

Effects of CagriSema on Appetite and Functional Brain Activity in People with Overweight/Obesity



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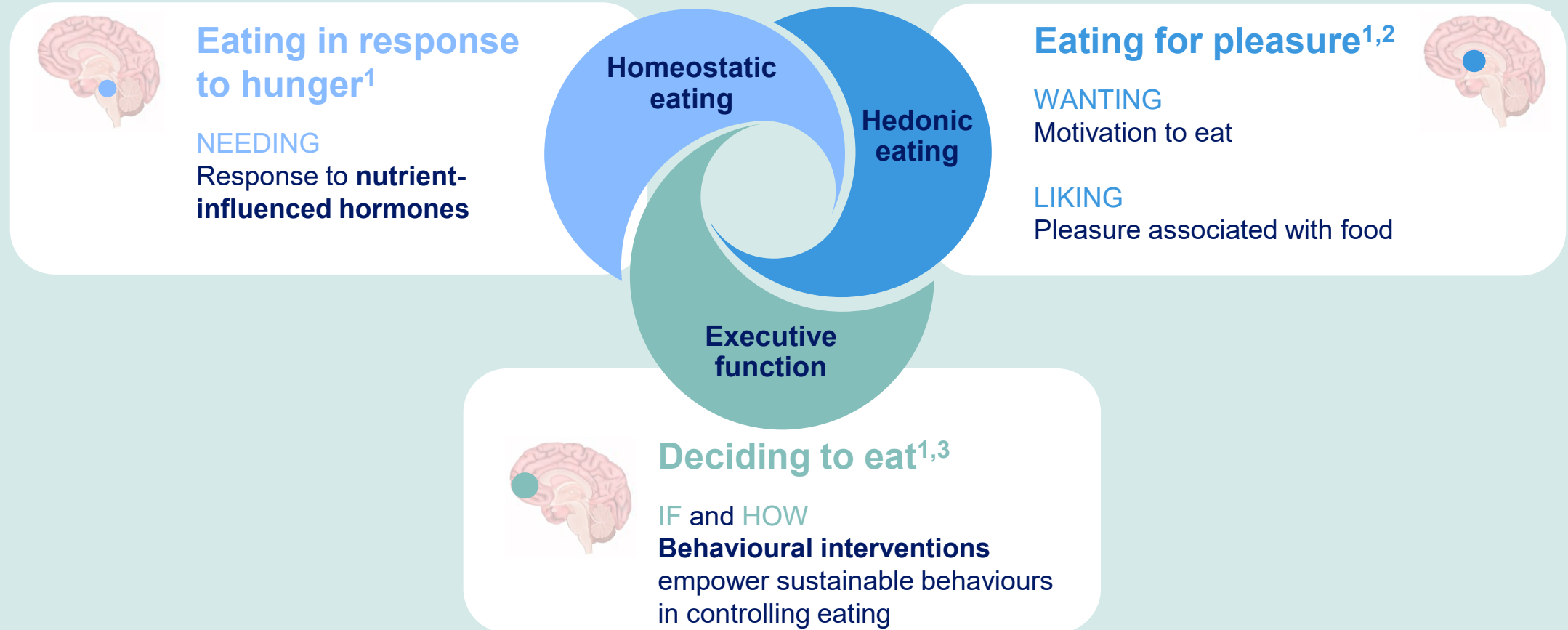
EASD 2026 oral presentation 122.

Disclosures

Anthony P. Goldstone reports the following disclosures:

- Speaker honoraria fees from Eli Lilly, Mission Kitchen, Novo Nordisk, Rhythm Pharmaceuticals, Soleno Therapeutics
- Consultancy fees from Asabys Partners, Bramble Partners, Eli Lilly, Evidera, Helsinn Healthcare S.A., Idera Pharmaceuticals Inc., Novo Nordisk, Rhythm Pharmaceuticals, Soleno Therapeutics, Tonix Pharmaceuticals
- Research funding from Novo Nordisk
- Dr Goldstone participated in medical advisory boards for Millendo Therapeutics and Radius Health
- Dr Goldstone was a Principal Investigator for trials sponsored by Rhythm Pharmaceuticals and Soleno Therapeutics and was part of a Data Safety Monitoring Committee for Novo Nordisk

Central regulation of eating behaviour



1. Clarke GS et al. *Pharmacol Res Perspect* 2024;12:e70027; 2. Berridge KC et al. *Brain Res* 2010;1350:43–64; 3. Vallis M. *Clin Obes* 2019;9:e12299.

Food noise



I can't stop thinking about food



When can I eat again?



These thoughts about food are distracting me...

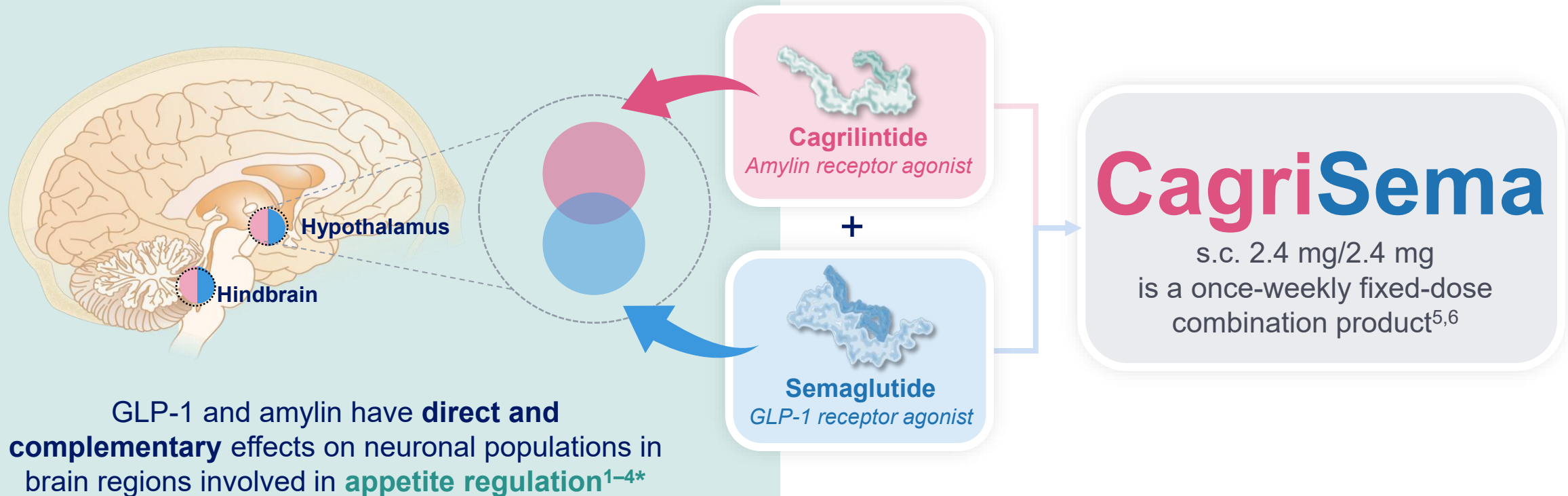
These thoughts about food are exhausting

Related assessments

- **Control of Eating Questionnaire:** eating behaviours and related psychological factors
- **DAILY EATS:** key eating-related factors
- **Power of Food scale:** food-related thoughts, feelings, and motivations
- **Yale Food Addiction scale:** food-related thoughts, feelings, and motivations

Images are visual representations of the patient, fully AI-generated (Magnific). Quotes provided for illustrative purposes only; not derived from a published scientific source. Dhurandhar EJ et al. Nutr Diabetes 2025;15:30; Diktas HE et al. Obesity (Silver Spring) 2025;33:289–97.

