Endoscopic Duodenal Mucosal Resurfacing for Post-GLP-1 Weight Maintenance: 6-Month Randomized, Sham-Controlled Results from the REMAIN-1 Midpoint Cohort Study

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Disclosures

- Research Support / Grants Last 24 Months
  - Allurion Technologies (ended), Fractyl Health, Viking Therapeutics
- Consulting / Employment Last 24 Months
  - Allurion Technologies (ended), Fractyl Health (ended), Biolinq, Olympus, Steris, Harbor Labs

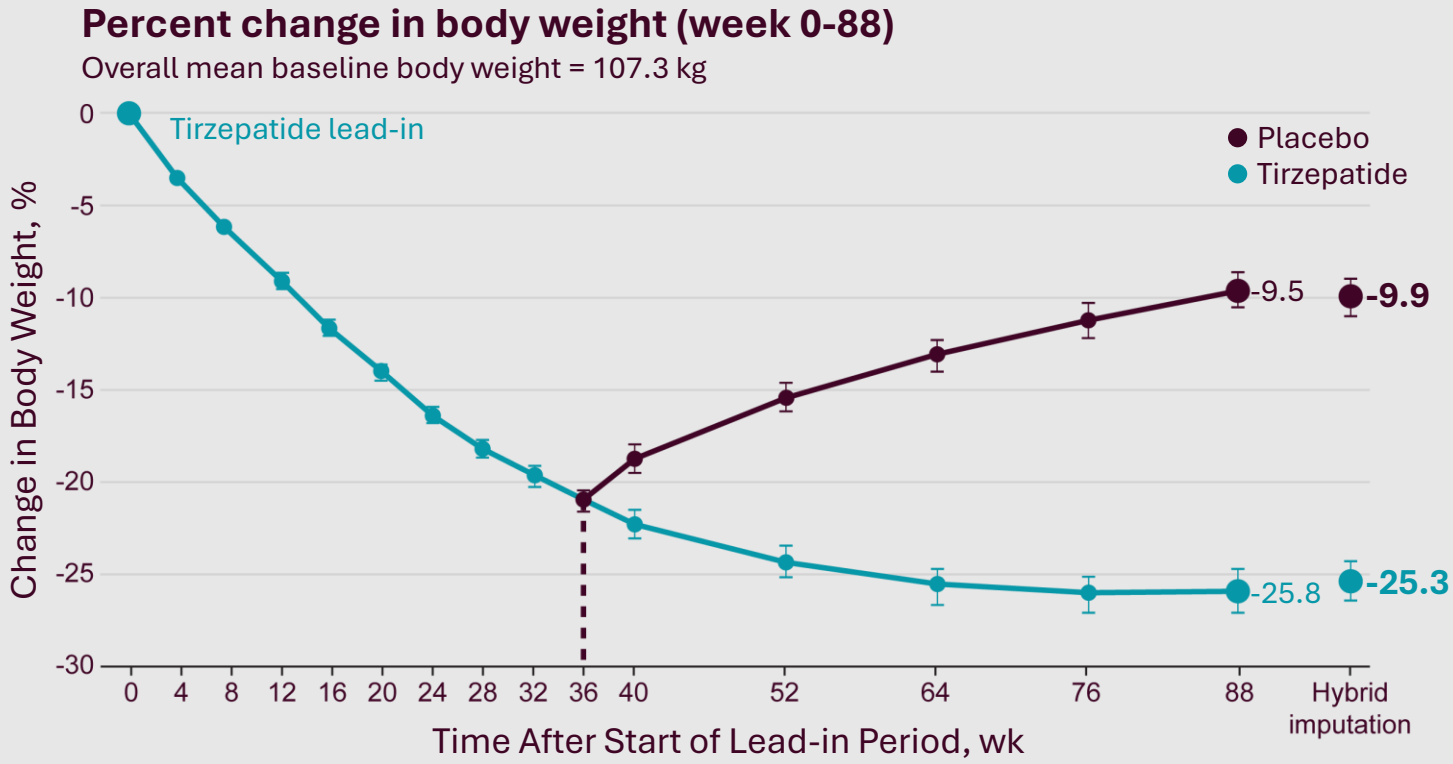
Post-GLP-1 Weight Rebound: The New Unmet Need in Obesity Care

~40% U.S. adults currently living with obesity[1]

~22% U.S. adults with obesity have tried a GLP-1 medication[2]

~65% Patients with obesity discontinue before one year[3]

85% Patients regain lost weight after GLP-1 discontinuation[4]



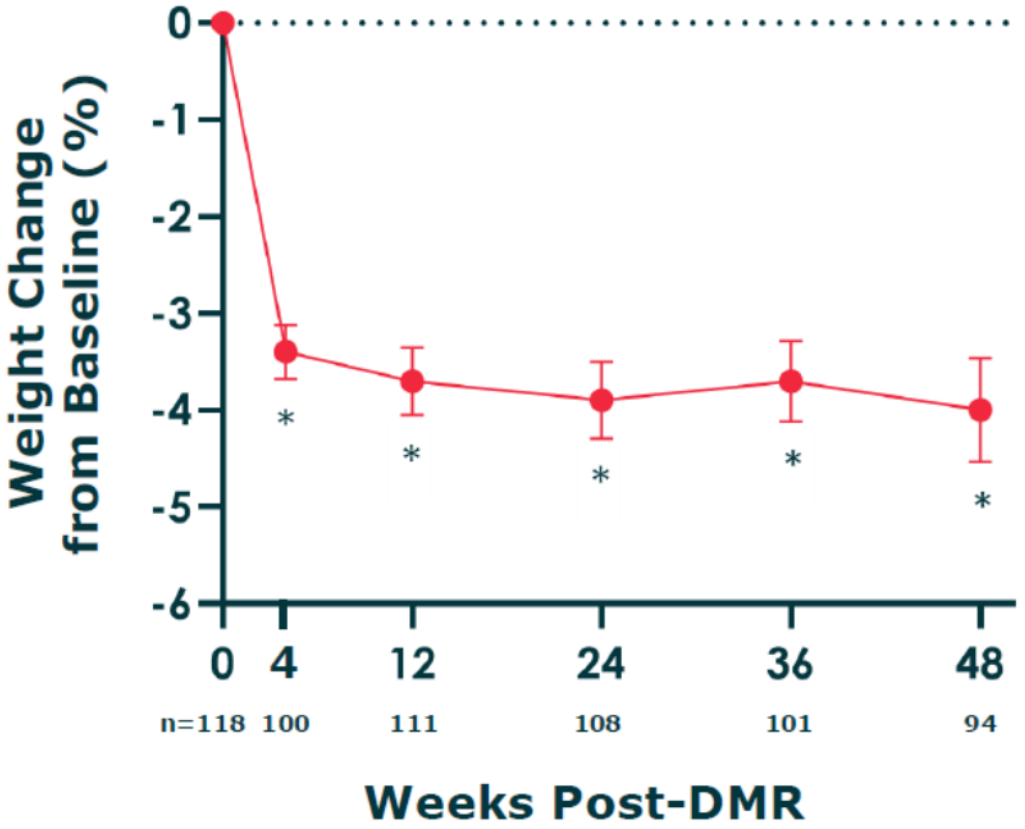
Durable weight maintenance after GLP-1 cessation represents a significant unmet clinical need

