FRACTYL health

Positive Randomized Data from REMAIN-1 Midpoint Cohort Study

Revita®: Unlocking Durable Weight Maintenance After GLP-1 Discontinuation

September 26, 2025

Revita is for Investigational Use Only in the US Under Federal Law

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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Revita: A Potential Breakthrough in Obesity Care

Pioneering the possibility of a durable metabolic reset without chronic therapy

Hypothesis:

Endoscopic duodenal ablation designed to provide:

- **Safe, well-tolerated, straightforward** procedure
- **Highly effective** metabolic disease modification
- **Durable weight and metabolic impact** designed to last for years

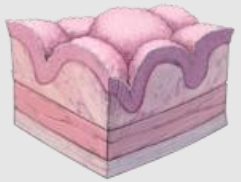
Evidence:

Revita clinical experience has already shown:

- **Sustained improvements** in weight and HbA1c[1,2,4]
- Early outcomes at 1 and 3 months translated to **2 years of durable benefit**[1, 2]
- **Excellent safety** and tolerability profile[2, 3, 4, 5]

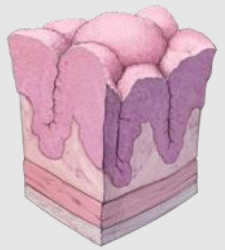
Targeting Duodenal Mucosa for a Durable Metabolic Reset

Healthy duodenum



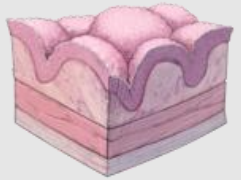
Normal gut-to-brain signaling via satiety hormones → **metabolic balance**

Diseased duodenum



Diet-induced mucosal changes → **duodenal dysfunction, insulin resistance, weight gain**

Post-Targeting



Regenerated mucosa → **restored signaling, durable weight maintenance and glycemic control**

1. Fractyl Health press release dated August 5, 2025. 2. van Baar et al. Diabetes Res Clin Pract. 2022 Feb:184:109194. 3. Mingrone et al. Gut. 2022 Feb;71(2):254-264. 4. van Baar et al. Gut. 2020 Feb;69(2):295-303. 5. van Baar et al. JHEP Rep. 2019 Nov 5;1(6):429-437

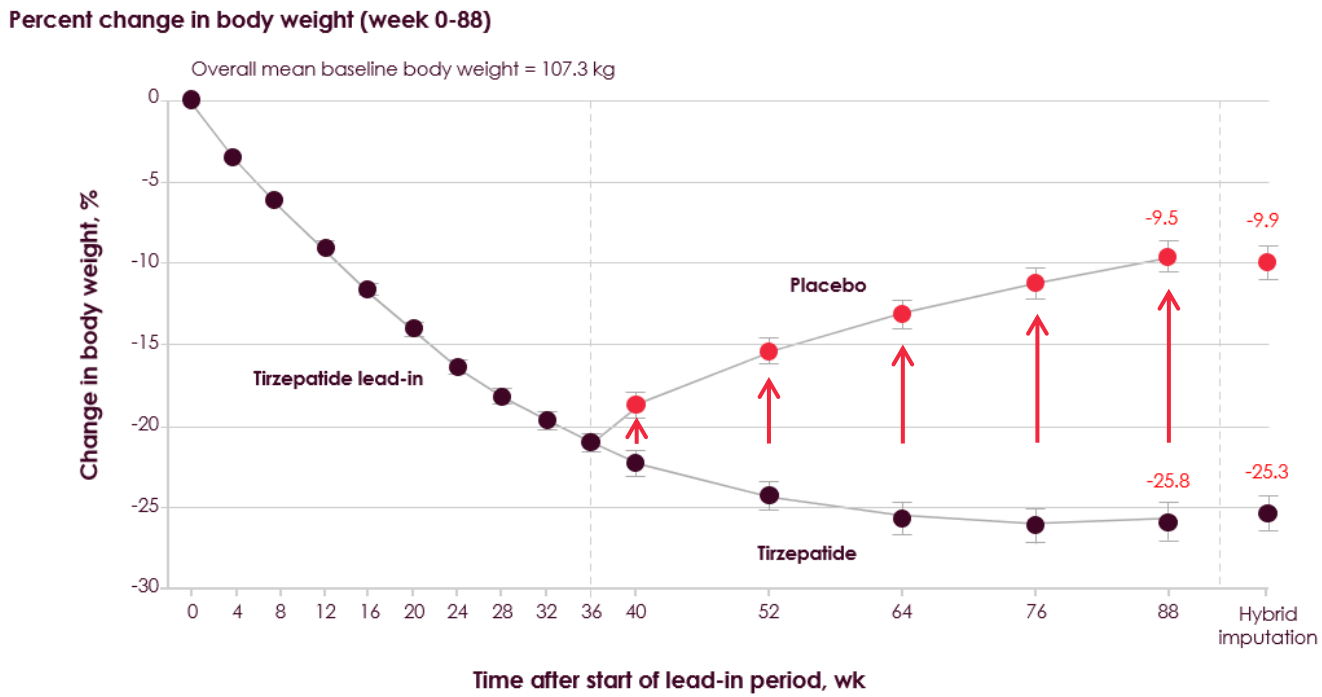
Why Lose 20 Pounds of Fat Just to Gain it All Right Back?

