R&D strategy

Mads Krogsgaard Thomsen
EVP and Chief Science Officer
Forward-looking statements

Novo Nordisk’s reports filed with or furnished to the US Securities and Exchange Commission (SEC), including the company’s Annual Report 2016 and Form 20-F, which are both filed with the SEC in February 2017 in continuation of the publication of the Annual Report 2016, 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.

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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 presentation, whether as a result of new information, future events or otherwise.

Important drug information

• Victoza® (liraglutide 1.2 mg & 1.8 mg) is approved for the management of type 2 diabetes only
• Saxenda® (liraglutide 3 mg) is approved in the US and EU for the treatment of obesity only
R&D organisation successfully advanced early and late-stage projects since last Capital Markets Day¹

<table>
<thead>
<tr>
<th>Project</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Submitted</th>
<th>Approved</th>
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</thead>
<tbody>
<tr>
<td>Xultophy®</td>
<td>Phase 1 initiated</td>
<td>Phase 2</td>
<td>Phase 3a</td>
<td>Submitted in US/EU/JP</td>
<td>US approval</td>
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<td>Fiasp®</td>
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<td></td>
<td>Phase 3a</td>
<td></td>
<td>US/EU approval</td>
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<td>oral semaglutide</td>
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<td>Phase 2</td>
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<td>Anti-IL 21 &amp; lira – T1D</td>
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<tr>
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<td>NN1406 - PI406</td>
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<tr>
<td>semaglutide obesity</td>
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<td>NN9277 – GG-co-agonist</td>
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<td>NN9499 – FGF21 obesity</td>
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<td>NN9423 – Tri-agonist 1706</td>
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<td>semaglutide NASH</td>
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</table>

1 The last Capital Markets Day took place 17 November 2015
2 Projects still in phase 1 (G530L, AM833, PYY1562 and LAI287) or discontinued projects (LATIN, OI338GT and OI320GT oral insulin) are not included
3 Study conducted in adult growth hormone disorder
QW: Once-weekly; Lira: Liraglutide; T1D: Type 1 diabetes; QD: Once-daily; GH: Growth hormone; sc: Subcutaneous; NASH: Non-alcoholic steatohepatitis
Innovation bar has been raised due to increased maturity of core areas and market access challenges

High level of innovation achieved within basal insulin

- Biology optimised insulin
- Once-weekly
- Long-acting
- Insulin analogue
- NPH
- Powder

Raised innovation bar for the GLP-1 franchise

- Second generation oral GLP-1 analogue
- First generation oral GLP-1 analogue
- Once-weekly human GLP-1 analogue
- Once-daily human GLP-1 analogue
- Native GLP-1

Growing market challenges

- Regulatory requirements
- Biosimilar competition
- Political scrutiny
- Market access constraints

NPH: Neutral protamine Hagedorn insulin
Novo Nordisk R&D strategy and priorities

**STRATEGIC PRIORITIES**

**Strengthen leadership in DIABETES CARE**

- Develop disruptive insulin and GLP-1 based products with distinct clinical and/or delivery advantages
- Develop novel mechanisms that reverse the course of diabetes, act as insulin sensitisers and improve hard clinical endpoints

**Strengthen leadership in OBESITY CARE**

- Develop new biologics combined with GLP-1 to achieve >15% weight loss

**Pursue leadership in HAEMOPHILIA**

- Pursue subcutaneous delivery of long-acting coagulation factors and bypassing agents

**Strengthen leadership in GROWTH DISORDERS**

- Bring once-weekly growth hormone to market and expand indications

**Expand into other SERIOUS CHRONIC DISEASES**

- Enter NASH, CVD and CKD by leveraging GLP-1 and other internal assets as well as licensing external opportunities

**Innovate to improve patient outcomes and drive growth**

CKD: Chronic kidney disease; CVD: Cardiovascular disease; NASH: Non-alcoholic steatohepatitis
Expansion into other serious chronic diseases with high unmet medical needs and market attractiveness

