FRACTYL® health

Freedom from Metabolic Disease

Corporate Presentation | May 2024

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Our purpose

To defend humanity from metabolic disease

Our mission

To develop transformative therapies that can prevent and hopefully cure metabolic disease

Pioneering metabolic therapeutics company

Differentiated assets, near term catalysts, capital efficient operating model

Targeting Unmet Needs in Major Metabolic Markets	Obesity and Type 2 Diabetes (T2D)
Revita® Duodenal Mucosal Resurfacing	Proprietary device and delivery system platform enables privileged access to gut and pancreas for durable glucose control and weight maintenance
Rejuva® Pancreatic Gene Therapy Platform	Novel locally administered, AAV-based pancreatic gene therapy with potential for remission of obesity and T2D
Multiple Anticipated Near-Term Catalysts	Revita Pivotal Studies in T2D and weight maintenance, Revita commercial pilot in Germany, Rejuva FIH in T2D
Strong Balance Sheet	IPO in Q1 2024 with capital to fund key Revita and Rejuva catalysts

Leadership team and BOD

Experience spanning biotechnology and medical technology

Management Team

Harith Rajagopalan, MD, Ph.D.
Co-founder & CEO

Jay Caplan
Co-founder, President, Chief Product Officer

Lisa Davidson
Chief Financial Officer

Tim Kieffer, Ph.D.
Chief Scientific Officer

Sarah Toomey
General Counsel and Corporate Secretary

Jon Fitzgerald
Quality Assurance and Regulatory Affairs

Len Rosberg
Manufacturing

Kelly White, PharmD
Clinical and Medical Affairs

Nancye Green
Corporate Communications

Board of Directors

Allan Will
Chairman and Former Chair, The Foundry

William W. Bradley
Former U.S. Senator

Harith Rajagopalan, MD, PhD
Co-founder & CEO, Fractyl Health

Marc Elia
Founder of M28 Capital

Amy Schulman
Partner, Polaris Partners

Kelly Barnes
Former Partner, PwC

Sam Conaway
President of Boston Scientific U.S. Cardiology Sales and Chair of Close the Gap

Clive Meanwell, MB, CHB, MD
Executive Chairman and Founder of Population Health Partners

Ajay Royan
Co-founder and Managing General Partner, Mithril

Metabolic diseases are a massive market

With significant CAGR

Highly potent drugs in GLP-1RA class are now available for T2D, obesity, and CV mortality

$65B in annual pharmaceutical spend on T2D and obesity in 2022

However, conventional GLP-1RA therapies limited by need for chronic administration and high discontinuation rates

- Over 50% discontinue within 1 year[1]
- Patients who discontinue are unlikely to experience durable benefit from GLP-1RA Rx[2]

Lowering glucose and weight is now easy, **but keeping it off is still hard**

Estimated Worldwide Market For Diabetes / Obesity Drugs By Class ($MM, Net Sales)[3]

	2022	2028	'22 – '28
Drug Class	**Market**	**Market**	**% CAGR**
Injectable Incretin Diabetes	**$18,769**	**$44,514**	**15%**
Injectable Incretin Obesity	**$2,519**	**$20,134**	**41%**
Oral Incretin Diabetes	**$1,657**	**$5,363**	**22%**

1. Rowley et al Population Health Mgmt 2017 2. Wilding JPH, Diabetes Obes Metab. 2022;24:1553–1564 and Aronne et al JAMA. 2024;331(1):38-48 3. Source: TD Cowen estimates

Successes & limitations of today's GLP-1RA therapies

Successes

Limitations

- Require chronic administration
- High discontinuation rates
- Lack of durable effect

Opportunity for differentiated therapies with durable benefit

Fractyl Health approach

Our assets are positioned to target previously unaddressable categories in obesity and T2D

Revita: Procedure that targets the duodenum to reverse pathology in the duodenal lining that is a root cause of obesity and T2D

Rejuva: Potentially best-in-class GLP-1 therapy that mimics human physiology to produce nutrient-stimulated hormones within the pancreas

Two technologies tackling root causes of obesity & T2D

Single-administration treatments for durable weight and glucose control

Revita®

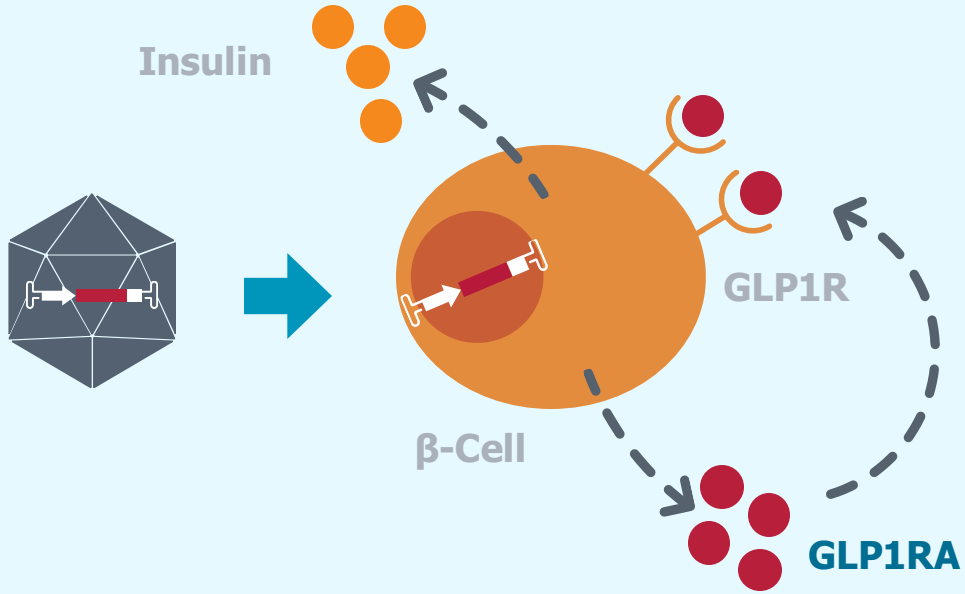
Targeting **duodenal dysfunction**

Hydrothermal ablation of dysfunctional duodenum

Rejuva®

Targeting **pancreatic islet dysfunction**

Local AAV gene therapy for islet dysfunction



Revita and Rejuva clinical pipeline

Financed to support operations through multiple near-term milestones

*Revita has been granted Breakthrough Device designation for the hydrothermal ablation of the duodenal mucosa to improve glycemic control and eliminate insulin needs in T2D patients inadequately controlled on long-acting insulin; and CE mark obtained from EU and UK in 2016 for Revita for the improvement of glycemic control in patients with inadequately controlled T2D despite oral and/or injectable glucose lowering medications and/or long-acting insulin; **Product candidates under our Rejuva gene therapy platform will undergo Phase 1, Phase 2 and Phase 3 clinical trials ***The Revitalize-1 study is a pivotal study in patients with inadequately controlled T2D despite being on up to three ADAs and daily insulin; ****If PMA approved *****subject to IND approval

IND = Investigational New Drug Application with FDA or comparable regulatory body; IDE = Investigational Device Exemption with FDA or comparable regulatory body; FIH = first-in-human; PMA = Premarket Approval

Revita

Targeting duodenal dysfunction to address obesity and T2D

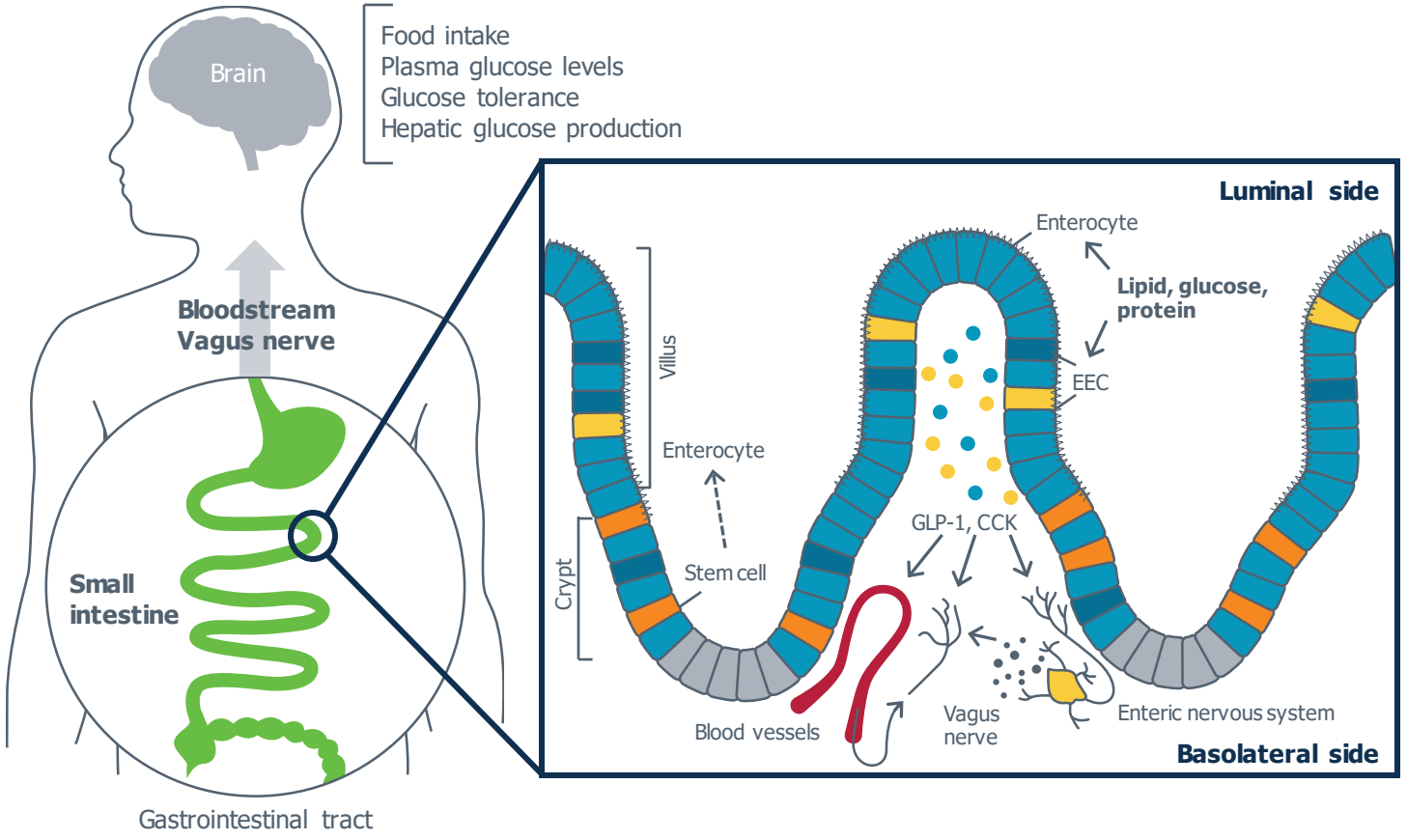
Duodenum is a central regulator of metabolic control

Key nutrient sensor and signaling beacon for brain

Duodenum is a critical neuro-endocrine organ

- First part of small intestine and key site for absorption, sensing, and signaling
- Blood + nerve signaling pathways from duodenal surface to brain
- Brain then regulates appetite and blood sugar

Known beneficial effects of duodenal bypass on weight maintenance and glucose control

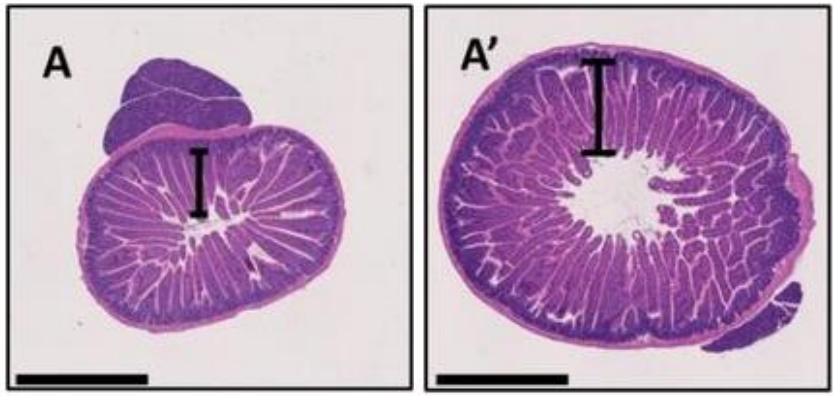


Adapted from Duca et al

Gut dysfunction is a root cause of obesity & T2D[1]

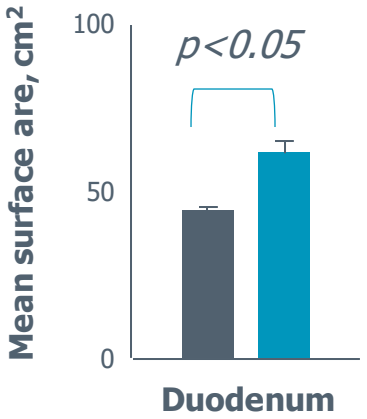
Driven by chronic exposure to high fat and high sugar diets[2]

HFHSD causes duodenal hyperplasia[3]

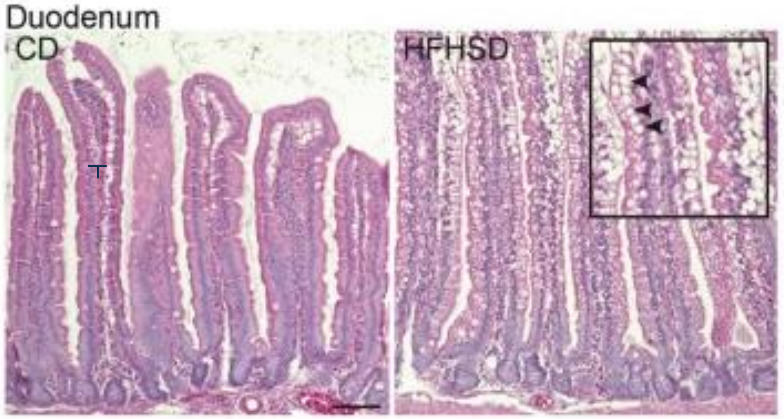


Normal diet HFHSD

50% greater mucosal surface area[3]



Increased enteroendocrine cell types[1]



Chronic high fat and high sugar diets cause gut dysfunction

Gut dysfunction alters gut-brain signaling[1-2]

Altered gut-brain signaling drives obesity and T2D[2]

[1]Aliluev et al Nat Metab. 2021 3:1202-1216 [2]Duca et al Cell Metab. 2015 22:367-380 [3] West et al bioRxiv 822122; CD = Chow Diet HFHSD = High Fat High Sugar Diet

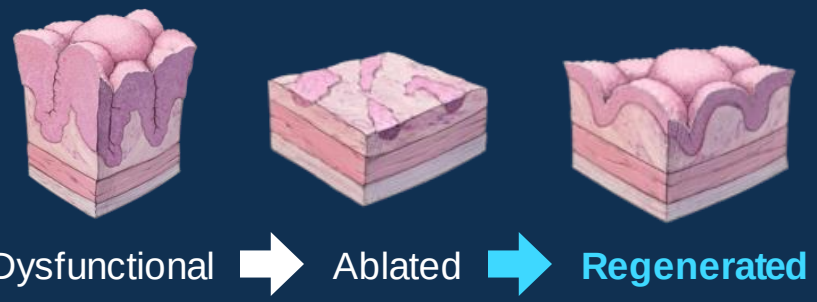
Revita summary

*Revita is an **outpatient endoscopic procedure** that targets the **duodenum** to reverse pathology in the duodenal lining that is a root cause of obesity and T2D*

CE mark in EU; reimbursement authorization in Germany

Initiated pilot commercial launch and Real World Registry study in 1H 2023 in Germany

Registrational studies underway in the U.S.