CagriSema leverages direct and complementary effects of amylin and GLP-1 on appetite regulation



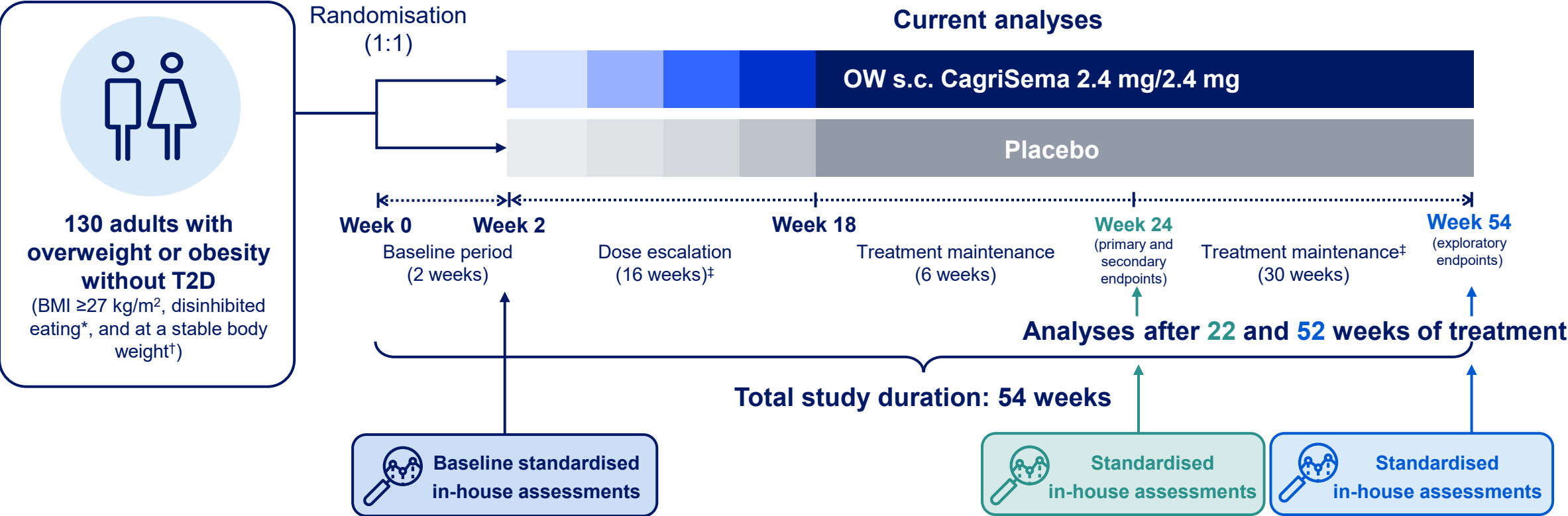
**Evidence from preclinical studies in rodents.*

GLP-1, glucagon-like peptide-1; s.c., subcutaneous.

1. Lundh S et al. Poster-569. Presented at Obesity Week 2024; San Antonio, TX, USA; 2-6 November 2024; 2. Morton GJ et al. Nat Rev Neurosci 2014;15:367-78; 3. Terrill SJ et al. Am J Physiol Regul Integr Comp Physiol 2016;311:R124-32; 4. Secher A et al. Nat Metab 2026;8:299-312; 5. Garvey WT et al. N Engl J Med 2025;393:635-47; 6. Davies MJ et al. N Engl J Med 2025;393:648-59.

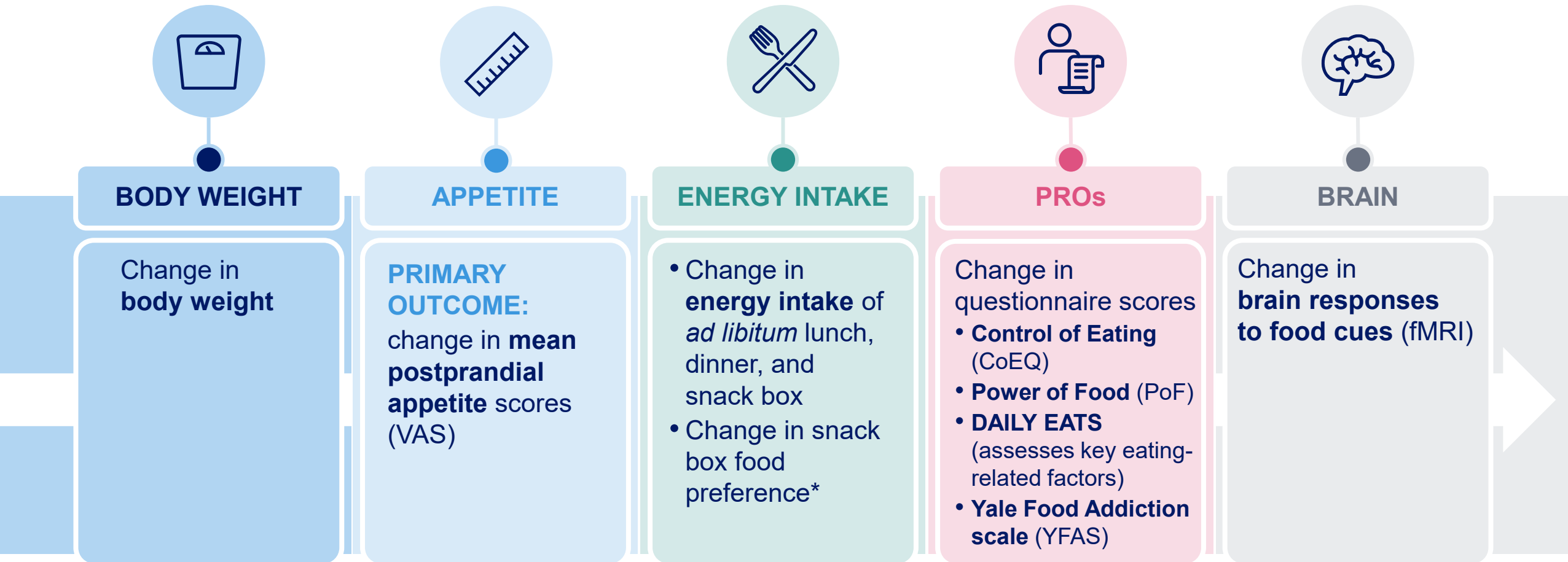
Study design

This study investigated the impact of CagriSema on self-reported appetite changes, eating behaviour and brain responses to food cues in adults with overweight or obesity



