Redefining Durable Weight Loss Maintenance in the Post-GLP-1 Era

Corporate Presentation | June 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.

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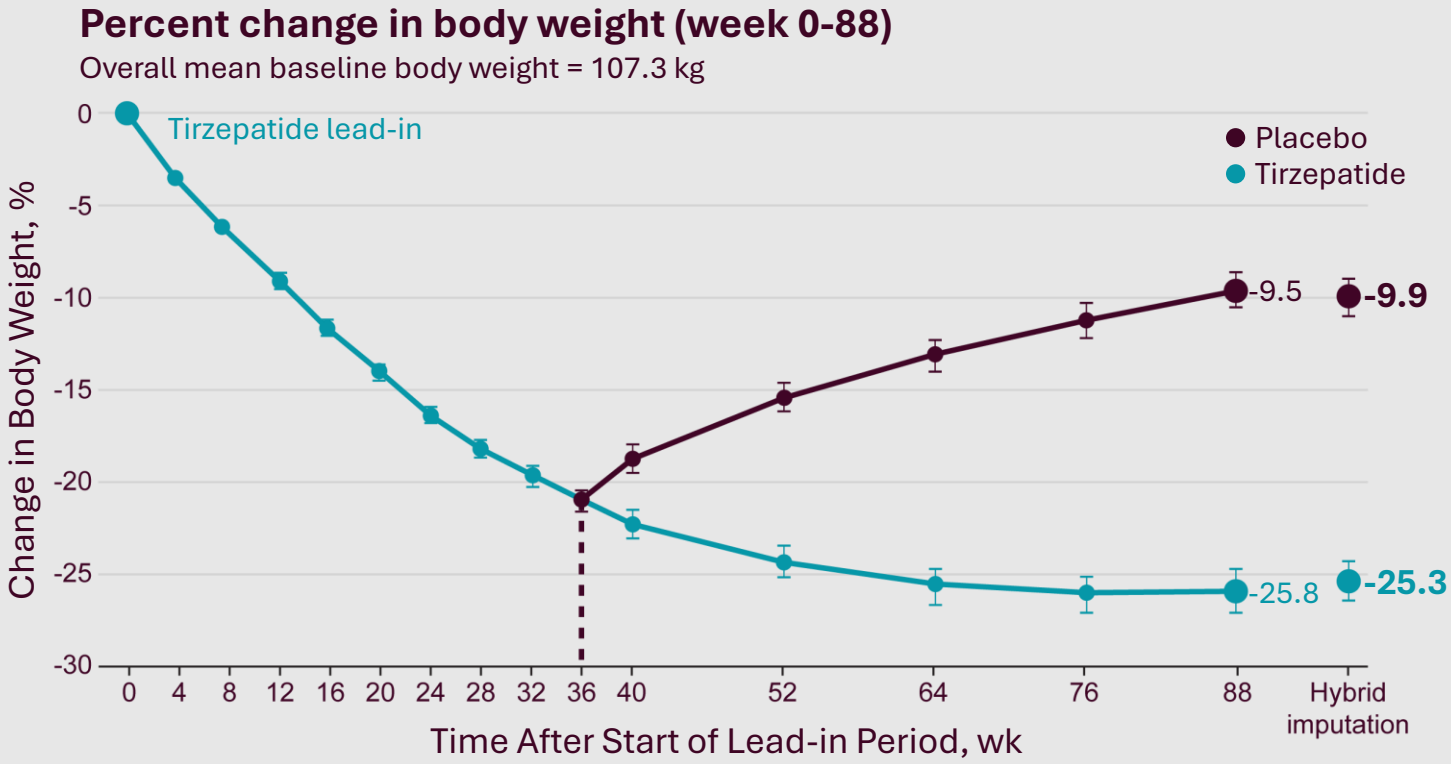
GLP-1s unlocked weight loss, but durability remains unsolved

~30M U.S. Patients projected to use GLP-1s for obesity by 2035[1]

~65% Patients with obesity discontinue before one year[2]

85% Patients regain lost weight after GLP-1 discontinuation[3]



The next phase of obesity care will be defined by weight maintenance, not weight loss

Figure adapted from Lilly's SURMOUNT-4 study.[3] [1]Morgan Stanley, Obesity Medications: The Broadening, Apr 24, 2025. [2]Rodriguez, Patricia J., et al. *JAMA Network Open 8.1* (2025): e2457349-e2457349. [3]Aronne et al. *JAMA*. 2023 Dec 11;331(1):38–48. [4]Revita is currently being studied under an open Investigational Device Exemption (IDE) in the US and holds FDA Breakthrough Device designation for weight maintenance in patients discontinuing GLP-1 therapy. Abbreviations: GLP-1, glucagon-like peptide-1; wk, week.

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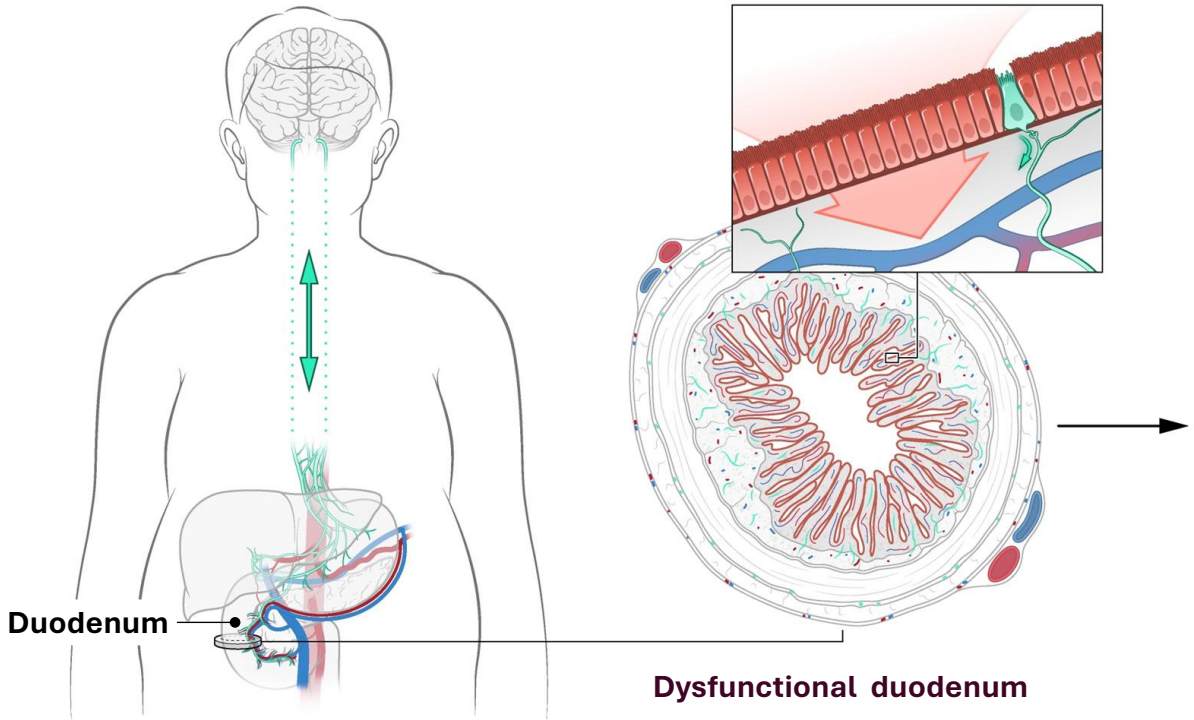
Gut dysfunction is a root cause of obesity

Weight regain is biologically driven – not behavioral failure

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]



Gut dysfunction caused by long-term exposure to high fat and high sugar diets is an underlying root cause of obesity and type 2 diabetes[2]

When GLP-1 therapy stops, underlying biology drives weight and blood sugar back to previous levels

Durable weight maintenance requires addressing gut-level root cause

[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.

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Revita®: Potential new backbone therapy in obesity

A one-time, endoscopic procedure designed to address gut-level metabolic dysfunction

Single outpatient endoscopic procedure

Performed by endoscopists; leverages familiar skills

Designed to complement pharmacology

Potentially used either as stand-alone treatment or alongside pharmacology

FDA Breakthrough Device designation

2026 is a pivotal and registrational year in post-GLP-1 weight maintenance

Comprehensive IP Estate

Robust portfolio protecting first-mover leadership

Revita is for investigational use only in the United States under Federal Law. Revita has a CE mark in the EU/UK.

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Near-term clinical catalysts and value-creation through to potential De Novo marketing application submission in Q4 2026

Revita *Outpatient endoscopic procedural therapy*

2026 Key Anticipated Milestones[1]

Indication	Program	Recent accomplishments	Q2	Q3	Q4
Weight Maintenance	REVEAL-1 Cohort (Open Label)	✓ Durable 6-mo data shared (Dec '25)	✓ 1-year data		
	REMAIN-1 Midpoint Cohort	✓ Positive 6-month randomized data (Jan '26)		1-year data	
	REMAIN-1 Pivotal Cohort	✓ Completed randomization (Feb '26)			**Topline 6-mo randomized data & potential De Novo marketing application submission**

Rejuva *Local AAV-delivered pancreatic GLP-1 gene therapy*

Indication	Program	Research	Lead selection	IND/CTA enabling	Phase 1	2026 Key Anticipated Milestones[1]
Type 2 Diabetes	RJVA-001	**CTA authorized in Netherlands**				H2: FIH dosing, subject to site activation, and preliminary data
Obesity	RJVA-002	**Candidate nominated**				

[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: CTA, clinical trial application. FIH, first-in-human.

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Revita®

An endoscopic procedural approach designed for durable weight maintenance via hydrothermal ablation of duodenal mucosa

