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

Corporate Presentation | September 2026

NASDAQ:GUTS

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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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Forward-looking statements in this presentation include, without limitation, statements regarding: the expected initiation, timing, design, endpoints, site activation, and conduct of the REMAIN-1 clinical trial program; RJVA-001 first-in-human clinical trial in the Netherlands and the RJVA-001 clinical trial in Australia; the timing and results of first-in-human dosing and reporting of preliminary data; Fractyl's regulatory strategy, including submissions to and communications with regulators in the European Union, Australia, and other jurisdictions; the promise, potential impact, and mechanism of action of RJVA-001 and Fractyl's Rejuva platform; the promise, potential impact, and mechanism of action of the Revita DMR system and Fractyl's Revita platform; Fractyl's anticipated financial performance, including cash and cash equivalents, for any period of time; Fractyl's expected cash runway; the promise and potential impact of Fractyl's preclinical or clinical trial data and product candidates, including Revita's potential for maintaining weight loss after glucagon-like peptide (GLP-1) based therapy discontinuation; the design, initiation, timing and results of clinical enrollment and any clinical studies or readouts, including readouts from the REVEAL-1 Cohort, the REMAIN-1 Midpoint Cohort and the REMAIN-1 Pivotal Cohort; the content, information used for, timing or results of any Investigational New Drug (IND)-enabling studies, IND applications, or CTAs; communications with regulators regarding the REVEAL-1 Cohort, the potential launch or commercialization of any of Fractyl's product candidates or products, the REMAIN-1 Midpoint Cohort and the REMAIN-1 Pivotal Cohort; the potential treatment population or benefits for any of Fractyl's product candidates or products; Fractyl's regulatory strategy, including potential use and benefits of the De Novo pathway (U.S. Food and Drug Administration (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's commercial readiness activities and the development of commercial infrastructure; the timing and content of any planned Investor Day or similar event; Fractyl's strategic and product development objectives and goals; the potential sales and estimated total addressable markets, currently and in the future, for Fractyl's product candidates; the potential timeline for profitability following the launch of Revita;' and the timing of any of the foregoing. 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GLP-1s unlocked weight loss, but durability remains unsolved

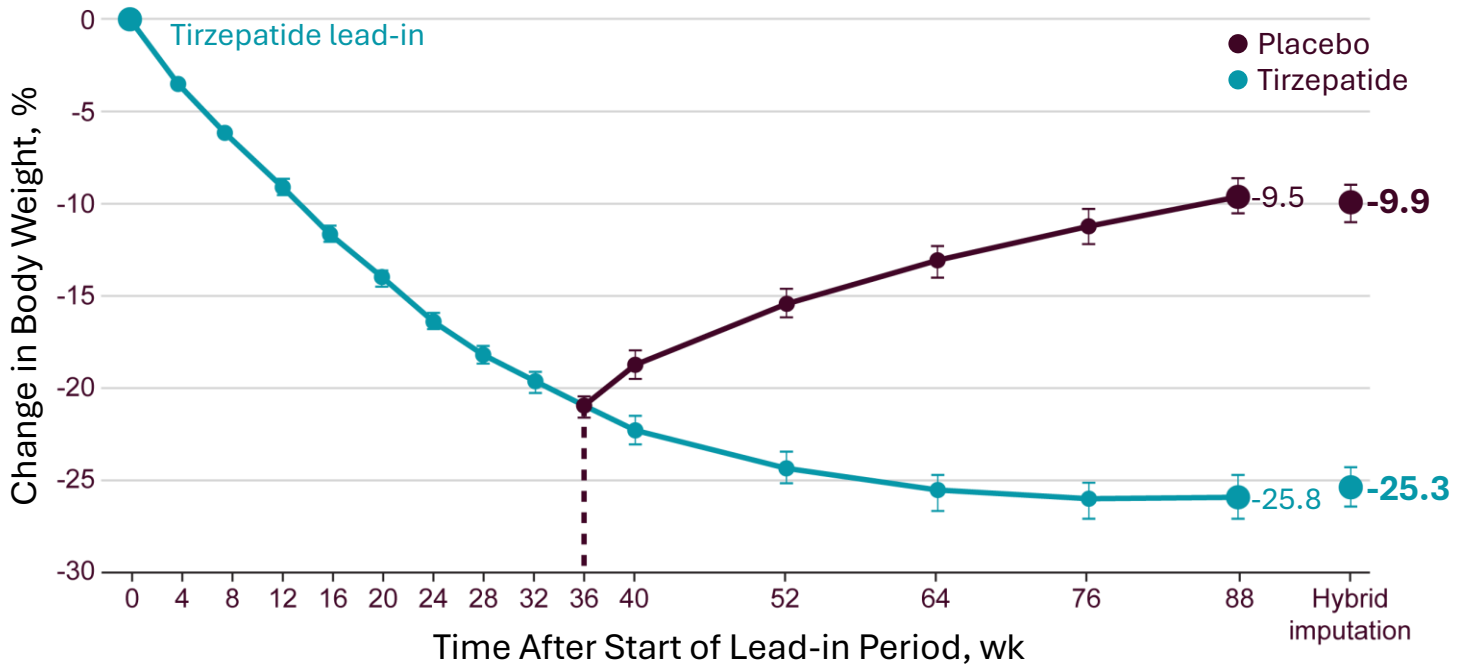
~29M Estimated U.S. patients on GLP-1s[1]

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

No FDA-approved therapies for post-GLP-1 weight maintenance

Percent change in body weight (week 0-88) from the SURMOUNT-4 Study[3]

Overall mean baseline body weight = 107.3 kg



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

[1]KFF Health Tracking Poll, Nov 2025: ~1 in 8 adults currently on a GLP-1 [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 U.S. 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

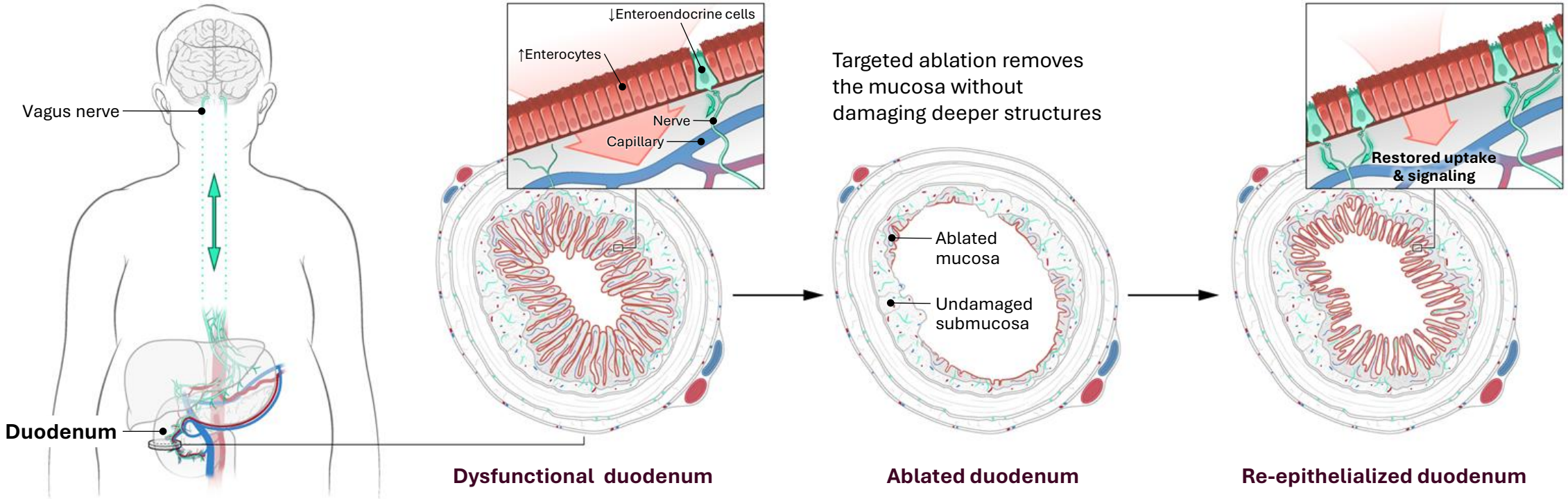
and mucosal ablation is a compelling modality for durable metabolic control

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]

Targeted ablation removes the mucosa without damaging deeper structures

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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Revita®

A one-time, outpatient procedure to ablate duodenal mucosa for durable weight maintenance

- A single outpatient endoscopic procedure
- Designed to complement pharmacology
- FDA Breakthrough Device designation
- Robust IP portfolio protecting first-mover leadership

Revita: a potential new backbone therapy in obesity

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

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Revita Duodenal Mucosal Resurfacing (DMR) procedure

Utilizes familiar skills, does not alter patient's anatomy, complements other approaches

Entire length of the post-papillar duodenum is treated through two primary actions:

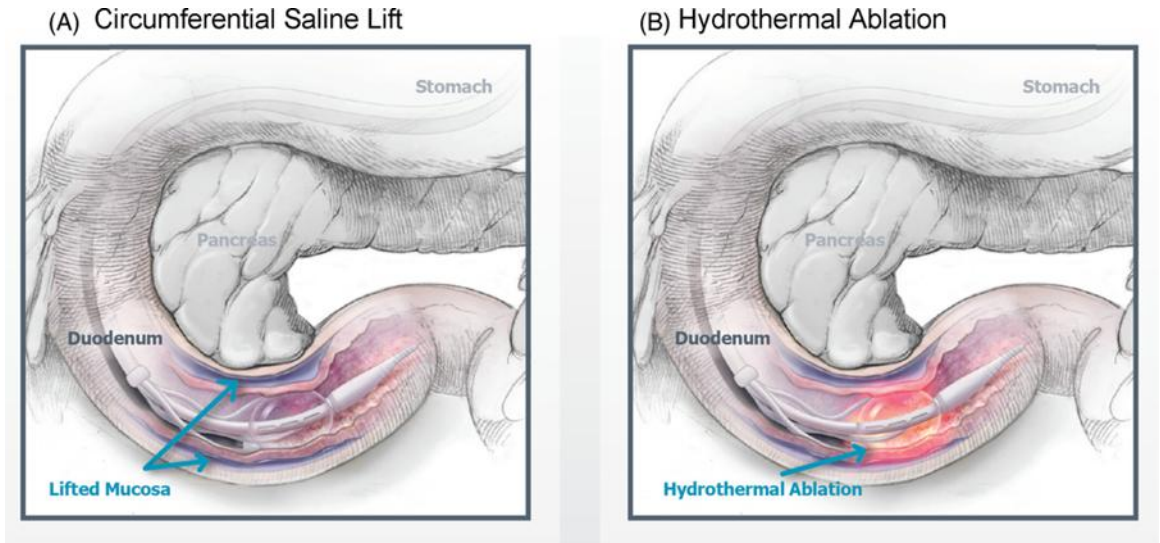
(A) **Circumferential saline lift**

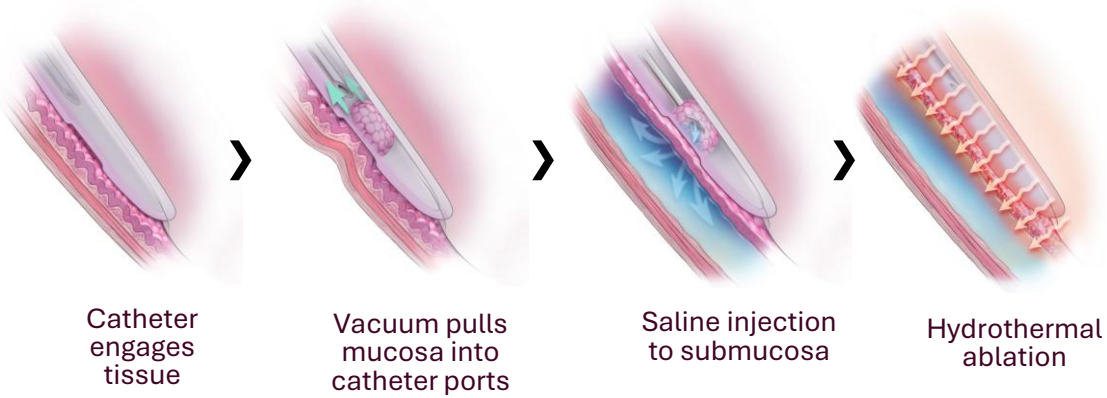
- Balloon engages tissue
- Vacuum pulls mucosa into ports
- Needle injects saline into submucosa

(B) **Hydrothermal ablation**

- Controlled hot water creates precise ablation at each lift site
- Steps repeated along full duodenal length (>14cm)

Utilizes familiar skills.
No implant or anatomy alteration.
Does not preclude any other therapeutic option.





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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** • **Topline 1-yr data: 1Q '27**

[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

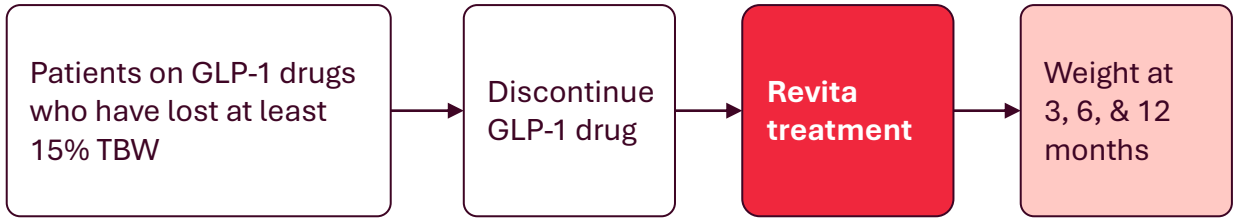
Primary endpoints

- 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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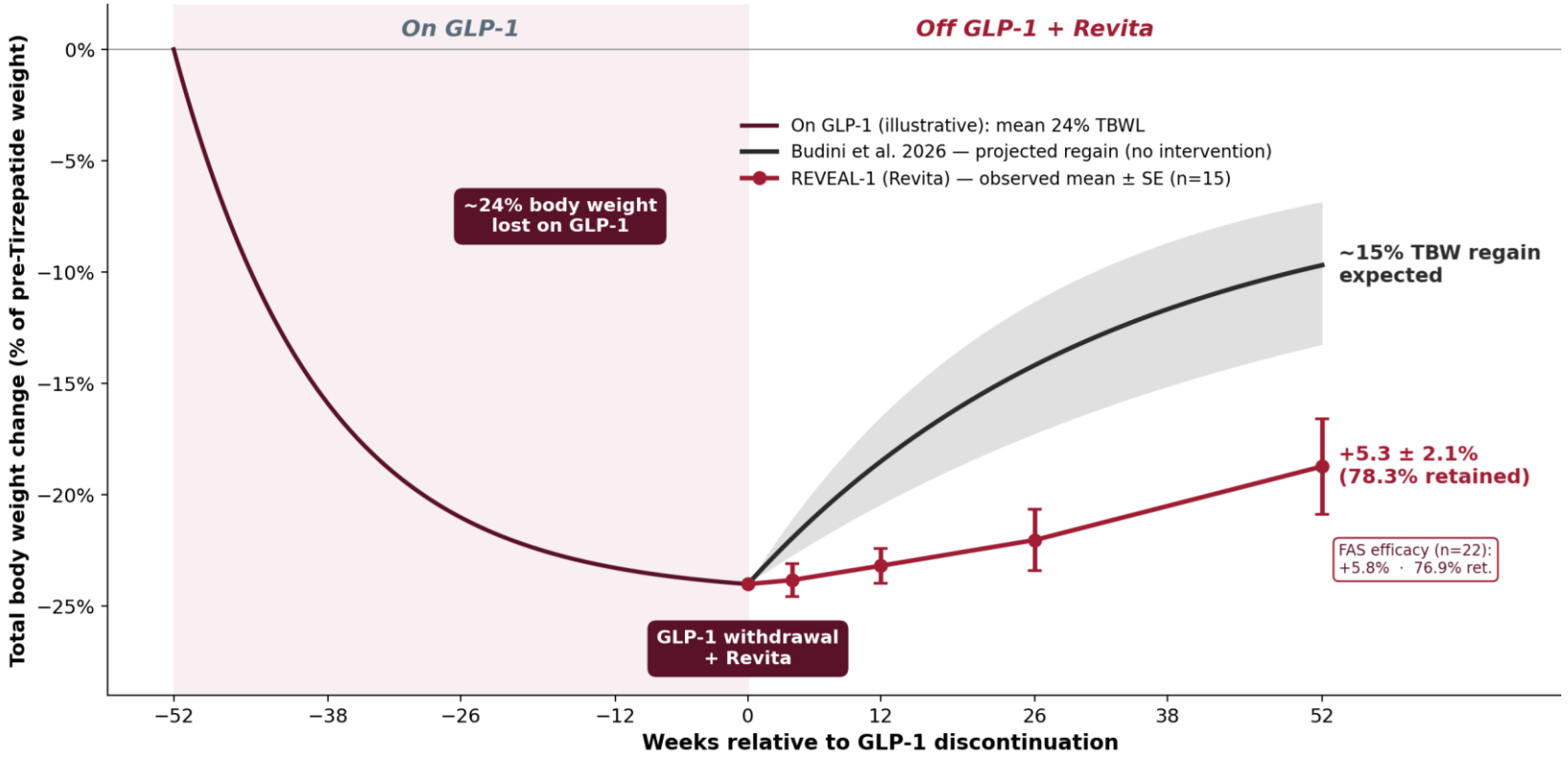
REVEAL-1 showed durable maintenance at 1 year

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

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

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REMAIN-1 Midpoint Cohort weight maintenance pilot

Designed to inform design and execution of 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

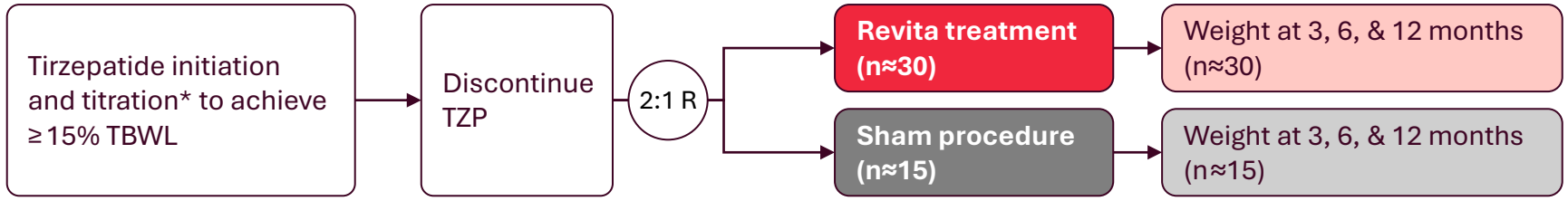
Study design

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

Key milestones

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

Study design



*Tirzepatide run-in modeled from SURMOUNT-4 trial. 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.

