Investor presentation
ADA 2019
Agenda

CV aspects of GLP-1s and clinical developments with Ozempic®

PIONEER highlights

Driving innovation in insulin

Obesity and NASH pipeline

The increasing focus on Real-World Evidence

Regulatory update
Forward-looking statements

Novo Nordisk’s reports filed with or furnished to the US Securities and Exchange Commission (SEC), including this presentation as well as the company’s statutory Annual Report 2018 and Form 20-F, which were both filed with the SEC in February 2019 in continuation of the publication of the Annual Report 2018, 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, 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, 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, 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, and failure to maintain a culture of compliance.

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 presentation, reference is made to the overview of risk factors in ‘Risk management enables better decision-making’ on pp 41-43 in the Annual Report 2018.

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 and 1.8 mg) is approved for the management of type 2 diabetes only
- Saxenda® (liraglutide 3 mg) is approved in the USA and the EU for the treatment of obesity only
Ozempic® now launched in 21 countries and continues to gain market shares in the USA

**USA GLP-1 NBRx market share**

- **Weekly NBRx share**
  - Jan 2018: 9.7%
  - May 2019: 50.6%
- **Monthy TRx share**
  - Feb 2017: 45.9%
  - May 2019: 44.5%

**USA GLP-1 volume market share**

- **Monthly NBRx share**
  - Jan 2018: 9.7%
  - May 2019: 50.6%
- **Monthy TRx share**
  - Feb 2017: 45.9%
  - May 2019: 44.5%

Source: NBRx-IQVIA LRx Weekly, week ending 19 May 2019
NBRx: New-to-brand prescriptions

Source: IQVIA monthly xponent, Apr 2019, weekly xponent for May, week ending 19 May 2019
Progress on several projects since ADA last year

- Bridging strategy for semaglutide CV labels
- PIONEER 5, 8 and 10 results
- Zylo acquisition for accelerating glucose responsive insulin
- PIONEER 9 and 6 results
- DUAL VIII completed for Xultophy®
- US filing of oral semaglutide and CV label for Ozempic® and oral semaglutide
- AM833 phase 2 initiated

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- OG2023 phase 1 initiated
- SELECT obesity CVOT phase 3 initiated
- REFLECT RWE trial completed for Tresiba®
- LAI287 phase 2 initiated
- EU and CA filings of oral semaglutide
- Partnership with Gilead Science announced

GLP-1, Insulin, Obesity & NASH, Real-World Evidence, Regulatory

Mads Krogsgaard Thomsen
Chief Science Officer
GLP-1s have positive effects beyond glycaemic control and treatment guidelines have been updated to particularly reflect the CV risk benefits

The multifactorial effects of GLP-1s

Pancreas
- Beta-cell function
- Beta-cell apoptosis
- Insulin biosynthesis
- Glucose-dependent insulin secretion
- Glucose-dependent glucagon secretion

Heart
- CV risk
- Fatty acid metabolism
- Cardiac function
- Systolic blood pressure
- Inflammation
- Atherosclerotic plaque progression

Liver
- Endogenous glucose production
- Hepatic insulin sensitivity
- De novo lipogenesis
- Lipotoxicity
- Steatosis

Brain
- Body weight
- Food intake
- Satiety

Incretin system
Replacement of deficient GLP-1 response

ADA/EASD diabetes treatment guidelines for second-line treatment with established ASCVC or CKD

First-line therapy is metformin and lifestyle management. If HbA1c above target, proceed as below

**Established ASCVD or CKD**

**Without established ASCVD or CKD**

If HbA1c above target

**GLP-1 with proven CVD benefit**
**SGLT-2 with proven CVD benefit**, if eGFR adequate

**NO**

**YES**

ASCVD predominates

**Simpliﬁed illustration**

All references and notes on slide 37
Key inclusion criteria defining established CVD differ between GLP-1 CVOTs but trial populations are more comparable with aligned definitions

### Key inclusion criteria defining established cardiovascular disease across selected CVOTs

<table>
<thead>
<tr>
<th>Established CVD</th>
<th>Without established CVD</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1 prior CVD</td>
<td>Age 55 to 60 years, the above, or evidence of other vascular or renal disease</td>
</tr>
<tr>
<td>MI</td>
<td>Age ≥60 years, the above, or 2 CV risk factors</td>
</tr>
<tr>
<td>Ischaemic stroke</td>
<td>LEADER: age ≥60 years with ≥1 CV risk factor</td>
</tr>
<tr>
<td>Revascularisation*</td>
<td>SUSTAIN 6: age ≥60 years with subclinical evidence of CVD</td>
</tr>
<tr>
<td>Hospitalisation for unstable angina</td>
<td>LEADER: age ≥50 years with ≥1 prior CVD</td>
</tr>
<tr>
<td>Myocardial ischaemia</td>
<td>SUSTAIN 6: age ≥50 years with clinical evidence of CVD</td>
</tr>
<tr>
<td>PCI</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>≥1 prior CVD</th>
<th>≥1 of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>• CVD</td>
</tr>
<tr>
<td>Ischaemic stroke</td>
<td>• CeVD</td>
</tr>
<tr>
<td>Revascularisation*</td>
<td>• PVD</td>
</tr>
<tr>
<td>Hospitalisation for unstable angina</td>
<td>• Chronic HF (NYHA class II or III)</td>
</tr>
<tr>
<td>Myocardial ischaemia</td>
<td>• Chronic kidney disease of stage 3 or higher</td>
</tr>
<tr>
<td>PCI</td>
<td></td>
</tr>
</tbody>
</table>

