Treatment with Oral VK2735 Results in Significant Weight Loss:

The Randomized, Placebo-Controlled, Dose-Finding, VENTURE-Oral Study

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INTRODUCTION

- In 2022, approximately 2.5 billion adults were overweight, of which 890 million were living with obesity (WHO, 2025)
- Obesity can cause weight-related co-morbidities, such as diabetes, cardiovascular disease, stroke, and liver disease
- The clinical benefits of 5% to >10% weight reduction have been demonstrated (Dhar, 2025; Tahrani, 2022)
- Activation of the glucagon-like peptide 1 (GLP-1) receptor decreases glucose, reduces appetite, lowers body weight, and improves insulin sensitivity. Activation of glucose-dependent insulinotropic polypeptide (GIP) receptors may potentiate satiety and insulin-sensitizing effects of GLP-1 receptor activation (Douros, 2025)
- VK2735 is a long-acting dual GLP-1/ GIP receptor agonist that has demonstrated significant weight reduction in a Phase 2 trial of the subcutaneous formulation (Bays, 2026)
- Orally administered VK2735 has also demonstrated promise in a Phase 1 study in healthy subjects with BMI ≥30 (Neutel, 2024)

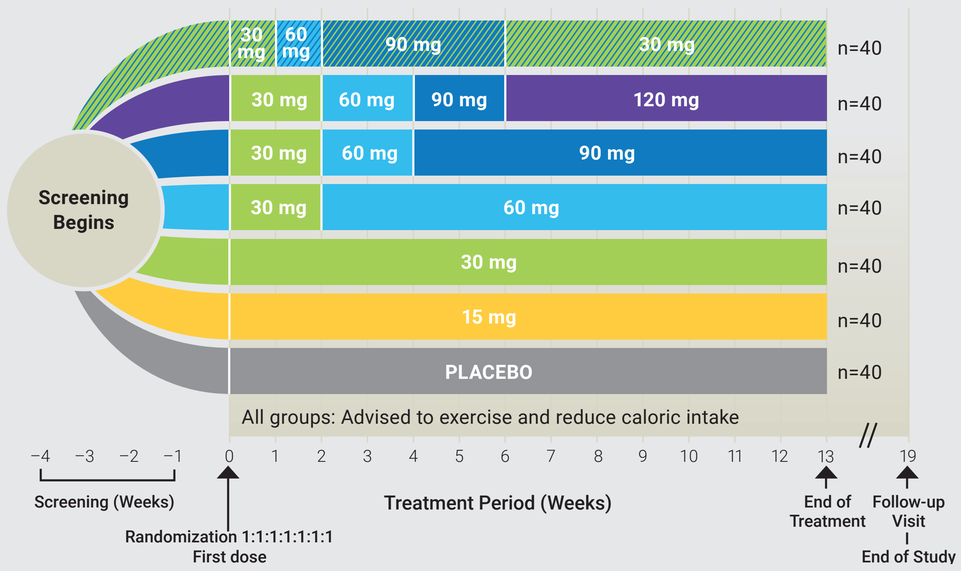
OBJECTIVE

- To evaluate the safety, tolerability, and efficacy of various doses of oral VK2735 on weight reduction in adults with obesity or overweight with ≥1 weight-related comorbidity

METHODS

- VENTURE-Oral was a Phase 2, randomized, double-blind, placebo-controlled study intended to evaluate the safety, tolerability, pharmacokinetics, and weight loss efficacy of oral VK2735, administered, once daily for 13 weeks
- The trial enrolled adults with obesity (BMI ≥30 kg/m^2), or overweight (BMI ≥27 kg/m^2) with ≥1 weight-related comorbid condition
- The primary endpoint of the study was the percent change in body weight from baseline to Week 13 among patients treated with oral VK2735 versus placebo in the modified intent-to-treat (mITT) population
- Secondary and exploratory endpoints evaluated a range of additional safety and efficacy measures

