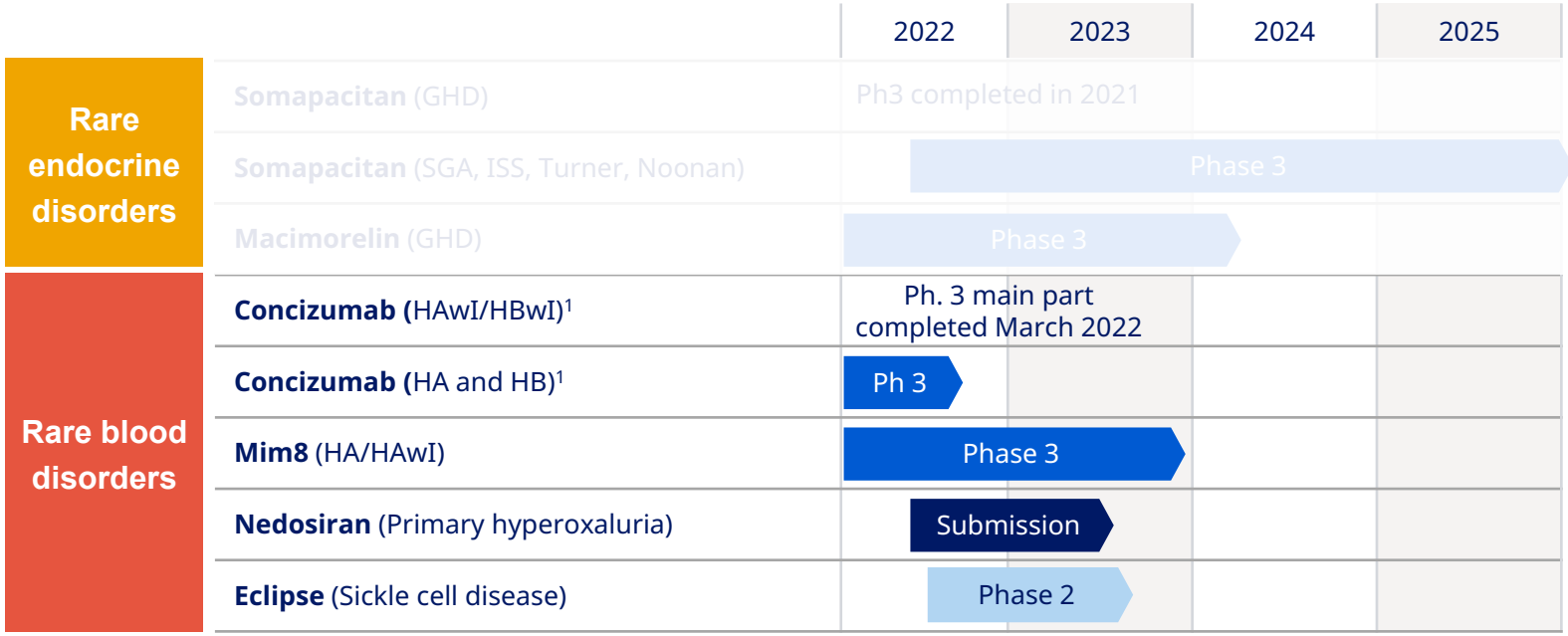
hGH: Human growth hormone; SGA: Small for gestational age, ISS; Idiopathic short stature
Source: IQVIA, MAT Dec 2021

Driving change and addressing the unmet need within Rare disease with a competitive late-stage pipeline

Strengthening and progressing the Rare disease pipeline

- Better individual patient outcomes with improved safety and efficacy across RBD and RED
- Accelerate innovation and speed of trial execution
- Develop integrated solutions (drug, data, diagnostics, digital, device)
- Maximise lifetime value of therapeutic solutions and develop full portfolio

