Cagrilintide

What Human Research Suggests About Appetite, Weight Loss, Metabolic Health and Combination Therapy

A conversational scientific review that starts with demonstrated human outcomes, then connects those findings to amylin-receptor biology, appetite signalling and current combination research.

Prepared: September 28, 2026

Literature reviewed through: September 28, 2026

Document version: 1.0

RESEARCH-USE SCOPE

This report discusses published human, translational and clinical-development research on cagrilintide. Findings obtained with regulated investigational products do not establish that a Vanguard Compound Research material is safe, effective or suitable for administration. This report does not provide a dose, route, treatment protocol or medical recommendation. For laboratory research only; not for human or veterinary use.

THE HUMAN QUESTION

What could cagrilintide realistically mean in people?

Cagrilintide has moved well beyond a purely theoretical peptide. Human randomized trials show that the long-acting amylin analogue can reduce body weight when studied alone, and larger phase 3 trials show substantial weight reduction when it is coadministered with semaglutide. The useful question is no longer whether the molecule has human biological activity; it is how much of that activity belongs to cagrilintide itself, how it changes eating behaviour, and what remains unproven about long-term outcomes. [1][2][5][6]

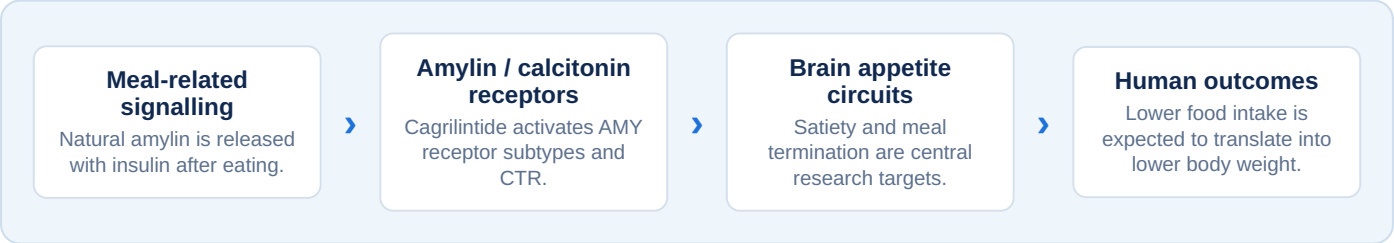


Figure 1. Translational model. Human weight-loss evidence is direct; the receptor and appetite steps are supported by amylin physiology, structural pharmacology and ongoing human-mechanism studies. [1][7][13]

Four questions worth separating

Standalone weight loss

Does cagrilintide reduce body weight by itself, without a GLP-1 receptor agonist?

Appetite and eating behaviour

How much of the weight effect is explained by less hunger, earlier fullness and lower energy intake?

Combination with GLP-1

What changes when amylin signalling and semaglutide's GLP-1 pathway are used together?

Metabolic and long-term outcomes

What happens to glucose control, waist circumference, cardiovascular risk and durability over time?

1 | STANDALONE WEIGHT LOSS

Does cagrilintide produce meaningful weight loss on its own?

Short answer

Yes. Randomized human studies show a clear dose-related weight-loss signal with cagrilintide monotherapy. A 26-week phase 2 trial reported mean losses up to 10.8%, and the cagrilintide-only arm of REDEFINE 1 later reported 11.8% weight loss at 68 weeks under the trial-product estimand. [2][11]

The phase 2 dose-finding trial enrolled adults with overweight or obesity without diabetes. Every tested cagrilintide dose produced greater mean weight reduction than placebo, with the largest tested dose reaching 10.8% at week 26 versus 3.0% with placebo. The 4.5 mg cagrilintide group also exceeded the 9.0% mean reduction reported with liraglutide 3.0 mg in that study. [2]

Two direct human signals



Figure 2. Mean body-weight change reported in two different trials. *REDEFINE 1 values shown here use the trial-product estimand; they should not be directly compared as though the trials had identical populations, doses or estimands. [2][11]

What the longer trial adds

REDEFINE 1 was designed primarily around the cagrilintide-semaglutide combination, but it also included randomized cagrilintide and placebo arms. In the cagrilintide 2.4 mg arm, mean waist circumference fell by 10.6 cm versus 4.0 cm with placebo under the reported trial-product analysis. These findings reinforce that the standalone effect is not limited to a short dose-finding study. [11]

The most useful interpretation

Cagrilintide has a genuine human monotherapy signal. The evidence is strongest for body-weight reduction in adults with overweight or obesity; it does not yet establish cardiovascular benefit, long-term durability after discontinuation or an approved treatment protocol.

