



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

Corporate Presentation | 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.

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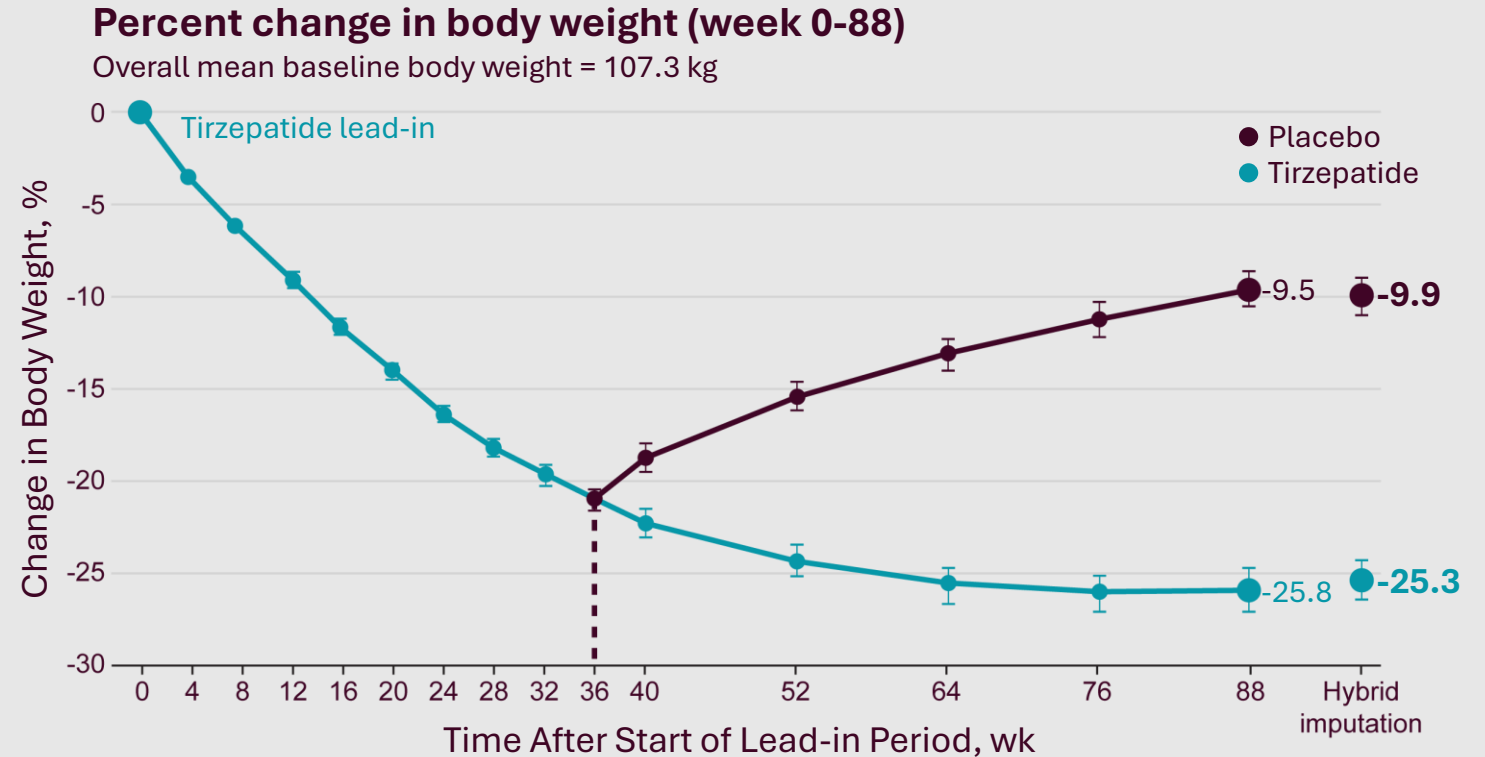
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GLP-1s unlocked weight loss, but durability remains unsolved

~30M U.S. Patients projected to use GLP-1s for obesity by 2035¹

~65% Patients with obesity discontinue before one year²

85% Patients regain lost weight after GLP-1 discontinuation³



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

Figure adapted from Lilly's SURMOUNT-4 study.³ ¹Morgan Stanley, Obesity Medications: The Broadening, Apr 24, 2025. ²Rodriguez, Patricia J., et al. *JAMA Network Open* 8.1 (2025): e2457349-e2457349. ³Aronne et al. *JAMA*. 2023 Dec 11;331(1):38-48. ⁴Revita 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.

Gut dysfunction is a root cause of obesity

Weight regain is biologically driven – not behavioral failure

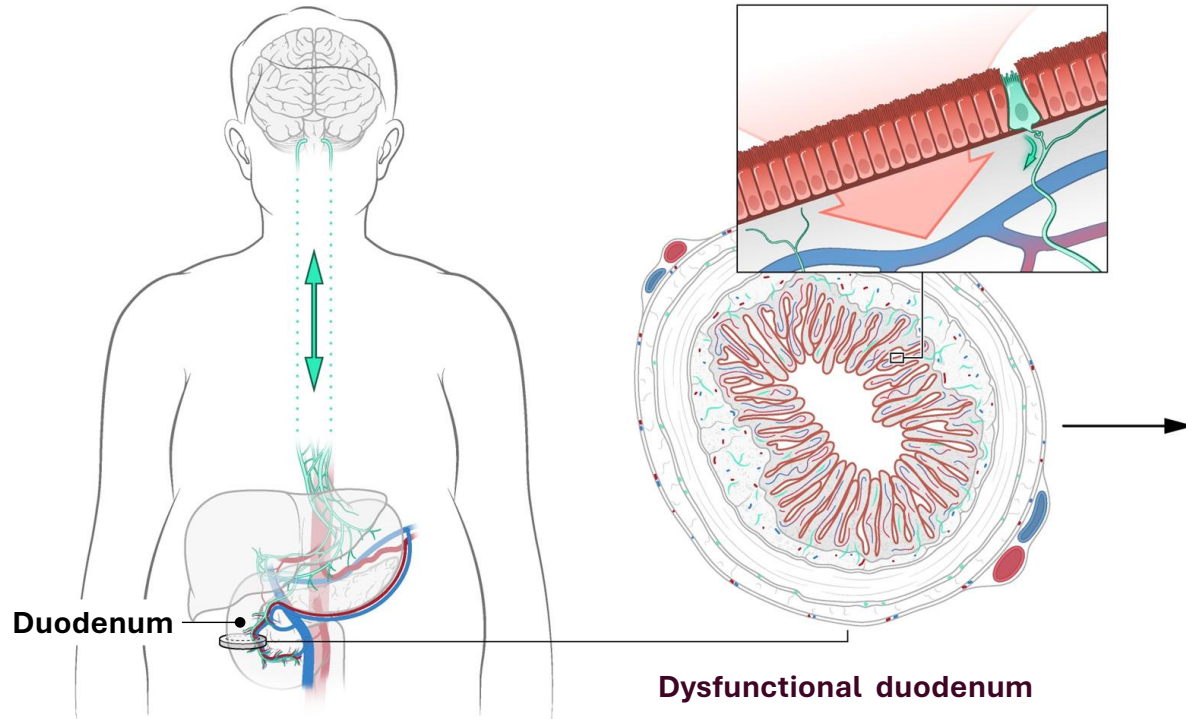
Nutrient signals from the duodenum travel via the vagus nerve to regulate hunger and metabolism¹

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 diabetes²

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



¹Kentish, Stephen J., and Amanda J. Page. "The role of gastrointestinal vagal afferent fibres in obesity." *The Journal of Physiology* 593.4 (2015): 775-786.

²Aliluev, 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[®]: Potential new backbone therapy in obesity

A one-time, < 1 hr 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.

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 Milestones¹

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	CTAs submitted				Q2: Regulatory feedback on CTAs H2: FIH dosing, subject to CTA authorization, and preliminary data
Obesity	RJVA-002	Candidate nominated				

¹These 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.



Revita[®]

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

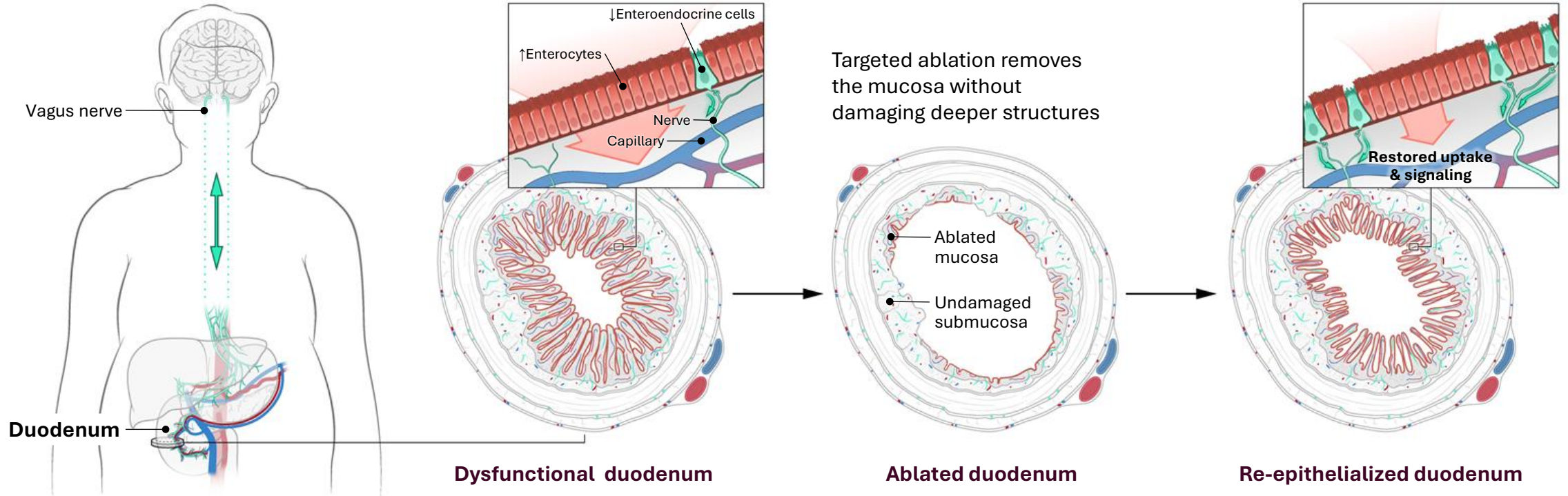
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The duodenal mucosa: A compelling target for durable metabolic control

