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TERN-601 Phase 1 Trial Top-Line Results

NASDAQ: TERN

Sept 9, 2024

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Agenda and Participants

- **Opening Remarks** / Amy Burroughs
- **Phase 1 Top-Line Results** / Emil Kuriakose
- **Closing Remarks** / Amy Burroughs
- **Q&A** / Amy Burroughs, Emil Kuriakose, Mark Vignola

Terns Pipeline: Broad Rights to Multiple Wholly-owned Opportunities Targeting Serious Diseases

PROGRAM	MECHANISM	INDICATION	PRECLINICAL	EARLY-STAGE CLINICAL DEVELOPMENT	LATE-STAGE CLINICAL DEVELOPMENT	STATUS / NEXT MILESTONE
Oncology						
TERN-701	Allosteric BCR-ABL Inhibitor	CML	Phase 1 CARDINAL		*Anticipated registrational trial following Ph 1 trial*	**Ph1 CARDINAL trial initiated** Interim data from initial cohorts in Dec '24
Metabolic						
TERN-601	Oral GLP-1R Agonist	Obesity	Phase 2 Ready			**Positive top-line Ph1 data (28-day PoC) Sept '24** Phase 2 initiation 2025
TERN-501 Combination	Oral THR-β Agonist + Metabolic Agent	Obesity	Phase 2 Ready			**Positive Ph2a NASH data** Preclinical data in combo with GLP-1 (enhanced and higher quality weight)
TERN-800 Series	Oral GIPR Modulators	Obesity	GIPR Antagonist Lead Opt.			**GIPR antagonist lead optimization underway**

CML: chronic myeloid leukemia, GIPR: glucose-dependent insulinotropic polypeptide receptor, GLP-1R: glucagon-like peptide-1 receptor, NASH: non-alcoholic steatohepatitis, opt: optimization, PoC: proof of concept, THR-β: thyroid hormone receptor beta

Positive Phase 1 Results Demonstrate TERN-601 is Well Positioned for Phase 2 and Long-Term Differentiation

- **Statistically significant** and **dose-dependent** weight loss over 28 days with QD dosing
- **Well tolerated** with unremarkable safety findings despite **rapid titration to high doses**
- **Distinct drug properties** enabled sustained target coverage and a flat PK curve, and may lead to a differentiated clinical profile in subsequent studies
- Potential to be a leading GLP-1R agonist with promising **efficacy, tolerability and manufacturing scalability**
- **Plan to initiate Phase 2** trial in 2025

GLP-1R: glucagon-like peptide-1 receptor, PK: pharmacokinetic, QD: once-daily

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Phase 1 Top-Line Results

Emil Kuriakose, M.D., Chief Medical Officer

Clinical Data Support TERN-601 as an Oral, Once-Daily GLP-1R Agonist with a Distinct and Compelling Profile

Over 28 days, TERN-601 dosed once-daily:

- ✓ Showed significant mean weight loss up to 5.5% (4.9% placebo-adjusted)
  - 67% of participants lost ≥ 5% baseline body weight at top dose
- ✓ Was well tolerated with unremarkable safety findings
  - No treatment-related dose interruptions, reductions, or discontinuations at any dose
  - All GI adverse events were mild to moderate and consistent with the GLP-1R agonist class
  - No clinically meaningful changes in liver enzymes, vital signs or ECGs
- ✓ Demonstrated distinct drug properties, allowing sustained target coverage with once-daily dosing and enabling evaluation of doses up to 740 mg
- ✓ Identified pharmacodynamically and clinically active dose range warranting further evaluation in subsequent studies

ECG: electrocardiogram, GI: gastrointestinal, GLP-1R agonist: glucagon-like peptide-1 receptor agonist

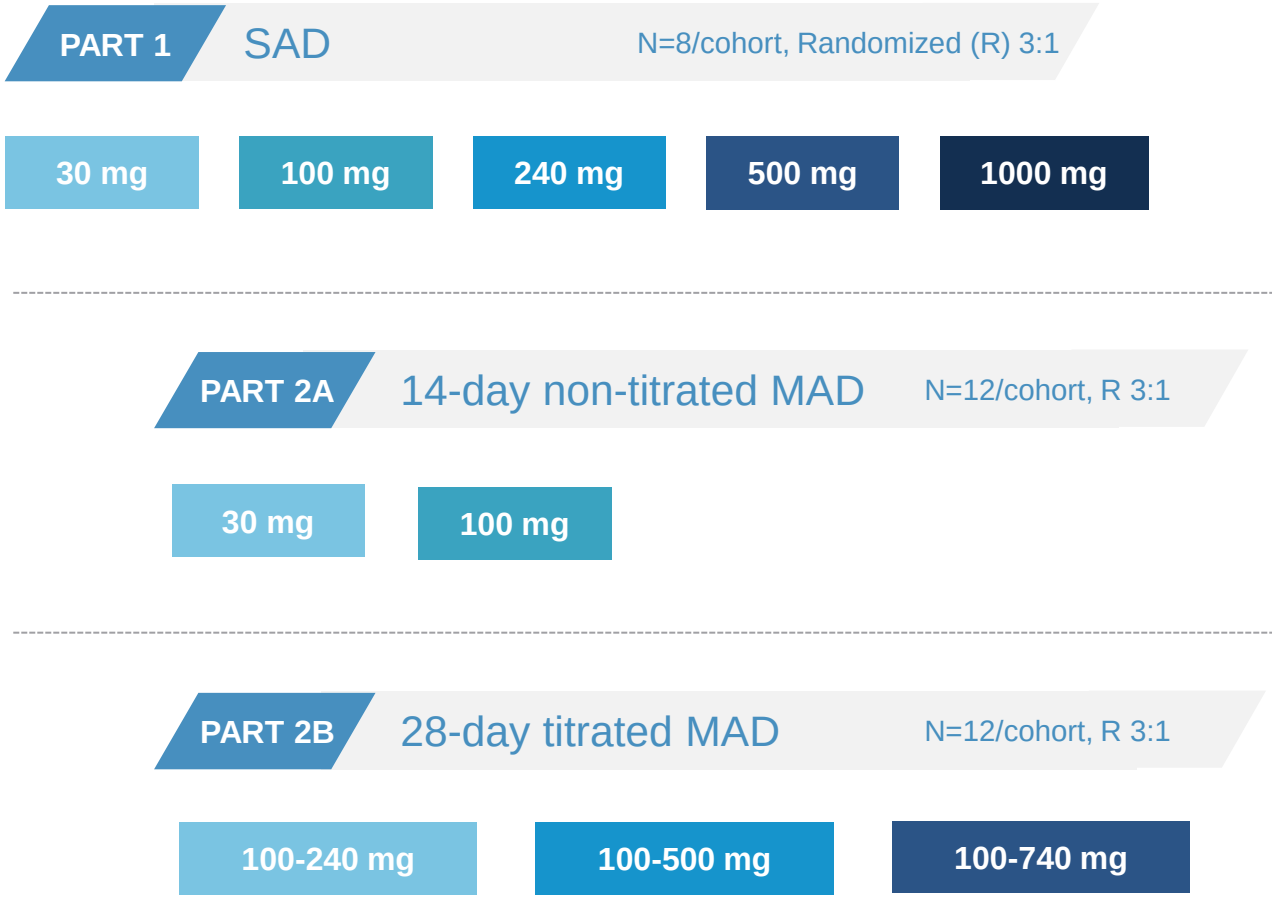
TERN-601 First-In-Human Study Leveraged an Efficient Design to Explore a Wide Dose Range