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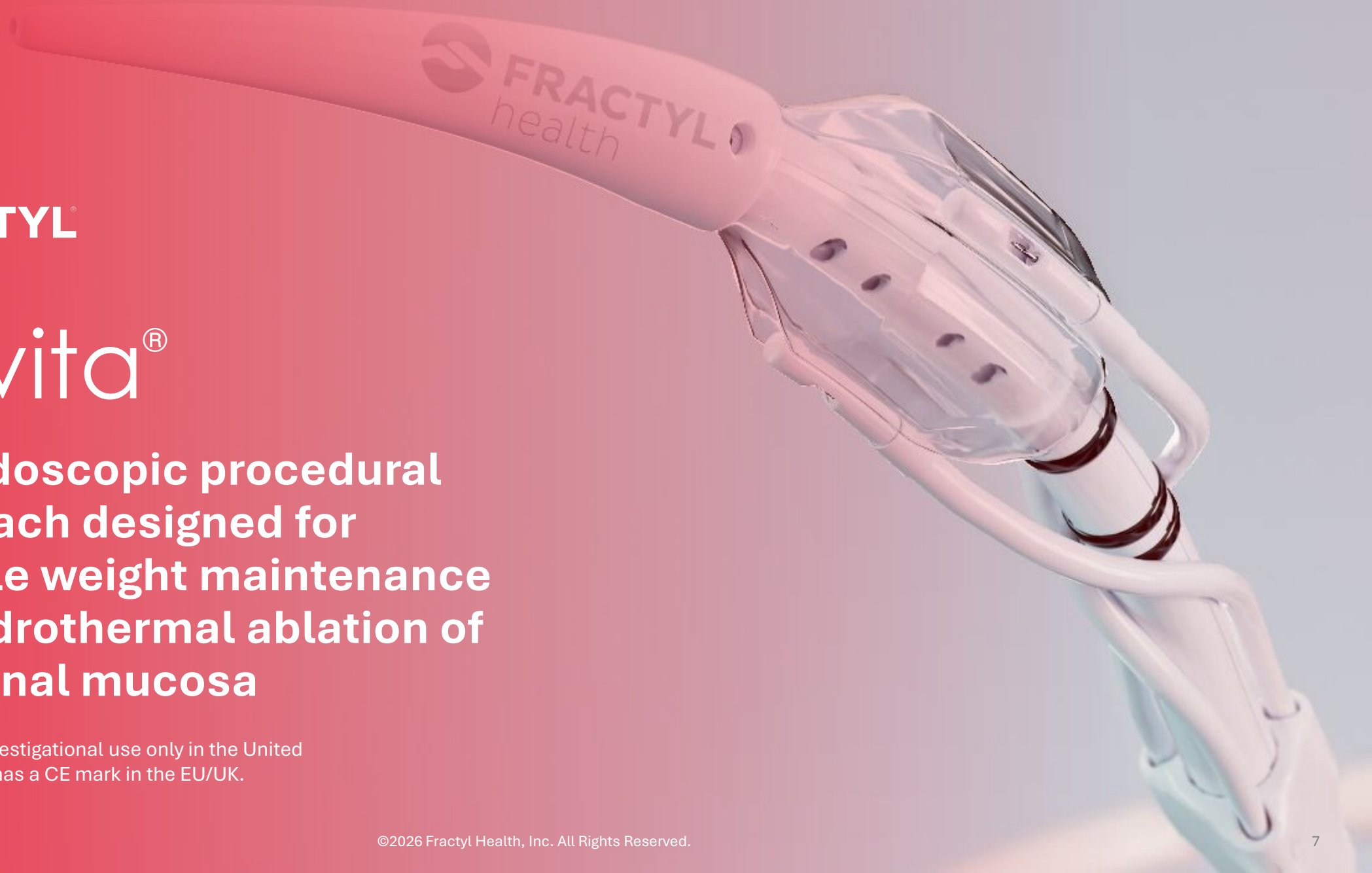
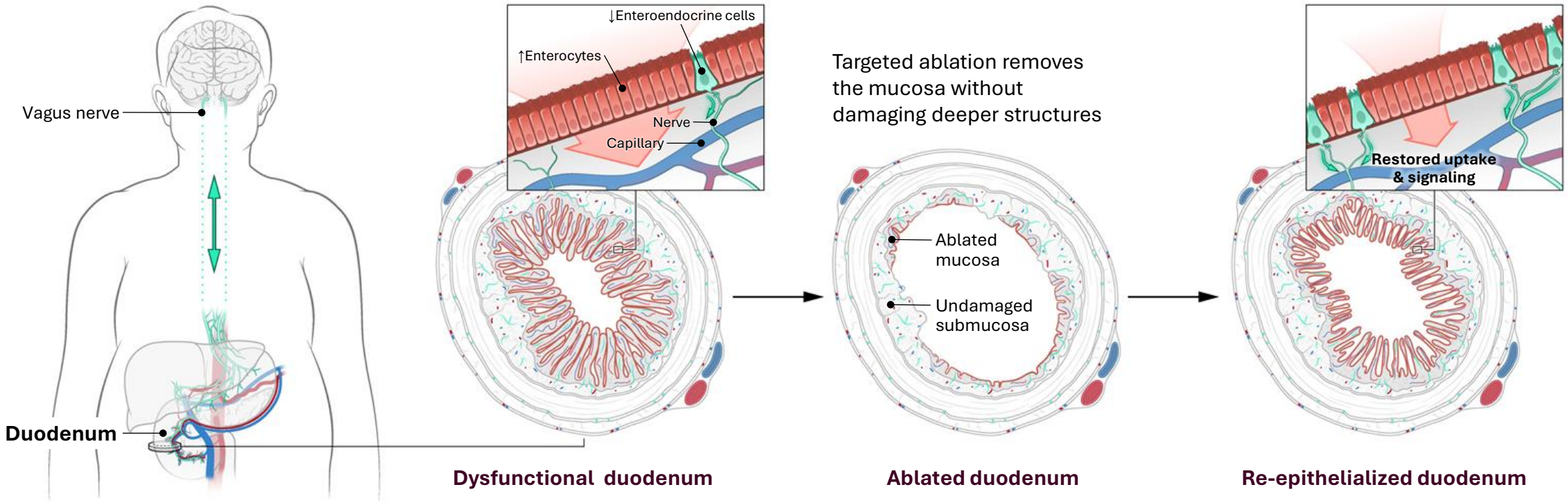


The duodenal mucosa: A compelling target for durable metabolic control

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.

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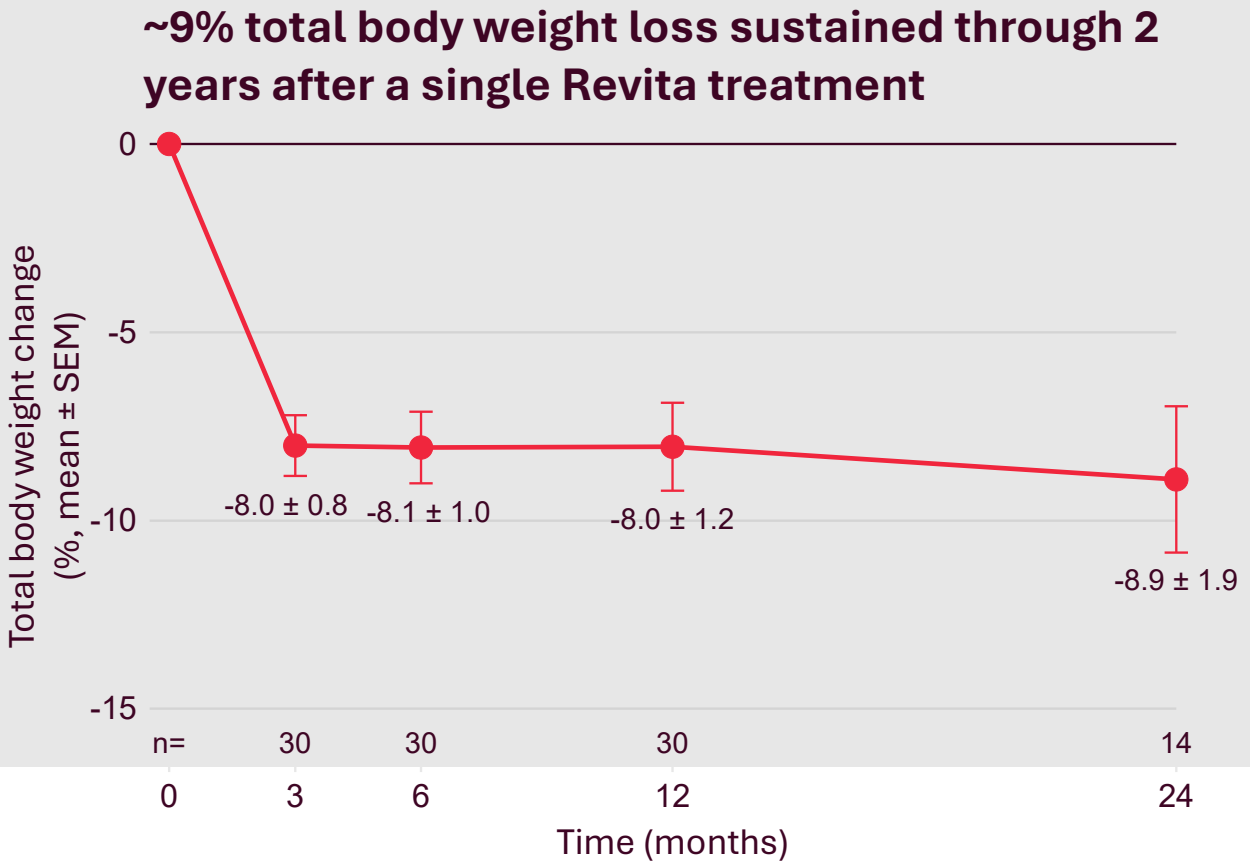
Real-world data show sustained 2-year metabolic benefits after a single Revita treatment



- **Metabolic control:** Mean HbA1c ↓1.7% from baseline (9.1% → 7.4%)
- **Reduced medicines:** 86% of patients on stable or fewer glucose-lowering drugs
- **Patient satisfaction:** At 2 yrs, 93% would repeat or recommend Revita
- **Real-world data:** Outcomes maintained despite reduced clinical surveillance
- **Safety:** No device- or procedure-related SAEs reported

The Germany Real-World Registry study is a prospective, post-market, clinical follow-up study to evaluate the Revita procedure in patients with inadequately controlled T2D. Entry criteria included a baseline HbA1c between 7-10% (inclusive), a BMI of ≤45 kg/m2, and use of at least one glucose-lowering agent (GLA). Baseline demographics: mean age of 60 years, a mean weight of 102 kg (225 lbs; BMI 33 kg/m^2), a mean HbA1c of 8.8%, despite being on up to three GLAs. Fractyl Health internal data, October 2025.
Abbreviations: QOL, quality of life; SAE, serious adverse event.

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REMAIN-1 Program

Clinical evaluation of durable post-GLP-1 weight maintenance

- Clinical & real-world data support durability after a single treatment
- Post-GLP-1 weight regain represents the critical unmet need
- REMAIN-1 is designed to directly test durable weight maintenance

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Durability is the binding constraint in obesity post-GLP-1s

Interest in prescription weight-loss drugs falls from 45% to 14% when regain risk is disclosed

45% **Percent who say they would be very or somewhat interested in taking a prescription weight loss medicine** *if they heard it was safe and effective*

Percent who say they would still be interested if…

14% *…they heard they may gain the weight back if they stopped using the prescription drug*

2/3rds of those initially interested in taking a prescription weight loss drug subsequently lose interest when informed about risk of weight regain

KFF Health Tacking Poll (July 11-19, 2023)

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REMAIN-1 weight maintenance program

Stepwise validation through potential De Novo marketing application submission in late Q4 26[1]

	Open-label exposure	Sham-controlled pilot	Sham-controlled pivotal
	REVEAL-1 Cohort (n≈20)	**REMAIN-1 Midpoint Cohort** (n≈45)	**REMAIN-1 Pivotal Cohort** (n≈315)
Rationale	Post-GLP-1 weight maintenance in a **real-world** setting	Randomized, double-blind, sham controlled	Randomized, double-blind, sham-controlled
Design	• Open-label	• Tirzepatide run-in phase • Revita vs sham (2:1)	• Tirzepatide run-in phase • Revita vs sham (2:1)
Participants	With obesity (BMI > 30 kg/m^2) prior to GLP-1 *and* ≥15% TBWL with GLP-1 drug	With obesity (BMI 30-45 kg/m^2) without T2D *and* GLP-1 drug naïve	With obesity (BMI 30-45 kg/m^2) without T2D *and* GLP-1 drug naïve
Anticipated milestones[1]	✓ 3-mo data: June '25 ✓ 6-mo data: Dec '25 ✓ 1-yr data: Q2 '26	✓ 3-mo data: Sept '25 ✓ 6-mo data: Jan '26 • 1-yr data: Q3 '26	✓ Enrollment: Q2 '25 ✓ Randomization: Feb '26 • **Topline 6-mo data: early Q4 '26** • **Potential De Novo marketing application submission: late Q4 '26**

[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; T2D, type 2 diabetes; TBWL, total body weight loss.

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REVEAL-1 cohort study in weight maintenance

Ongoing, open-label cohort designed to provide early, real-world insights

Patient population

- Patients living with obesity (BMI ≥30) without T2D and achieving at least 15% TBW loss with tirzepatide or semaglutide
- n≈20 patients who need to or want to stop tirzepatide

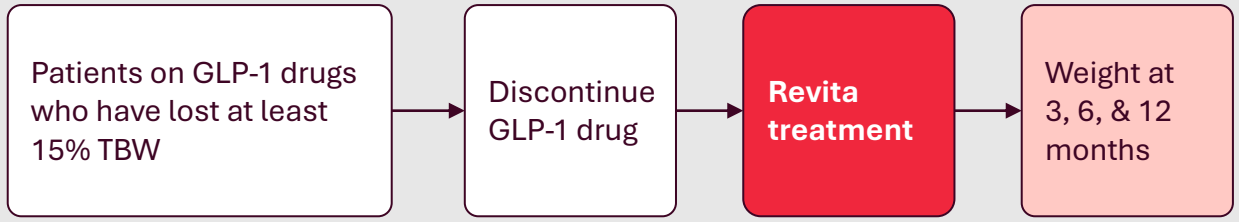
Primary endpoints

- Change from baseline in weight
- Comparison to historical controlled studies of GLP-1 withdrawal

Study design

- Single-arm, open-label, cohort study of Revita after GLP-1 drug discontinuation
- Diet and lifestyle counseling throughout

Study design



[1]Aronne et al. *JAMA*. 2024;331(1):38–48. doi:10.1001/jama.2023.24945. REVEAL-1 is an open label cohort as part of the REMAIN-1 pivotal IDE. Missing post-baseline data were not imputed.
Abbreviations: BMI, body mass index; GLP-1, glucagon-like peptide; LTFU, lost to follow-up; T2D, type 2 diabetes; TBW, total body weight; TBWL, total body weight loss.