Nutrient signals from the duodenum travel via the vagus nerve to regulate hunger and metabolism¹

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

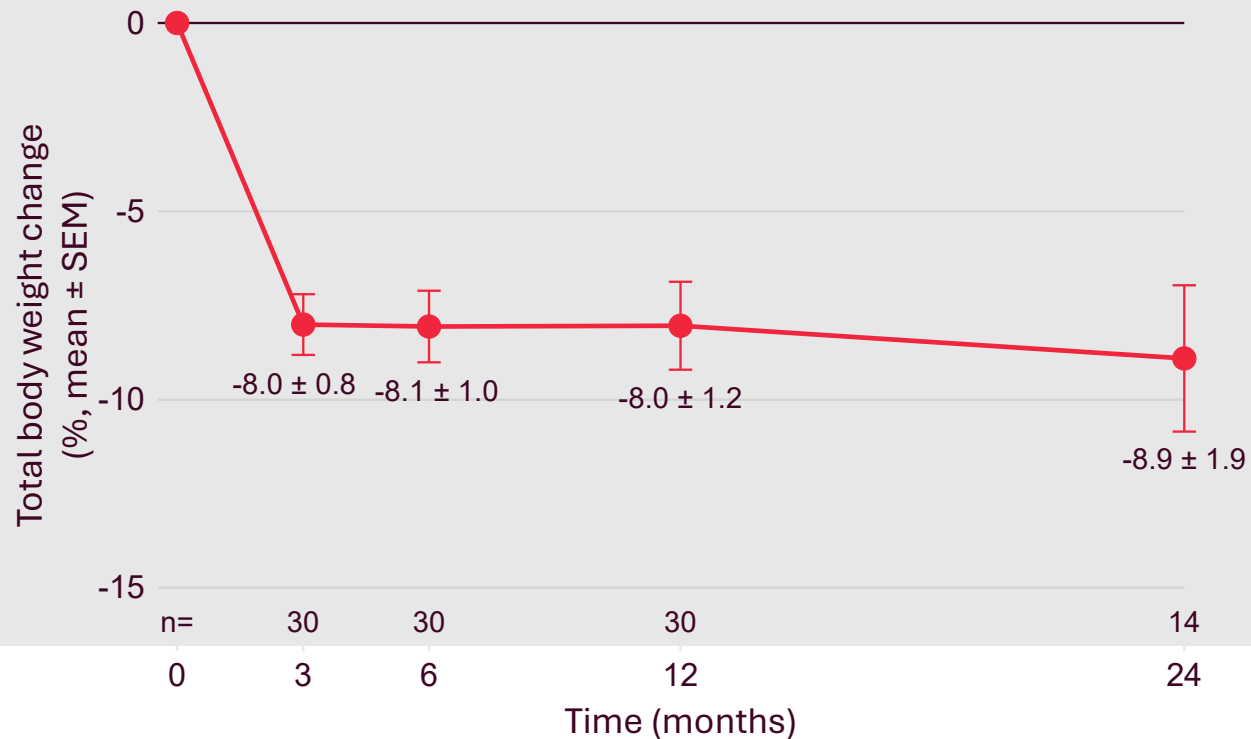



¹Kentish, Stephen J., and Amanda J. Page. "The role of gastrointestinal vagal afferent fibres in obesity." *The Journal of Physiology* 593.4 (2015): 775-786.


²Aliluev, Alexandra, et al. "Diet-induced alteration of intestinal stem cell function underlies obesity and prediabetes in mice." *Nature Metabolism* 3.9 (2021): 1202-1216.


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


~9% total body weight loss sustained through 2 years 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/m²), 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.



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

REMAIN-1 weight maintenance program

Stepwise validation through potential De Novo marketing application submission in late Q4 '26¹

	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	<ul style="list-style-type: none"> • Open-label 	<ul style="list-style-type: none"> • Tirzepatide run-in phase • Revita vs sham (2:1) 	<ul style="list-style-type: none"> • Tirzepatide run-in phase • Revita vs sham (2:1)
Participants	With obesity (BMI > 30 kg/m ²) prior to GLP-1 <u>and</u> ≥15% TBWL with GLP-1 drug	With obesity (BMI 30-45 kg/m ²) without T2D <u>and</u> GLP-1 drug naïve	With obesity (BMI 30-45 kg/m ²) without T2D <u>and</u> GLP-1 drug naïve
Anticipated milestones¹	<ul style="list-style-type: none"> ✓ 3-mo data: June '25 ✓ 6-mo data: Dec '25 • 1-yr data: Q2 '26 	<ul style="list-style-type: none"> ✓ 3-mo data: Sept '25 ✓ 6-mo data: Jan '26 • 1-yr data: Q3 '26 	<ul style="list-style-type: none"> ✓ Enrollment: Q2 '25 ✓ Randomization: Feb '26 • Topline 6-mo data: early Q4 '26 • Potential De Novo marketing application submission: late Q4 '26

¹These 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.

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
- $n \approx 20$ patients who need to or want to stop tirzepatide

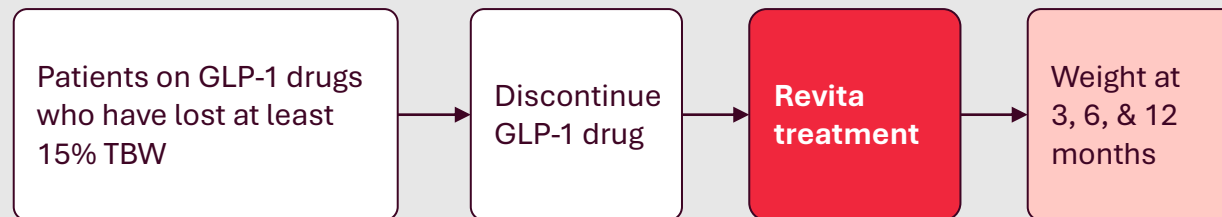
Primary endpoints

- 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



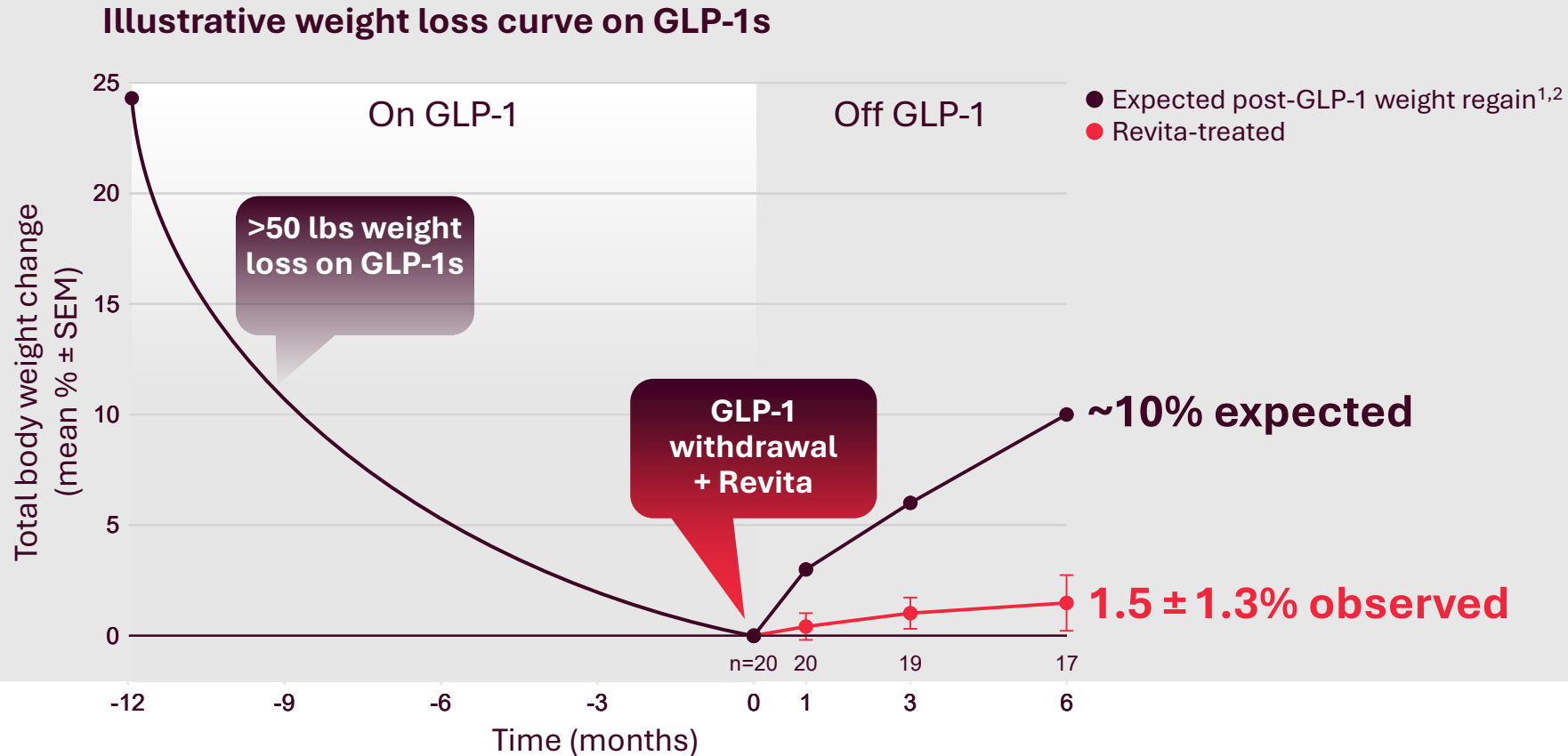
22 patients enrolled and treated with Revita

