REMAIN-1 Weight Maintenance Program Update

March 2026

NASDAQ:GUTS

Legal disclaimer

The study database has not been locked as this is an ongoing study, and the data are subject to further cleaning and validation.

Forward-looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact are forward-looking statements. These statements may be identified by words such as “aims,” “anticipates,” “believes,” “could,” “estimates,” “expects,” “forecasts,” “goal,” “intends,” “may,” “plans,” “possible,” “potential,” “seeks,” “will” and variations of these words or similar expressions that are intended to identify forward-looking statements, although not all forward-looking statements contain these words. 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Four pillars driving our conviction in Revita for post-GLP-1 weight maintenance

1

The Clinical Signal Is Real

- **Ablation length (i.e., dose)-responsive treatment effect** in Revita arm
- **~70% reduction in weight regain** with widening separation from sham in high GLP-1 responders

2

Pivotal Is Built to Win

- **Powered at >90%** with conservative assumptions
- **Dose-response and high-responder subgroup** are well represented and pre-specified in pivotal SAP
- **Fully randomized**

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Clear Path to Commercial Value

- **Favorable FDA De Novo feedback received**
- **Potential FDA De Novo submission** in post-GLP-1 weight maintenance late Q4 2026
- **Large, defined, and growing market** with established patient journey on GLP-1s

4

Funded Through Definitive Data

- **Cash runway extends into early 2027 and through pivotal readout in early Q4 2026**
- **Funded to key value inflection** without planned incremental capital raise

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REMAIN-1 midpoint cohort study in weight maintenance

Sham-controlled pilot study validating design and powering assumptions for the REMAIN-1 Pivotal

Patient population

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

Efficacy endpoints

- % TBW change Revita vs sham at 3 and 6 months

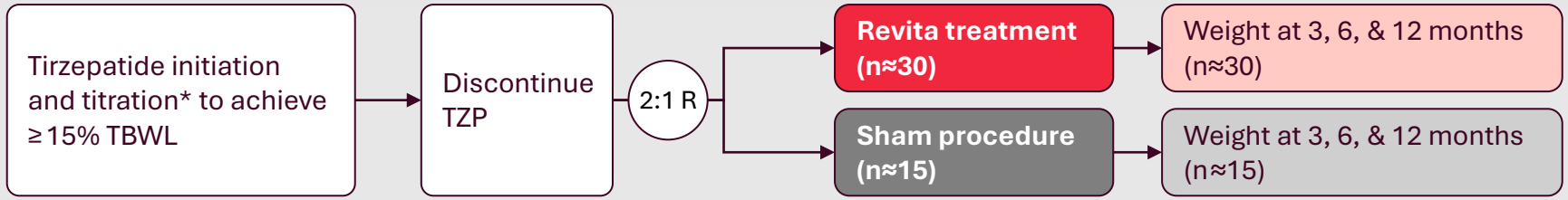
Study design

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

Anticipated milestones[1]

- **Midpoint cohort 3-mo data:** Sept ‘25
- **Midpoint cohort 6-mo data:** Jan ‘26
- **Midpoint cohort 12-mo data:** Q3 '26

Study design



*Tirzepatide run-in modeled from SURMOUNT-4 trial.[2]

[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. [2]Aronne et al. *JAMA*. 2023 Dec 11;331(1):38–48.