Phase 1 Trial Design

Population
- Healthy adults with obesity or overweight
- Non-diabetic
- BMI ≥ 27 to < 40 kg/m^2 (Part 2)

Endpoints
- Primary: safety and tolerability
- Secondary / exploratory: PK, change in body weight over 28 days, etc.

Location
- U.S. inpatient Phase 1 center



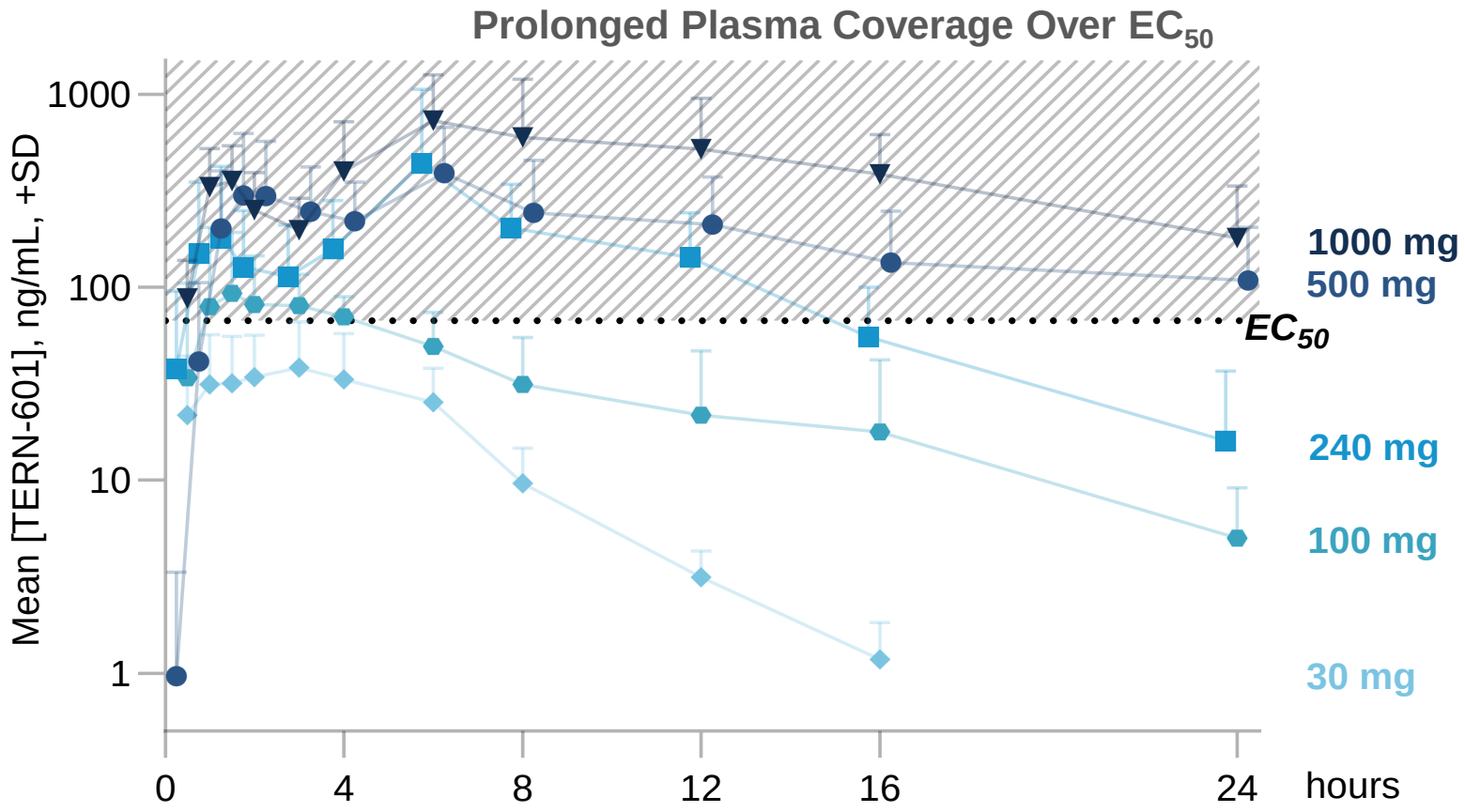
Study objectives

- Use PK data to identify once-daily target doses for 28-day titration
- Use safety/tolerability and PD data to identify optimal starting dose for 28-day titration
- Assess safety / tolerability of fast titration to target doses and weight loss over 28 days

BMI: body mass index, MAD: multiple ascending dose, PD: pharmacodynamic, PK: pharmacokinetic, SAD: single ascending dose

Prolonged Absorption of TERN-601 at Target Doses Drove Sustained Target Coverage with Once-Daily Dosing

- Prolonged absorption at ≥240 mg led to sustained 16-24 hour target coverage in plasma despite ~4-6 hour elimination half-life
- SAD PK identified 240 mg and above as potentially efficacious target doses for 28-day MAD cohorts



Note: Dotted line represents estimated protein-binding adjusted EC_{50} (concentration at which 50% of maximal activity is observed) in CHO-K1 cells (subclone of the Chinese hamster ovary cell line) expressing hGLP-1R (humanized GLP1 receptor)
MAD: multiple ascending dose, PK: pharmacokinetic, SAD: single ascending dose, SD: standard deviation

