Petrelintide
Topline data
16-week trial (MAD Part 2).

Zealand Pharma

June 20, 2024

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Information concerning pharmaceuticals (including compounds under development) contained within this material is not intended as advertising or medical advice.

Agenda

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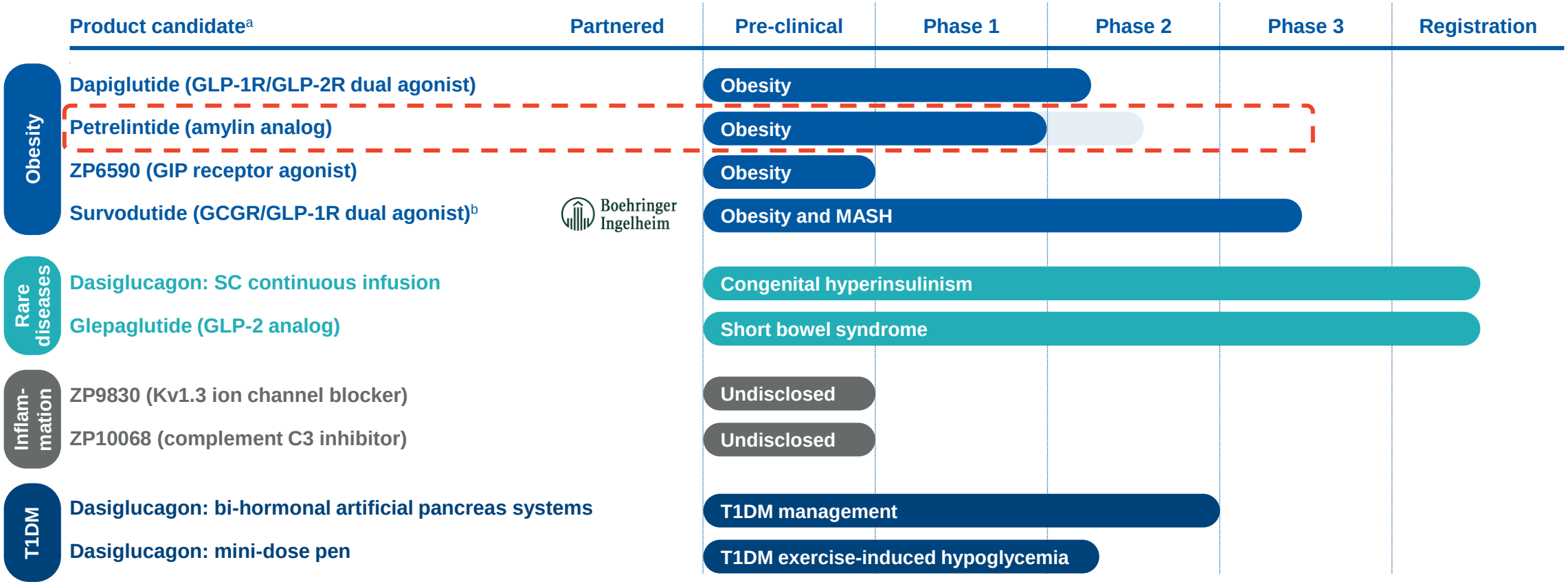
Opening remarks

Adam Steensberg, CEO

June 20, 2024

Our R&D pipeline addresses unmet medical needs across several therapeutic areas



[a]**Investigational compounds whose safety and efficacy have not been evaluated or approved by the U.S. Food and Drug Administration (FDA) or any other regulatory authority.**
[b]Survodutide is licensed to Boehringer Ingelheim from Zealand Pharma, with Boehringer solely responsible for development and commercialization globally (subject to Zealand's co-promotion rights in the Nordic countries): EUR 315 million outstanding potential development, regulatory and commercial milestones + high single to low double digit % royalties on global sales.

GCGR=glucagon receptor; GIP=gastric inhibitory polypeptide; GLP-1R=glucagon-like peptide-1 receptor; GLP-2=glucagon-like peptide-2; GLP-2R=glucagon-like peptide-2 receptor; MASH=metabolic dysfunction-associated steatohepatitis (formerly NASH, or nonalcoholic steatohepatitis); SC=subcutaneous; T1DM=type 1 diabetes mellitus.