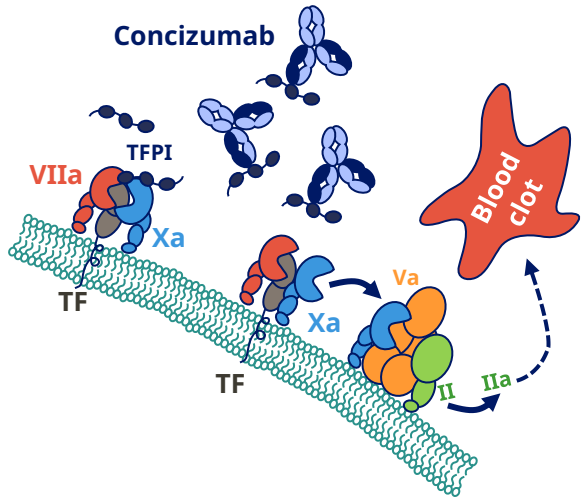
Rare disease development pipeline



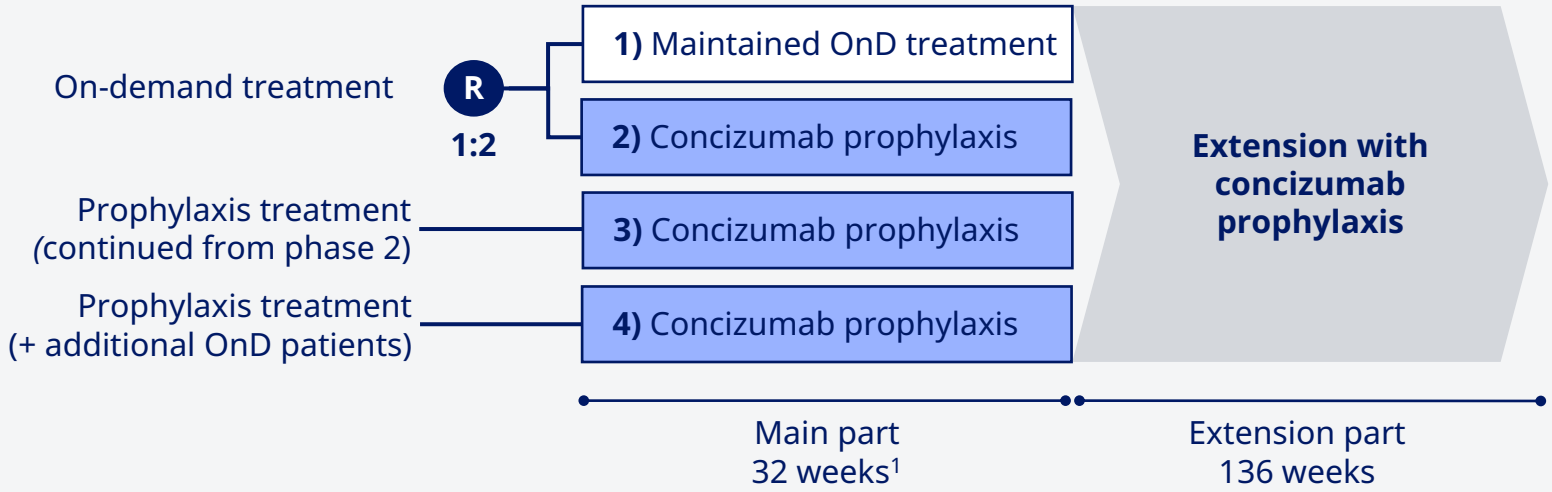
[1]Arrow indicative of main part; extension part of trials continuing until 2024
RBD: Rare blood disorders; RED: Rare endocrine disorders; Ph: Phase; HA/HB: Haemophilia A and Haemophilia B; HAwI/HBwI: Haemophilia A and B with inhibitors; GHD: Growth hormone deficiency; SGA: Small for gestational age; ISS: Idiopathic short stature

Explorer 7 trial evaluated safety and efficacy of concizumab in 132 haemophilia A and B patients with inhibitors

Concizumab binds TFPI, enabling thrombin generation and clot formation



Explorer 7 trial design



Trial Objective

Assess the efficacy of concizumab prophylaxis vs no prophylaxis in reducing number of bleeding episodes in adults and adolescents with haemophilia A and B with inhibitors

Primary endpoint

Number of treated bleeding episodes from start of treatment to the end of the main phase

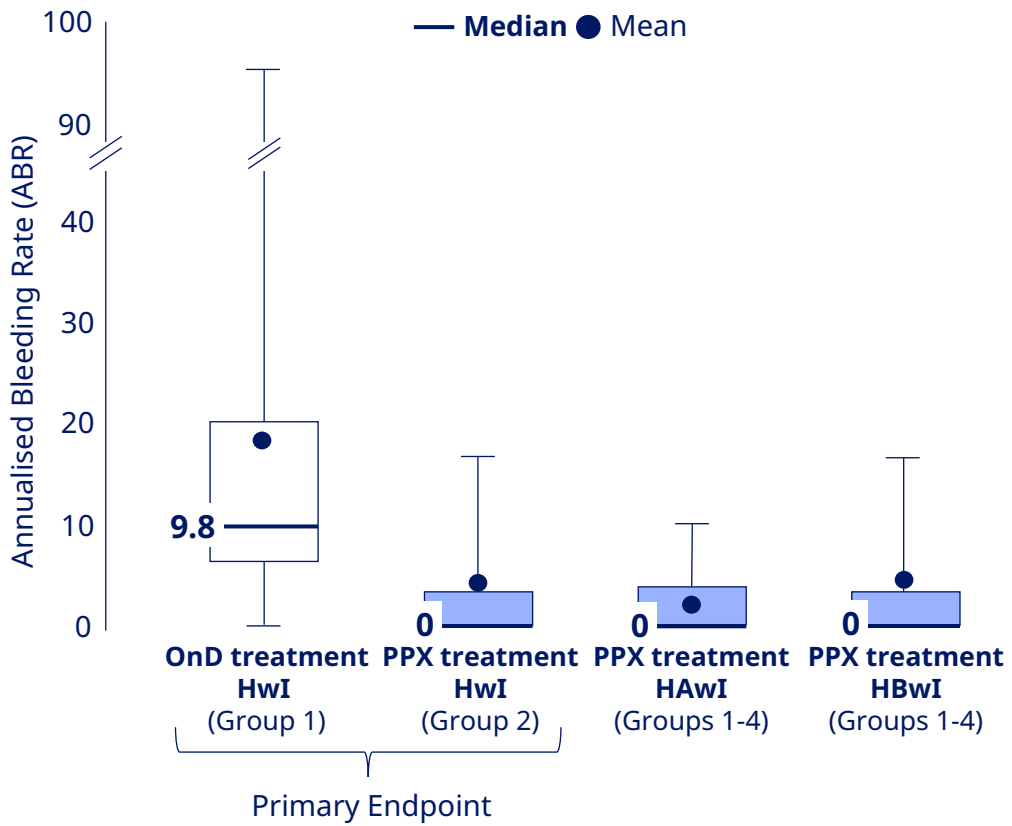
Key inclusion criteria

- Males ≥12 years with haemophilia and inhibitors, treated with bypassing agents within last 24 weeks
- For on-demand, minimum six bleeding episodes within last 24 weeks

