Safety, Pharmacokinetics, and Pharmacodynamics of CT-996, an Oral Small-Molecule, Signal-Biased GLP-1 Receptor Agonist Over 4 Weeks in Adults With Obesity

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Disclosures

- **MV Chakravarthy**, **J Wu**, and **S Toussaint Touson** are full-time employees of Roche and may hold Roche stock and/or stock options
- **P Wabnitz** is an employee of Avance Clinical, which has a consulting agreement with Carmot/Roche
- **MA Elliott** is a former employee of Carmot Therapeutics (now Roche), currently employed by ME Clinical Research Consulting, LLC
- **CC Chang** is an employee of Nucleus Network, which has a consulting agreement with Carmot/Roche. She is also an employee of Alfred Hospital (Melbourne, Victoria, Australia) and Monash University (Melbourne, Victoria, Australia)
- **J Lickliter** is an employee of Nucleus Network, which has a consulting agreement with Carmot/Roche

Challenges and Opportunities in the Treatment of Obesity

Worldwide adult prevalence (2020)[1]

With obesity or overweight	**2.2B** (growing to **3.3B by 2035**)
With obesity	**810M** (growing to **1.3B by 2030**)

Disease burden[2]

Approximate lifetime risk of CVD in people with obesity without diabetes	**1 in 2 women** **2 in 3 men**

The cost of obesity is expected to surpass

$4.3T by 2035[1]

Addressing obesity should have a broad impact on population health and healthcare cost

Approved medications are effective for weight loss[3–5]
However, challenges remain:

Access[6,7] | Adherence[7] | Tolerability[6,7]

Need for simpler, cost-effective solutions that can be applied at scale with adequate global reach

Oral treatment options with convenient dosing

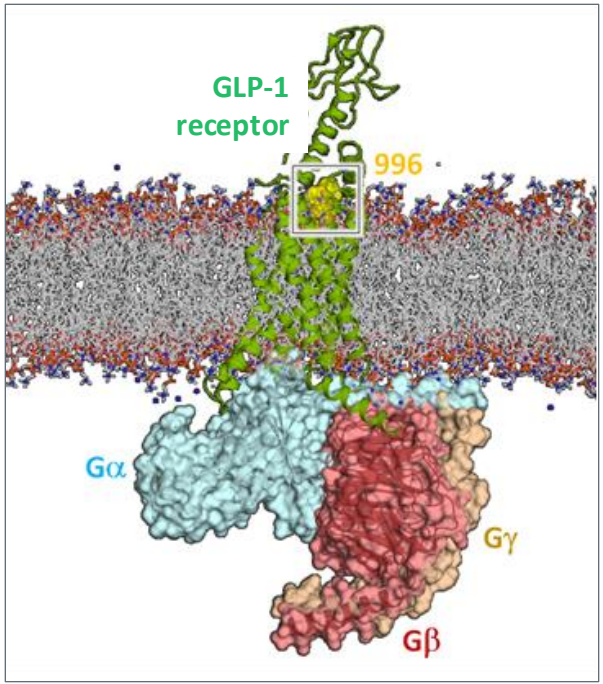
Efficacy = injectable GLP-1 receptor agonists

B, billion; CVD, cardiovascular disease; M, million; T, trillion.

1. World Obesity Federation. World Obesity Atlas 2024. Accessed August 14, 2024. https://data.worldobesity.org/publications/WOF-Obesity-Atlas-v7.pdf. 2. Fox CS, et al. *Diabetes Care*. 2008;31(8):1582–1584. 3. Rosenstock J, et al. *Lancet*. 2021;398:143–155. 4. Davies M, et al. *Lancet*. 2021;397:971–984. 5. Jastreboff AM, et al. *N Engl J Med*. 2022;387(3):205–216. 6. Brandfon S, et al. *Cureus*. 2023;15(10): e46623. 7. Gleason PP, et al. *J Manag Care Spec Pharm*. 2024;30(8):860–867. 8. Rybelsus (semaglutide). Prescribing information. Novo Nordisk; 2021. Accessed August 2, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/213051s006lbl.pdf.

CT-996 Is a Small-Molecule Oral GLP-1 Receptor Agonist

Intended for once-daily oral administration for T2D, obesity, and obesity-related comorbidities



Courtesy of: R Chowdhury, Roche-Genentech

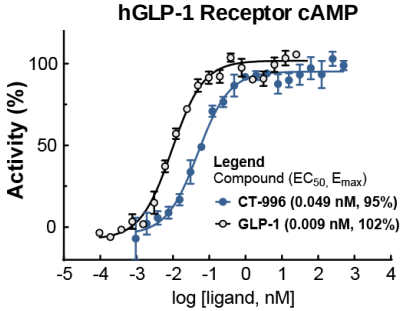
Required design elements to achieve meaningfully differentiated attributes	CT-996[1,2]
Highly potent, cAMP biased, selective GLP-1 receptor agonist	✓
Robust in vivo efficacy in preclinical models	✓
High oral bioavailability and PK to support QD dosing with no significant food effect	✓
Low DDI potential	✓
No GSH adduct formation	✓
No significant toxicology findings and with large exposure margins	✓

cAMP, cyclic adenosine monophosphate; DDI, drug-drug interactions; GLP-1, glucagon-like peptide-1; GSH, glutathione; PK, pharmacokinetic; QD, once daily; T2D, type 2 diabetes.