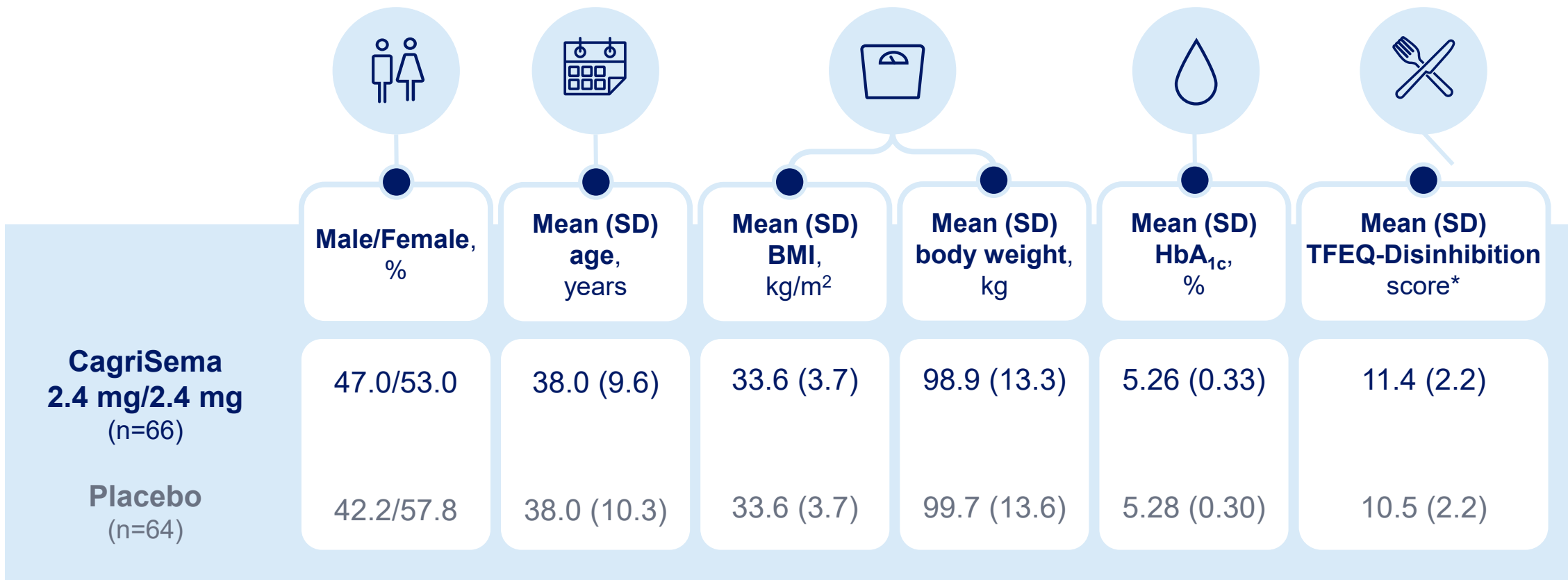
*Indicated by a score of ≥ 8 out of 16 in the Disinhibition subscore of the Three-Factor Eating questionnaire. †Stable body weight defined as $<5\%$ self-reported change in body weight within 90 days before screening. ‡Dose escalation represented by darkening blue colours in the CagriSema treatment arm in the trial design diagram; dose-escalation period protocol was an initial dose of 0.25 mg/0.25 mg of CagriSema or placebo for 4 weeks and then increasing every 4 weeks until week 18 (0.5 mg/0.5 mg at weeks 5–8, 1.0 mg/1.0 mg at weeks 9–11, 1.7 mg/1.7 mg at weeks 12–15, and 2.4 mg/2.4 mg at week 16 onwards). §Treatment maintenance phase represented by checkered colours in trial design diagram; dose adjustments were allowed after week 24. After the end of the treatment period, participants underwent a minimum of 38 days of follow-up. BMI, body mass index; OW, once-weekly; s.c., subcutaneous.

Evaluating effects of CagriSema on appetite, eating behaviour and brain responses to food cues



*The snack box consisted of four categories: high-fat sweet food, high-fat non-sweet food, low-fat sweet food and low-fat non-sweet food.
fMRI, functional magnetic resonance imaging; PRO, patient-reported outcome; VAS, Visual Analog Scale.

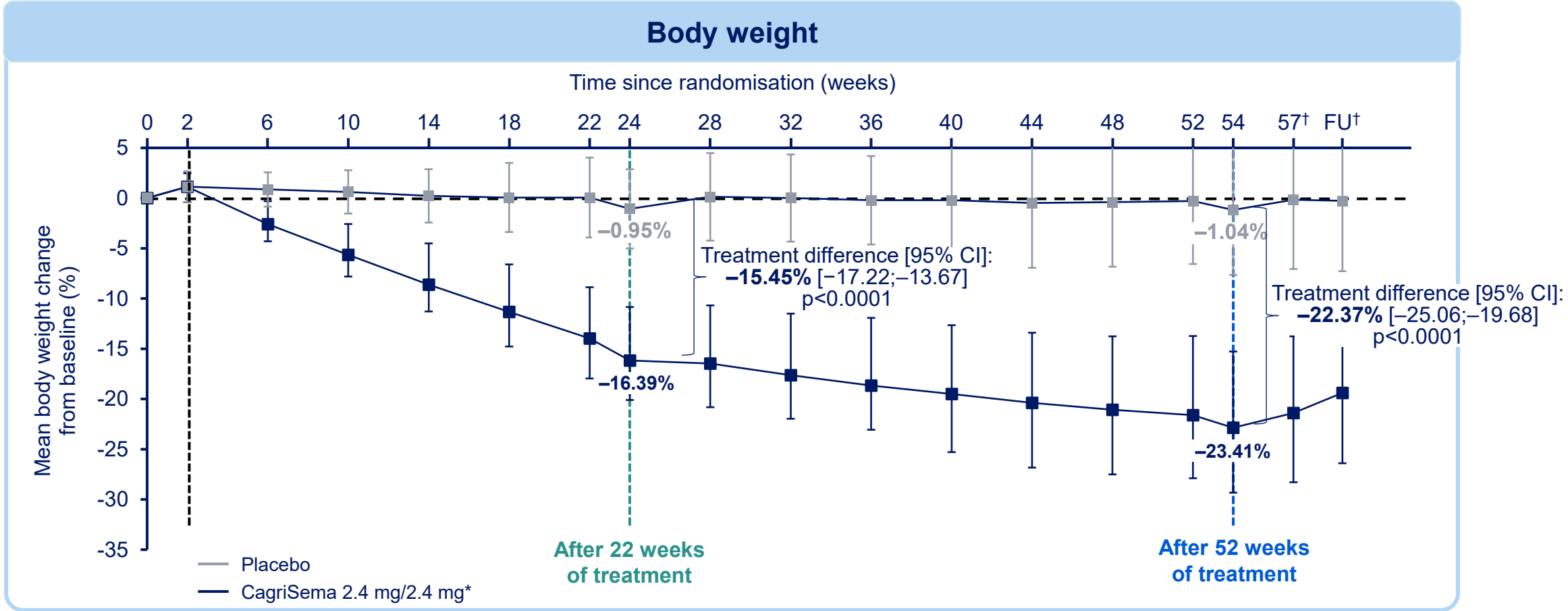
Baseline characteristics were comparable across treatment groups