[1]At least 24 weeks for arm 1
TF: Tissue factor; TFPI: Tissue factor pathway inhibitor; OnD: On-demand: R: Randomisation

In the Explorer 7 trial, concizumab reduced the number of bleeds in adults and adolescents with inhibitors

Explorer 7 trial results: Annualised bleeding rate per patient group



Key highlights

Efficacy

- **Median ABR was 0** for concizumab prophylaxis treatment, compared to 9.8 in the on-demand treatment group
- Estimated mean ABR was 1.7 for concizumab prophylaxis treatment, compared to 11.8 in the on-demand treatment group
- For patients on concizumab prophylaxis, **64% had 0 bleeds** in Group 2

Safety

- Concizumab appeared to have a **safe and well tolerated** profile

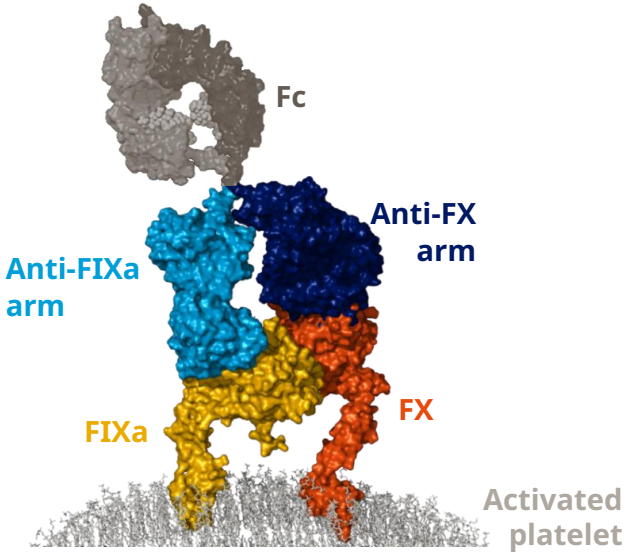
Next steps

- US submission for inhibitor indications expected later in 2022
- Explorer8 in non-inhibitor patients is ongoing
- US submission for non-inhibitor indications (HA/HB), and EU submission in all indications, expected in 2023

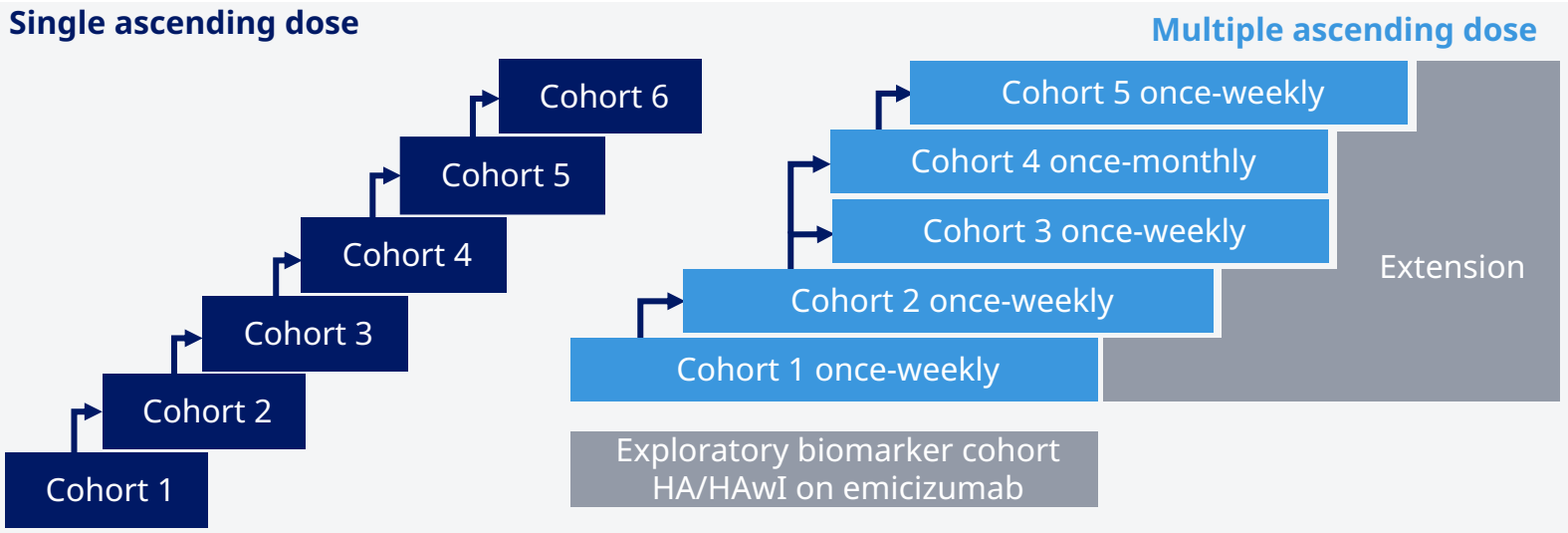
Note: The box represents Q1-Q3 (25th to 75th percentile). Whiskers are 5th and 95th percentile.
HA: Haemophilia A; HB: Haemophilia B; HAwI: Haemophilia A with inhibitors, HBwI: Haemophilia B with inhibitors; OnD: On-demand; PPX: Prophylaxis; ABR annualised bleeding rate