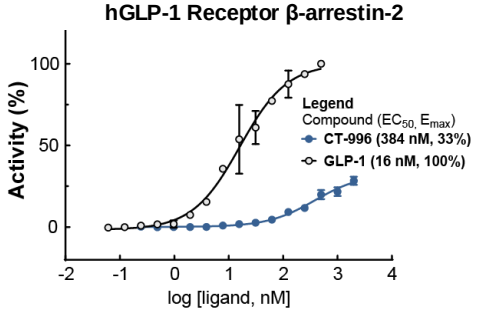
1. Luo J, et al. Efficacy of CT-996, an Oral Small Molecule GLP-1 Receptor Agonist, in Human GLP-1 Receptor Knock-in Mice and Obese Cynomolgus Monkeys. Poster presented at: the American Diabetes Association 84th Scientific Sessions; June 21–24, 2024; Orlando, FL. Poster 771-P. 2. Roche Therapeutics, Data on File.

CT-996: In Vitro and In Vivo Properties

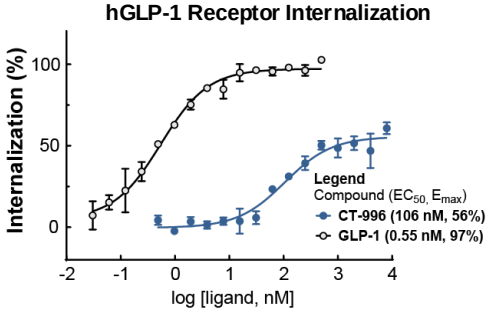
CT-996 is a potent and cAMP-biased GLP-1 receptor agonist[1]



Sub-nM potency on hGLP-1 receptor

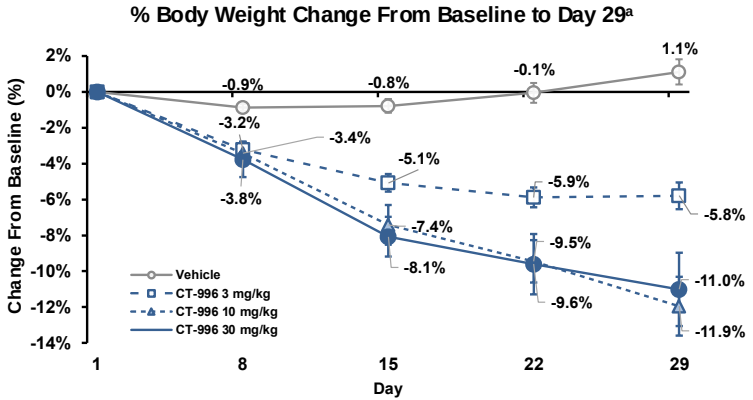


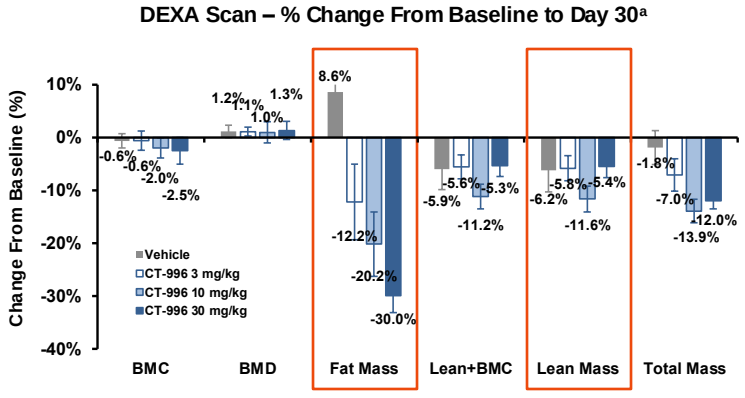
~20-fold weaker β-arrestin-2 recruitment to hGLP-1 receptor



~200-fold weaker internalization of hGLP-1 receptor

CT-996 induced weight loss in obese monkeys with once-daily oral administration *(preferential reduction in fat mass by DEXA)*[1]





BMC, bone mineral content; BMD, bone mineral density; cAMP, cyclic adenosine monophosphate; DEXA, dual-energy X-ray absorptiometry; EC_{50}, half maximal effective concentration; E_{max}, maximum effect change; GLP-1, glucagon-like peptide-1; hGLP-1, human GLP-1; nM, nanomolar.

Data are presented as mean (SE).

1. Luo J, et al. Efficacy of CT-996, an Oral Small Molecule GLP-1 Receptor Agonist, in Human GLP-1 Receptor Knock-in Mice and Obese Cynomolgus Monkeys. Poster presented at: the American Diabetes Association 84th Scientific Sessions; June 21–24, 2024; Orlando, FL. Poster 771-P.

[a]n = 6 per group.

Study CT-996-201

First-in-Human, 3-Part, Multi-Cohort, Phase I, Randomized, Double-Blind, Placebo-Controlled Study

Part 1: SAD (Overweight/Obesity, n = 40) | Part 2: MAD (Obesity, n = 25) | Part 3: MAD (Obesity + T2D, n = ~30)

Overall Study Objective

To investigate the safety, tolerability, pharmacokinetics, and pharmacodynamics of single and multiple ascending doses (up to 4 weeks) of CT-996 in adults with overweight or obesity, with or without T2D

This presentation focuses on results from the 4-week MAD portion of the study in adults with obesity without T2D

MAD, multiple ascending dose; SAD, single ascending dose; T2D, type 2 diabetes.
NCT05814107.