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### Trial population based on previous MI/stroke vs CV risk factors

<table>
<thead>
<tr>
<th>Trial</th>
<th>MI/Stroke</th>
<th>CV risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>REWIND</td>
<td>72%1</td>
<td>40%</td>
</tr>
<tr>
<td>LEADER</td>
<td>78%</td>
<td>60%</td>
</tr>
<tr>
<td>SUSTAIN 6</td>
<td>59%</td>
<td>41%</td>
</tr>
</tbody>
</table>

Comparison of post-hoc analyses of SUSTAIN 6, LEADER and REWIND for prior and no prior MI/stroke subgroups

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Prior MI/stroke</th>
<th>No. events*</th>
<th>Hazard ratio (95% CI)</th>
<th>Interaction p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SUSTAIN 6</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.75</td>
</tr>
<tr>
<td>3-point MACE</td>
<td>With</td>
<td>66</td>
<td>88</td>
<td>0.76 (0.55 ; 1.05)</td>
</tr>
<tr>
<td></td>
<td>Without</td>
<td>42</td>
<td>58</td>
<td>0.70 (0.47 ; 1.04)</td>
</tr>
<tr>
<td><strong>LEADER</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.56</td>
</tr>
<tr>
<td>3-point MACE</td>
<td>With</td>
<td>322</td>
<td>372</td>
<td>0.84 (0.72 ; 0.97)</td>
</tr>
<tr>
<td></td>
<td>Without</td>
<td>286</td>
<td>322</td>
<td>0.89 (0.76 ; 1.05)</td>
</tr>
<tr>
<td><strong>REWIND</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.18</td>
</tr>
<tr>
<td>3-point MACE</td>
<td>With</td>
<td>196</td>
<td>236</td>
<td>0.79 (0.66 ; 0.96)</td>
</tr>
<tr>
<td></td>
<td>Without</td>
<td>396</td>
<td>423</td>
<td>0.93 (0.81 ; 1.07)</td>
</tr>
</tbody>
</table>

*First events

Poullier N et al. Abstract 86477, presented at the European Society of Cardiology Congress, Barcelona, 28 August 2017
CI: confidence interval; CV: cardiovascular; MI: myocardial infarction; PYO: patient-years of observation; Lira: Liraglutide; Sema: Semaglutide; Dula: dulaglutide Pbo: Placebo
The FLOW trial is the first dedicated GLP-1 renal outcomes trial to demonstrate that semaglutide delays renal impairment

End-stage renal disease (ESRD) often results in chronic dialysis treatment or kidney transplantation

Healthy kidney ~20-25 years ESRD kidney

- 2 in 5 people living with type 2 diabetes will develop chronic kidney disease

- Up to 70% of people with type 2 diabetes and chronic kidney disease experience continued deterioration of the kidney function despite the current standard of care

- ~10% of the population worldwide is suffering from chronic kidney diseases

- The global dialysis market is currently estimated to be around USD 80 billion

FLOW trial design

Randomised: >3,000 patients with type 2 diabetes

Semaglutide 1.0 mg

Placebo

Event driven

Trial objective

The FLOW trial is the first dedicated GLP-1 renal outcomes trial and is carried out to demonstrate that semaglutide delays the progression of renal impairment and lowers the risk of renal and cardiovascular mortality in people with type 2 diabetes and chronic kidney disease

Inclusion criteria

- Patients with type 2 diabetes
- HbA1c ≤10%
- Impaired kidney function measured by estimated Glomerular Filtration Rate (eGFR)*

Trial initiation: Q3 2019

* eGFR ≤75 to ≥50* and UACR >300 to <5,000 mg/g or eGFR <50 to ≥25* and UACR >100 to <5,000 mg/g (20% cap of patients having eGFR ≥60*)
The FOCUS trial will evaluate long-term effects of semaglutide vs placebo regarding diabetic retinopathy

Poor glucose control causes damage to blood vessels which can lead to diabetic retinopathy

Healthy eye

Diabetic eye

- 1 in 3 people living with type 2 diabetes have some degree of diabetic retinopathy\(^1\)
- About 5-10% of people living with diabetes will develop a vision threatening form of the disease\(^2\)
- The global market for treating diabetic retinopathy is currently estimated to be around USD 6 billion\(^3\)

FOCUS trial design

Randomised: ~1,500 patients with type 2 diabetes

Antidiabetic SOC + semaglutide 0.5-1.0 mg sc QW

Antidiabetic SOC + placebo

5 years

Trial objective

To assess the long-term effects of semaglutide compared with placebo, both added to standard of care, with respect to diabetic retinopathy development and progression

Inclusion criteria

- Diabetes duration >10 years
- HbA\(_{1c}\) 7-10%
- Exclusion: unstable or active eye disease

Trial initiation: Q2 2019

\(^1\) IDF Atlas, Eighth edition 2017, \(^2\) Tien Y. Wong, Chui Ming Gemmy Cheung, Michael Larsen, Sanjay Sharma and Rafael Simó, Diabetic retinopathy, Nature Reviews, Disease Primers, VOLUME 2, 2016, \(^3\) Grand View Research; Diabetic Retinopathy Market Analysis Report By Type, published February 2018
SUSTAIN FORTE will evaluate high-dose semaglutide in type 2 diabetes and is expected to conclude by end of 2020