Revita aims to be the non-drug alternative to control weight and glucose by targeting the gut

In **obesity**, Revita is a potential non-drug alternative that can offer durable weight maintenance and other metabolic benefits for patients after discontinuing GLP-1RA therapies

In **T2D**, Revita is a potential non-drug alternative for patients with inadequately controlled T2D despite standard of care, who need to improve metabolic control while reducing insulin burden

Revita console and catheter system

Designed to seamlessly integrate into high volume endoscopy workflow

Designed for durable and repeatable metabolic improvement

80+ issued patents covering methods, systems, devices

CE Mark in EU/UK

Reimbursed in Germany

Breakthrough Designation from FDA in insulin-treated T2D

Control console with user-friendly touch screen interface automates majority of procedure

Real-time sensors designed to monitor procedure and ensure technical success and safety

½ day training
< 1 hour procedure time
< 4 cases for proficiency

Single-use catheter optimized with over 300 clinical procedures to date

Revita is for investigational use only in the United States. Revita has a CE mark in the European Union. Prototype rendering

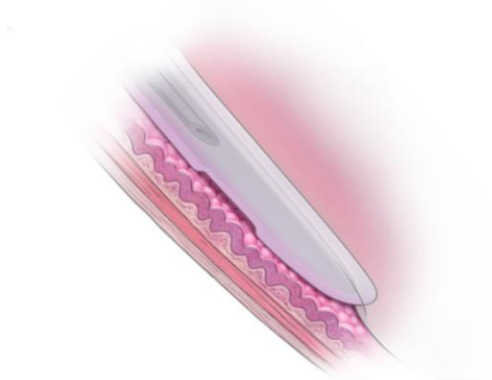
Revita endoscopic procedural therapy

Procedure designed to provide a thermal protection before ablation

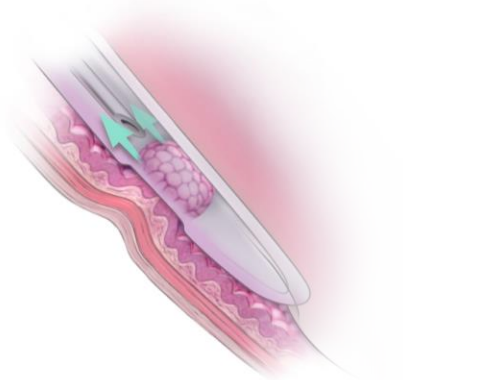
Thermal protection designed to protect deeper layers before ablation (or potentially repeat treatments)

Sequence progresses from Ampulla of Vater to end of duodenum (> 10-14 cm)

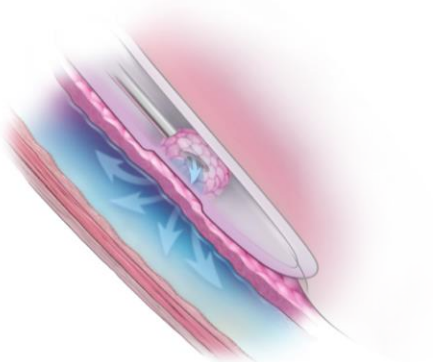
Conducted under direct endoscopic visualization of entire procedure



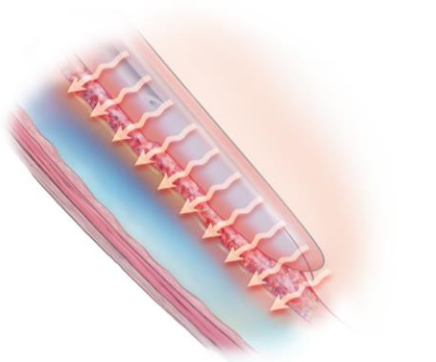
1 Revita catheter engages duodenal lining



2 Catheter port vacuums mucosa and advances needle into submucosa



3 Needles inject saline circumferentially into submucosa



4 Hydrothermal ablation follows in thermally protected area

Encouraging tolerability and AE profile

Well validated experience in > 300 trial participants and multiple centers

- No long-term device or procedure-related AEs
- Gastrointestinal AEs infrequent, mild and transient in nature
- Typically lasting 1-2 days and mostly mild in severity
- Consistent with routine upper endoscopic procedures
- Abdominal pain, abdominal distention, nausea, and diarrhea most commonly reported
- Few hypoglycemic events were mild in severity and only associated with medicines known to cause hypoglycemia
- No clinical or laboratory signs or reports of malabsorption, nutrient deficiency, pancreatitis, or infection

AE = adverse event

Revita for T2D

Goal: durably improve glucose control, maintain weight loss, and reduce medication burden for millions of people with inadequately controlled T2D

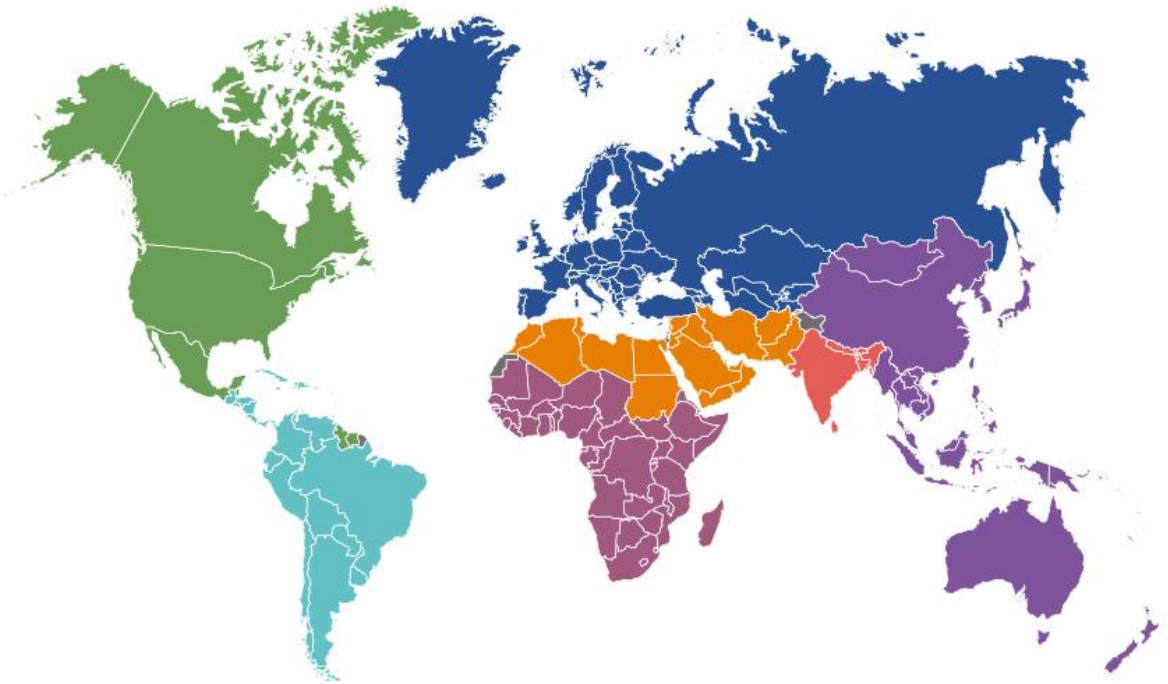
T2D is a high unmet need market opportunity

60+ approved drugs but market continues to grow

> $350B annual cost of T2D in 2022[1]

> $20B in branded GLP-1 sales for T2D in 2022 (15% CAGR)[2]

> 50M in US projected to have diagnosed T2D by 2030[3]



537M with diabetes globally in 2021[4]

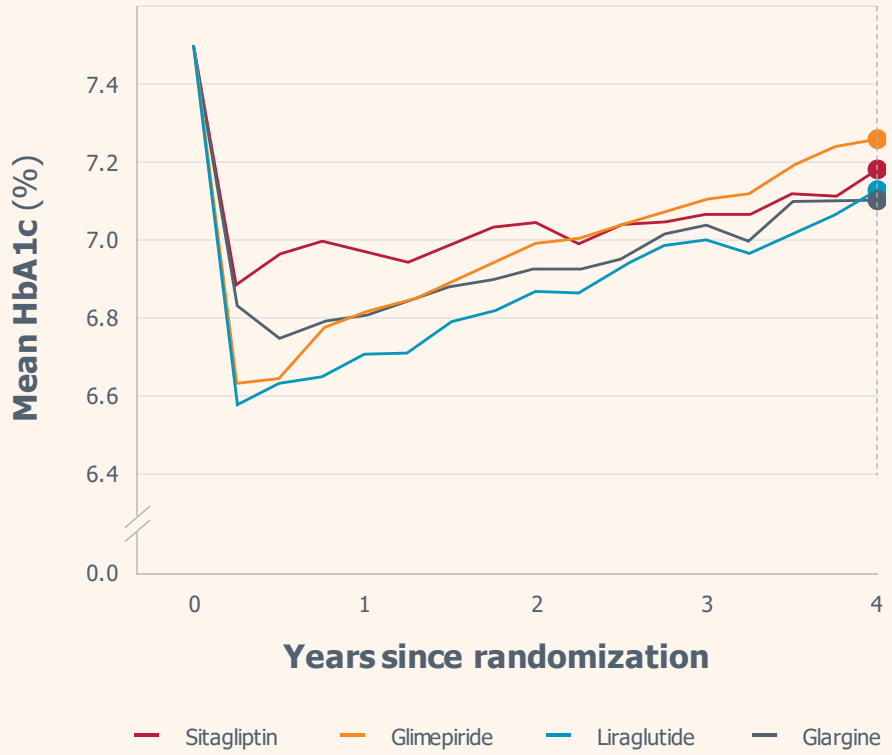
Map: Number of people with diabetes worldwide and per IDF Region in 2021–2045 (20–79 years)

1. CDC 2. TD Cowen estimates 3. Rowley et al Pop Health Mgmt 2017 4. IDF Diabetes Atlas 2021

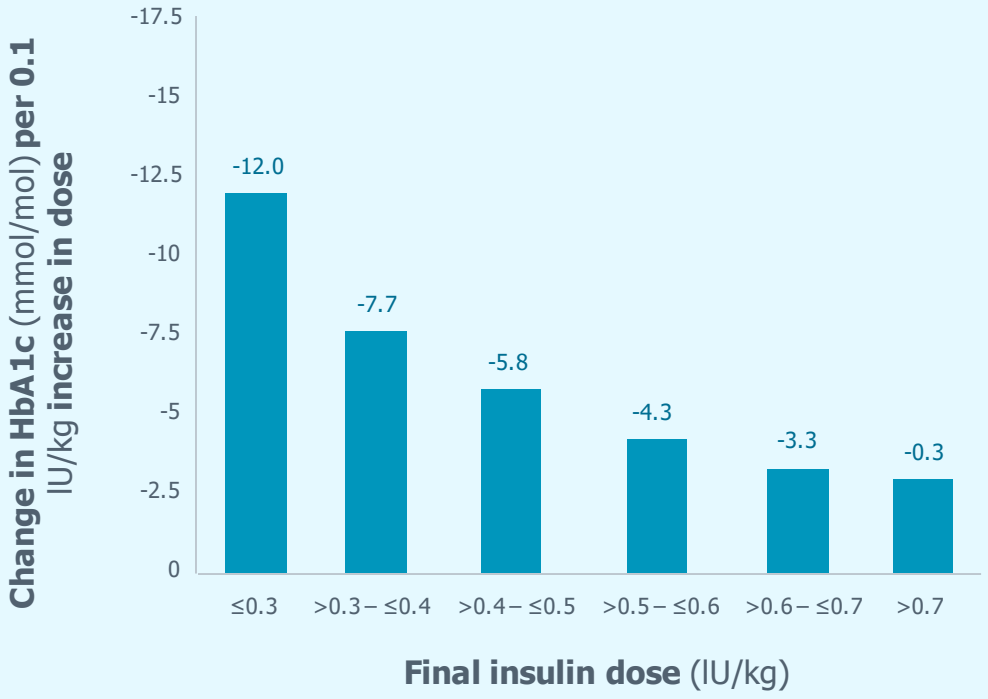
Decreased effectiveness of T2D therapies over time

