VRB-101 IS A POTENT ORAL GLP-1 TABLET WITH ONCE-WEEKLY DOSING POTENTIAL

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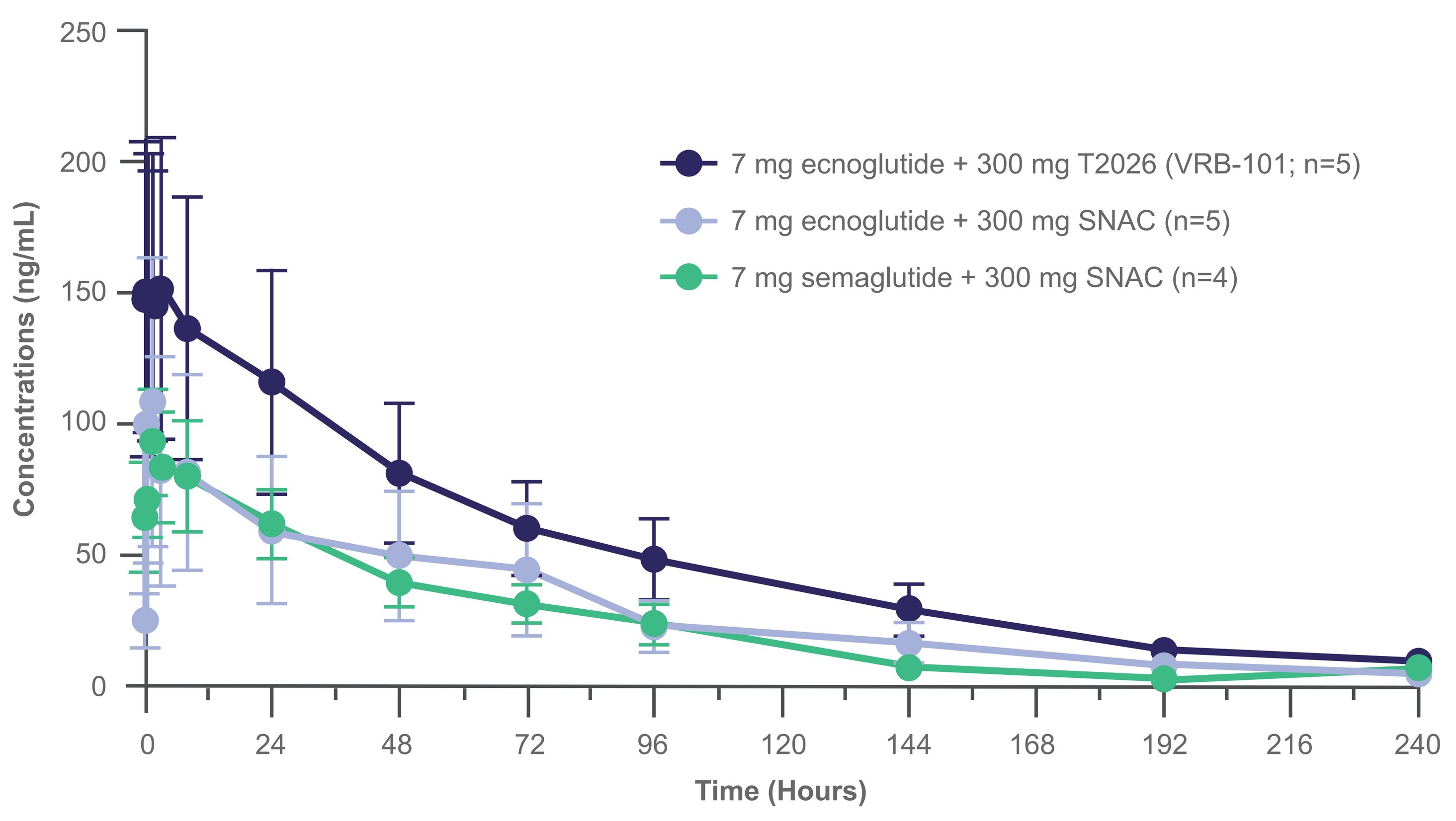
Background

- VRB-101 is an oral tablet formulation of ecnoglutide, a cAMP-biased, long-acting GLP-1 analog being developed for the treatment of obesity and other cardiometabolic diseases[1]
- VRB-101 was designed with rational peptide engineering and administered with proprietary oral delivery technology (T2026) to address the limitations of currently available oral peptide treatments
- VRB-101 contains novel amino acid substitutions that may enable cAMP-biased signaling, extend peptide half-life, increase resistance to stomach pepsin, and may enhance receptor potency relative to unbiased GLP-1 peptides[2]
- The addition of the T2026 absorption enhancer demonstrated improved oral bioavailability, oral absorption, and gastric stability at low pH compared to SNAC[2]