GLP-1s drive weight loss – but can't deliver long-term results alone

Majority of patients discontinue GLP-1s within 1 year[2]:

- Weight and metabolic rebound occur rapidly upon discontinuation[1]
- First symptoms are profound hunger and food noise, usually occurring within weeks of treatment discontinuation
- Revita is the first and only FDA Breakthrough Device targeting this gap[3]
- High unmet need and hard-to-treat patient population for Revita's first clinical demonstration in obesity

REMAIN-1 program modeled off Lilly's SURMOUNT-4 tirzepatide discontinuation study[1]:



1. Adapted from Aronne et al. JAMA. 2023 Dec 11;331(1):38–48. 2. Blue Health Intelligence, Issue Brief May 2024. 3. 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. GLP-1=glucagon-like peptide-1

Remain-1 Midpoint Cohort Supports Revita's Safety Profile, Efficacy, and Strategic Potential

Key Takeaways

1. **Clear evidence of Revita activity**: At 3 months, Revita patients experienced 2.5% *further* weight loss after stopping GLP-1s, vs 10% weight regain in sham-treated patients (p=0.014)
2. **Excellent safety and tolerability through 3 months**: No Revita-related SAEs or Grade II+ AEs observed, consistent with prior Revita clinical study experience
3. **Positive readthrough to pivotal study**: Midpoint data supports the rapidly progressing pivotal study. Pivotal Cohort is on track to complete randomization in early 2026; 6-month topline primary endpoint and potential PMA filing in H2 2026[1]
4. **Potential backbone therapy in obesity**: Addressing high unmet need in post-GLP-1 weight maintenance population opens the door for Revita as a potential backbone therapy across the spectrum of obesity and metabolic disease

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. AE=adverse event, PMA=premarket approval, SAE=serious AE, GLP-1=glucagon-like peptide-1

REMAIN-1 Pivotal Program Overview

Midpoint Cohort: designed to reinforce confidence in pivotal study

	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, controlled **pilot** study	Randomized, controlled **pivotal** study
Design	• Open-label	• Tirzepatide run-in phase • Double-blind Revita vs sham (2:1)	• Tirzepatide run-in phase • Double-blind 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 naive	With obesity (BMI 30-45 kg/m^2) without T2D and GLP-1 drug naive
Anticipated Milestones[1]	✓ 1-mo data: April 2025 ✓ 3-mo data: June 2025 • 6-mo data: Q4 2025 • 1-yr data: Q2 2026	✓ Enrollment: Q4 2024 ✓ 3-mo data: Sept 2025 • 6-mo data: Q1 2026	✓ Enrollment: Q2 2025 • Randomization: Early 2026 • 6-mo primary endpoint and potential PMA filing: H2 2026

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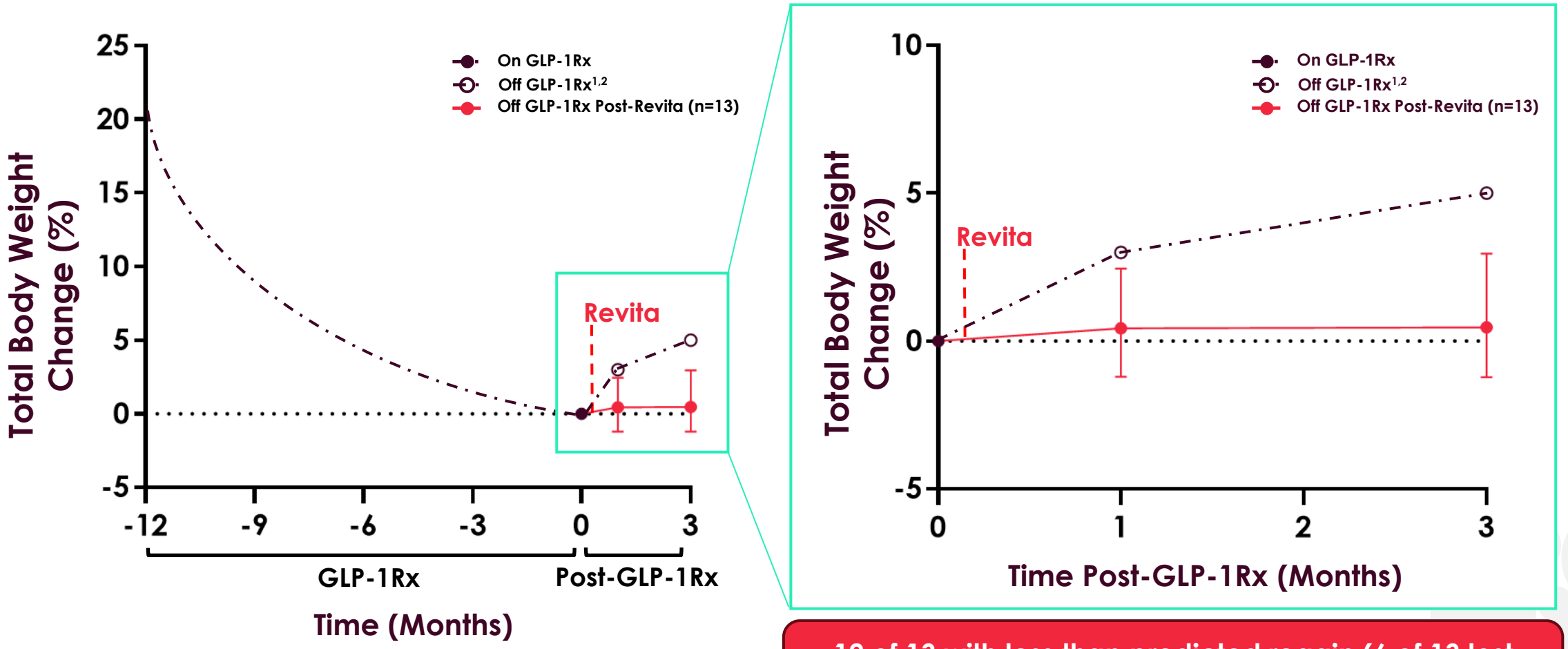
Shared in June 2025[3]

