IMPACT OF SUBCUTANEOUS VK2735 ON OBESITY SEVERITY AND CARDIOMETABOLIC PARAMETERS IN THE VENTURE STUDY

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INTRODUCTION

- Nearly 75% of US adults have overweight or obesity, with approximately 42% having obesity[1,2]
- Obesity is a major driver of weight-related comorbidities, premature death, and healthcare spending [3]
- Increasing obesity severity is directly related to increased mortality, cardiovascular disease, and cardiometabolic (CM) risk factors[4]
- Glucagon-like peptide 1 (GLP-1)/glucose-dependent insulinotropic polypeptide (GIP) dual receptor agonists may potentiate the satiety and insulin-sensitizing effects of GLP-1 receptor activation, leading to enhanced clinical benefits[5]
- VK2735 is a long-acting dual agonist of the GLP-1/GIP receptors that has demonstrated significant weight reduction in the VENTURE Phase 2 study[6]

OBJECTIVE

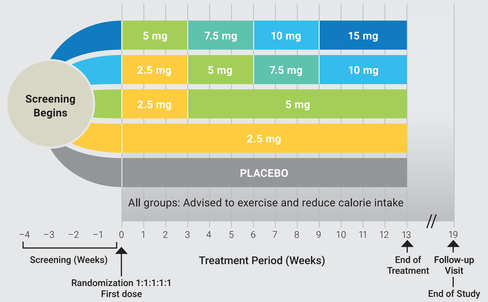
- This analysis reports the effect of subcutaneous (SC) VK2735 on body mass index (BMI) category and CM parameters applicable to weight category change following 13 weeks of treatment

METHODS

- VENTURE was a phase 2, randomized, double-blind, placebo-controlled study that evaluated the safety, tolerability, pharmacokinetics, and weight loss efficacy of SC VK2735 after 13 weeks of treatment (NCT06068946)
- Adults with BMI ≥30 kg/m² or ≥27 kg/m² and ≥1 weight-related comorbid condition received once-weekly SC injections of VK2735 or matched placebo for 13 weeks
- Primary endpoint was percent change in body weight from baseline to week 13 versus placebo
- Exploratory analyses included obesity severity category shift and change in CM parameters from baseline to week 13

Study Design

- Phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel arm study
- The duration of the study was 13 weeks, with a 6-week safety follow-up period
- 176 participants were randomized



Demographics Were Well Matched Across Groups (N=176)

Characteristic	Placebo (n=35)	All VK2735 (n=141)
Age, years, mean (SD)	47.6 (16.4)	49.9 (14.2)
Female, n (%)	29 (83)	101 (72)
Race, n (%)		
White	26 (74)	113 (80)
Black or African American	8 (23)	25 (18)
Ethnicity, n (%)		
Not Hispanic or Latino	28 (80)	117 (83)
Weight, kg, mean (SD)	104 (22.2)	101 (17.4)
BMI, kg/m², mean (SD)	38.9 (6.3)	36.78 (4.8)
Pre-diabetes,[a] n (%)	14 (40)	74 (52)
MetS,[b] n/N (%)	18/34 (53)	70/140 (50)

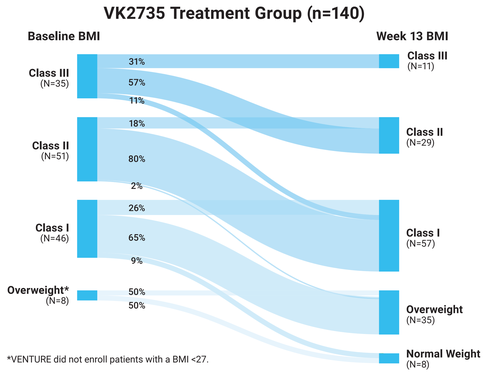
[a]Pre-diabetes defined as FPG 100 – 125 mg/dL or HbA1c 5.7 – 6.4%.

[b]Participants who met Metabolic Syndrome (MetS) criteria at BL. MetS criteria are having ≥3 of 5 factors: abdominal obesity (ie, waist circumference >40 inches [101.6 cm] in men and >35 inches [88.9 cm] in women), high blood pressure, high fasting blood sugar, high triglycerides, low HDL (good) cholesterol.

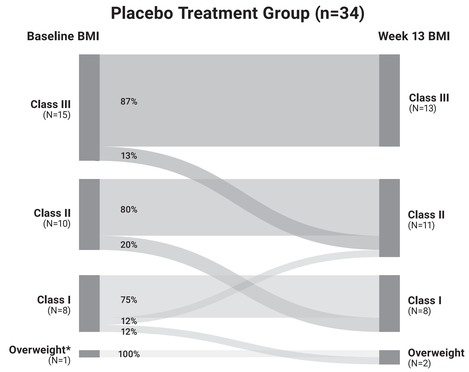
Abbreviations: BMI, body mass index; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; SD, standard deviation.