CT-996-201 MAD: 3 Sequential Dose Escalation Cohorts Over 4 Weeks

Eligibility criteria:
- Adults aged 18–65 years
- BMI ≥ 30 kg/m^2 and otherwise healthy

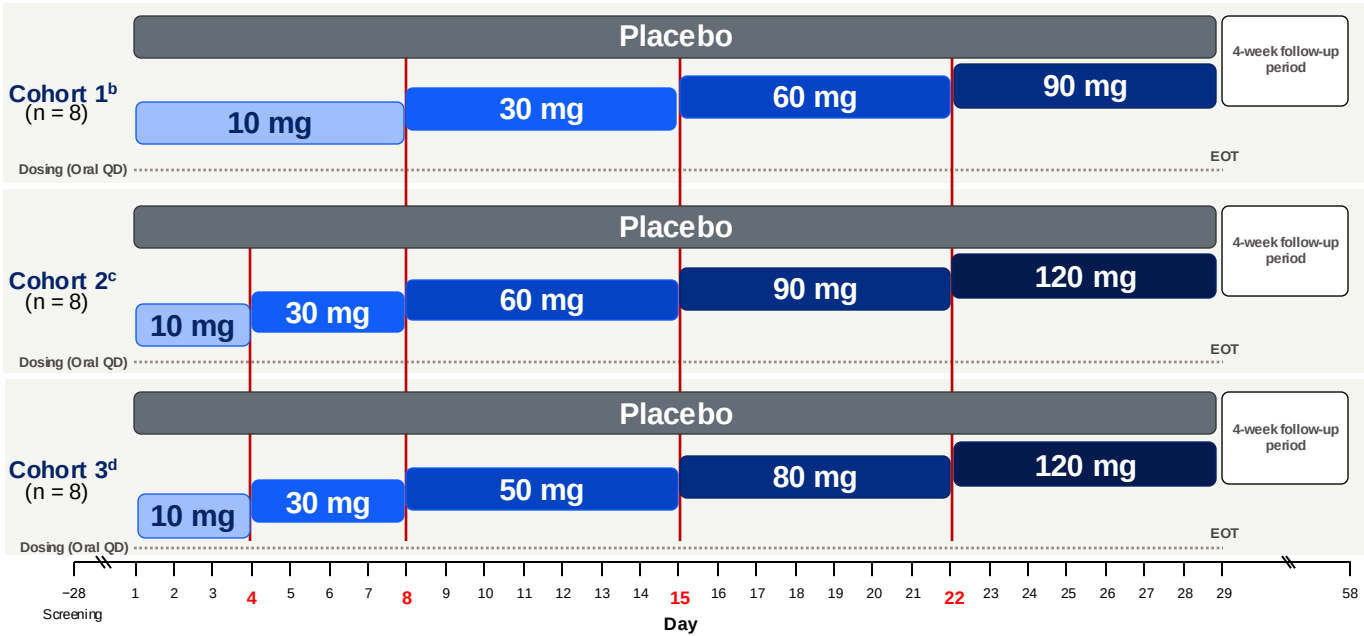
n = 8 per cohort planned
3:1 randomization [CT-996 (6):Placebo (2)]

Single-center MAD study conducted in Australia[a]

Primary endpoint
- Safety and tolerability

Secondary endpoints
- PK
- Weight loss
- Glucose homeostasis

Flexibility was provided to attain target doses



BMI, body mass index; d, day; EOT, end of trial; MAD, multiple ascending dose; PK, pharmacokinetic; QD, once daily.
[a]NCT05814107; 3 MAD study cohorts were run sequentially.
[b]Cohort 1 (CT-996 10/30/60/90): planned 10/30/60/90 mg: each dose for 7 days.
[c]Cohort 2 (CT-996 10/30/60/90/120): planned 10 mg × 3d, 30 mg × 4d, 60 mg × 7d, 90 mg × 7d, 120 mg × 7d.
[d]Cohort 3 (CT-996 10/30/50/80/120): planned 10 mg × 3d, 30 mg × 4d, 50 mg × 7d, 80 mg × 7d, 120 mg × 7d.

Rationale for Rapid Up-Titration Design in the Phase 1 Study

"Fail fast" approach early in development

Titration approaches that "start low and go slow" have been known to improve the tolerability profile of incretin therapies

Objective

Rapid determination if unexpected safety signals or efficacy patterns might exist
- Early de-risking (primarily for safety/tolerability; not for maximizing efficacy)

Approach

Brisk up-titration
- Higher starting dose (10 mg), frequent (3 days to weekly), and 2-3x dose step-ups

Hypothesis

Reasonable safety and tolerability in this setting, together with robust efficacy, provide support for continued investigation of CT-996 in studies of longer duration and larger sample sizes using slower titration approaches

The MAD Portion of the Study Included Participants With Obesity and Without T2D

Study enrolled 25 participants in 3 sequential cohorts
3:1 randomization [CT-996 (6):Placebo (2)] in each cohort