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

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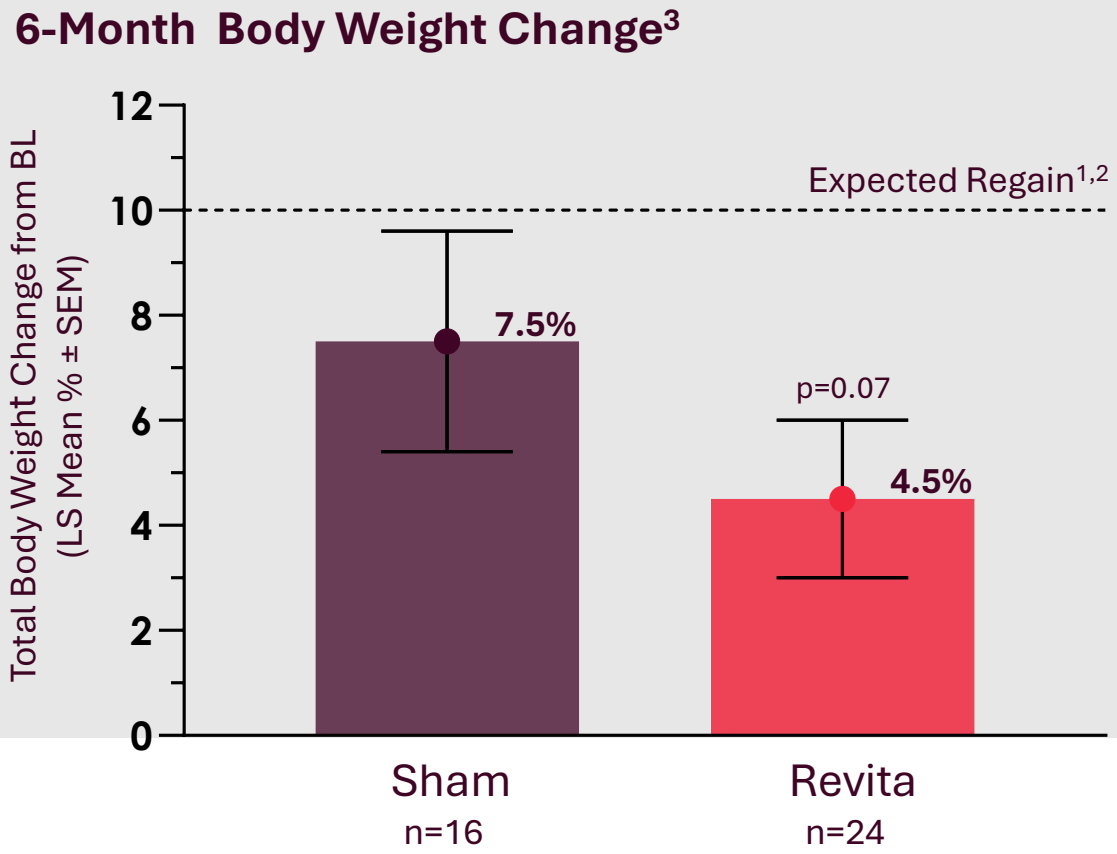
REMAIN-1 midpoint cohort confirms Revita activity and informs pivotal execution

- Revita reduced post-tirzepatide weight regain vs. sham at 6 months (p=0.07, n=40[3])
- Early analysis suggested site-level heterogeneity potentially attenuating treatment effect in some patients
- Investigation of this site heterogeneity uncovered shorter ablation length (dose response) as the key driver of efficacy rather than site operational issues



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.

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What the Midpoint Cohort exploratory analyses taught us and how the pivotal is built to win

Midpoint Cohort learnings have been systematically incorporated into Pivotal Cohort design and execution

Midpoint Observation	Pivotal Optimization
Dose-response observed Strong correlation between ablation length and weight maintenance across all 29 Revita participants, as in prior Revita T2D work[1]	**Pivotal mean ablation length > 16 cm** Pivotal study enriched for participants receiving longer ablation length treatments. Dose-response pre-specified in pivotal SAP
Greatest effect size in participants with most weight lost on GLP-1s High GLP-1 responders (total body weight loss of > 17.5% on GLP-1s) showed clinically meaningful and widening separation vs. sham through 6 months	**Pivotal mean run-in weight loss 18.3%** Pivotal study enriched for participants with higher run-in total body weight loss. High GLP-1 responder population pre-specified in pivotal SAP
	8x larger sample size with > 90% powering in Pivotal Cohort