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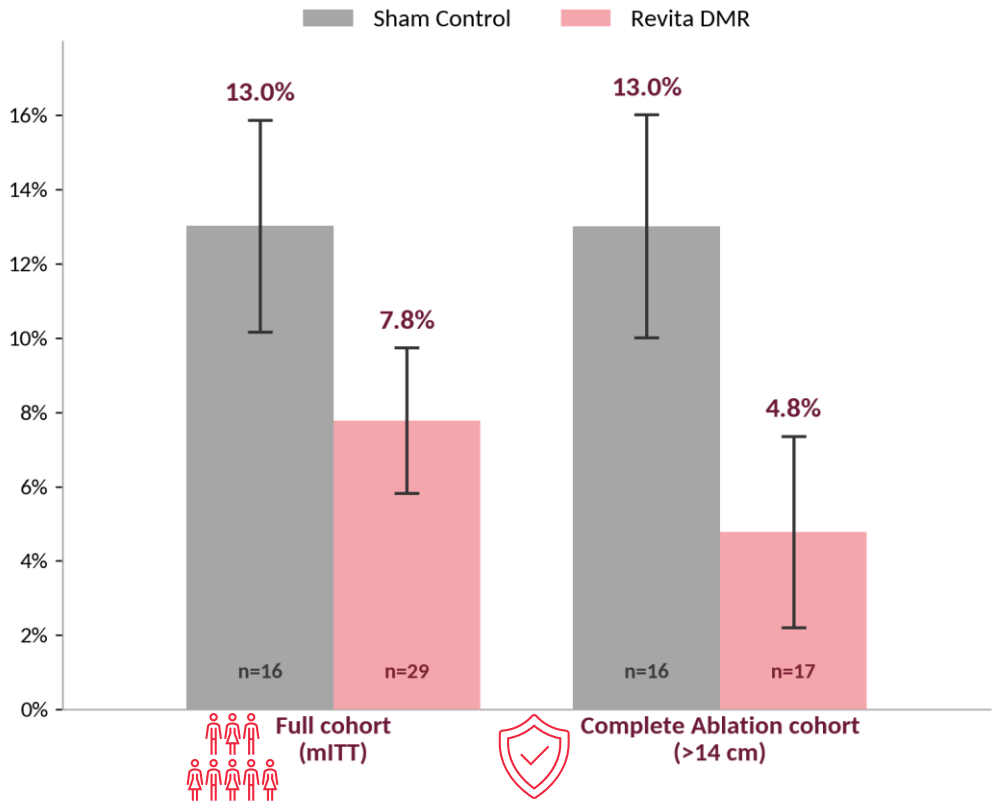
Revita reduces weight regain and benefits patients most when adequate dose of ablation is used

% Weight Change from Baseline at 12 months



- At 12 months, Revita reduced weight regain vs sham: 40% in the full cohort, rising to > 60% in patients with complete ablations > 14 cm
- Sham regain at 12 months consistent with 14% regain reported in SURMOUNT-4[1]

Full cohort (mITT): Sham n=16, Revita n=29. Complete Ablation cohort (> 14 cm ablation): Sham n=16, Revita n=17. LS-mean % total body-weight change from baseline at 12 months; MMRM, compound-symmetry covariance, estimated at 20% run-in weight loss; error bars ±SE. Exploratory REMAIN-1 Midpoint Cohort analysis; not powered for formal inference. 1. Aronne LJ, et al. Continued treatment with tirzepatide for maintenance of weight reduction (SURMOUNT-4). JAMA. 2024;331(1):38-48. Abbreviations: mITT, modified intention-to-treat; MMRM, mixed-model repeated measures; LS-mean, least-squares mean; SE, standard error.

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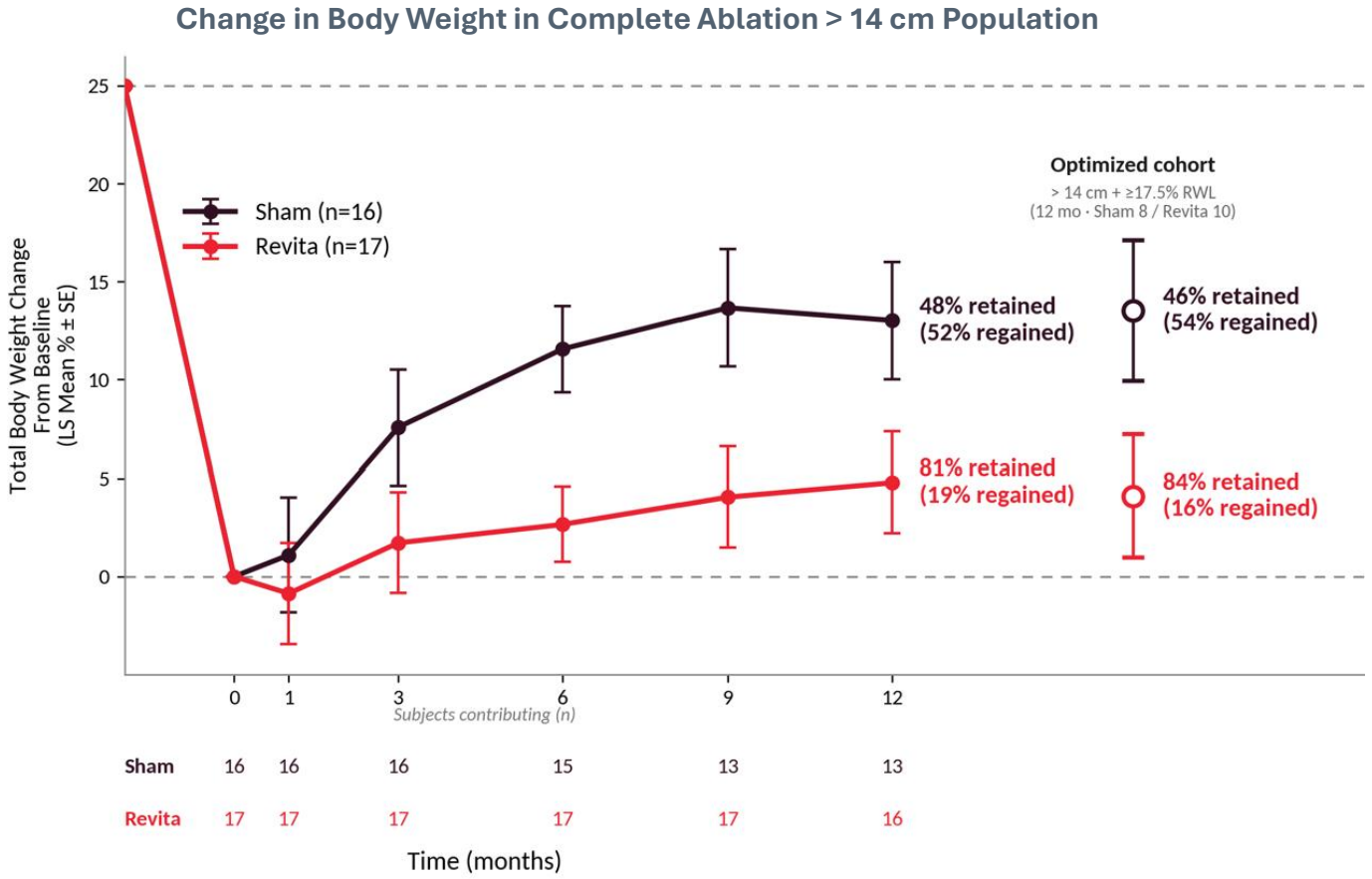
Revita cohort retained up to 84% of weight loss at 12 Months vs Sham Arm



Participants with complete ablations retained 81% of weight loss vs. 48% in sham at 12 months

The right patients, right dose (complete ablations and ≥ 17.5% RWL) **benefited most with 84% of their weight loss retained**

Pivotal Cohort implication:
Pivotal median ablation length is 16cm and mean TBWL on run-in is 18.3%, implying that the pivotal is enriched for both signals

Complete Ablation population: > 14 cm duodenal ablation, no run-in weight-loss restriction (Sham n=16, Revita n=17). Optimized population: complete ablation (> 14 cm) and run-in weight loss ≥ 17.5% (Sham n=8, Revita n=10). Y-axis: LS-mean % total body-weight change from baseline; MMRM, compound-symmetry covariance, estimated at 20% run-in weight loss; error bars ± SE; n contributing shown per visit below axis. Retention = % of run-in weight loss maintained at 12 months. Exploratory REMAIN-1 Midpoint Cohort analysis; not powered for formal inference. Abbreviations: MMRM, mixed-model repeated measures; LS-mean, least-squares mean; SE, standard error; SAP, statistical analysis plan.

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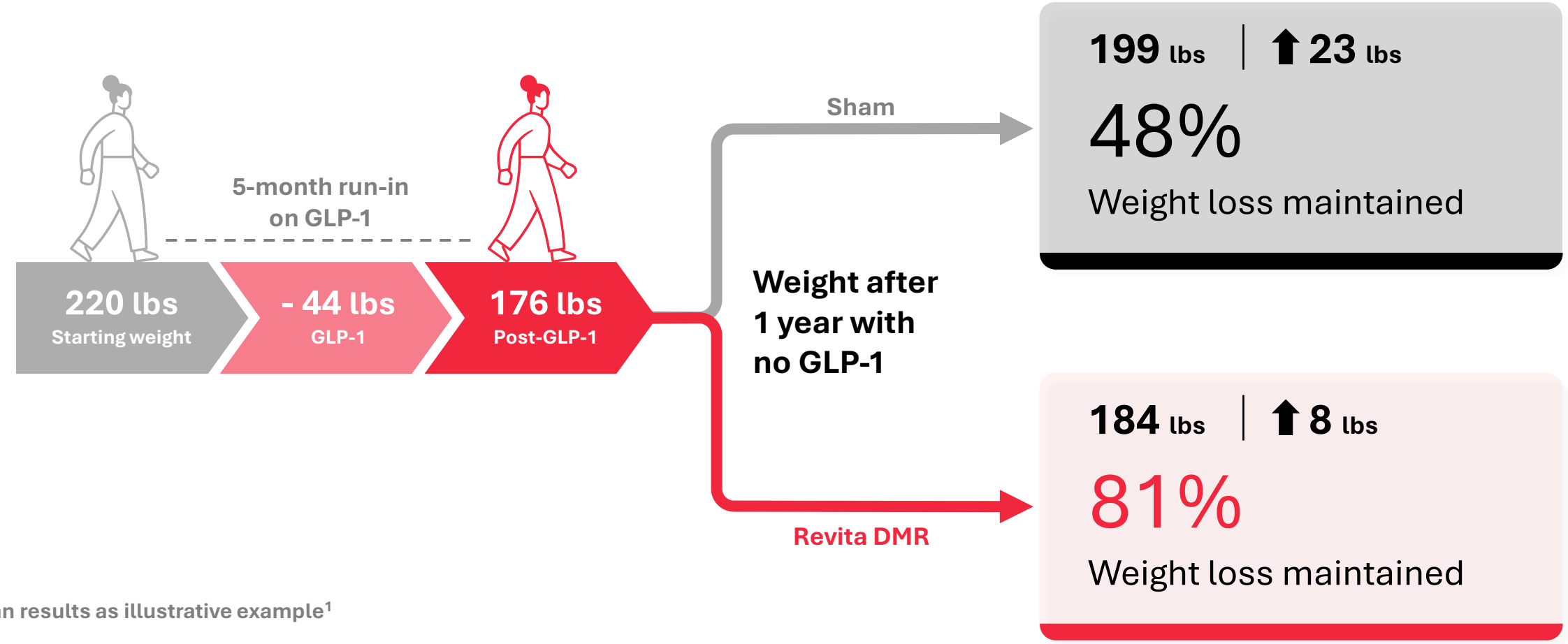
REMAIN-1 midpoint cohort at 1 year

Clinically meaningful effect size



Mean results as illustrative example[1]

[1]Complete ablation population in REMAIN-1 Midpoint Cohort.