Category	Placebo (n = 6)	Cohort 1[a] (n = 6)	Cohort 2[b] (n = 7)	Cohort 3[c] (n = 6)
Age, years	42.8 (9.3)	40.0 (8.6)	34.6 (8.6)	29.8 (8.8)
Sex, female, n (%)	4 (66.7)	4 (66.7)	3 (42.9)	4 (66.7)
Race, White, n (%)	5 (83.3)	4 (66.7)	5 (71.4)	4 (66.7)
Weight, kg	101.3 (21.2)	94.1 (8.0)	107.3 (19.4)	101.2 (18.7)
BMI, kg/m^2	36.2 (3.5)	32.9 (2.5)	36.3 (3.9)	33.9 (3.3)
HbA1c, %	5.1 (0.4)	5.1 (0.2)	5.2 (0.5)	4.8 (0.3)
Fasting Glucose, mmol/L	5.3 (0.2)	5.2 (0.3)	5.0 (0.2)	4.9 (0.3)
HOMA-IR	2.5 (0.9)	2.0 (0.9)	3.1 (1.9)	2.6 (0.5)

BMI, body mass index; d, day; HbA1c, glycated hemoglobin A1c; HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; MAD, multiple ascending dose; T2D, type 2 diabetes.
Values represent means (SD). HOMA-IR ≥ 2.0 signifies insulin resistance.[1,2]

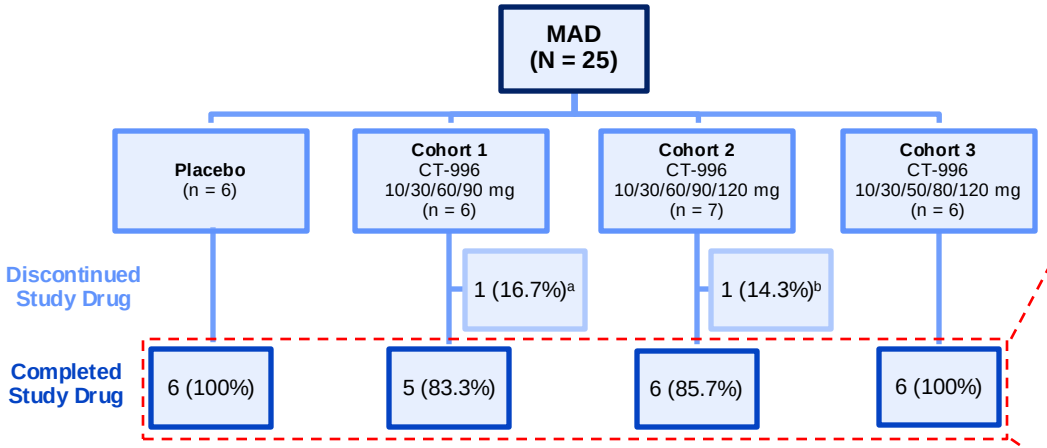
1. Lee S, et al. *J Clin Transl Endocrinol*. 2019;19:100210. 2. Gayoso-Diz P, et al. *BMC Endocr Disord*. 2013;13:47.

[a]Cohort 1 (CT-996 10/30/60/90): planned 10/30/60/90 mg: each dose for 7 days (actual: all participants followed planned titration path).
[b]Cohort 2 (CT-996 10/30/60/90/120): planned 10 mg × 3d, 30 mg × 4d, 60 mg × 7d, 90 mg × 7d, 120 mg × 7d (actual: 2 participants needed 3 additional days at 90 mg before escalating to 120 mg; 1 participant remained at 60 mg).
[c]Cohort 3 (CT-996 10/30/50/80/120): planned 10 mg × 3d, 30 mg × 4d, 50 mg × 7d, 80 mg × 7d, 120 mg × 7d (actual: all except 1 participant followed the planned path; 1 participant decreased their dose from 50 mg to 30 mg to 10 mg and completed the study at 10 mg).

92% of Participants Completed Study Drug Treatment

No study drug-related discontinuations

Participant Disposition



Titrations in study completers who received CT-996

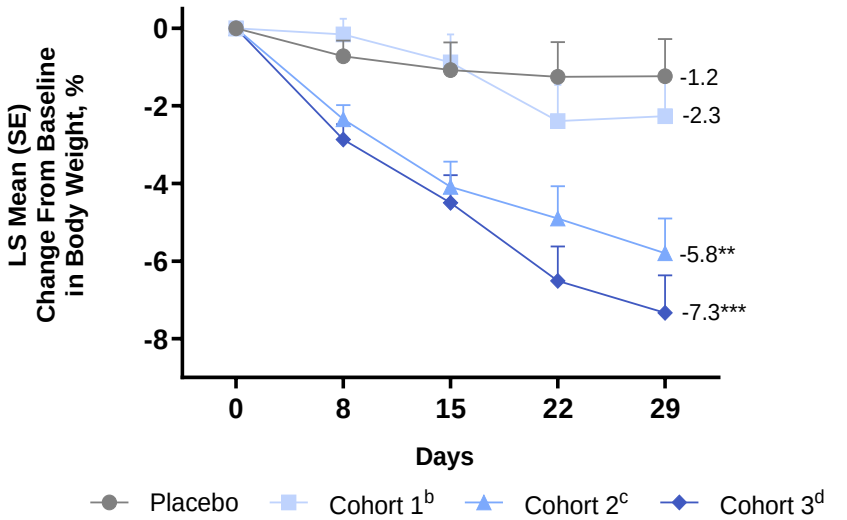
Cohort	Actual vs planned dosing
Cohort 1	All participants followed the planned titration path
Cohort 2	2 participants needed 3 additional days at 90 mg before escalating to 120 mg; 1 remained at 60 mg
Cohort 3	All followed the planned titration path, except for 1 participant – decreased dose from 50 mg to 30 mg to 10 mg and completed the study at 10 mg