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Weight Maintenance at 12 Months in Open Label Cohort

Single Revita procedure preserves GLP-1 induced weight loss through 1 year

Key Takeaways:

- **~78% of GLP-1-induced weight loss retained** at one year
- ~22% regained vs. 60-65% expected at 1 year[1] ➔ ~1/3 the expected regain
- **33% (5/15) lost additional weight** through 52 weeks off GLP-1
- **Clean AEs and tolerability:** No device/procedure-related SAEs, no TEAE-related discontinuations through 12 months, no device/procedure-related late AEs.
- **FDA protocol amendment filed** to extend follow-up beyond 1 year
- **Supports thesis:** REMAIN-1 pivotal topline data expected early Q4 ‘26*

1. Budini et al., *eClinicalMedicine*, March 2026. *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: CTA, clinical trial application. FIH, first-in-human.

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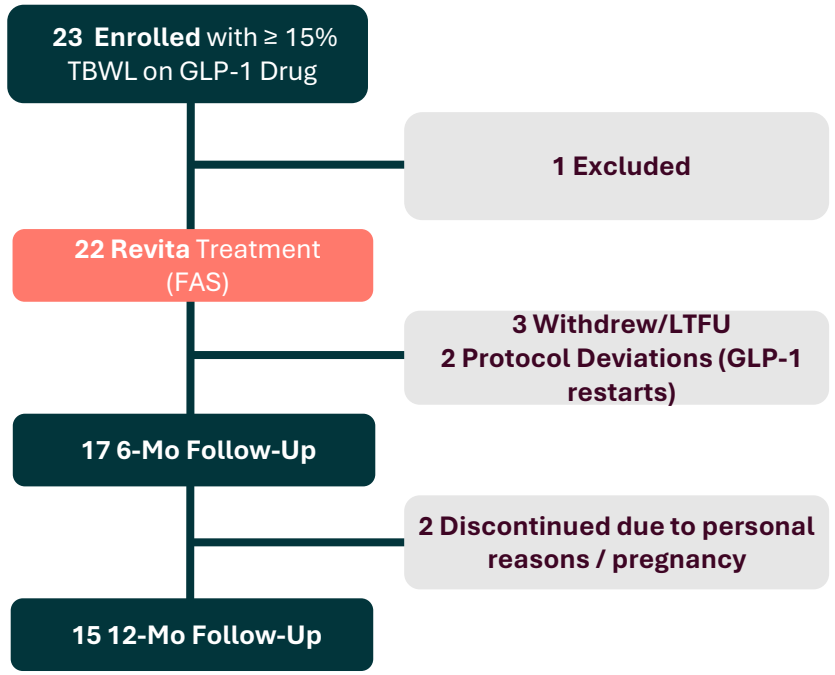
REVEAL-1 Open-Label Cohort Patient Disposition

Consistent procedure delivery; 12-mo retention in line with comparator trials

22 patients treated with Revita; 12-mo retention in line with comparator trials[1]

- **Consistent procedure delivery:** average ablation length ~16 cm
- **Analysis populations:**
  - 22 in Full Analysis Set (FAS)
  - 22 in Safety Analysis
  - 15 in Completer Analysis

Patient Disposition



[1]Aronne *et al.*, JAMA. 2023 Dec 11;331(1):38–48. FAS, full analysis set. GLP-1, glucagon-like peptide-1. LTFU, lost to follow-up,

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REVEAL-1 Cohort Reflects REMAIN-1 Pivotal and Real-World Post-GLP-1 Demographics

Strong GLP-1 responders at high risk of post-discontinuation regain[1]:

- **Substantial prior weight loss**: −24% ± 7% TBW (> 50 lbs avg) on GLP-1s
  - 17 of 22 participants ≥17.5% TBW loss on GLP-1s

Aligned with REMAIN-1 and real-world GLP-1 use:

- **21 of 22 (95%) on tirzepatide** — most relevant comparator to current real-world GLP-1 use
- Baseline characteristics align with REMAIN-1 Midpoint and Pivotal Cohorts[2,3]

Table 1: Demographics and Baseline Characteristics

Baseline Characteristics	Baseline Post-GLP-1 (n=22)
Age, yrs, mean (SD)	50 (12)
Sex, no. (%)	
Male	3 (14)
Female	19 (86)
Pre-diabetes*, no. (%)	3 (14)
On Tirzepatide, no. (%)	21 (95)
Body Weight Pre-GLP-1, kg, mean (SD)	105 (19)
Body Weight Post-GLP-1, kg, mean (SD)	80 (15)
TBW Change on GLP-1, %, mean (SD)	-24 (7)
BMI Post-GLP-1, kg/m^2, mean (SD)	29 (4)
HbA1c Post-GLP-1, % mean (SD)	5.1 (0.4)

*prediabetes in participant medical history or per protocol definition: HbA1c 5.7-6.5 and/or fasting plasma glucose 100-125 mg/dL at baseline. 1. Budini et al., eClinicalMedicine 2026. 2. Fractyl Health press release and conference call dated September 26, 2025. 3. Fractyl Health data on file. BMI=body mass index, GLP-1=glucagon-like peptide-1, HbA1c=Hemoglobin A1c, SD=standard deviation, TBW=total body weight

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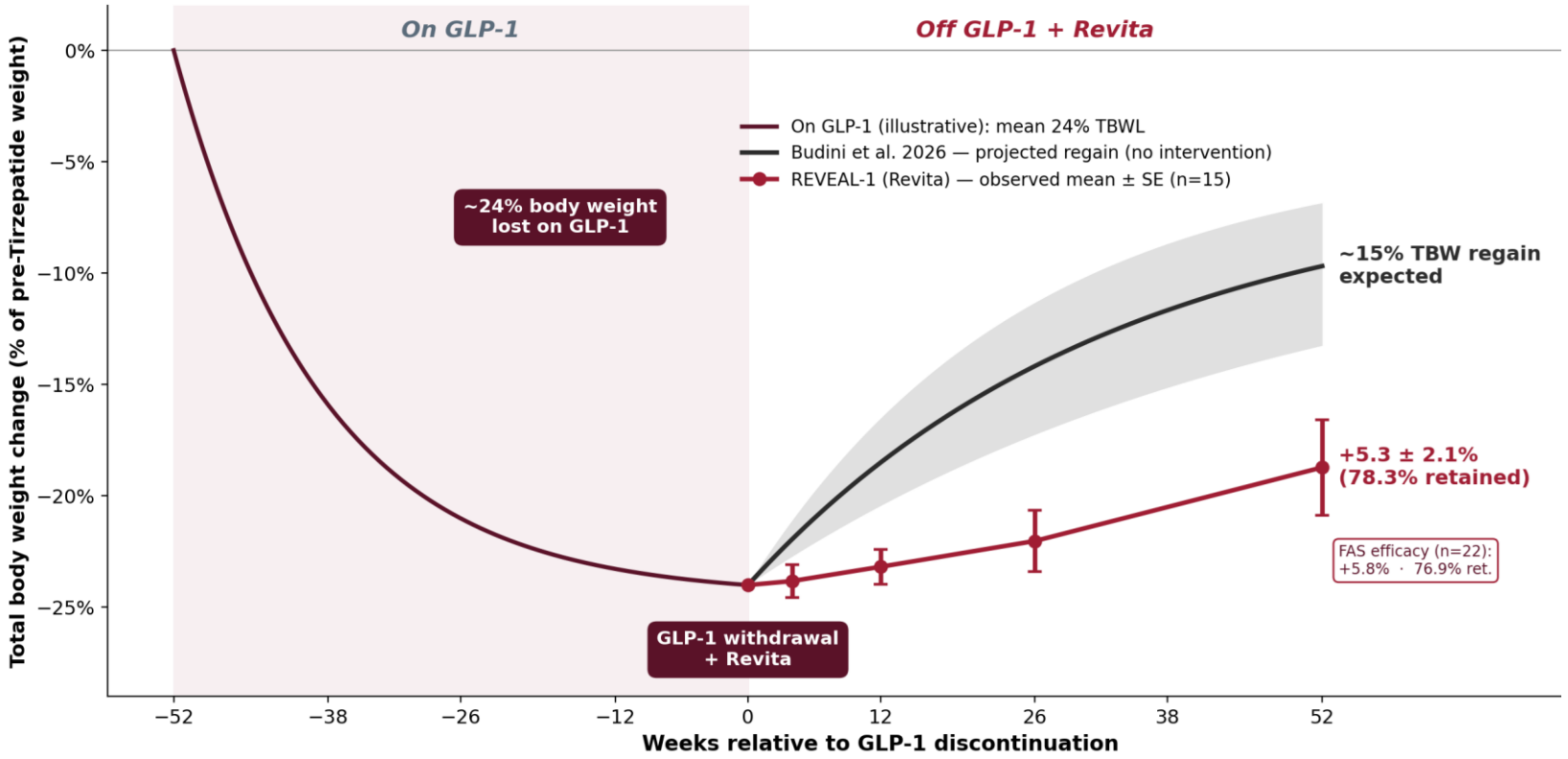
~1/3 the Expected Weight Regain at 1 Year Post-GLP-1

REVEAL-1 open-label cohort: n=15 completers (n=22 FAS); single Revita treatment, no ongoing GLP-1

- **78.3% of pre-Revita weight loss retained** at 52 weeks (+5.3% ± 2.1% SE n=15; FAS sensitivity: +5.8%; 76.9% retained n=22)
- **~22% regained** vs. **~60-65% literature-projected** regain at 1 year[1]
- **33% (5 of 15) continued to lose weight** past GLP-1 discontinuation

Prevention of Weight Regain with Revita Post-GLP-1 Discontinuation



[1] Budini *et al.*, eClinicalMedicine. 2026;93:103796

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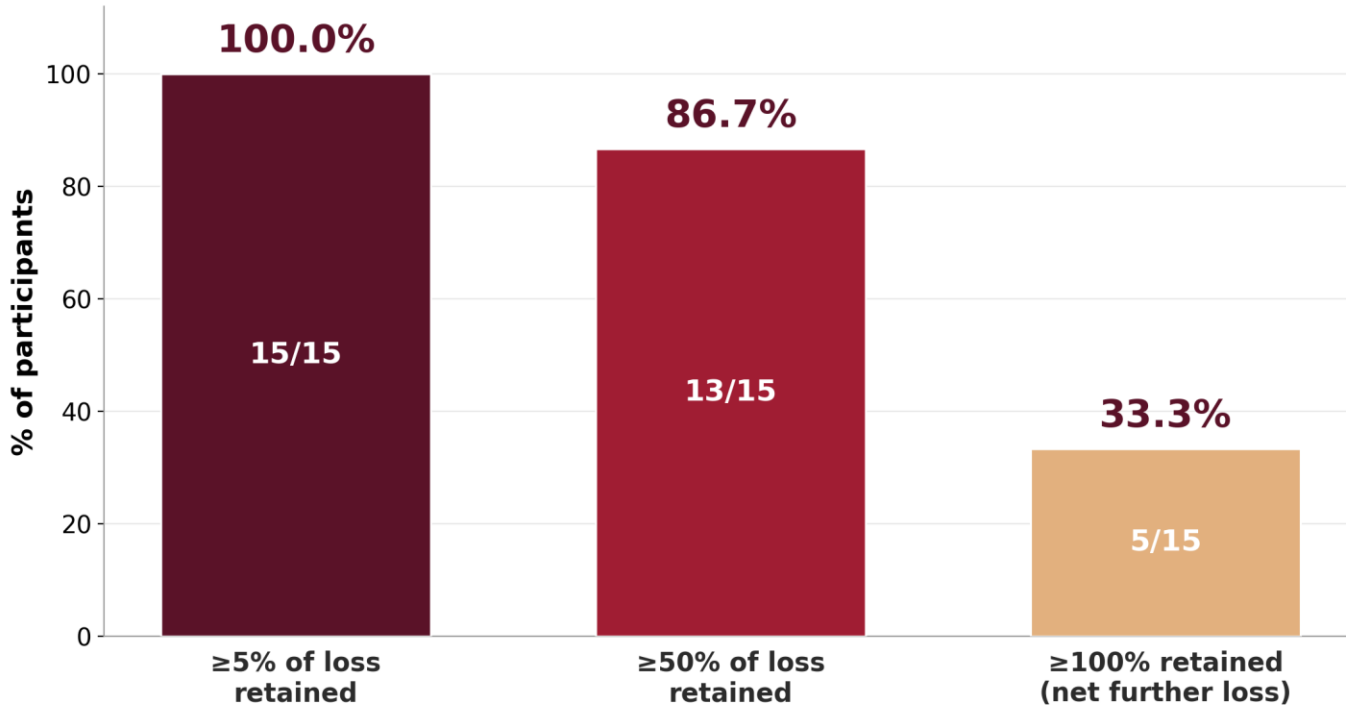
100% of REVEAL-1 Completers Hit the REMAIN-1 Pivotal Co-Primary Threshold at 52 Weeks