Addressing the greatest healthcare challenge of our time

GLP-1RA-based therapies are effective at reducing weight in PwO, but associated with GI tolerability issues[1]

There is a significant unmet need for alternative treatment options with different mechanisms of action

Today, **two QW GLP-1RA-based therapies are approved***, offering ~15-21% mean weight loss[2,3]

Up to **30%** of patients with obesity **discontinue GLP-1RA treatment** within **1 month**[4]

Up to **60-70%** of patients **discontinue GLP-1RA treatment** within **12 months**[5]

Petrelintide represents an alternative to GLP-1RA based therapies **targeting**:

- **15-20% mean weight loss**; high-quality weight loss with potential for preservation of lean mass
- **Non-incretin mechanism** that reduces food intake by increasing satiety and restoring leptin sensitivity
- **Significantly improved GI tolerability** with both lower frequency and severity of adverse events

*For chronic weight management: Wegovy and Zepbound.

1. Wang et al. Front Endocrinol (Lausanne) 2023;14:1085799; 2. Wegovy (semaglutide) US PI. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/215256s007lbl.pdf, accessed June 2024; 3. Zepbound (tirzepatide) US PI. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/217806s000lbl.pdf, accessed June 2024; 4. Blue Health Intelligence (2024) Real-world Trends in GLP-1 Persistence and Prescribing for Weight Management (May 2024); 5. Gasoyan et al. Obesity (Silver Spring). 2024;32(3):486-493. doi:10.1002/oby.2395.

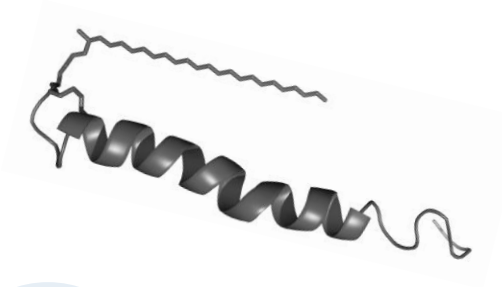
GI=gastrointestinal; GLP-1RA=glucagon-like peptide-1 receptor agonist; T2DM=type 2 diabetes mellitus; PwO=people with obesity; QW=once-weekly.

Topline data Phase 1b 16-week trial

David Kendall, CMO

June 20, 2024

Petrelintide is a potential best-in-class amylin analog in development as an alternative to GLP-1RA-based therapy

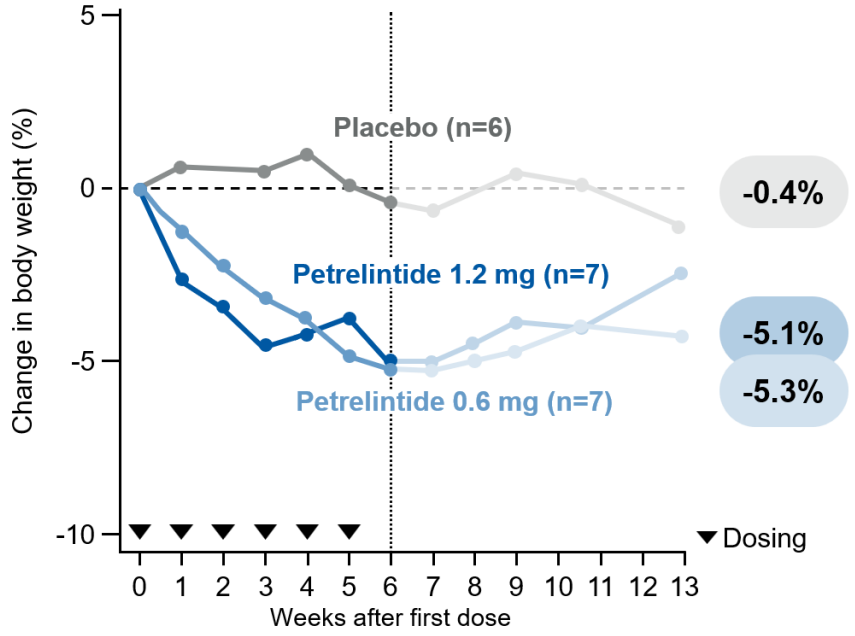


Petrelintide (ZP8396) is a 36-amino-acid acylated peptide, based on the peptide sequence of **human amylin**