**SUSTAIN FORTE trial design**
- Randomised: 964 patients with type 2 diabetes
- Semaglutide 2.0 mg
- Semaglutide 1.0 mg
- 40 weeks

**Trial objective**
To establish the effect of semaglutide sc 2.0 mg QW vs. semaglutide 1.0 mg QW on glycaemic control in patients with type 2 diabetes on a background of metformin with or without SU treatment

**Key SUSTAIN FORTE trial inclusion criteria**
- People with type 2 diabetes from 10 countries
  - HbA$_1c$ 8-10%
  - Stable dose of metformin +/- SU

**High-dose semaglutide**
- Supports individualised treatment
- Offers a simple treatment regimen for intensification

sc: subcutaneous; QW: once-weekly; SU: sulphonylurea

Trial initiation: Q2 2019
Progress on several projects since ADA last year

June 2018

- Bridging strategy for semaglutide CV labels
- STEP obesity phase 3 initiated
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GLP-1
Insulin
Obesity & NASH
Real-World Evidence
Regulatory
An overview of the PIONEER programme

<table>
<thead>
<tr>
<th>Diet and exercise</th>
<th>OAD</th>
<th>Insulin users</th>
<th>Special populations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PIONEER 1</strong></td>
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<tr>
<td><em>vs placebo</em></td>
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<tr>
<td><em>(Diet and exercise)</em></td>
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<td><strong>PIONEER 2</strong></td>
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<tr>
<td><em>vs SGLT-2</em></td>
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<tr>
<td><em>(Met)</em></td>
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<td><strong>PIONEER 3</strong></td>
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<tr>
<td><em>vs DPP-4</em></td>
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<td><em>(1–2 OADs: Met ± SU)</em></td>
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<td><strong>PIONEER 4</strong></td>
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<td><em>vs GLP-1/placebo</em></td>
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<tr>
<td><em>(1–2 OADs: Met ± SGLT-2)</em></td>
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<td><strong>PIONEER 7</strong></td>
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<td><em>Flexible dose adjustment vs DPP-4 with extension</em></td>
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<tr>
<td><em>(1–2 OADs: Met, SU, TZD, SGLT-2)</em></td>
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<td><strong>PIONEER 8</strong></td>
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<tr>
<td><em>Add-on to insulin</em></td>
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<tr>
<td><em>(Insulin ± Met)</em></td>
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<tr>
<td><strong>PIONEER 5</strong></td>
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<tr>
<td><em>Renal impairment</em></td>
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<tr>
<td><em>(± Met, ± SU, or ± insulin)</em></td>
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<tr>
<td><strong>PIONEER 6</strong></td>
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<tr>
<td><em>CVOT</em></td>
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<tr>
<td><em>(Standard of care)</em></td>
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<tr>
<td><strong>PIONEER 9</strong></td>
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<tr>
<td><em>vs GLP-1/placebo, Japan</em></td>
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<tr>
<td><em>(Monotherapy)</em></td>
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<td><strong>PIONEER 10</strong></td>
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<tr>
<td><em>vs GLP-1/placebo, Japan</em></td>
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<td></td>
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<tr>
<td><em>(1 OAD: SU, TZD, α-GI, glinide or SGLT-2)</em></td>
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</tbody>
</table>

The PIONEER programme showed consistent statistically significant reductions in HbA$_{1c}$ and body weight

Oral semaglutide lowered HbA$_{1c}$ by 1.0–1.8%-points by end of trial\(^1\)

<table>
<thead>
<tr>
<th>PIONEER trials</th>
<th>Mean change in HbA$_{1c}$ (%-points)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-1.3%*</td>
</tr>
<tr>
<td>2</td>
<td>-1.2%*</td>
</tr>
<tr>
<td>3</td>
<td>-1.1%*</td>
</tr>
<tr>
<td>4</td>
<td>-1.0%*</td>
</tr>
<tr>
<td>5</td>
<td>-1.4%*</td>
</tr>
<tr>
<td>6</td>
<td>-1.2%*</td>
</tr>
<tr>
<td>7</td>
<td>-1.5%*</td>
</tr>
<tr>
<td>8</td>
<td>-1.8%*</td>
</tr>
<tr>
<td>9</td>
<td></td>
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<tr>
<td>10</td>
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</tr>
</tbody>
</table>

Oral semaglutide lowered body weight by ~2–5 kg by end of trial\(^1\)

<table>
<thead>
<tr>
<th>PIONEER trials</th>
<th>Mean change in weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-4.1*</td>
</tr>
<tr>
<td>2</td>
<td>-4.7*</td>
</tr>
<tr>
<td>3</td>
<td>-3.5*</td>
</tr>
<tr>
<td>4</td>
<td>-3.7*</td>
</tr>
<tr>
<td>5</td>
<td>-2.9*</td>
</tr>
<tr>
<td>6</td>
<td>-2.8*</td>
</tr>
<tr>
<td>7</td>
<td>-4.2*</td>
</tr>
<tr>
<td>8</td>
<td>-4.3*</td>
</tr>
<tr>
<td>9</td>
<td>-2.9*</td>
</tr>
<tr>
<td>10</td>
<td>-1.9*</td>
</tr>
</tbody>
</table>

\(^1\) Hypothetical estimand, Mixed Model for Repeated Measurement (MMRM)

