# Placeholder - Document Produced Natively

semaglutide

# Update on Semaglutide

## Prospects, plans & timelines

[redacted]

**Jon Bugge/Lone Hoedt Hansen**

**Clinical Operations, Future GLP-1**

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# Agenda

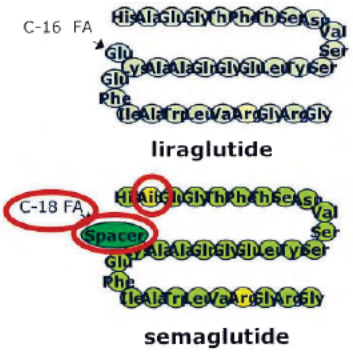
- Brief introduction
- Phase 2 results
- [redacted]
- [redacted]

- *Points for discussion*
  - [redacted]

[redacted] Confidential

# Semaglutide: Key features of the molecule

- [redacted]
  - Peptide backbone modified to protect against enzymatic degradation by DPP-IV
  - Acylation with C-18 fatty acid slows degradation and reduces renal clearance
  - Hydrophilic linker between Lys26 and fatty acid moiety improves albumin binding
- PK profile compatible with once weekly dosing

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# Semaglutide in the diabetes portfolio

- [redacted]
- [redacted]
- [redacted]

# Base case Product Profile

- [redacted]
  - [redacted]
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# Overall project status

- Phase 2 CPoC trial completed 2009
- End of Phase 2 consultation with EMA 2009
- FDA approval of liraglutide NDA January 2010
- EOP2 meetings with US and Japan Health Authorities planned [redacted]
- [redacted]
- [redacted]
- [redacted]

# Phase 2 results

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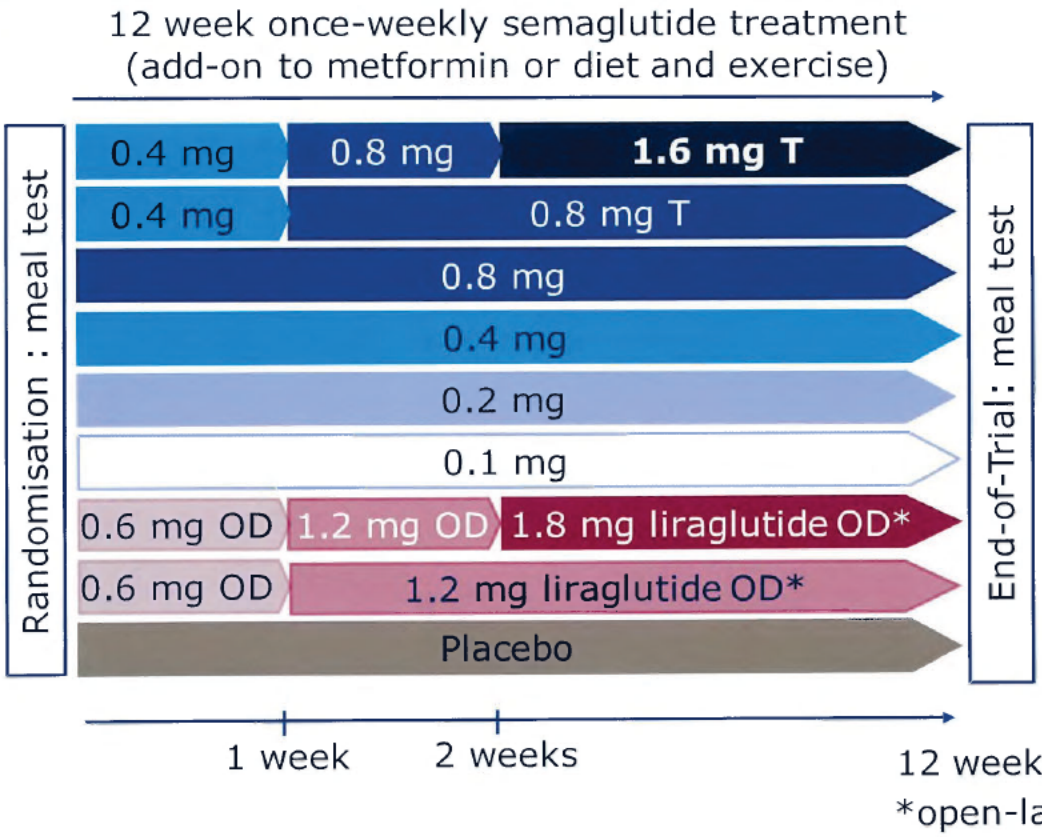
# NN9535-1821 trial design