- **Strong technical success:** Consistent procedure performance (average ablation length ~ 16 cm)
- **High retention rate:** Only 3 of 22 (14%) withdrew or LTFU (compared to 23% LTFU in SURMOUNT-4 study¹)
- **Analyses:** 22 in safety cohort and 17 in efficacy cohort

¹Aronne 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.

Robust weight maintenance in open-label cohort

Stable weight trajectory observed 6 months after single Revita treatment



*GLP-1 weight loss from months -12 to 0 are illustrative based on average weight loss and time on medication in REVEAL-1 subjects.

¹Aronne et al. *JAMA*. 2024;331(1):38–48. doi:10.1001/jama.2023.24945. ²Wilding et al. *Diabetes Obes Metab*. 2022 Aug;24(8):1553-1564.

Abbreviations: GLP-1, glucagon-like peptide-1; SEM, standard error of the mean.

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/m²)
- GLP-1 naïve; no T2D
- n≈45

Efficacy endpoints

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

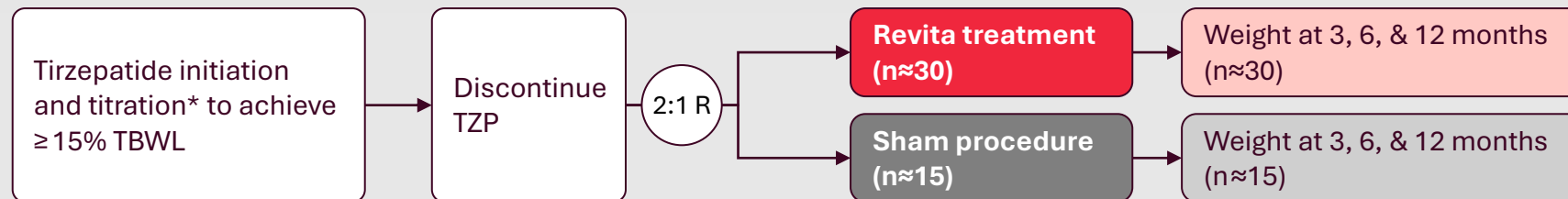
Study design

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

Anticipated milestones¹

- ✓ 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

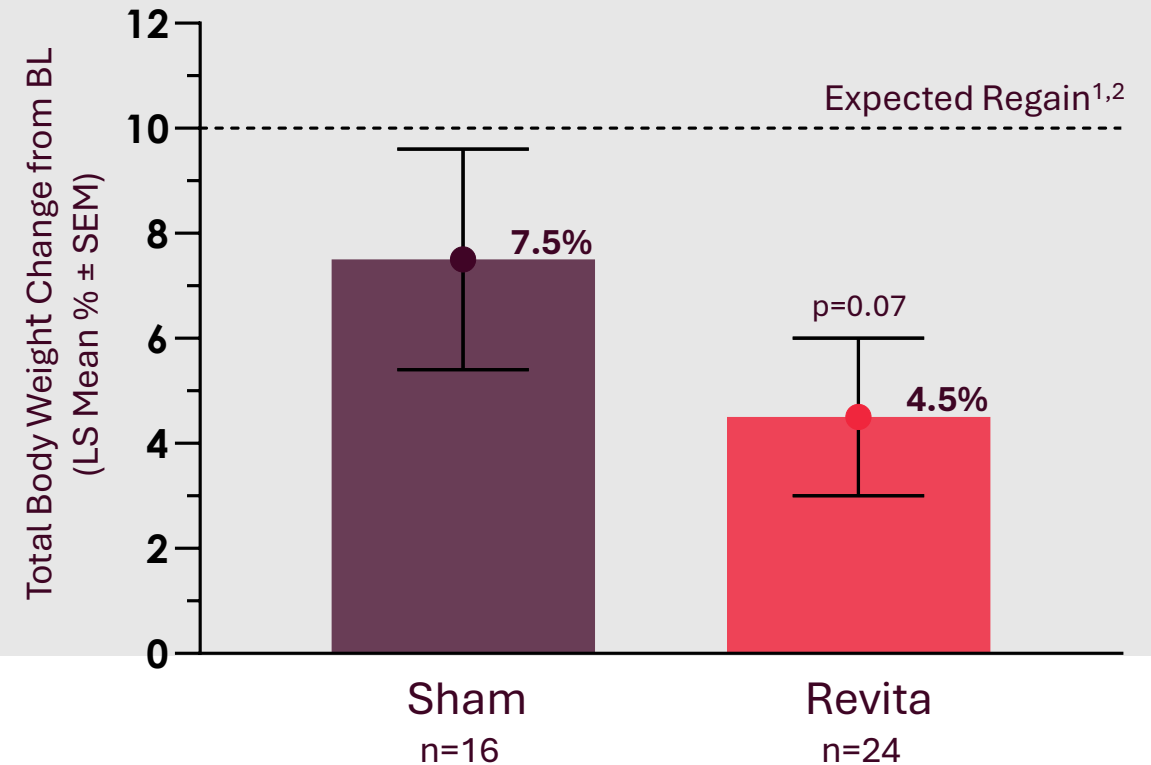
¹These forward-looking statements are based on management's current estimates and expectations. Refer to the latest disclosures filed with the SEC for a discussion regarding Risk Factors to these and other estimates and expectations. ²Aronne et al. *JAMA*. 2023 Dec 11;331(1):38–48.

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

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=40³)
- 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)

6-Month Body Weight Change³



Change from baseline through 6 months analyzed using a mixed model for repeated measures (MMRM); LS mean ± SEM shown; one-sided p-value reported.

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

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

Dose-response observed

Strong correlation between ablation length and weight maintenance across all 29 Revita participants, as in prior Revita T2D work¹

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 Optimization

Pivotal mean ablation length > 16 cm

Pivotal study enriched for participants receiving longer ablation length treatments. Dose-response pre-specified in pivotal SAP

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

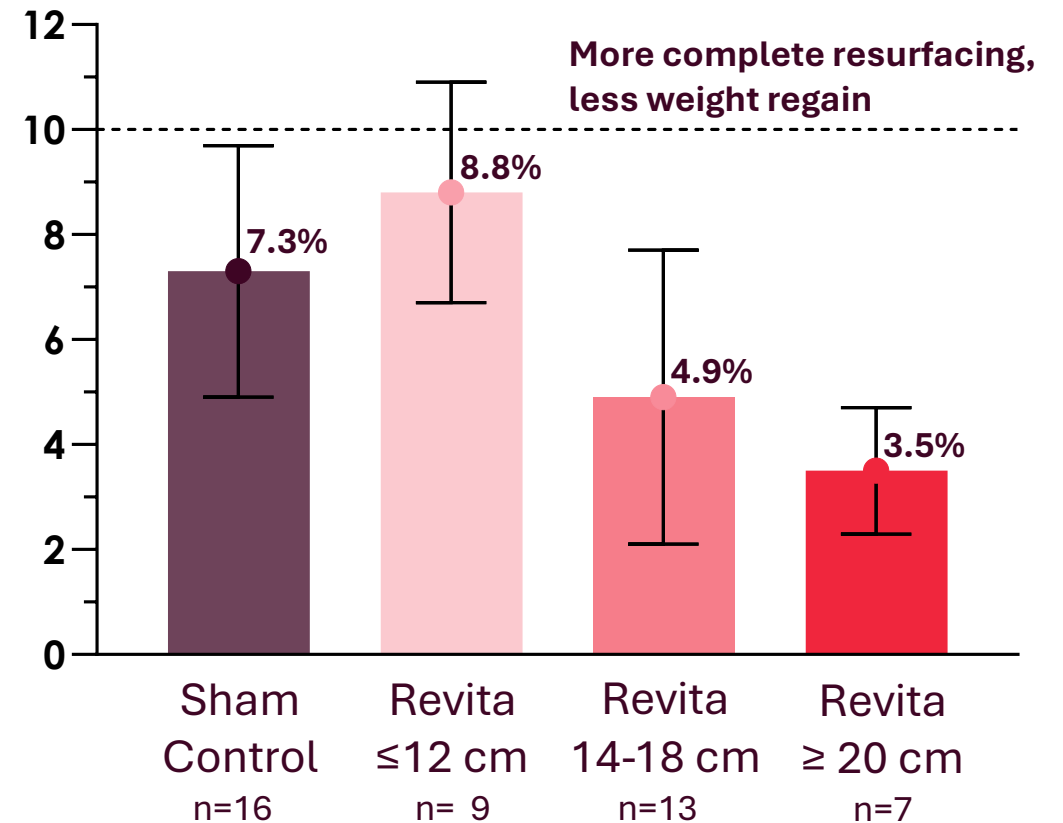
¹Rajagopalan et al Diabetes Care 2016 Dec;39(12):2254-2261

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 arm¹)
- 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 Change²



¹ Dose-response assessed by Spearman rank correlation between ablation count and weight regain at week 26 within the blinded DMR arm ²Observed 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.