Baseline Characteristics Well-Balanced Across 28-Day MAD Cohorts

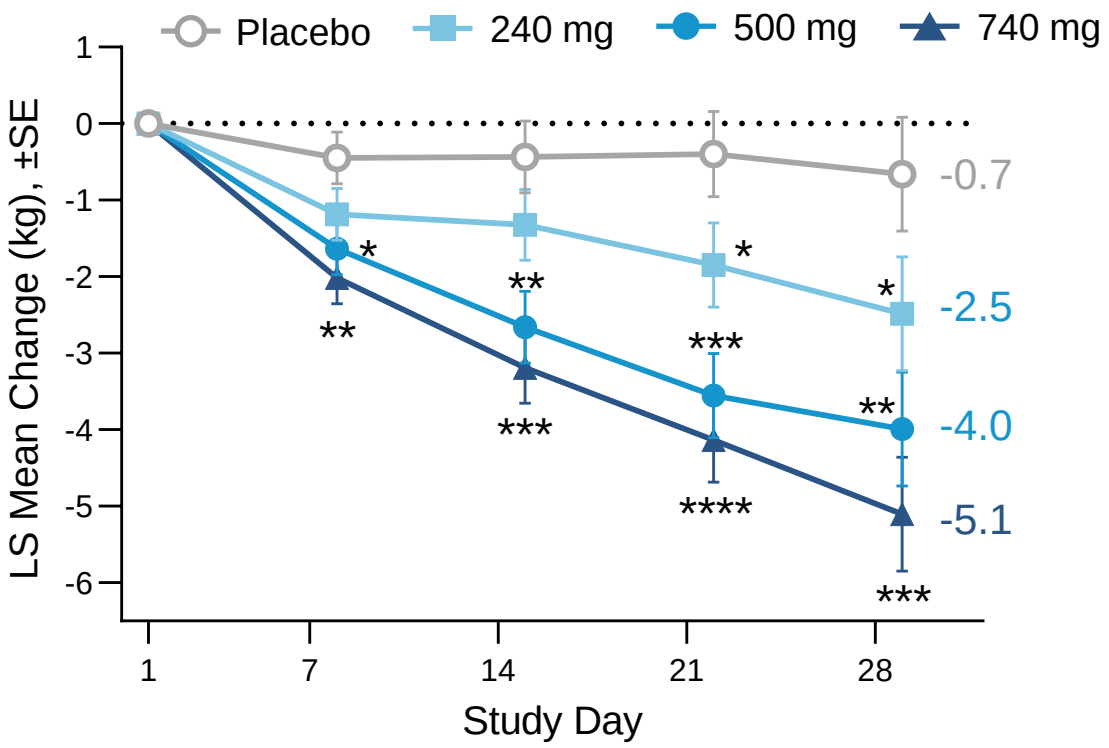
BMI consistent across groups (~30 kg/m^2), with predominantly male participants (≥70%)

Mean (SD) Median	Placebo pooled (N=9)	240 mg (N=10)	500 mg (N=9)	740 mg (N=9)
Age, year	41.4 (9.2) 40	44.7 (10.7) 49.5	46.7 (12.7) 45	46.7 (12.1) 50
Male, n (%)	7 (78%)	7 (70%)	8 (89%)	7 (78%)
Weight, kg	90.9 (7.8) 91.8	93.4 (14.2) 92.6	95.0 (10.6) 93.8	93.3 (13.7) 93.1
BMI, kg/m^2	29.7 (1.6) 28.8	30.6 (2.8) 30.3	31.2 (2.1) 30.4	30.1 (2.2) 29.4
HbA1c, %	5.6 (0.2) 5.5	5.5 (0.3) 5.7	5.6 (0.3) 5.6	5.5 (0.2) 5.5

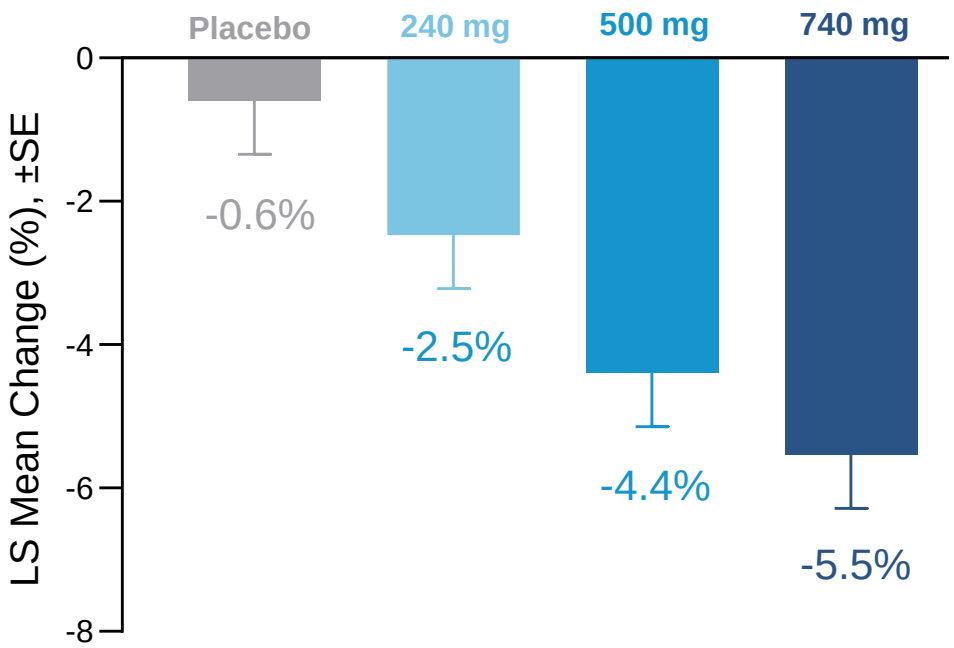
BMI: body mass index, HbA1c: hemoglobin A1c, MAD: multiple ascending dose, N: number of participants in analysis set, SD: standard deviation

TERN-601 Showed Dose-Dependent 28-Day Mean Weight Loss Up to 5.5%

Mean Body Weight Change from Baseline (kg)