[1]ICER. Semaglutide and Tirzepatide for Obesity: Effectiveness and Value. 2025. Montero A. [2]KFF Health Tracking Poll May 2024. https://www.kff.org/health-costs/kff-health-tracking-poll-may-2024-the-publics-use-and-views-of-glp-1-drugs/#:~:text=Among%20the%2012%25%20of%20adults,Get%20the%20dataDownload%20PNG. [3]Rodriguez PJ, et al. *JAMA Netw Open.* 2025;8(1):e2457349. [4]Aronne LJ, et al. *JAMA.* 2024;331(1):38-48. Figure adapted from SURMOUNT-4.

Duodenal Mucosal Resurfacing Leads to Sustained Weight Loss

Pooled Data from 5 Clinical

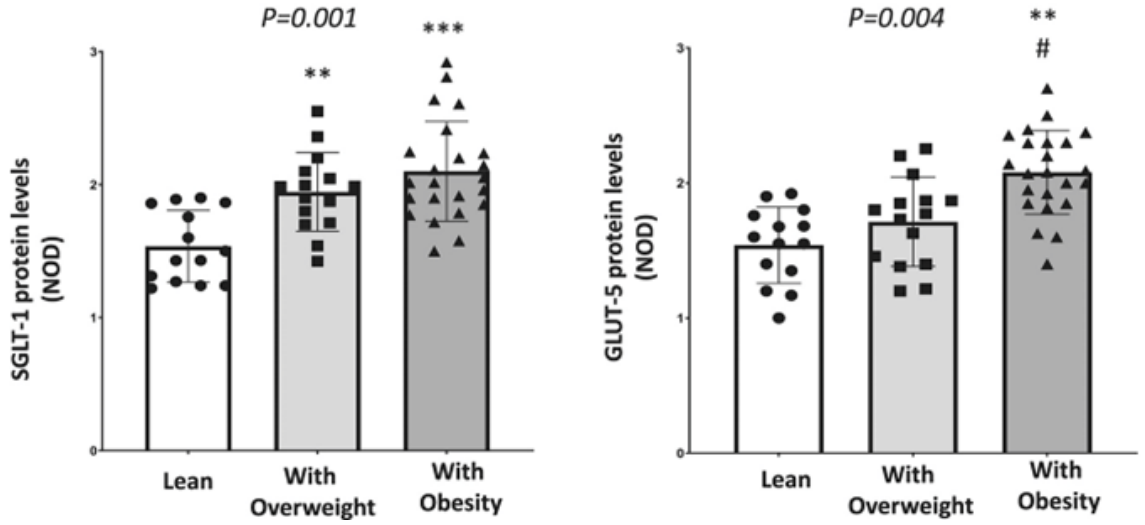
Demographic/Characteristic	N=118
Male, n(%)	88 (75%)
Age, years	58 (8)
Diabetes Duration, years	10 (5)
A1c, %	8.2 (0.7)
Body Weight, kg	93 (14)



White K. Duodenal mucosal resurfacing durably maintains weight loss in metabolic disease. *Obesity*. 2024;32:85

Duodenal Dysfunction Occurs in Patient with Obesity and Metabolic Disease

- Increased enterocyte mass[1]
- Increase in carbohydrate uptake
  - Increased protein levels of glucose and fructose transporters[2]
  - Altered nutrient absorption in human enteroids[3,4]
- Potential alterations in gut permeability[5]
- Altered duodenal mucosal microbiome[6]
- Increase in intestinal pro-inflammatory macrophages[7]