* Statistically significant vs comparator (vs placebo in PIONEER 1; vs empagliflozin 25 mg in PIONEER 2; vs sitagliptin 100 mg in PIONEER 3; vs Victoza® 1.8 mg in PIONEER 4; vs placebo in PIONEER 5; vs placebo in PIONEER 6; vs sitagliptin 100 mg in PIONEER 7; vs Victoza® 0.9 mg and placebo in PIONEER 9; vs 0.75 mg dulaglutide in PIONEER 10)

Note: Results shown are: PIONEER 1 and 5 for 26 weeks with 14 mg oral semaglutide, PIONEER 2, 4, 8, 9 and 10 for 52 weeks with 14 mg oral semaglutide; PIONEER 7 for 52 weeks with a mixed dose; PIONEER 3 for 78 weeks with 14 mg oral semaglutide; PIONEER 7 for 52 weeks with a mixed dose; PIONEER 6 following occurrence of 137 MACE with a median follow-up time of 16 months.

MACE: major adverse cardiovascular events; FDA: The US Food and Drug Administration
The PIONEER 6 trial investigated cardiovascular safety of oral semaglutide vs placebo

**PIONEER 6 trial design**

- Randomised: 3,176 patients with type 2 diabetes
  - Oral semaglutide 14 mg + standard of care
  - Placebo + standard of care

**137 MACE**

**Trial objective**
Confirm the cardiovascular safety of oral semaglutide in patients with type 2 diabetes

**Inclusion criteria**
- Age ≥50 years and clinical evidence of CV disease or age ≥50 years and subclinical evidence of CV disease
- Antidiabetic drug-naïve or current treatment with one or more oral or injectable antidiabetic agent(s) (excl. DPP-4 and GLP-1)

**PIONEER 6 headline results**

- 21% non-significant reduction of primary endpoint\(^1\) for oral semaglutide-treated patients compared to placebo-treated subjects (HR: 0.79)
  - CV death – significant (HR: 0.49)
  - Non-fatal MI – non-significant (HR: 1.18)
  - Non-fatal stroke – non-significant (HR: 0.74)

- All-cause mortality – significant (HR: 0.51)

- Results were based on 137 MACE with median follow-up of 16 months

\(^1\) The primary endpoint of the PIONEER 6 trial was defined as the MACE composite outcome of the first occurrence of cardiovascular death, non-fatal myocardial infarction or non-fatal stroke. CV: cardiovascular; DPP-4: dipeptidyl peptidase-4 inhibitor; GLP-1: glucagon-like peptide-1; MACE: major cardiovascular event; HR: hazard ratio; MI: myocardial infarction; PIONEER: peptide innovation for early diabetes treatment

**PIONEER symposium on Tuesday June 11\(^{th}\) from 9.45 – 11.45 (pacific time)**
The SOUL trial will provide robust evidence on the cardiovascular benefits of oral semaglutide in people with type 2 diabetes

**SOUL trial design**

- **Randomised:** 9,642 patients with type 2 diabetes
- **Oral semaglutide 14 mg + standard of care**
- **Placebo + standard of care**
- Event-driven

**SOUL trial key inclusion criteria**

- **People with type 2 diabetes from 34 countries with primarily moderate Chronic Kidney Disease**
  - **HbA1c ≤10%**
  - **Age ≥50 years**
  - **At least 1 of the following:** Coronary heart disease, Cerebrovascular disease, Symptomatic peripheral arterial disease, Chronic kidney disease

**Key endpoints**

**Primary:**
- Cardiovascular death, non-fatal myocardial infarction or non-fatal stroke (MACE)

**Secondary confirmatory:**
- 5-component composite CKD endpoints
- Cardiovascular Death
- A composite peripheral artery endpoint

Standard of care allows all glucose lowering drugs except GLP-1s; CKD: chronic kidney disease

**Trial initiation:** Q2 2019
Progress on several projects since ADA last year

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  - Ziylo acquisition for accelerating glucose responsive insulin
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- June 2019
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  - Partnership with Gilead Science announced
  - AM833 phase 2 initiated

GLP-1 | Insulin | Obesity & NASH | Real-World Evidence | Regulatory

Martin Lange
SVP Global Development
In Dual VIII, 66% of people on glargine U100 required treatment intensification compared to 37% on Xultophy®

**Trial design Dual VIII - durability**

- **Randomised:** 1,012 patients
- **Duration:** 104 weeks

**“need for treatment intensification”**

- **IDegLira QD + OAD(s)**
- **Insulin glargine QD + OAD(s)**

**“get to target”**

- 26 weeks
- Continued trial drug period 0-78 weeks
- End of trial

**“durability”**

**Time to need for treatment intensification**

- **IDegLira**
- **Glarigne U100**

- **66.2% patients required treatment intensification**
- **37.4% patients required treatment intensification**

**Trial objective**

To compare long-term glycaemic control of IDegLira vs. insulin glargine U100 in insulin naïve subjects with type 2 diabetes inadequately controlled on OAD(s)\(^1\)

---

\(^1\) According to the ADA definition of HbA\(_1c\) > 7%; *HbA\(_1c\) ≥7% at 2 consecutive visits. Full analysis set. Treatment policy strategy. Patients discontinuing treatment contribute to analyses as needing treatment intensification from time of discontinuation. IDegLira/Xultophy®: insulin degludec/liraglutide; Glargine U100: insulin glargine U100; n: number of patients; OAD: oral anti-diabetes drug; QD: once-daily
In Dual VIII, mean HbA$_{1C}$ was comparable for Xultophy® compared with glargine U100 but with a lower actual insulin dose.