2 | APPETITE + AMYLIN BIOLOGY

Is cagrilintide really an appetite signal rather than just another GLP-1?

Short answer

It is mechanistically distinct from GLP-1 receptor agonists. Cagrilintide was designed from the 37-amino-acid amylin framework and activates amylin receptor subtypes as well as the calcitonin receptor. Its long half-life and lipidation allow prolonged exposure, while direct human studies specifically isolating its effects on energy intake and appetite are still developing. [1][3][7]

Natural amylin is co-secreted with insulin and contributes to meal-related satiety signalling. Cagrilintide preserves amylin-like receptor engagement while adding structural modifications that improve stability and duration. In a phase 1b human study, cagrilintide showed an estimated half-life of roughly 159-195 hours across the tested dose range, supporting once-weekly clinical development. [1][3]

MOLECULAR DESIGN	RECEPTOR EVIDENCE	HUMAN QUESTION
Lipidation and sequence changes were selected to reduce fibrillation and extend exposure while retaining amylin-family receptor activity. [1]	2025 cryo-EM work visualized cagrilintide bound to AMY1R, AMY2R, AMY3R and CTR in active G-protein-coupled complexes. [7]	The remaining translational task is to connect receptor activity to measured hunger, food intake and long-term eating behaviour in people.

A combination study gives a strong appetite clue

A 2025 clinical-pharmacology study of CagriSema reported a 63% decrease in ad-libitum energy intake at week 20 versus a 2% increase with placebo, together with lower hunger, greater fullness and better control of cravings. The study did not isolate cagrilintide from semaglutide, so it is evidence for the combination rather than proof of the standalone mechanism. [8]

ONGOING HUMAN RESEARCH

The appetite mechanism is still being tested directly

A 2026 human-pharmacology trial is recruiting adults with overweight or obesity specifically to examine how cagrilintide influences food intake and appetite. That is a useful sign of scientific maturity: the field is moving from “does weight go down?” toward “why, how much, and through which measurable behaviour?” [13]

Mechanistic takeaway

Cagrilintide should not be described as simply another GLP-1 compound. It targets the amylin/calcitonin receptor family, creating a biologically different route to satiety and body-weight regulation.

3 | COMBINATION WITH GLP-1

What happens when cagrilintide is paired with semaglutide?

Short answer

The combination produces a larger weight-loss signal than either component alone in the same phase 3 trial. In REDEFINE 1, trial-product estimates were 22.7% with CagriSema, 16.1% with semaglutide, 11.8% with cagrilintide and 2.3% with placebo at 68 weeks. [5][11]

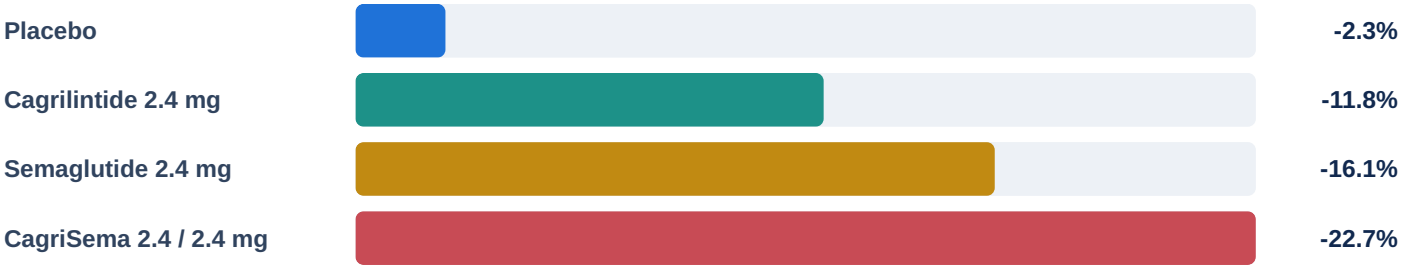


Figure 3. REDEFINE 1 trial-product estimand values reported for the four randomized arms. The primary treatment-policy estimate reported in the NEJM article was -20.4% for CagriSema versus -3.0% for placebo. Different estimands answer different questions and should not be mixed without explanation. [5] [11]

The biological attraction of the combination is straightforward: semaglutide acts through GLP-1 receptors, while cagrilintide acts through amylin/calcitonin-family receptors. Both can influence appetite, but they enter the system through different receptor pathways. A combination can therefore test whether broader signalling produces a larger effect than either pathway alone.