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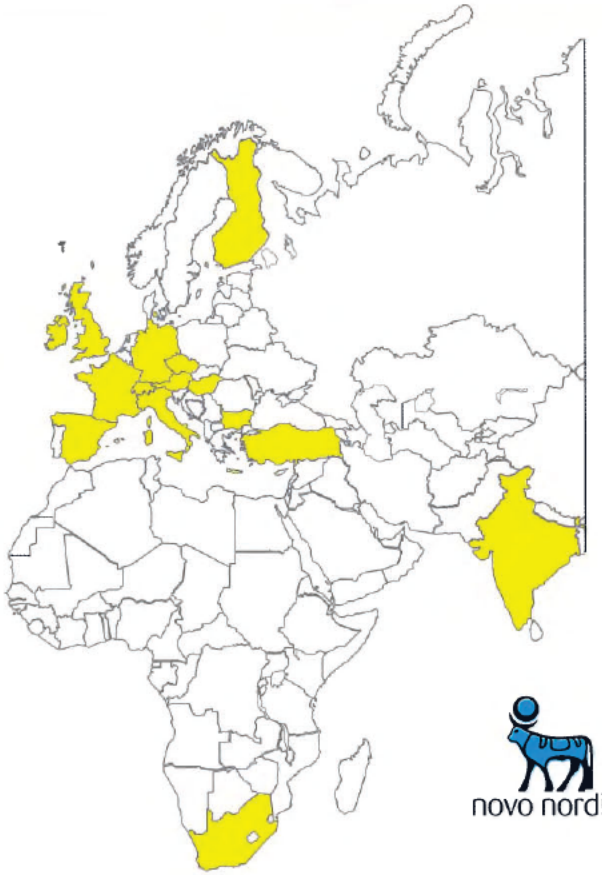
# Large multinational phase 2 trial

- 411 T2D subjects
  - White: 81.8%
  - Asian (India & South Africa): 16.3%
  - Black (South Africa): 1.9%
- 14 countries
- 67 active sites