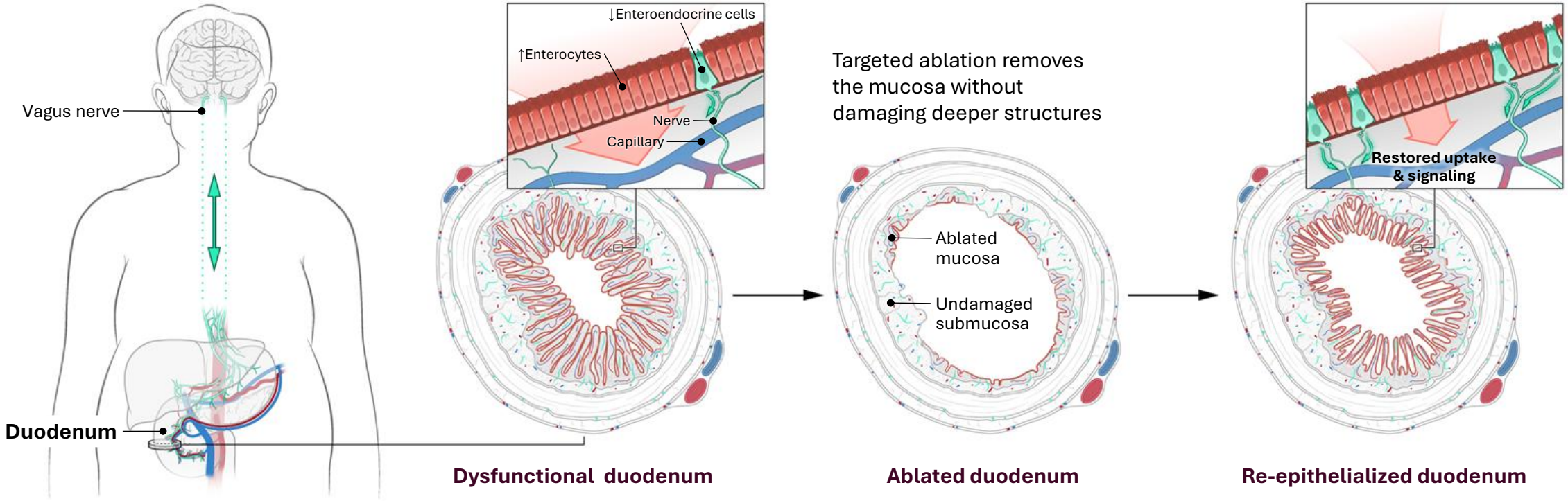
[1]Verdam et al. *J Clin Endocrinol Metab*. 2011 Feb;96(2):E379-83. [2]Fiorentino TV. *Obesity*. 2023:31(3):724-73. [3]Hasan NM. *Mol Metab*. 2021; 44:101129. [4]Badurdeen DS. DDW 2026 Presentation Number 731. [5]Hadefi A.*Gastro Hep Advances*. 2024; [6]Nardelili C. *Microorganisms*. 2020 Mar 29;8(4):485. [7]Rohm TV.*Front Immunol*. 12:668654. doi: 10.3389/fimmu.2021.668654

Duodenal dysfunction as a therapeutic target in obesity and metabolic disease

Nutrient signals from the duodenum travel via the vagus nerve to regulate hunger and metabolism[1]

Diet-induced mucosal changes lead to **increased** nutrient uptake and **impaired** gut-to-brain signaling[2]

Regenerated mucosa has potential to restore signaling and metabolic control

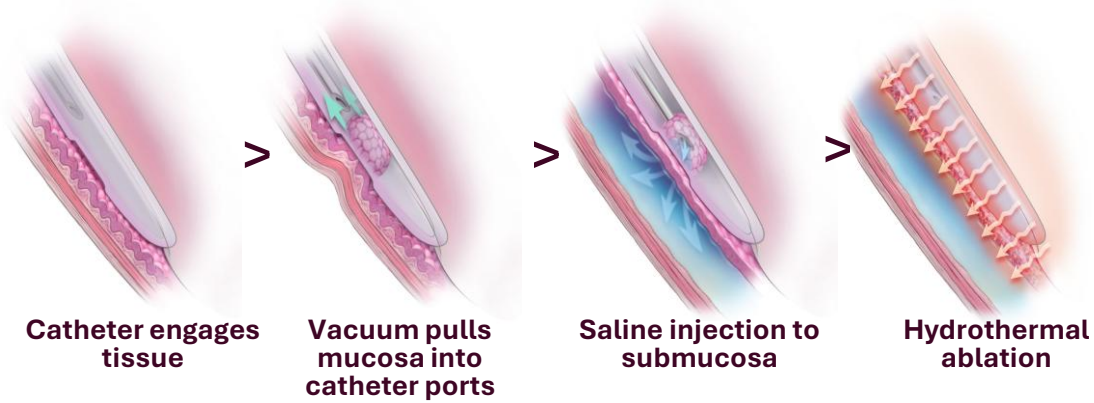


[1]Kentish, Stephen J., and Amanda J. Page. "The role of gastrointestinal vagal afferent fibres in obesity." *The Journal of Physiology* 593.4 (2015): 775-786.
[2]Aliluev, Alexandra, et al. 'Diet-induced alteration of intestinal stem cell function underlies obesity and prediabetes in mice." *Nature Metabolism* 3.9 (2021): 1202-1216.

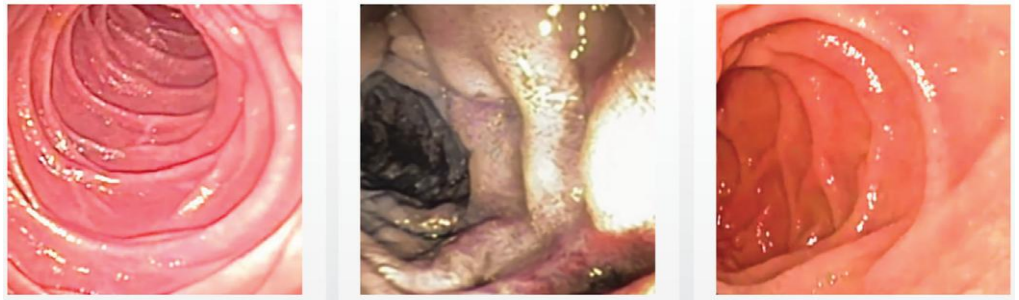
Revita Duodenal Mucosal Resurfacing Procedure

Targeted mucosal ablation designed to durably reset abnormal weight and metabolic setpoint[1-4]

Revita designed to achieve targeted mucosal ablation without damaging deeper structures via circumferential submucosal saline lift followed by hydrothermal ablation



Ablated mucosa is immediately evident via endoscopic visualization. Follow-up endoscopy shows normal appearing mucosa 1 mo later[5]



1. Mah AT et al. Endocrinology. 2014;155:3302-3314. 2. Mao J et al. Diabetes. 2013;62:3736-3746. 3. de Moura EGH et al. Endosc Int Open. 2019;7:E685-E690. 4. Haidry RJ, et al. Gastrointest Endosc. 2019;90:673-681.e2. 5. Rajagopalan H, et al. Diabetes Care. 2016;39:2254-2261. *Revita is investigational in the US. CE marked in the EU/UK.*