*The maximum score for the TFEQ-Disinhibition subscale is 16 (it is a 16-item questionnaire, each with a score of 0 or 1), with higher scores indicating a lower control over eating.
Data are expressed as mean (SD) unless stated otherwise, using data from the safety analysis set. Baseline information is defined as the measurement at the latest assessment before dosing (week 0).
BMI, body mass index; SD, standard deviation; TFEQ-Disinhibition, Three-Factor Eating Questionnaire Disinhibition subscale.



CagriSema substantially reduced body weight versus placebo

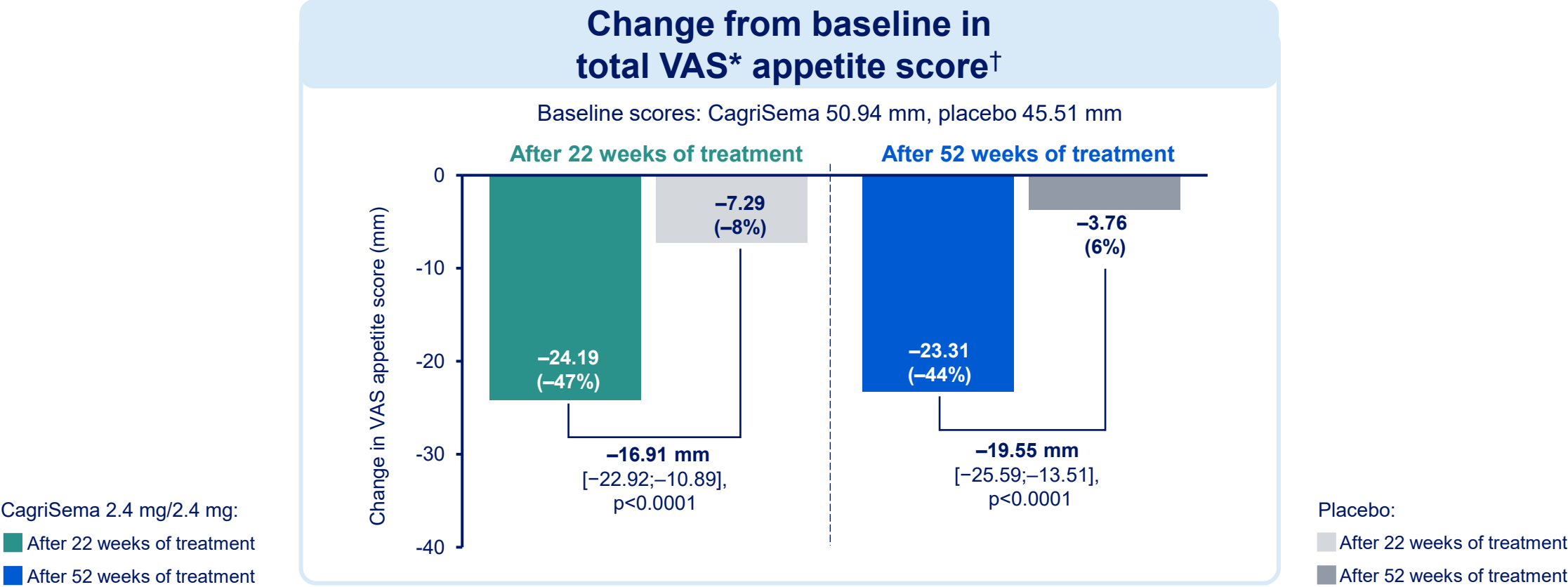


*No dose modifications were allowed prior to or during the week 24 clinic visit; after the week 24 clinic visit, up to two dose reductions were allowed. †Participants were not receiving treatment during the week 57 and FU visits (last treatment received at the week 54 visit).
Black vertical dashed line represents first dosing of CagriSema; green vertical dashed line represents after 22 weeks of treatment timepoint; blue vertical line represents after 52 weeks of treatment timepoint; horizontal black dashed line represents a zero change from baseline. Graph shows observed values over time; error bars represent standard deviation. Text values shown on slide are estimated data from the full analysis set.
CI, confidence interval; FU, follow-up.



CagriSema consistently reduced patient-reported appetite after 52 weeks of treatment

Hunger was reduced, and feelings of fullness and satiety were increased with CagriSema versus placebo



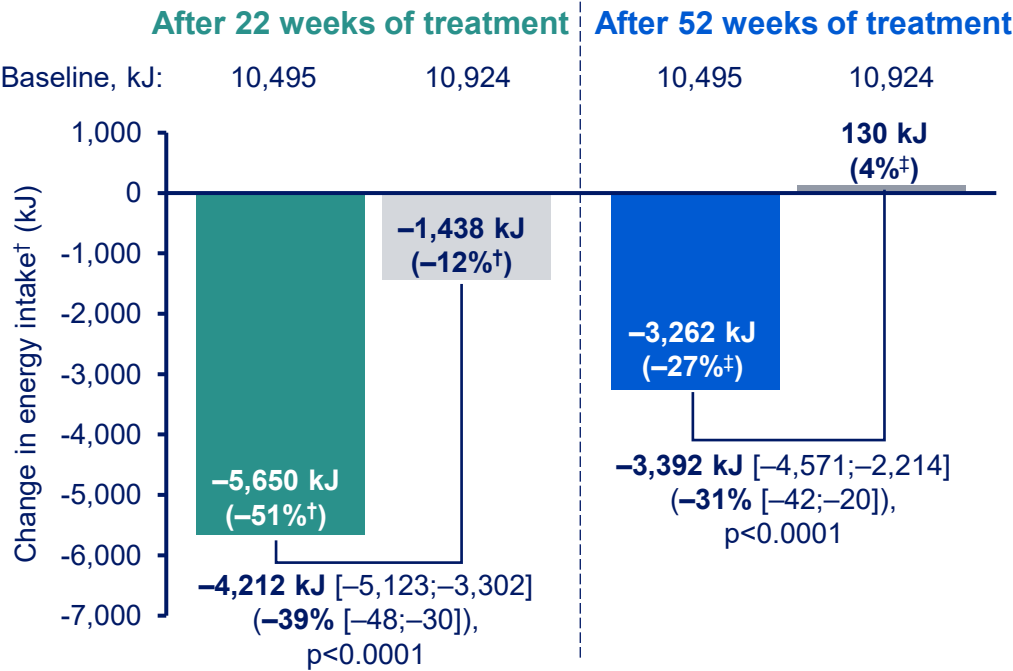
*The total VAS appetite score is based on sub-components including hunger, prospective food consumption, satiety, and fullness. [†]Participants were placed in meal bands calculated based on their age, gender, weight and physical activity (according to equations in Schofield WN. Hum Nutr Clin Nutr 1985;39(Suppl 1):5-41); energy content for the standardised breakfast meal was 303-740 kcal (1,268-3,098 kJ), which represented approximately 20% of their daily energy expenditure; VAS appetite scores were assessed within 5 minutes after the end of the meal. Data under bars show the treatment difference [95% CI] for CagriSema vs placebo. Data are based on on-treatment data from the full analysis set. CI, confidence interval; VAS, visual analogue scale.