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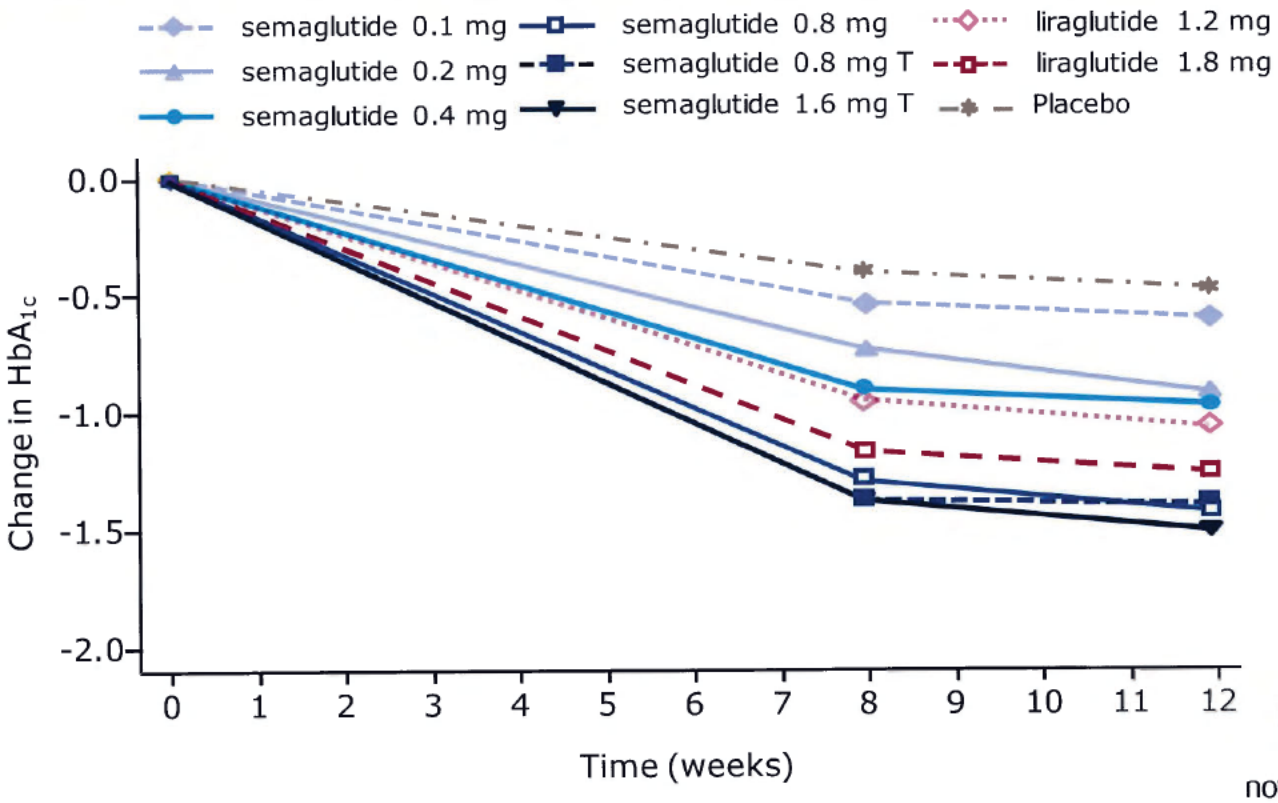
# Baseline characteristics

| | Mean (SD) |
|---|---|
| Exposed subjects, total | 411 |
| Subject per treatment group | 43–50 |
| D&E:metformin, % | 20:80 |
| Female:male, % | 35:65 |
| Age, years | 55.0 (9.8) |
| Duration of diabetes, years | 2.6 (3.1) |
| $HbA_{1c}$, % | 8.1 (0.8) |
| FPG, mmol/L | 9.3 (2.2) |
| Weight, kg | 87.5 (13.8) |
| BMI, $kg/m^2$ | 30.9 (4.4) |