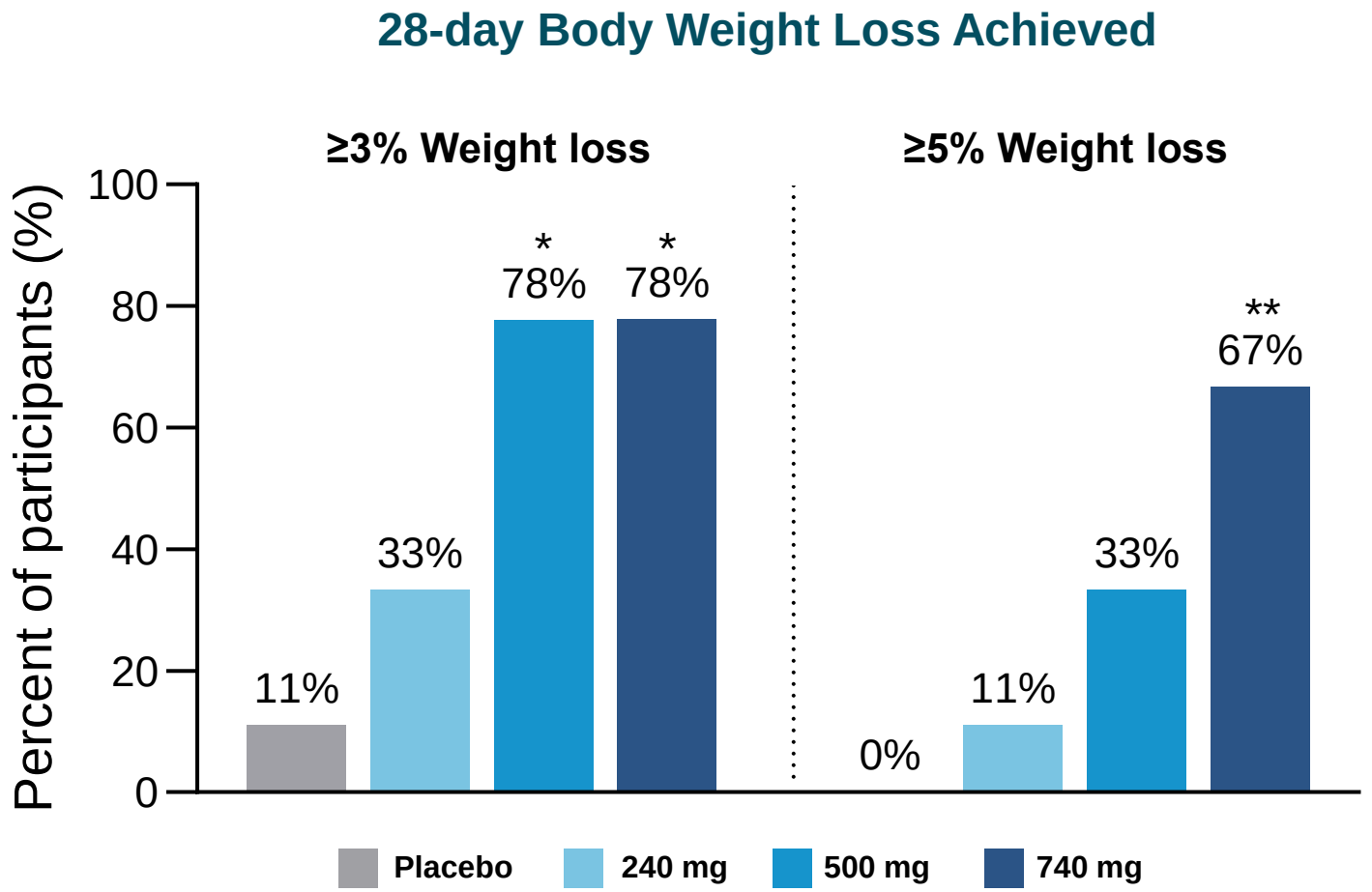
Mean Body Weight Change from Baseline (%)



N	9	9	9	9
PBO-adjusted	-	-1.9%	-3.8%	-4.9%
P-value	-	<0.1	<0.01	<0.0001

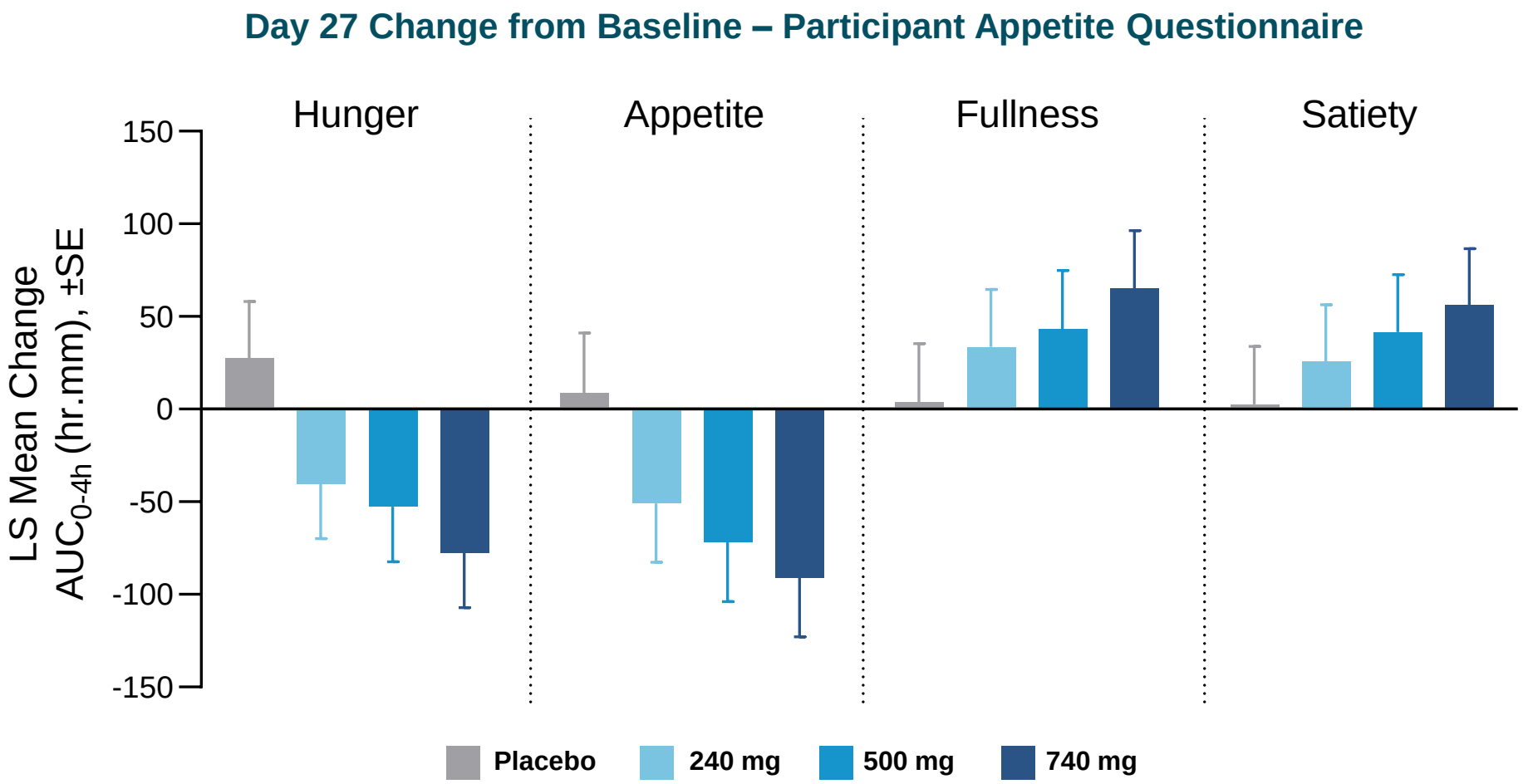
*p-value <0.1; **p-value <0.01; ***p-value <0.001, ****p <0.0001
LS: Least Squares, N: number of participants in analysis set, PBO: placebo, SE: standard error
Note: 1 participant (240mg) discontinued study early due to unrelated Grade 1 AE (menstrual bleeding determined to be unrelated to study drug); participant was replaced