REVEAL-1: Encouraging Weight Maintenance at 3 Months

Previously reported open-label data provided an early positive signal



12 of 13 with less than predicted regain (6 of 13 lost weight): median 0.46% at 3 months vs expected 5-6%[1,2]

1. Aronne et al. JAMA. 2024;331(1):38–48. doi:10.1001/jama.2023.24945. 2. Wilding et al. Diabetes Obes Metab. 2022 Aug;24(8):1553-1564. 3. Fractyl Health press release dated June 23, 2025. GLP-1Rx weight loss from months -12 to 0 are illustrative based on average weight loss and time on medication in REVEAL-1 subjects. Data for Revita shown are median ± interquartile range. GLP-1Rx=glucagon-like peptide-1 therapy

REMAIN-1 Midpoint Cohort Study in Weight Maintenance

First randomized sham-controlled study in post-GLP-1 weight maintenance

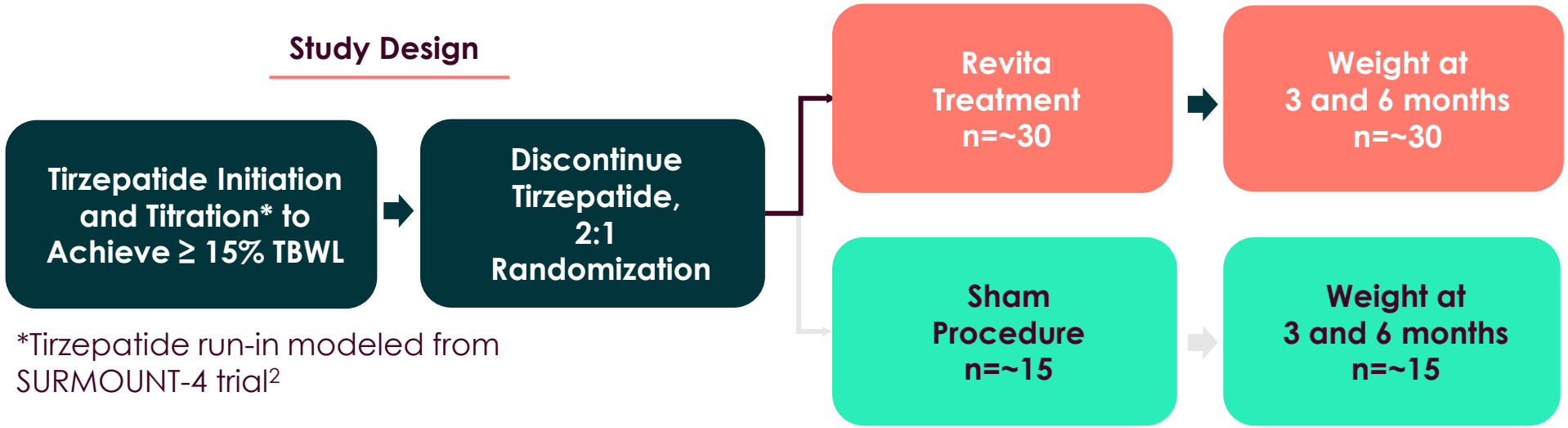
Patient Population
- Adults with obesity (BMI 30-45 kg/m^2)
- GLP-1 naïve; no T2D
- N=45

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

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

Anticipated Milestones[1]
- ✓ **Midpoint Cohort 3-mo data: Sept 2025**
- **Midpoint Cohort 6-mo data: Q1 2026**

Study Design



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

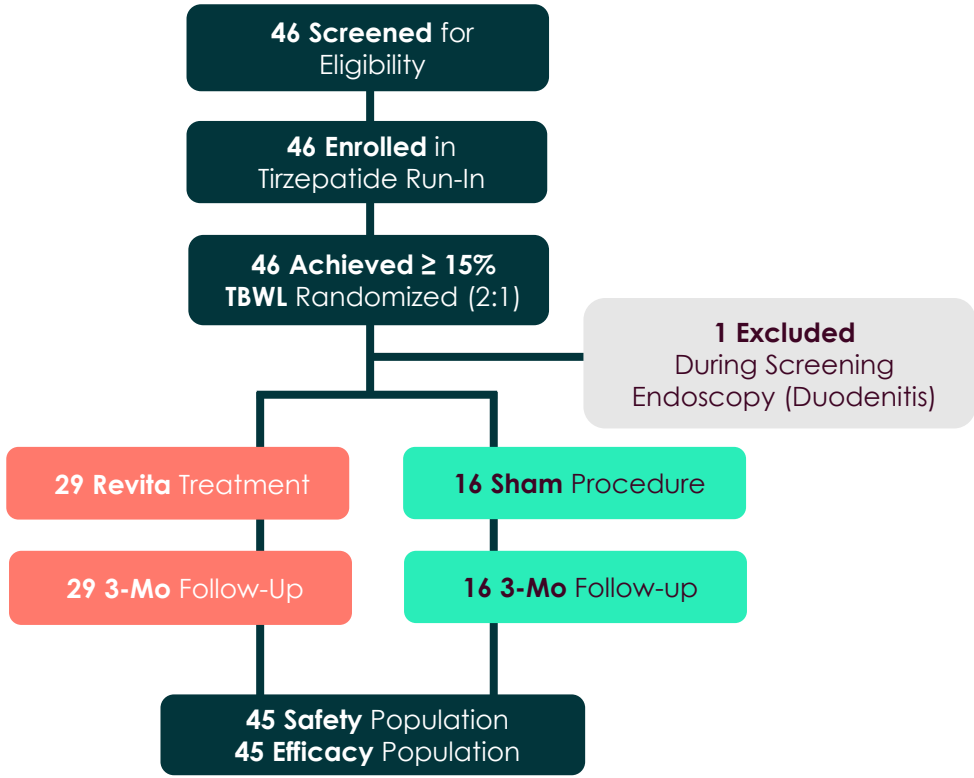
1. These forward-looking statements are based on management's current estimates and expectations. Refer to the latest disclosures filed with the SEC for a discussion regarding Risk Factors to these and other estimates and expectations. 2. Aronne et al. JAMA. 2023 Dec 11;331(1):38–48. GLP-1=glucagon-like peptide, TBW= total body weight, TBWL= total body weight loss, TZP= tirzepatide, T2D=type 2 diabetes