[redacted] Confidential

# Mean change in $HbA_{1c}$ from baseline (FAS, LOCF): by week

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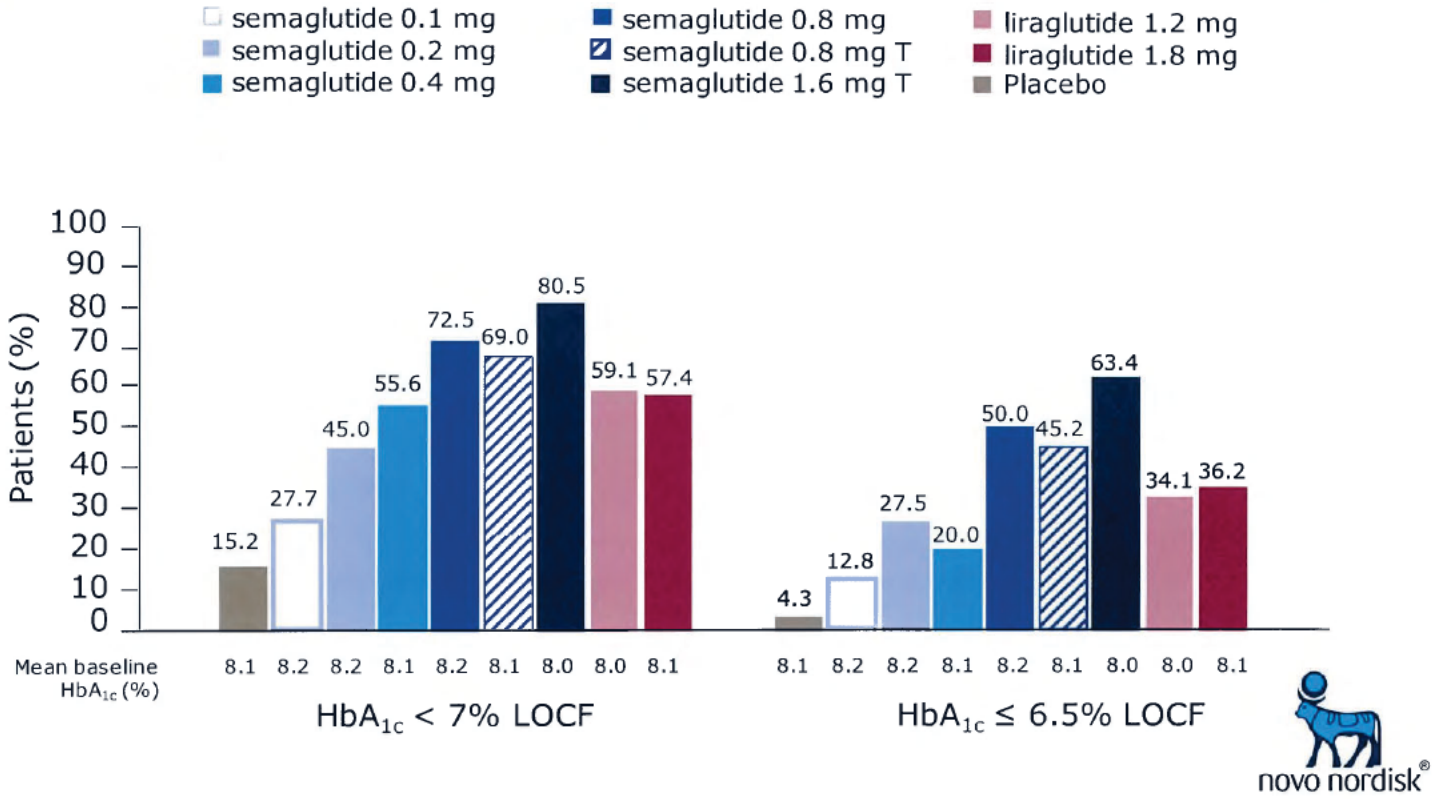
# Subjects reaching ADA/AACE criteria for glycaemic control (FAS, LOCF)