Need more effective and durable therapies for T2D

Lack of durability of current therapies drives need for medication escalation[1]



Decreased effectiveness of insulin with dose escalation[2]



Adapted from: 1. GRADE Study 2022 2. Umpierrez et al. Diabetes Obes Metab. 2019 21:1305-1310 3. Rubin et al. Diabetes Care. 2011 34:1723-1728
HbA1c=hemoglobin A1c, IU=international units, OR=odds ratio, *p<0.05

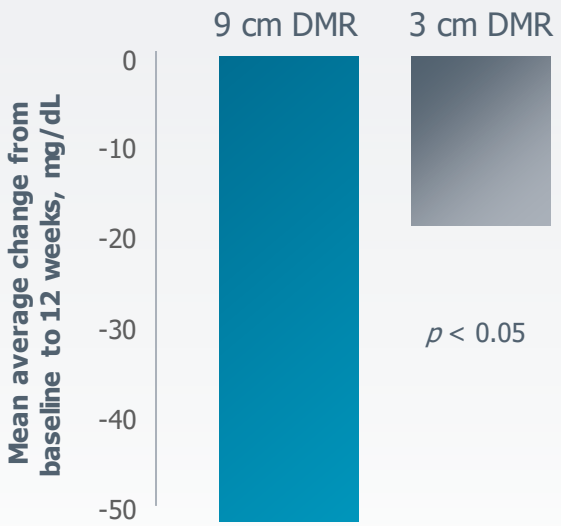
Revita T2D clinical program overview

Consistent effects on blood glucose across clinical studies

Revita FIH[1]

Dose-dependent glucose lowering

Dose-Dependent Efficacy

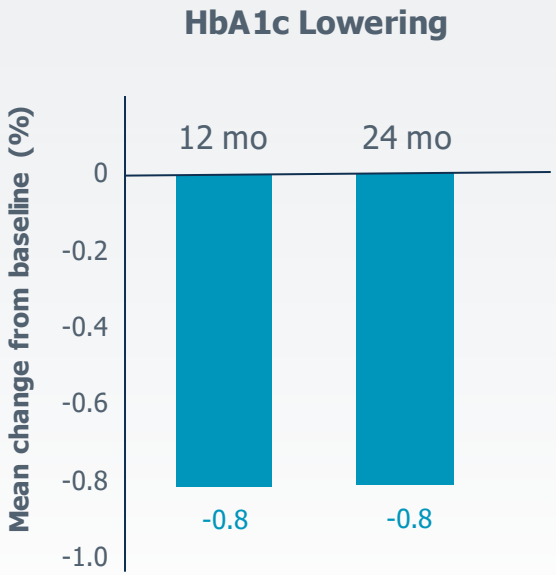


Axial length of treated intestine = treatment dose

Revita-1 Open Label[2]

2-year glucose lowering and weight control

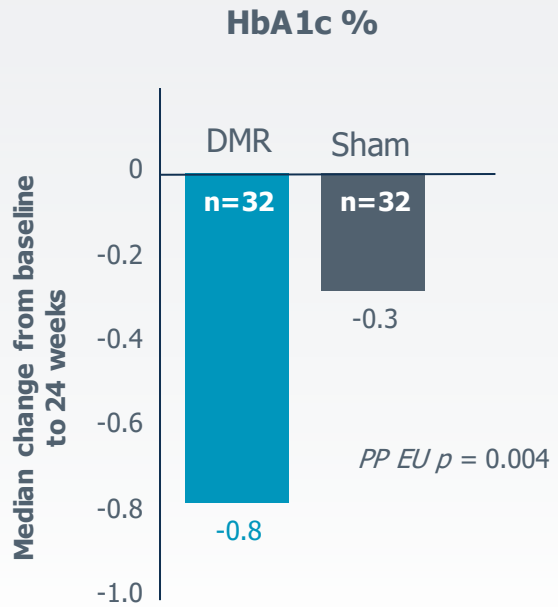
Durable Metabolic Improvements



Revita-2 Sham-Controlled[3]

Sham-controlled efficacy pilot study

Sham-Controlled Efficacy



1. Rajagopalan et al Diabetes Care 2016 2. van Baar et al. Diabetes Res Clin Pract. 2022 184:109194 3. Mingrone et al. Gut 2022 71:254-264 5. Interrupted due to COVID-19 epidemic 6. NCT04419779

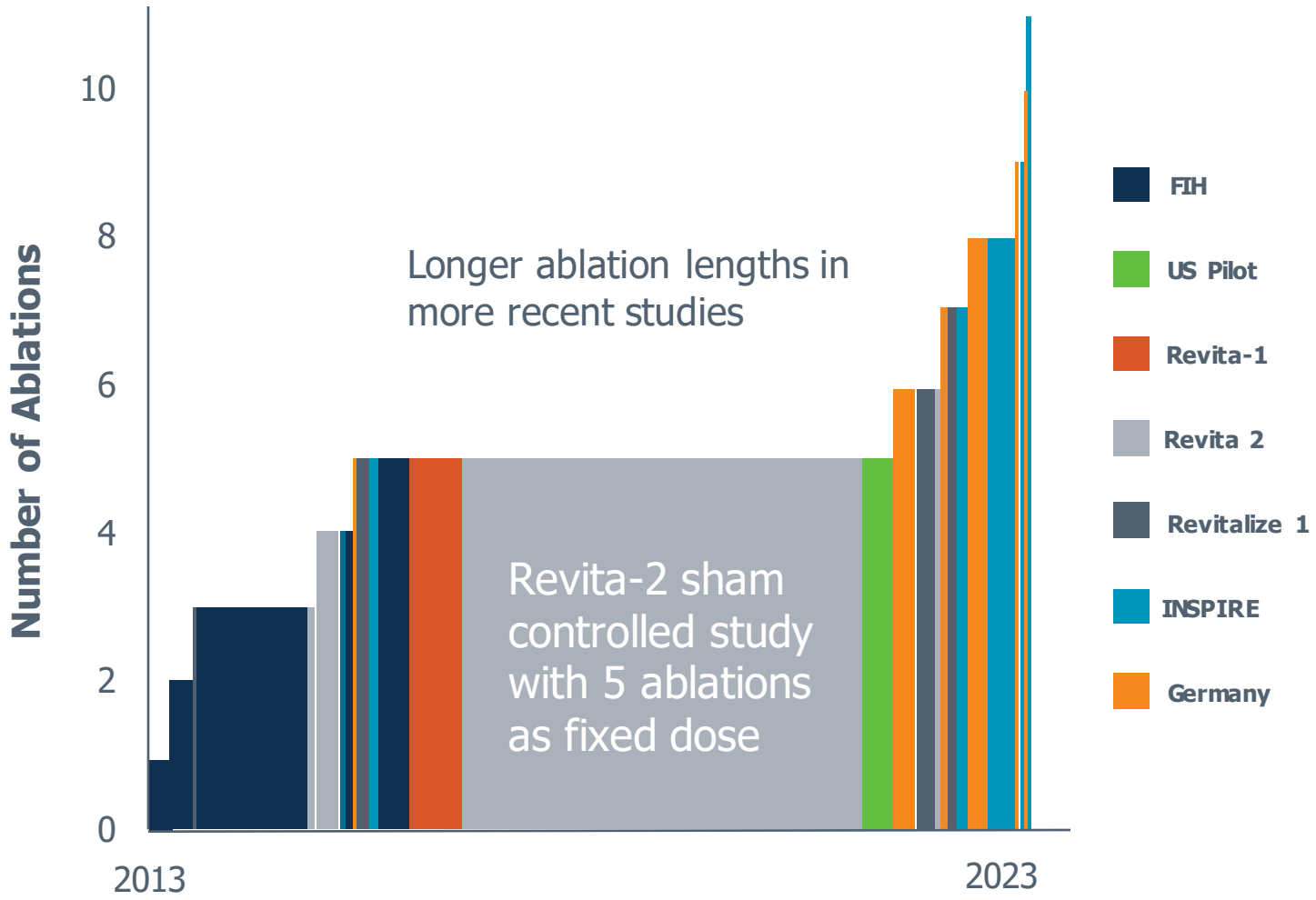
Revita profile optimization ongoing

Increased ablation length associated with greater efficacy

Early studies showed ablation length-dependent efficacy

Treatment "dose" has increased in current and ongoing clinical studies

No emergent safety signals with increased treatment dose



Revitalize-1 pivotal study underway

FDA Breakthrough designation and CMS reimbursement support

Patient population

High unmet need, inadequately controlled T2D (HbA1c > 7.5) after exhausting diabetes therapy including insulin, GLP-1RA, SGLT2i
320 subjects

Primary endpoint

Change from baseline in HbA1c at 24 weeks

Key secondary endpoints

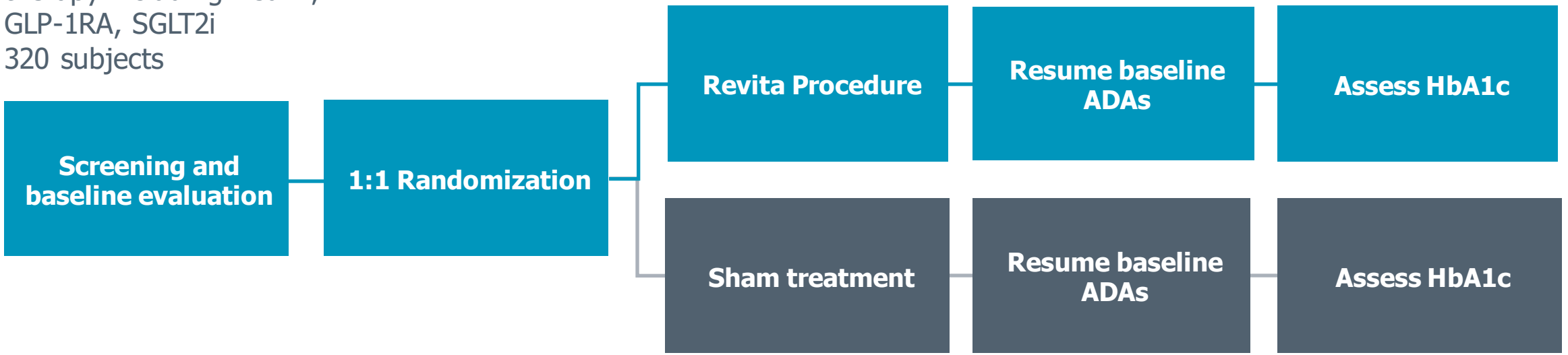
HbA1c targets
weight loss,
insulin requirement

Design

Randomized (1:1) double blind sham controlled

Anticipated timing

Primary endpoint EOY 2024



Revitalize 1 Study; ClinicalTrials.gov Identifier: NCT04419779

FDA breakthrough device and CMS reimbursement

Alignment of key stakeholders for regulatory and reimbursement next steps

Breakthrough device designation for insulin-treated T2D

- Potential for expedited PMA review
- Potential for TCET process through CMS

Modular PMA filing for Revitalize-1

- Design module and manufacturing modules to be submitted after completion of Revitalize-1 enrollment
- Clinical modules to be separated into a first filing with 24-week data and supplement with 48-week data

CMS Reimbursement Support

- Cost/healthcare burden in insulin-treated T2D is a major concern for payers
- CMS coverage granted for routine clinical expenses for Medicare beneficiaries in Revitalize-1

Revita: German commercial pilot

Opportunity to collect real world evidence for Revita in T2D

Revita system is approved in Europe for patients with inadequately controlled T2D under CE Mark

1H 2023: Secured reimbursement authorization for Revita in Germany

- Initiated limited commercial pilot launch in single center in Dusseldorf and German Real World Registry study to evaluate real-world evidence of Revita's safety and effectiveness
- Intend to continue to add centers in Germany, focusing on GI endoscopists with a focused interest in metabolic endoscopy and hospitals that have established reimbursement for Revita with statutory health insurers
- Intend to provide regular updates on registry enrollment and real-world data on effects of Revita on blood sugar and weight control

Real-world registry ongoing in Germany

Weight loss and glucose control[1]

Patient population

Patients with T2D on at least 1 ADA at baseline

Baseline demographics

62 years age
64% male
13 years duration T2D
BMI 32.1 kg/m^2

	Baseline n=14 **Median** (min,max)	**6 Month n=14** **Median** (min,max)
Weight (kg)	**111** (66,139)	**102** (62,127)
HbA1c (%)	**9.2** (7.3,12.8)	**7.6** (6.0,13.2)
FPG (mg/dL)	**153** (101,355)	**116** (79,198)

- The DMR procedure was well tolerated in registry participants with no DMR-related serious adverse events reported to date.