Long-acting amylin analog (half-life of 10 days), suitable for **once-weekly administration**[1]

Stability at **neutral pH**, **minimizing fibrillation** and allowing for co-formulation with other peptides[2,3]

Potent balanced agonist effect on **amylin and calcitonin receptors**[4,5]



In Part 1 of the Phase 1b MAD trial, all drug-related **GI side effects were mild**[6]

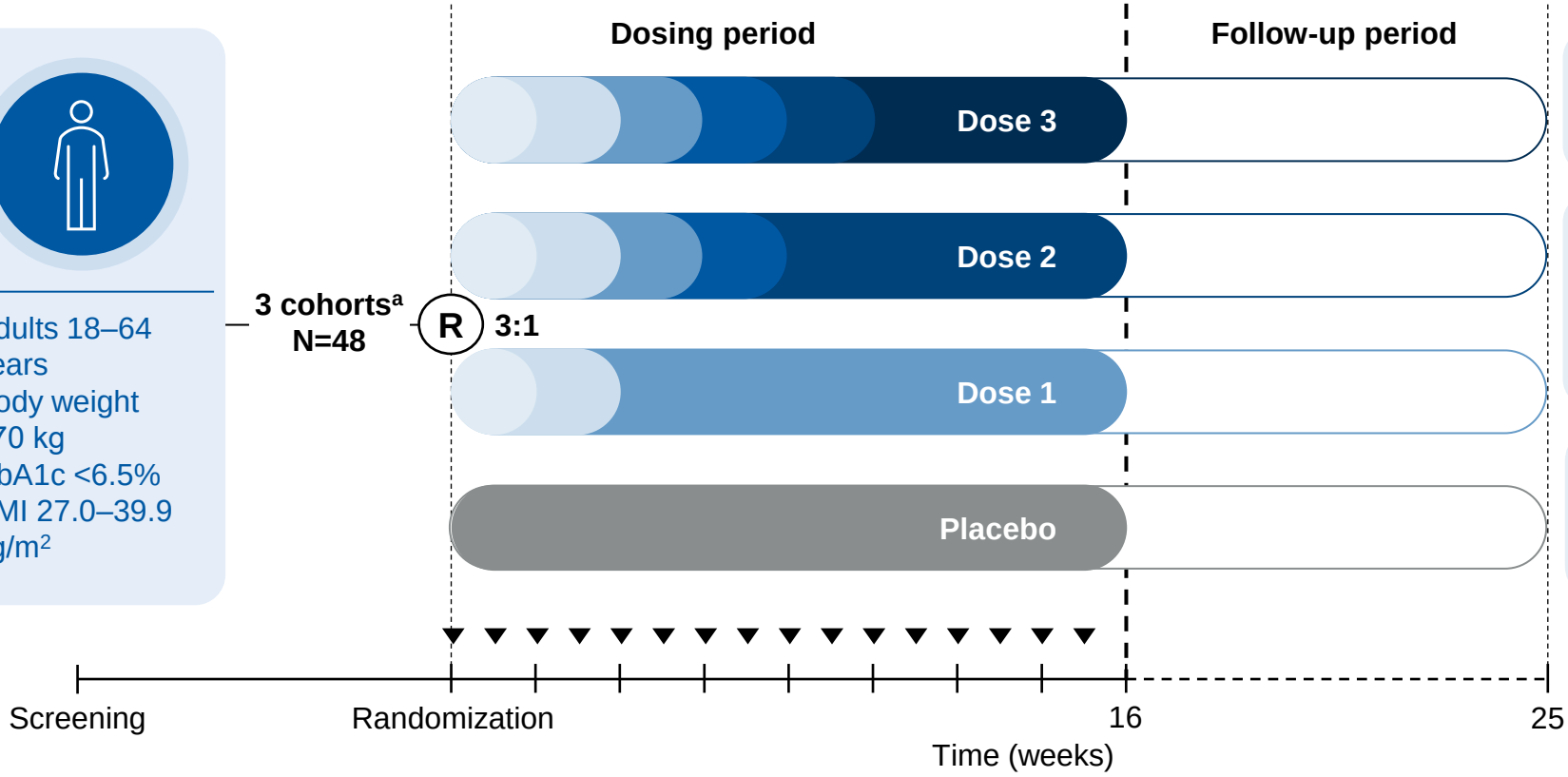
Sources: 1. Brændholt Olsen et al. Poster 92-LB. Presented at ADA 83rd Scientific Sessions, June 23–26, 2023, San Diego, CA; 2. Skarbaliene et al. Poster 1406-P. Presented at ADA 82nd Scientific Sessions, June 3–7, 2022, New Orleans, LA; 3. Eriksson et al. Poster 532. Presented at ObesityWeek, November 1–4, 2022, San Diego, CA; 4. Eriksson et al. Presentation at ObesityWeek, November 1–4, 2022, San Diego, CA; 5. Data on file; 6. Brændholt Olsen et al. Poster presented at ObesityWeek, October 14–17, 2023, Dallas, TX.
GI=gastrointestinal; MAD=multiple ascending dose.