Most if not all participants in cohorts 1 and 3 achieved and maintained their respective target dose(s) for the intended 1-week duration compared to those in cohort 2

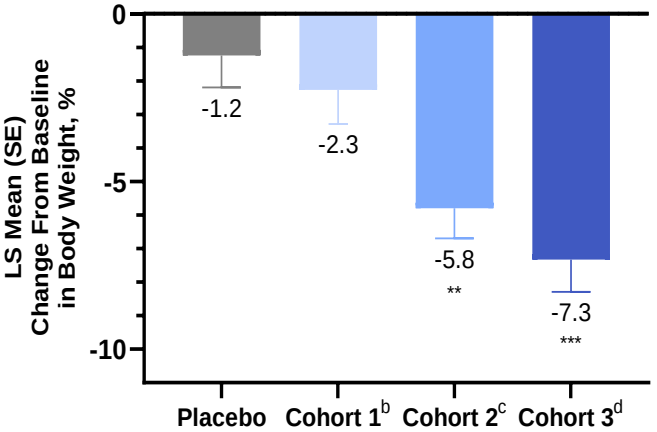
MAD, multiple ascending dose.
[a]Participant discontinued due to a Grade 2 psychotic disorder (underlying history of schizophrenia), not related to study drug.
[b]Participant discontinued due to a Grade 1 right bundle branch block (body weight ~140 kg, history of obstructive sleep apnea), not related to the study drug.

Once-Daily Oral Dosing of CT-996 Over 4 Weeks Yielded Weight Loss of up to 7.3%

Percent change in body weight appears to be linear over time (~2.0% [~1.8 kg] per week), with no plateau



Clinically meaningful placebo-adjusted weight loss of -6.1% for cohort 3 (*P* < 0.001)[a]



**$P < 0.01$[a]; ***$P < 0.001$.[a]

d, day; LS, least squares.

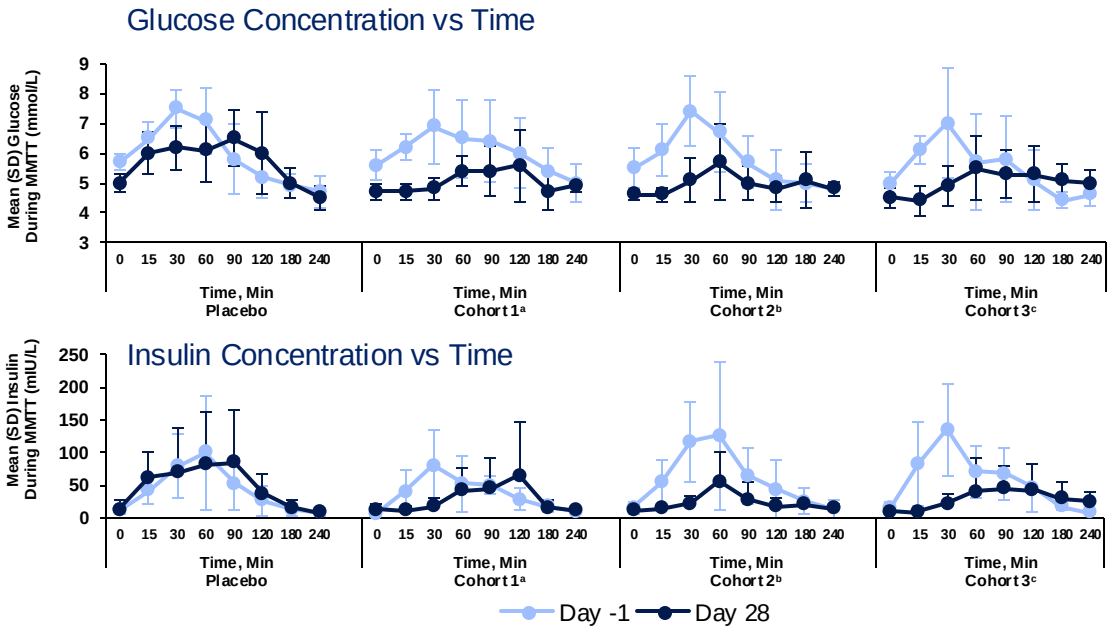
[a]*P* values are nominal and have not been adjusted for multiplicity.