REMAIN-1 Midpoint Cohort Patient Disposition

Strong study execution, high retention, scalable procedure

- No dropouts between baseline visit and screening endoscopy
- Consistent procedure performance (average ablation length ~16 cm) supports scalability of technique
- 100% retention through 3 months

Figure 1. Patient Disposition



Tirzepatide run-in and dose-escalation period was approximately 16-26 weeks. Sham procedure consisted of placing the Revita catheter into the duodenum for a minimum of 30 minutes with no manipulations of the device or activation of the catheter

Balanced, Representative Study Population Supports Generalizability of Results

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

Table 1: Screening Demographics and Characteristics

Demographic/Characteristic	Revita (n=29)	Sham (n=16)	Total (N=45)
Age, yrs, mean (SD)	44 (14)	40 (11)	43 (13)
Sex, no. (%)			
Male	6 (21)	3 (19)	9 (20)
Female	23 (79)	13 (81)	36 (80)
Body Weight Pre-TZP, kg, mean (SD)	**100 (16)**	99 (15)	99 (15)
BMI Pre-TZP, kg/m^2, mean (SD)	**37 (4)**	36 (4)	37 (4)
Pre-diabetes Diagnosis*, no. (%)	3 (10)	0 (0)	3 (7)
Pre-diabetes at Screening, no. (%)**	14 (48)	5 (31)	19 (42)

These demographics mirror the real-world obesity population discontinuing GLP-1s, underscoring Revita's broad relevance

1. Fractyl Health REVEAL-1 data disclosure https://ir.fractyl.com/static-files/8110e855-b50a-4333-b551-678d5e854663. 2. Fractyl Health data on file. *Patients with a diagnosis of pre-diabetes in their medical history. ** Per protocol definition of pre-diabetes: screening HbA1c between 5.7% and 6.5% and/or screening fasting plasma glucose between 100 to 125 mg/dL. Tirzepatide run-in and dose-escalation period was approximately 16-26 weeks. Sham procedure consisted of placing the Revita catheter into the duodenum for a minimum of 30 minutes with no manipulations of the device or activation of the catheter. BMI=body mass index, SD=standard deviation, TZP=tirzepatide, TBW=total body weight

Both Arms Achieved 18% Weight Loss on Tirzepatide Prior to Randomization

- Baseline and Run-in characteristics balanced across treatment arms
- Wide baseline weight range demonstrates relevance across diverse obesity patients

Table 2: Post-tirzepatide Run-in Characteristics

Characteristic	Revita (n=29)	Sham (n=16)	Total (N=45)
Body Weight, kg,			
Post-TZP Baseline, mean (SD)	82 (13)	81 (13)	82 (13)
Min, Max Baseline	64, 115	59, 103	59, 115
TBW Change on TZP, %, mean (SD)	-18 (2)	-18 (2)	-18 (2)
BMI, kg/m^2, mean (SD)			
Post-TZP Baseline, mean (SD)	30 (3)	30 (4)	30 (4)
Min, Max Baseline	25, 37	24, 38	24, 38
Post-TZP Waist Circumference, cm, mean (SD)	92 (10)	96 (13)	94 (11)