Why “synergy” should be used carefully

The side-by-side phase 3 results are consistent with a larger effect from coadministration, but they do not mean the percentages can simply be added or that every effect is pharmacologically synergistic. Weight loss is nonlinear, dose escalation matters, and the combination can change adherence, tolerability and eating behaviour in ways that are not captured by adding two monotherapy percentages.

IMPORTANT DISTINCTION

CagriSema evidence is not cagrilintide-alone evidence

When discussing appetite, glucose control or cardiovascular risk from combination trials, the contribution of semaglutide must remain explicit. A strong combination result cannot be re-labelled as a standalone cagrilintide effect.

4 | TYPE 2 DIABETES + METABOLIC SIGNALS

Does the amylin pathway affect more than body weight?

Short answer

Yes, but the human metabolic story is more developed for the combination than for cagrilintide alone. In a small phase 2 diabetes trial, cagrilintide monotherapy reduced body weight by 8.1% and HbA1c by 0.9 percentage points at 32 weeks, while CagriSema produced larger changes. [4]

Phase 2 study in type 2 diabetes

32-week outcome	Cagrilintide 2.4 mg	Semaglutide 2.4 mg	CagriSema 2.4 / 2.4 mg
Mean body-weight change	**-8.1%**	-5.1%	**-15.6%**
Mean HbA1c change	**-0.9 percentage points**	-1.8 points	**-2.2 points**
Study size	92 participants total; small exploratory phase 2 trial		

Table 1. Values reported in the randomized phase 2 type 2 diabetes trial. The study was small and should not be used to rank monotherapies broadly across different populations. [4]

Phase 3 combination evidence

-13.7%
Estimated mean body-weight change with CagriSema at week 68 in REDEFINE 2, versus -3.4% with placebo.

73.5%
Participants with HbA1c at or below 6.5% in the CagriSema group, versus 15.9% with placebo.

REDEFINE 2 enrolled 1,206 adults with overweight or obesity and type 2 diabetes. It confirmed that the combination can produce clinically measurable weight and glycaemic changes in a population that often loses less weight than people without diabetes. [6]

What an independent 2026 synthesis found

A 2026 systematic review and meta-analysis pooling four randomized trials reported a significant body-weight advantage for cagrilintide-based therapy. For cagrilintide alone, the pooled placebo-adjusted difference in percentage weight change was approximately -6.08 percentage points. The review found stronger glycaemic evidence for CagriSema than for cagrilintide monotherapy. [9]

Research interpretation

The direct monotherapy signal is strongest for body weight. Glycaemic improvement is biologically plausible and has been observed, but the combination data should not be used to overstate the glucose-lowering effect of cagrilintide by itself.

5 | SAFETY + TOLERABILITY

What does the human evidence say about trade-offs?

Short answer

Gastrointestinal symptoms are the dominant tolerability signal. Across trials, nausea, constipation, diarrhoea and vomiting occur more often with active cagrilintide treatment than placebo, especially during dose escalation. The available clinical programme is substantial enough to describe common events, but cagrilintide remains investigational and long-term rare-event risk is still being defined. [2][11]

REDEFINE 1 cagrilintide-only safety signal

Adverse event category	Cagrilintide 2.4 mg	Placebo
Any gastrointestinal adverse event	**~54%**	~40%
Nausea	23.8%	12.6%
Constipation	20.5%	11.6%
Diarrhoea	15.2%	12.1%
Vomiting	7.0%	4.1%

Table 2. EASD 2025 cagrilintide analysis from REDEFINE 1. GI-related discontinuation was reported at 1.3% in the cagrilintide group. [11]

Phase 2 monotherapy

GI events occurred in about 41%-63% across cagrilintide doses versus 32% with placebo; nausea was reported in 20%-47% versus 18%. [2]

Renal / hepatic impairment

Two 2026 single-dose studies found no clinically relevant pharmacokinetic differences across renal or hepatic impairment groups, with no new safety signal. Sample sizes were small. [10]

Combination therapy

REDEFINE 1 reported GI adverse events in 79.6% of the CagriSema group versus 39.9% with placebo. These results belong to the combination, not cagrilintide alone. [5]

What remains unknown

Rare adverse events, very long exposure, cardiovascular outcomes, pregnancy-related risk and broad population-specific safety require more data.