Responder Rates

- **100% retained at least 5% of GLP-1 induced weight loss** (co-primary endpoint in REMAIN-1 pivotal study)
- **87% retained at least 50% of GLP-1 induced weight loss** (industry clinical success threshold[1])
- **33% lost additional weight** at one year after discontinuing GLP-1 drugs
- Across this cohort, ablation length clustered narrowly around its median ablation length (16cm) and the study therefore does not have power to detect an ablation length dose response

100% Met Pivotal Co-Primary; 33% Lost Incremental Weight at 1 Year



1. Aronne LJ et al Nature Medicine 13 May 2026

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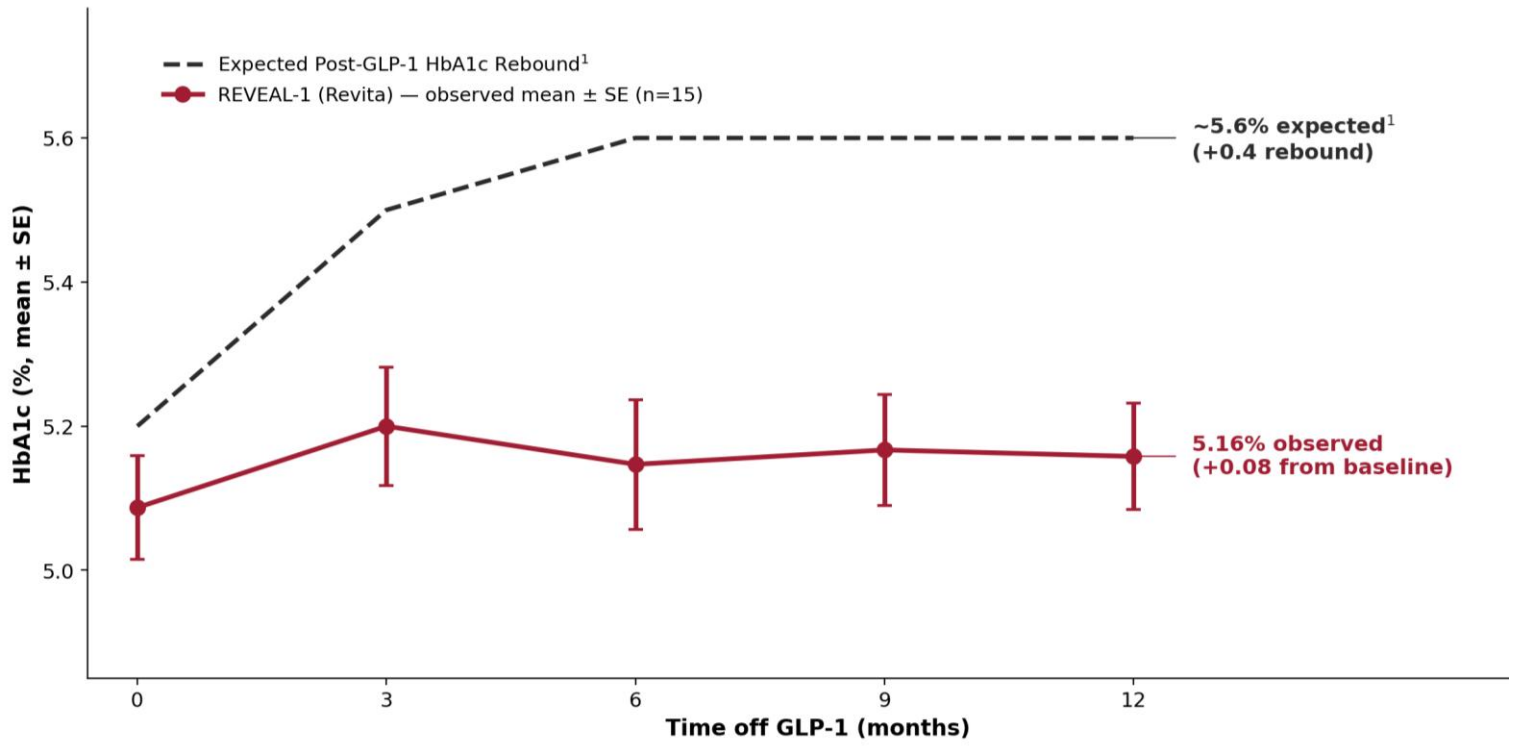
Sustained Glycemic Control Post-Revita

HbA1c held stable through one year off GLP-1

Glycemic Stability

- **HbA1c held flat at 5.16%** (+0.08 from baseline) through 52 weeks off GLP-1 which is within assay noise
- **No rebound observed** vs. ~0.4% increase expected post-GLP-1 trajectory[1]
- **Absence of glycemic deterioration** despite discontinuation of GLP-1

HbA1c change (%)



1. Wilding et al. Diabetes Obes Metab. 2022 Aug;24(8):1553-1564. GLP-1=glucagon-like peptide-1, HbA1c= hemoglobin A1c, SEM=standard error of the mean

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Excellent Safety and Tolerability Profile

No change to treatment emergent adverse events since last update

- No treatment-emergent serious adverse events related to device or procedure
- No TEAE-related study discontinuations
- No TEAE in long-term follow up
- Compelling safety and tolerability profile is consistent with prior Revita clinical experience

Table 2: Treatment-Emergent Adverse Events*

n=22	Patients, n (%)	Duration (days post-Revita)
Grade ≥III TEAEs	0 (0)	N/A
Grade II TEAEs	0 (0)	N/A
Grade I TEAEs	8 (36)	1-5
Sore Throat	4 (18)	1-5
Bloating	2 (9)	2-3
Swollen, blistered lips	2 (9)	5
Nausea	2 (9)	1-4
Vomiting	1 (5)	1
Diarrhea	1 (5)	4
Abdominal pain and bloating	1 (5)	5
Inflammation to face lips and throat	1 (5)	5

Clavien-Dindo Classification[1]: Standardized FDA recommended system for TEAE grading: Grade I: minor, any deviation from normal course without requiring treatment; Grade II: requiring treatment; Grade III: requiring surgical, endoscopic, radiologic intervention; Grade IV: Life-threatening, requiring ICU; Grade V: Death

*Related TEAEs are defined as definitely or probably related to the device and or procedure.

1. Dindo *et al.* Annals of Surgery 240(2):p 205-213, August 2004. TEAE= treatment-emergent adverse event.

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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 Cohort

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

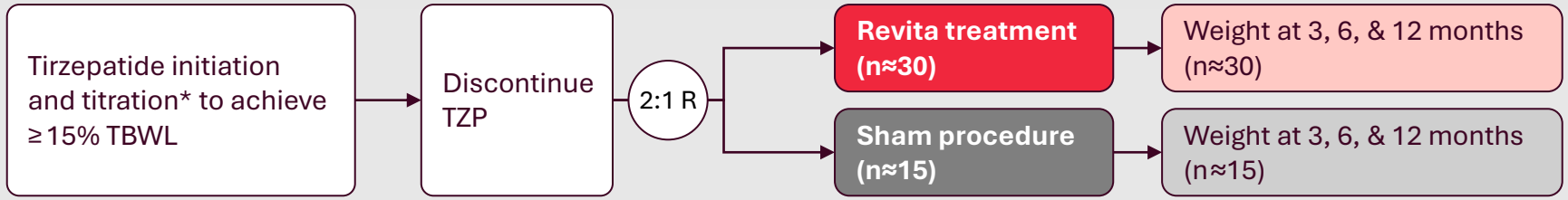
Study design

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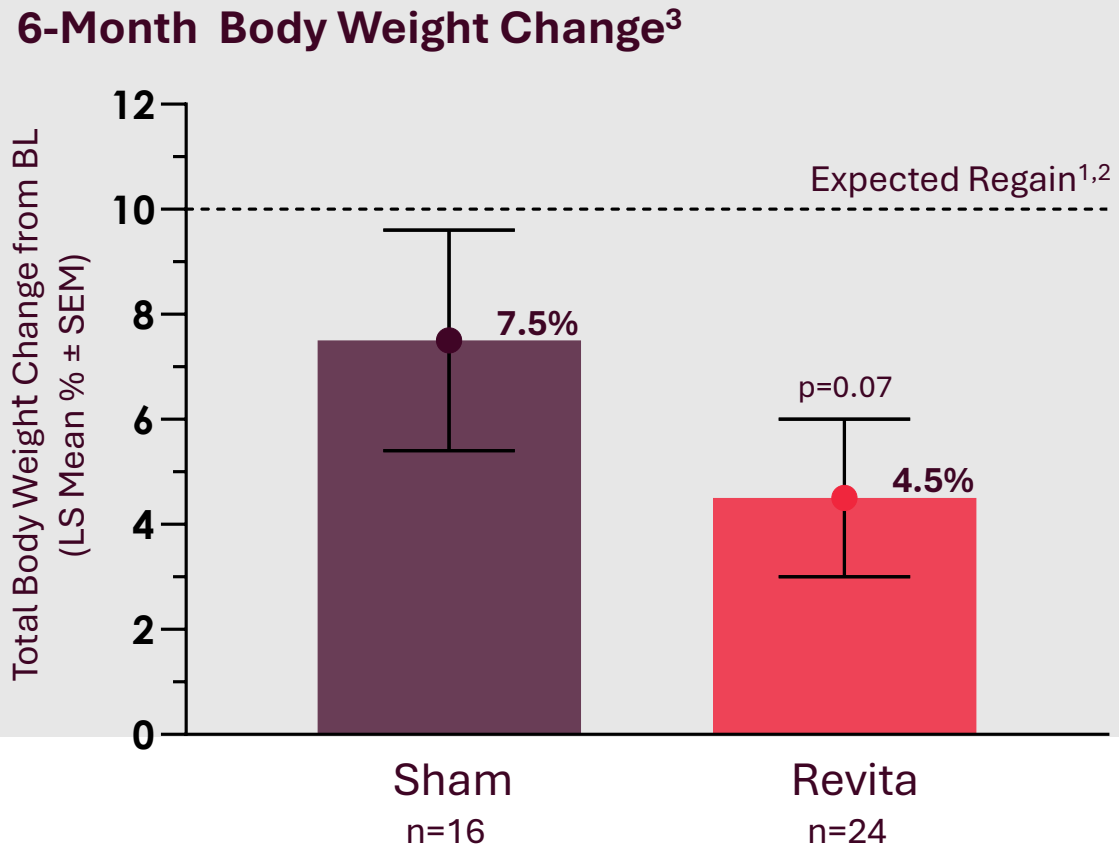
REMAIN-1 midpoint cohort confirms Revita activity and informs pivotal execution

- Revita reduced post-tirzepatide weight regain vs. sham at 6 months (p=0.07, n=40[3])
- Pilot study provides confidence in ongoing pivotal study effect size and durability
  - Dose-response identified (consistent with prior Revita studies in T2D)
  - Responder population identified (high GLP-1 responders at greatest risk of weight regain)



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; GLP-1, glucagon-like peptide-1; LS, least-squares; SEM, standard error of the mean.