WEEKLY SUBCUTANEOUS VK2735 TREATMENT WAS ASSOCIATED WITH DECREASED OBESITY SEVERITY AND IMPROVEMENT IN CARDIOMETABOLIC RISK FACTORS AT WEEK 13

BMI Category Flow from Baseline to Week 13



*VENTURE did not enroll patients with a BMI <27.

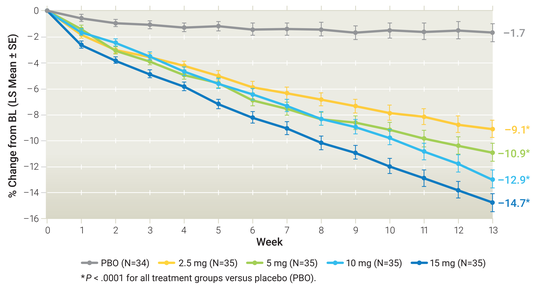


- At week 13, the majority (104/140; 74%) of the combined VK2735 group demonstrated ≥1 BMI category improvement versus 5/34 (15%) in the placebo group
- No VK2735-treated participants experienced worsening BMI category; one placebo participant demonstrated worsening BMI category

Categories of BMI[7]	
Underweight	15–19.9
Normal weight	20–24.9
Overweight	25–29.9
Class I obesity	30–34.9
Class II obesity	35–39.9
Class III obesity	≥40

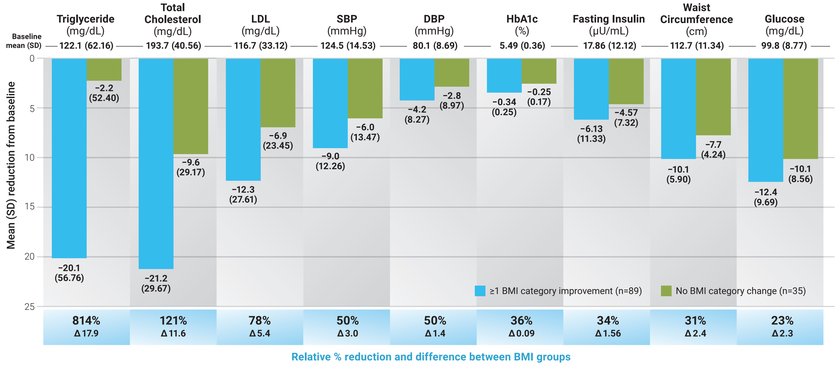
SC VK2735 Treatment Led to Significant Weight Loss by Week 13

- Participants in every VK2735 treatment group had significant weight loss from baseline within 13 weeks
- No weight loss plateau was observed at week 13



*P < .0001 for all treatment groups versus placebo (PBO).

Reduction in CM Risk Factors with SC VK2735 Treatment



Relative % Reduction = Δ ÷ mean change in no-change group.
Δ = difference in mean change from baseline (≥1 category improvement minus no change).
Abbreviations: BMI, Body mass index; DBP, diastolic blood pressure; HbA1c, Hemoglobin A1C; LDL, low-density lipoprotein; RR, Relative Reduction; SBP, systolic blood pressure; SD, standard deviation.

CONCLUSIONS

In this short duration study, weekly SC VK2735 treatment was associated with decreased obesity severity in individuals with obesity or overweight with ≥1 weight-related comorbidity

Treatment with SC VK2735 for 13 weeks resulted in improvements in cardiometabolic parameters, which were most pronounced in those with a BMI category shift

The Phase 3 VANQUISH-1 (NCT07104500) and VANQUISH-2 (NCT07104383) studies are currently ongoing and will further inform the efficacy and safety of VK2735 in participants with obesity or overweight.

REFERENCES

[1] Emmerich SD, et al. NCHS Data Brief, no 508. National Center for Health Statistics. 2024.

[2] Ng M. *Lancet*. 2024:404(10469):2278 – 2298.

[3] Thorpe, KE & Joski, PJ (2024). *JAMA Network Open*, 7(12), e2449200.

[4] Bays HE, et al. *Obes Pillars*. 2026;20:100283.

[5] Douros JD, et al. *Front Endocrinol*. 2025;16: 1530985.

[6] Bays HE, et al. *Obesity* (Silver Spring). 2026 Mar;34(3):537–549.

[7] Nuttall FQ. *Nutrition Today*. 2015;50(3):117–28.

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DISCLOSURES

The VENTURE study is supported by Viking Therapeutics, Inc (San Diego, CA). All authors are either principal site investigators for the study, with sites given remuneration for conducting the study, or are employees of Viking Therapeutics, Inc.