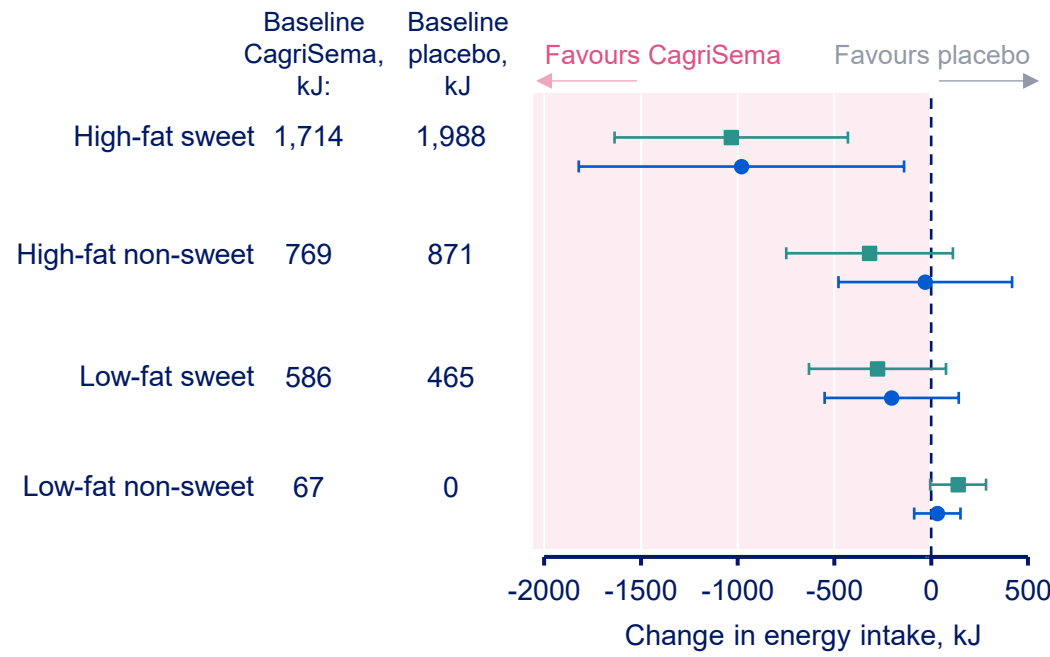
CagriSema substantially reduced food intake versus placebo

This was accompanied by a reduced preference for high-fat, sweet food

Change from baseline in total energy intake



Change from baseline in food preference*



CagriSema 2.4 mg/2.4 mg:
■ After 22 weeks of treatment
■ After 52 weeks of treatment