Mim8 was investigated in a combined phase 1/2 trial

Mim8 is a bispecific antibody with strong activity at site of bleeding



Single dose in healthy trial participants and 12 week[2] multiple dose haemophilia A patients with/without inhibitors



Trial Objective

- To investigate the safety and tolerability of subcutaneous Mim8
- To investigate the pharmacokinetics and pharmacodynamics of subcutaneous Mim8

Trial endpoints:

- Primary: Number of adverse events
- Secondary: Maximum concentration and thrombin peak height
- Exploratory: Number of treated bleeding episodes

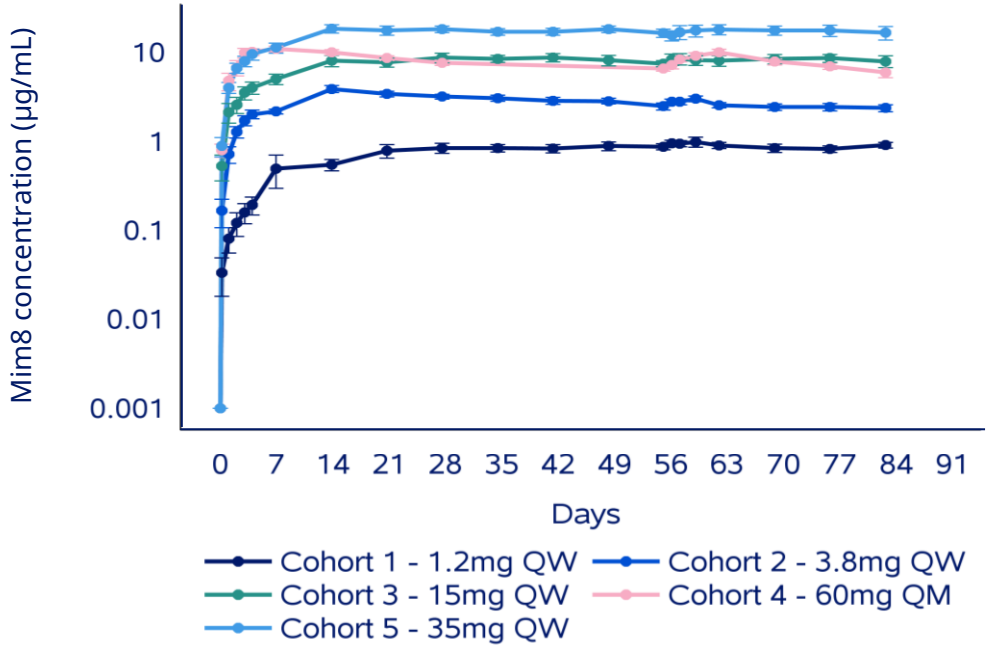
Key inclusion criteria

- Healthy trial participants (single ascending dose)
- Subjects with haemophilia A, with or without FVIII inhibitors (multiple ascending dose)

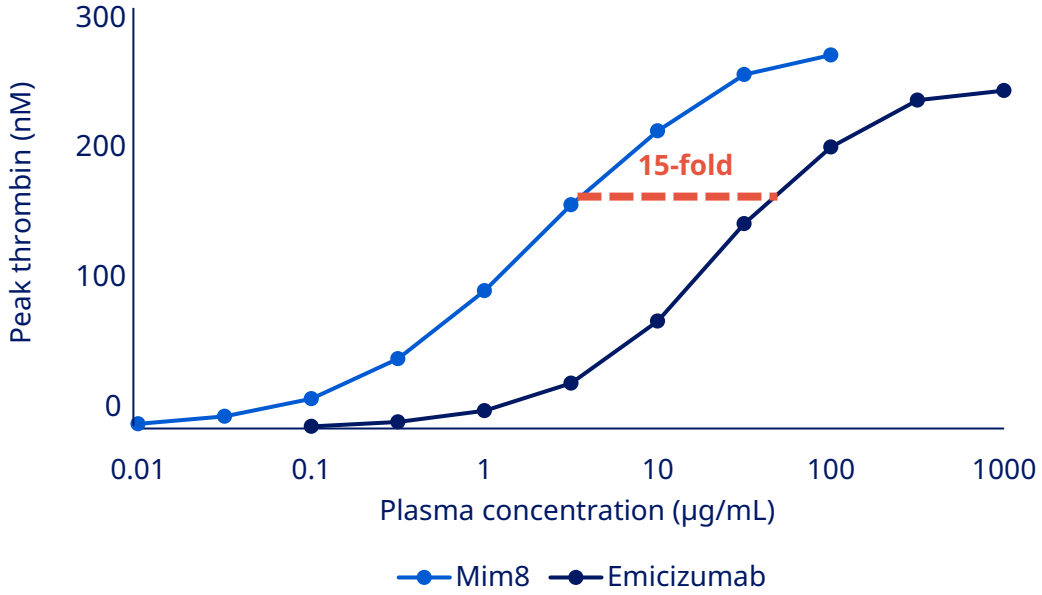
[1] 12-weeks followed by an extension period
HA: Haemophilia A; HAwI: Haemophilia A with inhibitors