[1]Rajagopalan et al Diabetes Care 2016 Dec;39(12):2254-2261

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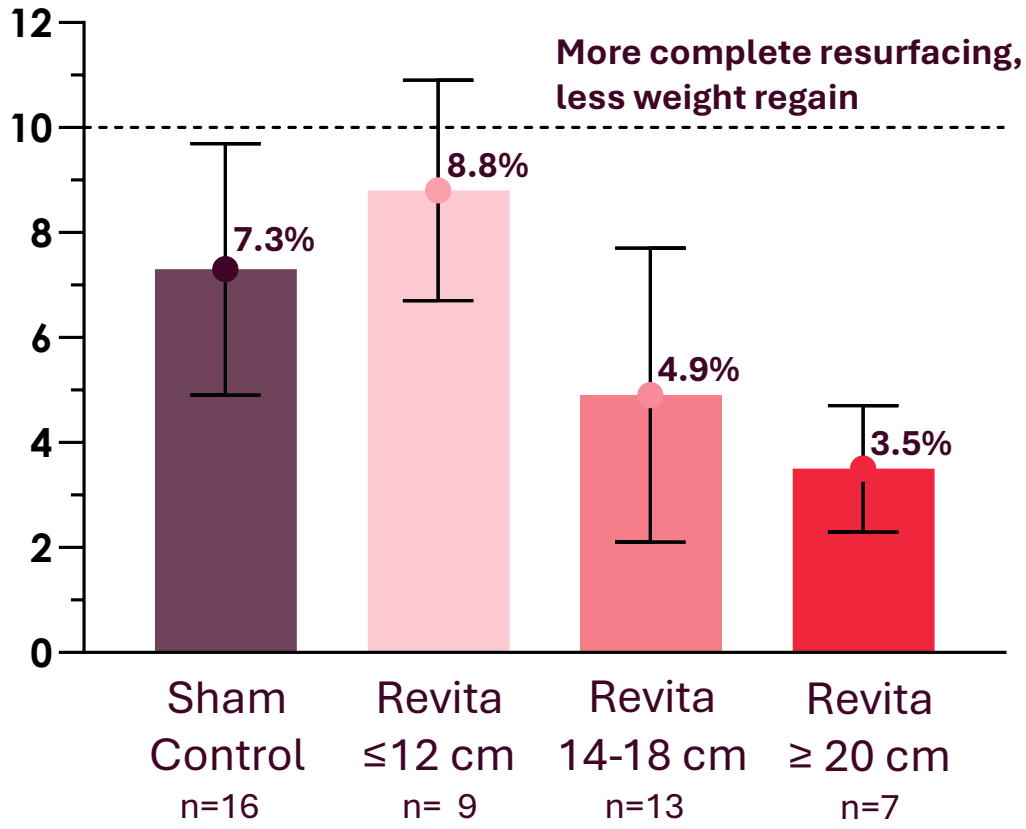
Dosing: Ablation completeness drives treatment effect and pivotal is optimized accordingly

- **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])
- Participants receiving >14 cm ablations regained ~ 50% the weight of sham at 6-months

Pivotal Cohort mean and median ablation length is 16cm, providing ample opportunity to demonstrate enhanced clinical signal

6-Month Body Weight Change[2]



[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.

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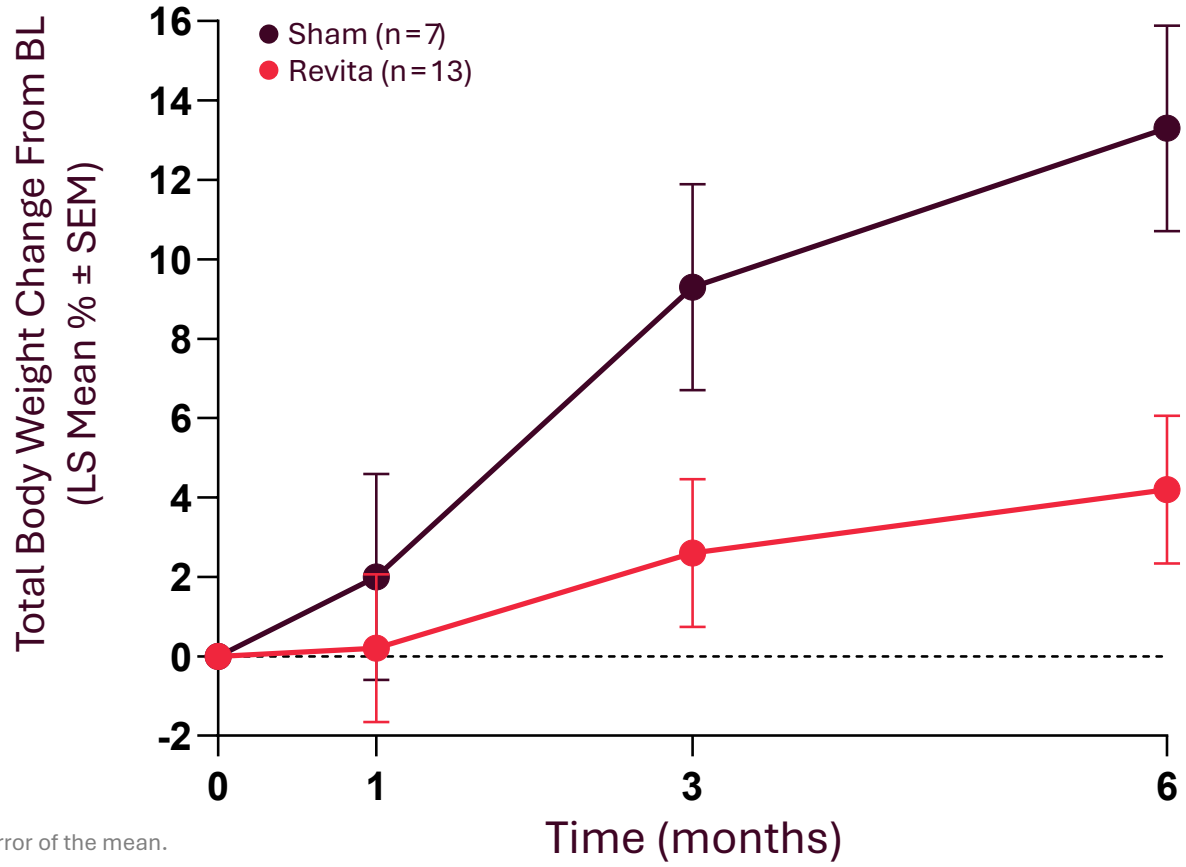
Patient selection: Revita effect is largest and growing in those who need it the most[1]