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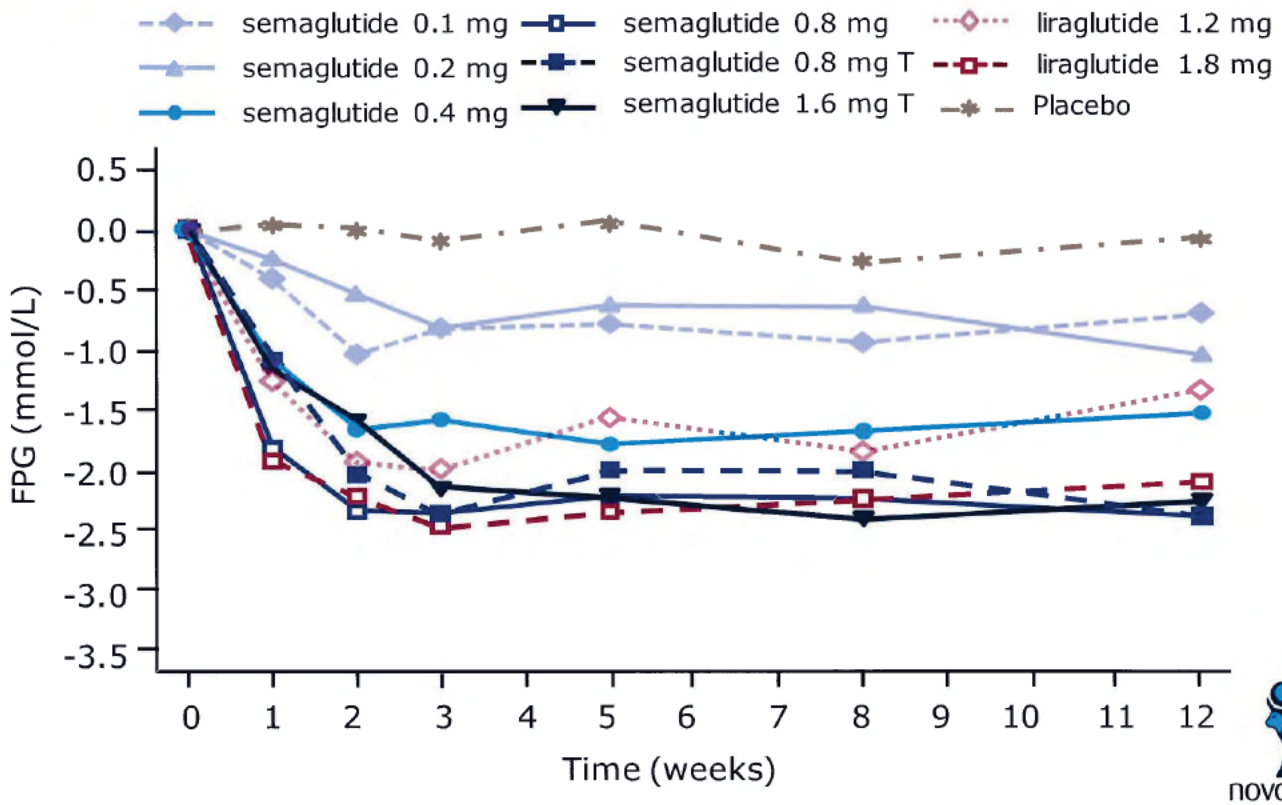
# Mean change in FPG from baseline (FAS, LOCF): by week



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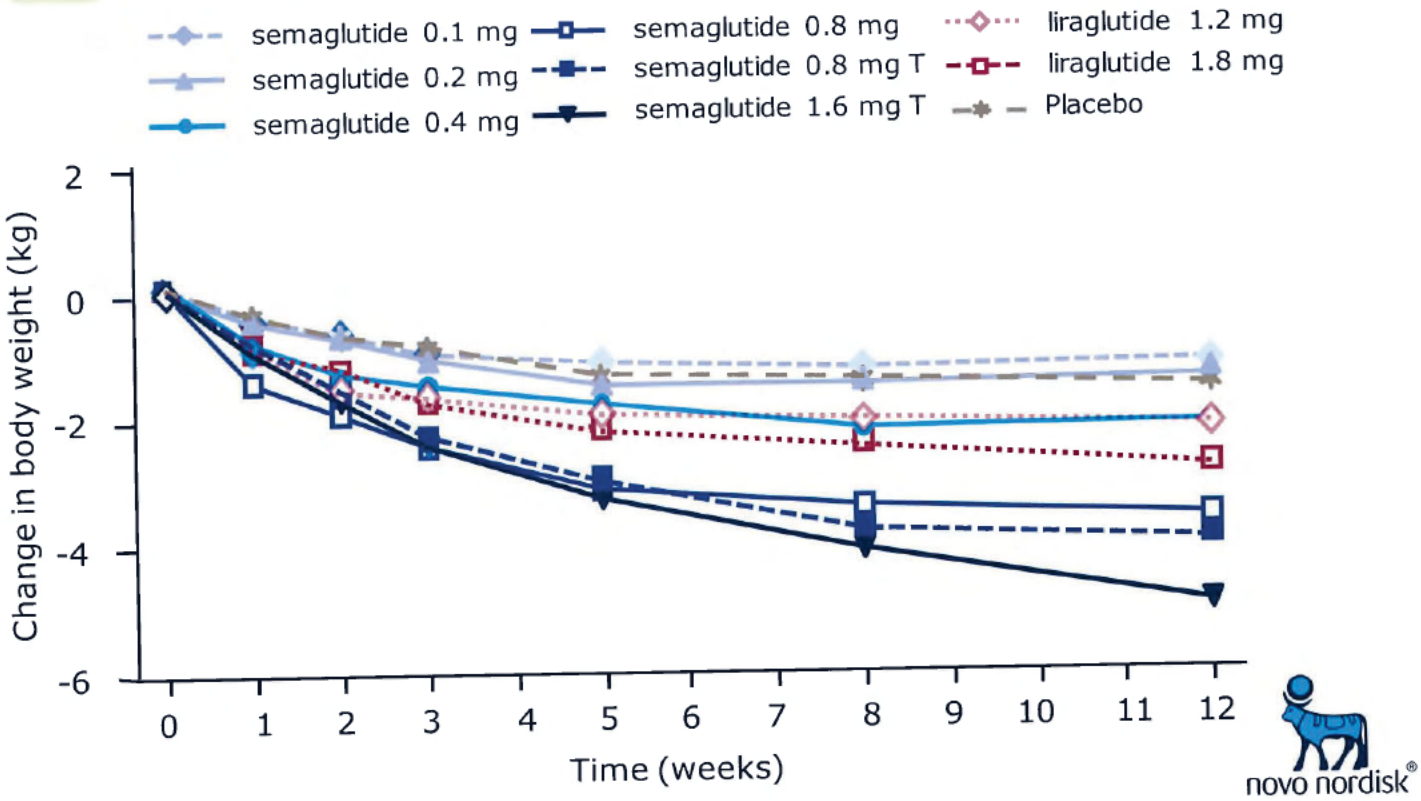
# Mean body weight change (FAS, LOCF)