Mim8 phase 1/2 trial reads out with PK/PD data supporting a once-monthly profile and improved dosing

Mim8 pharmacokinetic properties support weekly and monthly dosing



Higher potency of Mim8 vs emicizumab enabling a low dosing volume



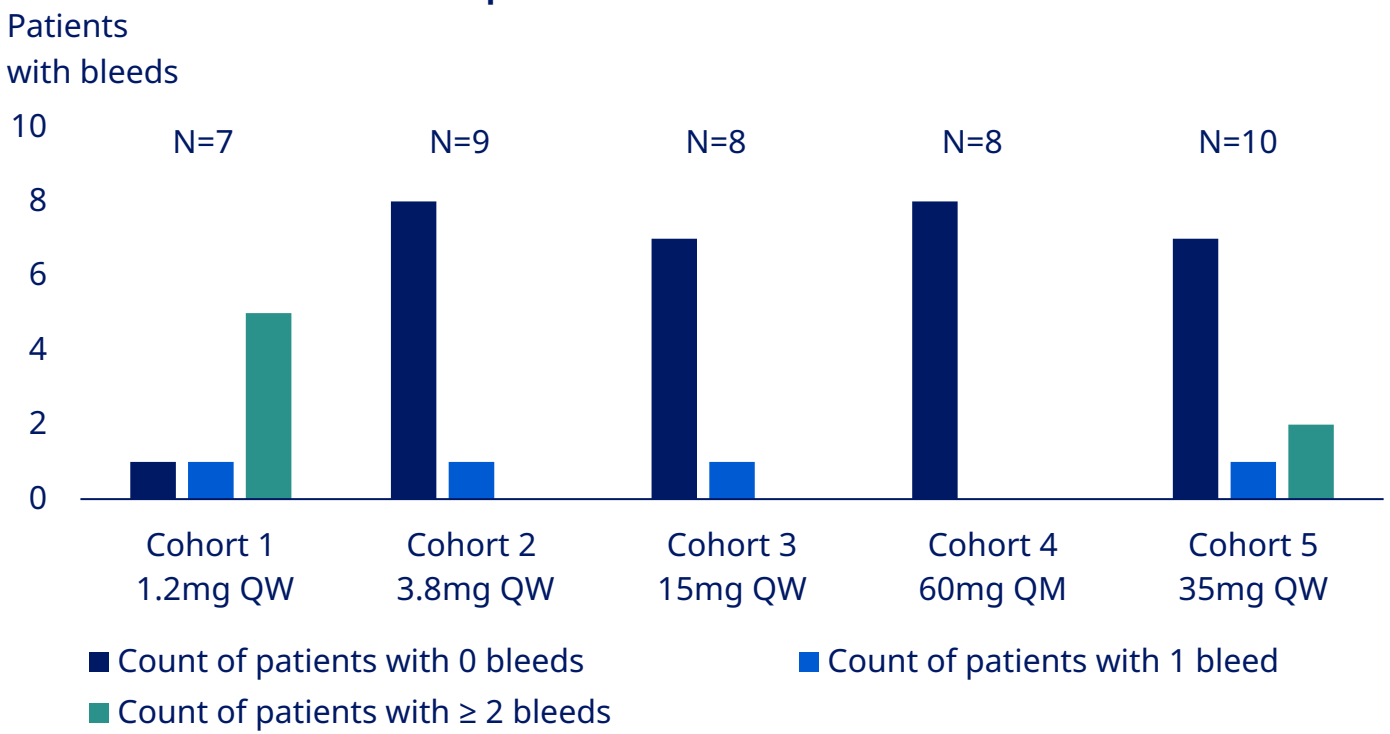
- Mim8 concentration profiles increased with dose
- Mean concentrations at steady state were comparable for Cohort 3 (QW) and Cohort 4 (QM)

- The PD marker, peak thrombin generation, increased with Mim8 dose
- In vitro exposure-response results show a 15-fold higher potency of Mim8 compared to emicizumab

PK: Pharmacokinetics; PD: Pharmacodynamics; QW: Once-weekly; QM: once-monthly

In the phase 1/2 trial, Mim8 appeared to have a safe and well tolerated profile and read out with exploratory efficacy

Low number of patients with treated bleeds after cohort 1



Exploratory analysis implied that >70% of patients enrolled had no bleeds in the 12 weeks

Mim8 safety summary in phase 1/2 trial

Adverse events

- No dose-dependency on rates, causality, type or severity of adverse events
- No thromboembolic events or thrombotic
- One serious adverse event deemed unrelated to trial product and two hypersensitivity
- Three mild injection site reactions

