Pharmacodynamic Effects of Oral Small Molecule GLP-1 Receptor Agonist TERN-601 in Healthy Participants with Obesity or Overweight

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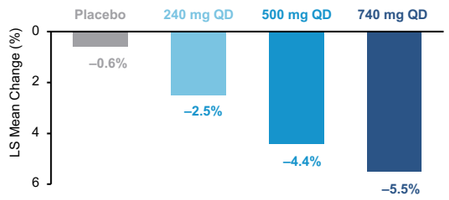
Summary Presentation 804

INTRODUCTION

- TERN-601 is an oral, small-molecule GLP-1 receptor agonist
- TERN-601 suppresses food intake, slows gastric emptying, and reduces blood glucose in mice expressing human GLP-1 receptor[1]
- In a first-in-human (FIH) study, TERN-601 was well-tolerated over 28 days of dosing and achieved weight loss of up to 5.5%[2]
- Several pharmacodynamic (PD) endpoints were measured in the FIH 28-day study to help determine the pharmacodynamically active dose range of TERN-601

Statistically Significant 28-Day Weight Loss[2]



Well-Tolerated Despite Fast Titration[2]

- ✓ No treatment-related discontinuations, interruptions or dose reductions
- ✓ Majority of GI-related AEs were mild
- ✓ No severe or serious AEs
- ✓ No clinically meaningful changes in liver enzymes

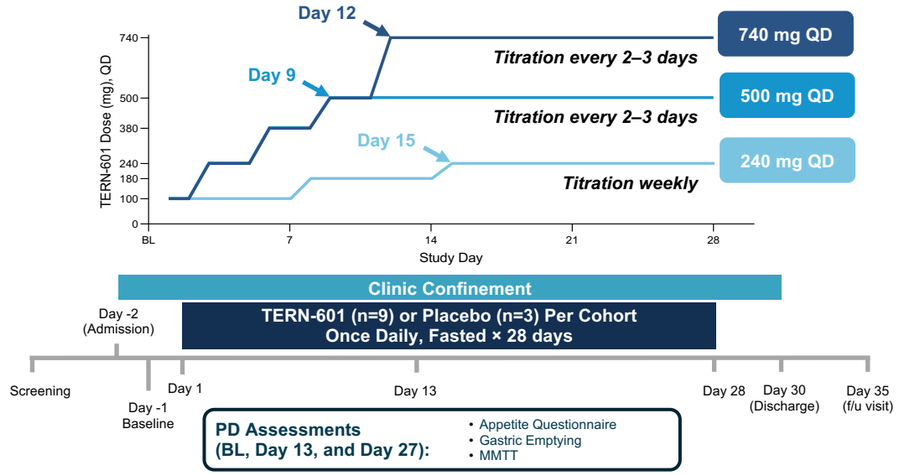
METHODS

Appetite Questionnaire:
- Visual analogue scale 0–100 mm
- Four questions:
  1. How hungry do you feel?
  2. How satisfied do you feel?
  3. How full do you feel?
  4. How much do you think you can eat?
- Assessed prior to a standardized meal and at 0.5, 1, 2, and 4 hours post-meal
- Area under the curve (AUC) calculated

Gastric Emptying:
- 1.5 grams of acetaminophen (APAP)/paracetamol administered orally as a solution
- Plasma samples collected at from 0 to 5 hrs post-APAP administration

Mixed-Meal Tolerance Test (MMTT):
- Standardized meal (16 oz Ensure Plus®) administered after overnight fast
- Blood samples collected 0 to 5 hours after mixed meal

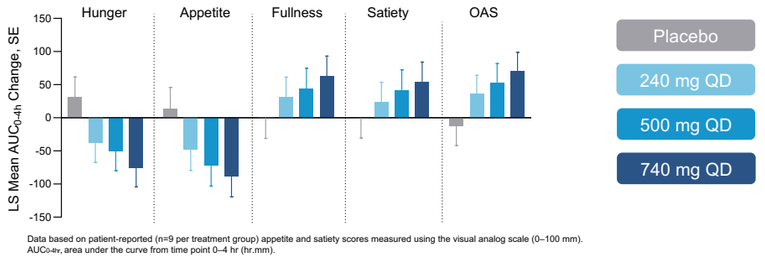
Study Population:
- Adults (18–65 yrs)
- BMI 27 to <40 kg/m^2
- HbA1c <6.5%



RESULTS

- Once-daily dosing of TERN-601 resulted in dose-dependent decreases in hunger and appetite with corresponding increases in fullness and satiety
- Overall appetite score (OAS), which is a composite score of hunger, appetite, fullness, and satiety, also increased in a dose-dependent manner
- Observed changes in appetite are likely predictive of weight loss in longer term studies