FRACTYL health

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

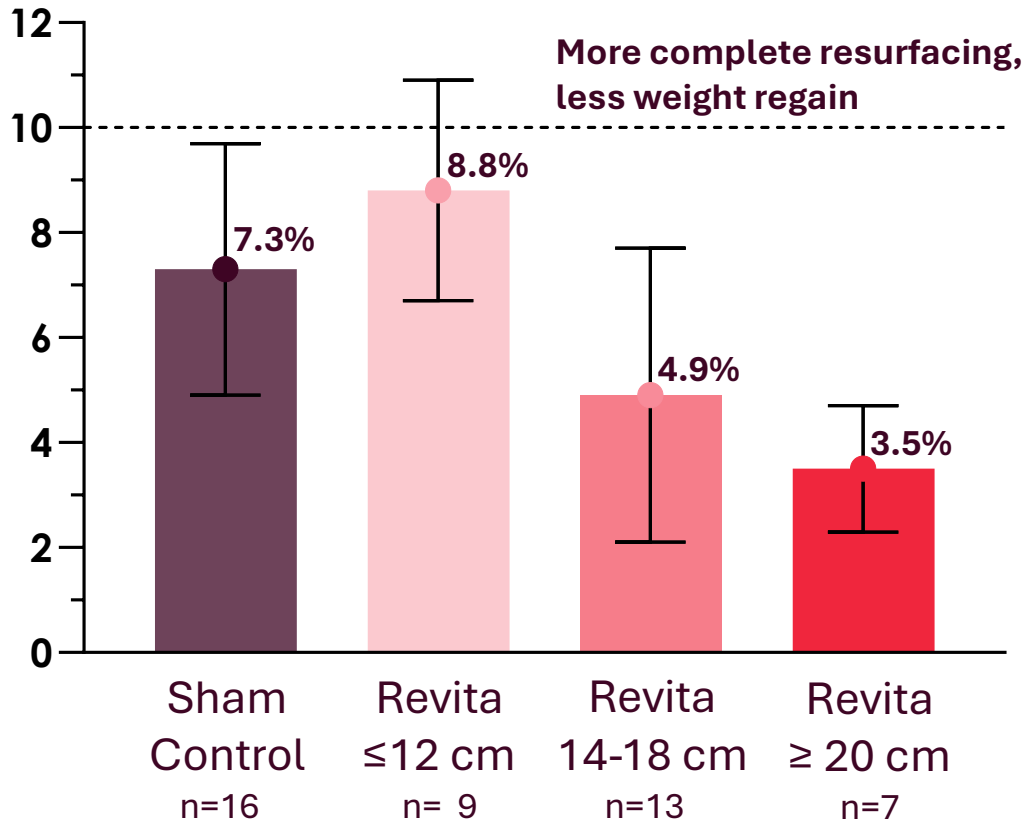
FRACTYL health

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.

FRACTYL health

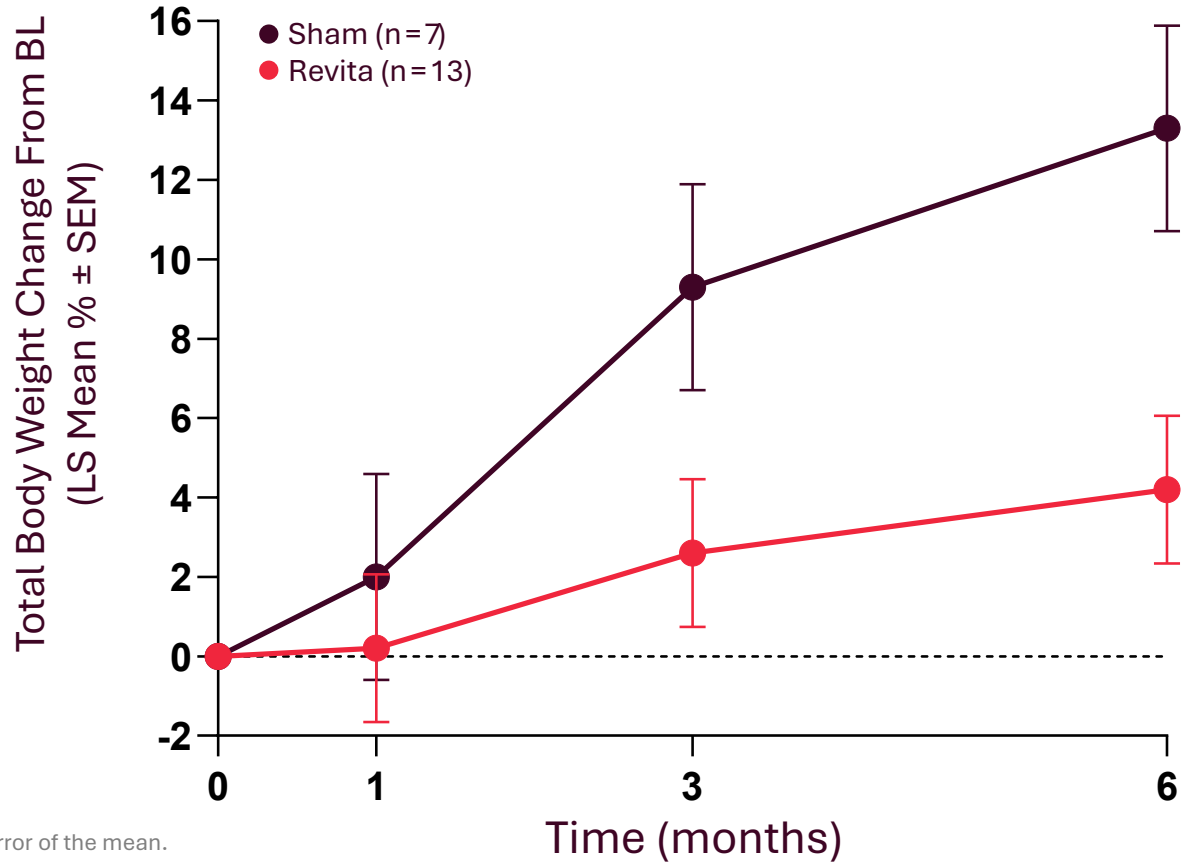
Patient selection: Revita effect is largest and growing in those who need it the most[1]

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

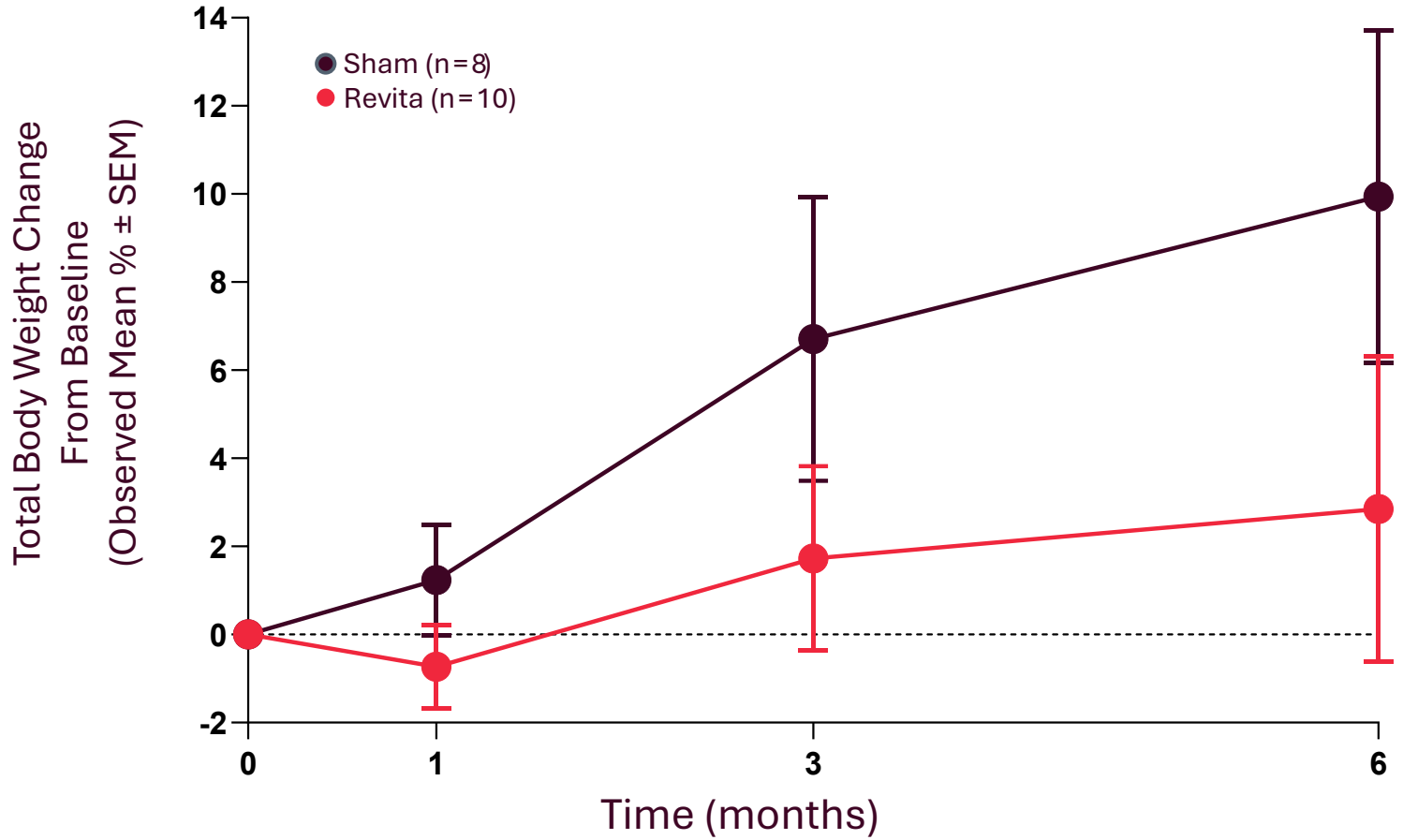


[1]Participants with run-in weight loss above a median ~ 18%.
Abbreviations: BL, baseline; GLP-1, glucagon-like peptide-1; LS, least-squares; SEM, standard error of the mean.

FRACTYL health

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

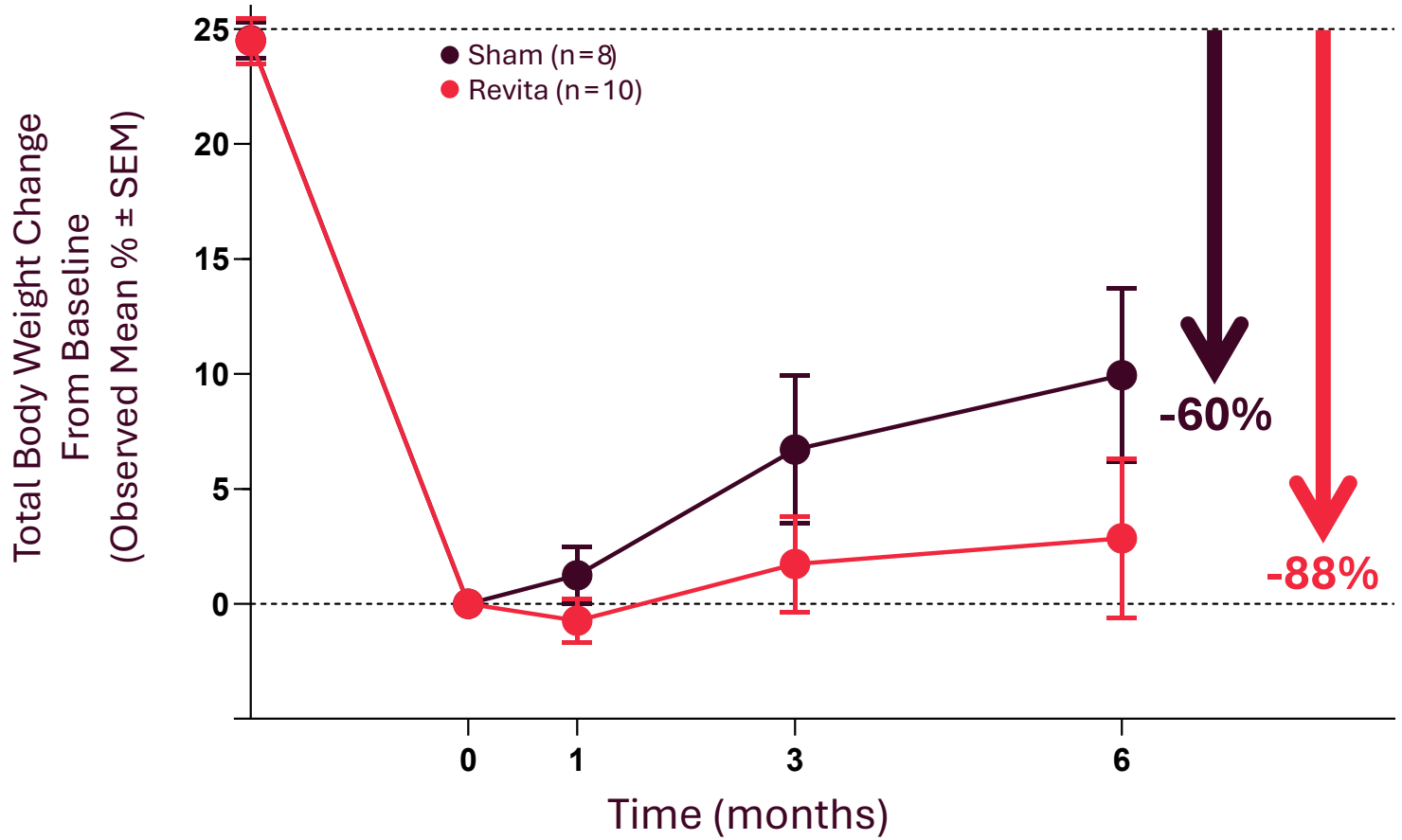
Revita-treated participants experienced only 2.9% weight regain at six months, compared to 9.9% in the sham arm in this optimized patient cohort

[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.