Serious chronic diseases are often associated with diabetes and obesity

- 70% of people with diabetes die from atherosclerotic CVD
- 40% of people hospitalised for heart failure have diabetes

- 80% of people with NASH are obese and 35% have diabetes

- 40% of people with diabetes have diabetic nephropathy and 50% are obese

New therapeutic areas represent patient populations with high unmet medical needs

<table>
<thead>
<tr>
<th></th>
<th>Estimated patients</th>
<th>Number of related deaths</th>
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<td>CVD</td>
<td>~420 million</td>
<td>~20 million annually</td>
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<table>
<thead>
<tr>
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<th>Estimated patients</th>
<th>Diagnosis rate</th>
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<tr>
<td>NASH</td>
<td>~15-40 million(^1)</td>
<td>~20%(^2)</td>
</tr>
<tr>
<td>CKD</td>
<td>~200 million</td>
<td>~20%</td>
</tr>
</tbody>
</table>

\(^1\) Internal forecast comprising US, Europe and Japan
\(^2\) Diagnosis rate is considered a major uncertainty to the forecast

Source: Ahera SF et al. Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015, 2017; Heart Disease and Stroke Statistics, American Heart Association, 2017; Williams CD et al. Prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy, 2011; Addressing the global burden of chronic kidney disease through clinical and translational research, 2014

CVD: Cardiovascular disease; NASH: Non-alcoholic Steatohepatitis; CKD: Chronic kidney disease
Source: Diabetes Care 2005 Jan; 28(1): 164-176
The R&D strategy focuses on innovation and expansion of current patient base

- **Innovation**
  - Diabetes
  - Obesity
  - Haemophilia

- **Expansion**
  - CVD
  - CKD
  - NASH

- **Externalisation**

  - Raise the innovation level within our core therapy areas
  - Expand into new therapy areas spearheaded by semaglutide
  - Intensify external innovation activities

CVD: Cardiovascular disease; NASH: Non-alcoholic Steatohepatitis; CKD: Chronic kidney disease
Research strategy and priorities

Peter Kurtzhals
SVP Global Research

ALEX SILVERBERG, Sweden
Alex has type 1 diabetes
Strengthening leadership in diabetes by improving patient outcomes

Significant unmet needs remain within diabetes

- Need for reducing hypoglycaemia, co-morbidities and oral drug delivery
- Opportunities to provide patients with new innovative treatment options

Research priorities

- Pursue next-generation insulin and GLP-1 with benefits in addition to classic glucose regulation
- Identify new anti-diabetics with novel modes of action and co-morbidity benefits
- Explore new technologies and other modalities besides peptides and proteins
- Pursue all attractive external innovation opportunities

Current activities

- Once-weekly insulin 287
- Liver preferential insulin 406
- PYY 1562
- Anti-IL-21/liraglutide
- Stem cell research: Type 1 diabetes project in progress
- External diabetes assets at all development stages are evaluated
## Expanding the obesity pipeline with new targets

### High growth and unmet needs in the obesity market

<table>
<thead>
<tr>
<th>Unmet medical needs in an immature pharmaceutical market</th>
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<tbody>
<tr>
<td>A unique and attractive growth opportunity</td>
</tr>
<tr>
<td>Numerous peptide- and protein-based opportunities</td>
</tr>
</tbody>
</table>

### Research priorities

<table>
<thead>
<tr>
<th>Pursue all relevant options with &gt;15% weight reduction potential</th>
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</thead>
<tbody>
<tr>
<td>Target pathways with new modes of action complementary to GLP-1</td>
</tr>
<tr>
<td>Explore new targets with co-morbidity benefits</td>
</tr>
<tr>
<td>Monitor external opportunities on an ongoing basis</td>
</tr>
</tbody>
</table>

### Current activities

- Target discovery in Seattle/Beijing
  - G530L
  - GG-co-agonist
  - Tri-agonist 1706
Improving patient outcomes by expanding into other serious chronic diseases