Patient selection: Revita effect is largest and growing in those who need it the most¹

In participants who were high GLP-1 responders¹, Revita showed **early and sustained separation vs sham through 6 months** (per Pivotal Cohort pre-specified SAP; p=0.004)

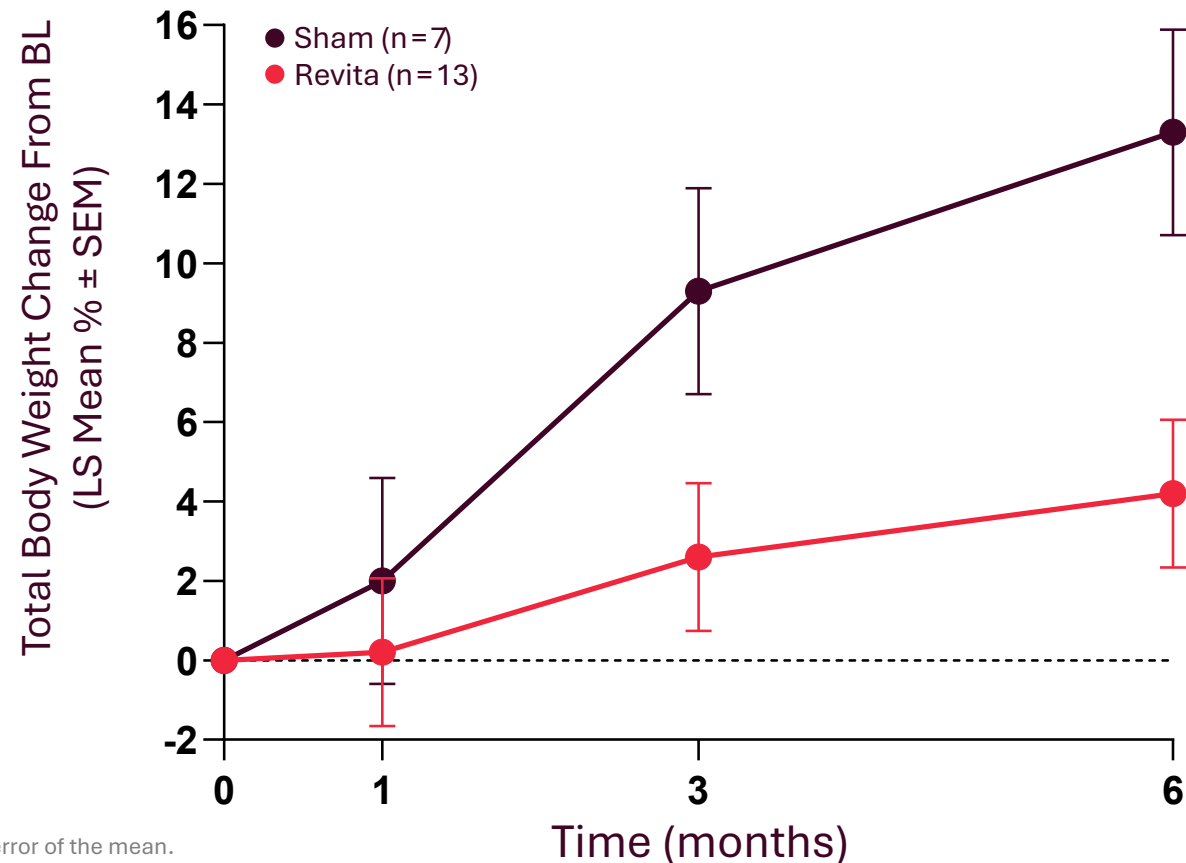
Curve trajectories continue to diverge at 6 months, **indicating potential for sustained biological activity**

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

¹Participants with run-in weight loss above a median ~ 18%.

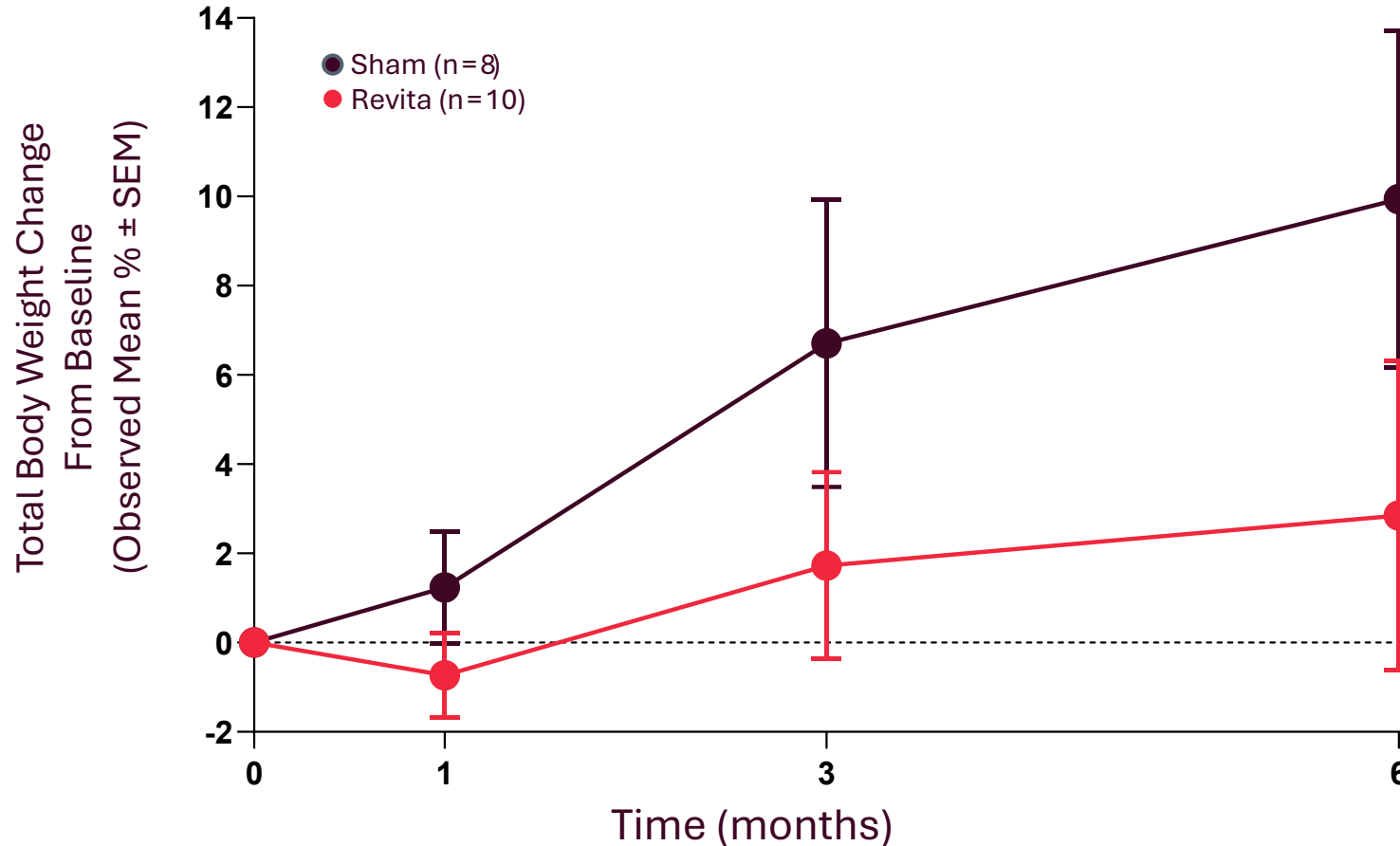
Abbreviations: BL, baseline; GLP-1, glucagon-like peptide-1; LS, least-squares; SEM, standard error of the mean.