1. Fractyl Health, Data on File NCT06256497 ADAs = Anti-diabetic agents

Revita for obesity

Goal: Provide durable, effortless weight maintenance for millions of people with obesity

Obesity is the largest metabolic disease market opportunity

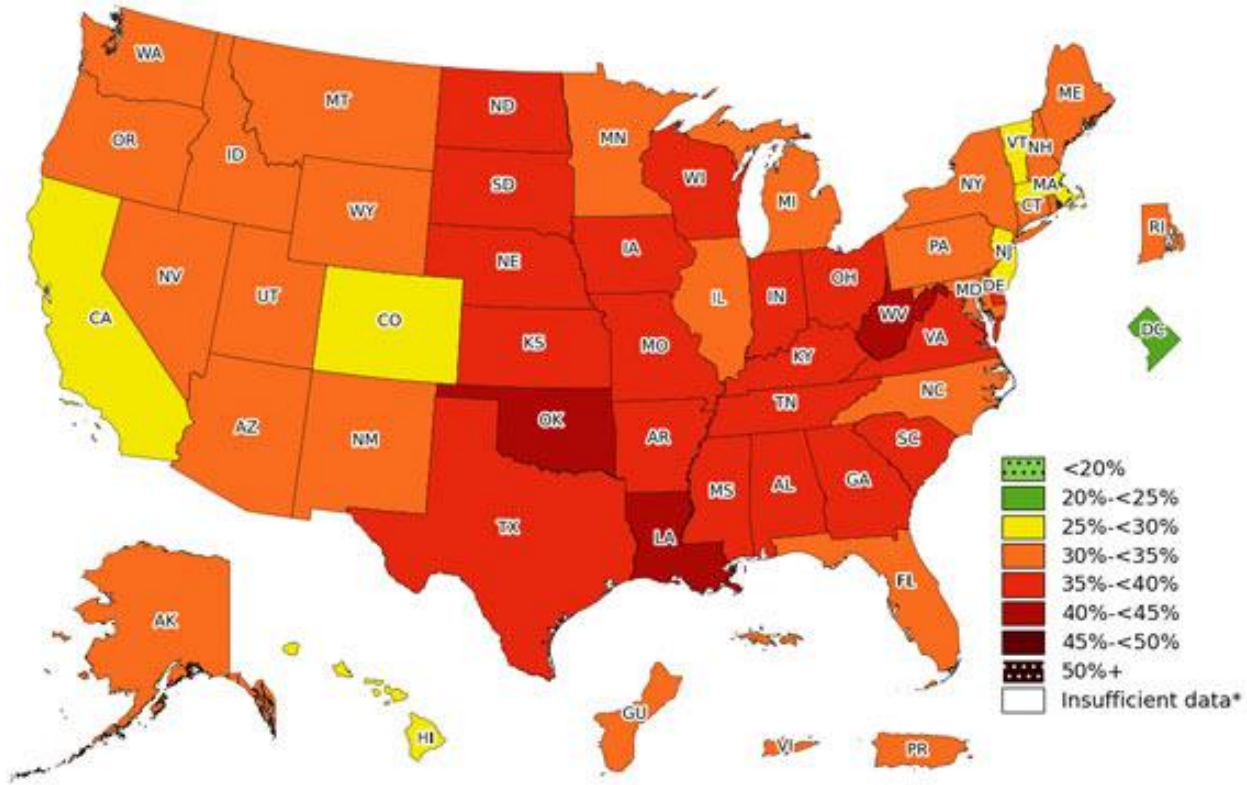
Unmet need has shifted from weight loss to weight maintenance

> 40%
of adult US population is obese[1]

$2.5B
in branded GLP-1 drug sales in 2022 with 41% CAGR[2]

> 50%
who start GLP-1RAs discontinue within 1 year[3]

CDC 2022 Adult Obesity Prevalence[1]



1. CDC 2. TD Cowen estimated 3. Polonsky et al. Diabetes Ther. 13, 175–187 (2022)

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HEALTH NEWS ✓ Fact Checked

Ozempic Rebound: Why Most People Regain Weight After Stopping Semaglutide

Taking semaglutide medications like Wegovy and Ozempic can help once they stop. Sergey Mironov/Getty Images

- Research has found that when people stop using Ozempic and Wegovy, weight rebound occurs
- Experts say this is because the drug is not a cure but a temporary adaptation that occurs during weight loss

CNN health | Life, But Better | Fitness | Food | Sleep | Mindfulness | Relationships

To keep pounds off, patients may need to continue taking weight loss drug, study suggests

By Brenda Goodman, CNN

6 minute read · Published 10:00 AM EST, Mon December 11, 2023

Eli Lilly and Company

...e or overweight with at least one health problem related to their weight.

WSJ | Barron's | MarketWatch | IBD

DJIA 37804.43 0.01% ▼ | S&P 500 4879.16 0.22% ▲ | Nasdaq 15513.09 0.20% ▲ | U.S. 10 Yr 2/32 Yield 4.162% ▲ | Crude Oil 76.46 1.82% ▲ | Euro 1.0834 0.49% ▼

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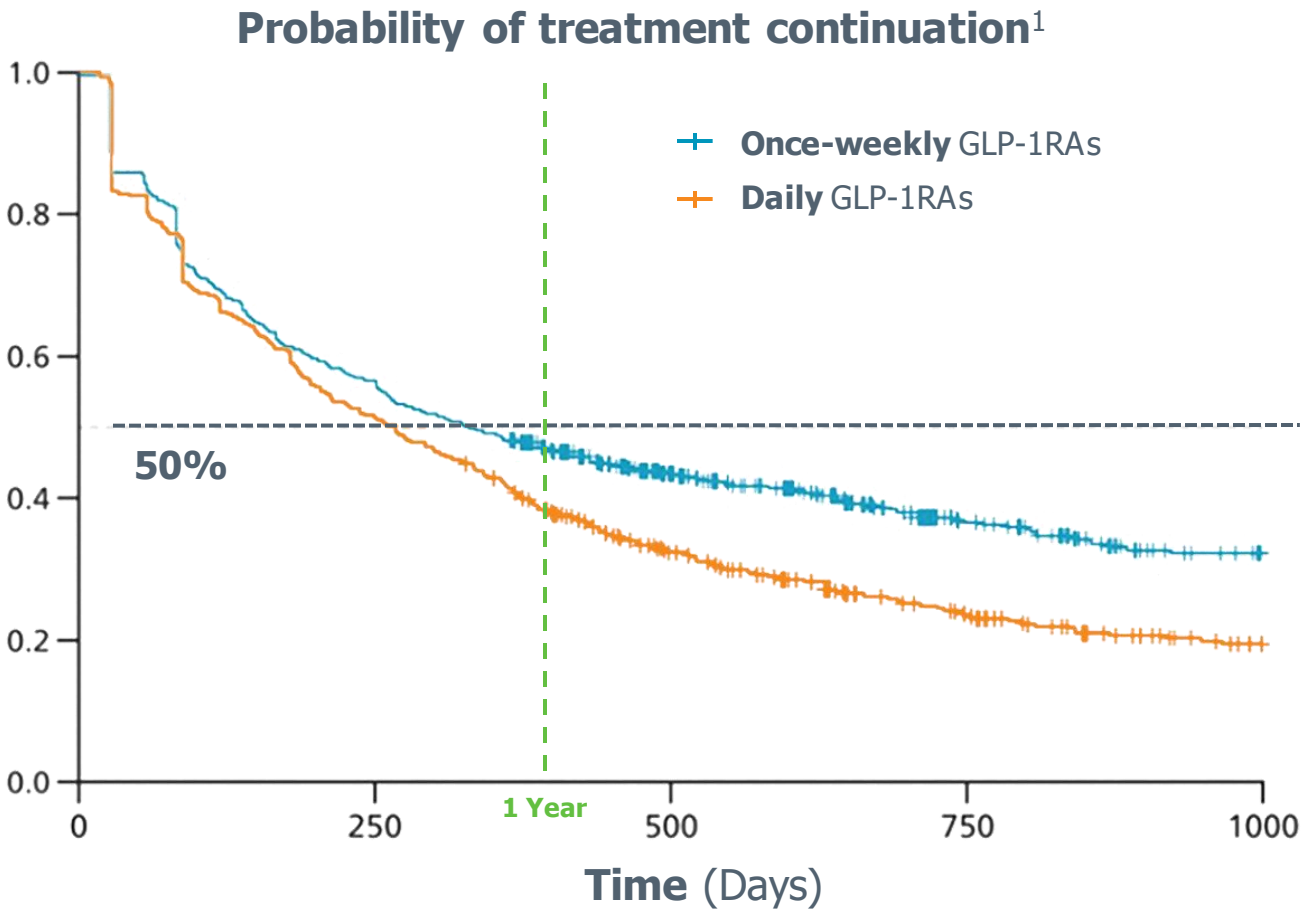
HEALTH

What Happens When You Stop Taking Ozempic?

Many people become heavier after halting the use of semaglutide to manage weight

GLP-1RAs have a persistence problem

Rates of persistence with GLP-1RAs in US clinical practice - STAY study

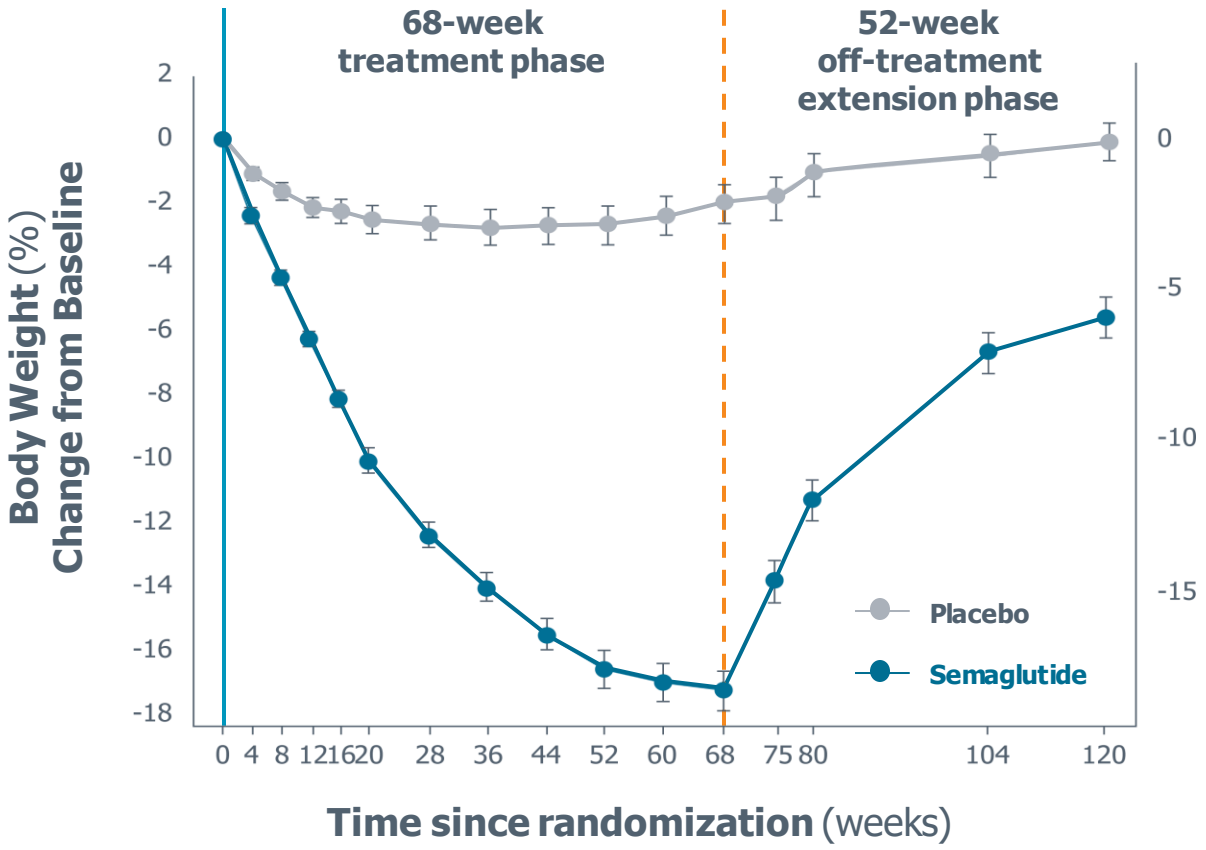


Persistence drops below 50% at about one year even with once-weekly GLP-1RA

William Polonsky et al. 1. Polonsky et al. Diabetes Ther. 13, 175–187 (2022) (Funded by Novo Nordisk A/S)

Weight regain after GLP-1RA discontinuation

67% weight regain after one year in STEP 1 trial extension[1]



> **Preventing regain of lost weight is the most difficult challenge** in the treatment of obesity.[2]

- Loss of glucose lowering benefit
- Loss of cardiometabolic benefit
- Regain of fat mass > lean mass

1. Wilding JPH, Diabetes Obes Metab.2022;24:1553–1564 (Funded by Novo Nordisk) 2. Laughlin MR, Obesity. 2021 April; 29(Suppl 1):S5-s8

Revita weight maintenance results

Pooled weight loss data in T2D including overweight subjects[1]

