Carmot Therapeutics Highlights Clinical Data from its Pipeline of Treatments for Obesity and Diabetes at the 83rd American Diabetes Association Scientific Sessions

– Once-weekly administration of CT-388 delivers clinically meaningful weight loss and metabolic control with a favorable tolerability profile over a 4 week treatment period in overweight and obese otherwise healthy participants –

– Mechanism of Action study achieves robust weight-independent effect of CT-868 on glucose homeostasis in overweight and obese adults with type 2 diabetes –

SAN DIEGO, Calif., June 23, 2023 (GLOBE NEWSWIRE) — Carmot Therapeutics, Inc. (Carmot), a clinical-stage biotechnology company developing disease-modifying therapies for metabolic diseases, today announced positive results from the following studies: a Phase 1 clinical trial of CT-388 assessing safety, tolerability, pharmacokinetics and pharmacodynamic activity in overweight and obese otherwise healthy participants, a mechanism of action (MOA) clinical study of CT-868 in overweight and obese adults with type 2 diabetes (T2D) to assess weight independent effects on glucose homeostasis, and a preclinical study in rodent models of type 1 diabetes (T1D) to support the effects of CT-868 as an adjunct to insulin treatment. The results are summarized in three poster presentations taking place at the American Diabetes Association (ADA) Annual Meeting (June 23-26, 2023).

“We are extremely excited about the results from our CT-388 and CT-868 dual GLP-1/GIP receptor modulator programs to date. These data provide critical translational support to our hypothesis that finely tuning GPCR signalling could lead to differentiated pharmacology,” said Manu Chakravarthy, MD, PhD, Carmot's Chief Scientific & Medical Officer. “To see more than 8% weight loss in 4 weeks with a favorable tolerability profile after CT-388 dosing, is highly encouraging and sets the stage to test additional patient-friendly dosing regimens and titrations to maximize the potential benefit-risk profile for people living with obesity and its many comorbidities."

Chakravarthy added, "Mechanistic data from CT-868 is equally exciting as it suggests that with a fully biased twincretin, weight-independent and potentially, insulin-independent effects on glucose disposal is possible, which could provide an effective therapeutic solution to people living with type 1 diabetes. We are now keenly focused on executing additional Phase 2 clinical trials across both programs this year, and to key data readouts over the next 6 to 12 months."

Summaries of the three presentations are as follows:

Poster No. 75-LB: CT-388, a novel once-weekly dual GLP-1 and GIP receptor modulator, is safe, well-tolerated, and produces more than 8% weight loss in 4 weeks in overweight and obese adults

As part of a larger Phase 1/2 clinical trial, the Phase 1 results presented at ADA comprised single ascending doses (SAD; 0.5-7.5 mg) and multiple ascending doses (MAD; 5-12 mg) for 4 weeks administered to overweight/obese adults. The primary objective, safety and tolerability of CT-388, was evaluated across a total of 64 participants who received at least one dose of CT-388 or placebo. The results were as follows across the three MAD cohorts:

- Favorable tolerability profile in both overweight and obese participants with most common adverse events (AEs) being GI-related, consistent with the incretin class. No temporal patterns for AEs around dose up-titration periods.
- Pharmacokinetic (PK) profile supports once weekly dose administration.
- CT-388 dosed at 5/8/12/12 mg produced 8.4% weight loss (7.7 kg, ~17 lbs) accompanied by a decrease in waist and hip circumference, and improvement in markers of insulin sensitivity (HOMA-IR). Initial profile suggests that obese patients might benefit the most given the higher weight loss and more favorable tolerability.

These data warrant further clinical evaluation of CT-388, possibly with minimal to no titration, for the treatment of obesity, type 2 diabetes and other weight-related comorbidities. Carmot has designed the Phase 1/2 CT-388 clinical trial to evaluate not only higher doses across longer treatment durations (e.g. 12-24 weeks), but also cohorts with minimal to no titrations. Carmot expects data from these additional cohorts in the first half of 2024. Additional Phase 2 clinical trials in overweight and obese adults are planned to commence in 2023.