At week 104, 90 patients (27.36%) had max dose of IDegLira. 75.3% were at target <7%; IDegLira/Xultophy®: insulin degludec/liraglutide; glargine U100: insulin glargine U100.
In Dual VIII, mean body weight gain was 1.7 kg lower for Xultophy® and with lower risk of hypoglycaemia compared with glargine U100.

**Body weight – change from baseline**

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Mean change body weight (Kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>-1.0</td>
</tr>
<tr>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>26</td>
<td>1.0</td>
</tr>
<tr>
<td>52</td>
<td>2.0</td>
</tr>
<tr>
<td>78</td>
<td>3.0</td>
</tr>
<tr>
<td>104</td>
<td>4.0</td>
</tr>
</tbody>
</table>

**Severe or blood glucose confirmed symptomatic hypoglycaemic episodes over 104 weeks**

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Number of episodes per patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>0.0</td>
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<tr>
<td>16</td>
<td>0.2</td>
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<td>24</td>
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<td>32</td>
<td>0.6</td>
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<td>40</td>
<td>0.8</td>
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<td>48</td>
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<td>56</td>
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<tr>
<td>64</td>
<td>1.4</td>
</tr>
<tr>
<td>72</td>
<td>1.6</td>
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<tr>
<td>80</td>
<td>1.8</td>
</tr>
<tr>
<td>88</td>
<td>2.0</td>
</tr>
<tr>
<td>96</td>
<td>2.2</td>
</tr>
<tr>
<td>104</td>
<td>2.4</td>
</tr>
</tbody>
</table>

Means from the MMRM model.

* statistically significant vs. insulin glargine U100 after 104 weeks; Kg: kilograms; CI: confidence interval; ETD: estimated treatment difference; IDegLira/Xultophy®: insulin degludec/liraglutide; glargine U100: insulin glargine U100; LS: least squares; MMRM: mixed model repeated measurement.

Severe or blood glucose confirmed symptomatic hypoglycaemia: An episode that is severe according to the American Diabetes Association classification or BG confirmed by a plasma glucose value < 3.1 mmol/L (56 mg/L) with symptoms consistent with hypoglycaemia.

CI: confidence interval; conf., confirmed; ERR: estimated rate ratio; Symp: symptomatic.
# Innovation and convenience for patients on basal insulin with once-weekly insulin LAI287

**Rationale for a once-weekly insulin**

Provide an efficacious, safe and convenient once-weekly alternative to once-daily basal insulin for patients with type 2 diabetes

- Fewer injections
- Lower treatment burden could lead to higher compliance

**LAI287 phase 2 programme**

<table>
<thead>
<tr>
<th>2019 H1</th>
<th>2019 H2</th>
<th>2020 H1</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2D, insulin naïve + OAD vs glargine ~250 patients, 26 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2D, insulin naïve Different titrations vs glargine ~200 patients, 16 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2D, + OAD With and without loading dose vs glargine ~150 patients, 16 weeks</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Expected phase 2 programme completion: H1 2020

T2D: type 2 diabetes; OAD: oral antidiabetes drugs
Connected insulin pen resulting in improved adherence and ‘time in range’ in Swedish study

NovoPen® 6 with Glooko/Diasend® system

1. NovoPen® 6
2. Data capture
3. Data storage
4. HCP review of data

- In-clinic data box
- FGM/CGM blood glucose data
- Storage of data on cloud
- Visualisation of patient data (insulin dosing and glucose data) on same interface using HCP platform

More accurate data leading to better doctor-patient conversations and treatment results

- 43% fewer missed meal-time insulin injections
- 28% increase in dose of meal-time insulin
- 2 more hours in good glucose control per person per day

Anonymised data transfer to Novo Nordisk for research and product development purposes

For more details, see ADA 2019 Late-breaking poster presentation 126-LB and Poster presentation 1076-P; HCP: healthcare professional; FGM: flash glucose monitor; CGM: continuous glucose monitor
Progress on several projects since ADA last year

- Bridging strategy for semaglutide CV labels
- PIONEER 5, 8 and 10 results
- Ziylo acquisition for accelerating glucose responsive insulin
- PIONEER 9 and 6 results
- DUAL VIII completed for Xultophy®
- US filing of oral semaglutide and CV label for Ozempic® and oral semaglutide
- AM833 phase 2 initiated
- June 2018
- STEP obesity phase 3 initiated
- OG2023 phase 1 initiated
- SELECT obesity CVOT phase 3 initiated
- REFLECT RWE trial completed for Tresiba®
- LAI287 phase 2 initiated
- EU and CA filings of oral semaglutide
- Partnership with Gilead Science announced
- June 2019

Martin Lange
SVP Global Development
Clinical projects in obesity and NASH

**Obesity**
- Phase 1:
  - PYY 1562 analogue
  - GG-co-agonist
  - Tri-agonist 1706
  - PYY 1875 analogue

- Phase 2:
  - Amylin AM833

- Phase 3:
  - Semaglutide obesity

- Marketed:
  - Saxenda® (injection)

**NASH**
- Semaglutide NASH
- Semaglutide NASH + Gilead Science

Develop new biologics combined with GLP-1 to achieve >20% weight loss

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

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PYY: peptide YY; GG: GLP-1 and glucagon; NASH: nonalcoholic steatohepatitis; GLP-1: glucagon-like peptide-1
The phase 3a programme STEP and the CV outcomes study SELECT were initiated in 2018 for semaglutide in obesity