FRACTYL health

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.

FRACTYL health

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

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

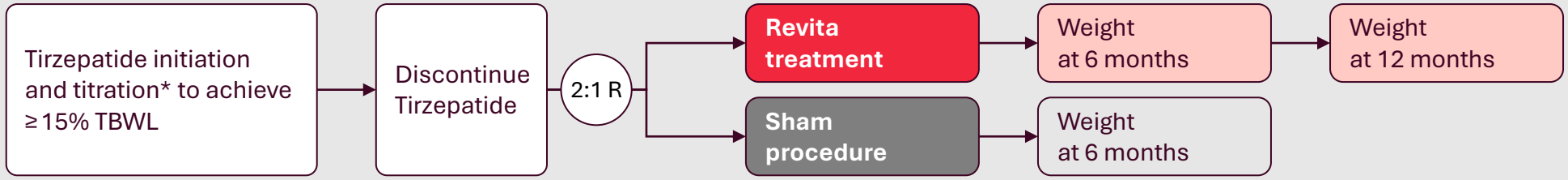
Study design

- 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]

- **Complete randomizations:** Feb '26
- **Topline 6-month pivotal data:** Early Q4 '26
- **Potential De Novo marketing application submission:** Late 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.

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

[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. FDA pre-submission feedback is advisory and non-binding, and there is no assurance that FDA will accept a De Novo marketing application submission or that the Revita DMR System will receive marketing authorization

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.

FRACTYL health

US regulatory and reimbursement alignment

Leveraging well-understood FDA Breakthrough and CMS TPT timelines

FDA Breakthrough Device Designation

Initial US Reimbursement with Category III CPT Code and CMS TPT Payment

FDA Breakthrough Device designation and CMS TPT profile may support early US commercialization at hospital-based Centers of Excellence (COEs), if approved

Timing subject to regulatory, CMS and AMA review cycles. [1]TCET (Transitional Coverage of Emerging Technologies) represents potential upside and not required for launch.
Abbreviations: AMA, American Medical Association; CMS, Centers of Medicare and Medicaid Services; COE, centers of excellence; CPT, Current Procedural Terminology; FDA, Food and Drug Administration; TPT, Transitional Pass-Through. FDA pre-submission feedback is advisory and non-binding, and there is no assurance that FDA will accept a De Novo marketing application submission or that the Revita DMR System will receive marketing authorization

FRACTYL health

Targeted and efficient commercial model at Revita Centers of Excellence if approved

Candidate Sites for Revita Launch

Revita Midpoint & Pivotal Sites

- Delivered in endoscopy suites (~ 2,000–4,000 endoscopy suites across the U.S. alone)
- Planned COE launch with a targeted sales force in centers of excellence (likely ~50 centers in year 1, with already established relationships at clinical centers and Everself)
- Estimated capacity of ~1,200 procedures annually per center once fully operational
- Procedure has a short learning curve (typically mastered within ~4 cases)

Capital-efficient model may leverage existing infrastructure

Abbreviation: CMS, Centers of Medicare and Medicaid Services; COE, centers of excellence; CPT, Current Procedural Terminology

FRACTYL health

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.

FRACTYL health

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**

3

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

FRACTYL health

Durable weight maintenance creates a substantial, procedure-based market opportunity

$3-5B Market penetration opportunity[1]

800K GLP-1 patients already flowing through GI suites each year[1]

~ 60% Procedure volume[2] from top 250 US centers[2]

>1M Annual procedures at peak[1]

Recurring, high-margin revenue

+80% gross margin: Single-use catheter

~15% gross margin: One console per suite

~1,200 procedures[2] per center per year

Revita is for investigational use only in the United States. Revita has a CE mark in the EU/UK.

[1]Fractyl estimates. [2]Based on market research commissioned by Fractyl Health.

FRACTYL health

Rejuva®

Rejuva®: Advancing targeted pancreatic gene therapy for durable metabolic control

←PROPRIETARY TARGETED INTRAPANCREATIC DELIVERY SYSTEM

←"SMART GLP-1" GENE THERAPY

Rejuva is an investigational preclinical asset which has received Clinical Trial Authorization in the Netherlands. Rejuva is currently under review for clinical research in additional countries in the EU and AUS. It has yet to be assessed by the FDA.

Reimagining gene therapy economics for metabolic disease

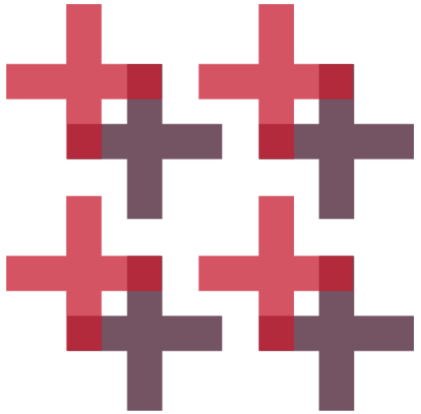
Large patient population

~27M with T2D in US[1]
~100M with Obesity in US[2]

Low cost of goods

< $10K COGs per patient enabled by local delivery

High economic value



~$10K price per year ICER price benchmark[3]

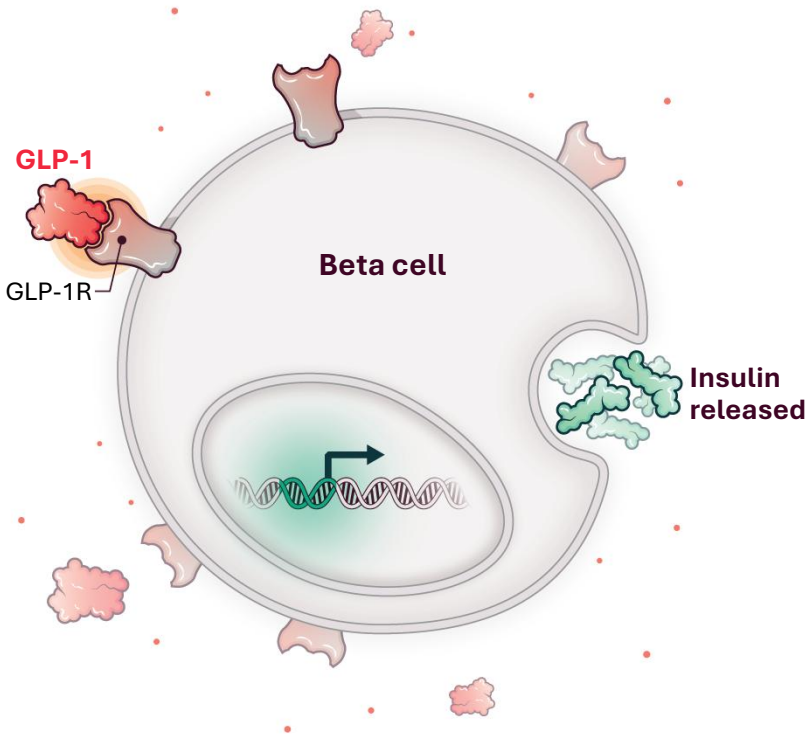
[1]CDC National Diabetes Statistics Report 2026, [2]CDC NCHS Data Brief No. 508. Obesity and Severe Obesity Prevalence in Adults: United States, August 2021– 2023, [3]ICER Medications for Obesity Mgmt 2022.

FRACTYL health

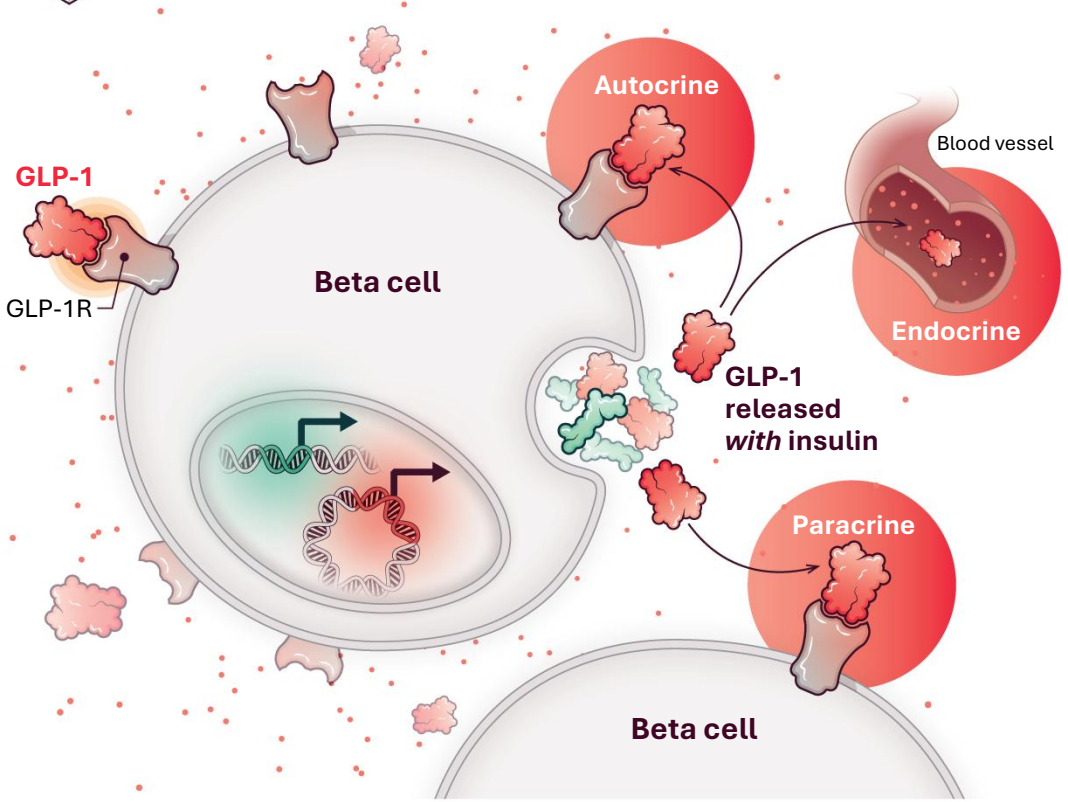
RJVA-001 for T2D

Nutrient-responsive “Smart” GLP-1 via intrapancreatic gene therapy

Type 2 Diabetes
Insufficient pancreatic GLP-1 signaling[1]



Rejuva
Nutrient-responsive GLP-1 expression



Product design

- Proprietary targeted endoscopic delivery
- AAV9 vector
- Insulin promoter
- Human GLP-1 transgene

Smart GLP-1 differentiation

- Single intrapancreatic administration
- Designed to transduce pancreatic islets
- Expression regulated by the insulin promoter
- Enables nutrient-responsive GLP-1 expression

Abbreviations: GLP-1, glucagon-like peptide 1.