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# Overall tolerability

| | Placebo | semaglutide | | | | | | liraglutide | |
|---|---|---|---|---|---|---|---|---|---|
| | | 0.1 mg | 0.2 mg | 0.4 mg | 0.8 mg | 0.8 mg T | 1.6 mg T | 1.2 mg | 1.8 mg |
| Exposed (safety analysis set) | 46 | 47 | 43 | 48 | 42 | 43 | 47 | 45 | 50 |
| SAE | **1** (2.2) 1 | **1** (2.1) 1 | **1** (2.3) 1 | **2** (4.2) 2 | **0** (0.0) 0 | **1** (2.3) 2 | **2** (4.3) 2 | **0** (0.0) 0 | **1** (2.0) 1 |
| AE | 20 **(43.5)** 48 | 28 **(59.6)** 76 | 24 **(55.8)** 55 | 35 **(72.9)** 134 | 36 **(85.7)** 141 | 31 **(72.1)** 142 | 44 **(93.6)** 219 | 25 **(55.6)** 83 | 31 **(62.0)** 90 |
| Withdrawn – total | 1 **(2.2)** | 5 **(10.6)** | 7 **(16.3)** | 10 **(20.3)** | 10 **(23.3)** | 10 **(23.3)** | 15 **(31.3)** | 3 **(6.5)** | 9 **(18.0)** |
| Withdrawn – AE | 0 **(0.0)** | 0 **(0.0)** | 3 **(7.0)** | 7 **(14.6)** | 6 **(14.3)** | 9 **(20.9)** | 14 **(29.8)** | 2 **(4.4)** | 5 **(10.0)** |
| Withdrawn – GI AE | 0 **(0.0)** | 0 **(0.0)** | 2 **(4.7)** | 5 **(10.4)** | 6 **(14.3)** | 8 **(18.6)** | 13 **(27.7)** | 1 **(2.2)** | 5 **(10.0)** |

N (% of exposed) E
60% of n=70 withdrawals due to AE, of which 85% were due to GI AE

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# NN9535-1821 Overall conclusions

- [redacted]
  - [redacted]
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# Considerations for phase 3 development

# Selection of doses and dosing regimen

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# Global phase 3a programme

# Phase 3a programme design considerations

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# Current phase 3 timelines

[redacted]