High GLP-1 Responders¹ Change in Body Weight Over Time



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

Change in Body Weight in Optimized Patient Cohort¹



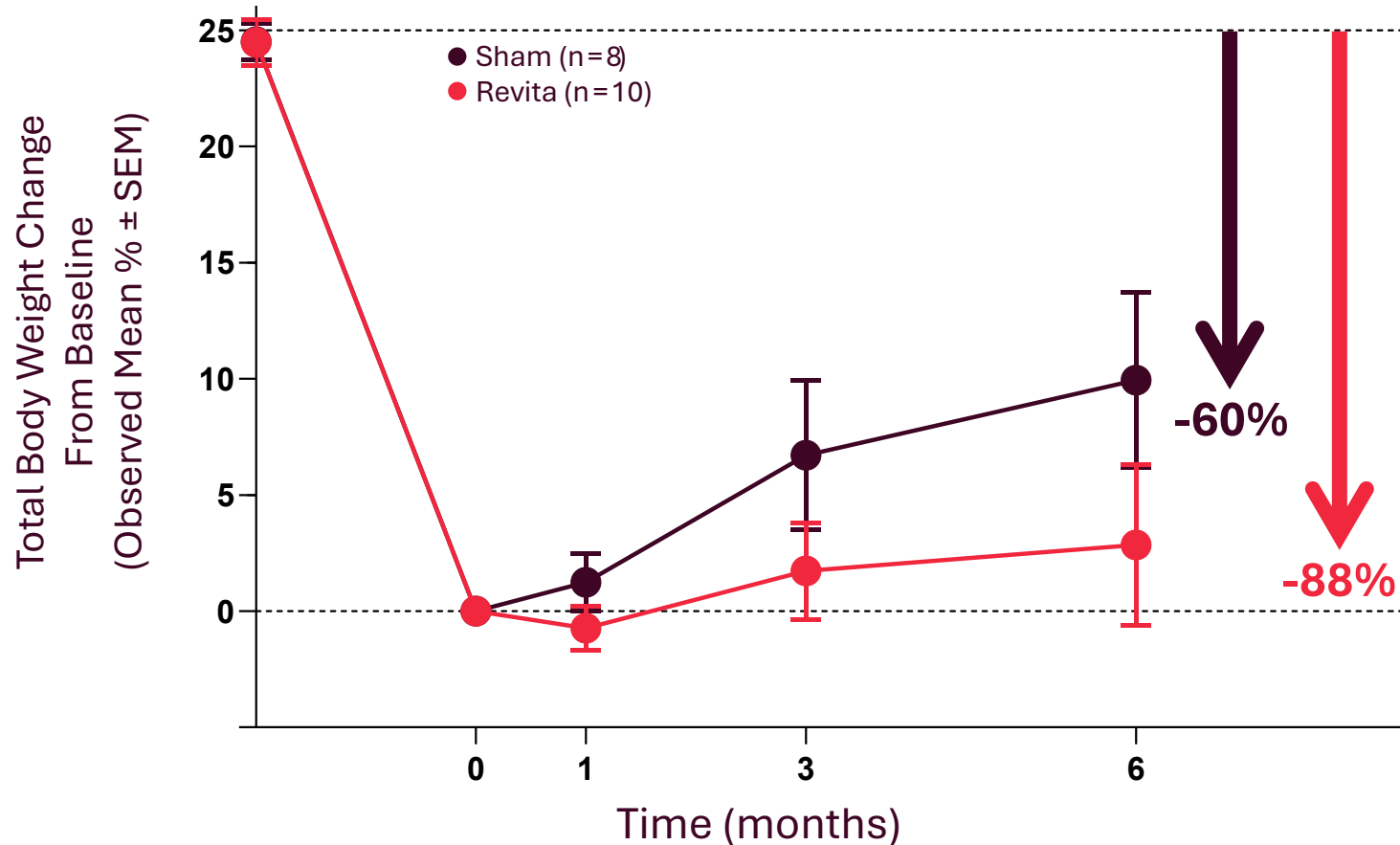
This optimized cohort reflects the profile of the Pivotal Cohort population — participants with high GLP-1 weight loss and per-protocol ablation standards

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

¹Participants 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.

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

Change in Body Weight in Optimized Patient Cohort¹



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

¹Participants 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.

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 Classification¹: 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. ¹Dindo *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/m²)
- 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

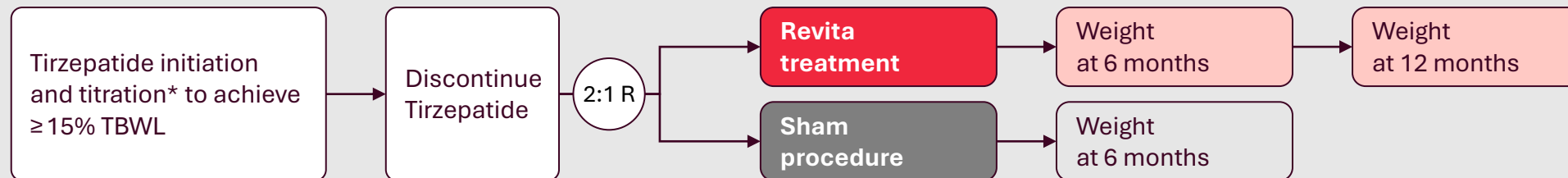
Study design

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

Anticipated milestones¹

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

Study design



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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.

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

¹These 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.

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. ¹TCET (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

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

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.

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.

2 Dose-Dependent, Standardized Delivery

Clear dose-response.

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

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.

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

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

\$3-5B Market penetration opportunity¹

800K GLP-1 patients already flowing through GI suites each year¹


~ 60% Procedure volume² from top 250 US centers²

>1M Annual procedures at peak¹

 **Recurring, high-margin revenue**

 **+80% gross margin:**
Single-use catheter

 **~15% gross margin:**
One console per suite

 **~1,200 procedures²**
per center per year



← SINGLE-USE CATHETER

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

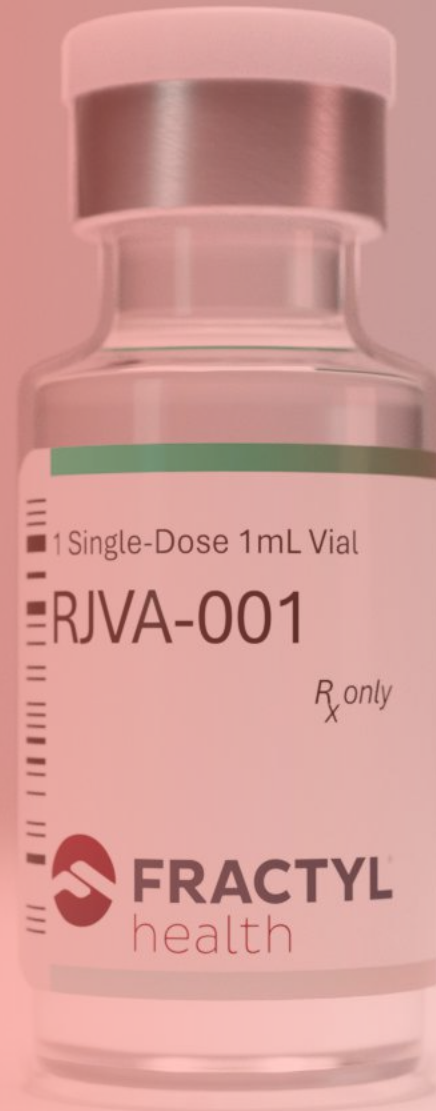
¹Fractyl estimates. ²Based on market research commissioned by Fractyl Health.



Rejuva[®]

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

Rejuva is an investigational preclinical asset and is currently under review for clinical research in the EU and AUS. It has yet to be assessed by the FDA.



← PROPRIETARY TARGETED INTRAPANCREATIC DELIVERY SYSTEM

← "SMART GLP-1" GENE THERAPY

Reimagining gene therapy economics for metabolic disease

Large patient population



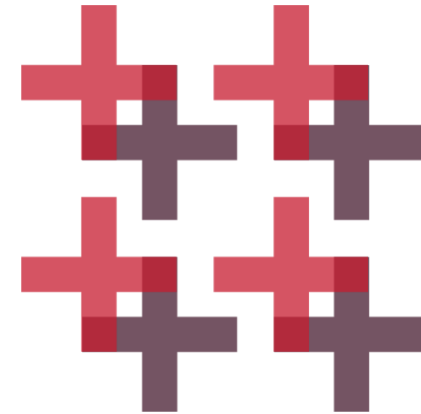
~**27M** with T2D in US¹
~**100M** with Obesity in US²

Low cost of goods



< **\$10K** COGs per patient
enabled by local delivery

High economic value



~**\$10K** price per year
ICER price benchmark³

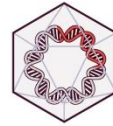
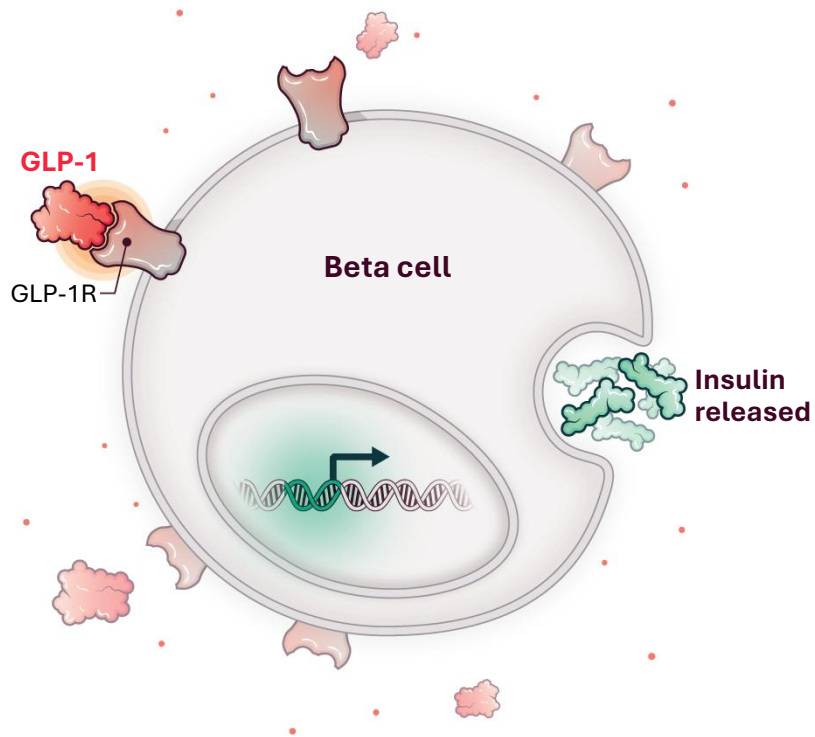
¹CDC National Diabetes Statistics Report 2026, ²CDC NCHS Data Brief No. 508. Obesity and Severe Obesity Prevalence in Adults: United States, August 2021–2023, ³ICER Medications for Obesity Mgmt 2022.