Patient population

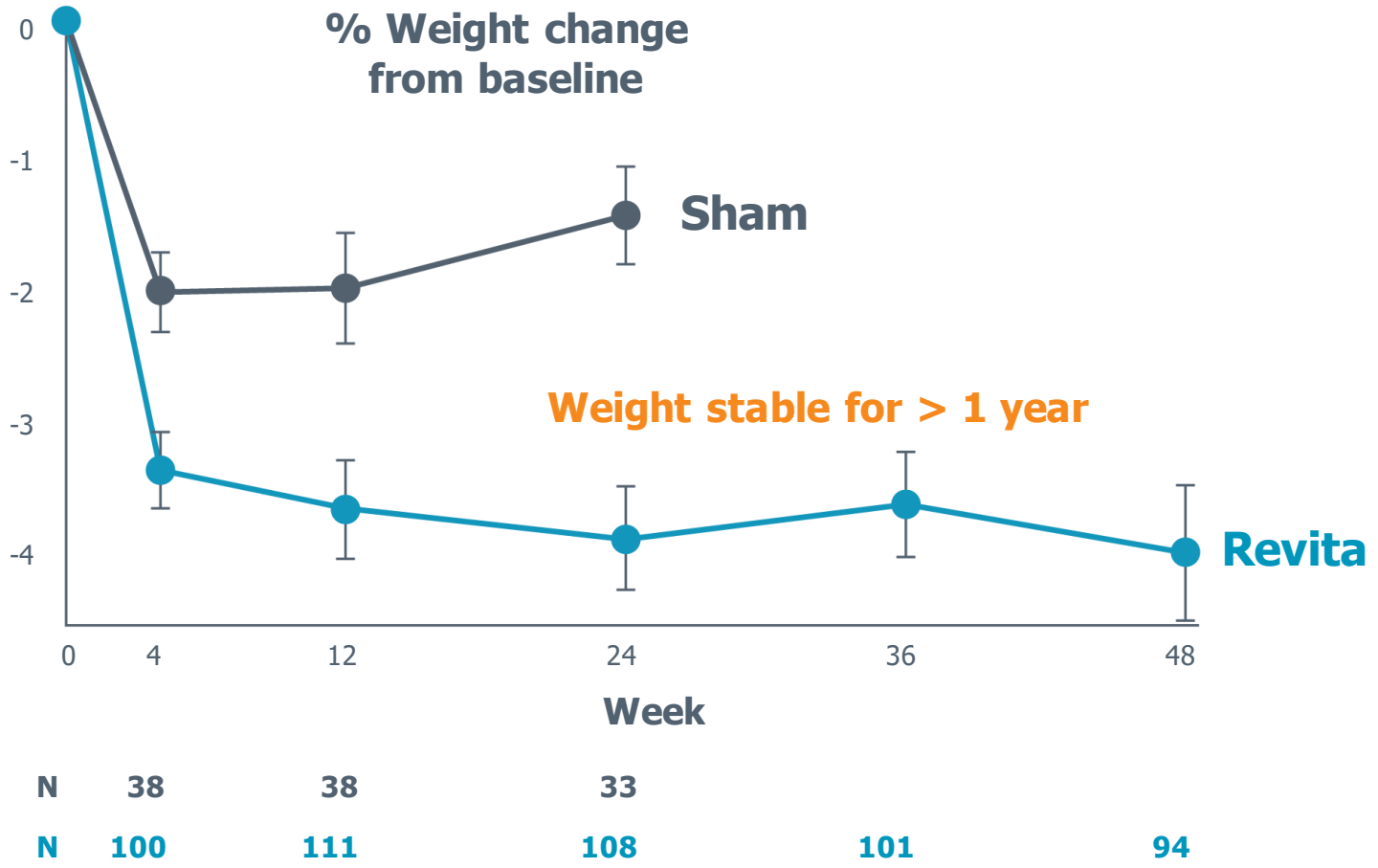
Patients with advanced T2D on multiple ADAs

Baseline Demographics

Baseline 93 kg (BMI 31.1)

HbA1c 8.3%

T2D Duration 10 years



Ozempic 1mg demonstrated similar body weight loss (~ 5% at wk 30) in similar T2D patients[2]

1. Fractyl Health, Data on File. 2. Sorli C et al. The Lancet Diabetes & Endocrinology 2017; 5(4)251-260. ; we have not conducted any head-to-head studies of Revita with Ozempic

Reveal-1 Open-Label Cohort[1]

Weight maintenance after GLP-1RA discontinuation

Patient population	Primary endpoint	Key secondary endpoints	Design	Anticipated timing
Obese patients (BMI ≥ 30) without T2D and achieving at least 15% TBW loss with tirzepatide or semaglutide *or* GLP-1 drug naïve with run-in period to achieve at least 15% TBW loss with tirzepatide ~ 50 participants	Change from baseline in weight	Glucose, CV risk factors	Single-arm, open-label, cohort study of Revita after GLP-1RA discontinuation Diet and lifestyle counseling throughout	Open-label study updates starting H2 2024

TBW = total body weight 1. Reveal-1 is an open label cohort as part of the Remain-1 pivotal IDE. Participants may either already be taking GLP-1 based semaglutide or tirzepatide and have achieved at least 15% TBW loss or will initiate tirzepatide to achieve at least 15% TBW loss before Revita

Remain-1 Pivotal Study

Aim to reduce weight regain from baseline by at least 50% compared to sham at 24 and 48 weeks

Patient population

Obese patients (BMI ≥ 30) without T2D and GLP-1 drug naive

Run-in period to achieve at least 15% TBW loss with tirzepatide

315 participants with sample size re-estimation after 75% of participants randomized

Co-Primary endpoints

Change from baseline in weight to week 24
and
% of Revita participants who maintain at least 5% TBW loss at week 24

Key secondary endpoints

Glucose,
CV risk factors

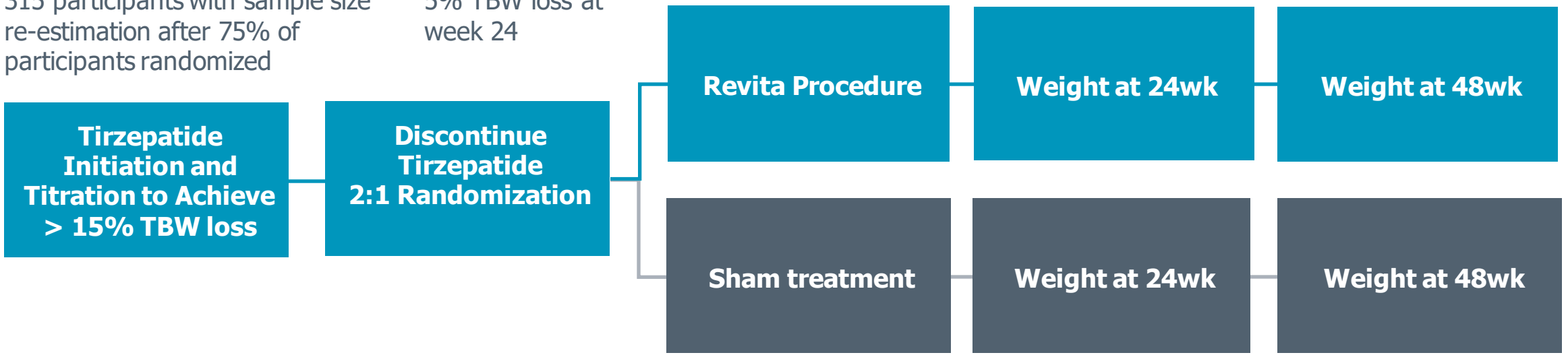
Study Design

Randomized (2:1), double blind, sham controlled after GLP-1RA discontinuation

Diet and lifestyle counseling throughout

Anticipated timing

IDE approved Q1 2024
Study initiation H2 2024



TBW = total body weight

Rejuva

Pancreatic gene therapy platform for remission of obesity and T2D

RJVA-001 for Type 2 Diabetes (T2D)

Nutrient-responsive GLP-1 via intrapancreatic gene therapy

High Unmet Medical Need

- Highly variable tolerability to GLP-1RA drugs
- Frequent injections
- Patient/physician adherence issues
- Incomplete responders

Epidemiology: US

- ~ 27M prevalence

Product Design

- Vector: AAV9
- Transgene: human GLP-1
- Promoter: insulin
- Delivery: Endoscopic needle

Differentiation

Effectively transduces pancreatic islets
One-time intrapancreatic administration
Nutrient-responsive GLP-1 expression

Status

IND-enabling studies

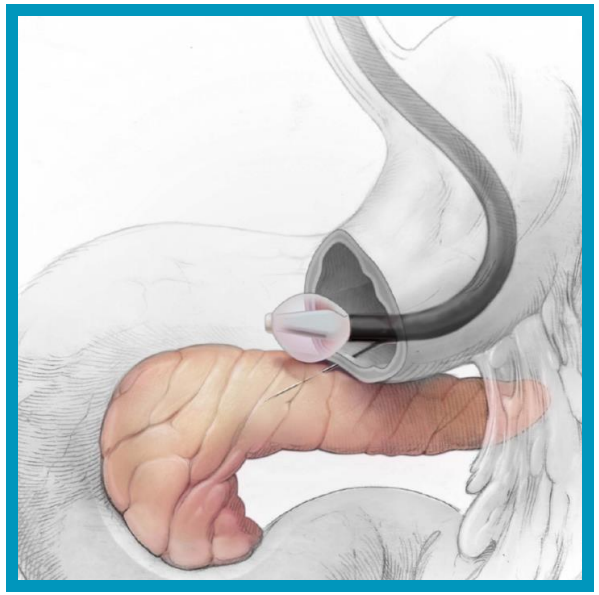
Expected Milestone

Initiate Clinical Trial in H1 2025

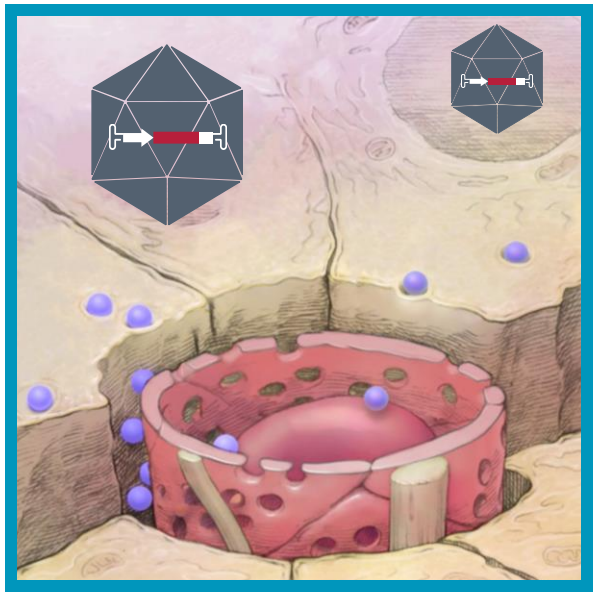
GLP-1-based Pancreatic Gene Therapy (PGTx)

Designed to mimic human physiology

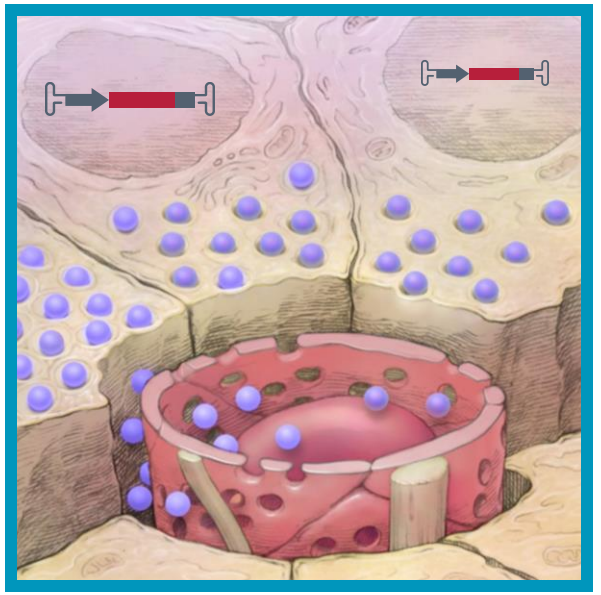
1. Local delivery



2. Low-dose AAV9



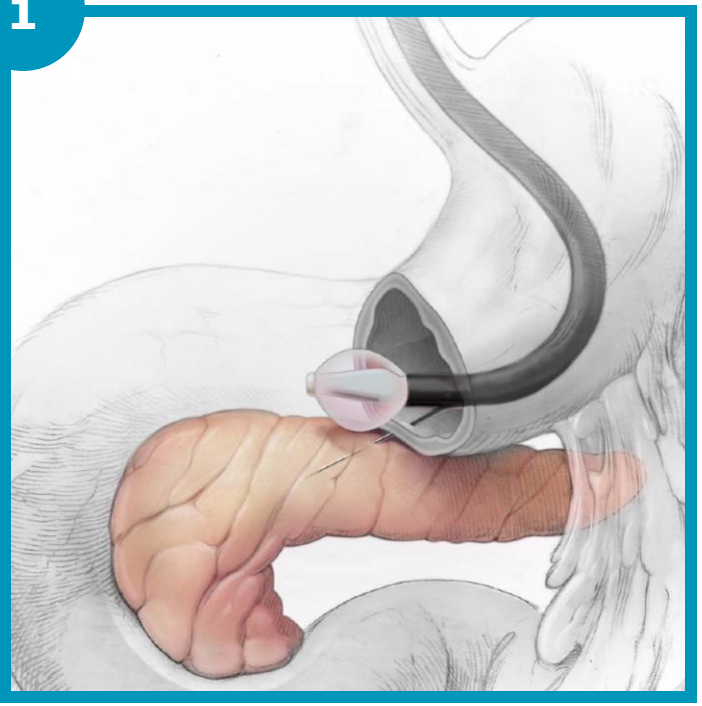
3. GLP-1 Transgenes



Rejuva delivery device

Designed to reduce procedural risk of pancreatic injection

1 Local Delivery



Endoscopic ultrasound-based needle injection is already a standard diagnostic tool for pancreatic lesions[1]

Rejuva procedure designed to reduce risk with key device design elements (needle gauge, pressure regulation) and procedure steps (directed at tail of pancreas, avoiding pancreatic duct)

Proprietary device and endoscopic procedure enabled by Revita system[2,3]

1. Cazacu et al. Endosc Ultrasound. 2018 May-Jun; 7(3): 141–160 2. Thompson et al. DDW 2023 poster presentation. Control no. 3862948.
3. Rajagopalan et al. ASGCT 2023 oral presentation. Abstract no. 191

Local, AAV-delivered PGTx designed to improve islet function

AAV can achieve durable genetic modification of islet cells[1,2]

Intra-islet GLP1 can restore beta cell health and function[3,4]

GLP1-based PGTx (driven by the insulin promoter) may offer differentiated benefit by high local levels of GLP1 with low systemic exposure

