Media & Investor Release

Roche announces positive Phase II results for petrelintide, an amylin analog developed for people living with overweight and obesity

- **Petrelintide achieved up to 10.7% mean body weight reduction at week 42 versus 1.7% with placebo (p-value<0.001) while demonstrating placebo-like tolerability**
- **At the maximally effective dose, there were no cases of vomiting and no treatment discontinuations due to gastrointestinal adverse events**
- **The data support further development of petrelintide in chronic weight management as monotherapy and its tolerability profile also confirms its value as a combination partner**

Basel, 05 March 2026 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today positive topline results from the Phase II ZUPREME-1 trial evaluating investigational petrelintide versus placebo in 493 people living with overweight and obesity (mean BMI of 37 kg/m²) in a gender-balanced trial population. The study met its primary endpoint, demonstrating that once-weekly subcutaneous injections of petrelintide (escalated every fourth week) resulted in statistically significant and clinically meaningful weight loss from baseline after 28 weeks in all five treatment arms compared to placebo.

The weight loss was sustained through week 42 with participants achieving up to 10.7% mean weight loss from baseline using the efficacy estimand, compared to 1.7% with placebo. In the cohort that achieved the greatest reduction in body weight, 98% of trial participants treated with petrelintide reached the maintenance dose underscoring its favorable tolerability profile. Accordingly, body weight reduction using the treatment regimen estimand was largely consistent with the efficacy estimand. Notably, female participants lost considerably more weight than male participants in this trial.

“Petrelintide achieved meaningful weight loss with a well-tolerated dosing approach, which is essential to support long-term and sustained benefits in people living with obesity,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “Therefore, these data reinforce our confidence in petrelintide’s potential to address important unmet medical needs in chronic weight management.”

Petrelintide demonstrated a favourable tolerability profile which is comparable to placebo; no unexpected safety signals were observed. The treatment discontinuation rate due to adverse events (AEs) was 4.8% with petrelintide in the maximally effective treatment arm versus 4.9% with placebo. The most frequently reported AEs were gastrointestinal-related, the vast majority of which were mild. The proportion of participants across all petrelintide treatment arms who experienced vomiting was lower than that observed with placebo, with no vomiting in the maximally effective treatment arm. The rates of diarrhea and constipation

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were consistent with those seen with placebo and remained in the single-digit range. Nausea was less common than in the prior 16-week Phase 1b trial of petrelintide, which used dose escalation every second week, and the vast majority was mild. Almost no events of nausea were reported after participants reached their maintenance dose. Trial withdrawal due to any reason was 8.4% across petrelintide treatment arms compared to 13.6% with placebo.

The final ZUPREME-1 data, including a nine-week safety follow-up, will be presented at an upcoming medical congress and will inform the optimal Phase III designs and settings to evaluate petrelintide. Topline results from the second Phase II petrelintide monotherapy trial, ZUPREME-2, which is evaluating petrelintide versus placebo in people living with obesity or overweight and type 2 diabetes, are expected in the second half of 2026. A Phase II trial exploring the combination of petrelintide and CT-388, will be initiated later in 2026.

With its growing cardiometabolic portfolio and strong diagnostic expertise, Roche is advancing a portfolio of solutions providing optionality to adequately address the diverse needs of people living with obesity and its comorbidities.

Obesity is recognised as the greatest single risk factor for chronic disease globally. By 2035, over four billion people (more than half of the global population) are projected to be living with overweight and obesity, a trend affecting nearly every country. This rise is driven by a complex mix of genetics and biology as well as behavioural, environmental and socioeconomic factors, placing an increased strain on healthcare systems due to the associated burden of comorbidities and reduced quality of life.

In 2025, Roche and Zealand entered into an exclusive collaboration & licensing agreement to co-develop and co-commercialise petrelintide for people living with overweight and obesity.

About ZUPREME-1 [NCT06662539]

ZUPREME-1 is a 42-week randomised, double-blind, placebo-controlled, dose-finding Phase II clinical trial with 493 participants with a mean baseline body weight of 107 kg, a mean body mass index (BMI) of 37 kg/m², and a mean age of 48 years. The trial population was 53% female, representing a well-balanced cohort designed to maximise learning across genders. The trial compares five doses of once-weekly petrelintide with placebo, when added to a reduced-calorie diet and increased physical activity in people with obesity or overweight with weight-related comorbidities.

The trial includes a screening period, a dose escalation period up to 16 weeks with dose escalation every fourth week, followed by a maintenance period until week 42, and a follow-up period after treatment is completed until week 51. ZUPREME-1 has enrolled participants across 33 sites in the United States, Poland, and Romania. The primary endpoint in the trial is the percentage change in body weight from baseline to week 28. Secondary endpoints include, but are not limited to, percentage change in body weight from baseline to week 42,

change in waist circumference, change in haemoglobin A1c (HbA1c), change in high-sensitivity C-reactive protein (hsCRP), change in fasting lipids, and change in fasting glucose. Change in body composition at week 42 measured by Magnetic Resonance Imaging (MRI) is included as an exploratory endpoint in the trial.

About Petrelintide

Petrelintide is an investigational long-acting amylin analog suitable for once-weekly subcutaneous administration that has been designed with chemical and physical stability with no fibrillation around neutral pH, allowing for co-formulation and co-administration with other peptides.[1] Amylin is produced in the pancreatic beta cells and co-secreted with insulin in response to ingested nutrients. Amylin receptor activation has been shown to reduce body weight by restoring sensitivity to the satiety hormone leptin[2,3] inducing a sense of feeling full faster.

About Roche

Founded in 1896 in Basel, Switzerland, as one of the first industrial manufacturers of branded medicines, Roche has grown into the world's largest biotechnology company and the global leader in in-vitro diagnostics. The company pursues scientific excellence to discover and develop medicines and diagnostics for improving and saving the lives of people around the world. We are a pioneer in personalised healthcare and want to further transform how healthcare is delivered to have an even greater impact. To provide the best care for each person we partner with many stakeholders and combine our strengths in Diagnostics and Pharma with data insights from the clinical practice.

For over 125 years, sustainability has been an integral part of Roche's business. As a science-driven company, our greatest contribution to society is developing innovative medicines and diagnostics that help people live healthier lives. Roche is committed to the Science Based Targets initiative and the Sustainable Markets Initiative to achieve net zero by 2045.

Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan.

For more information, please visit www.roche.com.

References

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