Clear Dose Response With 67% of Participants Losing ≥ 5% Baseline Body Weight at Top Dose



*p-value <0.1; **p-value <0.01, relative to placebo

Meaningful Changes in Hunger/Satiety Scores Seen at All Doses with Clear Dose Relationship



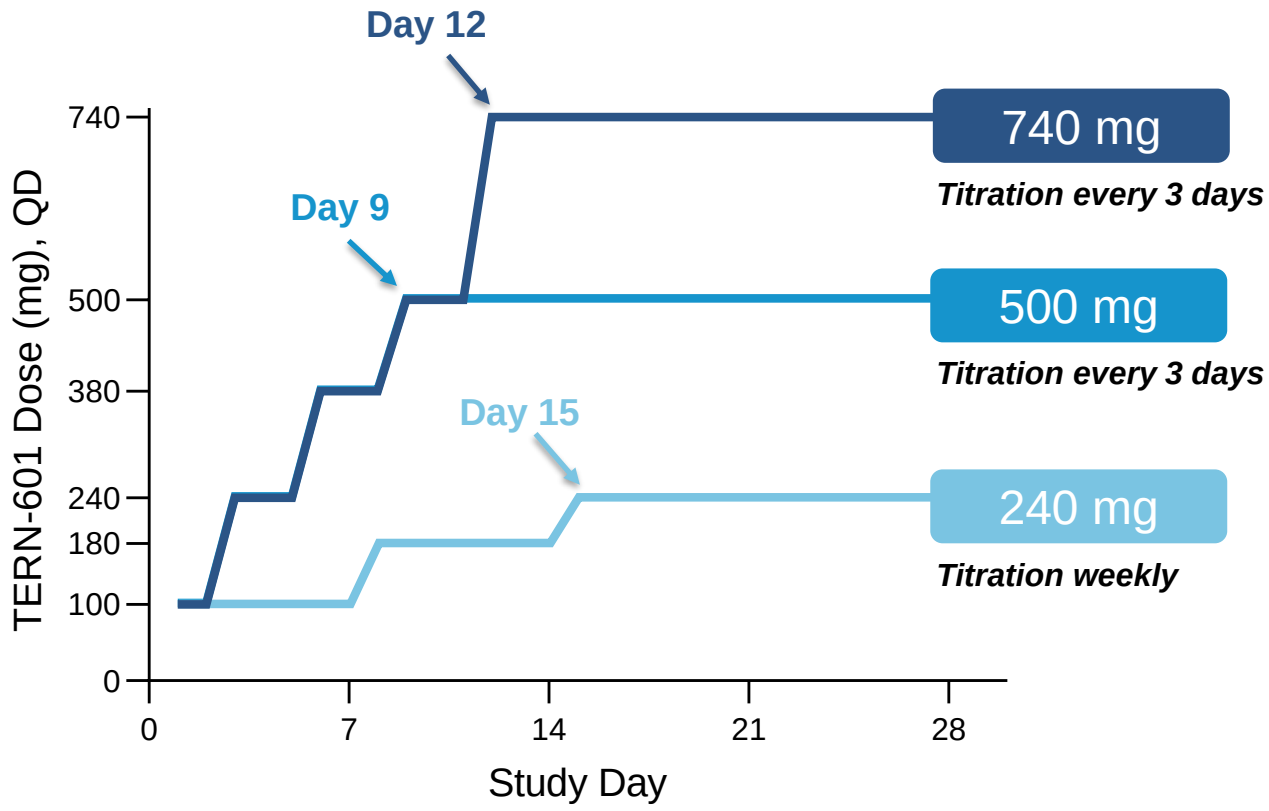
Data based on patient-reported appetite and satiety scores measured using the visual analog scale (0-100 mm)
$AUC_{0\text{-}4hr}$ = area under the curve from timepoint 0 to 4 hr (hr.mm), LS: least squares, SE: standard error

28-Day MAD Design Assessed Tolerability of Fast Titration to High Doses

Well tolerated despite fast titration suggests potential for improved tolerability in subsequent studies with slower titration

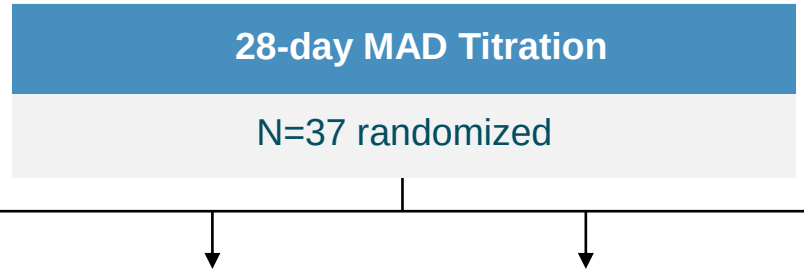
- Safety / tolerability data from completed cohorts guided titration speed and target dose for subsequent cohorts
- Primary measures of tolerability guiding escalation / titration decisions were:
  - Dose interruptions / reductions / discontinuations
  - Severity of GI AEs

All Cohorts Completed Titration Within the First 2 Weeks



GI AEs: gastrointestinal adverse events, MAD: multiple ascending dose, QD: once-daily

No Drug-Related Discontinuations, Interruptions or Dose Reductions



	Placebo pooled (N=9)	240 mg (N=10)	500 mg (N=9)	740 mg (N=9)
Completed Treatment	9 (100%)	9 (90%)*	9 (100%)	9 (100%)
Discontinued Study Drug Due to Related-AE	0	0	0	0
Dose Interruption Due to AE	0	0	0	0
Dose Reduction Due to AE	0	0	0	0

* 1 participant discontinued study early due to unrelated Grade 1 AE (menstrual bleeding determined to be unrelated to study drug); participant was replaced
AE: adverse event, MAD: multiple ascending dose, N: number of participants in analysis set

Favorable Safety Profile with No Severe or Serious Adverse Events

>95% of treatment emergent adverse events were mild (Grade 1)

Treatment Emergent AEs by Maximum Severity

Event, N (%)	Placebo pooled (N=9)	240 mg (N=10)	500 mg (N=9)	740 mg (N=9)
Grade 1 (Mild)	5 (55.6%)	5 (50%)	9 (100%)	3 (33.3%)
Grade 2 (Moderate)	0	1 (10%)	0	6 (66.7%)
Grade ≥3 (Severe)	0	0	0	0
Serious Adverse Events	0	0	0	0

- Majority of AEs were consistent with known effects of GLP-1R agonist class (e.g. gastrointestinal)
- No clinically meaningful changes in ECGs, heart rate or blood pressure

AE: adverse event, ECG: electrocardiogram, N: number of participants in analysis set, GLP-1R agonist: glucagon-like peptide-1 receptor agonist