In participants who were high GLP-1 responders[1], Revita showed **early and sustained separation vs sham through 6 months** (per Pivotal Cohort pre-specified SAP; p=0.004)

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

Pivotal Cohort mean run-in weight loss 18.3%; treatment effect in high GLP-1 responders is a pre-specified subgroup in pivotal SAP

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.

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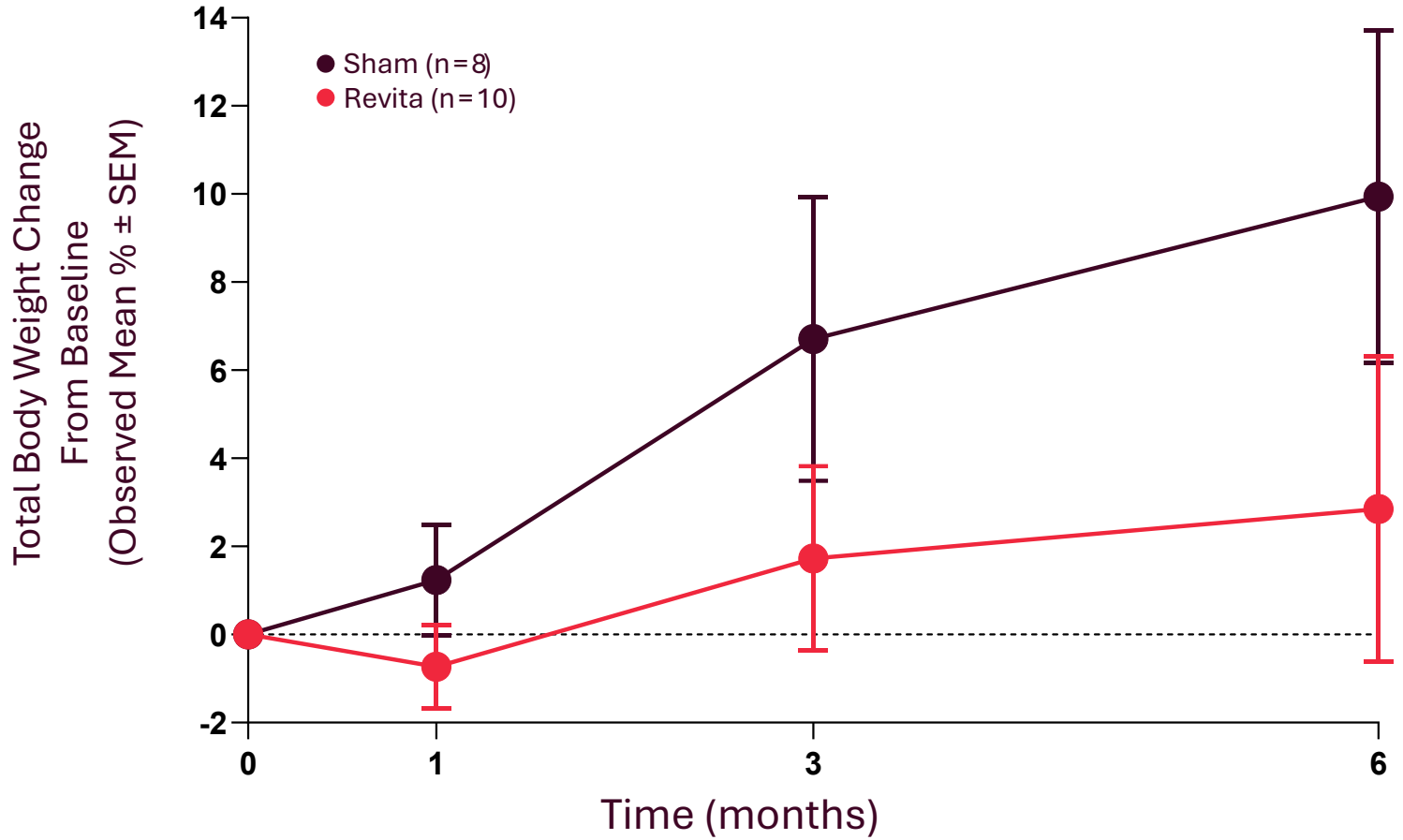
Right “dose” in the right patient: Revita showed large and growing treatment effect through 6 months