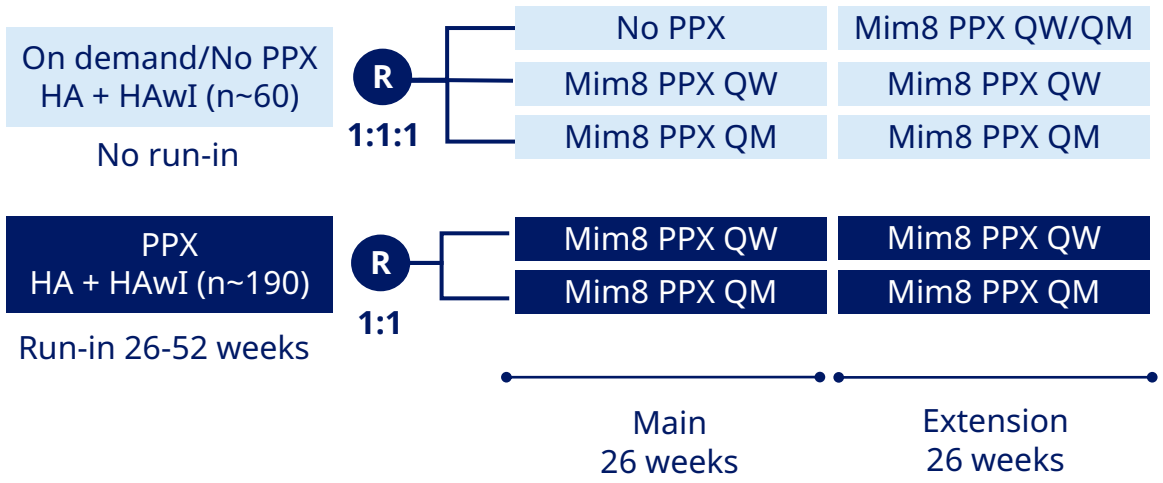
Anti-Mim8 antibodies

- No antibodies detected

QW: Once-weekly, QM: Once-monthly; N=Number of patients

Accelerated phase 3 programme towards establishing Mim8 as a once-monthly treatment reducing burden of care

FRONTIER 2: Mim8 phase 3 pivotal trial



Trial design

- Novel and accelerated design minimising time from phase 2 into phase 3, with phase 3 dosing expected to start in Q4 2022
- Testing for weekly and monthly prophylaxis treatment for previously on-demand or prophylaxis patients
- Trial population: Adults and adolescent patients with HA/HAwI

Trial objective

- On-demand: Superiority of Mim8 prophylaxis (PPX) vs no prophylaxis
- Prophylaxis: Non-inferiority of Mim8 prophylaxis vs standard of care[2] prophylaxis run-in period

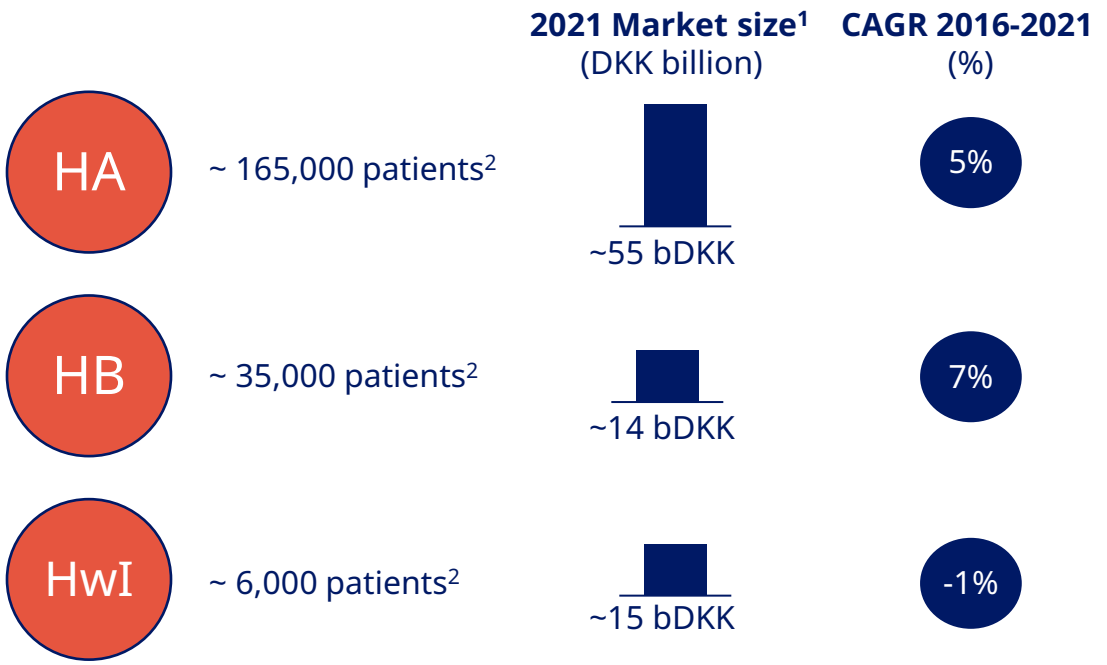
Key trial endpoints

- ABR for treated bleeds over 26 weeks of treatment
- Overall safety of Mim8 prophylaxis including occurrence of anti-Mim8 antibodies and injection site reactions

[1] Run-in only applicable for prophylaxis arms. [2] Standard of care implies standard half-life FVIII product or FVII product or extended half-life FVIII product
PPX: Prophylaxis; HA: Haemophilia A; HAwI: Haemophilia A with inhibitors; R: Randomisation; ABR: Annual bleeding rate; QW: Once-weekly; QM: once-monthly; N=Number of patients

Haemophilia is a competitive market, but with a severe unmet medical need where no single therapy is right for every patient

Overview of the global haemophilia market



+20,000 patients suffering from adjacent bleeding disorders[3] and ~85,000 suffering from von Willebrand disease