Placebo:
■ After 22 weeks of treatment
■ After 52 weeks of treatment

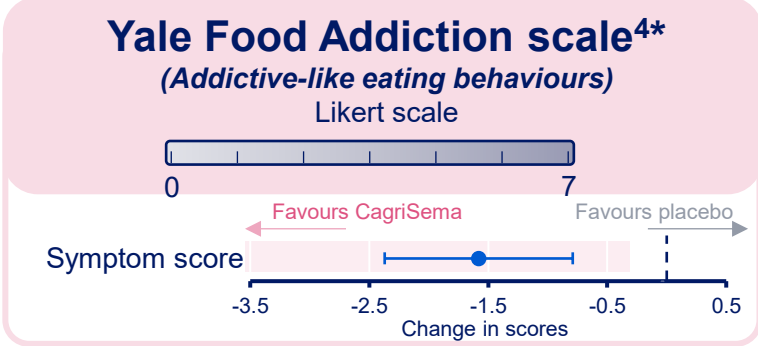
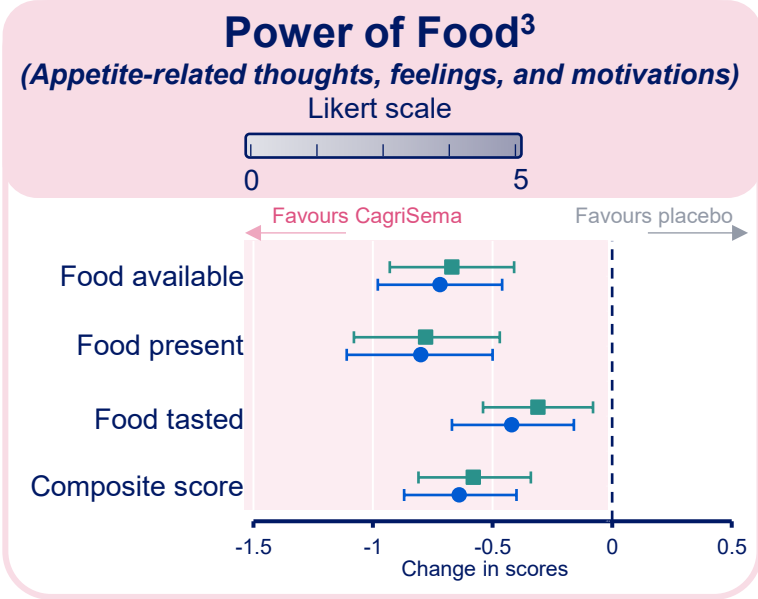
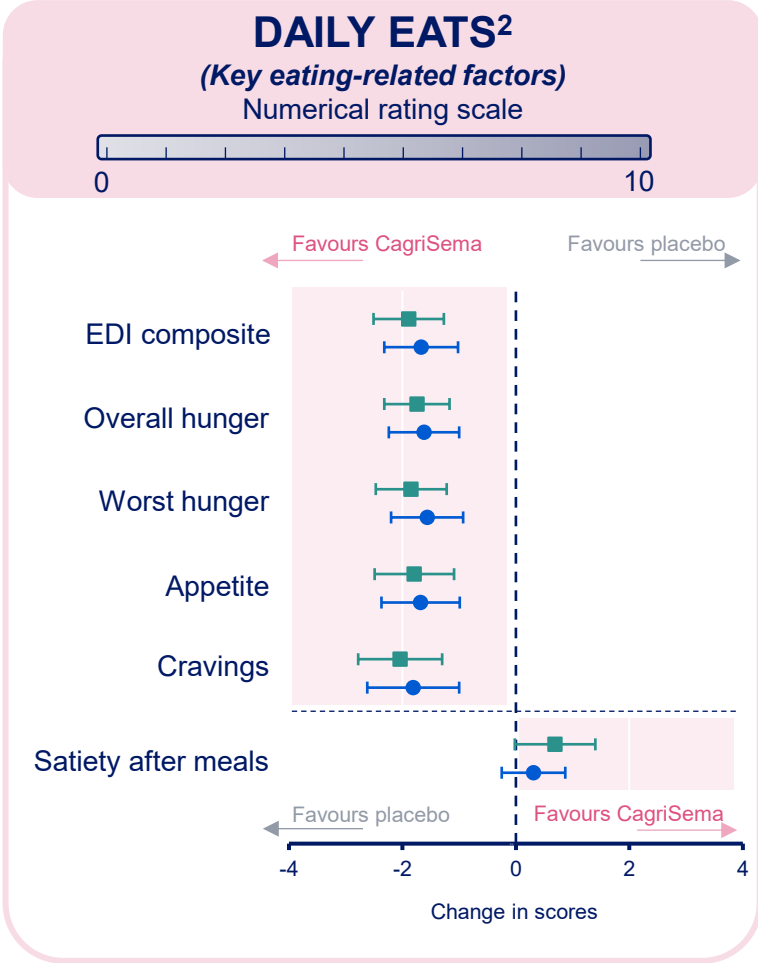
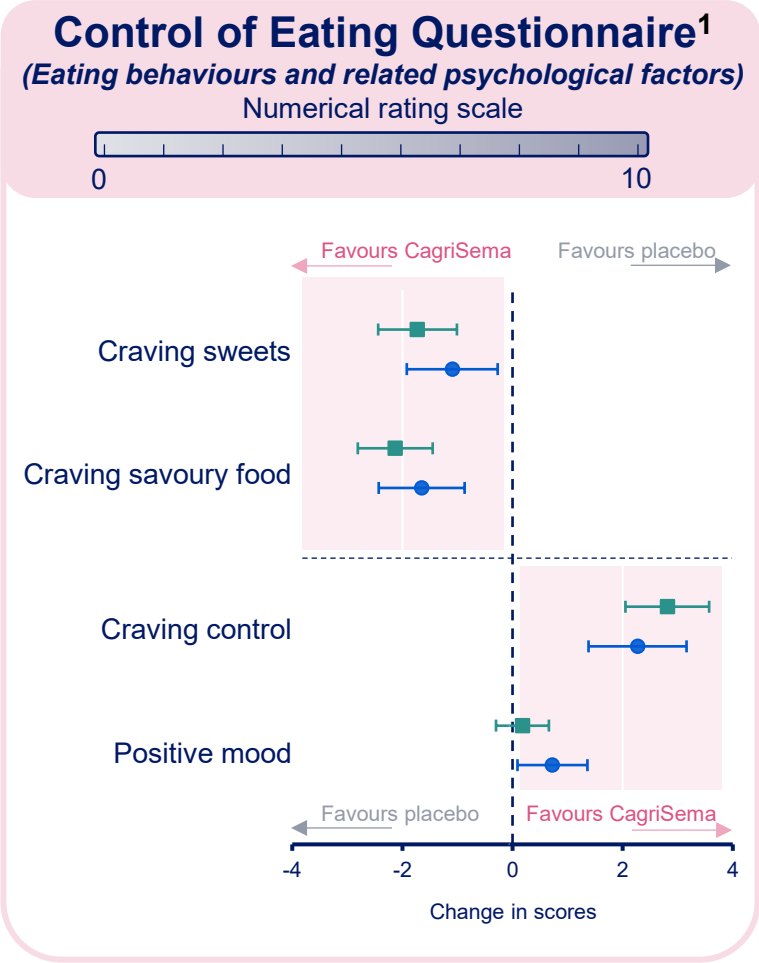
kJ to kcal conversion factor:
10 kJ ≈ 2.4 kcal

■ After 22 weeks of treatment
● After 52 weeks of treatment

*Consumption of high-fat non-sweet and low-fat sweet foods also decreased with CagriSema versus placebo, and consumption of low-fat non-sweet foods was increased with CagriSema versus placebo, but not significantly (p>0.05). †Percentage change from baseline to 22 weeks of treatment or ‡from baseline to 52 weeks of treatment. Data under bars show the treatment difference [95% CI] for CagriSema vs placebo. Data are based on on-treatment data from the full analysis set. CI, confidence interval.



CagriSema sustainably improved self-reported eating behaviour



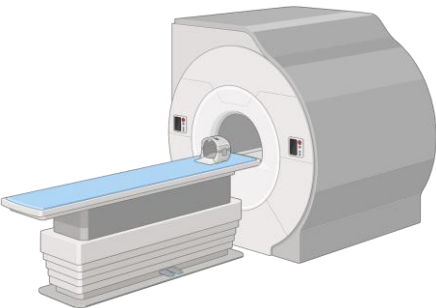
*The Yale Food Addiction scale (YFAS) evaluates changes over the previous 6 months; it was therefore not included after 22 weeks of treatment because the assessing timeframe would overlap with the baseline period. Data are from the on-treatment population. Questionnaires were completed in week 2, week 24 and week 54 assessment windows as follows: DAILY EATS, at the end of the day on 7 consecutive days within the assessment window; CoEQ, following 3 hours of fasting during the clinic visit; POF and YFAS, after the MRI examination. CoEQ, Control of Eating Questionnaire; EDI, Eating Drivers Index; MRI, magnetic resonance imaging; POF, Power of Food. 1. Dalton M et al. Eur J Clin Nutr 2015;69:1313–7; 2. Lowe MR et al. Appetite 2009;53:114–8; 3. Fastenau J et al. J Patient Rep Outcomes 2020;4:99; 4. Gearhardt AN et al. Appetite 2009;52:430–6.