Semaglutide in obesity phase 3a programme, STEP, expected to include ~4,500 patients

Inclusion criteria: Male or female, age ≥18 years, BMI: ≥30 kg/m² or ≥27 kg/m² and ≥1 comorbidity

Note: All treatment arms are adjunct to diet and exercise

CV: cardiovascular; T2D: type 2 diabetes; BMI: body mass index

- STEP 1: Weight loss
  1,950 patients, 68 weeks

- STEP 2: T2D non-insulin patients
  1,200 patients, 68 weeks

- STEP 3: Maximising weight loss
  600 patients, 68 weeks

- STEP 4: Maintained weight loss
  900 patients, 68 weeks

Expected phase 3a programme completion: 2020

Cardiovascular outcomes study, SELECT, initiated for semaglutide in obesity

Inclusion criteria: Male or female >45 years, BMI >27 kg/m², myocardial infarction or stroke >60 days, HbA₁c <6.5%

QW: once-weekly; sc: subcutaneous; BMI: body mass index

Semaglutide 2.4 mg sc QW

Placebo

Event-driven

Completion: Pre-defined number of events

1 Inclusion criteria: Male or female, age ≥18 years, BMI: ≥30 kg/m² or ≥27 kg/m² and ≥1 comorbidity
   Note: All treatment arms are adjunct to diet and exercise
   CV: cardiovascular; T2D: type 2 diabetes; BMI: body mass index

1 Inclusion criteria: Male or female >45 years, BMI >27 kg/m², myocardial infarction or stroke >60 days, HbA₁c <6.5%
   QW: once-weekly; sc: subcutaneous; BMI: body mass index
Amylin AM833 could become the next step in getting closer to the ambition of >20% weight loss

**Phase 1b amylin and semaglutide combination multiple dose trial**

- **Randomised:** 80 people with obesity
- **Cohort 5:** QW sema + QW AM833 Dose E
  - 4* 4-week escalation steps (fixed ratio)
- **Cohort 4:** QW sema + QW AM833 Dose D
  - 4* 4-week escalation steps (fixed ratio)
- **Cohort 3:** QW sema + QW AM833 Dose C
  - 4* 4-week escalation steps (fixed ratio)
- **Cohort 2:** QW sema + QW AM833 Dose B
  - 4* 4-week escalation steps (fixed ratio)
- **Cohort 1:** QW sema + QW AM833 Dose A
  - 4* 4-week escalation steps (fixed ratio)
- **20 weeks treatment**
- **~19 months**

**Trial objective**
To assess the safety, tolerability, and PK properties, and to explore PD effects of multiple subcutaneous doses of amylin AM833 initiated simultaneously with semaglutide in people with overweight or obesity (BMI 27-39.9 kg/m2)

**Phase 2 dose finding trial**

- **Randomised:** 700 people with obesity
- **AM833, 4.5 mg QW**
- **AM833, 4.1 mg QW**
- **AM833, 3.5 mg QW**
- **AM833, 2.4 mg QW**
- **AM833, 2.0 mg QW**
- **AM833, 1.2 mg QW**
- **AM833, 0.6 mg QW**
- **AM833, 0.3 mg QW**
- **Liraglutide, 3.0 mg QD**
- **Placebo**
- **Diet and physical activity counselling**
- **26 weeks + 6 weeks follow-up**

**Trial rationale**
To find optimal dose of sc. administered amylin AM833 QW for weight loss in people being overweight or with obesity (BMI 27-39.9 kg/m2)

**Primary endpoint**
Change from baseline to week 26 in body weight (%)

**Trial initiation:** Q1 2019

**QW:** once-weekly; **sema:** semaglutide; **sc:** subcutaneous
Novo Nordisk is investigating opportunities within NASH

### Semaglutide NASH phase 2 programme

- **2016**
  - Semaglutide 0.1, 0.2 and 0.4 mg QD vs placebo in patients with NASH (~320 patients, 72 weeks)

- **2017**
  - Semaglutide 0.4 mg QD vs placebo in patients with NASH (~70 patients, 72 weeks)

- **2018**
  - Semaglutide 2.4 mg QW vs placebo in patients with NASH (~70 patients, 48 weeks)

- **2019**
  - Semaglutide 0.4 mg QD vs placebo in patients with NASH (~70 patients, 72 weeks)

- **2020**
  - Expected phase 2 programme completion: H2 2020

### Proof of concept phase 2 combination trial design

- Sema 2.4 mg once weekly sc
- Sema 2.4 mg + FIR 20 mg once daily oral
- Sema 2.4 mg + CIL 30 mg once daily oral
- Sema 2.4 mg + CIL 100 mg once daily oral
- Sema 2.4 mg + FIR 20 mg + CIL 30 mg

- 24 weeks + 7 weeks follow-up

### Trial information
- Safety and tolerability trial
- Initiation Q3 2019
- MRI-PDFF, MRE & biomarkers at least at: 0, 12, 24 weeks

**Notes:**
- QD: Once-daily; QW: once-weekly; sc: subcutaneous; MRI-PDFF: magnetic resonance imaging–estimated proton density fat fraction; MRE: magnetic resonance elastography; NASH: nonalcoholic steatohepatitis; NAFLD: Nonalcoholic fatty liver disease; kPa: kilopascals; FIR: firsocostat (ACC inhibitor); CIL: cilofexor (FXR agonist); ACC: acetyl-CoA carboxylase; FXR: Farnesoid X receptor