FRACTYL health Revita is for Investigational Use Only under US Law

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Midpoint cohort: favorable safety through 12 months

No device-related serious AEs: a mild, periprocedural profile that supports outpatient use

- **No new device-related TEAEs between 6 and 12 months**
- **No device-related SAEs:** one SAE (blocked bile duct) adjudicated as unrelated to the device or procedure
- **No excess AEs with Revita:** any-TEAE rates matched sham (24% vs 25%)
- **Mild and periprocedural:** all 4 related events were Grade 1, on procedure day, and transient
- **1 new diagnosis of Type 2 Diabetes in sham arm vs zero in Revita arm**

Treatment-Emergent Adverse Events	**Revita** (n=29)	**Sham** (n=16)	**Total** (N=45)
Patients experiencing any TEAE n, (%)	**7 (24)**	**4 (25)**	**11 (24)**
TEAEs by grade, n (%)	**12**	**5**	**17**
Grade ≥3 TEAEs	1 (8)	0	1*
Grade 2 TEAEs	1 (8)	1 (20)	2**
Grade 1 TEAEs	10 (83)	4 (80)	14 (82)
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

Exploratory REMAIN-1 Midpoint Cohort analysis; not powered for formal inference.
*1 SAE: blocked bile duct (Grade IIIb, day 65); unrelated to device or procedure. **2 Grade 2 AEs: Revita worsening hypertension (day 258); Sham urinary tract infection (day 239); both unrelated.
Related TEAEs = probably related to device/procedure; all Grade 1, onset day 0. Two Sham AEs previously ungraded in EDC: nausea (day 0), Type 2 diabetes (day 363) are now classified Grade 1.REMAIN-1 Stage 2a, through 52 weeks (12 months). Abbreviations: AE, adverse event; TEAE, treatment-emergent adverse event; SAE, serious adverse event.

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REMAIN-1 randomized pivotal study in weight maintenance

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

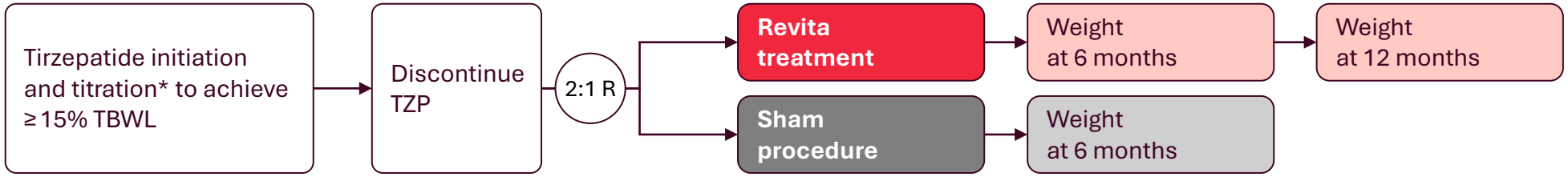
Study design

- 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



Top line results expected early Q4 2026 – de novo marketing submission to follow

*Tirzepatide run-in modeled from SURMOUNT-4 trial. 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; R, randomization; TBW, total body weight; TBWL, total body weight loss; TZP, tirzepatide; T2D, type 2 diabetes.

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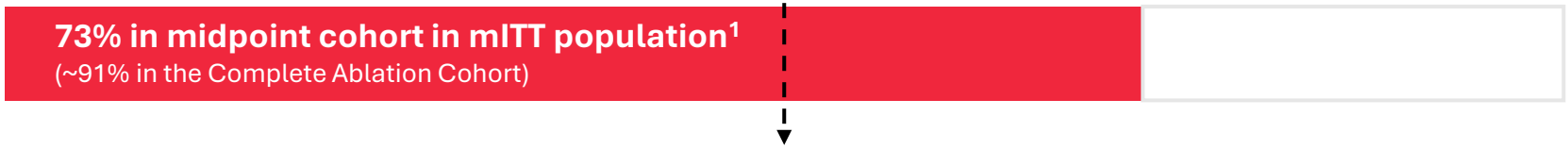
Co-primary endpoints well powered for pivotal trial success

First co-primary:
% TBW regain: Revita vs sham at 6 months

Illustrative sham 6-mo regain in mITT[1]	Revita regain needed to win[1,2]	Observed in midpoint cohort[1,3]	Projected pivotal p-value[4]
10%	≤ 7.4%	5.1%	*p<0.05*
11.6% (base case, current)	≤ 9.0%	5.1%	*p<0.05*
12.5%	≤ 9.9%	5.1%	*p<0.05*

Second co-primary: Responder rate:
% of Revita patients maintain ≥ 5% TBWL at 12 months



50% = FDA-mandated pre-specified performance goal (single-arm)

[1]Values shown are model-based estimates (mITT MMRM at the 20% run-in weight-loss reference). REMAIN-1 Midpoint Cohort, exploratory. [2]Maximum Revita weight regain at which the pivotal reaches statistical significance vs the sham scenario shown (~ 2.5-point gap at pivotal N=315). [3]5.1% = LS-mean percent total body-weight regain from post-run-in baseline at 6 months (Week 26); mITT MMRM at 20% run-in weight-loss reference; n=29 Revita. REMAIN-1 Midpoint Cohort, exploratory. [4]Two-sided; Revita vs sham, pivotal N=315, randomized 2:1 (Revita:sham). Sham values illustrative.
Abbreviations: LS-mean, least-squares mean; mITT, modified intention-to-treat; MMRM, mixed-model repeated measures; TBW, total body weight; TBWL, total body weight loss; .

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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
- One pivotal study is the registrational package
- A successful de novo would make Revita the reference device for the category
- 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.

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~4M eligible patients for Revita translates to $40-120B opportunity*

US GLP-1 users → patients clinically eligible for Revita (post-GLP-1 weight maintenance)

Bars: ● share of prior step retained (point estimate)

~4M

eligible patients

* TAM is an internal figure developed by management based on certain assumptions that management believes to be reasonable as of the date hereof. Please refer to the disclaimer titled "Market Data, Estimates and Industry Information" set forth on Slide 2 of this presentation.[1]Gallup 2026 — ~11% of ~262M US adults currently on a GLP-1 for weight loss. [2] 65% discontinuation rate is for individuals without T2D - Rodriguez et al., JAMA Netw Open 2025;8(1):e2457349. [3]30% base · Monte Carlo median 29.3% based on Fractyl market estimates. [4]On-label BMI 30–45 (~70%; RWE / Fractyl est.) Abbreviations: TAM, total addressable market

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Targeted and efficient COE launch strategy

Focused on top 10-20% high volume comprehensive metabolic centers across the U.S.

~1,000

Accredited centers, U.S. and Canada[1]

100–200

Early launch starts with top 10–20% of potential COEs

First wave includes Revita clinical centers and established ASMBS COEs

Locations approximated from the ASMBS center locator. Illustrative. 1 https://www.facs.org/quality-programs/accreditation-and-verification/metabolic-and-bariatric-surgery-accreditation-and-quality-improvement-program/

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Site-level volume potential is material and credible

Initial target centers

100–200

High-volume systems

GLP-1 patients/center/year

>2000

Patients at ready COEs[1]

Potential procedures /center/year

250–500

Procedures during ramp[1]

1. Company estimates

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Reimbursement execution already underway

Hospitals have a clear path to permanent reimbursement and Medicare coverage of GLP-1s is expanding right as Revita would launch.

1 Coverage

Pivotal data & real-world registry to support Medicare & commercial coverage

2 Coding

Dedicated Cat III CPT code at launch with defined path to permanent Category I code

3 Payment

Transitional Pass-Through & New Tech APC to establish new payment category

Tailwind at Launch: Medicare's GLP-1 Bridge Program

Medicare began covering GLP-1s for obesity July 1st, 2026 - expanding potential discontinuation pool just as Revita approaches a potential launch

Potential upside: CMS pathways like RAPID could speed national coverage after FDA authorization but not required for launch

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TPT, CPT coding, and coverage pathways are subject to CMS, AMA, and payer review cycles; outcomes are not assured. RAPID is a proposed CMS model. Statements assume FDA marketing authorization, which is not assured.