Proprietary platform encompasses methods, delivery systems, and gene constructs

2 Low-dose AAV9

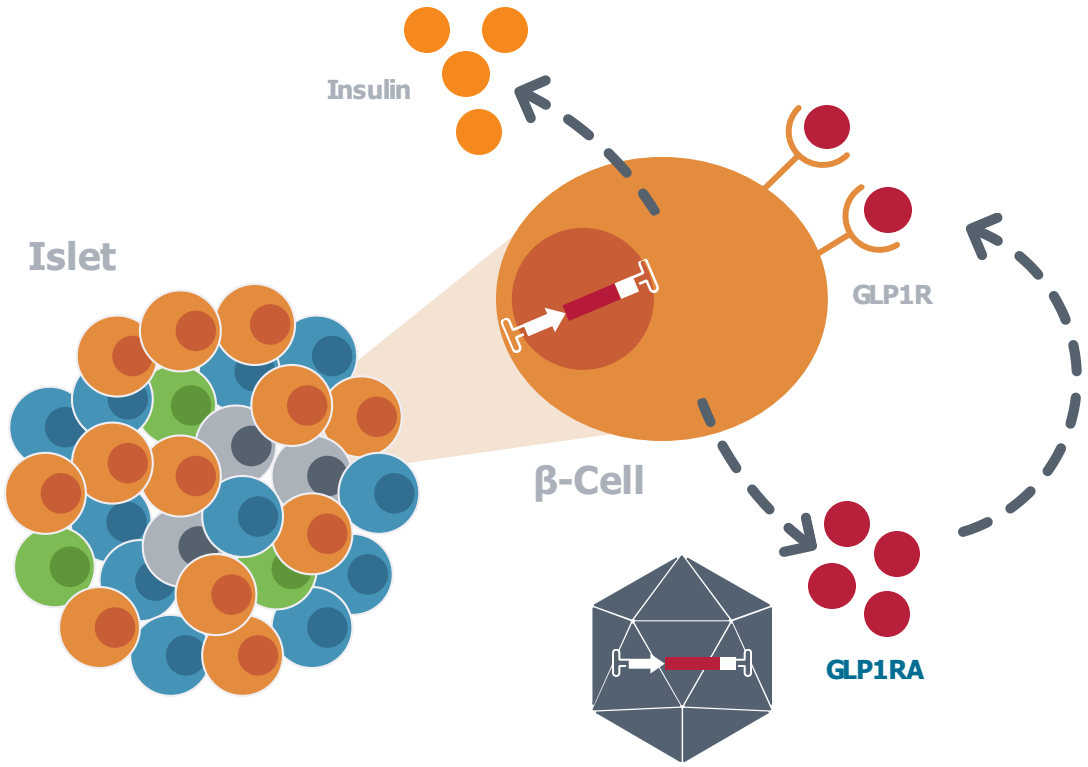


Figure adapted from Saikia et al. JCI Insight. 2021 6:e1418511. 1. Ju et al. Diabetologia. 1998 41:736-739. 2. Kapturczak et al. Mol Ther. 2002 5:154-160. 3. Campbell and Drucker. Cell Metab. 2013 17:819-837. 4. Riedel et al. Gene Ther. 2010 Feb; 17(2):171-80. AAV=adeno-associated virus, GLP1=glucagon-like peptide 1, GLP1R=GLP1 receptor, GLP1RA=GLP1R agonist, PGTx=pancreatic gene therapy

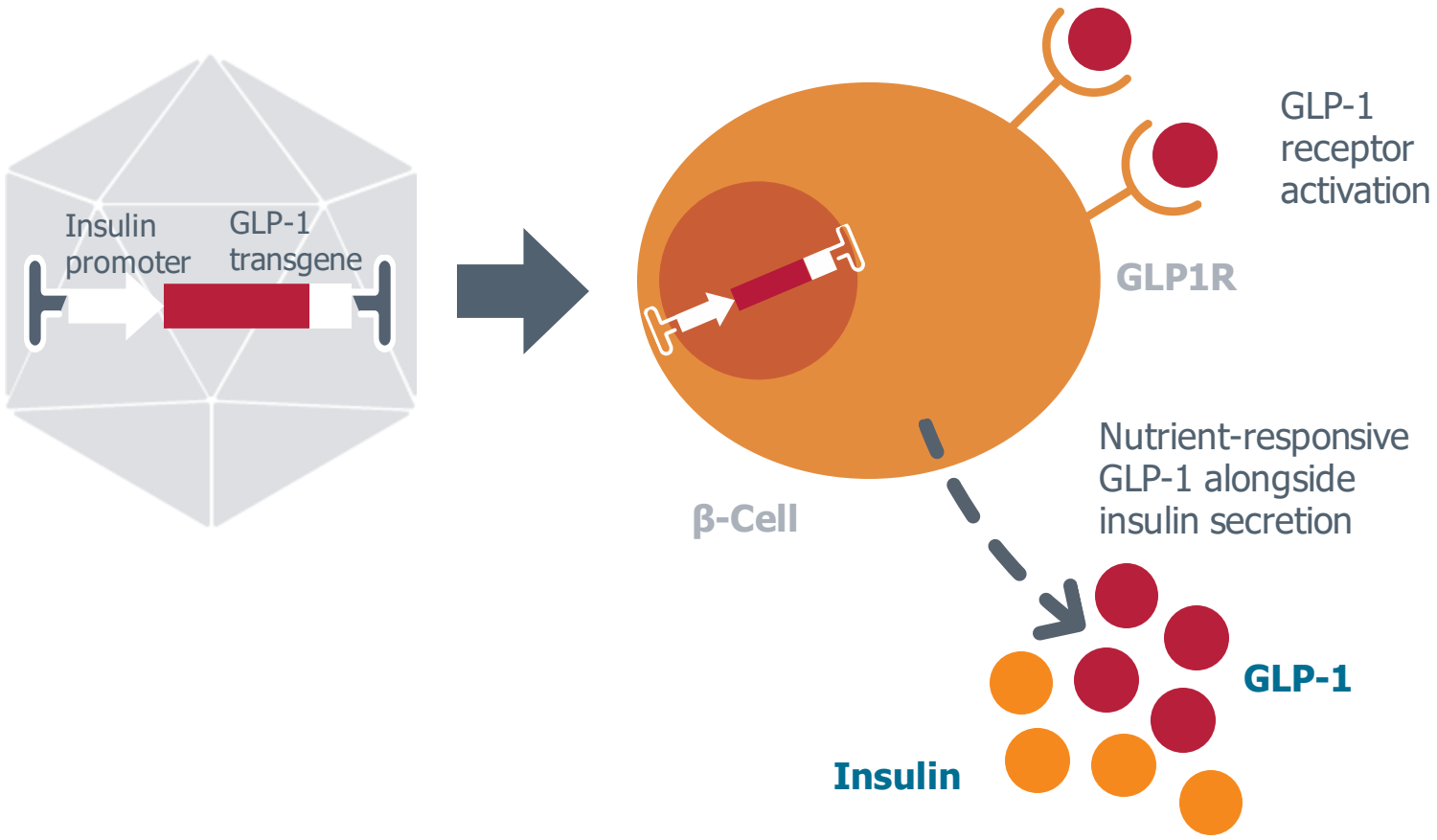
RJVA-001 for T2D

Insulin promoter designed to mimic human physiology

3 Insulin promoter

Insulin promoter and regulatory elements designed to maximize benefit and minimize risk:

- Where you need it: Transgene expression restricted to beta cells (reducing risk of off target expression)
- When you need it: Rapid and tightly regulated secretion
- How much you need: Glucose concentration-dependent transgene expression
- Why? Augmented, autoregulated, native GLP-1 signaling designed to mimic healthy physiology

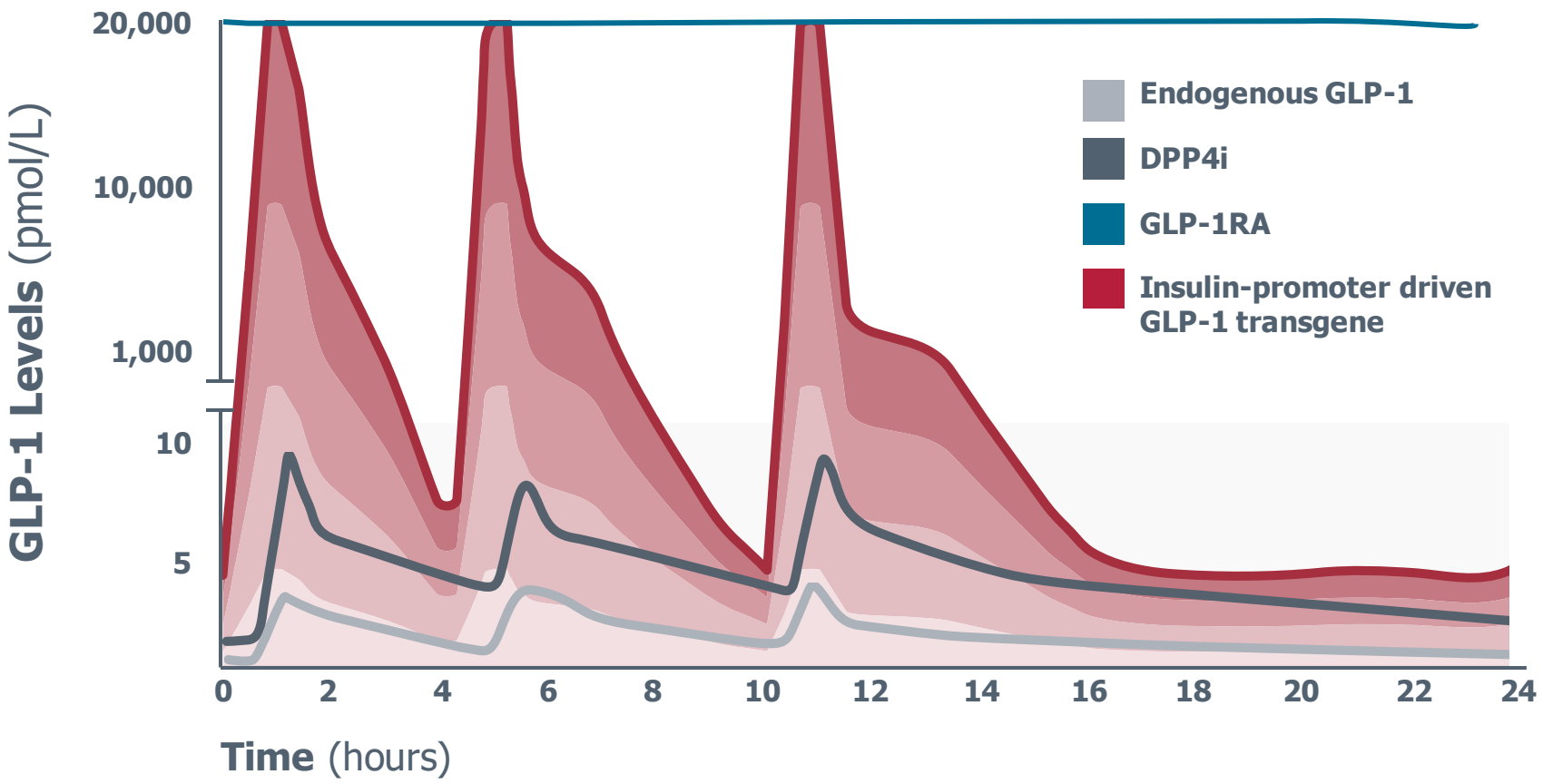


Goal is to produce physiologic GLP-1

Insulin promoter designed to offer meal-regulated GLP-1 expression

Insulin promoter designed to provide a superior GLP-1 profile:

- DPP4i increases endogenous GLP-1 levels by 2-4x (~10 pM serum concentrations)
- GLP-1RA drugs designed to achieve much higher and stable basal levels of GLP-1 (~20 nM serum concentrations)
- RJVA-001 designed to provide physiologically regulated GLP-1 expression over the course of the day