**Data:**
- 100 NAFLD/NASH MRI-PDFF with ≥ 10% steatosis
- FibroScan with liver stiffness ≥ 7 kPa or historical liver biopsy
Progress on several projects since ADA last year

- Bridging strategy for semaglutide CV labels
- PIONEER 5, 8 and 10 results
- Ziylo acquisition for accelerating glucose responsive insulin
- PIONEER 9 and 6 results
- DUAL VIII completed for Xultophy®
- US filing of oral semaglutide and CV label for Ozempic® and oral semaglutide
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- REFLECT RWE trial completed for Tresiba®
- LAI287 phase 2 initiated
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- AM833 phase 2 initiated
- Partnership with Gilead Science announced

Stephen Gough
Global Chief Medical Officer
Novo Nordisk continues to invest in post-approval trials across the portfolio to support clinical findings in real-world settings

- Semaglutide in patients with type 2 diabetes: real-world analysis in the Canadian LMC Diabetes Registry: the SPARE study (poster presentation 995-P)
- Real-world effectiveness of semaglutide in early users from a US commercially insured and Medicare Advantage population (poster presentation 1006-P)

- The outcomes associated with use of iDegLira in a large real-world cohort of patients with type 2 diabetes in Sweden (poster presentation 1110-P)
- The first real-world study describing change in glycated hemoglobin (HbA1c) among US patients initiating iDegLira (publication only)

- A multicenter, prospective, observational study that evaluates the safety and effectiveness of switching from other basal insulins to degludec, as part of routine clinical care, in patients with type 1 or type 2 diabetes: the ReFleCT study (poster presentation 374-P)

- A prospective, non-interventional pilot study running including twelve diabetes clinics from different parts of Sweden. Patients with type 1 diabetes using CGM were included if their treating physicians decided to offer them a NovoPen® 6 (Late-breaking poster presentation 126-LB)
ReFLeCT is a RWE trial investigating the safety and efficacy profile of Tresiba® for degludec naïve patients with T1D/T2D

ReFLeCT trial design

![Diagram of ReFLeCT trial design]

N=1,267 T1D and T2D patients planned to initiate degludec

Degludec QD + standard of care

Hypoglycaemia recording

Weeks

-4 0 3 6 9 12

Months

Key ReFLeCT trial inclusion criteria

People with type 1 and 2 diabetes from 7 countries

- T1D and/or T2D adults
- Male or female ≥ 18 years
- Insulin using, planned initiation with degludec
- No previous use of degludec

Trial objective

To confirm the safety and effectiveness of degludec in patients with T1D or T2D in routine clinical practice

Primary endpoint

Change in rate of any hypoglycaemia of patients before and after treatment change to degludec

RWE: real-world evidence; QD: once daily; T1D: type 1 diabetes; T2D: type 2 diabetes
ReFLeCT demonstrated lower hypoglycaemia risk-profile of Tresiba® as well as increased quality of life vs other basal insulins

**Significant reduction of all types of hypoglycaemic events**

<table>
<thead>
<tr>
<th>Hypoglycaemic Event</th>
<th>Rate Ratio (follow-up/baseline)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1D any hypoglycaemic episodes</td>
<td>0.80 [0.75;0.87]</td>
<td>*&lt;0.001</td>
</tr>
<tr>
<td>T2D any hypoglycaemic episodes</td>
<td>0.49 [0.41;0.60]</td>
<td>*&lt;0.001</td>
</tr>
<tr>
<td>T1D non-severe hyp. episodes</td>
<td>0.81 [0.75;0.87]</td>
<td>*&lt;0.001</td>
</tr>
<tr>
<td>T2D non-severe hyp. episodes</td>
<td>0.49 [0.41;0.59]</td>
<td>*&lt;0.001</td>
</tr>
<tr>
<td>T1D nocturnal hyp. episodes</td>
<td>0.58 [0.49;0.70]</td>
<td>*&lt;0.001</td>
</tr>
<tr>
<td>T2D nocturnal hyp. episodes</td>
<td>0.36 [0.21;0.61]</td>
<td>*&lt;0.001</td>
</tr>
<tr>
<td>T1D ADA-defined severe hyp. episodes</td>
<td>0.41 [0.23;0.73]†</td>
<td>=0.003</td>
</tr>
<tr>
<td>T2D ADA-defined severe hyp. episodes</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

**Patients’ treatment satisfaction and quality of life**

**Observed treatment difference at 12 months follow-up from baseline with Tresiba®**

- **T1D**: Baseline = 26.0, 12 months follow-up = 29.9
- **T2D**: Baseline = 25.7, 12 months follow-up = 30.0

**DTSQ-s total score**

*Favours degludec* 0.125 0.25 0.5 1 2 4 8 0

- **T1D**: Baseline = 26.0, 12 months follow-up = 29.9
- **T2D**: Baseline = 25.7, 12 months follow-up = 30.0

Percentages are based on the number of patients who responded that they used the specific flexibility option one or more times and calculated based on number of patients with evaluable data.

DTSQ: Diabetes Treatment Satisfaction Questionnaire; QoL: quality of life; SF: Short Form; T1D: type 1 diabetes; T2D: type 2 diabetes

---

*Favours previous basal insulin*

- **T1D**: Baseline = 26.0, 12 months follow-up = 29.9
- **T2D**: Baseline = 25.7, 12 months follow-up = 30.0

---

Negative binomial regression model with log link and log of exposure as offset.