Change in Body Weight in Optimized Patient Cohort[1]



This optimized cohort reflects the profile of the Pivotal Cohort population — participants with high GLP-1 weight loss and per-protocol ablation standards

Revita-treated participants experienced only 2.9% weight regain at six months, compared to 9.9% in the sham arm in this optimized patient cohort

[1]Participants with run-in weight loss above ~18% with > 14 cm of duodenal ablation.
Abbreviations: GLP-1, glucagon-like peptide-1; SEM, standard error of the mean.

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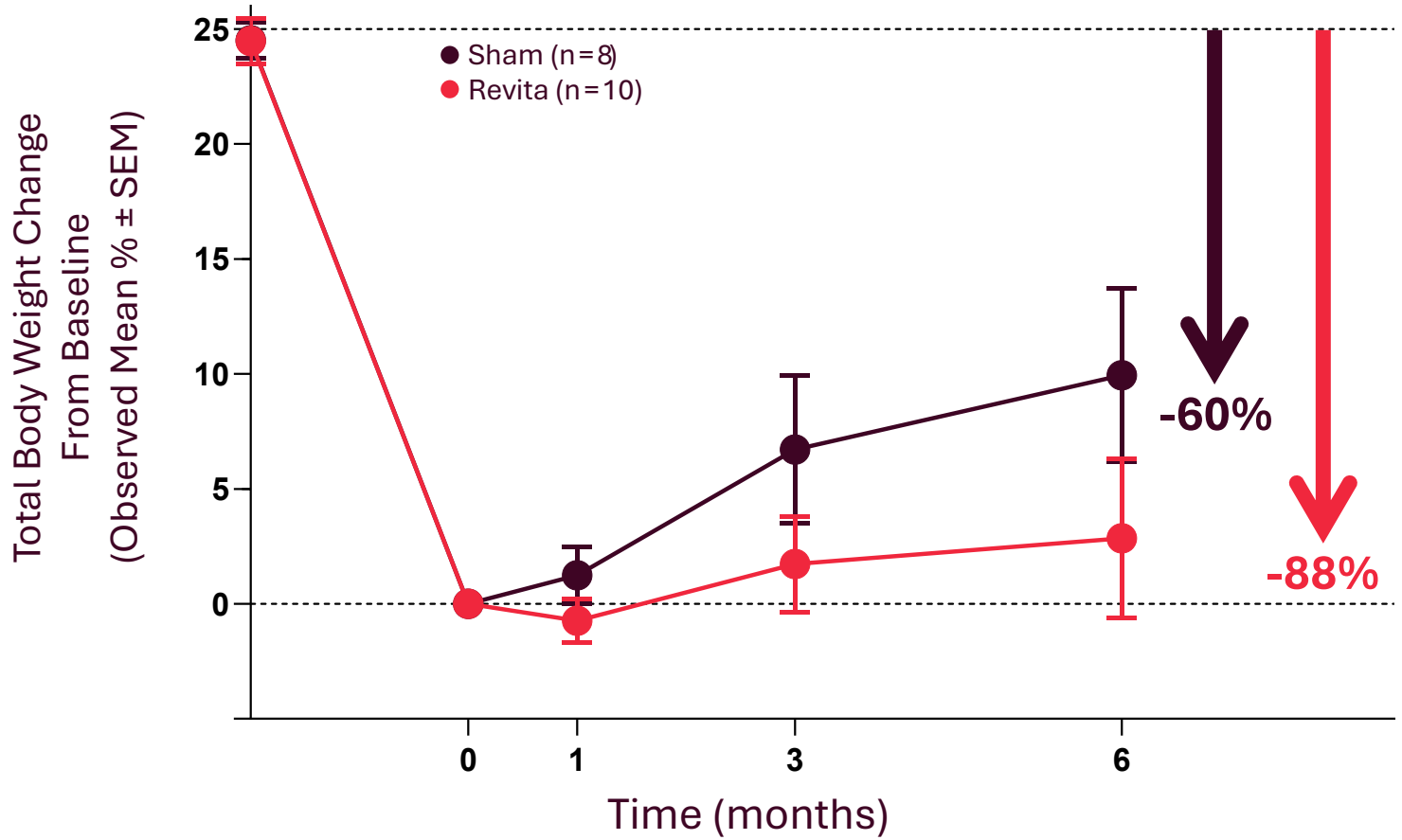
Right “dose” in the right participant: Revita showed up to 88% weight loss maintenance at 6 months