The opportunity of other serious chronic diseases

- High unmet medical needs and high market attractiveness
- Can be addressed with in-house assets and/or R&D capabilities
- Opportunity for external collaborations

Research priorities

Cardiovascular disease
- Leverage internal assets and capabilities to develop drug candidates
- Build dedicated research unit to drive internal and external innovation
- Access external projects with strong biological foundation

NASH
- Utilise internal cardio-metabolic and obesity assets to provide entry
- Build dedicated research unit
- External search for new MoAs targeting liver inflammation and fibrosis

Chronic kidney disease
- Explore internal assets and monitor external opportunities for in-licensing

Dedicated area for serious chronic diseases established

NASH: Non-alcoholic steatohepatitis; CV: Cardiovascular; MoA: Mode of action
Global Research organised to ensure successful execution of the revised R&D strategy

Research investment reflects revised R&D strategy

- **Diabetes**
- **Obesity**
- **Biopharm**
- Other serious chronic disease areas

**Examples**

- Research centers

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Note: Inflammation and devices excluded from the charts. The relative size of the pie charts depicts the development in overall spend, but is illustrative only.
Late-stage product portfolio

Peter Kristensen
SVP Global Development
Post-approval trials support the association between severe hypoglycemia and increased mortality risk

Lower rates of severe hypoglycaemia demonstrated in DEVOTE

<table>
<thead>
<tr>
<th>Subjects with one or more severe events</th>
<th>Number of overall severe events</th>
<th>Number of nocturnal severe events</th>
</tr>
</thead>
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<tr>
<td>252</td>
<td>472</td>
<td>73</td>
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<tr>
<td>187</td>
<td>280</td>
<td>37</td>
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Post-hoc analyses suggest higher all-cause mortality following severe hypoglycaemia

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<th>Time after event</th>
<th>LEADER</th>
<th>DEVOTE</th>
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<tr>
<td>Any time</td>
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<td>180 days</td>
<td><img src="image3" alt="Graph" /></td>
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<tr>
<td>60 days</td>
<td><img src="image5" alt="Graph" /></td>
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<tr>
<td>15 days</td>
<td><img src="image7" alt="Graph" /></td>
<td><img src="image8" alt="Graph" /></td>
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</tbody>
</table>

Hazard ratio all-cause mortality with/without prior severe hypoglycemia

0.1 1 100 0.5 1 16

* Statistically significant
Source: European Association for the Study of Diabetes - 53rd Annual Meeting, A-17-739-EASD, Sep 2017
SUSTAIN phase 3a trials with semaglutide successfully completed

SUSTAIN

Baseline

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
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<tbody>
<tr>
<td></td>
<td>8.1%</td>
<td>8.1%</td>
<td>8.3%</td>
<td>8.2%</td>
<td>8.4%</td>
<td>8.7%</td>
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</table>

Change in HbA$_1c$ (%)

<table>
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<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>-1.6 *</td>
<td>-1.5 *</td>
<td>-1.6 *</td>
<td>-1.5 *</td>
<td>-1.8 *</td>
<td>-1.4 *</td>
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</tbody>
</table>

Baseline

Change in weight (kg)

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<thead>
<tr>
<th></th>
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<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
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<tbody>
<tr>
<td></td>
<td>92 kg</td>
<td>89 kg</td>
<td>96 kg</td>
<td>93 kg</td>
<td>92 kg</td>
<td>92 kg</td>
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<tr>
<td></td>
<td>-4.5 *</td>
<td>-6.1 *</td>
<td>-5.6 *</td>
<td>-5.2 *</td>
<td>-6.4 *</td>
<td>-6.1 *</td>
</tr>
</tbody>
</table>