Functional magnetic resonance imaging (fMRI)

fMRI method

Measures changes in **brain activity** by detecting changes in blood oxygenation dependent (BOLD imaging)



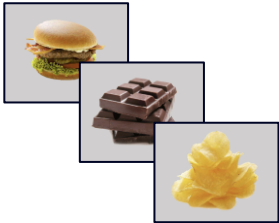
Participants received a standardised breakfast (303–740 kcal*) 1 hour prior to the MRI

fMRI assessment

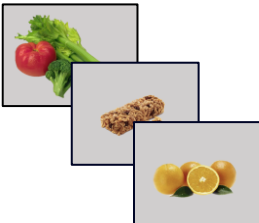
Participants were **shown images of**

- **high-calorie food**
- **low-calorie food**
- **non-food objects**

High-calorie foods



Low-calorie foods



Non-food objects



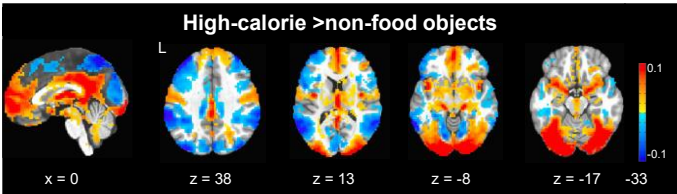
To induce maximal craving responses, participants were instructed to imagine tasting the food items and imagine holding (or holding onto) the non-food items

fMRI imaging

Whole-brain analyses[†] were performed to compare **brain responses**

Validation of results

Food cues activated regions of the brain relevant to reward and craving



*Participants were placed in meal bands calculated based on their age, gender, weight and physical activity (according to equations in Schofield WN. Hum Nutr Clin Nutr 1985;39(Suppl 1):5–41); energy content for the standardised breakfast meal was 303–740 kcal (1,268–3,098 kJ), which represented approximately 20% of their daily energy expenditure. [†]Covariates assessed in the whole-brain analyses included BMI, VAS responses, mean cerebral blood flow, age, FSH (colinear with gender), time between scans, block order, and scanner for each timepoint (BMI and VAS response were centred within group and timepoint to preserve group/timepoint integrity). Image of MRI scanner created with BioRender.

BMI, body mass index; BOLD, blood oxygen level dependent; FSH, follicle-stimulating hormone; fMRI, functional magnetic resonance imaging; MRI, magnetic resonance imaging; VAS, visual analogue scale.

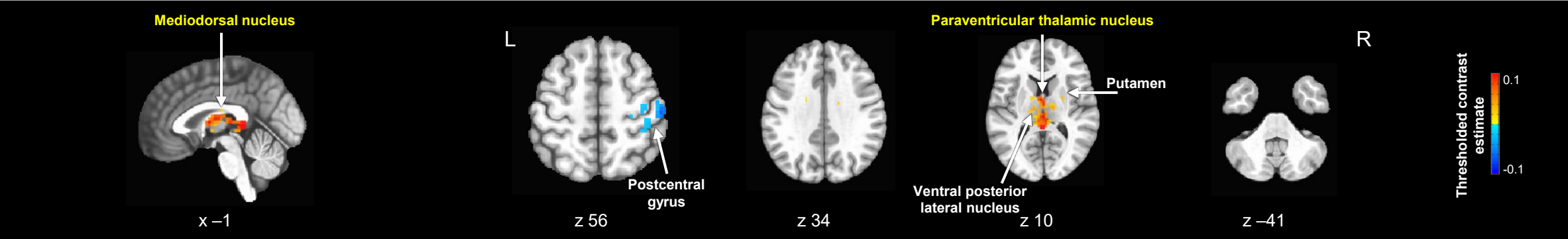


CagriSema modulates high-calorie food cue reactivity

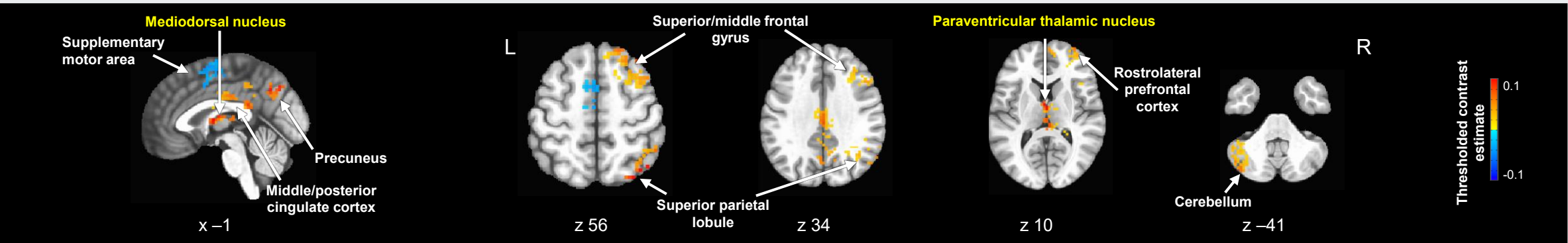
Modulated areas are involved in appetite regulation, reward processing and executive control

Treatment difference versus baseline high-calorie food versus non-food, CagriSema (n=65) versus placebo (n=62)