AQA: American Diabetes Association; NA: not available; T1D: type 1 diabetes; T2D: type 2 diabetes; hyp.: hypoglycaemic.
Progress on several projects since ADA last year

June 2018

- Bridging strategy for semaglutide CV labels
- PIONEER 2, 3, 4 and 7 results
- STEP obesity phase 3 initiated
- OG2023 phase 1 initiated
- SELECT obesity CVOT phase 3 initiated
- PIONEER 9 and 6 results

June 2019

- US filing of oral semaglutide and CV label for Ozempic® and oral semaglutide
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- REFLECT RWE trial completed for Tresiba®
- LAI287 phase 2 initiated

Robin Evers
SVP Medical Affairs, Regulatory Affairs & Safety
Oral semaglutide filed in the USA, the EU and Canada, and Ozempic® CV risk reduction indication filed in the USA

**Expected timelines for the FDA review**

<table>
<thead>
<tr>
<th>Quarter</th>
<th>Oral semaglutide</th>
<th>Oral semaglutide (CV indication)</th>
<th>Ozempic® (CV indication)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 2019</td>
<td>Expected review time: 6 months</td>
<td>Expected review time: 10 months</td>
<td>Expected review time: 10 months</td>
</tr>
</tbody>
</table>

**Oral semaglutide filed in key markets**

- **Three FDA filings:**
  - NDA for oral semaglutide for glycaemic control
  - NDA for oral semaglutide CV indication
  - sNDA for Ozempic® CV indication

- **Regulatory filing** in the EU for oral semaglutide for type 2 diabetes treatment

- **Regulatory filing** in Canada for oral semaglutide for type 2 diabetes treatment

CV: Cardiovascular; FDA: the US Food and Drug Administration; Q: Quarter; NDA: New Drug Application; sNDA: Supplementary New Drug Application
R&D milestones in 2019

<table>
<thead>
<tr>
<th>Project</th>
<th>Q1 2019</th>
<th>Q2 2019</th>
<th>Q3 2019</th>
<th>Q4 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tresiba®</td>
<td></td>
<td></td>
<td>Phase 3b results (vs glargine U300)</td>
<td></td>
</tr>
<tr>
<td>Ryzodeg®</td>
<td></td>
<td></td>
<td>CN regulatory decision</td>
<td></td>
</tr>
<tr>
<td>Ozempic®</td>
<td>US submission</td>
<td></td>
<td>FOCUS trial initiation (OT²)✓</td>
<td></td>
</tr>
<tr>
<td>Anti-IL-21</td>
<td>Phase 1 initiation✓</td>
<td></td>
<td>FORTE initiation (dose trial)✓</td>
<td></td>
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<tr>
<td>LAI287</td>
<td>US submission</td>
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<td>Phase 2 results</td>
<td></td>
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<tr>
<td>LAIsemia</td>
<td>Phase 1 initiation✓</td>
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<tr>
<td>Oral semaglutide</td>
<td>US submission✓</td>
<td></td>
<td>SOUL trial initiation (CVOT)✓</td>
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</tr>
<tr>
<td>Amylin - AM833</td>
<td>US submission (CV)✓</td>
<td></td>
<td>EU submission✓</td>
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<tr>
<td>Tri-agonist 1706</td>
<td>Phase 2 initiation✓</td>
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<tr>
<td>PYY 1562</td>
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<tr>
<td>Semaglutide combination</td>
<td></td>
<td></td>
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<tr>
<td>Esperoct®/N8-GP</td>
<td>US regulatory decision✓</td>
<td></td>
<td>PoC phase 2 initiation</td>
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<tr>
<td>Concizumab</td>
<td>CHMP recommendation✓</td>
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<tr>
<td>Somapacitan</td>
<td>Phase 3 initiation✓</td>
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</tr>
</tbody>
</table>

1 Expected to be published in the given quarter or in the subsequent quarterly company announcement; ² Diabetic retinopathy outcome trial; ³ Diabetes kidney disease outcome trial; GG-co-agonist in obesity phase 1 decisive results are now expected in 2020; OT: Outcomes trial; GHD: Growth hormone deficiency; AGHD: Adult growth hormone deficiency; CVOT: Cardiovascular outcomes trial; CV: Cardiovascular; PoC: proof of concept; NASH: nonalcoholic steatohepatitis
Investor contact information

Share information
Novo Nordisk’s B shares are listed on the stock exchange in Copenhagen under the symbol ‘NOVO B’. Its ADRs are listed on the New York Stock Exchange under the symbol ‘NVO’.

For further company information, visit Novo Nordisk on: www.novonordisk.com

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Upcoming events
09 Aug 2019  Financial statement for the first six months of 2019
01 Nov 2019  Financial statement for the first nine months of 2019
05 Feb 2020  Financial statement for the full year of 2019
References and notes for slide 6


*Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 strongest evidence for liraglutide>semaglutide>exenatide extended release. For SGLT-2 evidence modestly stronger for empagliflozin>canagliflozin. ASCVD: atherosclerotic cardiovascular disease; CKD: chronic kidney disease; CV: cardiovascular; CVD: cardiovascular disease; CVOT: cardiovascular outcome trial; DPP-4: dipeptidyl peptidase-4 inhibitor; eGFR: estimated glomerular filtration rate; GLP-1: glucagon-like peptide-1 receptor agonist; HF: heart failure; SGLT-2: sodium glucose co-transporter-2 inhibitor