Statistically significant; 1 SUSTAIN 1: Once-weekly semaglutide versus placebo in drug-naive subjects with type 2 diabetes; SUSTAIN 5: Once-weekly semaglutide versus placebo in subjects with type 2 diabetes added to insulin; SUSTAIN 6: Once-weekly semaglutide versus placebo, added to standard-of-care
ER: Extended-release
Semaglutide demonstrated superiority on both glucose control and weight loss vs dulaglutide in SUSTAIN 7 trial

Note: Inclusion criteria: Male or female, age ≥18 years, stable treatment with metformin, HbA₁c 7.0-10.5%
Statistically significant difference in both low and high dose comparisons

ADA: American Diabetes Association

- Clinically meaningful and statistically significant differences of 0.4% HbA₁c and 2-4 kg between the compared treatments
- Low events of diabetic retinopathy in both semaglutide and dulaglutide groups (4 and 5 events, respectively)
- Semaglutide was well-tolerated and showed an adverse event profile consistent with previous SUSTAIN trials

Next steps
- SUSTAIN 7 results expected to be published in a medical journal in early 2018
- Regulatory feedback expected in the US and the EU in the fourth quarter of 2017

Significantly more semaglutide patients reached target for glucose control in the SUSTAIN 7 trial vs dulaglutide

**Percentage of patients achieving the ADA recommended HbA₁c target below 7.0%**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% of patients at HbA₁c &lt;7.0%</th>
</tr>
</thead>
<tbody>
<tr>
<td>semaglutide 0.5 mg</td>
<td>68%*</td>
</tr>
<tr>
<td>dulaglutide 0.75 mg</td>
<td>52%</td>
</tr>
<tr>
<td>semaglutide 1.0 mg</td>
<td>79%*</td>
</tr>
<tr>
<td>dulaglutide 1.5 mg</td>
<td>67%</td>
</tr>
</tbody>
</table>

* Statistically significant difference in both low and high dose comparisons
ADA: American Diabetes Association
PIioneer programme for oral semaglutide investigates the entire treatment cascade

1. Monotherapy vs Placebo
   - Drug-naïve
   - OAD

2. SGLT-2 vs empagliflozin

3. DPP-IV vs sitagliptin

4. GLP-1 vs liraglutide 1.8 mg

5. Renal impairment vs Placebo

6. CVOT vs Placebo

7. DPP-IV Flexible dose vs sitagliptin

8. Add-on to insulin vs Placebo

9. Monotherapy vs Placebo and liraglutide
   - Japanese patients

10. OAD combination vs dulaglutide

SGLT-2: Sodium-glucose co-transporter-2; DPP-IV: Dipeptidyl peptidase-4; OAD: Oral anti-diabetic; CVOT: Cardiovascular outcomes trial
Full PIONEER programme expected to read out during 2018\(^1\)

**Monotherapy vs Placebo**

- **Q1 2018\(^1\)**: **SGLT-2** vs empagliflozin
- **Q2 2018\(^1\)**: **DPP-IV** vs sitagliptin
- **Q3 2018\(^1\)**: **Renal impairment** vs Placebo
- **Q4 2018\(^1\)**: **OAD combination** vs dulaglutide

**Add-on to insulin vs Placebo**

- **Q2 2018\(^1\)**: **GLP-1** vs liraglutide 1.8 mg
- **Q4 2018\(^1\)**: **CVOT** vs Placebo

**Monotherapy vs Placebo and liraglutide**

- **Q4 2018\(^1\)**: **DPP-IV** vs sitagliptin

Note: Estimated timing of trials from first patient first visit to last patient last visit and subsequent completion of trial.