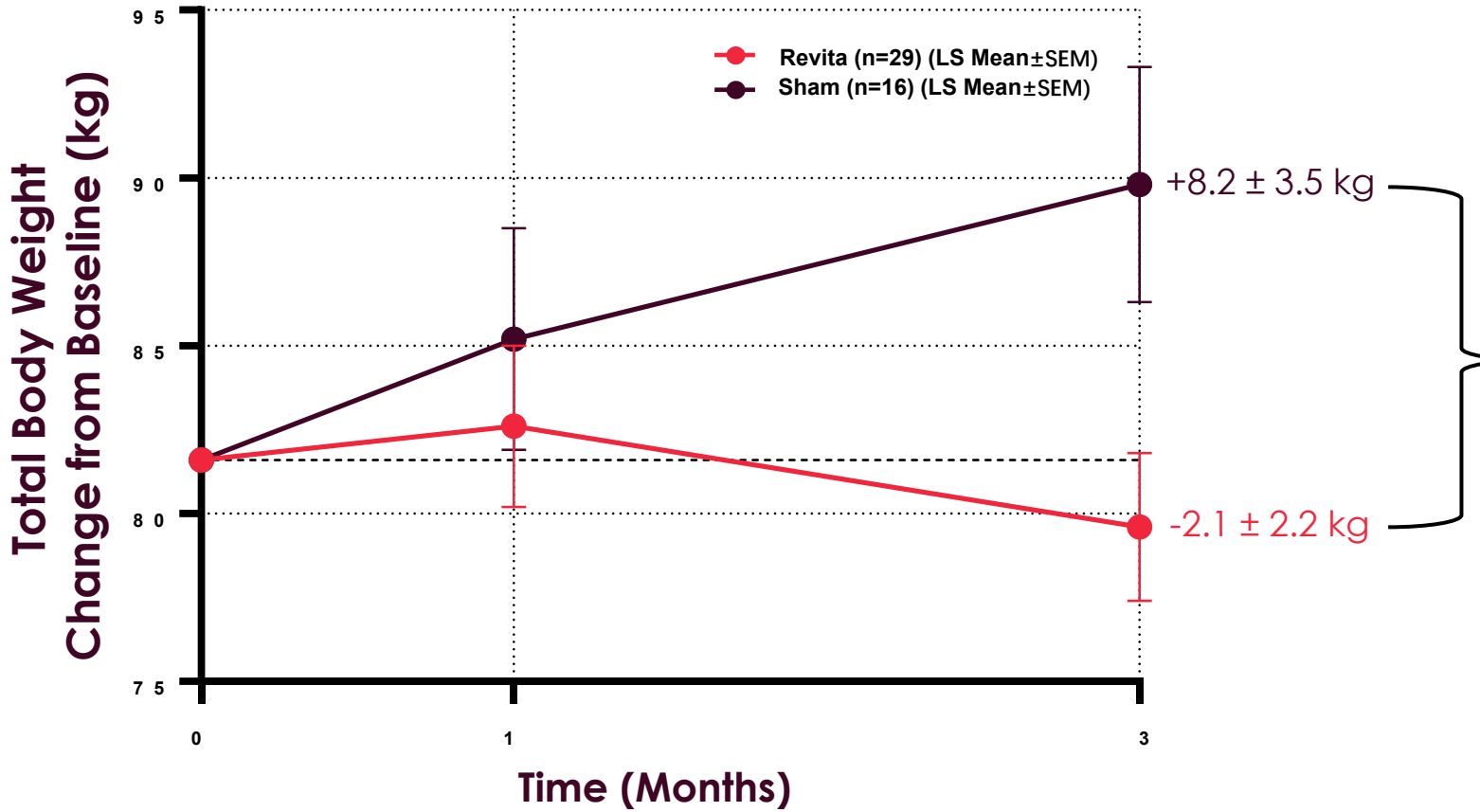
All patients achieved meaningful weight loss on GLP-1s, creating a rigorous "stress test" of Revita's ability to prevent weight regain

Tirzepatide run-in and dose-escalation period was approximately 16-26 weeks. Sham procedure consisted of placing the Revita catheter into the duodenum for a minimum of 30 minutes with no manipulations of the device or activation of the catheter. TZP=tirzepatide.

Clear Evidence of Revita Activity

Study met 3-month efficacy endpoint with strong statistical significance

Figure 2: Total Body Weight Change by Month



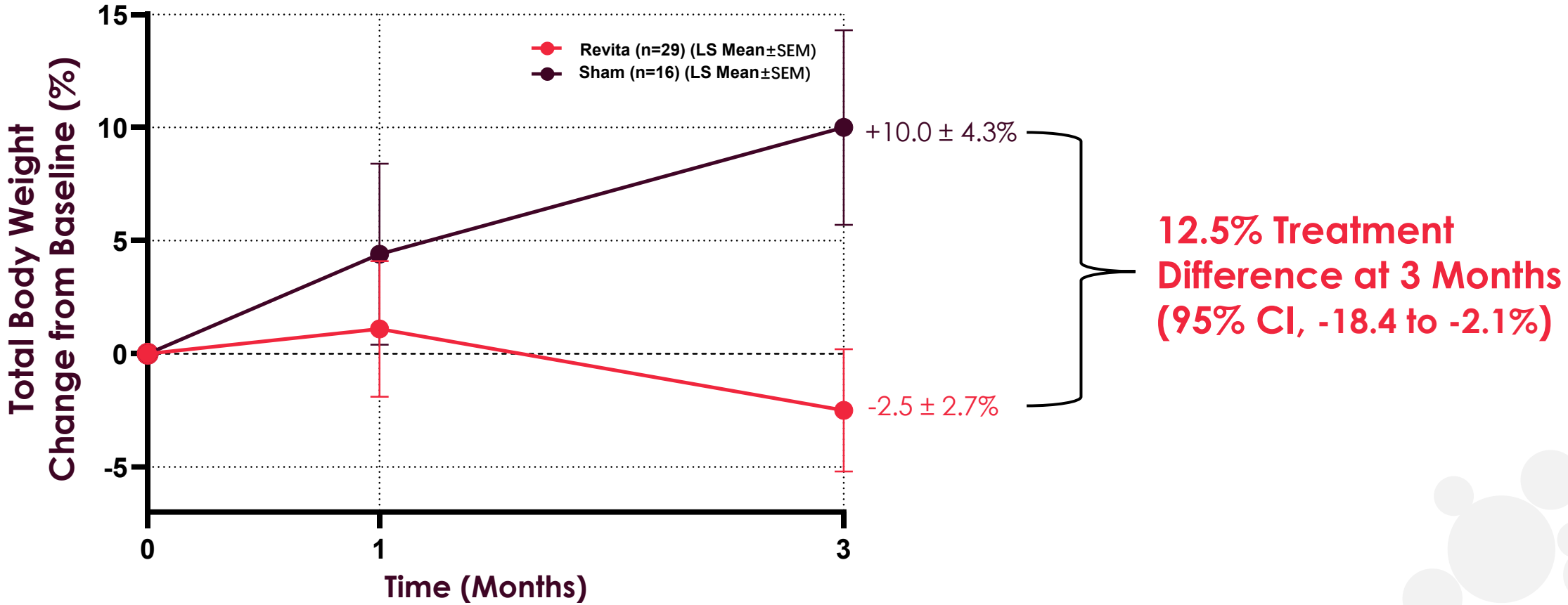
10.3 kg Treatment Difference at 3 Months (p=0.014)