Change in Body Weight in Optimized Patient Cohort[1]



This optimized cohort reflects the profile of the Pivotal Cohort population — participants with high GLP-1 weight loss and per-protocol ablation standards

In this cohort, **Revita patients retained 88% of GLP-1 induced weight loss at six months** compared to only 60% in sham participants

[1]Participants with run-in weight loss above ~18% with > 14 cm of duodenal ablation.
Abbreviations: GLP-1, glucagon-like peptide-1; SEM, standard error of the mean.

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Excellent safety and tolerability through 6 months

No new related Treatment-Emergent AEs between 3-month and 6-month follow-up

- No Treatment-Emergent Serious AEs 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.

FRACTYL health

Advancing toward a more efficient US regulatory path

FDA pre-submission feedback received; De Novo submission planned late Q4 2026

- **Received favorable pre-submission feedback from the FDA in March 2026**
  - Safety profile of the Revita DMR System is consistent with a Class II (De Novo) device classification
- Company intends to submit De Novo marketing application in late Q4 2026[1,2]

FDA Regulatory Pathways: De Novo vs. PMA

	De Novo Classification	PMA (Premarket Approval)
Intended Device Risk	Class I or II (low to mid risk)	Class III (high risk)
Clinical Evidence Required	"Reasonable assurance of safety and effectiveness"	"Valid scientific evidence"
Statutory FDA Review Timeline	150 FDA days	180 FDA days
Downstream Optionality	Creates predicate for future 510(k)s	No predicate created
Capital Efficiency	Potentially more capital-efficient	Potentially capital-intensive

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Source: FDA device classification regulations (21 CFR); FDA device classification regulations (21 CFR). *Both De Novo and PMA pathways require demonstration of reasonable assurance of safety and effectiveness.*

Abbreviations: FDA, Food and Drug Administration; PMA, premarket approval.

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Large, defined, and growing market with a clear path to potential market adoption

1 Large & Growing Patient Population

30M+ projected to be on GLP-1s.

As drugs grow more effective, the need for a durable off-ramp from chronic therapy grows. This market expands with GLP-1 success.

2 Dose-Dependent, Standardized Delivery

Clear dose-response.

All pivotal investigators successfully trained to achieve >14cm ablations. Anticipate standardizing dosing guidance in commercial setting.

3 Defined Population with Large Effect

Clinically significant weight maintenance

Large effect size and population clarity in high GLP-1 responders enable high-probability commercial conversion.

4 Pivotal Data with Breakthrough Pathway

Breakthrough Device. De Novo pathway.

Anticipated pivotal read out early Q4. CMS Transitional Pass-Through de-risks reimbursement. Clear path from data to value.

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