Study Design



Baseline Demographics

Baseline Characteristics (Safety Population)	Placebo (n=40)	15 mg (n=40)	30 mg (n=40)	60 mg (n=40)	90 mg (n=40)	120 mg (n=40)
Age, mean years	51	54	53	49	52	50
Sex, % M:F	30:70	20:80	45:55	15:85	32:68	28:72
White, %	85	80	73	68	88	83
Non-Hispanic, %	70	78	80	85	75	73
Weight, mean kg	105	99	103	103	103	102
BMI, mean kg/m²	38	37	35	37	37	37
Prediabetes,[a] (%)	53	45	60	38	68	63

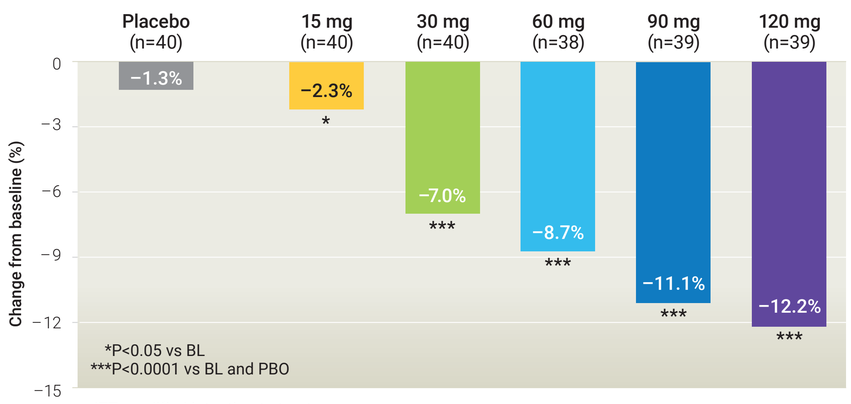
Abbreviations: BMI, body mass index; F, female; M, male.

[a]Prediabetes defined as fasting plasma glucose (FPG) 100 – 125 mg/dL or hemoglobin A1c (HbA1c) 5.7 – 6.4%.

- Majority of participants were non-Hispanic, White, female
- Mean age was 51 years for entire population, 83% of participants were <65 years

TREATMENT WITH ORAL VK2735 LED TO SIGNIFICANT WEIGHT REDUCTION FROM BASELINE AT WEEK 13

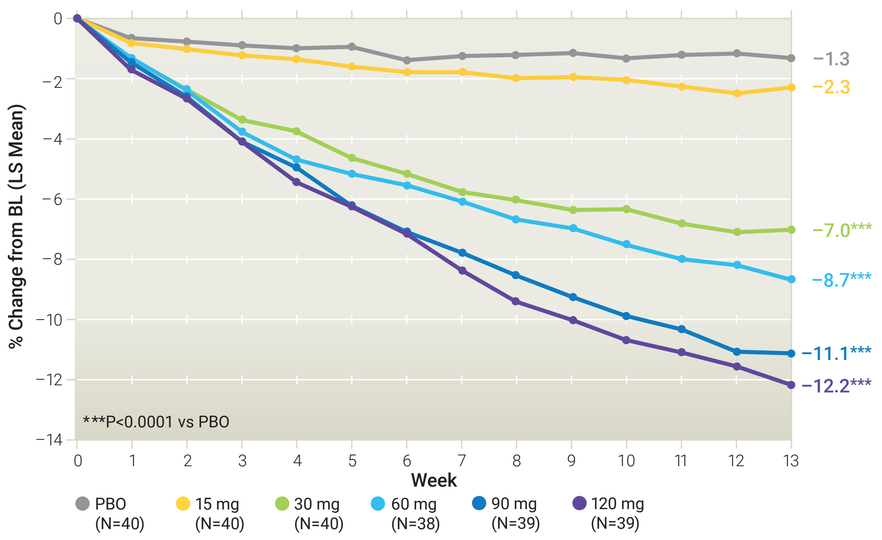
Mean percent change in body weight at week 13 (mITT)



mITT, modified intention-to-treat

- Primary end point was significantly improved versus baseline for all oral VK2735 doses at Week 13
  - It was significantly improved versus placebo for all doses >15 mg
- Dose dependent effect was observed across cohorts
- 12% reduction from baseline was obtained with highest dose