Trial design: Petrelintide Phase 1b MAD Part 2

A randomized, double-blind, placebo-controlled, Phase 1b, MAD trial of petrelintide – Part 2[1,2]

Aim: to evaluate the safety, tolerability, PK and PD of multiple SC doses of petrelintide, with dose escalation

- Adults 18–64 years
- Body weight ≥70 kg
- HbA1c <6.5%
- BMI 27.0–39.9 kg/m^2



Primary endpoint:
- Incidence of TEAEs

Secondary endpoints:
- PK parameters of petrelintide
- PD parameters related to MTM

Exploratory endpoint:
- Change in body weight

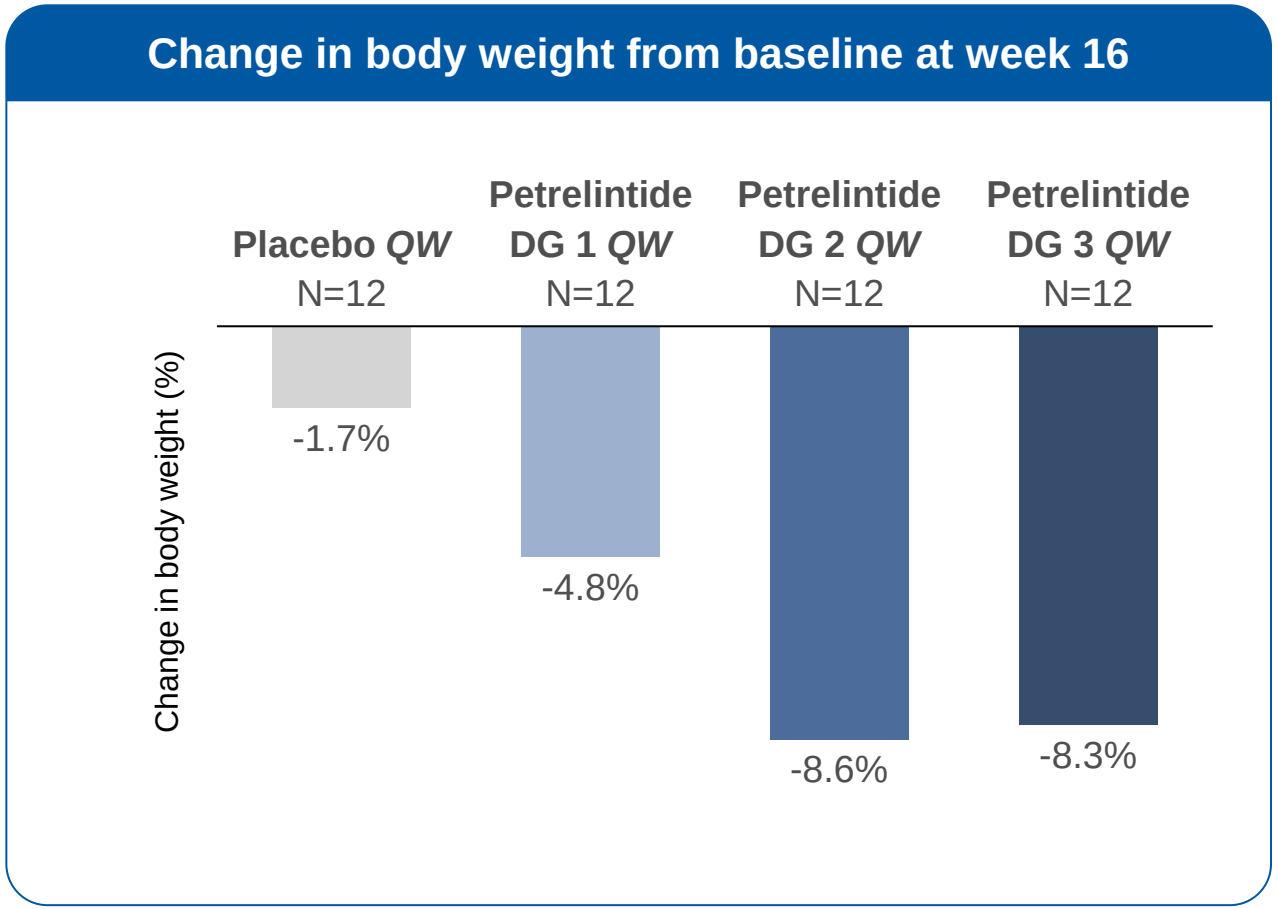
[a]Safety evaluation occurred after 4 weeks of treatment at the target dose for each cohort. Initiation of the next, higher dose cohort only occurred following safety evaluation for the previous cohort.
Sources: 1. ClinicalTrials.gov (NCT05613387), accessed June 2024; 2. Data on file.
BMI=body mass index; HbA1c=glycated hemoglobin; MAD=multiple ascending dose; MTM=mixed test meal; PD=pharmacodynamic; PK=pharmacokinetic; SC=subcutaneous; TEAE=treatment-emergent adverse event.

Baseline characteristics were balanced across the dose cohorts

Gender	**79%** of participants were **male**
Age	Median **49 years**
Weight	Median **92.4 kg**
BMI	Median **29.2 kg/m²**

Source: Data on file.
BMI=body mass index;