CLINICAL EVIDENCE IS PRODUCT-SPECIFIC

A high-purity research sample is not the same as a clinical-trial product

Clinical studies use investigational products manufactured under defined pharmaceutical controls. HPLC purity cannot establish exact active quantity, sterility, endotoxin level, particulate burden, formulation stability, container-closure integrity or suitability for administration.

6 | WHAT WOULD MOVE THE SCIENCE FORWARD?

The next studies should answer narrower human questions

Cagrilintide already has direct human weight-loss evidence. The next useful step is not repeating the broad question of whether it “works,” but separating mechanism, durability, comparative benefit and long-term clinical outcomes.

Human research question	Most meaningful measurement	Why it matters
How much does cagrilintide change eating behaviour by itself?	Ad-libitum energy intake, hunger, satiety, cravings and food-choice measures.	Connects amylin-receptor biology to the human weight-loss mechanism.
How durable is weight loss after stopping?	Long off-treatment follow-up with weight, appetite and metabolic markers.	Separates temporary pharmacologic suppression from durable change.
Does it improve cardiovascular outcomes?	Major cardiovascular events and validated risk endpoints in large trials.	Weight loss does not automatically equal proven cardiovascular benefit.
What does it do to body composition?	DXA/MRI measures of fat mass, lean mass and visceral adiposity.	Shows whether scale-weight change reflects favourable tissue distribution.
What is the best role beside GLP-1/GIP therapy?	Randomized add-on and head-to-head trials.	Clarifies whether the amylin pathway adds value after another therapy is established.
Do higher doses improve benefit-risk?	Phase 3 dose-response with discontinuation and adverse-event analysis.	Determines whether greater weight loss is worth additional tolerability burden.

What the evidence supports today

Strong standalone human signal

Randomized trials consistently show meaningful body-weight reduction with cagrilintide monotherapy. [2][11]

Clear mechanistic identity

Cagrilintide engages amylin and calcitonin-family receptors rather than functioning as a GLP-1 receptor agonist. [7]

Strong combination signal

Phase 3 CagriSema trials show larger weight reduction than placebo and substantial metabolic effects. [5][6]

Still unresolved

Cardiovascular outcomes, long-term rare-event safety, durability after stopping and the full standalone appetite mechanism remain open questions.

Bottom line

Cagrilintide has one of the more developed human evidence packages among investigational amylin analogues: direct monotherapy weight-loss trials, phase 3 combination data, human pharmacokinetics and structural receptor evidence. The strongest conclusion remains specific: it can reduce body weight in studied populations. Broader claims need their own controlled evidence.

7 | PRODUCT AND REGULATORY BOUNDARIES

A scientific result is inseparable from the material that produced it

Clinical cagrilintide is a specifically manufactured investigational product. A research powder can have the same nominal molecule name and still differ in quantity, impurities, counterions, water content, aggregation state, microbiological quality and formulation. Human trial results therefore cannot be transferred automatically to a separate research material.

Question	Method or evidence that addresses it	What remains separate
Is cagrilintide-like molecular material present?	LC-MS / high-resolution mass spectrometry with a suitable reference.	Exact quantity, purity profile, sterility and formulation performance.
How pure is the principal chromatographic component?	Validated HPLC or UPLC method.	Absolute content, water, counterions, endotoxin and microbiological quality.
How much active material is present?	Qualified quantitative assay against an appropriate standard.	Sterility, stability and clinical suitability.
Is the material equivalent to the product used in a trial?	Requires comprehensive pharmaceutical comparability, not one analytical test.	Manufacturing controls, excipients, stability, sterility, container closure and authorization.

Canadian status as of September 28, 2026

Health Canada's public Submissions Under Review list includes **cagrilintide with semaglutide** as a new active substance submission from Novo Nordisk Canada, dated March 2026. A submission under review is not the same as market authorization. [12]

Cagrilintide monotherapy also remains in clinical development. Novo Nordisk reported that its RENEW phase 3 programme for cagrilintide 2.4 mg was initiated in late 2025, with studies in obesity populations with and without type 2 diabetes. [15]

Canadian and European trial registries also list ongoing cagrilintide studies, including work examining cagrilintide as an add-on to GLP-1 or GIP/GLP-1 therapy and a human-pharmacology study focused on food intake and appetite. [13][14]

REGULATORY BOUNDARY

Research relevance does not authorize human use

Published human trials demonstrate the pharmacological potential of cagrilintide, but they do not authorize independently manufactured research material for treatment, compounding or administration. This report does not provide dosing, reconstitution or administration instructions.