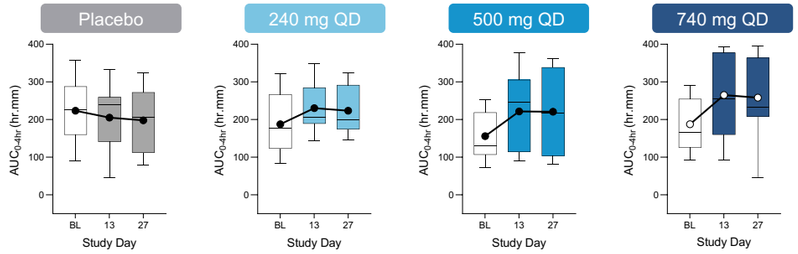
Figure 1. Day 27 Change from Baseline — Participant Appetite Questionnaire



Data based on patient-reported (n=9 per treatment group) appetite and satiety scores measured using the visual analog scale (0–100 mm).
$AUC_{0\text{-}4hr}$, area under the curve from time point 0–4 hr (hr.mm).

- Dose-dependent increases in overall appetite score (OAS), correspond to decreases in hunger and appetite and increases in fullness and satiety
- Increases in OAS were observed at Day 13 of dosing and remained relatively consistent on Day 27

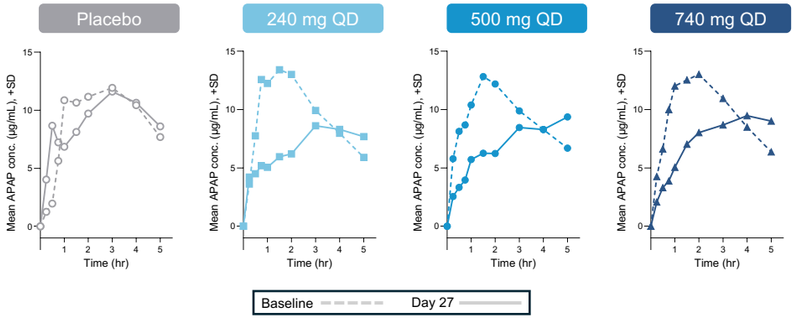
Figure 2. Baseline, Day 13, and Day 27 — Overall Appetite Score



Data based on patient-reported hunger and satiety scores measured using the visual analog scale (0–100 mm).
$AUC_{0\text{-}4hr}$, area under the curve from time point 0–4 hr (hr.mm).
Boxes provide the 25th to 75th percentiles with a line at the median. Whiskers extend to the smallest and largest values observed. Line plot overlays represent mean values.

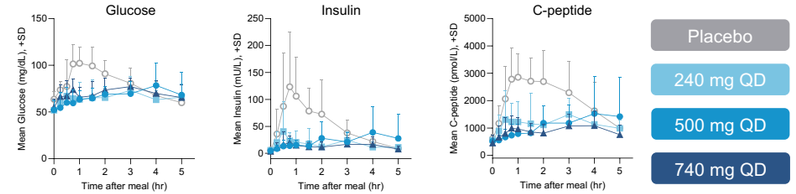
- Slowing of acetaminophen (APAP) absorption (a marker of delayed gastric emptying) on Day 27 (solid lines) was observed at all TERN-601 doses
- Delayed gastric emptying is consistent with the GLP-1RA class and likely contributes to observed effects on appetite and weight loss

Figure 3. Baseline and Day 27 — Gastric Emptying



- All TERN-601 doses suppressed increases in blood glucose, insulin, and C-peptide in response to an MMTT in participants without diabetes relative to placebo treatment
- Delayed gastric emptying (Figure 3) may have contributed to these effects on glycemic parameters

Figure 4. Mixed-Meal Tolerance Test (MMTT) Analytes on Day 27



CONCLUSIONS

- TERN-601 reduced appetite and increased satiety in a dose-dependent manner
- TERN-601 delayed gastric emptying and prevented rises in glucose, insulin, and C-peptide following MMTT to a similar extent at all doses
- TERN-601 PD effects were consistent with GLP-1RA mechanism of action
- 28-day PD data, along with safety and weight loss data, supported dose and titration schedule selection for ongoing Phase 2 12-week study (FALCON; NCT06854952) in participants with obesity or overweight

GLOSSARY

APAP, acetaminophen (paracetamol); BL, baseline (Day –1); DCs, discontinuations; FIH, first-in-human; GI AEs, gastrointestinal adverse events; GLP-1RA, glucagon-like peptide-1 receptor agonist; LS, least squares; MMTT, mixed meal tolerance test; OAS, overall appetite score; PD, pharmacodynamic; QD, once-daily; SD, standard deviation; SE, standard error

DISCLOSURES

- All authors are employees or paid consultants of Terns Pharmaceuticals
- All employees are stock/shareholders of Terns Pharmaceuticals
- This study was paid for by Terns Pharmaceuticals

REFERENCES

1. Jones C, et al. Diabetes. 2023;72(Suppl 1):767-P.
2. Nelson C, et al. Diabetes. 2025;74(Suppl 1):307-OR.

ACKNOWLEDGMENTS

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