Least-squares mean (LS mean) estimates were derived from a mixed model for repeated measures (MMRM), with treatment, visit, and treatment×visit interaction as fixed effects, and baseline weight and as a covariate. LS means are presented at the overall mean baseline to standardize comparisons between groups. Error bars represent standard errors of the LS means. Absolute total body weight changes calculated from post-tirzepatide grand mean baseline value at week -1. GLP-1= glucagon-like peptide 1, LS=least squares, SEM=standard error of the mean

Clear Evidence of Revita Activity

Study met 3-month efficacy endpoint with strong statistical significance

Figure 3: Percent Total Body Weight Change by Month



Least-squares mean (LS mean) estimates were derived from a mixed model for repeated measures (MMRM), with treatment, visit, and treatment×visit interaction as fixed effects, and baseline weight as a covariate. LS means are presented at the overall mean baseline to standardize comparisons between groups. Error bars represent standard errors of the LS means. Percent total body weight changes calculated from post-tirzepatide baseline value at week -1. CI=confidence interval, GLP-1= glucagon-like peptide 1, LS=least-squares, SEM=standard error of the mean

Excellent Safety and Tolerability Profile through 3 Months

Consistent with prior Revita clinical study experience

- **No treatment-emergent serious adverse events related to device or procedure**
- *1 SAE (cholecystitis) > 60 days post-randomization - unrelated to device or procedure
- 4 mild procedure-related events (Grade I) in Revita, 0 in Sham
- **No TEAE-related study discontinuations**
- Compelling safety and tolerability profile consistent with prior Revita clinical experience

Table 3: Treatment-Emergent Adverse Events

	Revita (n=29)	Sham (n=16)	Total (N=45)
Patients Experiencing Any TEAE n, % of subjects with events	7 (24)	1 (6)	8 (18)
TEAEs by Grade, n	12	1	13
Grade ≥III TEAEs, n, %	1* (8)	0 (0)	1* (8)
Grade II TEAEs, n, %	0 (0)	0 (0)	0 (0)
Grade I TEAEs, n, %	11 (92)	1 (100)	12 (92)
Related TEAEs, n**	4	0	4
Diarrhea	0	0	0
Abdominal discomfort	1	0	1
Nausea	1	0	1
Vomiting	0	0	0
Dry mouth	1	0	1
Sore Throat	1	0	1

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. Interim data reported are subject to further clinical evaluation committee review and adjudication. 1. Dindo *et al.* Annals of Surgery 240(2):p 205-213, August 2004. ICU=intensive care unit, GLP-1=glucagon-like peptide-1, TEAE= treatment-emergent adverse event.

REMAIN-1 Pivotal Study in Weight Maintenance

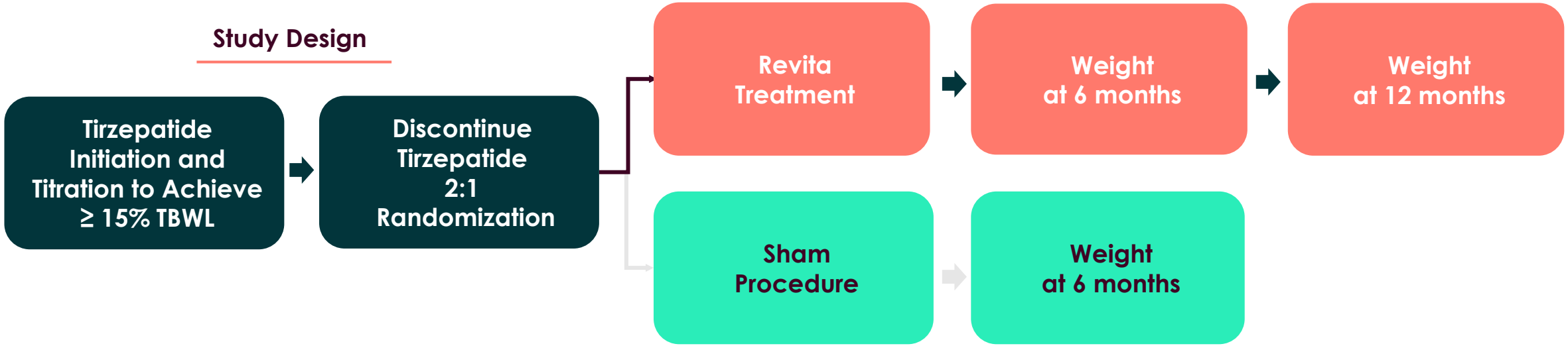
Pivotal Cohort data anticipated in H2 2026

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: early 2026**
- **Pivotal Cohort data: 6-month primary endpoint H2 2026**
- **Potential PMA filing: H2 2026**