FRACTYL health

The Rejuva approach is differentiated from GLP-1 drugs

Intrapancreatic, nutrient-responsive: “Smart GLP-1” gene therapy

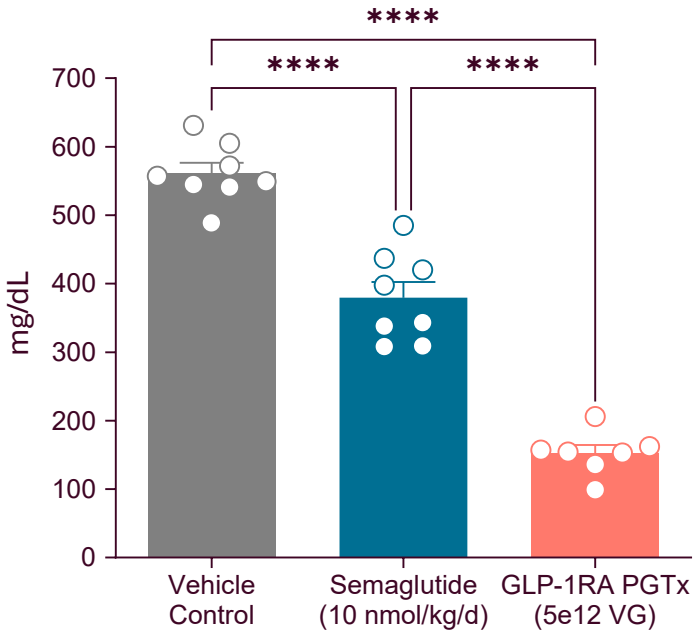
Feature	Rejuva	GLP-1 Drugs
MOA	Simulates endogenous GLP-1 secretion kinetics	Exogenous, pharmacologic activation of GLP-1R
GLP-1 Biodistribution	High pancreas and portal exposure with limited systemic exposure	Systemic, with widespread receptor activation
Safety/Tolerability	Better GI tolerability expected	Broad CNS activation with associated nausea, vomiting risk
Regulation	Nutrient-responsive expression and secretion	Chronic high levels independent of physiologic need
Durability	Long-term (AAV9)	Short-term (while adherent/persistent)
Potency	Potentially superior to SOC	SOC

Abbreviations: AAV, adeno-associated virus; CNS, central nervous system; GI, gastrointestinal; GLP-1, glucagon-like peptide-1; GLP-1R, GLP-1 receptor; MOA, mode of action; SOC, standard of care.

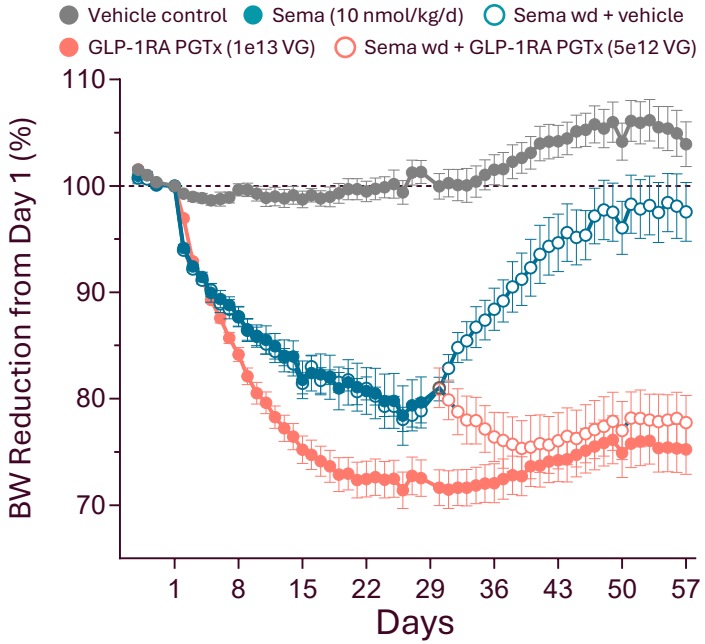
FRACTYL health

Potent efficacy in T2D & obesity mouse models with no toxicity observed in large animal model

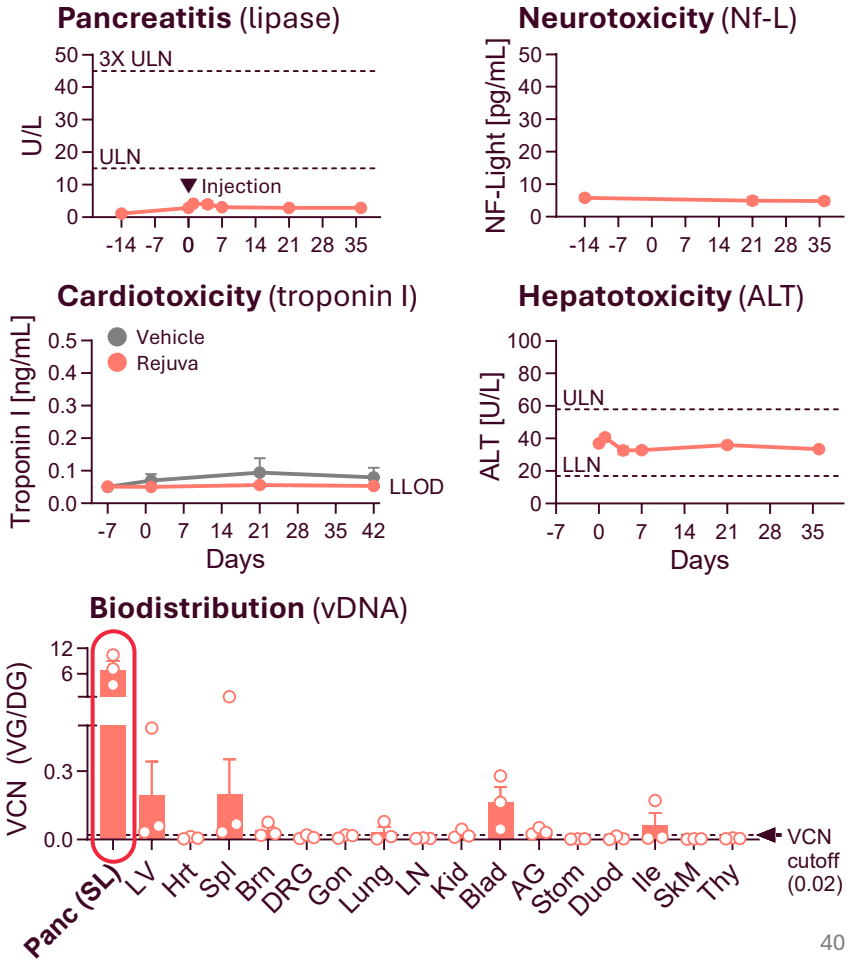
Glucose-lowering activity in *db/db* mouse model[1]



Sustained weight loss in DIO mouse model[2]



No toxicity observed in Yucatan pig model[3]



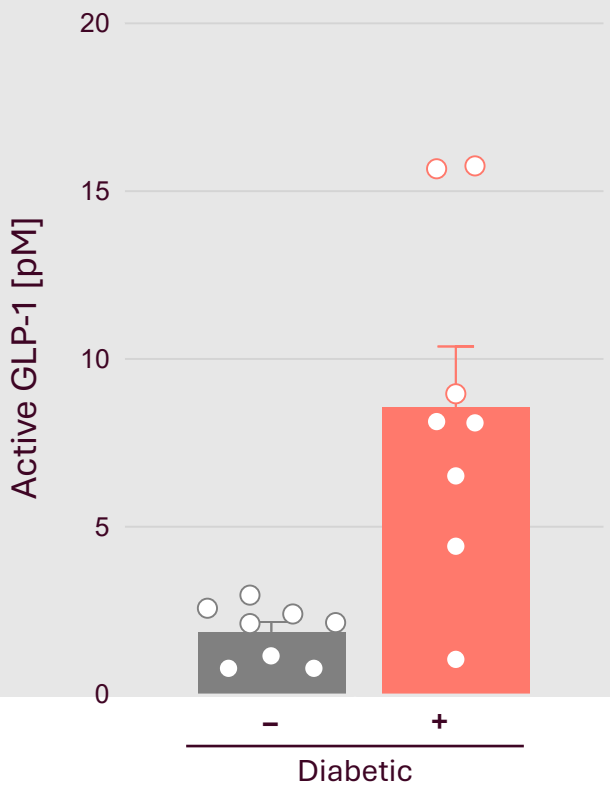
One-Way ANOVA, post-hoc Tukey Test: ****: P<0.0001. [1]Mean ± SEM shown; n=7-8 per group, day 29 shown, Rajagopalan et al. DDW 2024 oral presentation. Abstract no. 4029196. [2]Mean ± SEM shown; n=5-10 per group. Fitzpatrick et al. WCIRDC 2023 oral presentation. Abstract no. 0077. [3]Fitzpatrick et al., ASGCT 2025 oral presentation. Data are mean ± SEM, n=2-6 pigs per group. Abbreviations: AG, adrenal gland; ALT, alanine transaminase; Blad, bladder; BW, body weight; Brn, brain; DIO, diet-induced obesity; DRG, dorsal root ganglion; GLP-1RA, glucagon-like peptide 1 receptor agonist; Gon, gonad; Hrt, heart; Ile, ileum; Kid, kidney; LLN, lower limit of normal; LN, lymph node; LV, liver; NF-L, neurofilament light chain; Panc, pancreas; PGTx, pancreatic gene therapy; SkM, skeletal muscle; SL, single-lobe; Spl, spleen; Stom, stomach; Thy, thyroid; ULN, upper limit of normal; VCN, vector copy number; VG/DG, vector genome/diploid genome; wd, withdrawal.

FRACTYL health

Robust efficacy without high systemic GLP-1 exposure

May be less likely to cause tolerability issues

Rejuva active GLP-1 (circulating)[1]



Circulating active GLP-1 Levels[2]

Modality	Levels	Tolerability
Physiological	<5 pM	✓
DPP4 inhibition	~10 pM	✓
Rejuva GLP-1	**10-20* pM**	**TBD in FIH clinical study**
Roux-en-Y gastric bypass	~20 pM	✓
GLP-1RA drugs	50-150 pM	✗

[1]Fitzpatrick et al., ASGCT 2025 oral presentation. Data are mean ± SEM, n=8 per mice group from day 44 post IP AAV injection [2]Smits and Holst et al. Diabetes Metab Res Rev. 2023 Nov;39(8):e3699. *Levels detected at highest Rejuva dose tested in db/db mice. Circulating GLP-1 levels in db/db mice were more than twice those of healthy controls (db/+) (data on file). Abbreviations: DPP4, dipeptidyl peptidase-4; FIH, first-in-human; GLP-1, glucagon-like peptide 1; GLP-1RA, GLP-1 receptor agonist; TBD, to be determined.

FRACTYL health

RJVA-001 planned FIH dose escalation study design

Aligned with regulators to assess safety, tolerability, PK, preliminary PD

Patient population

- Adults with T2D and obesity and preserved pancreatic function on GLP-1RA therapy
- HbA1c 7-10%; BMI 30-40 kg/m^2
- Not yet on insulin therapy
- No prior AAV9 exposure

Endpoints

- Primary: Safety and tolerability across dose levels
- Secondary: PK profiling, exploratory PD biomarkers (blood glucose, metabolic markers)

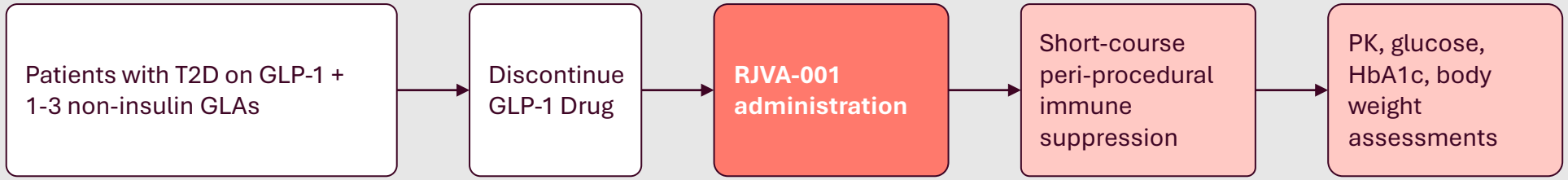
Study design

- GLP-1 drug therapy washout prior to therapy
- Sequential dose cohorts receiving escalating single doses of RJVA-001

Anticipated milestones[1]

- **FIH dosing, subject to site activation, and preliminary data:** H2 2026
- **Australian regulatory feedback on CTA:** Q3 2026

Study design: Ph 1/2 open-label, dose escalation



[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: AAV, adeno-associated virus; CTA, clinical trial application; FIH, first-in-human; GLP-1, glucagon-like peptide 1; PD, pharmacodynamics; PK, pharmacokinetics; T2D, type 2 diabetes.