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Major payers already cover obesity procedures

Bariatric surgery + GLP-1 coverage provide tailwinds for potential Revita coverage

Payer	2025 commercial lives[1]	GLP-1s for obesity[2]	Bariatric surgery[3]
United Healthcare	~35M	Prior Auth + opt-in	Covered
Elevance Health	~30M	Prior Auth + opt-in	Covered
aetna™	~20M	Prior Auth + opt-in	Covered
Cigna	~18M	Prior Auth + opt-in	Covered
HCSC Health Care Service Corporation	~14M	Prior Auth + opt-in	Covered
CMS (Medicare)	~68M[4]	GLP-1 Bridge	Covered

~190M lives sit with the six payers already reimbursing bariatric surgery

[1]Total U.S. medical enrollment, all lines — Mark Farrah Associates / Peterson–KFF, 2025; CMS row is Medicare Part D enrollment, not commercial. [2]Obesity indication; PA + employer election typically required (CVS Caremark 7/25; Evernorth 5/25). [3]Payer commercial medical policies; typical criteria BMI ≥40 or ≥35 + comorbidity (UnitedHealthcare policy, 2026). [4]Medicare GLP-1 Bridge: CMS §402 demonstration, Jul 1 2026–Dec 31 2027, outside Part D payment flow; $50/mo copay, central processor for PA (CMS, 2026). BALANCE Model indefinitely delayed. Bariatric surgery per NCD 100-1.1.

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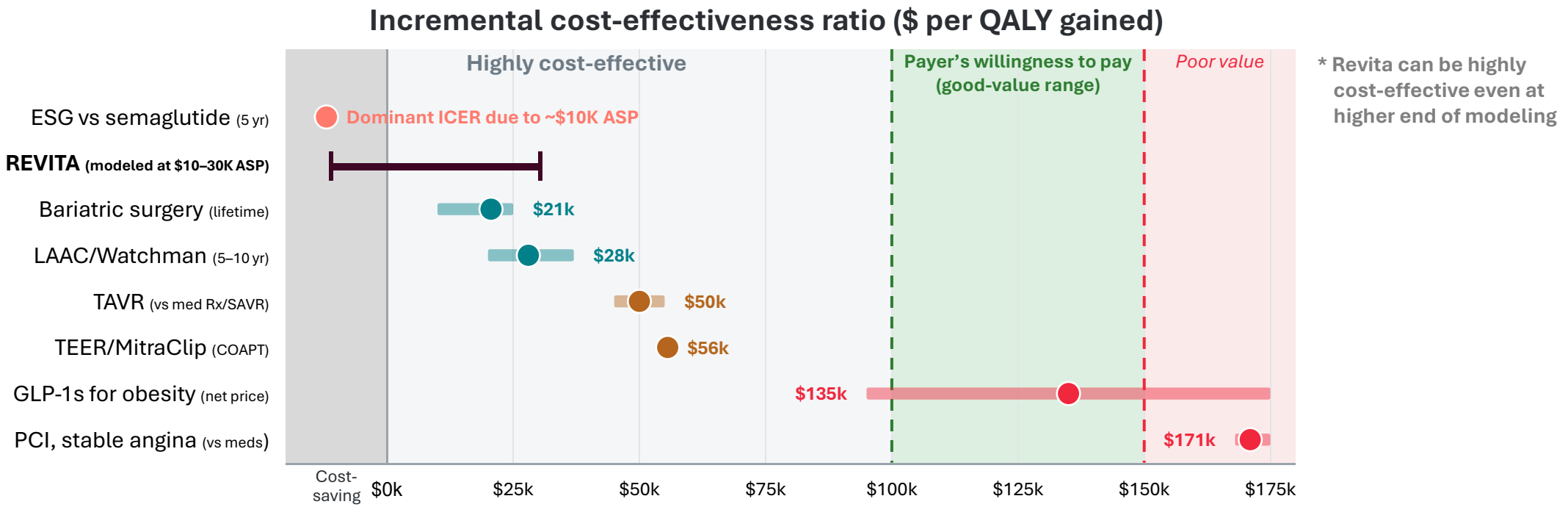
A one-time procedure that maintains post-GLP-1 weight loss can be highly cost-effective

We believe Revita's modeled cost-effectiveness is highly favorable: Better cost per QALY than widely covered CV procedures, bariatric surgery, and comparable to ESG-vs-GLP-1 at lower ASP



Based on published cost to payers and cost-effectiveness benchmarks for obesity therapies and other device-based interventions

Sources: JAMA Netw Open 2024 (ESG vs semaglutide, dominant at ~$10K ASP); ACS Clinical Congress 2024 & lifetime CE literature (bariatric surgery $10k–$25k/QALY); Stroke 2018 / PROTECT AF (LAAC); PARTNER economic substudies (TAVR); COAPT (TEER); ICER 2025 net-price review (GLP-1s); COURAGE (PCI). Revita value is internal model, not peer-reviewed. IVL omitted — no published ICER. Cross-study comparisons are directional: populations, comparators, & horizons differ.

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Revita pricing corridor

Bracketed by the endoscopic and surgical benchmarks that payers already pay

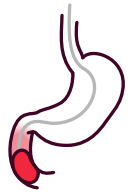
Endoscopic sleeve gastroplasty

~$11,600[1]+

CPT 43889 – APC 5362
Category I code effective Jan 1, 2026

Medicare, hospital outpatient
$10,860 facility + $720 physician

Self-pay market
$8,000 – $15,000, bundled



Revita DMR

Pricing to be determined

Outpatient endoscopic
Under one hour, same-day discharge

No resection or anatomic change
Repeatable; no permanent implant

Duodenal target
Distinct mechanism from restriction

Bariatric surgery

Up to $33,000[2]

Sleeve gastrectomy, CPT 43775
Inpatient only under Medicare

Commercial/uninsured
$20,000 – $33,000

[1] ESG Lower bound is the CY2026 Medicare national average in the hospital outpatient setting: $10,860 facility (OPPS APC 5362, a Comprehensive APC — device cost is bundled, not separately paid; CMS-1834-FC) plus $720 physician (PFS at a $33.40 conversion factor; CMS-1832-F), before the 2% sequestration reduction. Upper bound is the published US self-pay range for ESG, typically $8,000–$15,000 as a bundled package.
[2] Bariatric surgery Lower bound is CY2026 Medicare for an uncomplicated laparoscopic sleeve gastrectomy: MS-DRG 621 at $10,976 (IPPS) plus $1,000 physician (CPT 43775); MS-DRG 619 with a major complication or comorbidity pays $21,011. Upper bound is self-pay and uninsured list pricing from published market surveys — a charge, not a payer-allowed amount. Published commercial episode payments sit materially below it.

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Potentially attractive unit economics at the center and at the company

Unit economics potentially favorable for hospital and Fractyl

The hospital's view

- Endoscopy and bariatrics are major drivers of hospital contribution margin
- TPT enables positive contribution margin by passing disposable costs through to CMS
- No new capital footprint to justify

Fractyl's view

- High gross margin of ~80%
- Capital-light: no high cost, long lead-time sales cycle per site
- Commercial cost scales with sites, not linearly with volume

Recurring, high-margin procedure revenue concentrated in high-throughput centers

Hospital economics assume pass-through plus facility payment.

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Potential Revita unit economics and breakeven

Potential 80% gross margin leads to cash break even 5-8 quarters after launch

Price per procedure

$11[1]–33K[2]

Published benchmark range

ESG: $11,600 Medicare

Bariatric: $20,000 private payer

Bariatric: $33,000 self-pay list

×

Gross margin at scale

~80%

Held constant across scenarios

Margin held flat across scenarios rather than modeled; higher-ASP cases would carry higher margin and earlier break-even than shown

›

Procedures to breakeven

80% gross margin, $22M quarterly operating cash burn

ASP	GP/proc	Procedures/qtr	Break-even
$10,000	$8,000	2,750	**2H 2029**
$20,000	$16,000	1,375	**1H 2029**
$30,000	$24,000	920	**Q1 2029**

Key Assumptions | Anticipated De novo clearance in late 2027 — CMS coverage and transitional pass-through early 2028

Price benchmarks: CY2026 Medicare national averages (OPPS APC 5362; IPPS MS-DRG 621) and a derived private-payer estimate. Gross margin, operating cash run-rate and center productivity are Fractyl assumptions. Break even quarters are contingent on De Novo authorization, coverage and financing, and are not guidance.

[1] ESG Lower bound is the CY2026 Medicare national average in the hospital outpatient setting: $10,860 facility (OPPS APC 5362, a Comprehensive APC — device cost is bundled, not separately paid; CMS-1834-FC) plus $720 physician (PFS at a $33.40 conversion factor; CMS-1832-F) [2] Bariatric surgery Lower bound is CY2026 Medicare for an uncomplicated laparoscopic sleeve gastrectomy: MS-DRG 621 at $10,976 (IPPS) plus $1,000 physician (CPT 43775); MS-DRG 619 with a major complication or comorbidity pays $21,011. Upper bound is self-pay and uninsured list pricing from published market surveys

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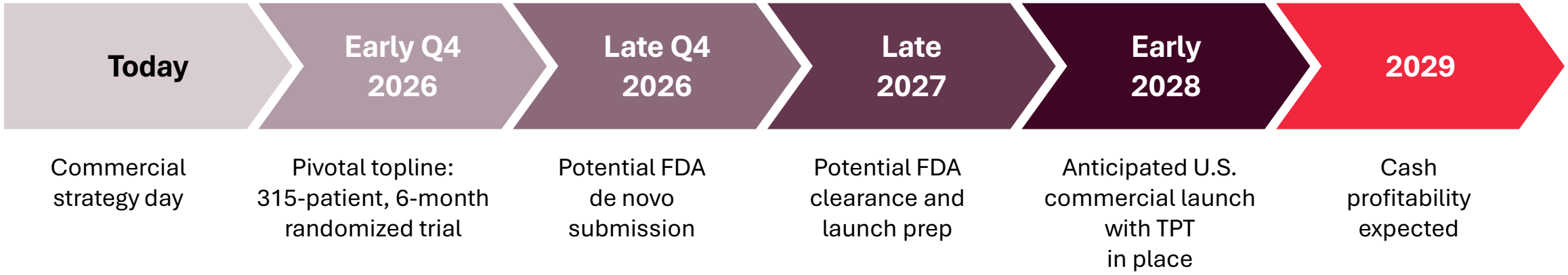
Clear commercial strategy to potential cash profitability within 5–8 quarters of launch



Timelines are management estimates and forward-looking; actual events may differ. Revita is investigational — commercialization is subject to REMAIN-1 results and FDA marketing authorization, neither of which is assured.