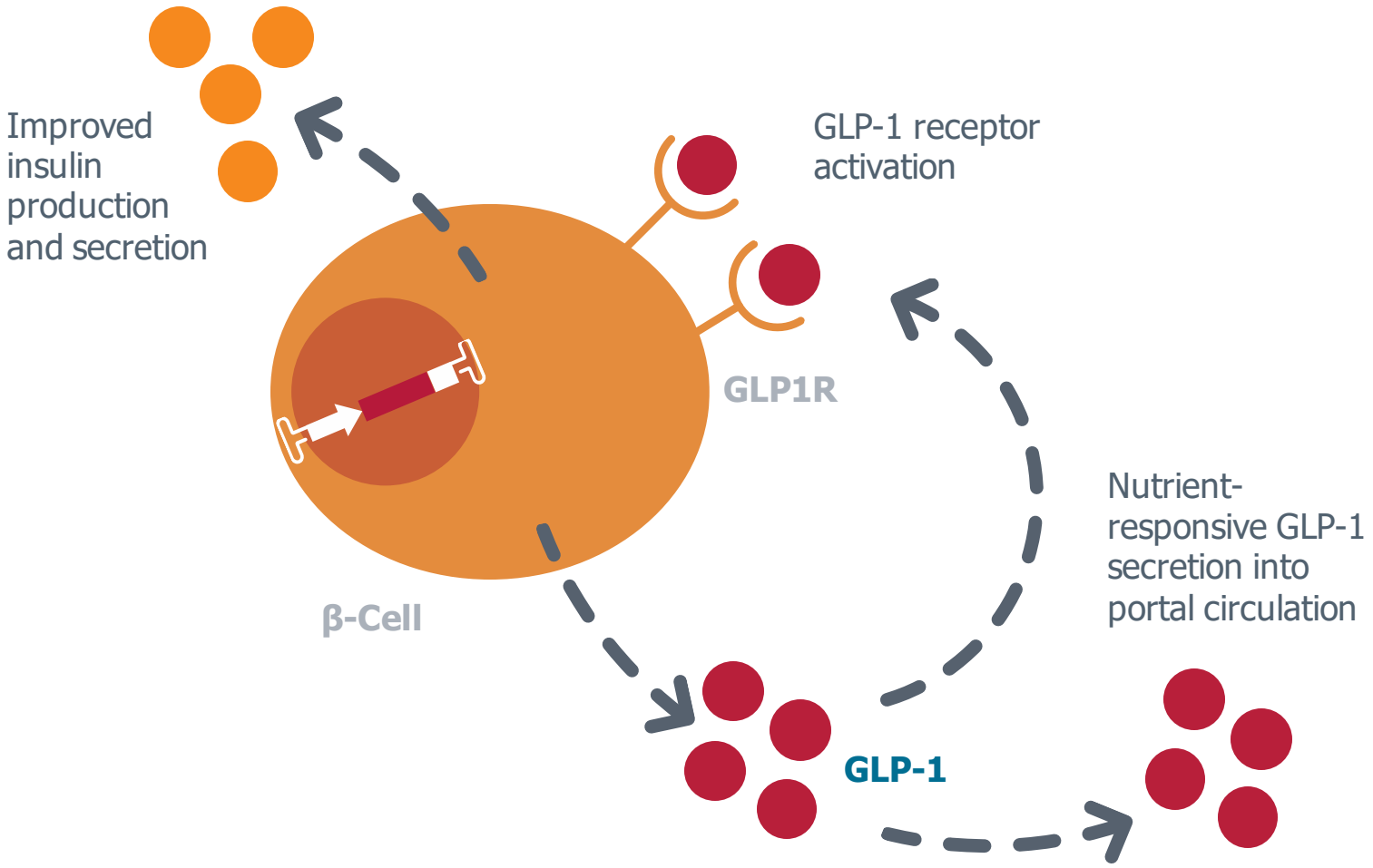


RJVA-001 for T2D

GLP-1 transgene mimics native hormone biology

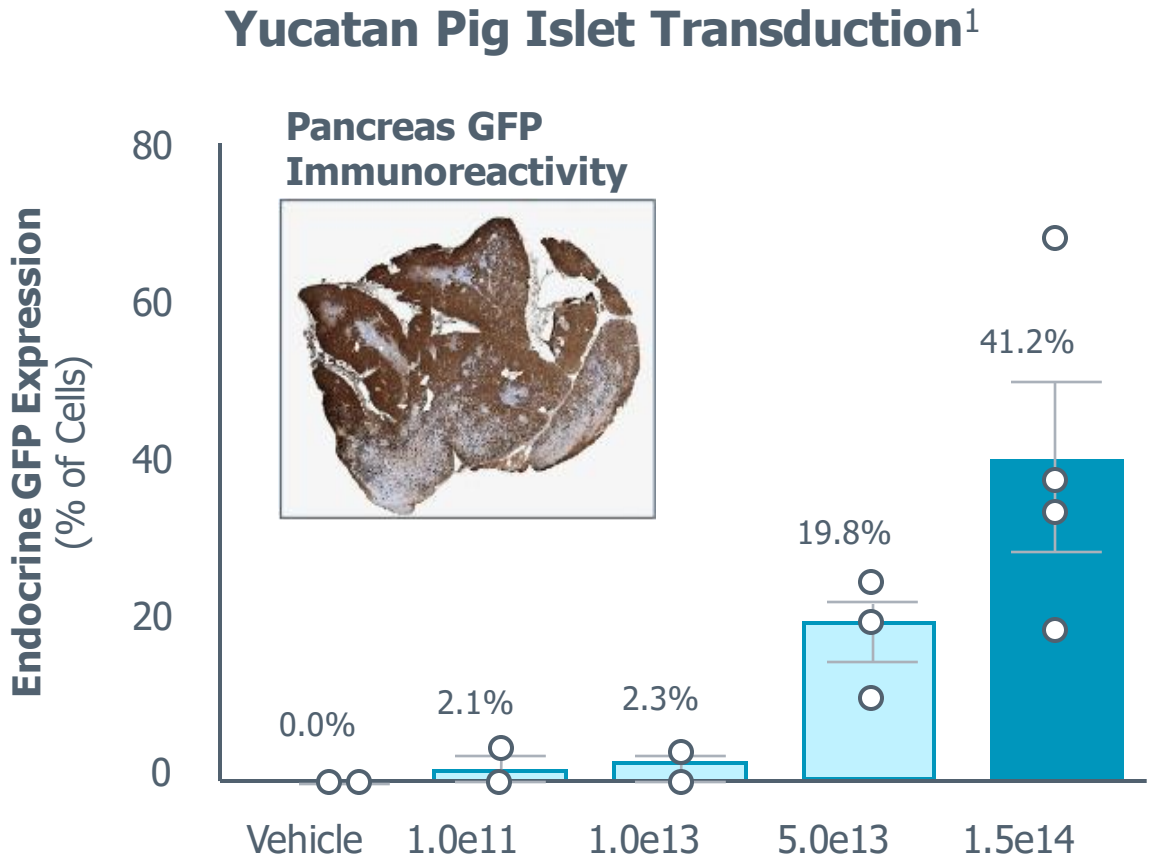
GLP-1 expression designed to provide:

- Protection from immunogenicity (GLP-1 transgene is native)
- Restoration of beta cell function
- Therapeutic leverage: Only a minority of beta cells need to be transduced due to autocrine and paracrine effects of GLP-1
- Nutrient-responsive secretion into portal circulation (like native GLP-1)



Intrapancreatic delivery of AAV9

5.0e13 total VG in Yucatan pig ~ 5e11 VG/kg human dose



>50 animals treated with 100% technical success;
no adverse safety signals to date

Low viral genome dose with limited systemic virus exposure[1]

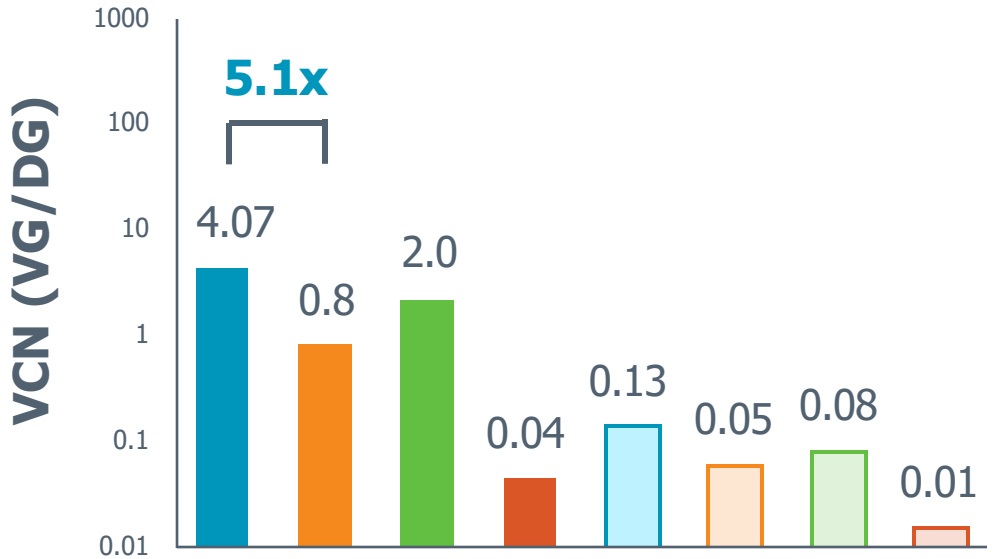
Designed to be 2-3 orders of magnitude less AAV9 than used in Zolgensma®

Mean ± SD shown; n=2-4 per group. 1. Presented at Rajagopalan et al. ASGCT 2023. Abstract no. 191. Oral Presentation

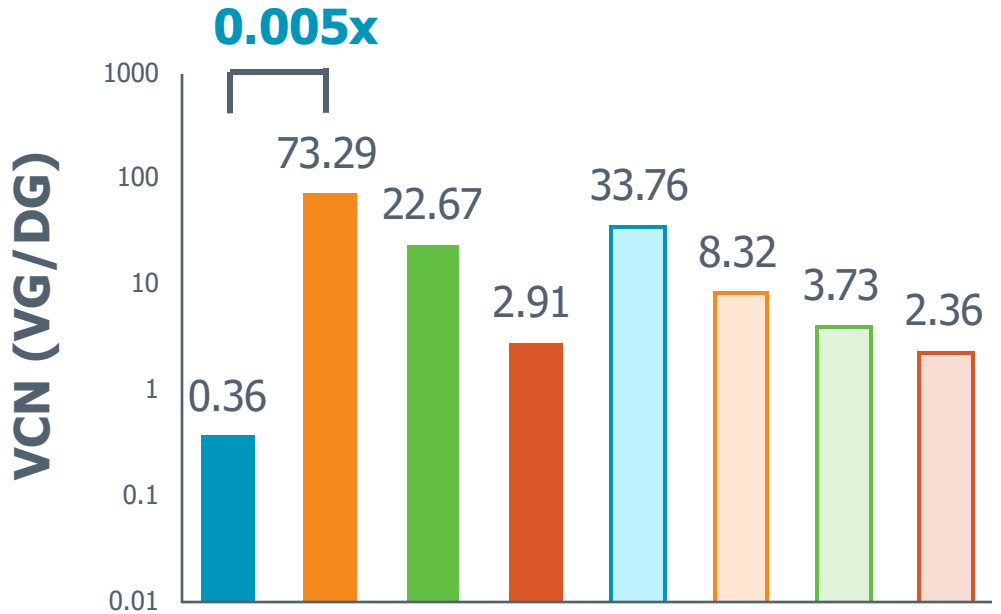
Intrapancreatic AAV9: Biodistribution

Local delivery de-targets liver and kidney vs I.V. administration

A) Intra-pancreatic delivery (4.2e12 VG/kg)



B) I.V. delivery (8.3e12 VG/kg, Li et al. 2022[1])



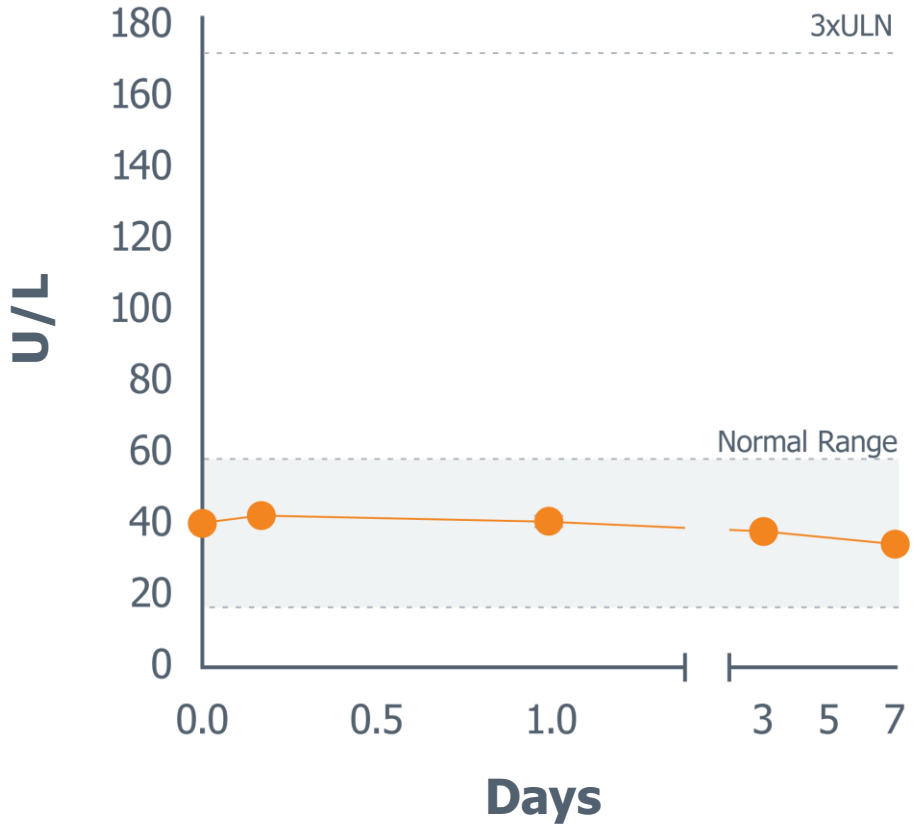
Pancreas | Liver | Spleen | Heart | Kidney | Lung | Cerebral Cortex | Skeletal Muscle

Figure adapted from 1. Li et al. Physiol Genomics 54: 261–272, 2022. EUS, N=4; I.V., N=2; EUS=endoscopic ultrasound, ROA=Route of administration, AAV=adeno-associated virus, VCN=vector copy number, VG=vector genomes, DG=diploid genomes, I.V.=intravenous