\(^1\) Expected to be published in the given quarter or in the subsequent quarterly company announcement; \(^2\) Trial to rule out cardiovascular risk; \(^3\) To be followed by 52-week extension trial.
Trials in obesity and other serious chronic disease areas building on the semaglutide molecule

**Planned or ongoing trials with semaglutide addressing other serious chronic diseases**

- **Obesity**
- **NASH**
- **CVD**
- **CKD**

**Ongoing phase 2 trial with daily semaglutide vs placebo in patients with NASH**

- **372 patients**
  - Semaglutide 0.4 mg sc QD
  - Semaglutide 0.2 mg sc QD
  - Semaglutide 0.1 mg sc QD
  - Placebo 0.1, 0.2 or 0.4 mg

- **Liver biopsy** (recent or new)
- **72 weeks**

**Next steps:**
- Phase 2 trial expected to complete 2020
- An MR imaging trial initiated in November 2017

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1 Inclusion criteria: Histological confirmation of NASH, BMI 25–45 kg/m², NASH fibrosis stage 2 or 3, Histological NAFLD Activity Score ≥ 4 mg: Milligram; sc: Subcutaneous; QD: Once-daily; MR: Magnetic resonance; NAFLD: Non-alcoholic fatty liver disease

CVD: Cardiovascular disease; NASH: Non-alcoholic steatohepatitis; CKD: Chronic kidney disease
REN YANXIA, China
Yanxia has type 2 diabetes

Regulatory update

Robin Evers
SVP Medical Affairs, Regulatory and Safety
The global regulatory organisation handled over 300 submissions and obtained ~200 approvals in 2016.

- **North America**
  - ~60 employees
  - 14 submissions
  - 2 approvals

- **Europe**
  - ~65 employees
  - 163 submissions
  - 6 approvals

- **Japan & Korea**
  - ~20 employees
  - 1 submission
  - 0 approvals

- **Latin America**
  - ~25 employees
  - 21 submissions
  - 51 approvals

- **Region China**
  - ~20 employees
  - 2 submissions
  - 3 approvals

- **AAMEO**
  - ~70 employees
  - 130 submissions
  - 132 approvals

Note: Numbers for submissions and approvals for full year 2016, employee numbers as of 1 Sep 2017.
AAMEO: Africa, Asia, Middle-East and Oceania; HQ: Headquarters.
Medical Affairs is responsible for early scientific dialogue ahead of product launches

Medical Affairs activities

- Clinical activities
- KOL engagement
- Publication planning
- Medical education
- Medical guidance

Key preparations ahead of a product launch

- Ensure scientific dialogue
- Secure congress presence
- Publish scientific publications
- Conduct medical education to secure safe patient use of launched products
- Obtain external advice on medical needs and appropriate use from Key Opinion Leaders (KOLs) and International Professional Associations (IPAs)
# Regulatory review for semaglutide is progressing as planned

<table>
<thead>
<tr>
<th>Regulatory status - USA</th>
<th>Regulatory status – rest of world</th>
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</thead>
<tbody>
<tr>
<td>USA</td>
<td></td>
</tr>
<tr>
<td>• Semaglutide advisory committee meeting held on 18 October with a 16-0 vote in favour of recommending approval of semaglutide</td>
<td>• CHMP opinion expected in Q4 2017, followed by final decision by the EU commission in Q1 2018</td>
</tr>
<tr>
<td>• Regulatory decision expected in Q4 2017</td>
<td>• Pending approval, launch is expected in the first European countries during 2018</td>
</tr>
<tr>
<td>• Pending approval, launch is expected Q1 2018</td>
<td>• Regulatory decision expected Q1 2018</td>
</tr>
<tr>
<td></td>
<td>• Pending approval, launch is expected mid-2018</td>
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</table>

**Total countries**
• Semaglutide has been submitted in 35 countries in total

CHMP: Committee for Medicinal Products for Human Use in the EU
# R&D milestones in 2018

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<th>Project</th>
<th>Q1 2018</th>
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<th>Q3 2018</th>
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<td>Japan submission</td>
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1 Expected to be published in the given quarter or in the subsequent quarterly company announcement
Closing remarks

Innovation bar raised following increased maturity of core areas and market access challenges

Significant unmet needs remain within core therapy areas and other serious chronic diseases

Semaglutide demonstrated unprecedented clinical benefits vs comparators in the SUSTAIN programme, spearheading expansion to new areas