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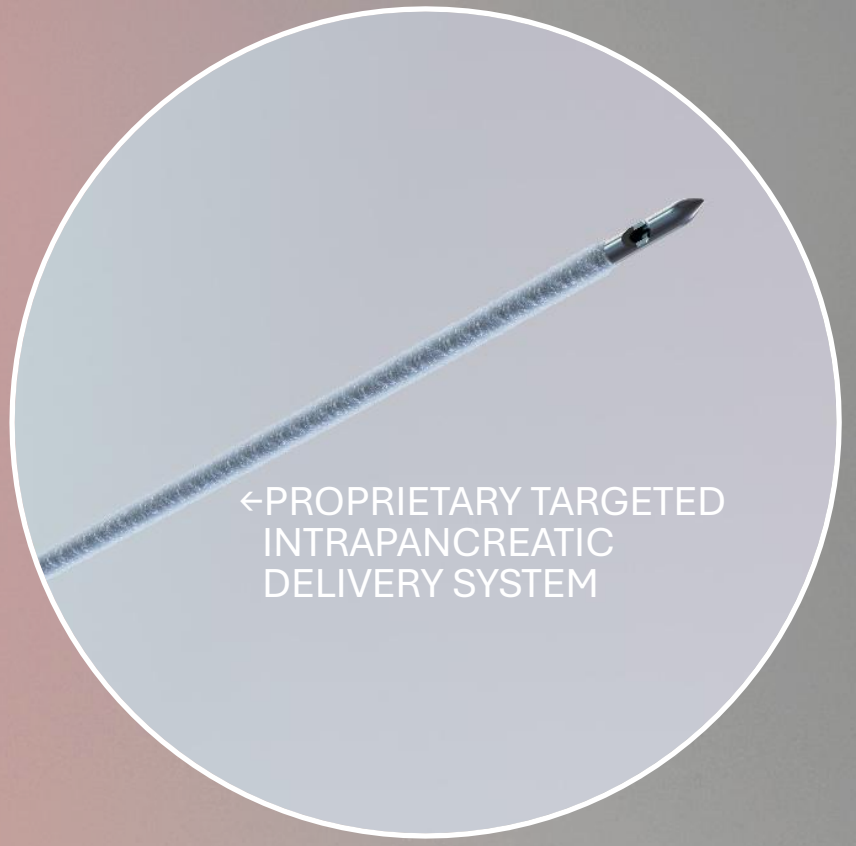
Rejuva®

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.

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Reimagining gene therapy economics for metabolic disease

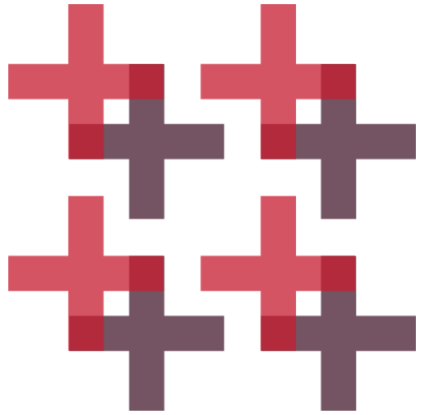
Large patient population

~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.

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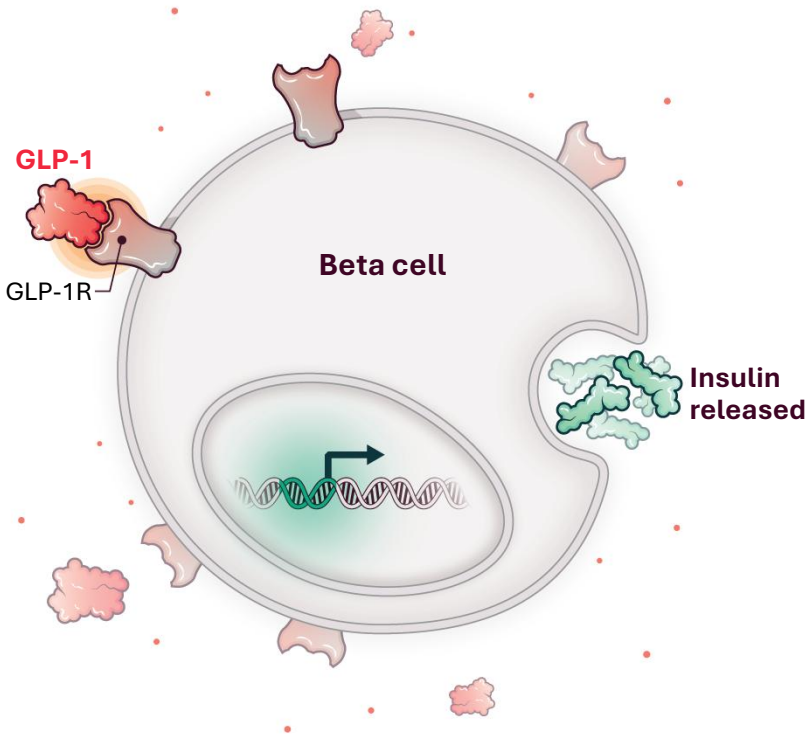
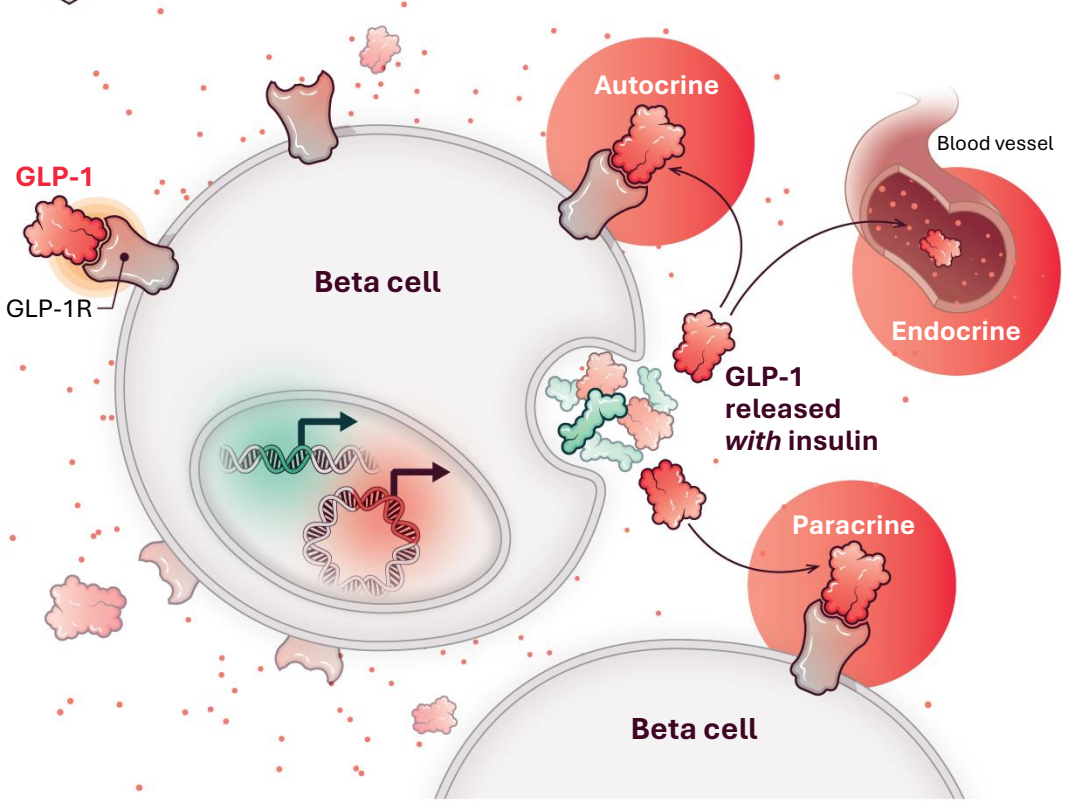
RJVA-001 for T2D

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.

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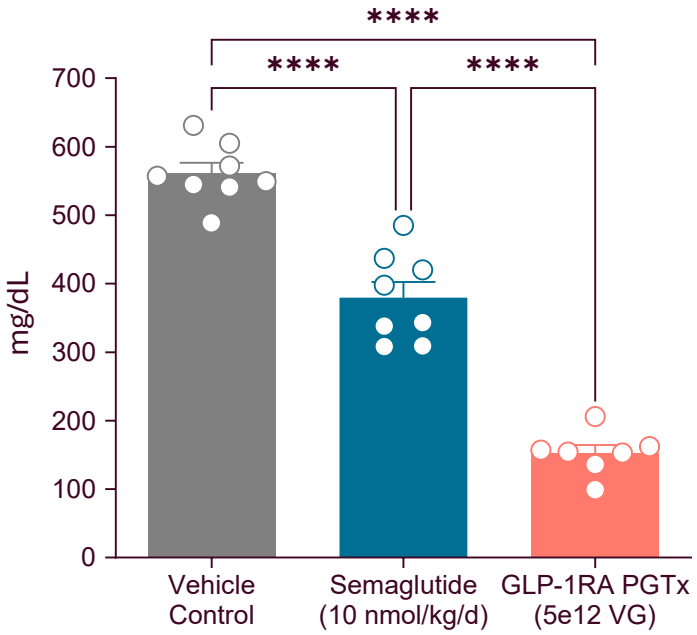
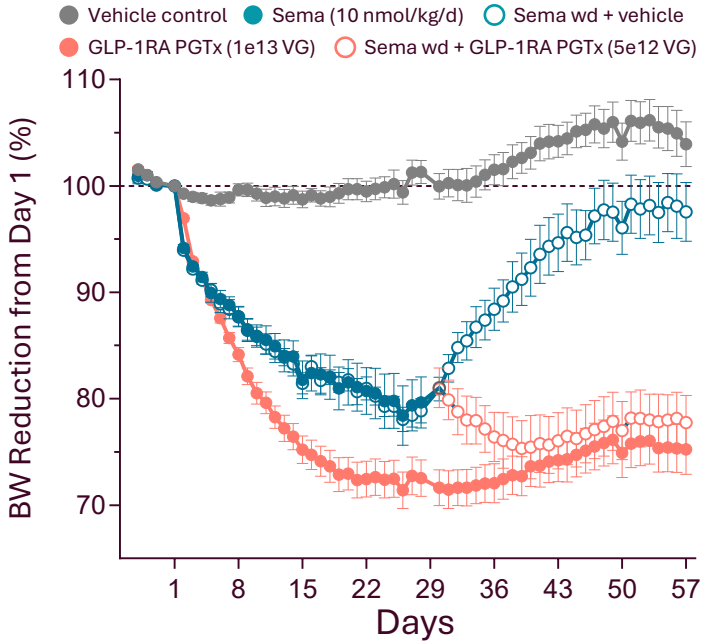
Potent efficacy in T2D & obesity mouse models with no toxicity observed in large animal model