Change from baseline body weight over 13 weeks (mITT)



mITT, modified intention-to-treat

- Progressive weight loss observed with all oral VK2735 doses >15 mg
- Dose dependent effects were observed
- All doses >15 mg resulted in significantly greater weight loss than placebo starting in Week 1 and maintained through Week 13

CONCLUSIONS

- Oral VK2735 dosed daily for 13 weeks led to progressive weight loss of up to 12.2% from baseline
- Promising tolerability, with 98% of drug related TEAS reported as mild to moderate
- Mild GI AE profile consistent with incretin axis activation; generally waned following initial exposures
- VENTURE-Oral results will inform planned Phase 3 clinical trial design

SAFETY & TOLERABILITY

Treatment-Emergent Adverse Events (TEAEs)

Category, n (%)	Placebo (n=40)	15 mg (n=40)	30 mg (n=40)	60 mg (n=40)	90 mg (n=40)	120 mg (n=40)
TEAEs, n (%)	34 (85)	35 (88)	33 (83)	33 (83)	37 (93)	36 (90)
Treatment-related TEAEs[a]	27 (68)	28 (70)	30 (75)	31 (78)	37 (93)	34 (85)
Discontinued treatment early[b]	7 (18)	8 (20)	8 (20)	11 (28)	10 (25)	15 (38)
TEAE leading to treatment discontinuation	5 (13)	2 (5)	5 (13)	7 (18)	8 (20)	12 (30)
Drug-related TEAE leading to treatment discontinuation	3 (8)	1 (3)	5 (13)	6 (15)	8 (20)	11 (28)
Discontinued study early[b]	2 (5)	4 (10)	5 (13)	5 (13)	3 (8)	5 (13)
TEAE leading to study discontinuation	1 (3)	0	1 (3)	0	1 (3)	0
Drug-related TEAE leading to study discontinuation	1 (3)	0	1 (3)	0	1 (3)	0

[b]Three participants (pts) had drug-related SAEs: 1 pt with angioedema/urticaria in the 60 mg tx group; 1 pt with dehydration and 2 pts with nausea/vomiting in the 120 mg tx group. None led to withdrawal from study.

[b]Participants could discontinue treatment and remain in study.

- Among participants receiving VK2735, the majority (98%) of drug-related TEAEs were mild or moderate in severity
- TEAEs leading to study discontinuation were low and similar across study arms

Gastrointestinal (GI) Tolerability

Severity[a]	Placebo (n=40)	15 mg (n=40)	30 mg (n=40)	60 mg (n=40)	90 mg (n=40)	120 mg (n=40)
Any Drug-Related GI TEAE, n (%)						
Mild - Grade 1	17 (43)	18 (45)	16 (40)	18 (45)	21 (53)	18 (45)
Moderate - Grade 2	6 (15)	6 (15)	11 (28)	12 (30)	13 (33)	11 (28)
Severe - Grade 3	1 (3)	0	0	0	0	2 (5)
Most Common Individual GI TEAEs, mild / moderate / severe, % of participants						
Nausea	40/8/0	30/5/0	38/18/0	33/20/0	55/18/0	38/18/5
Constipation	13/10/0	13/10/0	10/10/0	20/10/0	33/10/0	25/3/0
Vomiting	3/8/0	5/0/0	8/8/0	18/3/0	30/5/0	15/15/5
Diarrhea	10/0/3	5/0/0	8/0/0	15/0/0	10/5/0	15/10/0

[a]Severity was rated by investigators using the Common Terminology Criteria (CTC) for Adverse Events 1 to 5 grading scale. There were no Grade 4/5 (life-threatening/death) drug-related TEAEs.

- The majority of GI-related TEAEs were mild or moderate in severity
- Most common TEAEs were GI related: nausea, constipation, vomiting and diarrhea (known drug class TEAEs), which substantially subsided after titration

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DISCLOSURES

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