REMAIN-1 midpoint cohort study in weight maintenance

Pilot randomized study designed to inform effect size and powering of pivotal study

Patient population

- Adults with obesity (BMI 30-45 kg/m^2)
- GLP-1 naïve; no T2D

Efficacy endpoints

- % TBW change from baseline Revita vs sham at 3, 6 and 12 months

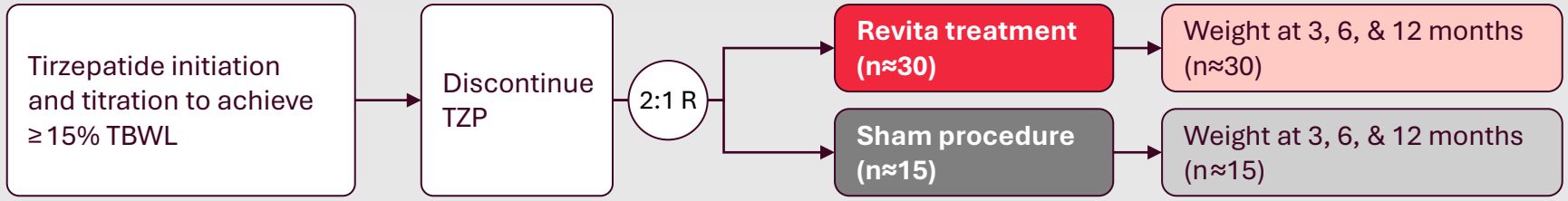
Study design

- TZP administration to achieve ≥15% TBWL, then discontinued
- Randomized (2:1 Revita vs Sham), double-blind, sham-controlled
- Diet and lifestyle counseling throughout

Sample size

- n=45
- Not powered for formal hypothesis testing[1]

Study design



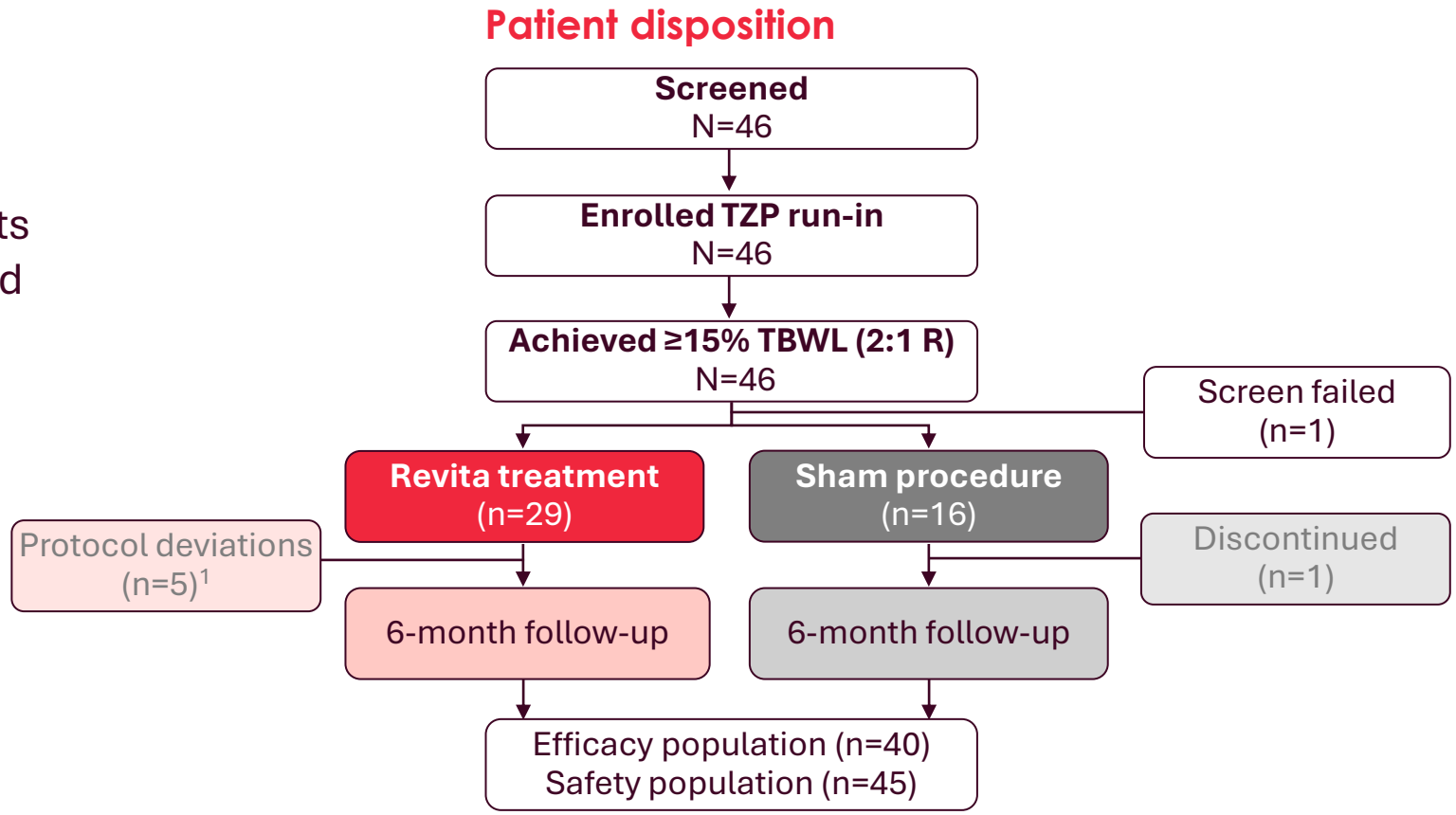
[1] p values are provided to describe the strength and consistency of observed treatment effects

Abbreviations: GLP-1, glucagon-like peptide; R, randomization; T2D, type 2 diabetes; TBW, total body weight; TBWL, total body weight loss; TZP, tirzepatide.