Poster No. 774-P: Weight-independent effects of CT-868, a signaling biased dual GLP-1 and GIP receptor modulator, on glucose homeostasis in overweight and obese adults with Type 2 Diabetes

In a Phase 1 randomized, double-blind crossover trial in 20 overweight and obese patients with T2D, each of three treatments (CT-868, liraglutide and placebo) was administered to all participants for 4 days to examine its effect on glucose homeostasis independent of weight loss. The results were as follows:

- CT-868 demonstrated a robust insulin secretory response from beta cells in patients with T2D relative to placebo; this response was similar between CT-868 and liraglutide.
- CT-868 treatment lowered appetite and hunger scores accompanied by significantly decreased food intake relative to placebo; no significant changes were observed between placebo and liraglutide.
- During the mixed meal tolerance test (MMTT), patients with T2D who were treated with CT-868 demonstrated lower blood glucose accompanied by significantly less insulin excursion compared to both placebo and liraglutide. The concomitantly reduced glucose and insulin excursions suggest enhanced insulin sensitivity and/or enhanced insulin independent glucose disposal induced by CT-868, independent of weight loss.
- Consistent with the intent of the study design, body weight was not significantly changed following any of the treatments during the study periods.
- CT-868 was well tolerated with no significant adverse effects in patients with T2D.

A Phase 2, double-blind, randomized, placebo-controlled, dose-ranging clinical trial to assess the efficacy and safety of CT-868 over 26 weeks in overweight and obese patients with T2D has recently completed; results from the clinical trial will be submitted to an upcoming medical conference. CT-868 is also being evaluated in a Phase 1b randomized, placebo and active comparator-controlled crossover clinical trial to assess the effects of CT-868 on glucose homeostasis in patients with T1D. Carmot expects to initiate a Phase 2 proof-of-concept clinical trial in overweight and obese patients with T1D in the second half of 2023.

Poster No. 1649-P: Biased GLP-1 improves weight loss with additional benefits on glucose homeostasis via biased GIP in diabetic rodent models

These data provide additional mechanistic support for CT-868 in the treatment of T1D:

- In Akita mice, a mouse model of type 1 diabetes, adding CT-868 to sub-optimal doses of insulin normalized glucose levels to the same extent as that of high doses of insulin.
- Blood glucose reduction was accompanied without hyperinsulinemia.
- These effects appear to be GIP-mediated in part as a result of suppression of endogenous glucose production.

"Obesity and diabetes remain serious and ongoing public health problems, consequences from which are far-reaching and can lead to a significant burden on individuals and families. The results generated by Carmot with their dual GLP-1/GIP receptor modulators are highly encouraging and have the potential to provide the type of disease-modifying solutions that these patients sorely need," said Ildiko Lingvay, MD, MPH, MSCS, Professor of Medicine, Department of Internal Medicine/Endocrinology at UT Southwestern Medical Center. Dr. Lingvay was not involved with the conduct of the above studies.

All posters can be found on the Carmot website.

About CT-388
CT-388 is being developed as a novel therapeutic candidate for chronic weight management in obese adults with weight-related comorbidities including type 2 diabetes (T2D). CT-388 is a once-weekly investigational unimolecular GLP-1/GIP receptor modulator being studied in a multi-part, multi-cohort Phase 1/2 clinical trial to assess its safety, tolerability, pharmacokinetic and pharmacodynamic effects vs. placebo in overweight and obese healthy volunteers as well as in cohorts of overweight and obese participants with T2D.

About CT-868
CT-868 is being developed as a novel therapeutic candidate as an adjunct to insulin for glycaemic control in overweight and obese adults with type 1 diabetes (T1D). CT-868 is a once-daily investigational unimolecular GLP-1/GIP receptor modulator being studied in two clinical trials: CT-868-004, a Phase 2 multi-center, double blind, randomized, placebo-controlled, dose-ranging trial assessing efficacy and safety of CT-868 over 16 weeks in overweight and obese participants with T1D; CT-868-005, a randomized, double-blind, placebo and active comparator-controlled crossover trial to assess the weight-independent effects of CT-868 on glucose homeostasis in overweight and obese participants with T1D.

About Carmot Therapeutics.
Carmot Therapeutics is a clinical-stage biotechnology company that is focused on the discovery and development of disease-modifying therapies for people living with metabolic diseases including obesity and diabetes. We have three clinical candidates: CT-388 (once-weekly, dual GLP-1/GIP receptor modulator), CT-868 (once-daily, dual GLP-1/GIP receptor modulator) and CT-996 (oral, small molecule GLP-1 receptor agonist), and other candidates in the preclinical pipeline. All of these assets are proprietary novel compounds, wholly-owned by Carmot, and were developed utilizing Chemotype Evolution, a pioneering drug discovery platform, to identify novel incretin receptor signalling targets and develop a broad pipeline of therapeutics that have the potential to produce significant weight loss and improved glycaemic control. For more information, visit the Carmot Therapeutics website and follow us on LinkedIn.

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