RJVA-001 for T2D

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

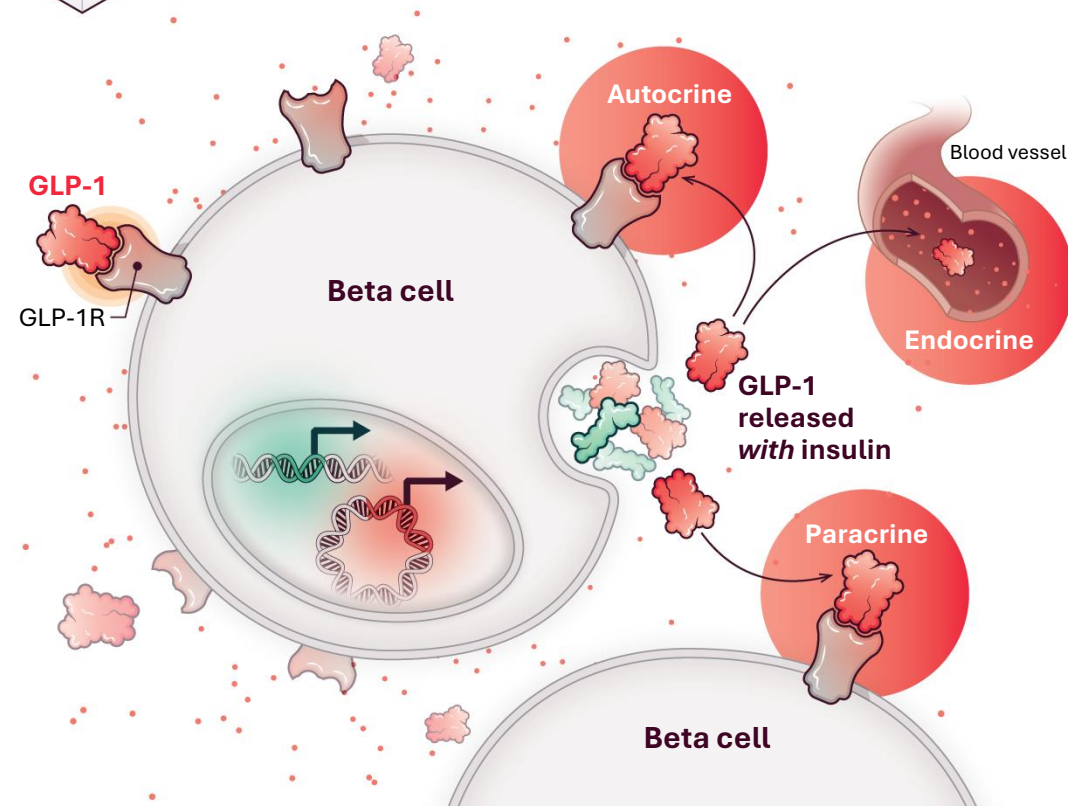
Type 2 Diabetes

Insufficient pancreatic GLP-1 signaling¹



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

Rejuva is an investigational preclinical asset and has yet to be assessed by regulatory agencies. Abbreviations: GLP-1, glucagon-like peptide 1.

The Rejuva approach is differentiated from GLP-1 drugs

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

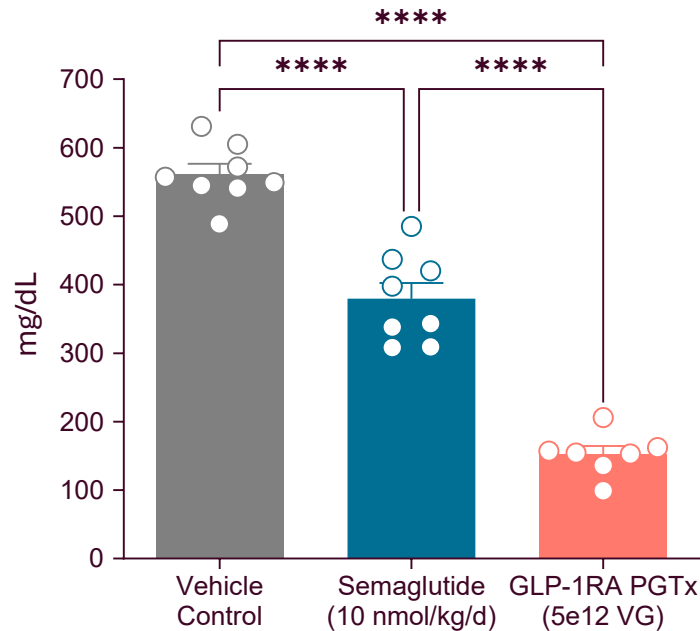
Feature	Rejuva	GLP-1 Drugs
MOA	✓ Simulates endogenous GLP-1 secretion kinetics	Exogenous, pharmacologic activation of GLP-1R
GLP-1 Biodistribution	✓ High pancreas and portal exposure with limited systemic exposure	Systemic, with widespread receptor activation
Safety/Tolerability	✓ Better GI tolerability 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

Rejuva is an investigational preclinical asset and has yet to be assessed by regulatory agencies.

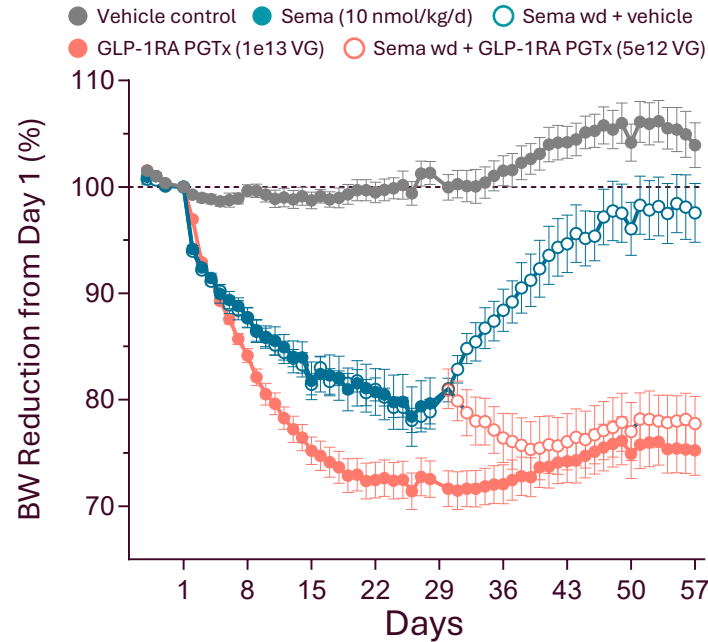
Abbreviations: AAV, adeno-associated virus; CNS, central nervous system; GI, gastrointestinal; GLP-1, glucagon-like peptide-1; GLP-1R, GLP-1 receptor; MOA, mode of action; SOC, standard of care.

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

Glucose-lowering activity in *db/db* mouse model¹

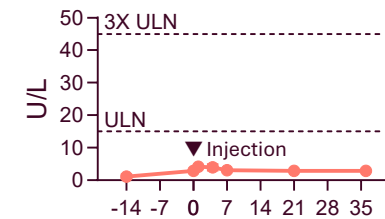


Sustained weight loss in DIO mouse model²

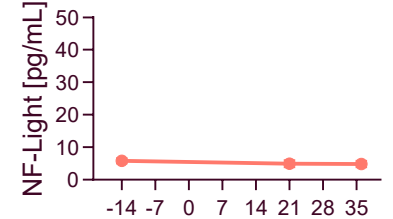


No toxicity observed in Yucatan pig model³

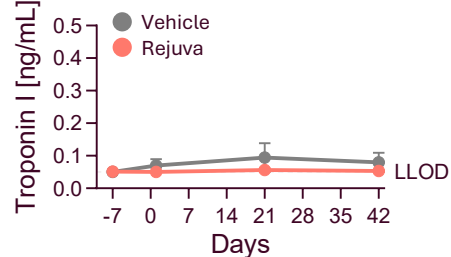
Pancreatitis (lipase)



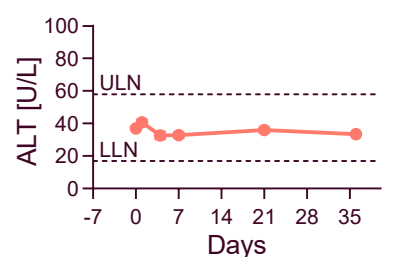
Neurotoxicity (Nf-L)



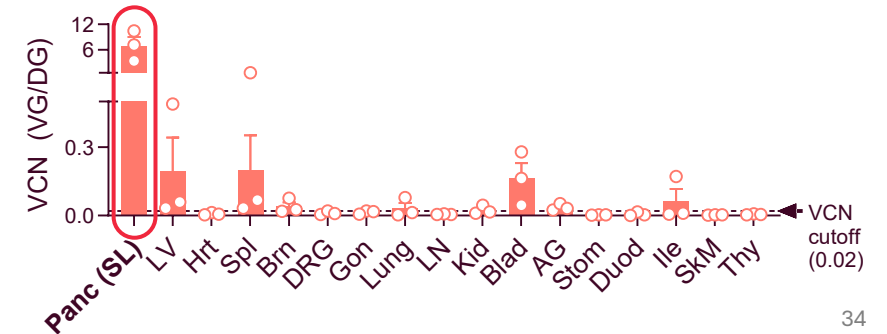
Cardiotoxicity (troponin I)