REMAIN-1 midpoint cohort patient disposition

High retention rate through 6 months of follow-up

- 44/45 participants (98%) completed 6-month follow-up
- Efficacy analysis includes all participants who followed protocol-specified diet and exercise requirements



Abbreviations: R, randomization; TBWL, total body weight loss; TZP, tirzepatide. 1. Prospectively defined pre-specified protocol deviations due to consecutive non-adherence to diet/lifestyle requirements per blinded dietitian

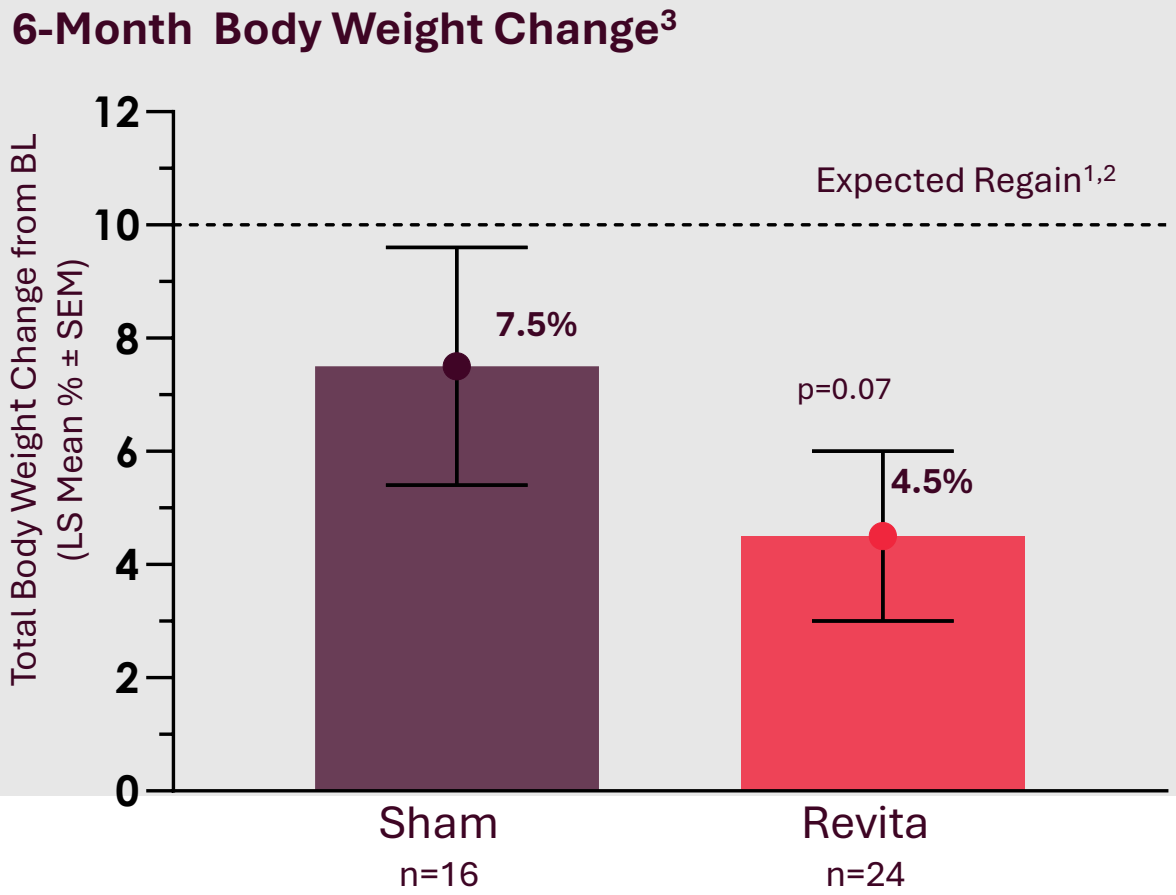
Balanced, Representative Study Population Supports Generalizability of Results

- Reflects broad US GLP-1 obesity population and REMAIN-1 Pivotal Cohort (BMI ~ 37 kg/m^2; 80% female)[1,2]
- Balanced across study arms
- High rate of underdiagnosed pre-diabetes (42%)

Demographic/Characteristic	Revita (n=29)	Sham (n=16)	Total (N=45)
Age, yrs, mean (SD)	44 (14)	40 (11)	43 (13)
Sex, no. (%)			
Male	6 (21)	3 (19)	9 (20)
Female	23 (79)	13 (81)	36 (80)
Body Weight Pre-TZP, kg, mean (SD)	100 (16)	99 (15)	99 (15)
Body Weight Post-TZP, kg, mean (SD)	82 (13)	81 (13)	82 (13)
Pre-diabetes at Screening, no. (%)**	14 (48)	5 (31)	19 (42)

1.Fractyl Health data on file. *Patients with a diagnosis of pre-diabetes in their medical history. ** Per protocol definition of pre-diabetes: screening HbA1c between 5.7% and 6.5% and/or screening fasting plasma glucose between 100 to 125 mg/dL. Tirzepatide run-in and dose-escalation period was approximately 16-26 weeks. Sham procedure consisted of placing the Revita catheter into the duodenum for a minimum of 30 minutes with no manipulations of the device or activation of the catheter. BMI=body mass index, SD=standard deviation, TZP=tirzepatide, TBW=total body weight