FIGURE 1. THE T2026 ORAL ABSORPTION ENHANCER DELIVERS MORE PEPTIDE INTO SYSTEMIC CIRCULATION THAN SNAC[2]



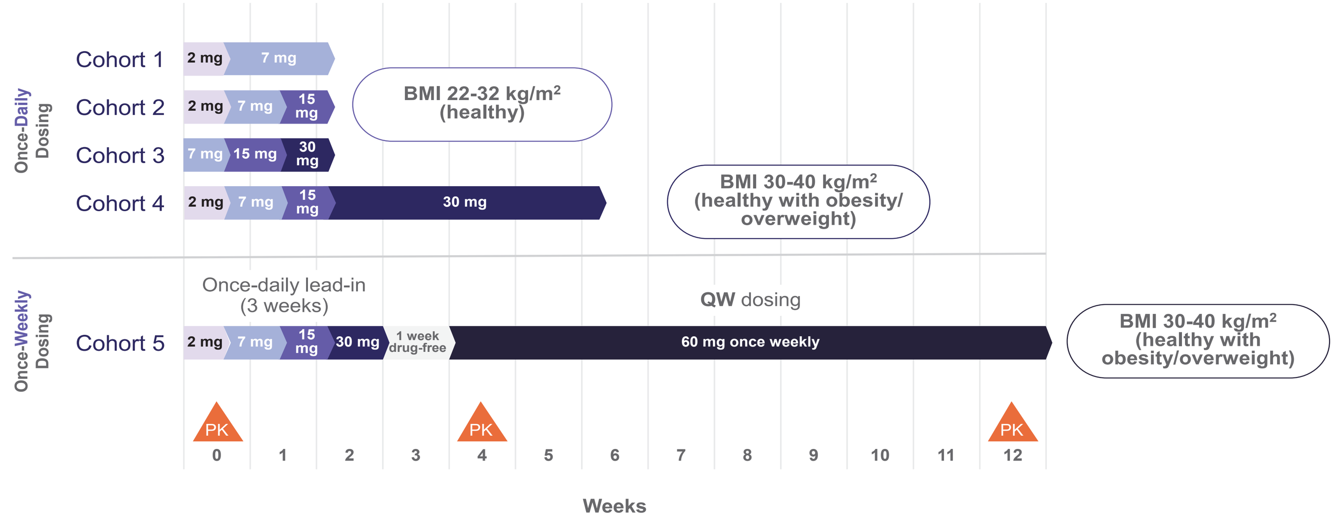
- The enhanced bioavailability provided by T2026 may allow for QW oral administration of VRB-101
- Phase 1 clinical efficacy, safety, and tolerability data were presented previously[3]
- Here we present PK analysis of 30 mg daily dose of VRB-101 and the modeled PK data supporting the potential of VRB-101 as a QW oral GLP-1 tablet for the treatment of obesity

Methods

- We conducted a randomized, double-blind, placebo-controlled Phase 1 study in healthy adults with and without obesity[4]
- Participants were randomized to receive VRB-101 escalated to the target doses of 7, 15, or 30 mg QD for up to 6 weeks[4]
- PK samples were collected, including up to 7 days after the last daily dose; these data were used to model the PK profile of QW dosing with VRB-101

FIGURE 2. PHASE I CLINICAL STUDY DESIGN[4]

Objective: To evaluate the safety and tolerability of repeat doses of oral VRB-101 designed with T2026 (an absorption enhancer) in healthy participants with or without obesity/overweight.



Each cohort is controlled by placebo and T2026 placebo groups (n=2 for each).

Key Inclusion Criteria[4]

- 18-55 years of age and in good general health
- Cohorts 1, 2, and 3: BMI ≥22 kg/m² and <32 kg/m²; body weight ≥55 kg
- Cohorts 4 and 5: BMI ≥30 kg/m² and <40 kg/m²; body weight ≥75 kg
- Stable body weight for at least 3 months

Key Exclusion Criteria[4]

- Prior or ongoing medical conditions, including diabetes, hypoglycemic episodes, acute or chronic pancreatitis, and more
- Participation in any diet and/or exercise program
- Use of weight-reduction medications

Endpoints[4]