Hepatotoxicity (ALT)



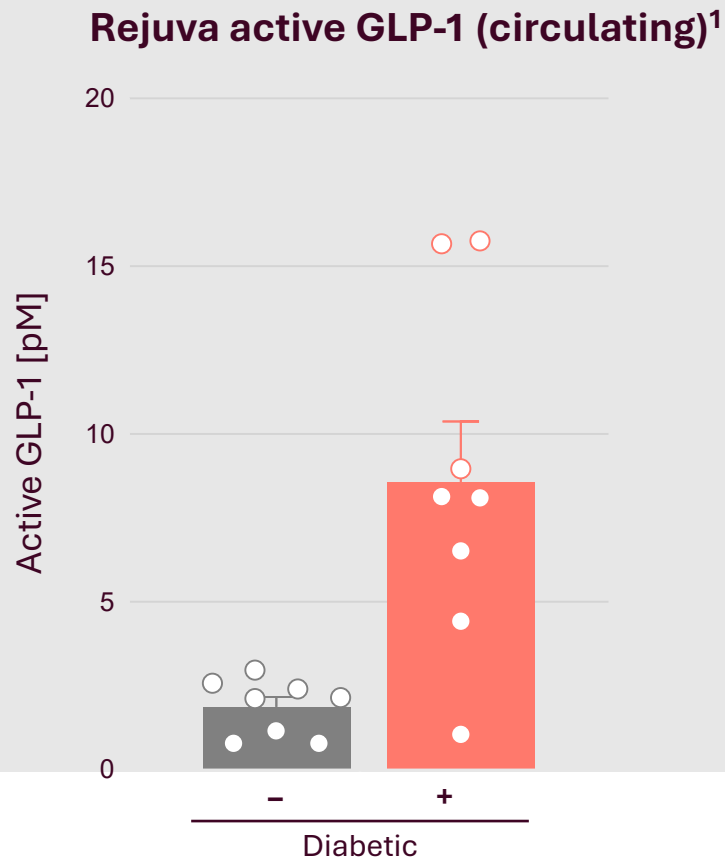
Biodistribution (vDNA)



One-Way ANOVA, post-hoc Tukey Test: ****: $P < 0.0001$. Rejuva is an investigational preclinical asset and has yet to be assessed by regulatory agencies. ¹Mean \pm SEM shown; $n=7-8$ per group, day 29 shown, Rajagopalan et al. DDW 2024 oral presentation. Abstract no. 4029196. ²Mean \pm SEM shown; $n=5-10$ per group. Fitzpatrick et al. WCIRDC 2023 oral presentation. Abstract no. 0077. ³Fitzpatrick et al., ASGCT 2025 oral presentation. Data are mean \pm 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.

Robust efficacy without high systemic GLP-1 exposure

May be less likely to cause tolerability issues



Circulating active GLP-1 Levels²

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	✗

¹Fitzpatrick et al., ASGCT 2025 oral presentation. Data are mean ± SEM, n=8 per mice group from day 44 post IP AAV injection ²Smits 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). Rejuva is an investigational preclinical asset and has yet to be assessed by regulatory agencies. 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.

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/m²
- 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)

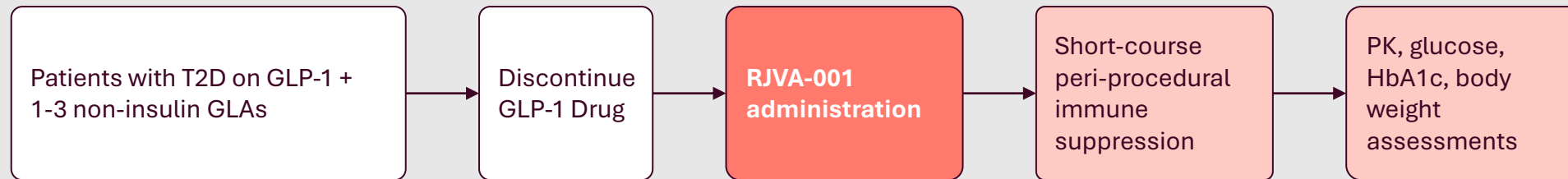
Study design

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

Anticipated milestones¹

- **Regulatory feedback on CTA:** Q2 2026
- **FIH dosing, subject to CTA authorization, and preliminary data:** H2 2026

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



¹These 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.




Rejuva

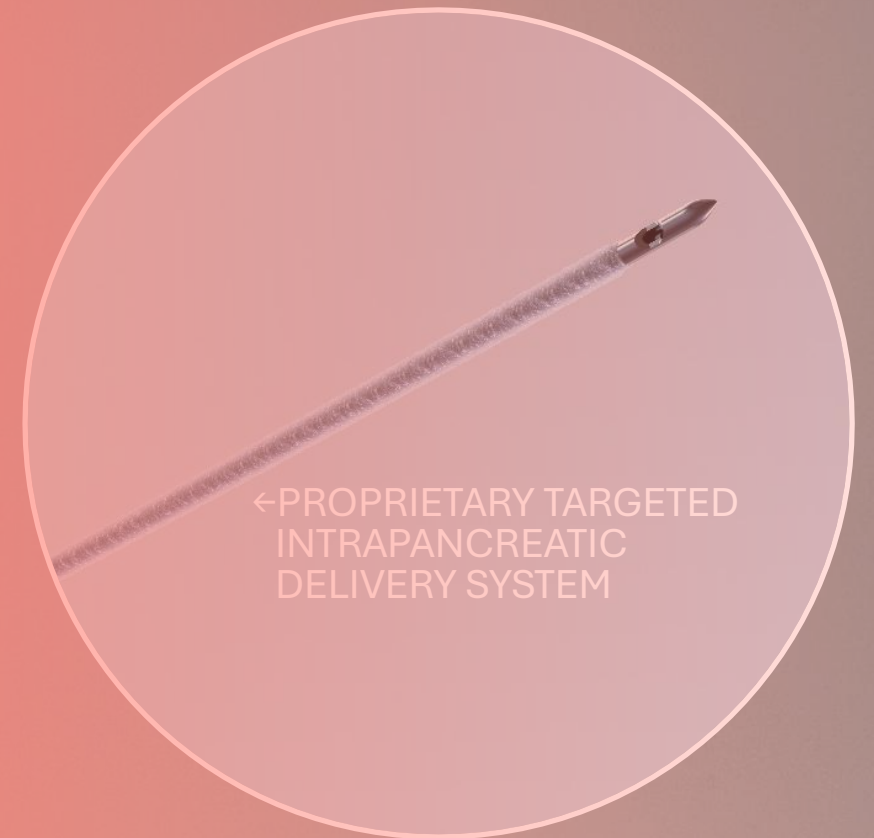
Nutrient-responsive GLP-1 via intrapancreatic gene therapy

-  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

 Submitted CTA in EU and AUS

 Anticipate 1st patient dosing & preliminary data in H2 2026
Assuming CTA is authorized

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



← "SMART GLP-1" GENE THERAPY

Rejuva is an investigational preclinical asset and is currently under review for clinical research 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 footprint¹

35 Active patent families	<ul style="list-style-type: none">✓ 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	<p>Issued claims cover devices, systems, methods of treatment</p> <p>IP Portfolio focus includes:</p> <ul style="list-style-type: none">• Methods of treating critical region of duodenum• Devices for treating target tissue in the duodenum• Gene therapy infusion devices, methods, constructs <p>Leadership in thermal & non-thermal DMR ablation</p> <p>Proactive continuation strategy extends protection to improvements & emerging technologies</p>
100+ Patents issued globally		
36 Patents issued in the US		
70+ Pending patent applications		

Diverse Protection

¹As of March 2026.

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 Milestones¹

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	CTAs submitted				Q2: Regulatory feedback on CTAs H2: FIH dosing, subject to CTA authorization, and preliminary data
Obesity	RJVA-002	Candidate nominated				

¹These 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.

Leadership team & BOD

Experience spanning biotechnology and medical technology



Harith Rajagopalan, MD, PhD
Co-Founder & CEO



Jay Caplan
Co-Founder,
President, & CPO



Lara Smith Weber
CFO



Sarah Toomey
General Counsel
& Corp. Secretary



Jon Fitzgerald
Sr VP of Regulatory,
Quality, & Clinical



Len Rosberg
VP of Manufacturing

Board of Directors

Ajay Royan (Chair)
Co-founder &
Managing General
Partner, Mithril Capital

William Bradley
Former U.S. Senator

Harith Rajagopalan
Co-founder & CEO,
Fractyl Health

Marc Elia
Founder of M28
Capital

Kelly Barnes
Former Partner, PwC

Samuel Conaway
President of Boston
Scientific U.S.
Cardiology Sales &
Chair of Close the Gap

Clive Meanwell
Executive Chairman
& Founder of
Population Health
Partners

Christopher Thompson
Prof of Medicine,
Harvard Medical
School & Dir of
Endoscopy, Brigham &
Women's Hospital

Ian Sheffield
Managing Partner,
North Country
Holdings, LLC



Thank you

Investor Relations

Brian Luque, Head of IR & Corp. Dev.