After 22 weeks of treatment



After 52 weeks of treatment

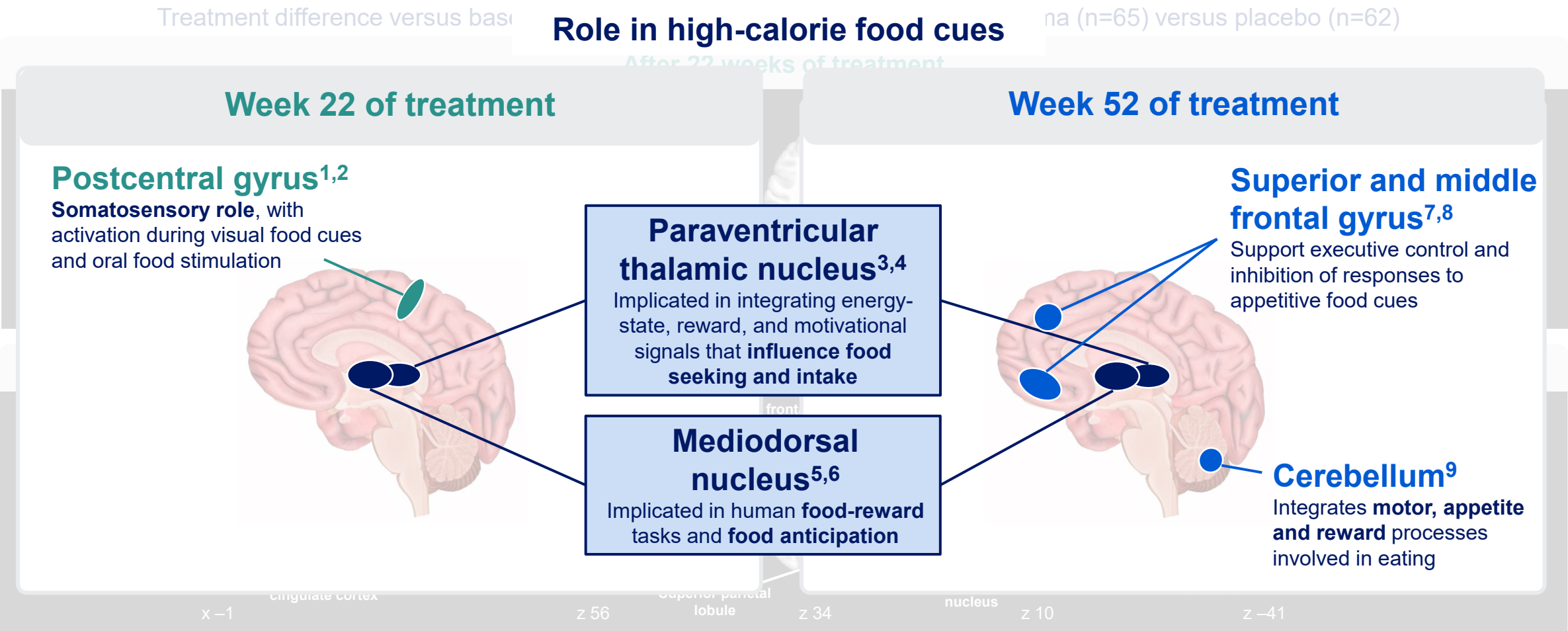


Selected anatomical regions within significant whole-brain group-by-time interaction clusters are labelled on the slide. Images show analyses conducted in the intention-to-treat population. Group by timepoint interaction effect for high-calorie foods versus non-food objects in participants receiving CagriSema versus placebo, intention-to-treat analysis. BOLD, blood oxygenation-level dependent; fMRI, functional magnetic resonance imaging; x, slice location in the sagittal plane coordinate; z, slice location in the axial plane coordinate.



CagriSema modulates high-calorie food cue reactivity

Modulated areas are involved in appetite regulation, reward processing and executive control



1. DiGiuseppi J, Tadi P. Neuroanatomy, Postcentral Gyrus. [Updated 2023 Jul 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-.; 2. Huerta CI et al. Obesity (Silver Spring) 2014;22:1439–46; 3. Petrovich GD. Front Behav Neurosci 2021;15:671096; 4. Ong ZY et al. Neuropsychopharmacology 2017;42:2387–97; 5. Sescousse G et al. Neurosci Biobehav Rev 2013;37:681–96; 6. Small DM et al. Neuron 2008;57:786–97; 7. Simmonds DJ et al. Neuropsychologia 2008;46:224–32; 8. Batterink L et al. Neuroimage 2010;52:1696–703; 9. Iosif CI et al. Cerebellum 2023;22:1002–19.

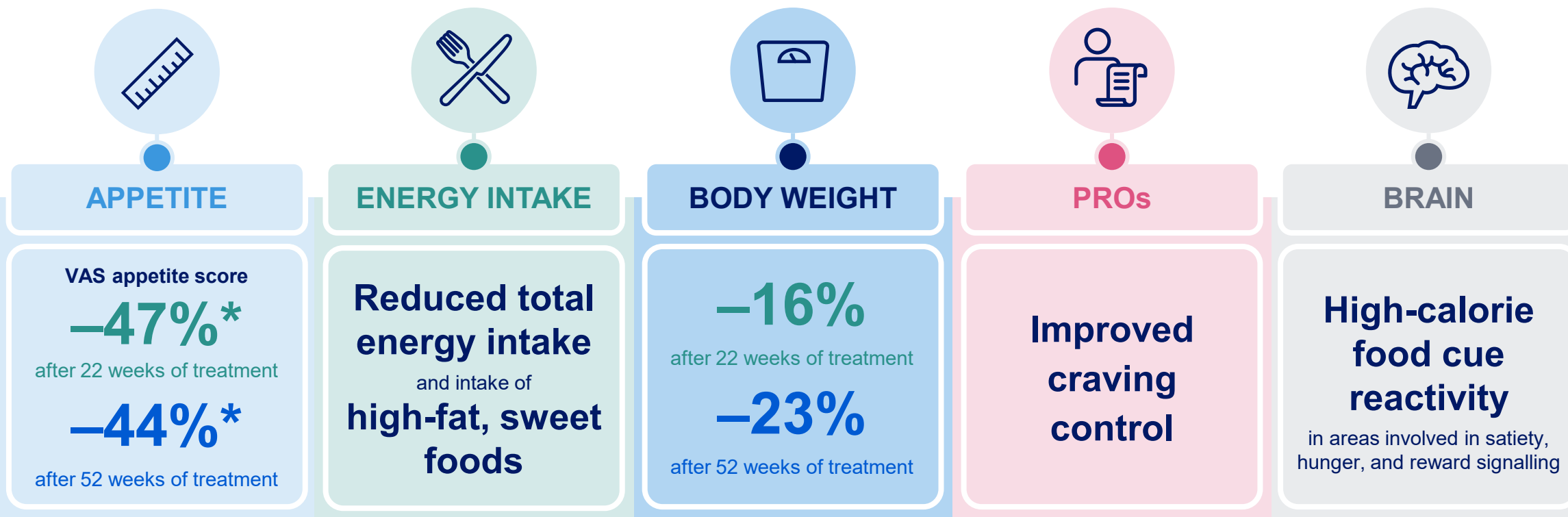
CagriSema had an acceptable tolerability profile, and no unexpected safety signals were observed

After 52 weeks of treatment		
	CagriSema 2.4 mg/2.4 mg (n=66)	Placebo (n=64)
AEs	65 (98.5)	59 (92.2)
GI-related AEs	59 (89.4)	28 (43.8)
Decreased appetite*	59 (89.4)	23 (35.9)
AE severity		
Mild	64 (97.0)	55 (85.9)
Moderate	37 (56.1)	42 (65.6)
Severe	0	0
Serious AEs	3 (4.5)	4 (6.2)
AEs leading to study withdrawal†	12 (18.2)	2 (3.1)

**Decreased appetite might be related to the mode of action of CagriSema. †The most common AEs leading to study withdrawal in the CagriSema group were nausea and vomiting; other events leading to withdrawal were bladder cancer, constipation, fatigue, and depressed mood in the CagriSema group and appendicitis and cardiac disorders (New York Heart Association heart failure Class II, atrial fibrillation, atrioventricular block, all observed in one participant) in the placebo group.*
Data are from the safety analysis set, expressed as n (%).
AE, adverse event; GI, gastrointestinal.

CagriSema improves eating behaviour and modulates neural drivers involved in appetite, reward and executive functions

The improvements with CagriSema were consistently maintained across the full study duration



CagriSema durably addresses the biological drivers that make weight management difficult – not just calories, but the hunger, cravings, and food preoccupation that undermine sustained weight loss

*Equating to a decrease of 24.19 mm after 22 weeks of treatment and 23.31 mm after 52 weeks of treatment. PRO, patient-reported outcome; VAS, visual analogue scale.

THANK YOU

Do you have any questions?