Media & Investor Release

Ad hoc announcement pursuant to Art. 53 LR

Roche reports positive Phase I results for its dual GLP-1/GIP receptor agonist CT-388 in people with obesity

- **Over 24 weeks, a once-weekly subcutaneous injection of CT-388 achieved a clinically meaningful and statistically significant mean placebo-adjusted weight loss of 18.8% ($p < 0.001$)**
- **At week 24, 100% of CT-388 treated participants achieved >5% weight loss, 70% achieved >15% and 45% achieved >20% weight loss**
- **In a subgroup with pre-diabetes at baseline, CT-388 treatment normalised glycemia in all patients, indicating its strong impact on glucose homeostasis**
- **No new or unexpected safety signals were detected. Overall, CT-388 demonstrated a safety and tolerability profile consistent with its drug class**

Basel, 16 May 2024 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today positive results from the Phase I clinical trial of CT-388, a dual GLP-1/GIP receptor agonist being developed for the treatment of obesity and type 2 diabetes. The study found that a once-weekly subcutaneous injection of CT-388 over 24 weeks resulted in significant weight loss in healthy adults with obesity compared to placebo. The weight loss achieved with CT-388 was clinically meaningful, with a mean placebo-adjusted weight loss of 18.8% (p-value < 0.001). At week 24, 100% of CT-388 treated participants achieved a weight loss of >5%, 85% achieved >10%, 70% achieved >15%, and 45% achieved >20%. The treatment was well tolerated, with mild to moderate gastrointestinal-related adverse events being the most common, consistent with the incretin class of medicines that CT-388 belongs to. All participants with a pre-diabetes status at baseline became normoglycemic after 24 weeks of CT-388 treatment, whereas glycemic status of participants treated with placebo remained largely unchanged during this period.

“We are very pleased to see the significant and clinically meaningful weight loss in people treated with CT-388,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “The results are highly encouraging for further development of CT-388 for both obesity and type 2 diabetes and underscore its potential to become a best-in-class therapy with durable weight loss and glucose control.”

Obesity is one of the most urgent health challenges in the world with extensive comorbidities, such as type 2 diabetes, cardiovascular diseases, steatohepatitis and chronic kidney disease. Over four billion people - about 50% of the world’s population - are estimated to be impacted

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by obesity or being overweight by 2035. The growing number puts an incredible strain on societies and healthcare systems around the world.

CT-388 belongs to the class of incretin-based medicines that aim to regulate blood sugar and reduce appetite. It selectively targets and activates two specific receptors in the body, known as GLP-1 and GIP, which integrate nutrient-derived signals to control food intake, energy absorption and assimilation. It is hypothesised that the dual targeting effect of CT-388 could result in a meaningful durable glucose reduction and weight loss, in addition to a favourable safety profile.

An additional cohort from the ongoing placebo-controlled Phase I trial of CT-388 will evaluate obese patients (BMI>30 kg/m2) with type 2 diabetes over a 12-week treatment duration. Roche expects data from this additional cohort in the second half of 2024.

About the CT-388 study

The CT-388-101 trial is a multi-arm, multi-cohort Phase I randomised, double-blind, placebo-controlled study designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of CT-388 in otherwise-healthy adult participants with overweight or obesity and in participants with obesity and type-2 diabetes mellitus.

The primary endpoint of the trial is safety and tolerability of CT-388; secondary endpoints include its effect on body weight and glucose homeostasis. Pharmacokinetics and other pharmacodynamic effects of CT-388 were also assessed.

About CT-388

CT-388 is a once-weekly subcutaneous injectable, dual GLP-1/GIP receptor agonist being developed for the treatment of obesity and type 2 diabetes (T2D). CT-388 was designed to have potent activity on both the GLP-1 and GIP receptors but with minimal to no ß-arrestin recruitment on either receptor. This biased signalling significantly minimises receptor internalisation and consequent desensitisation, which is expected to lead to prolonged pharmacological activity. It is currently being studied in a multi-part, multi-cohort Phase 1 clinical trial in people with overweight/obesity with and without T2D.

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.

In recognising our endeavour to pursue a long-term perspective in all we do, Roche has been named one of the most sustainable companies in the pharmaceuticals industry by the Dow Jones Sustainability Indices for the fifteenth consecutive year. This distinction also reflects our efforts to improve access to healthcare together with local partners in every country we work.

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

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