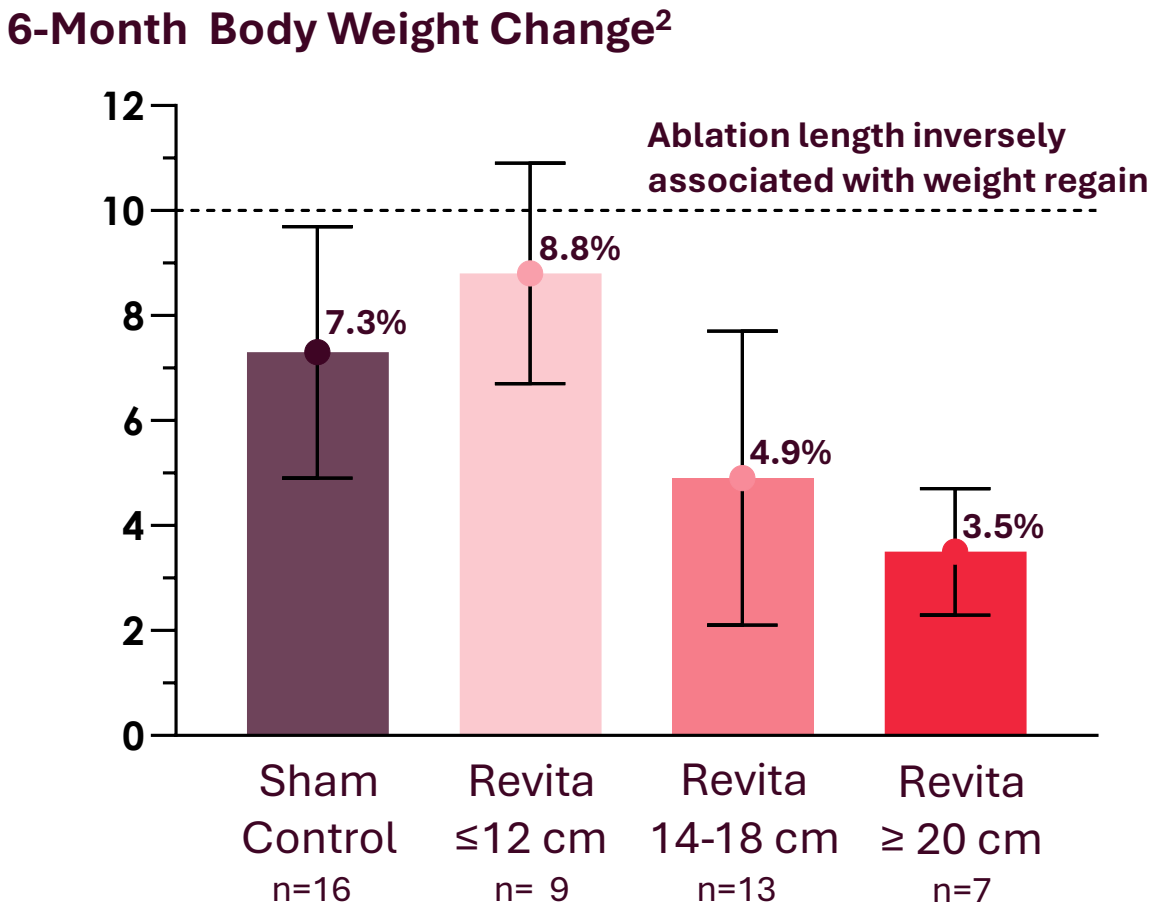
REMAIN-1 midpoint cohort: Revita reduced post-TZP weight regain at 6 months



Change from baseline through 6 months analyzed using a mixed model for repeated measures (MMRM); LS mean ± SEM shown; one-sided p-value reported.
[1]Aronne et al. *JAMA*. 2023 Dec 11;331(1):38–48 . [2]Wilding et al. Diabetes Obes Metab. 2022 Aug;24(8):1553-1564.
[3] Excluded 5 subjects per protocol from efficacy analysis; included in safety assessment Abbreviations: BL, baseline; LS, least-squares; SEM, standard error of the mean.

Dose-Response: Ablation length correlates with weight maintenance treatment effect

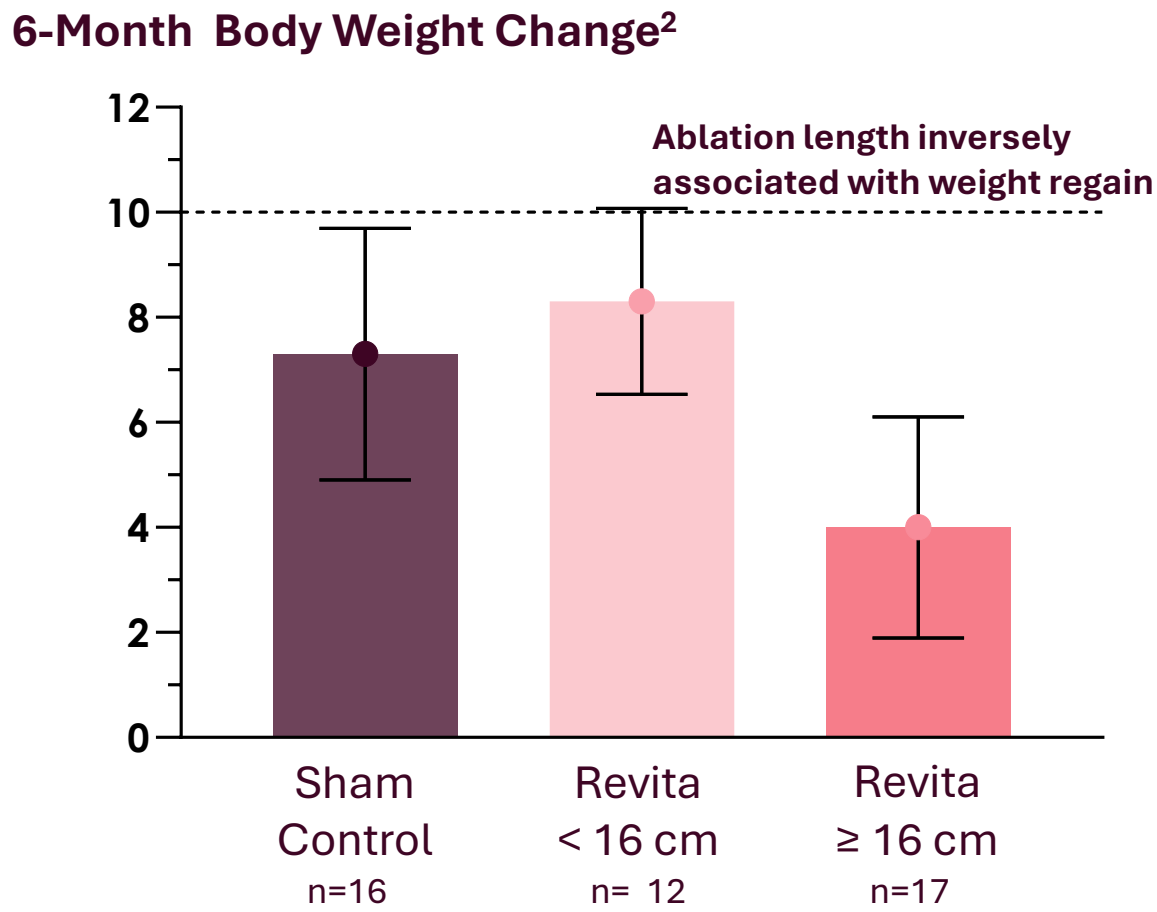
Dose-response: Significant correlation between ablation length and weight maintenance treatment effect (p=0.048 per Pivotal Cohort key secondary endpoint; n=29 Revita arm[1])