Petrelintide Phase 1b results: Substantial weight loss observed at 16 weeks

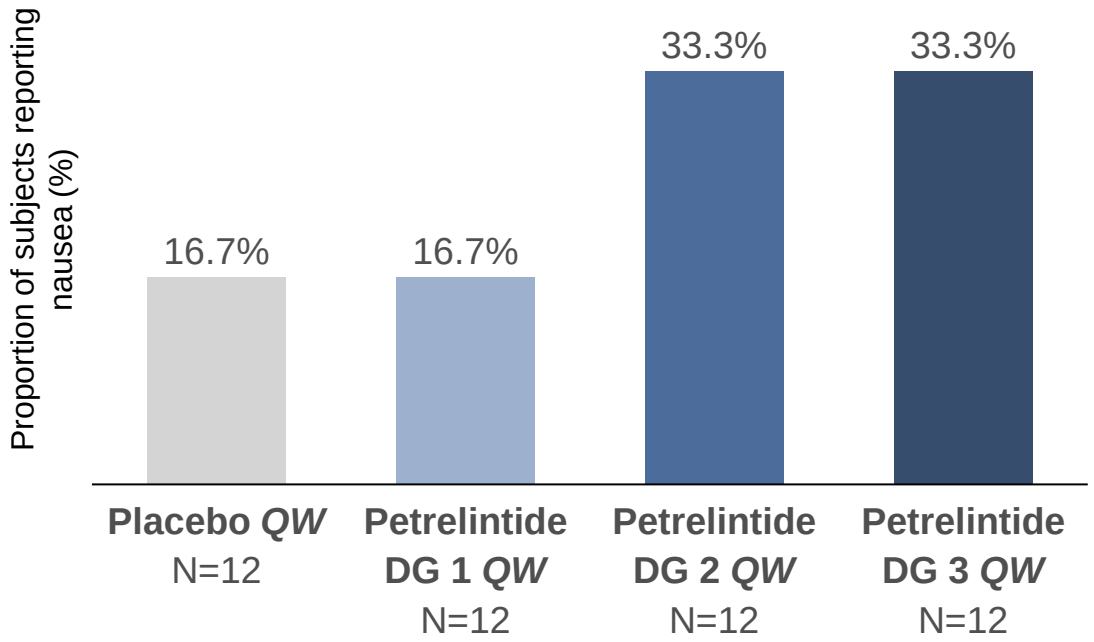


- Petrelintide treatment resulted in a **mean weight loss of up to 8.6%** from baseline after 16 weeks
- All participants treated with petrelintide lost weight during the trial
- Review of data from individual participants supports that separation at the higher doses is possible

Source: Data on file.
QW=once-weekly; DG=dose group.

Petrelintide treatment was safe and well-tolerated at all dose levels in the 16-week trial