Primary

- Incidence, frequency, and severity of TEAEs

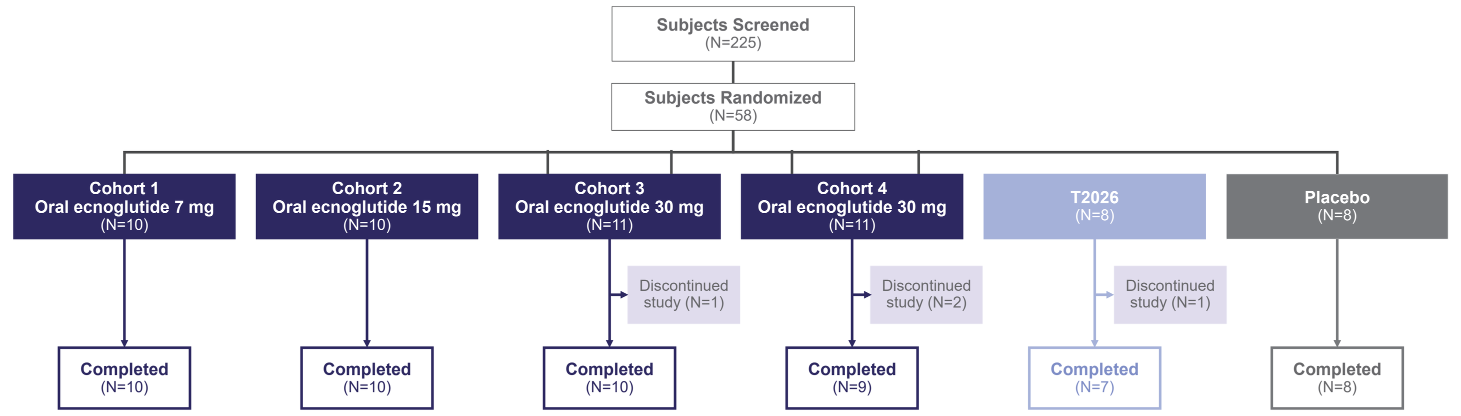
Key Secondary

- PK of initial and repeat doses of oral VRB-101 and T2026
- PD of repeat doses of oral VRB-101

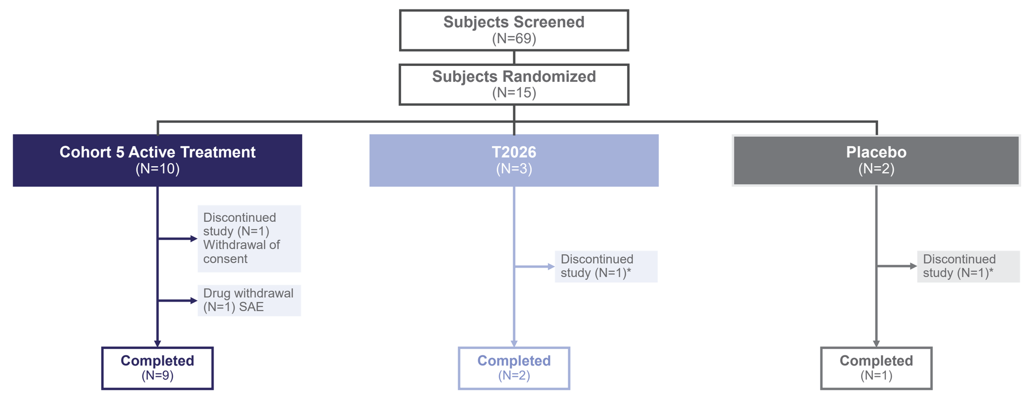
Results #1

FIGURE 3. DISPOSITION OF COHORTS 1-5

Disposition of Cohorts 1-4 (Once-Daily)[3]