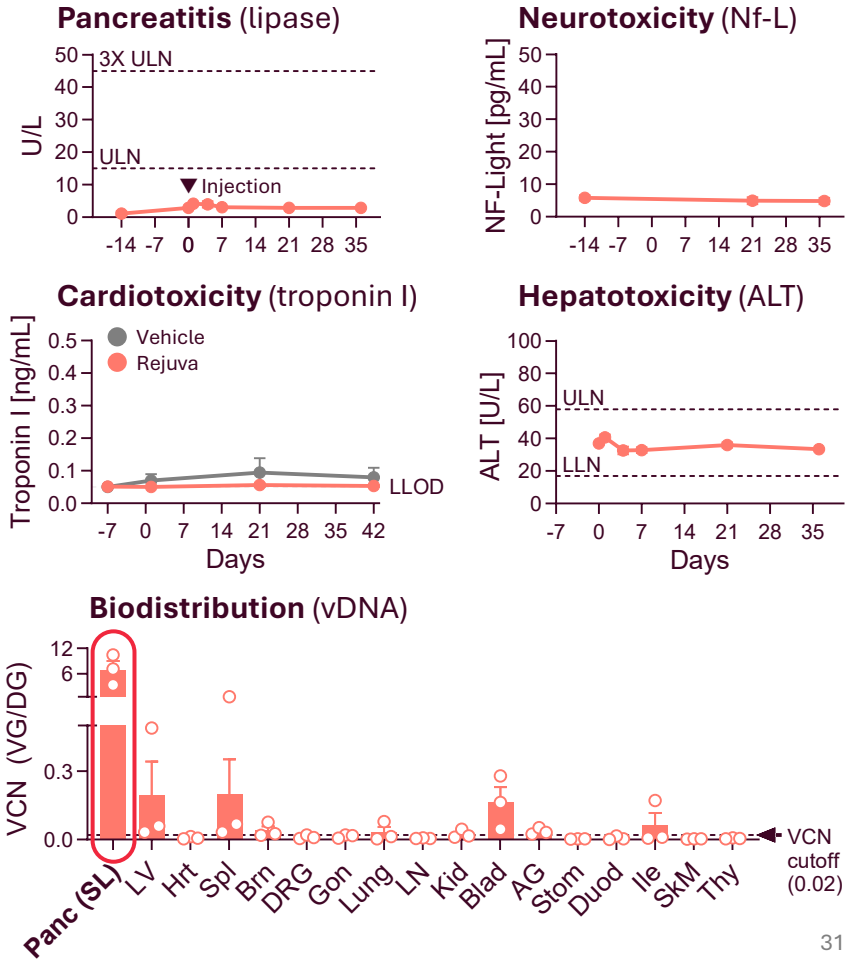
Glucose-lowering activity in *db/db* mouse model[1]



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.

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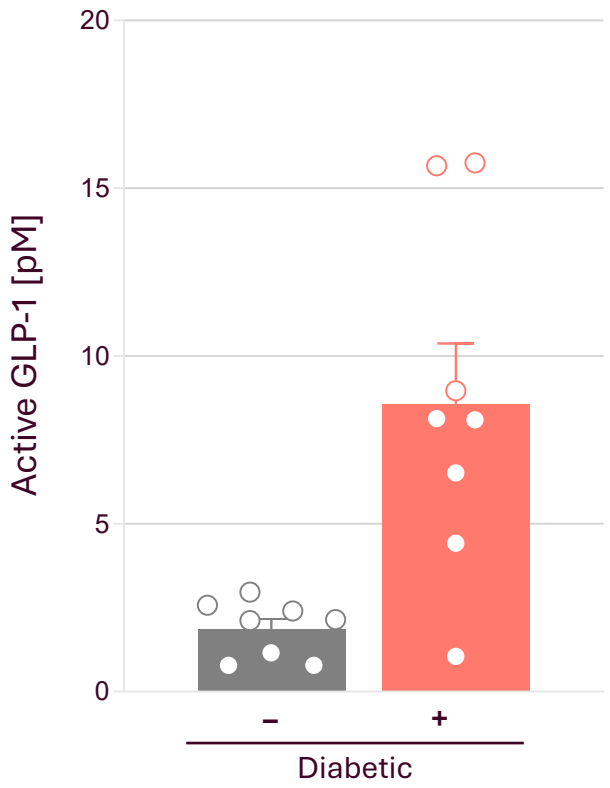
Robust efficacy without high systemic GLP-1 exposure

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.

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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)

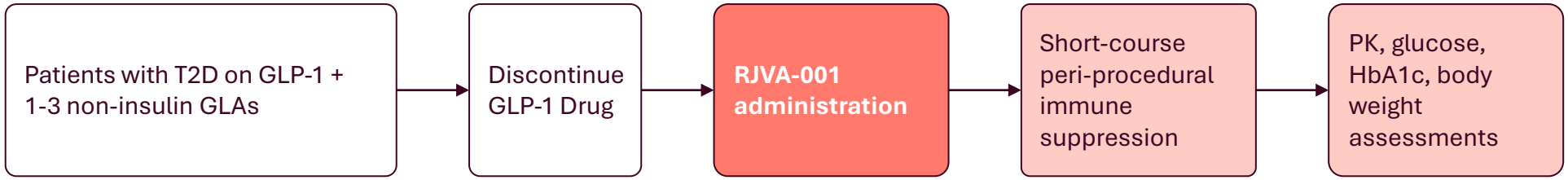
Study design

- 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

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.

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Robust IP estate covering Revita & Rejuva

Strategic platform for long-term value and optionality

Global footprint[1]

36	Active patent families
100+	Patents issued globally
37	Patents issued in the US
80+	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 August 2026.

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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*

Key Anticipated Milestones[1]

Indication	Program	Recent accomplishments	Q2'26	Q3'26	Q4'26	Q1'27
Weight Maintenance	REVEAL-1 Cohort (Open Label)	✓ Durable 1-year data shared (June '26)	✓ 1-year data			
	REMAIN-1 Midpoint Cohort	✓ Positive 1-year randomized data (July '26)		✓ 1-year data		
	REMAIN-1 Pivotal Cohort	✓ Completed randomization (Feb '26)			**Topline 6-mo randomized data & potential De Novo marketing application submission**	1-year data

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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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

Mike Zumdahl
Sr VP of Market Access & Commercial Strategy

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

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Thank you

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NASDAQ:GUTS

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Appendix

NASDAQ:GUTS

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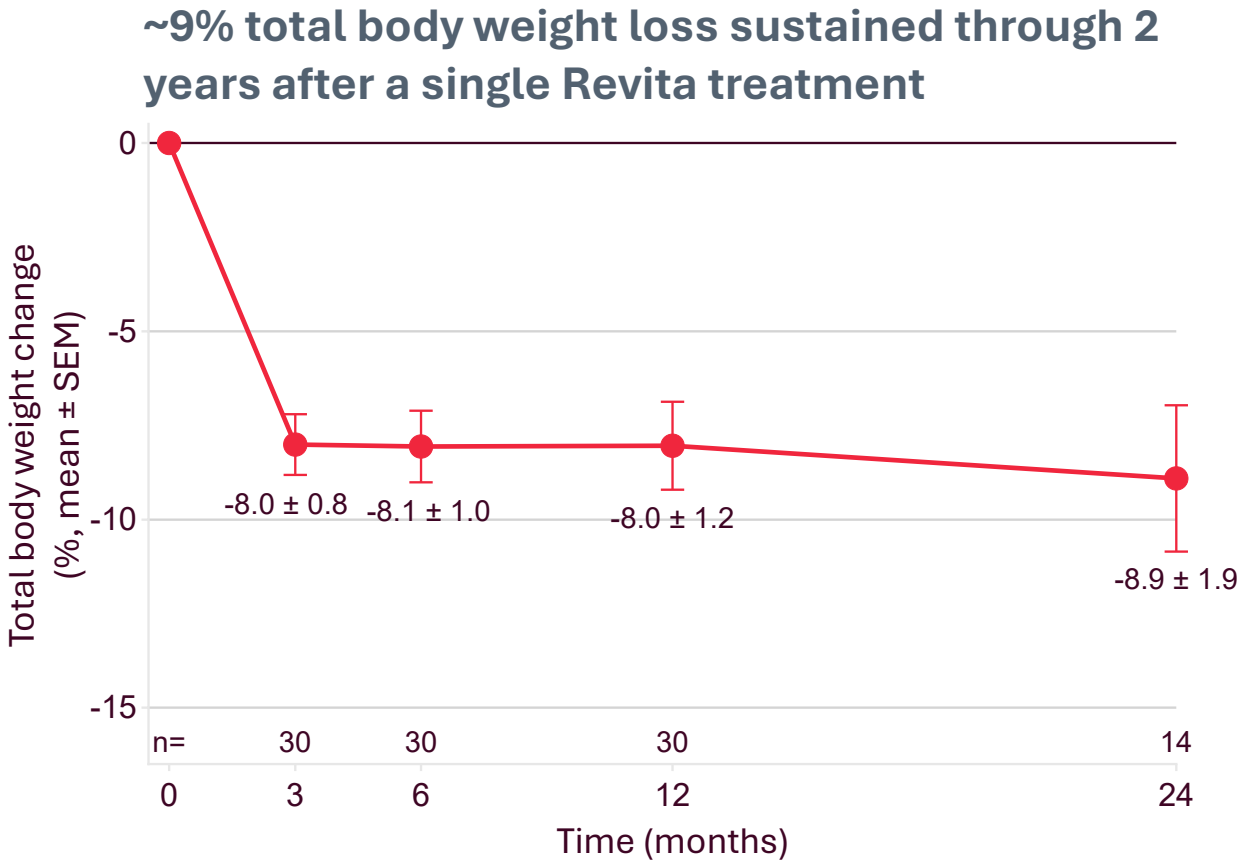
Real-world data show sustained 2-year metabolic benefits after a single Revita treatment