951.206.1200

IR@fractyl.com

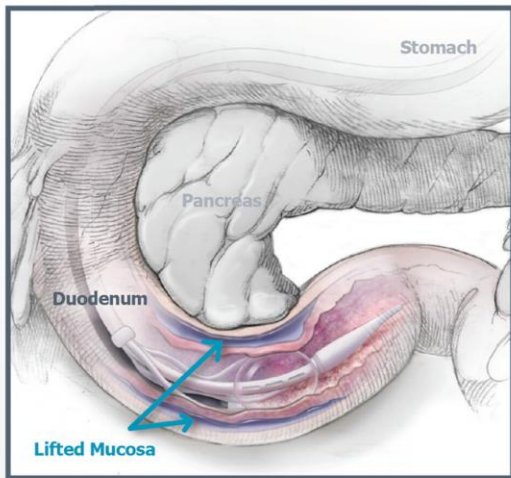
NASDAQ:GUTS

Revita Targets Duodenal Dysfunction

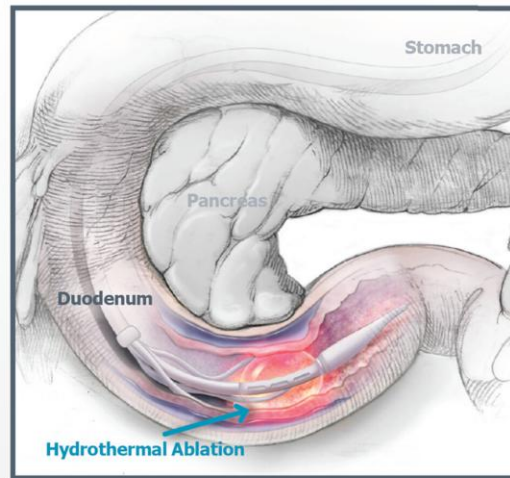
Potentially first-in-class procedural therapy designed to durably reset metabolism¹⁻⁴

Revita designed to achieve targeted mucosal ablation without damaging deeper structures

(A) Circumferential Saline Lift



(B) Hydrothermal Ablation



Images 7

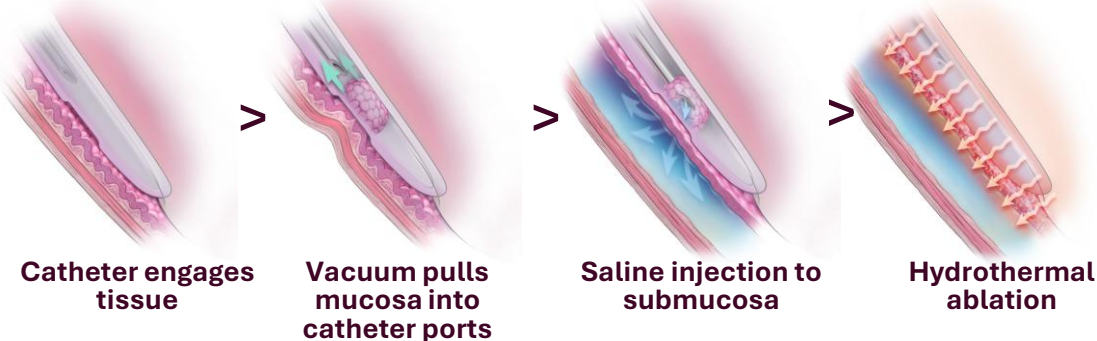
FDA Breakthrough Device designation for post-GLP-1 weight maintenance in obesity

Scalable intervention: Outpatient, < 1 hour procedure conducted via straightforward upper endoscopy

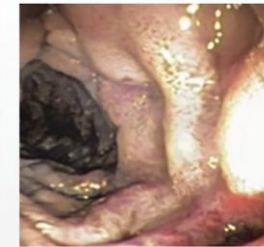
Designed with safety in mind: Engineered to deliver therapeutic ablation without compromising safety

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

Normal mucosa by one-month post-Revita⁵



Prior to DMR



Ablated Duodenum



1mo post-procedure

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 point¹⁻³

- 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 intervention⁴⁻¹¹

- 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

¹Habegger, et al. *Gut* 2014. ²Yang et al. *Photodiagnosis Photodyn Ther*. 2023 Dec;44:103733. ³Nie et al. *World J Diabetes*. 2025 Mar 15;16(3):102277. ⁴Haidry R, et al. *GIE* 2019.

⁵van Baar ACG, et al. *Endosc Int Open*. 2020 8:E1683-E1689. ⁶Rajagopalan H, et al *Diabetes Care*. 2016 39:2254-2261. ⁷van Baar ACG, et al. *Gut*. 2020 69:295-303. ⁸Mingrone G, et al. *Gut*. 2022 71:254-264. ⁹van Baar ACG, et al. *Gastrointest Endosc*. 2021 94:111-120.e3. ¹⁰van Baar, et al. *Diabetes Res. Clin. Pract*. 2022 184:109194. ¹¹Fractyl Health press release dated August 5, 2025.

REVEAL-1: Metabolic stability at 6 mo in open label cohort

REVEAL-1 Cohort (n≈20)

Rationale	Post-GLP-1 weight maintenance in a real-world setting
Design	• Open-label
Participants	With obesity (BMI > 30 kg/m ²) prior to GLP-1 <u>and</u> ≥15% TBWL with GLP-1 drug
Anticipated milestones¹	✓ 3-mo data: June 2025 ✓ 6-mo data: Dec '25 • 1-yr data: Q2 '26

Key takeaways

High risk of post-GLP-1 rebound:

- Participants lost 24% total body weight (>50 lbs) on GLP-1 drugs prior to enrollment
- Success in this population provides supportive context for upcoming REMAIN-1 results

Stable weight trajectory through 6 months:

- Mean total body weight change was only **1.5%**
- Published studies report **~10%** weight regain post-GLP-1 discontinuation^{2,3}

Stable HbA1c through 6 months:

- HbA1c change was only **0.04%**
- GLP-1 withdrawal typically results in glycemic rebound of **~0.4%**³

Excellent AE and tolerability profile:

- No procedure-related serious adverse events were observed
- Eight (36%) experienced mild, self-limited, transient TEAEs

¹These 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. ²Aronne et al. *JAMA*. 2023 Dec 11;331(1):38–48. ³Wilding et al. *Diabetes Obes Metab*. 2022 Aug;24(8):1553-1564.

Abbreviations: AE, adverse event; GLP-1, glucagon-like peptide-1; HbA1c, hemoglobin A1c; TEAE, treatment-emergent adverse event.

REVEAL-1 demographics mirror REMAIN-1 pivotal cohort & real-world obesity population on GLP-1s

Demographic/ Characteristic	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)

Population at high risk of weight rebound:

- Substantial weight loss on GLP-1s: 24% ± 7%; >50 lbs
- Patients on drug for 5 months to 5 years

Similar demographics to REMAIN-1:

- Other baseline characteristics closely align with REMAIN-1 midpoint and pivotal cohorts^{1,2}
- 21 of 22 on tirzepatide

*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.

¹Fractyl Health press release and conference call dated September 26, 2025. ²Fractyl Health data on file.

Abbreviations: BMI, body mass index; GLP-1, glucagon-like peptide-1; HbA1c, hemoglobin A1c; SD, standard deviation; TBW, total body weight.

Excellent safety & tolerability profile

TEAEs mild, transient, self-limited, as in prior Revita clinical studies

Treatment-Emergent Adverse Events*	Patients n (%)	Duration (days post-Revita)
Grade ≥3 TEAEs	0 (0)	N/A
Grade 2 TEAEs	0 (0)	N/A
Grade 1 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

- **No treatment-emergent serious adverse events related to device or procedure**
- **No TEAE-related study discontinuations**
- No patients experienced anything greater than a Grade 1¹ (minor) TEAE
- Grade 1 TEAEs were observed in 8 of 22 (36%):
 - Transient, mild, self-limited
 - Indistinguishable from routine upper endoscopy
 - No TEAEs after 5 days post-Revita
- **Compelling safety and tolerability profile is consistent with prior Revita clinical experience**

*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.

Clavien-Dindo Classification¹: Standardized FDA recommended system for TEAE grading: Grade 1: Minor, any deviation from 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. ¹Dindo *et al. Annals of Surgery* 240(2):p 205-213. ²Fractyl Health data on file.

Abbreviations: BMI, body mass index; GLP-1, glucagon-like peptide-1; HbA1c, hemoglobin A1c; SD, standard deviation; TBW, total body weight. TEAE, Treatment-emergent adverse effects

Cardiometabolic and food craving parameters consistent with attenuated post-GLP-1 rebound

- Improvements in cardiometabolic lipid profile at 6 months consistent with improved insulin sensitivity and lipid handling:
 - Improved HDL-C
 - Improved TG:HDL ratio
- Patient-reported outcomes suggest trend toward improved appetite regulation consistent with biological hypothesis of duodenal control of food craving
 - Reduced craving intensity, particularly for sweet foods

Cardiometabolic Parameter	LS Mean change from BL (SEM) ¹		p-value
	Revita (n=24)	Sham (n=16)	
Triglycerides, mg/dL	9.1 (11.2)	27.5 (15.2)	0.11
LDL-C, mg/dL	3.9 (6.2)	3.9 (8.9)	0.44
HDL-C, mg/dL	15.5 (3.1)	3.9 (4.3)	0.01
VLDL-C, mg/dL	1.9 (2.2)	5.7 (3.0)	0.10
Triglyceride : HDL ratio	-0.2 (0.2)	0.4 (0.3)	0.03
HbA1c, %	0.1 (0.04)	0.2 (0.06)	0.14

CoEQ Parameter	Revita (n=24)	Sham (n=16)	p-value
Craving control	2.3 (0.7)	3.1 (1.0)	0.21
Craving for sweet	1.8 (0.6)	3.4 (0.8)	0.04

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.

¹ Excluded 5 subjects per protocol from efficacy analysis; included in safety assessment