No Clinically Meaningful Changes in Liver Enzymes

Liver enzymes remained ≤ 1.5X ULN while on treatment at all doses

Mean (SD) Change from Baseline to Day 29	Placebo pooled (N=9)	240 mg (N=10)	500 mg (N=9)	740 mg (N=9)
ALT (U/L)	-3.4 (7.6)	-4.0 (6.4)	-9.0 (6.4)	-9.0 (9.7)
AST (U/L)	-2.4 (4.6)	-1.3 (3.3)	-7.0 (4.6)	-5.1 (8.7)
Bilirubin (mg/dL)	0.01 (0.11)	0.15 (0.14)	0.09 (0.35)	0.18 (0.47)

ULN: upper limit of normal; ALT: alanine transaminase; AST: aspartate transaminase; N: number of participants in analysis set; SD: standard deviation

Majority of GI-Related AEs Mild in Severity Despite Fast Titration

GI AEs consistent with class increased with faster titration to higher doses, as expected, and were not dose limiting

Treatment Emergent GI AEs by Maximum Severity

Event, N (%)	Placebo pooled (N=9)	240 mg (N=10)	500 mg (N=9)	740 mg (N=9)
Nausea				
Grade 1 (Mild)	2 (22.2%)	0	7 (77.8%)	2 (22.2%)
Grade 2 (Moderate)	0	0	0	6 (66.7%)
Vomiting				
Grade 1 (Mild)	0	0	4 (44.4%)	6 (66.7%)
Grade 2 (Moderate)	0	0	0	1 (11.1%)
Diarrhea				
Grade 1 (Mild)	0	0	2 (22.2%)	2 (22.2%)
Grade 2 (Moderate)	0	0	0	0
Constipation				
Grade 1 (Mild)	0	1 (10.0%)	0	5 (55.6%)
Grade 2 (Moderate)	0	1 (10.0%)	0	0

AE: adverse event, GI: gastrointestinal, N: number of participants in analysis set, GLP-1R agonist: glucagon-like peptide-1 receptor agonist

Compelling 28-Day Data Amongst Oral GLP-1R Agonist Peers

	TERN-601	danuglipron	GSBR-1290	orforglipron	RGT-075	CT-996
≥3% Placebo-Adjusted Weight Loss	✓	✓	✓	✓	✓	✓
No Dose Interruptions or Reductions Due to AEs	✓	✗	✓	?	✗	?
No Drug-Related AE Discontinuations	✓	✗	✓	✗	✗	✓
No Severe TEAEs	✓	✗	✓	✓	✓	?
Rapid Dose Titration (>50% of Days at Highest Dose)	✓	✓	✗	✗	✗	?

Note: Assessments based on entirety of Phase 1 28-day datasets of peer compounds (any/all doses/cohorts); no head-to-head study has been conducted with TERN-601 against the other drug product candidates. Differences exist in study designs and conditions, and caution should be exercised when comparing data across studies. Data are shown for illustrative purposes only.
Sources: danuglipron: Saxena A, et al. *Nature Medicine*. 2021;27:1079-87; GSBR-1290: Structure Therapeutics Corporate Presentation; GSBR-1290 Phase 1b MAD Results. 2023 September 29; orforglipron: Pratt E, et al. *Diabetes Obes Metab*. 2023;25:2642-49; RGT-075: Priner M. et al. *Diabetes* 2022;71(Supplement_1):94-LB; CT-996: Roche. (2024 July 16). *Roche Phase I results GLP-1 receptor agonist CT-996*

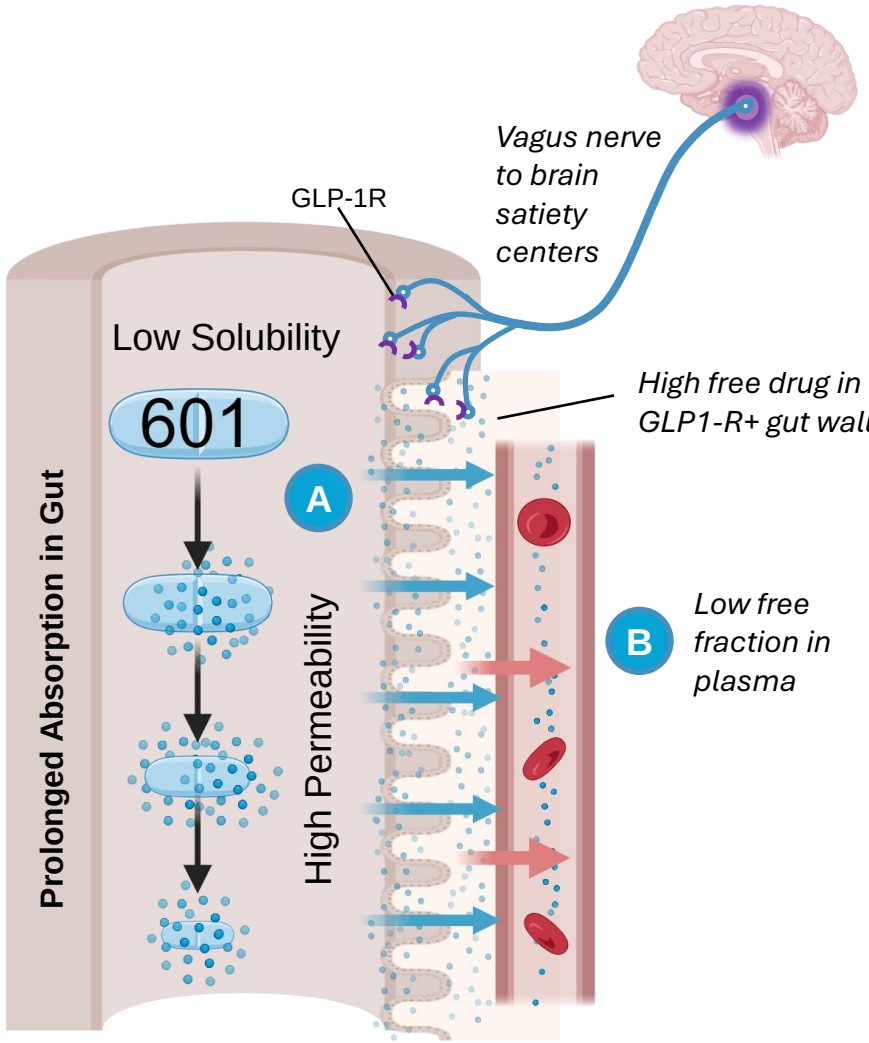
AE: adverse event, GLP-1R agonist: glucagon-like peptide-1 receptor agonist, TEAE: treatment emergent adverse event

Distinct Drug Properties May Confer Advantages For an Orally-Dosed GLP-1R Agonist