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NN9535-3744

# NN9535-3744 - summary

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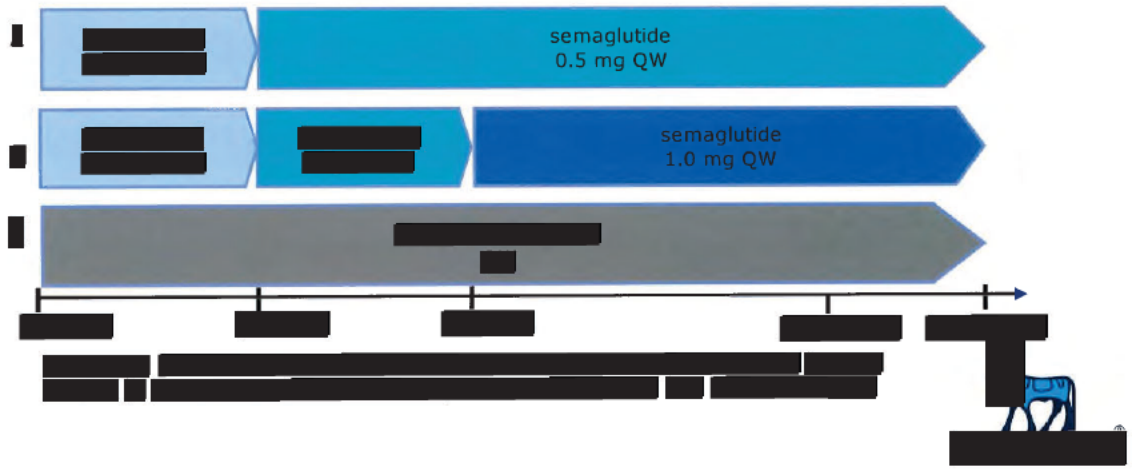

# NN9535-3744 - summary

- [redacted]

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# Inclusion criteria vs. LEADER

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# Inclusion criteria vs. LEADER

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# Exclusion criteria vs. LEADER

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# Timelines, Trial Outline

# Timelines, Trial Outline to Country allocation

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# Question – Country Allocation

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  - [redacted]

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# Country Allocation NN9535-3744 – [redacted]

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# NN9535-3744 Country Allocation

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# Question – Recruitment time

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# Current phase 3 timelines

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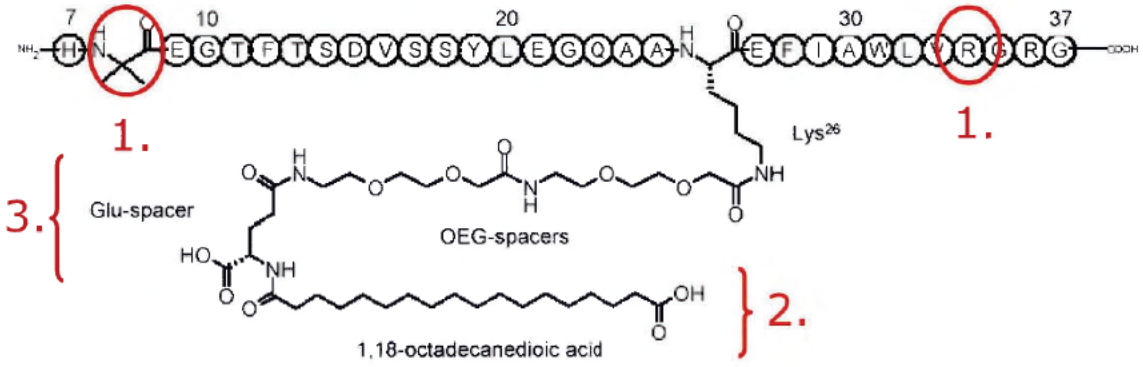
# Questions?

- Thank you for your attention

# Back-up slides

# Semaglutide: introducing the molecule

1. Peptide backbone modified at
   - position 8 (Ala to Aib*) to protect against enzymatic degradation by DPP-IV
   - position 34 (Lys to Arg) to avoid erroneous binding of fatty acid
2. Acylation in position 26 with a C-18 fatty acid slows degradation and reduces renal clearance
3. Hydrophilic linker (2 OEG & 1 Glutamic acid spacers) between Lys26 and the fatty acid moiety improves albumin binding




*∞-aminoisobutyric acid

# Summary of key safety data

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# Semaglutide device options

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