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Carmot closes $160M series D to advance metabolic disease candidates

By Michael Fitzhugh, Managing Editor

Carmot Therapeutics Inc. has raised $160 million in series D financing to support a trio of early to midstage clinical programs focused on treating diabetes and obesity with peptide-based small-molecule incretin receptor modulators. The Column Group led the financing alongside a significant investment from new investor RA Capital Management. Deep Track Capital, Willett Advisors, Horizons Ventures and other institutional investors also participated in the round.

The funding will support the completion of phase II studies for CT-388, a once-weekly, dual modulator of the glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) incretin receptors for the potential treatment of obesity and type 2 diabetes (T2D); phase I studies for CT-996, an oral small-molecule GLP-1 receptor agonist; and phase II studies for CT-868, a GLP-1/GIP modulator for overweight and obese patients with T2D and as a potential adjunct to insulin in type 1 diabetes. In addition, the funds will support advancement of several preclinical programs, the company said.

"It is a very exciting time for metabolic disease, especially for patients living with obesity," Manu Chakravarthy, Carmot's chief medical officer and head of R&D, told *BioWorld*, noting the significant clinical benefits that co-agonists of GLP-1 and GIP have brought to the table.

For example, in April 2022 a phase III readout for the most advanced candidate of the class, Eli Lilly and Co.'s Mounjaro (tirzepatide), found it delivered average weight reductions of 16% on a low dose and as much as 22.5% on a high dose.

The industry has now "entered an era of non-invasive therapeutics where you can get bariatric-surgery like weight loss. GLP-1/GIP as a modality is really at the leading edge of that," Chakravarthy said. "To the best of our knowledge, we are among the very few companies that have a clinical-stage dual GLP-1/GIP right behind Lilly. In a market that is so big, being second is not a bad thing."

Following its phase III readout, Lilly is awaiting the outcome of a priority review at the U.S. FDA and no doubt enjoying the recent receipt of a positive recommendation from the EMA's Committee for Medicinal Products for Human Use in July 2022.

But, to Chakravarthy's point, the market Carmot is pursuing is substantial. Sales of the GLP-1 and GLP-1/GIP receptor agonists will continue to increase in the years ahead, according to a Clarivate forecast, with anticipated combined sales of more than $44.7 billion in the near-term.

Manu Chakravarthy, chief medical officer and head of R&D, Carmot Therapeutics

Furthermore, he said, the Carmot team believes CT-388 has the potential for both superior safety and efficacy relative to other drugs in the market, merits it is out to prove in both an ongoing phase I/Ib study expected to wrap up in the first quarter of 2023, and a planned phase II/IIb study in the second quarter of 2023. Though the specific design of the midstage study hasn't been disclosed, it's likely to be typical of similar studies which generally test multiple doses over the course of about six months in obese people with T2D.

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Notable elements of the company's other chief pipeline programs include CT-868's status as a fully biased GLP-1/GIP modulator – meaning it is designed to only be active on cyclic AMP, a key secondary messenger employed by the incretin receptor and not beta-arrestin – and CT-996's status as a potential oral alternative to injectable GLP-1 receptor agonist.

Berkeley, Calif.-based Carmot, the name of which is pronounced "car-mott," previously raised a $47 million series C round, supported in part by its partner Amgen Inc., and a $15 million series B in addition to smaller earlier financings.

Carmot's molecules are products of the company's Chemotype Evolution (CE) platform, an iterative discovery and development tool validated by the May 2021 world-first U.S. FDA approval of Amgen Inc.'s cancer therapy Lumakras (sotorasib). Lumakras was developed using CE to identify novel binding sites and covalent inhibitors of KRASG12C, the drug's target. Under terms of their agreement, first announced in 2014, Carmot gained research funding, milestone payments and a royalty on commercial sales of products emerging from the collaboration. In addition, the partners have also worked on a Parkinson's disease program. Chakravarthy declined to comment on the status of the partnership due to deal terms common to Amgen partnerships that tend to restrict partners from public disclosures about the work outside joint announcements.

Incretin-focused therapies have proved to be a highly successful class of medicines, including products such as the insulin sensitizer and dipeptidyl peptidase IV inhibitor (DPP-4) Onglyza (saxagliptin, Kyowa Kirin Co. Ltd./Astrazeneca plc), GLP-1 receptor agonists such as Byetta (exenatide, Eli Lilly and Co./Astrazeneca); the dual DPP-4 inhibitor and GLP-1 modulator Januvia (sitagliptin, Merck & Co. Inc.); and the GLP-1 receptor agonist Saxenda (liraglutide, Novo Nordisk A/S).

SGLT2 inhibitors have surpassed at least DPP-4 inhibitors as the most valuable oral T2D drug class, with sales projected by Clarivate to peak at about $25 billion in 2024, driven by positive results from cardiovascular outcome trials and renal trials. With the number of total prevalent cases of T2D in developed markets forecast by Clarivate to increase by 13% in the decade ahead, from 77 million to 87 million, there's no shortage of ongoing need for new therapies.