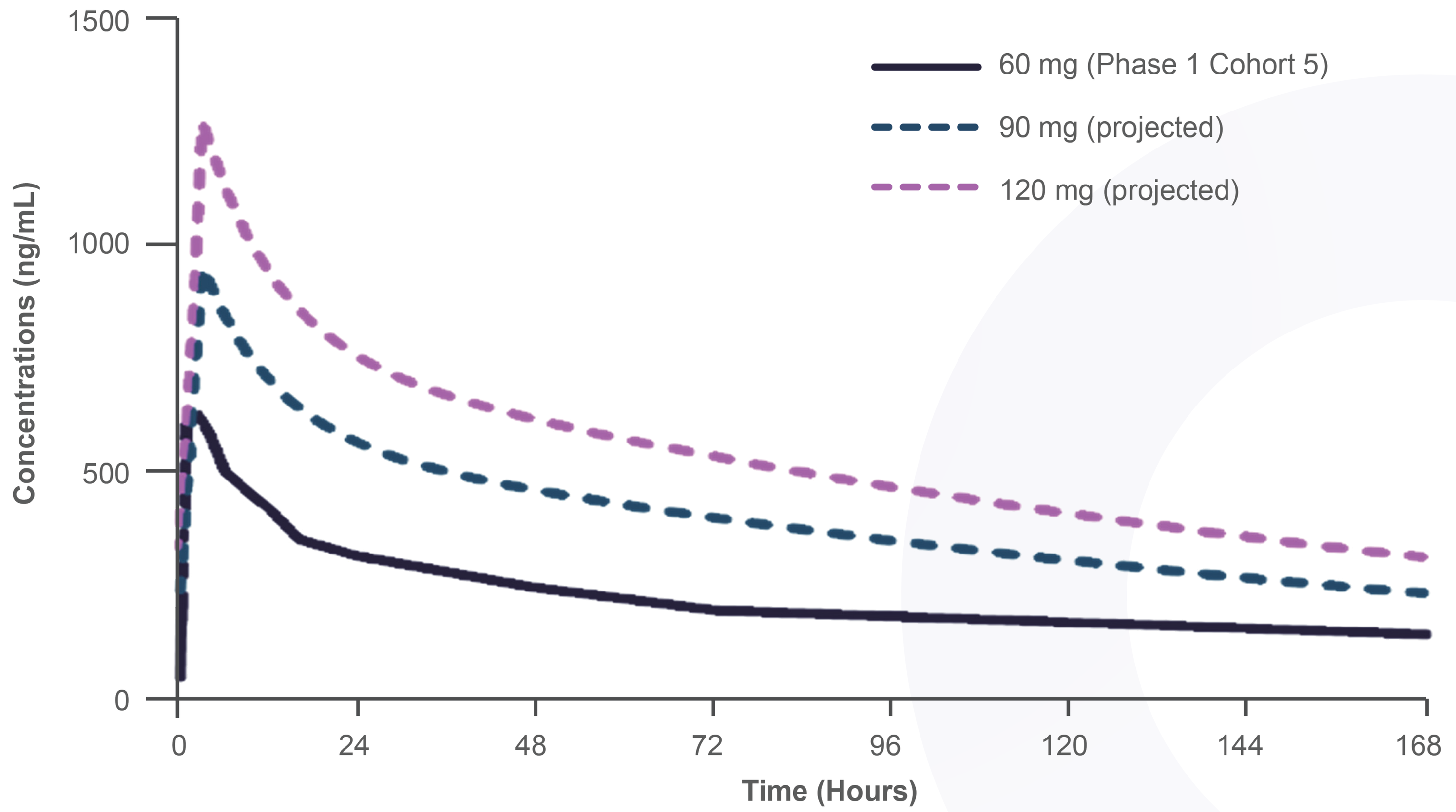


Disposition of Cohort 5 (Once-Weekly)[5]



*Withdrew consent, not due to drug.

FIGURE 4. PK PROFILE OF VRB-101[5]



Results #2

TABLE 1. PK MODELING SUPPORTS THAT ONCE WEEKLY ORAL DOSING WITH VRB-101 CAN MATCH OR EXCEED ONCE WEEKLY SUBCUTANEOUS DOSING WITH 2.4 MG SEMAGLUTIDE[5]

QW Dosing	Low 60 mg (Phase 1)	Mid 90 mg (Projected)	High 120 mg (Projected)	2.4 mg SC semaglutide[6]
$AUC_{0\text{-}t}$ (ng·h/mL)	42,377	69,934	93,243	55,500
C_{trough} (ng/mL)	159	239	319	221

- PK modeling projects 90 mg QW VRB-101 to match plasma exposure and C_{trough} of 2.4 mg SC semaglutide[6]
- This evidence supports moving into Phase 2 trials to pursue a dose-optimization study

Conclusions

- These data support the rationale for VRB-101 as a QW oral GLP-1 treatment
- QW oral 90 mg and 120 mg VRB-101 are projected to be similar to or exceed the weekly exposures of SC GLP-1 injections
- VRB-101 is expected to exert potent weight reduction and may improve adherence via a more patient-friendly dosing regimen
- QW oral administration represents a potential opportunity towards a more scalable treatment option than currently available injectable GLP-1 receptor agonists and may be preferred by patients given the oral route of administration, less frequent dosing schedule, and lack of refrigeration requirement

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$AUC_{0\text{-}t}$=area under the plasma concentration-time curve from time zero to time t. BMI=body mass index. cAMP=cyclic adenosine monophosphate. C_{trough}=trough concentration. GLP-1= glucagon-like peptide-1. PD=pharmacodynamic. PK=pharmacokinetic. QD=once-daily. QW=once-weekly. SNAC=sodium N-(8-[2-hydroxylbenzoyl] amino) caprylate. SAE=serious adverse event. SC=subcutaneous. TEAE=treatment-emergent adverse event.

1. Guo W, et al. *Mol Metab*. 2023;75:101762. 2. Data on File, VRB-101 Preclinical Report. 2024. Verdiva Bio. 3. Zhu Z, et al. American Diabetes Association Scientific Sessions. 2024. Poster Presentation. Abstract 1871-LB. 4. Data on File. VRB-101 Phase 1 Protocol. 2024. Verdiva Bio. 5. Data on File. VRB-101 Phase 1 Clinical Study Report. 2025. Verdiva Bio. 6. Novo Nordisk. Semaglutide Injection (Wegovy) New Drug Application. 2020.