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## **Novo Nordisk's CagriSema demonstrates superior weight loss in people with T2D and overweight or obesity in REDEFINE 2 trial – March 10, 2025**

*At 68 weeks, CagriSema demonstrated 14% weight loss, compared to 3% with placebo; results fall short of expectations of 20% weight reduction, similar to [REDEFINE 1](#) results in obesity*

Novo Nordisk [announced](#) today topline results of the phase 3 [REDEFINE 2](#) trial (n=1,206), evaluating CagriSema (fixed combination of cagrilintide 2.4 mg and semaglutide 2.4 mg) in people with T2D and overweight or obesity. In the trial, participants could modify their dosing flexibly, and 62% of the participants in the CagriSema group reached the highest dose at 68 weeks.

The trial met its primary endpoint, demonstrating statistically significant and superior weight loss with CagriSema compared to placebo. By treatment policy estimand, CagriSema conferred a 13.7% weight loss from a baseline body weight of 102 kg (225 lbs), compared to 3.4% with placebo. By trial product estimand (assuming full treatment adherence), CagriSema conferred 15.7% weight loss from a baseline body weight of 102 kg (225 lbs), compared to 3.1% with placebo. These results compare to 15.7% weight loss from Lilly's tirzepatide at Week 72 in the [SURMOUNT-2](#) trial (n=938).

The trial also met its coprimary endpoint with 89.7% of participants on CagriSema achieving a weight loss of  $\geq 5\%$ , compared to 30.3% on placebo. The safety and tolerability profile was consistent with the GLP-1 RA class, with the most common adverse events being mild-to-moderate gastrointestinal events.

Previously, Novo Nordisk management shared expectations that CagriSema would confer approximately 20% weight loss in T2D and 25% weight loss in obesity ([3Q24](#), [ADA 2023](#), [Capital Markets Day 2024](#)). Similar to [REDEFINE 1](#) results, which demonstrated 20.4% weight loss in people with overweight or obesity, today's REDEFINE 2 results fall short of this expectation. Looking forward, Novo Nordisk plans to file for regulatory approval in 1Q26 and present full results at an undisclosed conference in 2025.

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### **REDEFINE 1 trial showed 20% weight loss in people with overweight or obesity**

In [December 2024](#), Novo Nordisk shared topline results of the phase 3 [REDEFINE 1](#) trial (n=3,417), evaluating CagriSema in adults with obesity or overweight, with one or more comorbidities, and without T2D. CagriSema conferred weight loss of 20.4%, compared to a reduction of 11.5% with cagrilintide 2.4 mg, 14.9% with semaglutide 2.4 mg, and 3.0% with placebo. If all participants had adhered to treatment, CagriSema would confer 22.7% weight loss.

In a subgroup analysis shared during Novo Nordisk's [4Q24](#) update, participants who ended at a lower dose (average of 1.1 mg CagriSema; 29% of the study population) achieved 25.1% weight loss at 68 weeks, compared to 22.2% in those who ended at the highest dose (2.4 mg; 57% of the study population). Management highlighted the potential significance of careful dose escalation/re-escalation and announced a new phase 3 trial, REDEFINE 11, to assess dose escalation/re-escalation.

Also during Novo Nordisk's [4Q24](#) update, the company addressed that the REDEFINE 1 results fall short of previous [expectations of 25%](#) weight loss. Nonetheless, the company expressed encouragement to see CagriSema confer one of the most substantial weight reductions observed in a clinical phase 3a trial. **As a combination therapy of semaglutide, which mimics the gut GLP-1 hormone, and cagrilintide, which mimics the amylin hormone, we're curious how future**

results of CagriSema might shift the treatment paradigm for obesity.

## Ongoing REDEFINE and REIMAGINE trials evaluate CagriSema in overweight or obesity and T2D, respectively

CagriSema is currently being investigated in the REDEFINE trials for people with overweight or obesity and in the REIMAGINE trials for people with T2D. See below for details and expected completion dates.

REDEFINE trials	Description and results	Completion date
<a href="#">REDEFINE 1</a> (n=3,400)	68-week trial of CagriSema vs. placebo in adults with obesity or overweight with one or more comorbidities and without T2D; topline results announced in <a href="#">December 2024</a> and subgroup analysis results shared in <a href="#">4Q24</a> .	October 2026
<a href="#">REDEFINE 2</a> (n=1,206)	68-week trial of CagriSema vs. placebo in adults with T2D and either obesity or overweight; topline results announced in <a href="#">March 2025</a> .	January 2025
<a href="#">REDEFINE 3</a> (n=7,000)	235-week CVOT of CagriSema vs. placebo in adults with established CVD with or without T2D.	September 2027
<a href="#">REDEFINE 4</a> (n=809)	72-week trial of CagriSema vs. tirzepatide 15 mg in adults with obesity.	October 2027
REDEFINE 11	Trial to assess dose escalation/re-escalation of CagriSema.	Unknown

REIMAGINE trials	Description and results	Completion date
<a href="#">REIMAGINE 1</a> (n=180)	40-week trial of CagriSema vs. placebo in people with T2D treated with diet and exercise.	December 2025
<a href="#">REIMAGINE 2</a> (n=2,734)	68-week trial of CagriSema vs. semaglutide, cagrilintide, and placebo in T2D on metformin and with or without SGLT-2 inhibitor.	January 2026
<a href="#">REIMAGINE 3</a> (n=270)	40-week trial of CagriSema vs. placebo in people with T2D on once-daily basal insulin with or without metformin.	November 2025
<a href="#">REIMAGINE 4</a> (n=1,000)	68-week trial of CagriSema vs. tirzepatide in people with T2D on metformin and with or without SGLT-2 inhibitor.	April 2026
<a href="#">REIMAGINE 5</a> (n=1,000)	60-week trial of CagriSema vs. tirzepatide 5 mg in people with T2D on metformin, SGLT-2 inhibitor, or both.	August 2026

### Close Concerns' Questions

1. What are the effects of CagriSema on A1c and Time in Range data?
2. How does the safety and tolerability profile of CagriSema compare to semaglutide?
3. What were the discontinuation rates of the CagriSema group?
4. How did CagriSema affect body composition?
5. What might have contributed to CagriSema falling short of the expected 20% weight loss?

--by Kat Moon, Esther Min, Monica Oxenreiter, and Kelly Close