[1]Dose-response assessed by Spearman rank correlation between ablation count and weight regain at week 26 within the blinded DMR arm. [2]Observed means and SEM at Week 26. DMR patients (n=29) stratified by ablation tercile. Dashed line = expected weight regain based on SURMOUNT-4 GLP-1 withdrawal data. Mean run-in TBWL balanced across groups.

Dose-Response: Ablation length correlates with weight maintenance treatment effect

These findings inform standardized ablation length of 16 cm adopted for Pivotal Cohort



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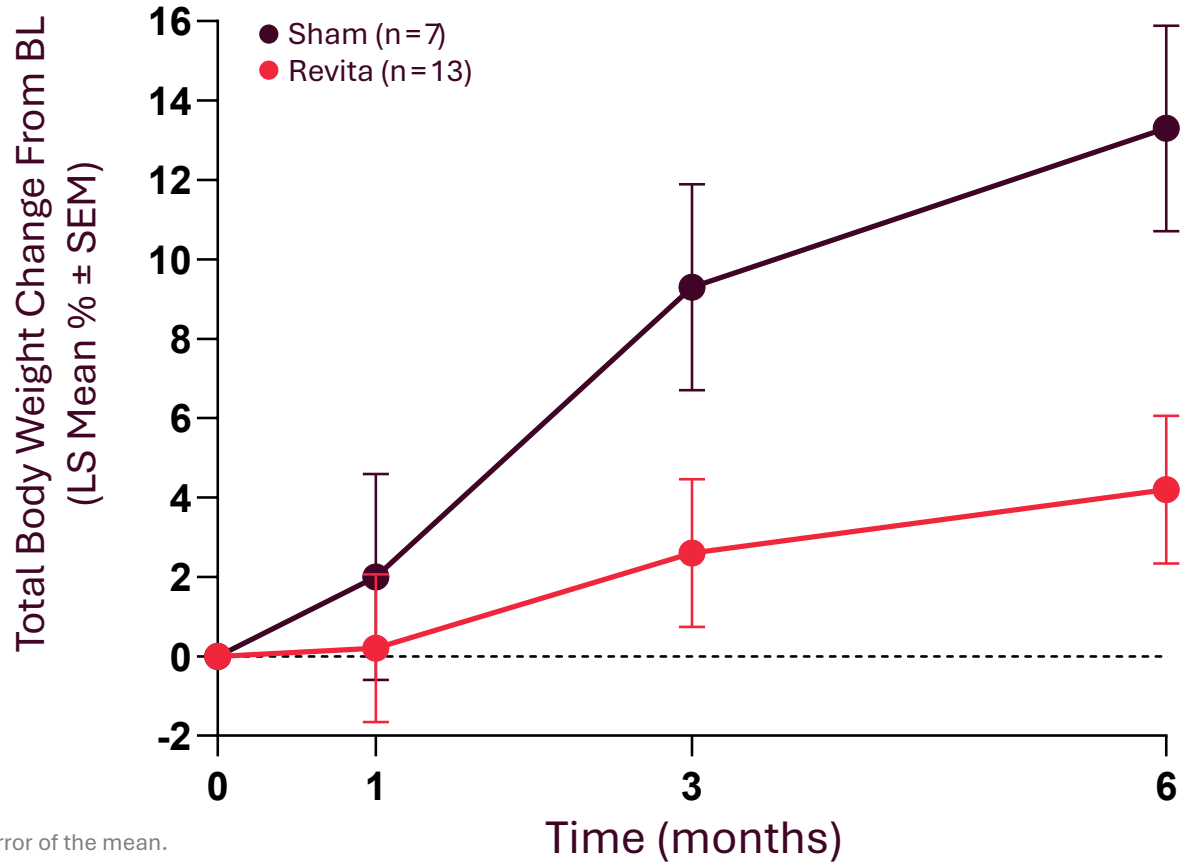
High GLP-1 responders showed sustained and growing treatment effect over time[1]

In participants who were high GLP-1 responders >18%[1], Revita showed **early and sustained separation vs sham through 6 months**

Curve trajectories continue to diverge at 6 months, **indicating potential for sustained biological activity**

Pivotal Cohort mean run-in weight loss 18.3%

High GLP-1 Responders[1] Change in Body Weight Over Time



[1]Participants with run-in weight loss above a median ~ 18%.
Abbreviations: BL, baseline; GLP-1, glucagon-like peptide-1; LS, least-squares; SEM, standard error of the mean.