Proportion of subjects reporting nausea in the 16-week trial



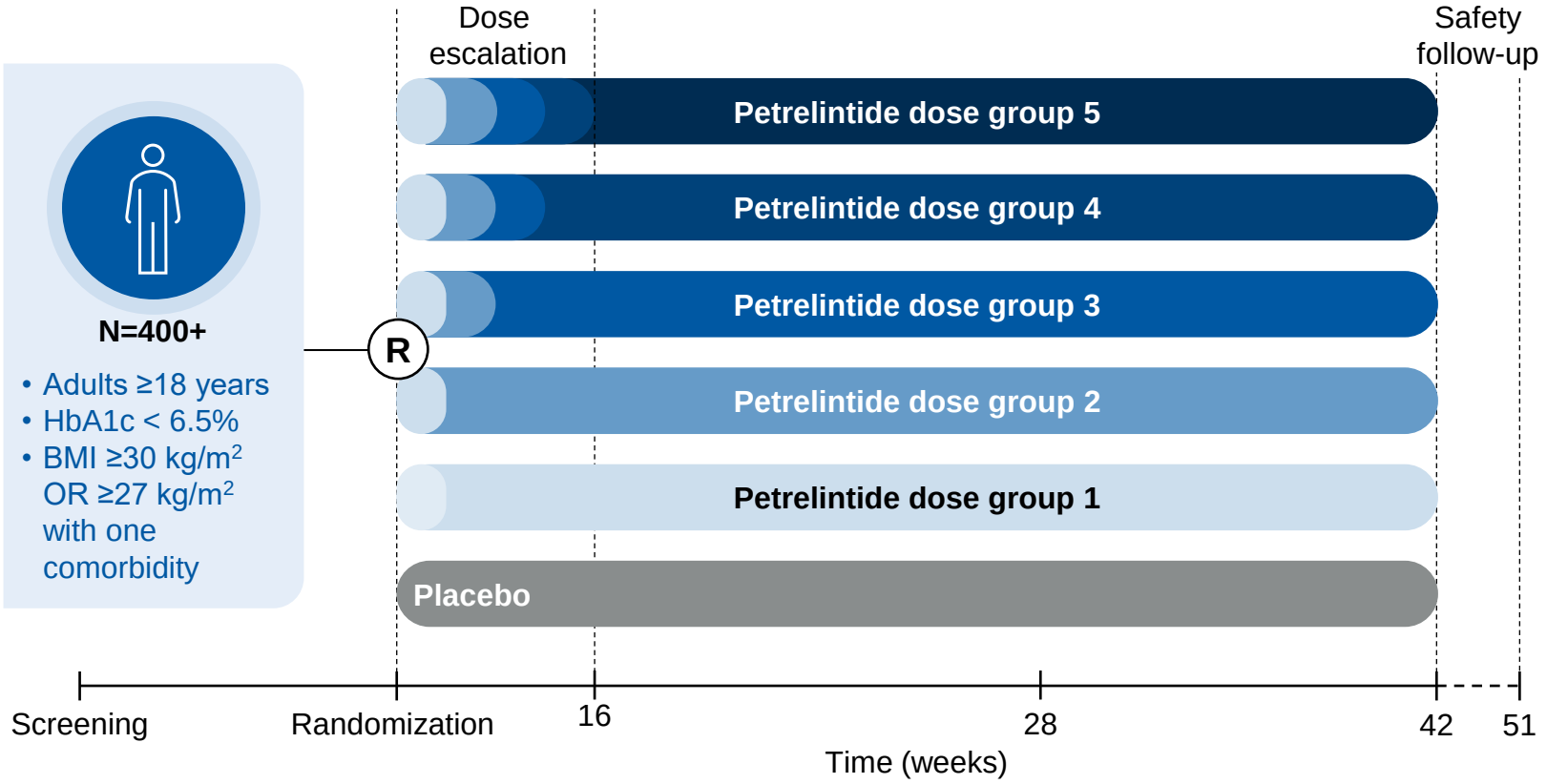
- No serious or severe AEs reported
- All GI AEs were mild except for two moderate events (nausea and vomiting) reported by one participant who discontinued treatment after the third dose
- No other participants discontinued treatment due to AEs and no other participants reported vomiting
- Two reports of diarrhea, both of which were mild
- No anti-drug antibodies were observed