- **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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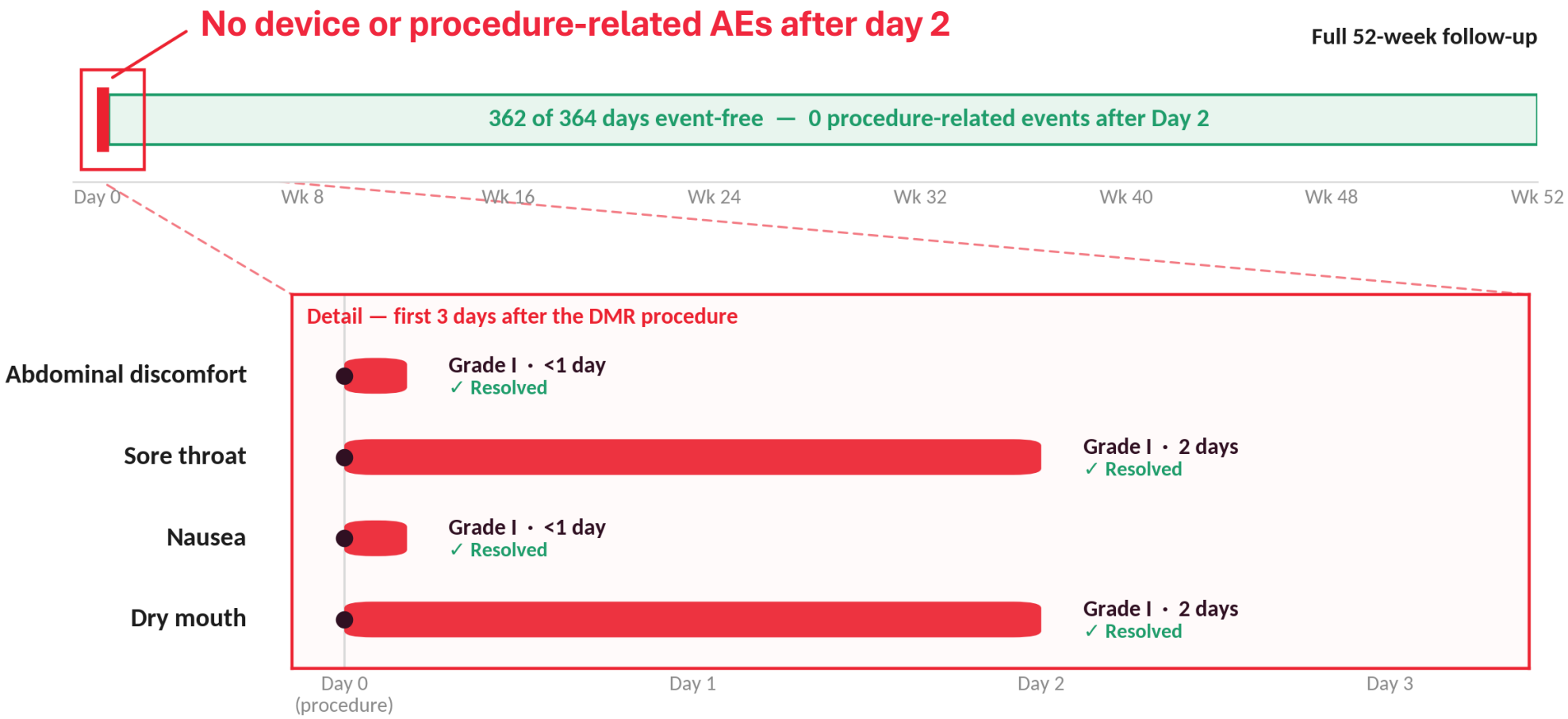
Procedure-related AEs: Mild, immediate, short-lived

No related SAEs: a mild, periprocedural profile that supports outpatient use



Exploratory REMAIN-1 Midpoint Cohort analysis; not powered for formal inference. Abbreviations: DMR, duodenal mucosal resurfacing; AE, adverse event; SAE, serious adverse event.

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Medicare alone is a multi-billion dollar opportunity

GLP-1 Bridge program may create a massive discontinuation pool Revita is designed to help

~4M

Medicare beneficiaries expected to access GLP-1s through the Bridge[1]

2–3M

expected to discontinue within a year | Bridge expires 12/31/2027[2]

600–970K

an estimated will achieve a deep response before stopping[3]

510K – 830K CMS beneficiaries eligible for Revita & TPT[3]

[1]https://www.kff.org/medicare/nearly-four-million-medicare-beneficiaries-met-the-eligibility-criteria-in-2023-for-the-medicare-glp-1-bridge . [2]CBO estimates 65% discontinuation - Publication 60441. [3]Company estimates

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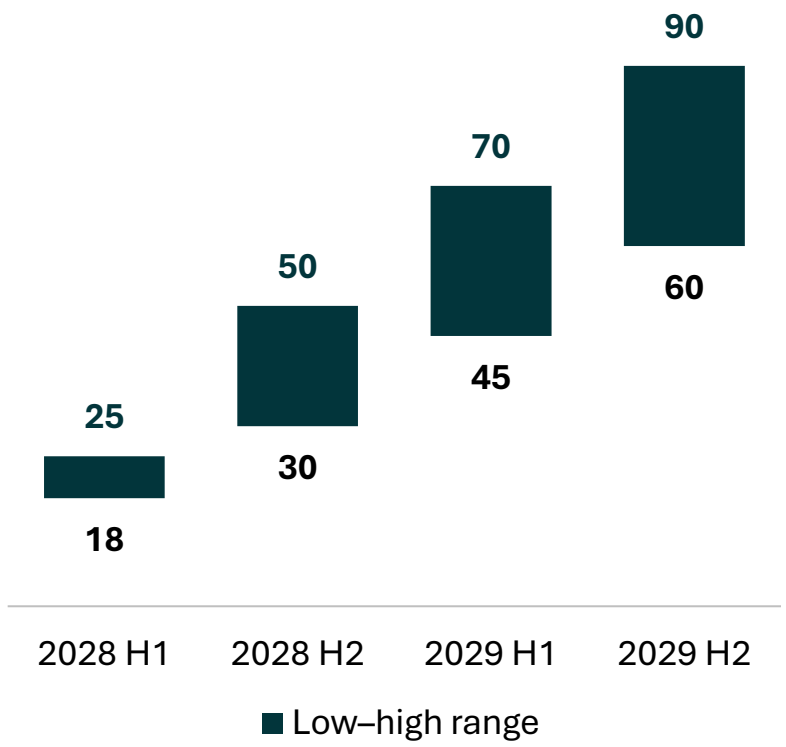
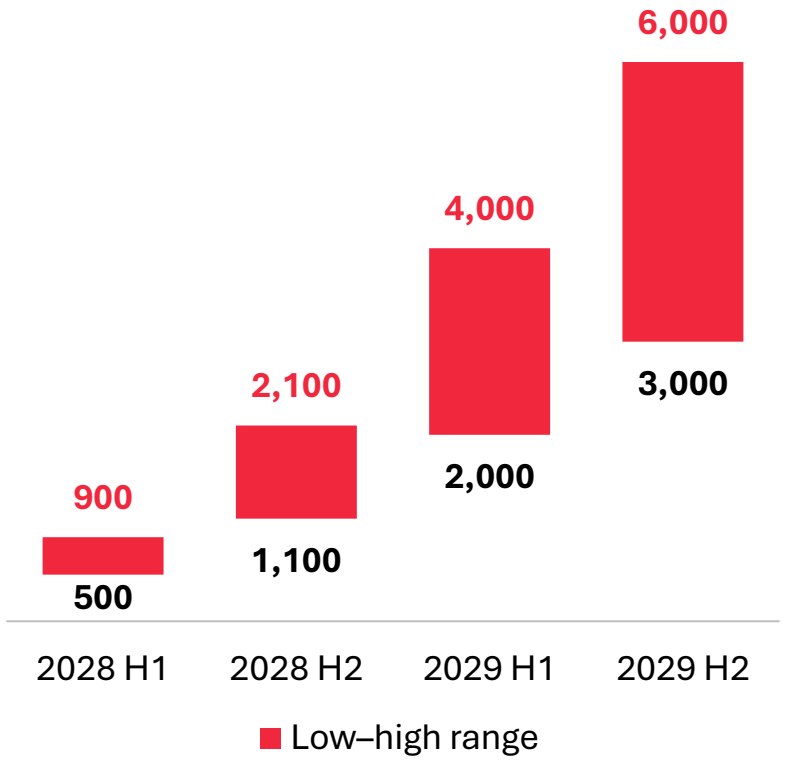
Potential launch expected early 2028: Center-led ramp with ~1,600–3,000 procedures by EOY 2028 and 5,000–10,000 procedures in 2029

Centers live (cumulative)[1]



Procedures (per half-year)[1]



Centers of excellence[1]

30-50
live at the end of 2028

60-90
live at the end of 2029

Procedure volume[1]

1,600 to 3,000
procedures in 2028

5,000 to 10,000
procedures in 2029

1. Figures presented are management estimates contingent on pivotal results and on FDA marketing authorization, neither of which is assured, and they are not guidance

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