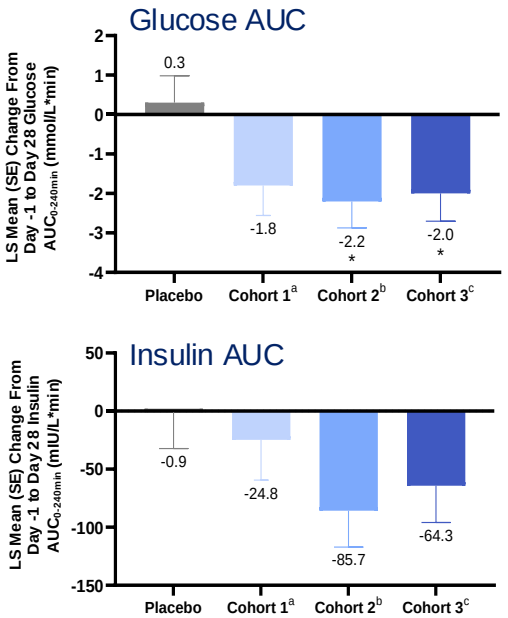
[b]Cohort 1 (CT-996 10/30/60/90): planned 10/30/60/90 mg: each dose for 7 days (actual: all participants followed planned titration path).

[c]Cohort 2 (CT-996 10/30/60/90/120): planned 10 mg × 3d, 30 mg × 4d, 60 mg × 7d, 90 mg × 7d, 120 mg × 7d (actual: 2 participants needed 3 additional days at 90 mg before escalating to 120 mg; 1 participant remained at 60 mg).

[d]Cohort 3 (CT-996 10/30/50/80/120): planned 10 mg × 3d, 30 mg × 4d, 50 mg × 7d, 80 mg × 7d, 120 mg × 7d (actual: all except 1 participant followed the planned path; 1 participant decreased their dose from 50 mg to 30 mg to 10 mg and completed the study at 10 mg).

CT-996 Treatment Over 28 Days Resulted in Reductions in Blood Glucose and Insulin During a Mixed Meal Tolerance Test





*$P < 0.05$.[d]

AUC, area under the concentration-time curve; d, day; LS, least squares; Min, minutes; MMTT, mixed meal tolerance test.

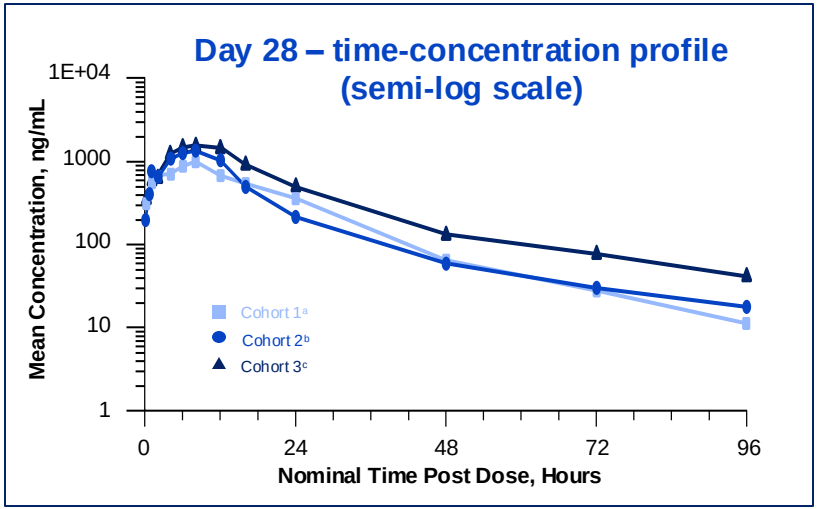
[a]Cohort 1 (CT-996 10/30/60/90): planned 10/30/60/90 mg: each dose for 7 days (actual: all participants followed planned titration path).

[b]Cohort 2 (CT-996 10/30/60/90/120): planned 10 mg × 3d, 30 mg × 4d, 60 mg × 7d, 90 mg × 7d, 120 mg × 7d (actual: 2 participants needed 3 additional days at 90 mg before escalating to 120 mg; 1 participant remained at 60 mg).

[c]Cohort 3 (CT-996 10/30/50/80/120): planned 10 mg × 3d, 30 mg × 4d, 50 mg × 7d, 80 mg × 7d, 120 mg × 7d (actual: all except 1 participant followed the planned path; 1participant decreased their dose from 50 mg to 30 mg to 10 mg and completed the study at 10 mg).

[d]*P* values are nominal and have not been adjusted for multiplicity.

PK Parameters Support Once-Daily Dosing



Day 28 – PK parameters

Parameters, mean (SD)	Cohort 1[a]	Cohort 2[b]	Cohort 3[c]
C_{max}, ng/mL	1070 (275)	1550 (752)	1620 (1130)
AUC_{last}, h*ng/mL	22,900 (3560)	23,900 (13,400)	37,900 (27,900)
T_{max}, h	9.6 (3.6)	8.0 (2.8)	9.2 (2.7)
$t_{1/2}$, h	17.1 (5.3)	18.7 (6.2)	21.8 (7.3)
Fe_{0-24}, %	1.1 (0.6)	1.0 (0.6)	0.4 (0.3)

C_{max} and AUC were generally dose proportional within each MAD cohort

No significant accumulation of CT-996 in plasma

Low urinary fractional excretion (< 1.1% over 24 hours)

No meaningful food effect on PK profile (from SAD portion of the study)

AUC, area under the concentration-time curve; AUC_{last}, area under the concentration-time curve from time 0 to the last measurable concentration; C_{max}, maximum observed concentration; d, day; Fe_{0-24}, fraction of dose excreted in urine; h, hour; MAD, multiple ascending dose; PK, pharmacokinetic; SAD, single ascending dose; $t_{1/2}$, elimination half-life; T_{max}, time to maximum concentration.