Cardiometabolic and craving signals consistent with Revita's proposed duodenal mechanism of action

- Secondary endpoints consistent with Revita's proposed mechanism of action
- Favorable lipid changes vs. sham consistent with improved insulin sensitivity and lipid handling
  - ↑ HDL-C
  - ↓ Triglycerides and TG:HDL ratio
- Patient-reported outcomes suggest reduced craving for sweet food compared to Sham

	LS Mean change from BL (SEM)[1]		
Cardiometabolic Parameter	**Revita** (n = 29)	**Sham** (n = 16)	**p-value**
Triglycerides, mg/dL	8.2 (10.2)	35.6 (14.9)	**0.04**
LDL-C, mg/dL	7.7 (5.4)	11.6 (8.1)	0.33
HDL-C, mg/dL	15.5 (2.7)	7.7 (3.9)	**0.02**
VLDL-C, mg/dL	1.7 (2.0)	7.3 (2.9)	**0.04**
Triglyceride : HDL ratio	-0.4 (0.2)	0.4 (0.3)	**0.01**
HbA1c, %	0.1 (0.04)	0.2 (0.05)	0.15
CoEQ Parameter			
Craving for sweet	1.9 (0.4)	3.4 (0.7)	**0.02**

[1] Included 5 subjects who did not follow protocol-specified diet and exercise tracking requirements.
Abbreviations: BL, baseline; GLP-1, glucagon-like peptide-1; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LS, least-squares; mg/dL, milligrams per deciliter; mg/L, milligrams per liter; SEM, standard error of the mean; TG:HDL, triglyceride-to-HDL ratio; VLDL-C, very low-density lipoprotein cholesterol.

Favorable safety and tolerability through 6 months

- No Treatment-Emergent Serious AEs definitely or probably related to device or procedure
- No TEAE-related study discontinuations
- Related TEAEs only mild in severity and temporary
- Safety and tolerability consistent with prior Revita clinical experience

Treatment-Emergent Adverse Events (TEAEs)	**Revita** (n = 29)	**Sham** (n = 16)	**Total** (N = 45)
Patients experiencing any TEAE n, (%) of subjects with event	8 (28)	2 (13)	10 (22)
TEAEs by grade, n (%)	13	3	16
Grade ≥3 TEAEs	1 (8)	0 (0)	1* (6)
Grade 2 TEAEs	1 (8)	1 (33)	2** (13)
Grade 1 TEAEs	11 (85)	2 (67)	13 (81)
Related TEAEs†, n	4	0	4
Abdominal discomfort	1	0	1
Nausea	1	0	1
Dry mouth	1	0	1
Sore throat	1	0	1

*1 SAE (cholecystitis) > 60 days post-randomization – unrelated to device or procedure. **2 Grade 2 AEs (Revita-hypertension/worsening high blood pressure, Sham-urinary tract infection) >200 days post-randomization - unrelated to device or procedure. †Related TEAEs are defined as definitely or probably related to the device and or procedure. Interim data reported are subject to further clinical evaluation committee review and adjudication. Clavien-Dindo Classification[1]: Standardized FDA-recommended system for TEAE grading: Grade 1: Minor, any deviation from the normal course without requiring treatment. Grade 2: Requiring treatment. Grade 3: Requiring surgical, endoscopic, radiologic intervention. Grade 4: Life-threatening, requiring ICU. Grade 5: Death. [1]Dindo *et al. Annals of Surgery* 240(2):p 205-213.
Abbreviations: AE, adverse event; ICU, intensive care unit; GLP-1, glucagon-like peptide-1; TEAE, treatment-emergent AE.

REMAIN-1 pivotal study in weight maintenance

Pivotal Cohort fully randomized; 6-mo topline pivotal data anticipated in early Q4 2026

Patient population

- Adults with obesity (BMI 30-45 kg/m^2)
- GLP-1 naïve; no T2D
- n≈315

Co-primary endpoints

- % TBW regain: Revita vs sham at 6 months *and*
- Responder rate: % participants who maintain weight loss at 12 months

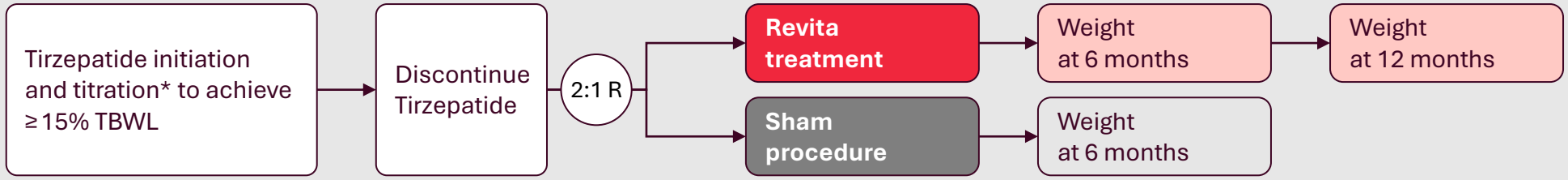
Study design

- TZP administration to achieve ≥15% TBWL, then discontinued
- Randomized (2:1 Revita vs Sham), double-blind, sham-controlled
- Diet and lifestyle counseling throughout

Anticipated milestones[1]

- **Complete randomizations:** Feb '26
- **Topline 6-month pivotal data:** Early Q4 '26

Study design



[1]These forward-looking statements are based on management's current estimates and expectations.
Refer to the latest disclosures filed with the SEC for a discussion regarding Risk Factors to these and other estimates and expectations.
Abbreviations: BMI, body mass index; GLP-1, glucagon-like peptide 1; R, randomization; TBW, total body weight; TBWL, total body weight loss; TZP, tirzepatide; T2D, type 2 diabetes.

Conclusions

- REMAIN-1 Midpoint is the first randomized, double-blind, sham-controlled study of a procedural intervention for post-GLP-1 weight maintenance
- Endoscopic duodenal mucosal resurfacing (Revita DMR) was safe and well-tolerated through 6 months, with no definite or probabe device- or procedure-related SAEs
- Revita reduced post-TZP weight regain relative to sham. A dose-response relationship between ablation length and treatment effect was identified in an exploratory analysis (p=0.048)
- Cardiometabolic analyses showed favorable changes in fasting HDL cholesterol, triglycerides, and sweet food craving compared to sham

Looking Ahead

- The REMAIN-1 Pivotal Cohort, fully enrolled with optimized ablation dosing (mean 16 cm), will test whether dose-response relationship translates to consistent, repeatable outcomes in a larger cohort - with 6-month primary endpoint data expected in early Q4 2026

Abbreviations: BL, baseline; DMR, duodenal mucosal resurfacing; GLP-1, glucagon-like peptide-1; ITT, intention-to-treat; LS, least-squares; SAE, serious adverse event; SAP, statistical analysis plan; SEM, standard error of the mean.