Source: Data on file.
Topline results are from an interim data cut at 16 weeks, which was at the end of the treatment period. Final results will be based on all collected data that include complete post-treatment follow-up.
QW=once-weekly; DG=dose group; GI=gastrointestinal; AE=adverse event.

Continuing development of petrelintide as monotherapy through a comprehensive Phase 2b trial

A randomized, double-blind, placebo-controlled, Phase 2b trial with petrelintide to be initiated in H2 2024

Aim: to evaluate change in body weight with multiple doses of petrelintide versus placebo



Primary endpoint:

- Percentage change in body weight from baseline to end of treatment

Secondary endpoints:

- Absolute change in body weight from baseline to end of treatment
- Proportion of patients with ≥5% and ≥10% weight loss from baseline to end of treatment
- Change in waist circumference at end of treatment

Exploratory endpoints:

- Body composition

Source: Data on file.
BMI=body mass index; HbA1c=glycated hemoglobin.

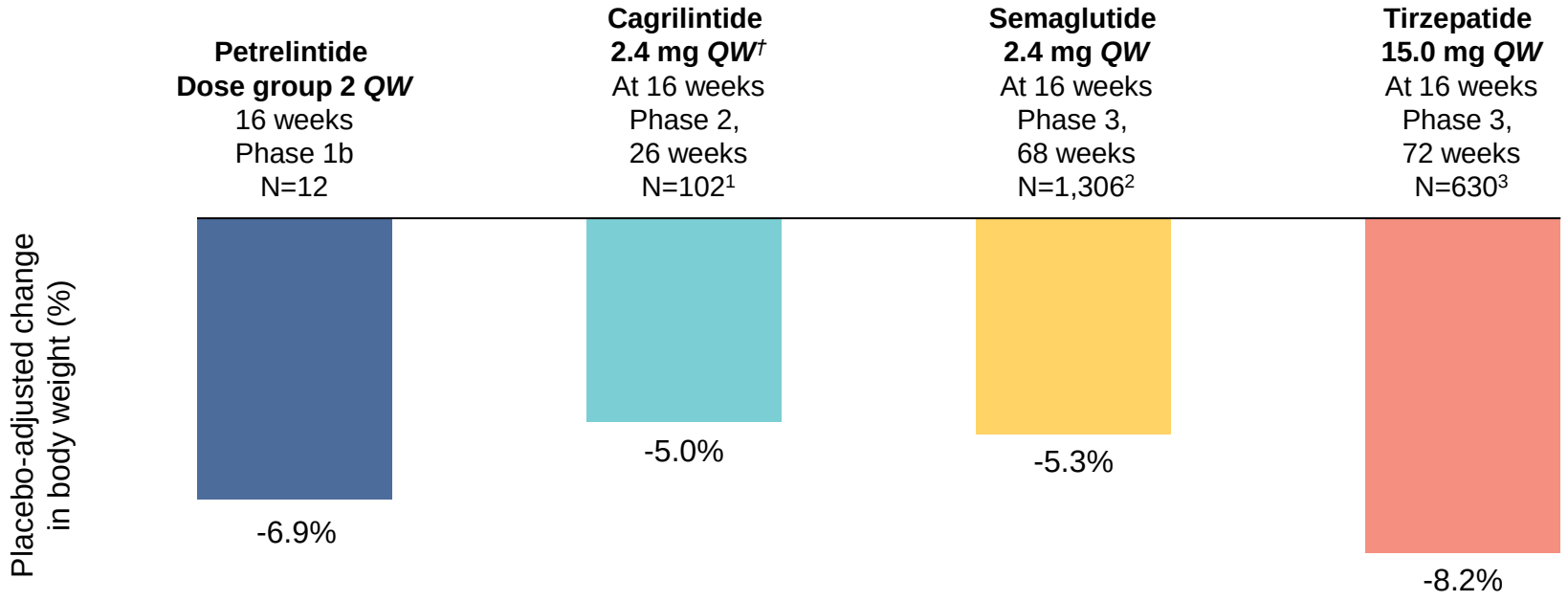
Concluding remarks

Adam Steensberg, CEO

June 20, 2024

16-week data position petrelintide as a potential best-in-class amylin analog for GLP-1RA-like weight loss

Indirect cross-trial comparison of placebo-adjusted percentage change in body weight from baseline at Week 16*



Baseline values

Mean BMI, kg/m^2	29.2	37.9	37.8	38.1
Female, %	21	74	73	68

***No head-to-head study has been conducted with petrelintide against the other drug product candidates. Differences exist in study designs and conditions, and caution should be exercised when comparing data across studies. Data presented were analyzed according to the trial product estimand.[1-3] Semaglutide data are shown for the on-treatment period.[2]**

†Cagrilintide 4.5 mg is not being advanced in clinical development but achieved a placebo-adjusted mean weight-loss of 5.9% at 16 weeks in the 26-week, Phase 2 trial.[1]