Data for cohorts 2 and 3 are included only for participants who completed the study at the 120-mg dose.

[a]Cohort 1 (CT-996 10/30/60/90): planned 10/30/60/90 mg: each dose for 7 days (actual: all participants followed planned titration path).

[b]Cohort 2 (CT-996 10/30/60/90/120): planned 10 mg × 3d, 30 mg × 4d, 60 mg × 7d, 90 mg × 7d, 120 mg × 7d (actual: 2 participants needed 3 additional days at 90 mg before escalating to 120 mg; 1 participant remained at 60 mg).

[c]Cohort 3 (CT-996 10/30/50/80/120): planned 10 mg × 3d, 30 mg × 4d, 50 mg × 7d, 80 mg × 7d, 120 mg × 7d (actual: all except 1 participant followed the planned path; 1participant decreased their dose from 50 mg to 30 mg to 10 mg and completed the study at 10 mg).

All TEAEs Were Mild or Moderate Across MAD Cohorts

- All TEAEs were mild or moderate in severity; no severe (Grade 3) TEAEs
- 1 serious AE (unrelated to study drug)
- No discontinuations related to study drug

Category, n (%)	Placebo (n = 6)	Cohort 1[a] (n = 6)	Cohort 2[b] (n = 7)	Cohort 3[c] (n = 6)
Participants with at least 1 TEAE	6 (100)	6 (100)	7 (100)	6 (100)
Serious TEAEs	0	1 (16.7)[d]	0	0
Discontinuations due to TEAE	0	1 (16.7)[d]	1 (14.3)[e]	0
Severity				
Grade 1	4 (66.7)	4 (66.7)	4 (57.1)	3 (50.0)
Grade 2	2 (33.3)	2 (33.3)	3 (42.9)	3 (50.0)
Grade 3	0	0	0	0

AE, adverse event; d, day; MAD, multiple ascending dose; TEAE, treatment-emergent adverse event.
[a]Cohort 1 (CT-996 10/30/60/90): planned 10/30/60/90 mg: each dose for 7 days (actual: all participants followed planned titration path).
[b]Cohort 2 (CT-996 10/30/60/90/120): planned 10 mg × 3d, 30 mg × 4d, 60 mg × 7d, 90 mg × 7d, 120 mg × 7d (actual: 2 participants needed 3 additional days at 90 mg before escalating to 120 mg; 1 participant remained at 60 mg).
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[d]One participant reported a Grade 2 psychotic disorder, not related to study drug.
[e]One participant reported a Grade 1 right bundle branch block, not related to study drug.

The Most Common TEAEs Were GI-Related, Consistent With Other Incretin Therapies

- Frequency of GI-related TEAEs consistent with brisk up-titration and early stage of development*
- Higher-dose cohorts exhibited more TEAEs, and a more gradual titration tended to improve tolerability

Most Frequently Reported[a] GI TEAEs[b] by PT, n (%)	Placebo (n = 6)	Cohort 1[c] (n = 6)	Cohort 2[d] (n = 7)	Cohort 3[e] (n = 6)
Nausea	1 (16.7)	5 (83.3)	6 (85.7)	5 (83.3)
Gastroesophageal reflux disease	0	2 (33.3)	6 (85.7) →	1 (16.7)
Vomiting	1 (16.7)	1 (16.7)	5 (71.4) →	2 (33.3)
Constipation	1 (16.7)	2 (33.3)	4 (57.1) →	3 (50.0)
Abdominal pain	1 (16.7)	0	4 (57.1) →	1 (16.7)
Abdominal distention	1 (16.7)	1 (16.7)	3 (42.9) →	0
Diarrhea	1 (16.7)	0	3 (42.9)	3 (50.0)
Decreased appetite	1 (16.7)	1 (16.7)	1 (14.3)	5 (83.3)

**High rates of GI-related AEs have typically been seen with oral incretin therapies early in development,[1,2] which generally improve with slower titrations over time[3]*

AE, adverse events; d, day; GI, gastrointestinal; PT, preferred term; TEAE, treatment-emergent adverse event.

1. Pratt E, et al. *Diabetes Obes Metab*. 2023;25(9):2642–2649. 2. Saxena AR, et al. *Nat Med*. 2021;27:1079–1087. 3. Wharton S, et al. *N Engl J Med*. 2023;389:877–888.

[a] ≥ 2 participants in any treatment group.

[b] Other common (≥ 2 participants in any treatment group) AEs included dysmenorrhea, chills, photosensitivity reaction, and presyncope.

[c] Cohort 1 (CT-996 10/30/60/90): planned 10/30/60/90 mg: each dose for 7 days (actual: all participants followed planned titration path).

[d] Cohort 2 (CT-996 10/30/60/90/120): planned 10 mg × 3d, 30 mg × 4d, 60 mg × 7d, 90 mg × 7d, 120 mg × 7d (actual: 2 participants needed 3 additional days at 90 mg before escalating to 120 mg; 1 participant remained at 60 mg).