Market dynamics

- **Unmet need** remains unserved
- Currently, ~**15% patients on prophylaxis** treatment
- I.V. and short half-life products (recombinant or plasma products) have **been standard of care** for many years
- Recently, **treatments have significantly progressed** with cross-segment, extended half-life and subcutaneously administered products
- Increased demand for **individualisation of care**
- Increased demand for **management of comorbidities**

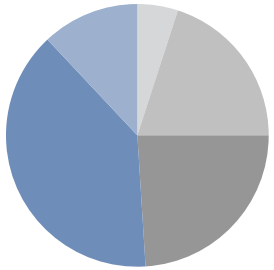
[1] Based on companies' reported sales 2021 and Evaluate pharma; [2] WFH annual survey 2020 (numbers may be understated as 120 out of 147 countries responded). [3] included in adjacent bleeding disorders are Glanzmann-Thrombasthenia, FXIII deficiency, FVII deficiency. Note: Patient numbers refer to diagnosed patients.
HA: Haemophilia A, HB; Haemophilia B, HwI; Haemophilia with inhibitors; I.V.: Intravenous

Concizumab and Mim8 to complement the existing portfolio and aim to add to the individualisation of patient care

Novo Nordisk Rare disease is well-placed with market expected to remain fragmented

Estimated global therapeutic split in HA as of 2030

ILLUSTRATIVE



Gene therapy
Extended half-life
Plasma derived
Cross-segment
Standard half-life

	HwI	HA	HB
Current	NovoSeven® RT Coagulation Factor VIIa (Recombinant)	esperoct® turoctocog alfa pegol novoeight®	refixia® nonacog beta pegol
Future	Concizumab		
Future	Mim8[2]		

Novo Nordisk's future offerings to answer increasing individual needs

Concizumab ambition

- Safe, effective and well tolerated with the ability to individualise
- Once-daily, subcutaneous administration for consistent level of everyday protection
- New MoA supporting PPX use across all haemophilia types

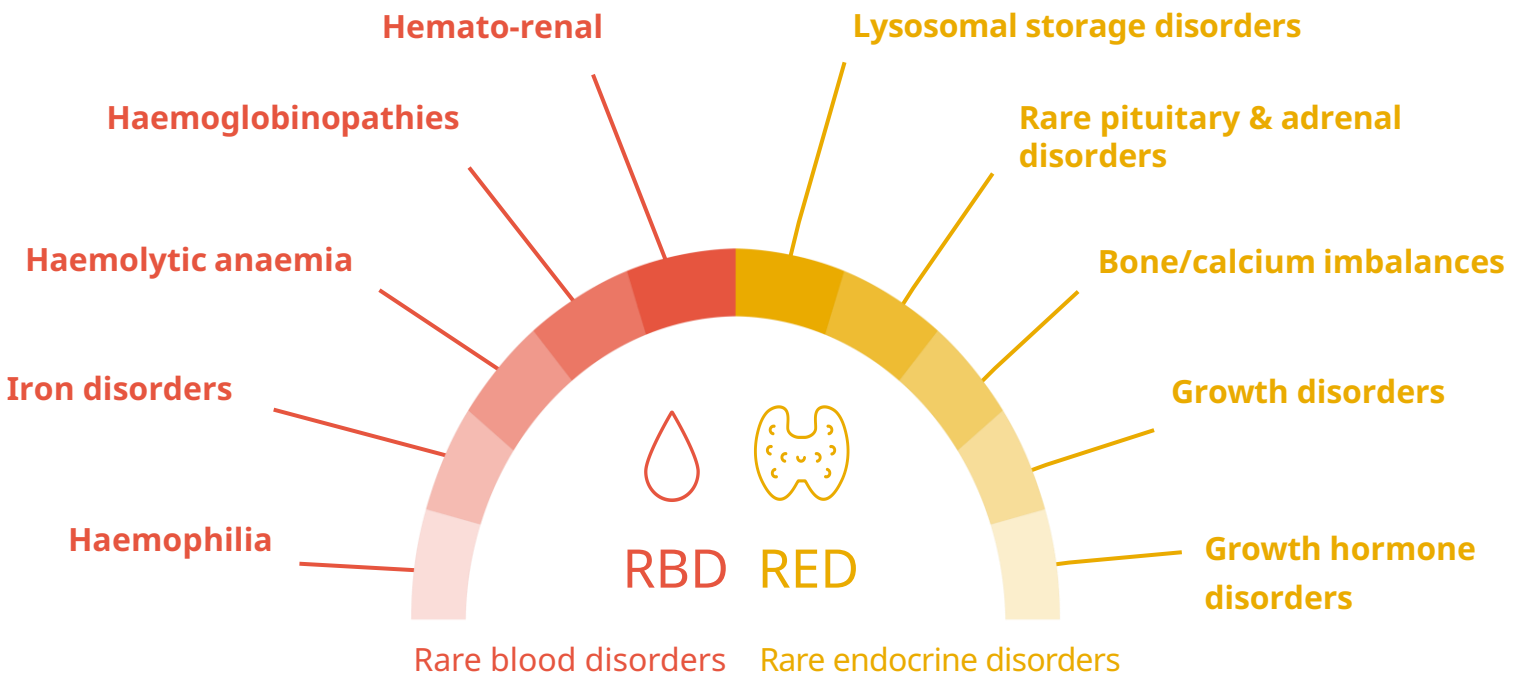
Mim8 ambition

- Safe, effective and well tolerated prophylaxis treatment
- → Subcutaneous once-weekly or once-monthly treatment in convenient device
- Lower treatment burden for patients