	TERN-601 Property	Advantage
Drug Product	Tablet	Convenient once-daily oral dosing
Solubility	Low	Prolonged absorption and flat PK curve
Gut Permeability	High	
Gut wall: Plasma Concentration Ratio	High	High levels of GLP-1R activation in gut
Plasma Protein Binding	High	Allows high doses with good tolerability

GLP-1R: glucagon-like peptide-1 receptor; PK: pharmacokinetic

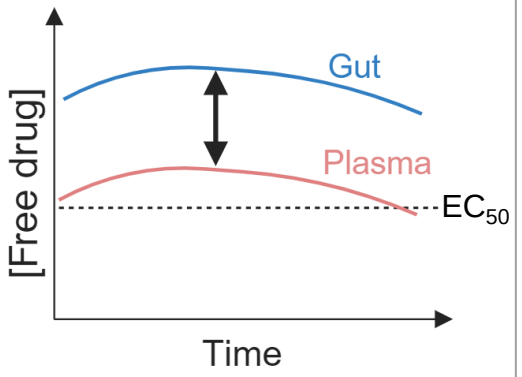
Distinct Properties Enable Tolerable Higher Doses that Achieve Robust GLP-1R Activation and Flat PK Curve



A

Low solubility & high permeability results in:

- **Prolonged absorption** and **flat PK curve** allowing **QD dosing**
- **High drug levels in gut wall** that strongly activate GLP-1R in gut triggering satiety centers in brain



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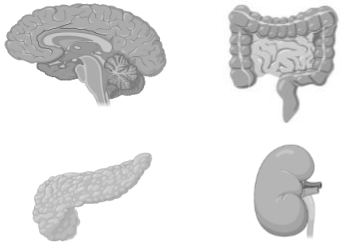
Low free fraction may allow:

- **Tolerable higher doses** that drive both **gut and systemic GLP-1R** activation



GLP-1R: glucagon-like peptide-1 receptor, PK: pharmacokinetic, QD: once-daily
EC_{50}: concentration at which 50% of maximal activity is observed

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Closing Remarks

Amy Burroughs, Chief Executive Officer

TERN-601 Well Positioned for Subsequent Studies: Plan to Initiate Phase 2 in 2025

Clinical Data To Date:		Potential Impact on Future Development:
✓ Thorough exploration of dose range	→	**No new dose range exploration anticipated**
✓ Well tolerated despite fast titration scheme	→	**Improved tolerability with slower titration**
✓ Flat PK with sustained target coverage	→	**Compelling weight loss over longer durations**
✓ Robust PD effects at all dose levels	→	**Optionality to pursue high/low doses for various patient segments**

PD: pharmacodynamic, PK: pharmacokinetic

Next Steps for TERN-601 in Obesity

Evaluating paths to run a comprehensive, efficient and expedient trial in Phase 2

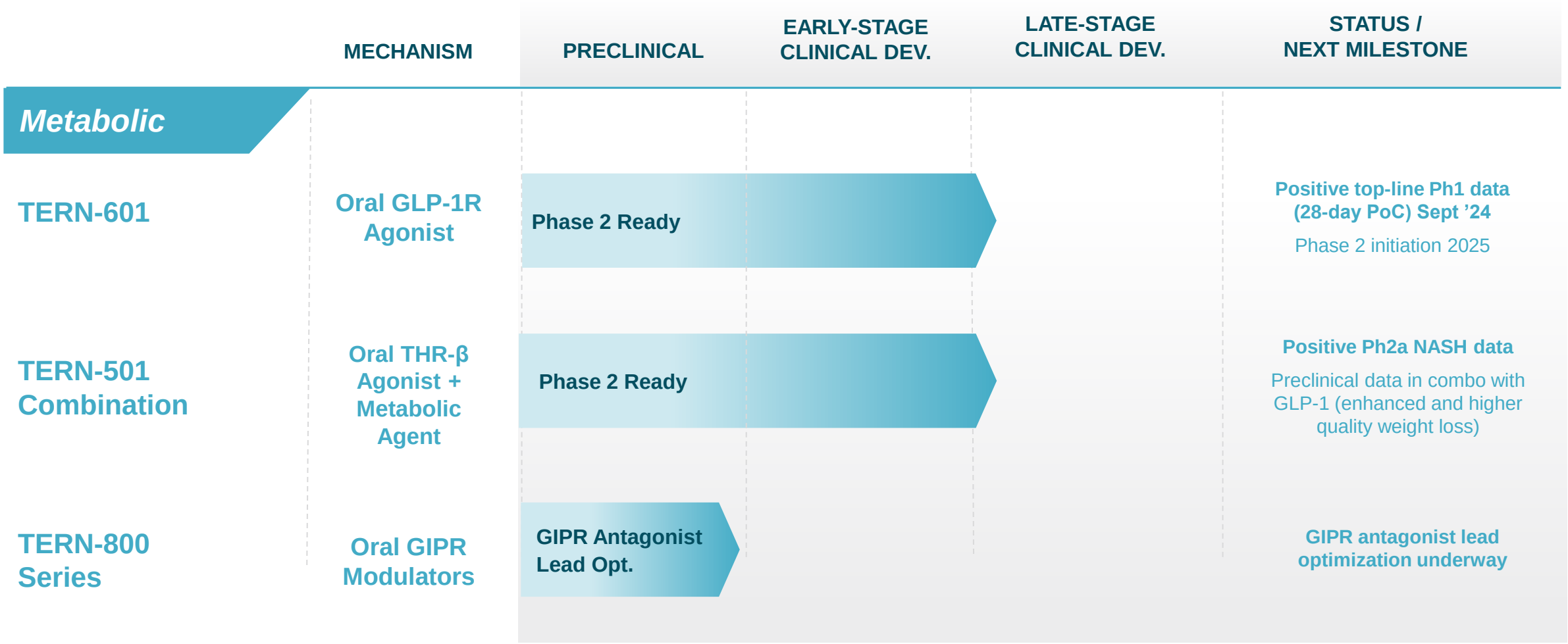
- ✓ **Positive Phase 1**
- ✓ **Operational and CMC Readiness**

Next Steps to Finalize Phase 2 Plans

- Gather additional feedback from scientific advisors based on the Phase 1 data
- Design Phase 2 to be informative and support an expeditious path to the pivotal trial
- Solicit regulatory feedback on development plan
- Plan to initiate Phase 2 in 2025