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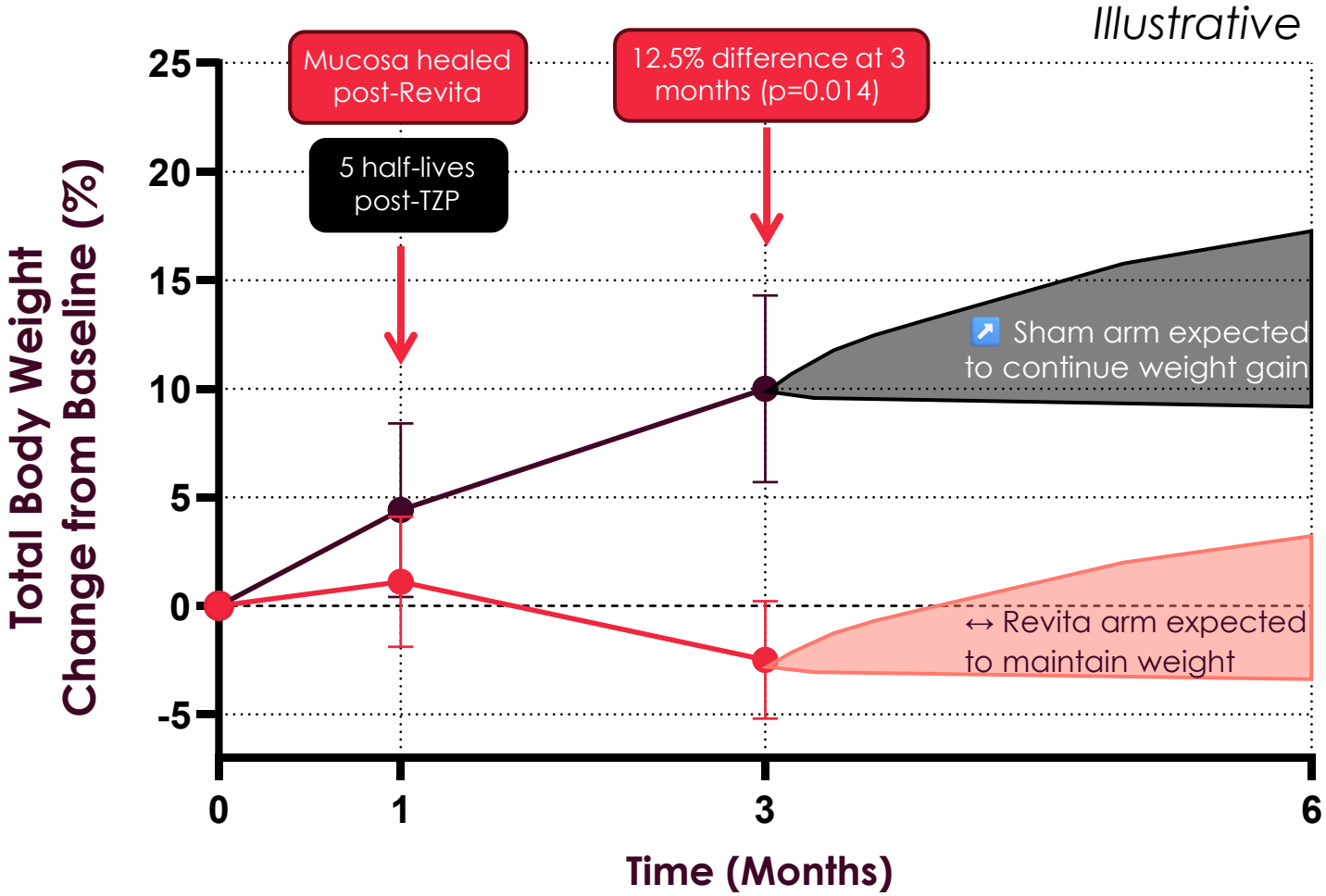
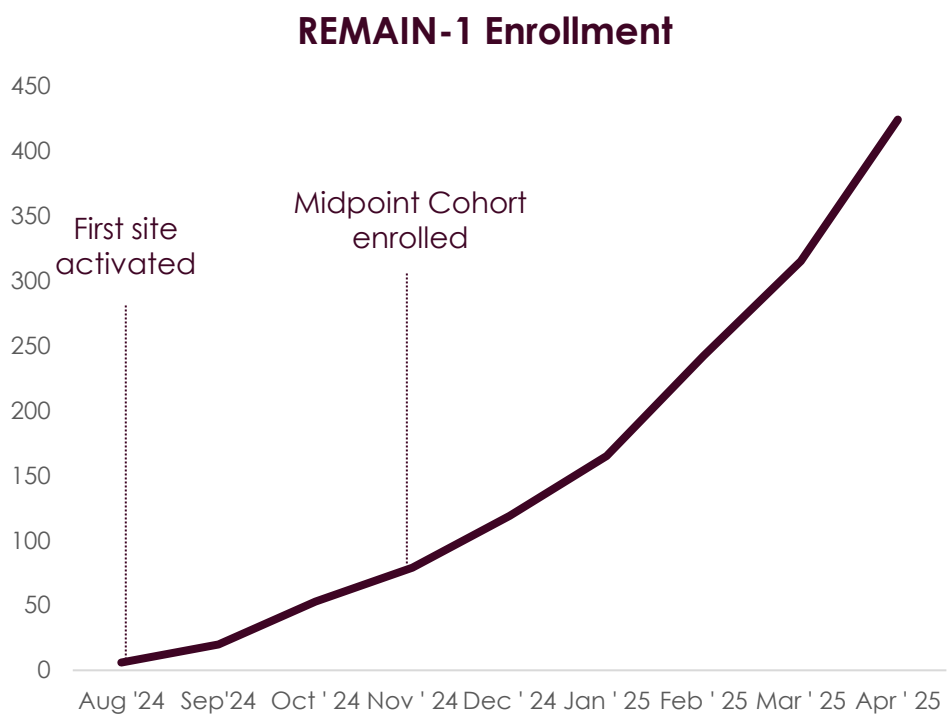
Observed 3-Month Treatment Effect Supports Potential Success in 6-Month Pivotal Cohort Primary Endpoint