[e] Cohort 3 (CT-996 10/30/50/80/120): planned 10 mg × 3d, 30 mg × 4d, 50 mg × 7d, 80 mg × 7d, 120 mg × 7d (actual: all except 1 participant followed the planned path; 1 participant decreased their dose from 50 mg to 30 mg to 10 mg and completed the study at 10 mg).

GI-Related TEAEs Were Mostly Mild

TEAE, n (%)	Placebo (n = 6)	Cohort 1[a] (n = 6)	Cohort 2[b] (n = 7)	Cohort 3[c] (n = 6)
Nausea	1 (16.7)	5 (83.3)	6 (85.7)	5 (83.3)
Grade 1	1 (16.7)	5 (83.3)	6 (85.7)	5 (83.3)
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Constipation	1 (16.7)	2 (33.3)	4 (57.1)	3 (50.0)
Grade 1	1 (16.7)	2 (33.3)	3 (42.9)	2 (33.3)
Grade 2	0	0	1 (14.3)	1 (16.7)
Grade 3	0	0	0	0
Vomiting	1 (16.7)	1 (16.7)	5 (71.4)	2 (33.3)
Grade 1	1 (16.7)	0	4 (57.1)	1 (16.7)
Grade 2	0	1 (16.7)	1 (14.3)	1 (16.7)
Grade 3	0	0	0	0
Diarrhea	1 (16.7)	0	3 (42.9)	3 (50.0)
Grade 1	1 (16.7)	0	2 (28.6)	3 (50.0)
Grade 2	0	0	1 (14.3)	0
Grade 3	0	0	0	0

- There were no Grade 3 (severe) GI-related AEs
- No more than 1 participant in each cohort experienced Grade 2 AEs
- GI events tended to improve over time (lower frequency-to-no events during days 23–29)

AE, adverse event; d, day; GI, gastrointestinal; TEAE, treatment-emergent adverse event.
[a]Cohort 1 (CT-996 10/30/60/90): planned 10/30/60/90 mg: each dose for 7 days (actual: all participants followed planned titration path).
[b]Cohort 2 (CT-996 10/30/60/90/120): planned 10 mg × 3d, 30 mg × 4d, 60 mg × 7d, 90 mg × 7d, 120 mg × 7d (actual: 2 participants needed 3 additional days at 90 mg before escalating to 120 mg; 1 participant remained at 60 mg).
[c]Cohort 3 (CT-996 10/30/50/80/120): planned 10 mg × 3d, 30 mg × 4d, 50 mg × 7d, 80 mg × 7d, 120 mg × 7d (actual: all except 1 participant followed the planned path; 1 participant decreased their dose from 50 mg to 30 mg to 10mg and completed the study at 10 mg).

Despite Rapid Up-Titration Approach, No Unexpected Safety Signals Were Observed

Changes in laboratory parameters and vital signs

- Laboratory investigations were generally NCS
- No signals of liver injury
- 1 participant in cohort 3 experienced mild-to-moderate lipase elevation (dosing was not changed or interrupted), reported as probably related to study drug[a]

- ECG findings (including QTc) were NCS, except for 1 participant who experienced an RBBB, reported as not related to study drug[b]
- Systolic blood pressure tended to decrease (up to 13 mmHg), and heart rate tended to increase (up to 15 bpm), consistent with the incretin class

bpm, beats per minute; ECG, electrocardiogram; NCS, nonclinically significant; QTc, corrected QT interval; RBBB, right bundle branch block.
[a]Participant was monitored with repeat amylase and lipase testing, and the issue was determined to be resolved.
[b]ECG parameters were generally within normal range over the 4-week period, and changes were not clinically significant, except for 1 participant in cohort 2 who experienced 1 event of isolated RBBB (participant had morbid obesity with body weight ~140 kg with obstructive sleep apnea). A complete cardiac evaluation was performed, including cardiac enzymes and echocardiography, all of which were normal. The participant was discontinued for abundance of caution. Not related to study drug.

Summary

- **CT-996 treatment produced robust weight loss** of up to 7.3% (7 kg) over 4 weeks
  - Slowing the pace of titration in cohort 3 tended to yield more weight loss than cohort 2 → suggests slower titration approaches may not compromise the weight loss efficacy of CT-996
  - Magnitude of weight loss appears to be more dependent on an exposure threshold and the duration it can be maintained
- **PK results support once-daily dosing of CT-996** ($t_{1/2}$ ~17–22 hours), with a generally dose-dependent increase in plasma exposure and with no meaningful food effect on PK
- **CT-996 exhibited a favorable safety profile and was generally well-tolerated** up to 120 mg despite brisk up-titration over 4 weeks
  - AE profile is consistent with the incretin drug class at a similar (early) stage of development
  - Starting at doses ≤ 10 mg with a shallower (smaller dose increments) and longer (eg, 2–4 weeks at each dose level) titration regimen is expected to further improve the tolerability profile, as demonstrated with other incretins
  - Individualized dosing regimens can benefit and empower people living with obesity

Together, these data support the continued investigation of CT-996 in studies of longer duration with larger sample sizes and slower titrations

AE, adverse event; PK, pharmacokinetic; $t_{1/2}$, elimination half-life.

Next Steps

1. Complete part 3 of the ongoing phase 1b study (4-week cohorts in participants with obesity and T2D)

2. Initiate phase 2 studies in 2025

T2D, type 2 diabetes.

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