FRACTYL health

FRACTYL health

Rejuva

Nutrient-responsive GLP-1 via intrapancreatic gene therapy

Uses Fractyl's intrapancreatic system
for local pancreatic gene delivery

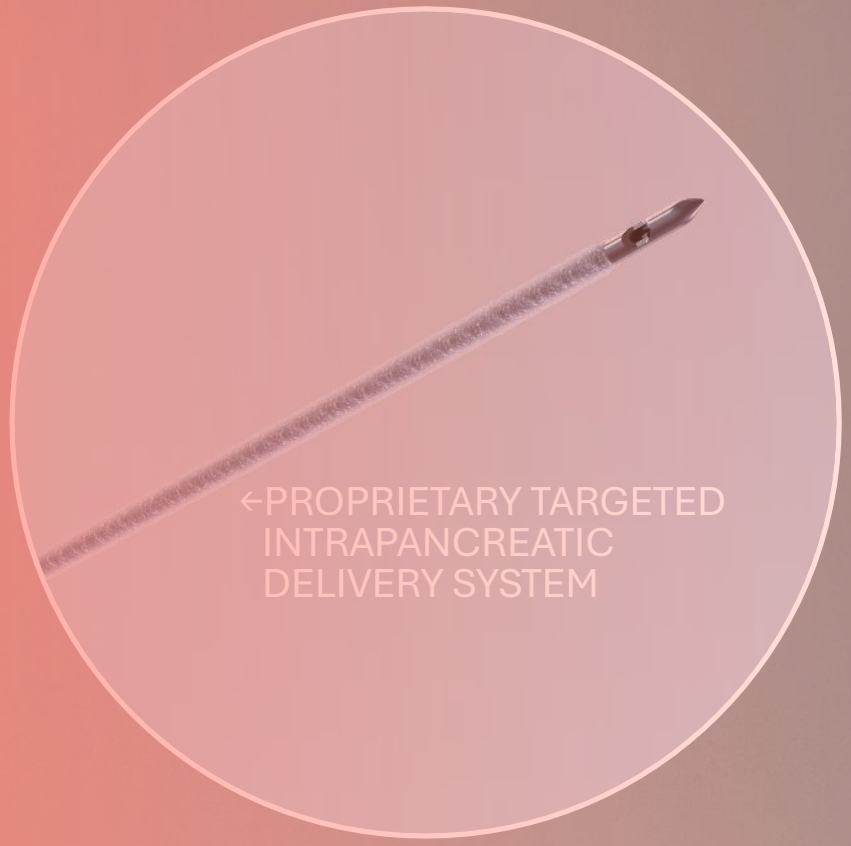
Designed for improved potency & tolerability
vs. systemic GLP-1 drugs

RJVA-001 outperforms chronic semaglutide
in *db/db* & DIO mouse T2D & obesity models

CTA authorized in NL
CTA submitted in AUS

Anticipate 1st patient dosing
& preliminary data in H2 2026
Assuming site activation

RJVA-002 smart GIP/GLP-1 demonstrated ~30% TBWL
achieved in hGIPR DIO mice



Rejuva is an investigational preclinical asset which has received Clinical Trial Authorization in the Netherlands. Rejuva is currently under review for clinical research in additional countries in the EU and AUS. It has yet to be assessed by the FDA.

Abbreviations: CTA, clinical trial application; DIO, diet-induced obese; GLP-1, glucagon-like peptide 1; hGIPR, human GIP receptor; T2D, type 2 diabetes; TBWL, total body weight loss.

Robust IP estate covering Revita & Rejuva

Strategic platform for long-term value and optionality

Global footprint[1]

35	Active patent families
100+	Patents issued globally
36	Patents issued in the US
70+	Pending patent applications

- **Protection across key jurisdictions** including: U.S., EU, China, Japan, Canada, Korea
- Foundational patents with **priority dates from 2011**
- IP is home-grown; **no in-licensing**

Diverse Protection

Issued claims cover devices, systems, methods of treatment

IP Portfolio focus includes:

- **Methods** of treating critical region of duodenum
- **Devices** for treating target tissue in the duodenum
- **Gene therapy** infusion devices, methods, constructs

Leadership in thermal & non-thermal DMR ablation

Proactive continuation strategy extends protection to improvements & **emerging technologies**

[1]As of March 2026.

FRACTYL health

Near-term clinical catalysts and value-creation through to potential De Novo marketing application submission in Q4 2026

Revita *Outpatient endoscopic procedural therapy*

2026 Key Anticipated Milestones[1]

Indication	Program	Recent accomplishments	Q2	Q3	Q4
Weight Maintenance	REVEAL-1 Cohort (Open Label)	✓ Durable 6-mo data shared (Dec '25)	✓ 1-year data		
	REMAIN-1 Midpoint Cohort	✓ Positive 6-month randomized data (Jan '26)		1-year data	
	REMAIN-1 Pivotal Cohort	✓ Completed randomization (Feb '26)			**Topline 6-mo randomized data & potential De Novo marketing application submission**

Rejuva *Local AAV-delivered pancreatic GLP-1 gene therapy*

Indication	Program	Research	Lead selection	IND/CTA enabling	Phase 1	2026 Key Anticipated Milestones[1]
Type 2 Diabetes	RJVA-001	**CTA authorized in Netherlands**				H2: FIH dosing, subject to site activation, and preliminary data
Obesity	RJVA-002	**Candidate nominated**				

[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: CTA, clinical trial application. FIH, first-in-human.

FRACTYL health

Leadership team & BOD

Experience spanning biotechnology and medical technology

Harith Rajagopalan, MD, PhD
Co-Founder & CEO

Jay Caplan
Co-Founder, President, & CPO

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Sr VP of Regulatory, Quality, & Clinical

Len Rosberg
VP of Manufacturing

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Thank you

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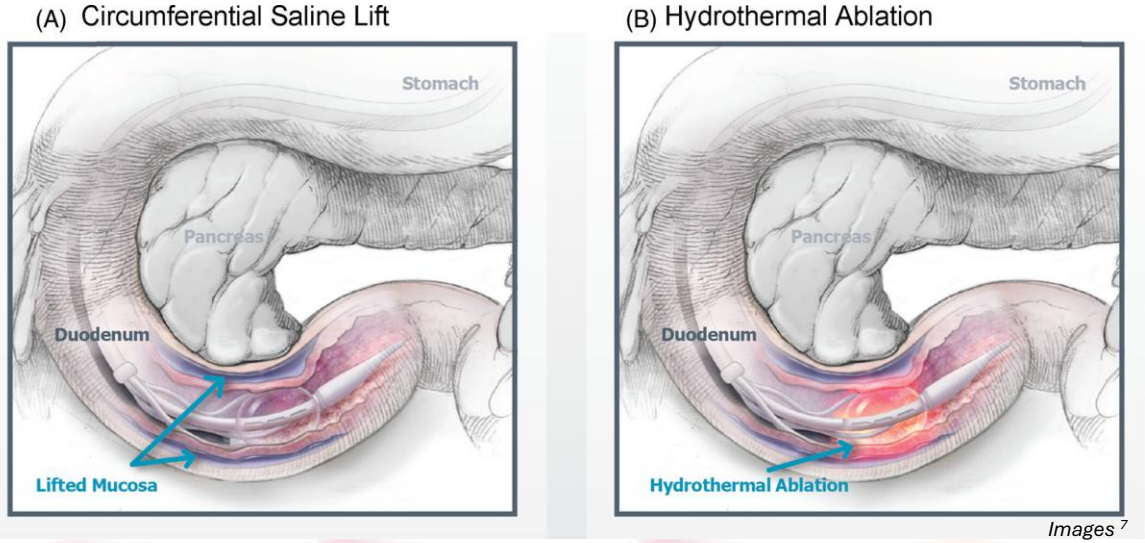
NASDAQ:GUTS

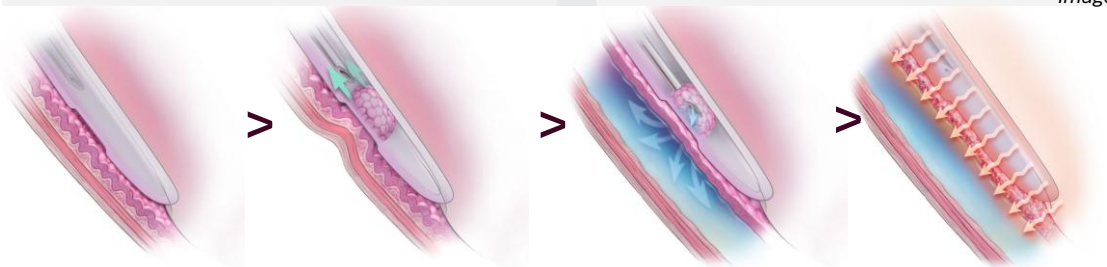
Revita Targets Duodenal Dysfunction

Potentially first-in-class procedural therapy designed to durably reset metabolism[1-4]

Revita designed to achieve targeted mucosal ablation without damaging deeper structures



Images [7]



Catheter engages tissue > **Vacuum pulls mucosa into catheter ports** > **Saline injection to submucosa** > **Hydrothermal ablation**

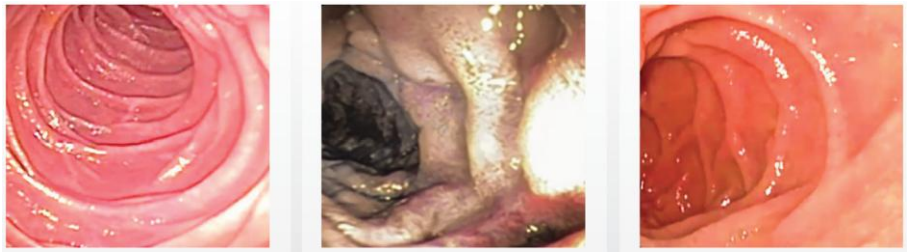
FDA Breakthrough Device designation for post-GLP-1 weight maintenance in obesity

Scalable intervention: Outpatient procedure conducted via straightforward upper endoscopy

Designed with safety in mind: Engineered to deliver therapeutic ablation without compromising safety

Refined training program: ½ day pre-procedure training, clinical proficiency < 4 cases

Normal mucosa by one-month post-Revita[5]



Prior to DMR | **Ablated Duodenum** | **1mo post-procedure**

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Revita is for investigational use only in the United States. Revita has a CE mark in the EU/UK 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. 7. Images from Hoyt et al. Diabetes Obes Metab 2024; 1-12.

Duodenal targeting: Three converging eras of evidence for durable metabolic benefit

Era 1: Bariatric surgery

Revealed metabolic impact of duodenal exclusion

- Surgical bypass of the duodenum produces rapid, durable improvements in weight and glycemic control
- Benefits often occur immediately after duodenal exclusion, implicating gut-driven signaling rather than restriction alone

Era 2: Foundational biology

Established duodenal mucosa as a metabolic control point[1-3]

- Nutrient sensing in the duodenal mucosa modulates gut-brain signaling, insulin sensitivity, and energy balance
- Diet-induced mucosal changes are associated with increased nutrient uptake and impaired signaling

Era 3: Revita clinical studies

Translates this biology into a scalable clinical intervention[4-11]

- Targeted mucosal ablation followed by regeneration is associated with sustained metabolic improvements
- Durable effects observed across multiple Revita clinical studies and real-world cohorts, totaling hundreds of patients

Across surgical, biological, and clinical evidence, targeting the duodenum has consistently been associated with durable metabolic benefit

[1]Habegger, et al. *Gut* 2014. [2]Yang et al. *Photodiagnosis Photodyn Ther*. 2023 Dec:44:103733. [3]Nie et al. *World J Diabetes*. 2025 Mar 15;16(3):102277. [4]Haidry R, et al. *GIE* 2019. [5]van Baar ACG, et al. *Endosc Int Open*. 2020 8:E1683-E1689. [6]Rajagopalan H, et al *Diabetes Care*. 2016 39:2254-2261. [7]van Baar ACG, et al. *Gut*. 2020 69:295-303. [8]Mingrone G, et al. *Gut*. 2022 71:254-264. [9]van Baar ACG, et al. *Gastrointest Endosc*. 2021 94:111-120.e3. [10]van Baar, et al. *Diabetes Res. Clin. Pract.* 2022 184:109194. [11]Fractyl Health press release dated August 5, 2025.

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