REMAIN-1 Rapid Enrollment Underscores Market Potential and Readiness



REMAIN-1 Pivotal Cohort **fully enrolled 3 months ahead of schedule**

High site and patient enthusiasm points to unmet need

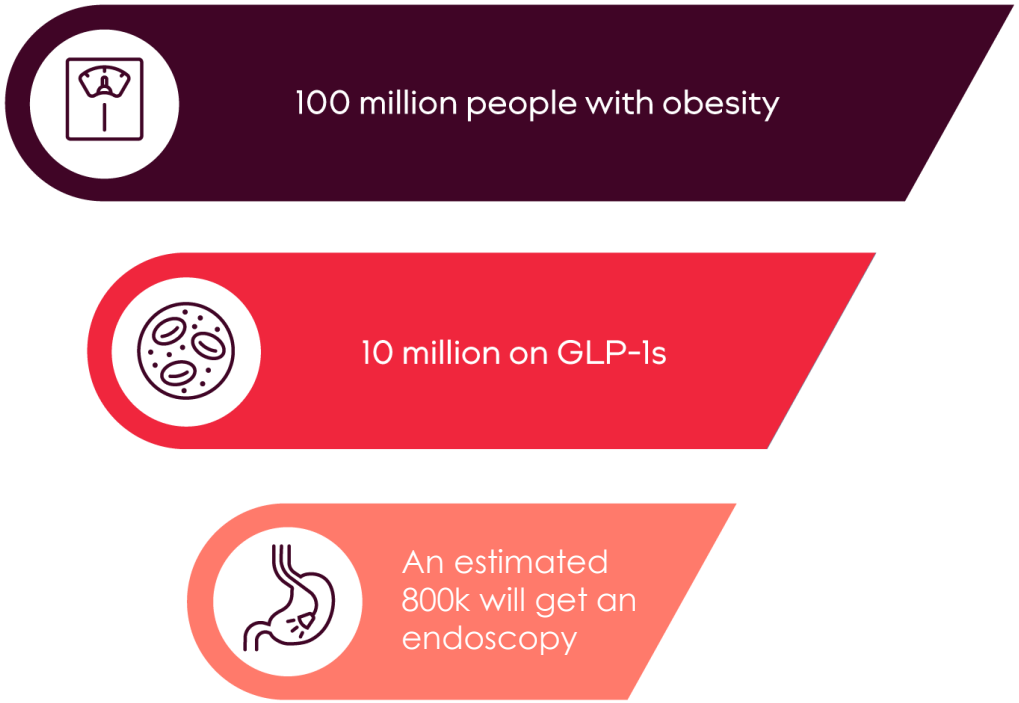
Multicenter U.S. study with **community and academic site participation**

Demand outstripped capacity at some centers

Rapid enrollment in first pivotal weight maintenance study reflects real-world clinical interest, physician engagement, and patient demand – key signals of commercial uptake potential

Revita targets a readily accessible patient population through routine upper endoscopy

- Of the estimated 10 million people on GLP-1s in the US today, we estimate ~ 800K will undergo an endoscopy this year – these are potential Fractyl patients
- Fractyl solutions are designed to fit into high volume, highly scalable workflow in endoscopy centers
- Strong clinical and economic value proposition for GI physicians
- GI endoscopists focused on obesity and metabolic disease therapies are currently participating in clinical studies



Potential candidates for Revita procedure

3-Month Midpoint Results Support Revita's Opportunity to Fundamentally Alter the Landscape of Obesity Treatment

- **Midpoint Cohort achieved its goal:**
  - Clear evidence of Revita's activity
  - Highly encouraging safety and tolerability profile
  - Builds confidence in powering assumptions for pivotal

- **Momentum and acceleration into next steps[1]:**
  - **Midpoint Cohort**: Anticipate 6-month results from these 45 subjects in Q1 2026
  - **Pivotal Cohort**: Study is fully enrolled and randomizing ahead of forecast. Anticipate completing randomizations in early 2026; topline primary endpoint and potential PMA filing in H2 2026

- **Potential backbone therapy in obesity**:
  - Proof-of-concept validated in post-GLP-1 weight maintenance
  - Opens the door for Revita as potentially first-line therapy in obesity and metabolic disease, add-on to GLP-1, etc.

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Significant Clinical Milestones for Revita in Weight Maintenance Over the Next 12 Months

				Key anticipated milestones[1]				
				2025	2026			
Platform	Indication	Program	Recent accomplishments	Q4	Q1	Q2	Q3	Q4
Revita (Outpatient endoscopic procedural therapy)	Weight Maintenance	REVEAL-1 Cohort (Open Label)	✓ Durable 3-mo data shared (June 2025)	**6-month open-label data in Q4 2025**		**1-year open-label data in Q2 2026**		
		REMAIN-1 Midpoint Cohort	✓ **3-mo sham-controlled data demonstrated prevention of weight regain (Sept 2025)**		**Randomized 6-month data in Q1 2026**			
		REMAIN-1 Pivotal Cohort	✓ Completed enrollment (May 2025)		**Complete randomization in early 2026**		**6-month primary endpoint data and potential PMA filing in H2 2026**	

- **Validated mechanism** – **potential backbone therapy** in obesity and related metabolic diseases
- **FDA Breakthrough Device designation** - **high unmet need** in post-GLP-1Rx weight maintenance clarifies regulatory and reimbursement pathway for Revita
- **Rapid clinical enrollment** – **strong signal** for motivated and ready patients and physicians
- **Product innovation** – ongoing product development designed to expand access to Revita for a broad population
- **Robust IP portfolio** – designed to **protect core inventions** of duodenal mucosal resurfacing **independent of ablation modality**
- **Substantial unmet need** – patients who cannot be served by drugs, signaling **significant market opportunity**
- **Express interest from potential customers** – signed LOI with leading outpatient provider of bariatric and metabolic endoscopy in the US

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. PMA=premarket approval