[1]Based on company reported sales 2021 and Evaluate. [2] Within inhibitor segment, Mim8 is targeting HAwI
MoA: Mode of action; PPx: Prophylaxis; HA/HB: Haemophilia A and Haemophilia B; HAwI/HBwI: Haemophilia A and B with inhibitors

In the early pipeline, efforts are ongoing to ensure next wave of innovative assets as treatments for severe conditions

A large and growing space of rare diseases exists



Well-positioned to further utilise competencies across RBD and RED

- Heritage and expertise in rare disease space
- Broad array of technological platforms[1]
- Accelerated internal innovation efforts
- External innovation and partnership co-creation

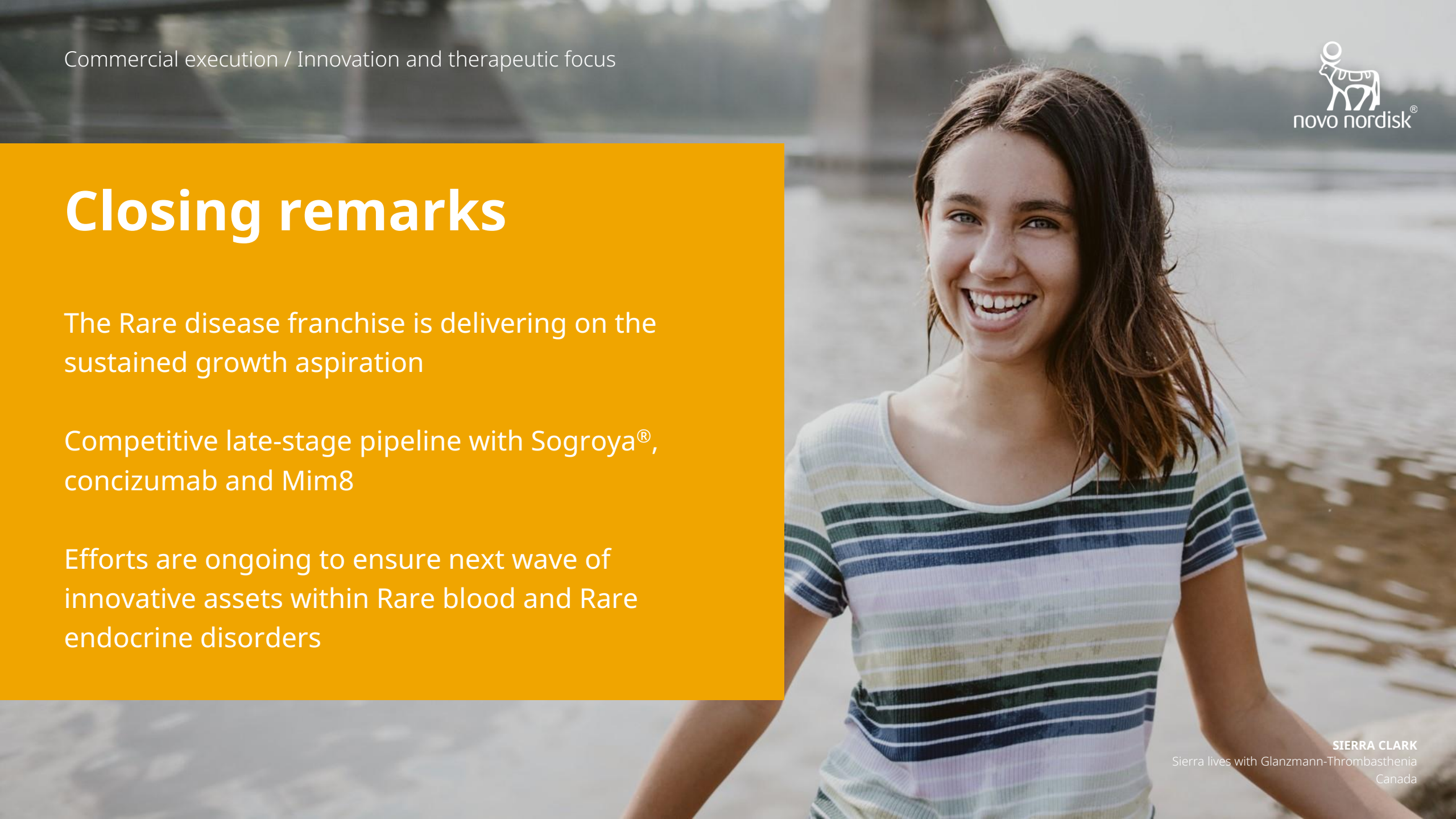
[1]Technological platforms include gene editing from 2SeventyBio, cell therapy, proteins and peptides, RNAi from Dicerna, oral platforms amongst others
RBD: Rare blood disorders; RED: Rare endocrine disorders

Closing remarks

The Rare disease franchise is delivering on the sustained growth aspiration

Competitive late-stage pipeline with Sogroya®, concizumab and Mim8

Efforts are ongoing to ensure next wave of innovative assets within Rare blood and Rare endocrine disorders



SIERRA CLARK
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