Advancing Terns' Metabolic Pipeline of Combinable Assets

Orally administered, small molecule and wholly-owned compounds for obesity



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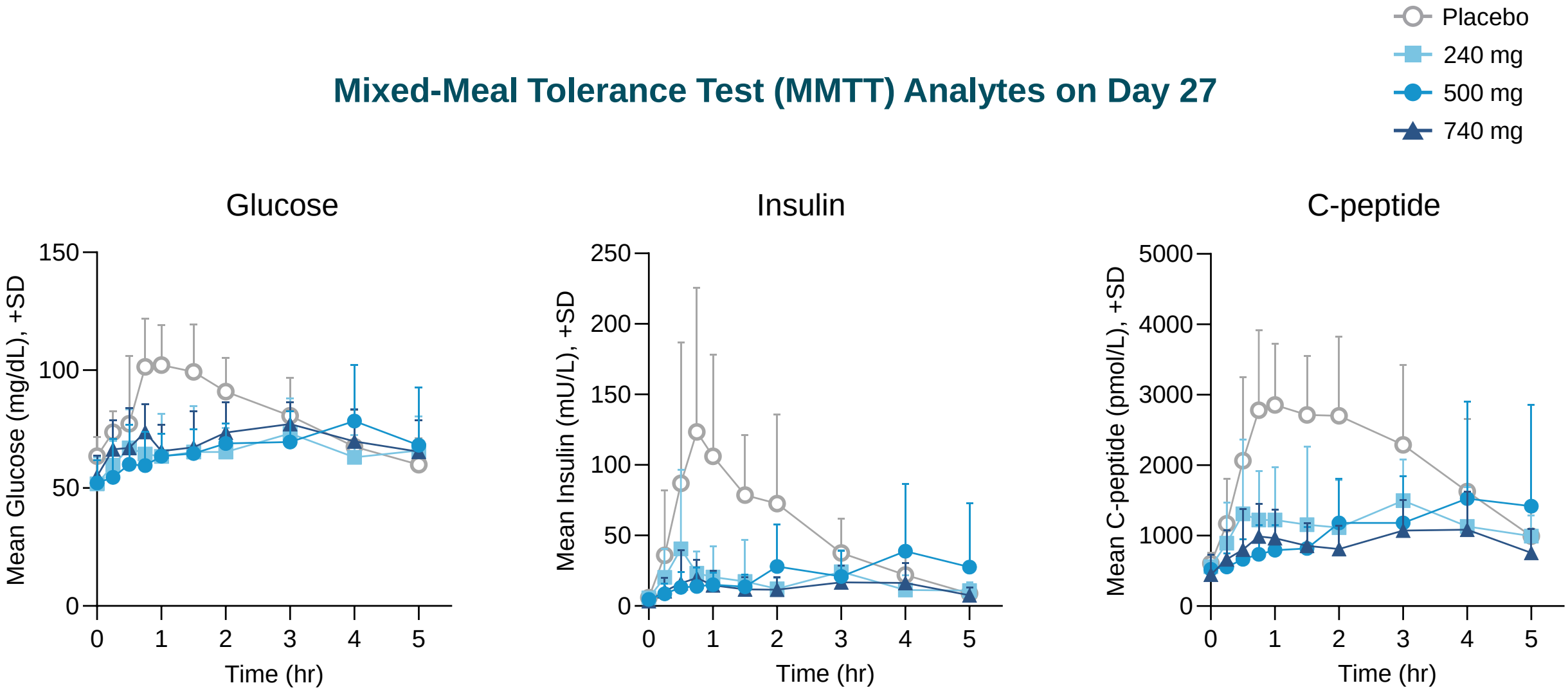
GLP-1R: glucagon-like peptide-1 receptor, PK: pharmacokinetic, QD: once-daily

Appendix

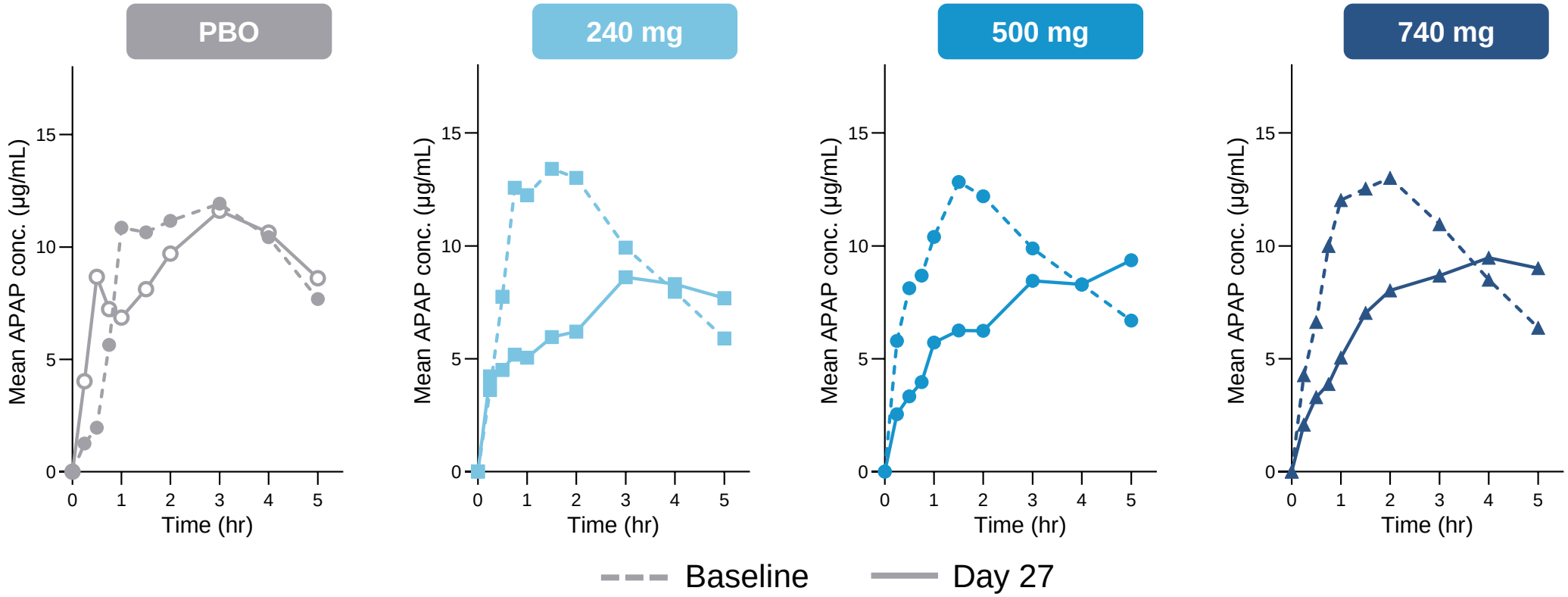
Evidence of On-Target Glycemic Control Effects at All Doses

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



Slowing of Gastric Emptying Seen at All Doses – Likely Contributes to Observed Effects on Appetite and Weight Loss

All doses appear pharmacodynamically active and warrant further evaluation



Slowing of acetaminophen absorption (a marker of delayed gastric emptying) was seen across dose levels

hr: hour, PBO: placebo