Sources: 1. Lau et al. Lancet 2021;398(10317):2160–2172; 2. Wilding et al. N Engl J Med 2021;384(11):989–1002; 3. Jastreboff et al. N Engl J Med 2022;387(3):205–216.

BMI=body mass index; GLP-1RA=glucagon-like peptide-1 receptor agonist; QW=once-weekly.

Petrelintide is a potential best-in-class alternative to GLP-1RA-based therapies: Target Product Profile of…

Weight loss – targeting 15-20% mean reduction in body weight as monotherapy, including high-quality weight loss with potential for preservation of lean mass[1-4]

MoA – mechanism reduces food intake by restoring leptin sensitivity and increasing satiety[5]
First non-incretin MoA that has shown potential for monotherapy with GLP-1RA-like weight loss[1-2,4]

Tolerability – potential for significantly better GI tolerability vs GLP-1RAs[1,2,6]

Cardiovascular disease – potential to reduce CVD risk (e.g., through effects on blood pressure, heart rate, lipids, and hsCRP)[2,7]

Sources: 1. Olsen et al. Poster presented at ObesityWeek, October 14–17, 2023, Dallas, TX; 2. Lau et al. Lancet. 2021;398(10317):2160–2172; 3. Wilding et al. N Engl J Med 2021;384(11):989–1002; 4. Data on file; 5. Roth et al. Proc Natl Acad Sci U S A 2008;105(20):7257–7262; 6. Olsen et al. Poster 92-LB. Presented at ADA 83rd Scientific Sessions, June 23–26, 2023, San Diego, CA; 7. Frias et al. Lancet 2023;402(10403):720–730.
CVD=cardiovascular disease; GLP-1=glucagon-like peptide-1; GLP-1RA=glucagon-like peptide-1 receptor agonist; hsCRP=high-sensitivity C-reactive protein; MoA=mechanism of action; GI=gastrointestinal.

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Q&A

June 20, 2024