Closing perspective

The evidence base is unusually informative for an investigational research compound: cagrilintide has direct monotherapy data, large phase 3 combination trials, mechanistic receptor structures and an active late-stage development programme. That makes precise language more important, not less: separate the molecule's clinical-development evidence from the quality and intended use of any individual research sample.

References

1. Kruse T, Hansen JL, Dahl K, et al. Development of Cagrilintide, a Long-Acting Amylin Analogue. *J Med Chem.* 2021;64(15):11183-11194. DOI: 10.1021/acs.jmedchem.1c00565. Source
2. Lau DCW, Erichsen L, Francisco AM, et al. Once-weekly cagrilintide for weight management in people with overweight and obesity: a multicentre randomized phase 2 trial. *Lancet.* 2021;398:2160-2172. PMID 34798060. Source
3. Enebo LB, Berthelsen KK, Kankam M, et al. Safety, tolerability, pharmacokinetics, and pharmacodynamics of concomitant cagrilintide with semaglutide 2.4 mg: phase 1b trial. *Lancet.* 2021;397:1736-1748. PMID 33894838. Source
4. Frias JP, Deenadayalan S, Erichsen L, et al. Efficacy and safety of once-weekly cagrilintide 2.4 mg with semaglutide 2.4 mg in type 2 diabetes: phase 2 trial. *Lancet.* 2023;402:720-730. PMID 37364590. Source
5. Garvey WT, Blüher M, Osorto Contreras CK, et al.; REDEFINE 1 Study Group. Coadministered Cagrilintide and Semaglutide in Adults with Overweight or Obesity. *N Engl J Med.* 2025;393:635-647. PMID 40544433. Source
6. Davies MJ, Bajaj HS, Broholm C, et al.; REDEFINE 2 Study Group. Cagrilintide-Semaglutide in Adults with Overweight or Obesity and Type 2 Diabetes. *N Engl J Med.* 2025;393:648-659. PMID 40544432. Source
7. Cao J, Belousoff MJ, Johnson RM, et al. Structural and dynamic features of cagrilintide binding to calcitonin and amylin receptors. *Nat Commun.* 2025;16. PMID 40204768. DOI: 10.1038/s41467-025-58680-y. Source
8. Bak N, Lee R, Sinn A, et al. Effect of CagriSema on energy intake, gastric emptying, and appetite in adults with overweight or obesity. *Diabetes.* 2025;74(Suppl 1):1969-LB. Source
9. Rao H, Kumar S, Ali SME, et al. Cagrilintide and CagriSema for weight reduction and metabolic risk modification in overweight or obesity: systematic review and meta-analysis. *J Diabetes Metab Disord.* 2026;25(1):140. PMID 42180166. Source
10. Nielsen MJF, Becker NP, Duus HHH, et al. Renal or Hepatic Impairment Does Not Affect Pharmacokinetics, Safety, or Tolerability of Subcutaneous Cagrilintide. *Clin Pharmacokinet.* 2026;65:1087-1099. PMID 42228334. Source
11. Novo Nordisk. Efficacy and safety of cagrilintide 2.4 mg in adults with overweight/obesity: data from REDEFINE 1. EASD 2025 scientific poster. Source
12. Health Canada. Drug and Health Product Submissions Under Review: New drug submissions under review. Cagrilintide, semaglutide - submission dated 2026-03. Source
13. European Union Clinical Trials Information System. Study 2025-524206-15-00: cagrilintide effects on food intake and appetite in overweight or obesity. Status updated 2026. Source
14. Health Canada Canadian Clinical Trial Search Portal. Study of cagrilintide as add-on to GLP-1 or GIP/GLP-1 for weight management in participants with obesity. Updated July 2026. Source
15. Novo Nordisk. Q2 2026 investor presentation: cagrilintide 2.4 mg and the RENEW phase 3 programme. Source

Document notice. This review reflects sources identified through September 28, 2026. Scientific understanding, clinical-development status and regulatory status may change. Charts reproduce or index values reported by the cited studies and are labelled by evidence type or estimand where relevant. This document is not a Certificate of Analysis and does not describe the release status of a specific batch.

Prepared by Vanguard Compound Research for public scientific reading and download. For laboratory research only. Not for human or veterinary use.