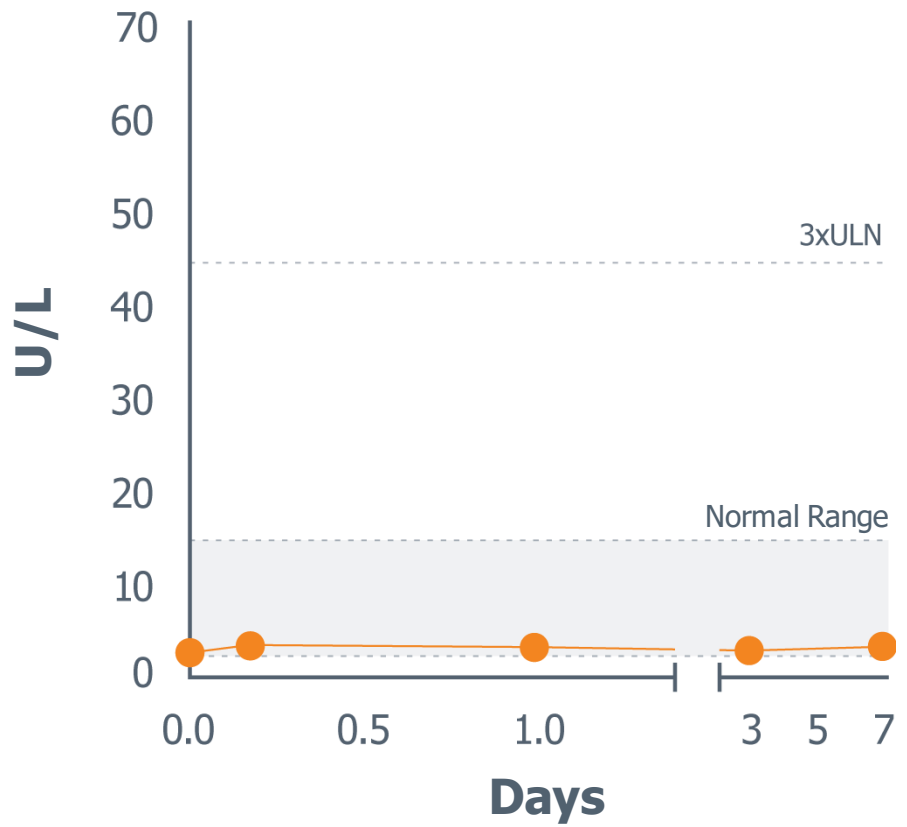
Intrapancreatic AAV9: Toxicology

ALT and lipase levels within normal range across all timepoints

A) 7-day ALT



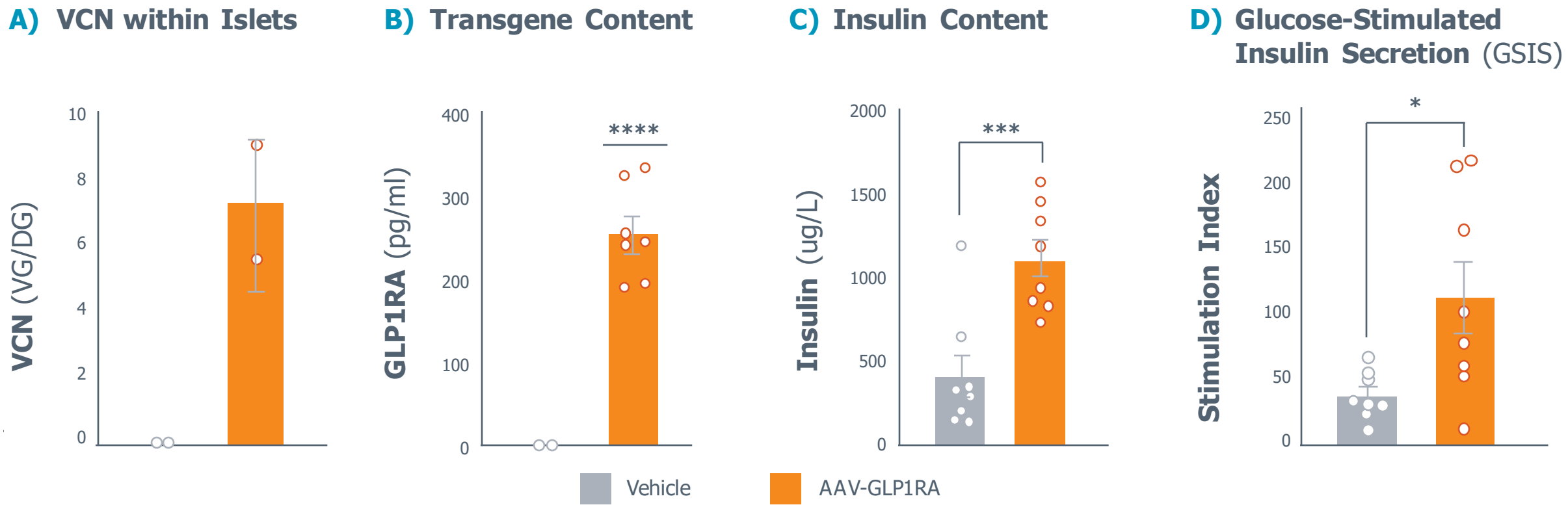
B) 7-day Lipase



Mean ± SEM shown; n=28. 1. Thompson et al. UEGW 2023 poster presentation. Abstract no. AS-UEG-2023-02238. ALT=alanine transaminase, ULN=upper limit of normal

RJVA-001 prototype* expression and activity

AAV9.MIP.GLP1RA 10 weeks after infusion in db/db mouse model

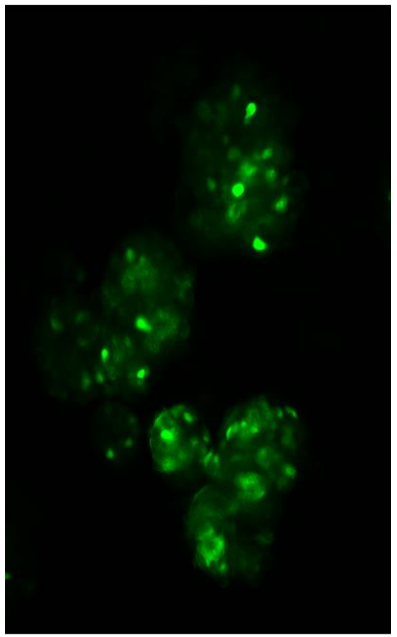


Mean ± SD shown; *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001; n=2-8 per group; AAV=adeno-associated virus, GLP1RA=GLP-1 receptor agonist, VCN=vector copy number, VG=vector genome, DG=diploid genome. MIP = mouse insulin promoter
RJVA-001 prototype = AAV9.MIP.GLP1RA Rajagopalan et al. ASGCT 2023 oral presentation. Abstract no. 191

RJVA-001 prototype* in vitro efficacy

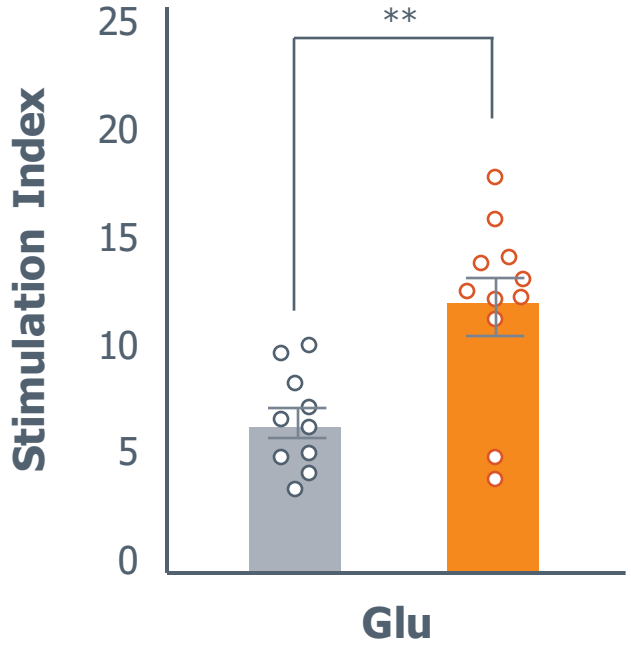
Improved insulin secretion in human islets and human β-cell Line

A) Human Islet Transduction

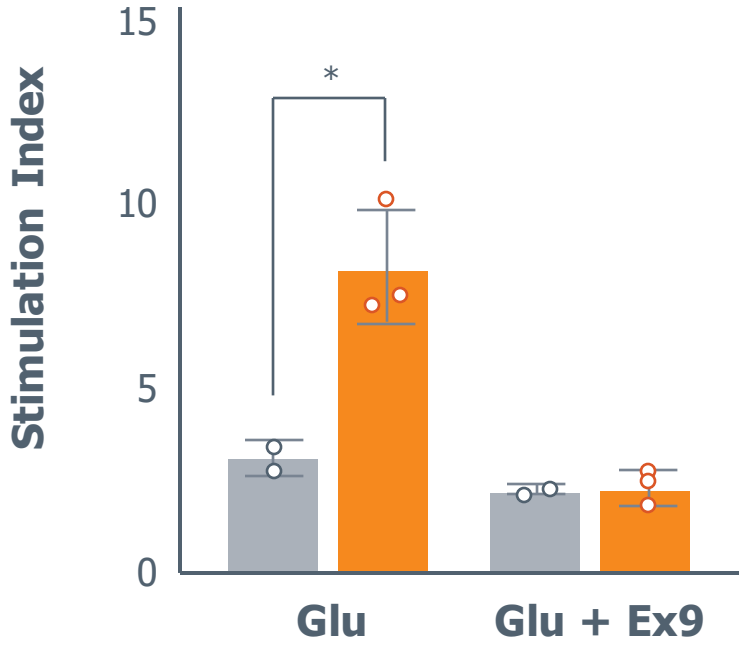


GFP Expression

B) Human Islet GSIS



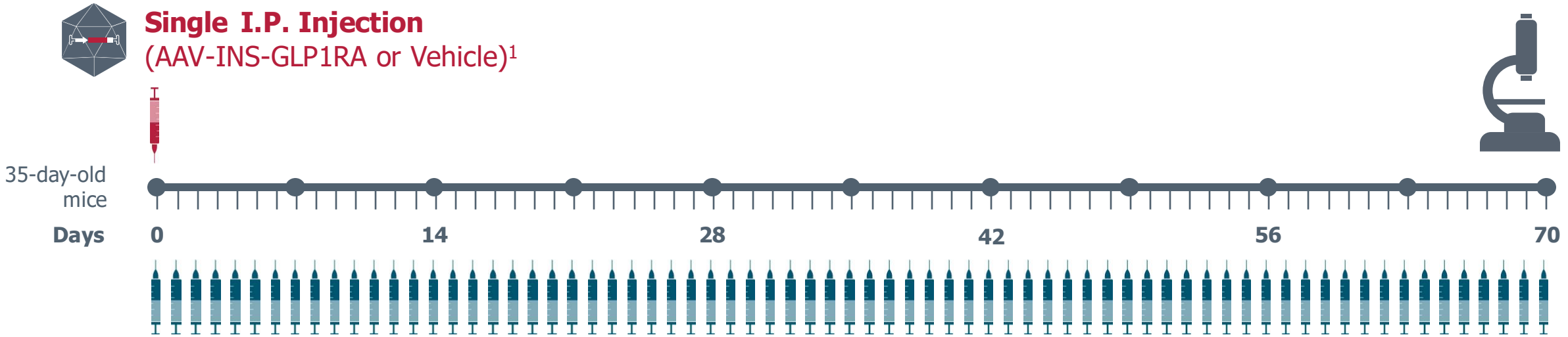
C) GLP-1R Antagonist Exendin-9 Blocks GLP-1RA in Human Beta Cell Line



Mean ± SEM shown; *p<0.05, **p<0.01; n=2-11 per group. B) Glucose stimulation of 16.7 mM from 2.8 mM baseline, C) Glucose stimulation of 11 mM from 0 mM baseline. Rajagopalan et al. ASGCT 2023 oral presentation. Abstract no. 191.. AAV=adeno-associated virus, Ex9=Exendin-9, GFP=green fluorescent protein, GLP1=glucagon-like peptide 1, GLP1R=GLP1 receptor, GLP1RA=GLP1R agonist, Glu=glucose, GSIS=glucose-stimulated insulin secretion, PGTx=pancreatic gene therapy RJVA-001 prototype = AAV9.MIP.GLP1RA

RJVA-001 prototype* vs Semaglutide

Design of POC efficacy study in db/db mouse (standard T2D model)



Daily S.C. Injection
Semaglutide (10 nmol/kg*) or Vehicle[1]

*Semaglutide dose selected for glucose-lowering optimization[2]

Efficacy/MOA (day 0-70)
Weekly Fasting Blood Glucose
Biweekly Insulin
Weight[1]

Sacrifice (days 58-70)
Organ Histology
Pancreatic GLP1RA Protein
Serum GLP1RA Protein[1]

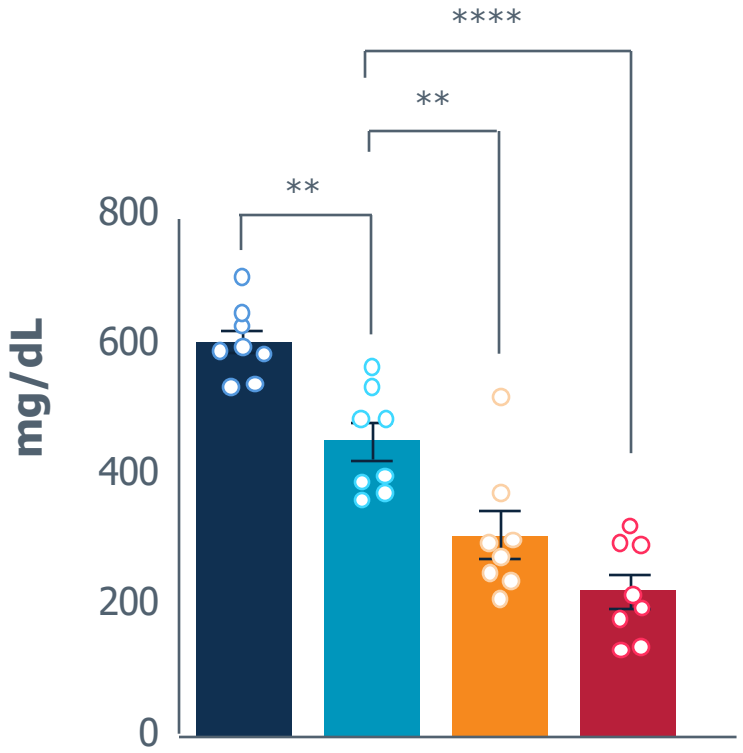
1. Rajagopalan et al. ADA 2023 oral presentation. Control #2023-A-3216-Diabetes 2. CDER (2017) Semaglutide NDA Application (209637Orig1s000), Section 4.4 Nonclinical Pharmacology/Toxicology. AAV=adeno-associated virus, GLP1=glucagon-like peptide 1, GLP1RA= GLP1 receptor agonist, INS=insulin promoter, I.P.=intraperitoneal, MOA=mechanism of action, PGTx=pancreatic gene therapy, S.C.=subcutaneous

RJVA-001 prototype* vs Semaglutide

Glucose and insulin levels after 8 weeks in db/db mice

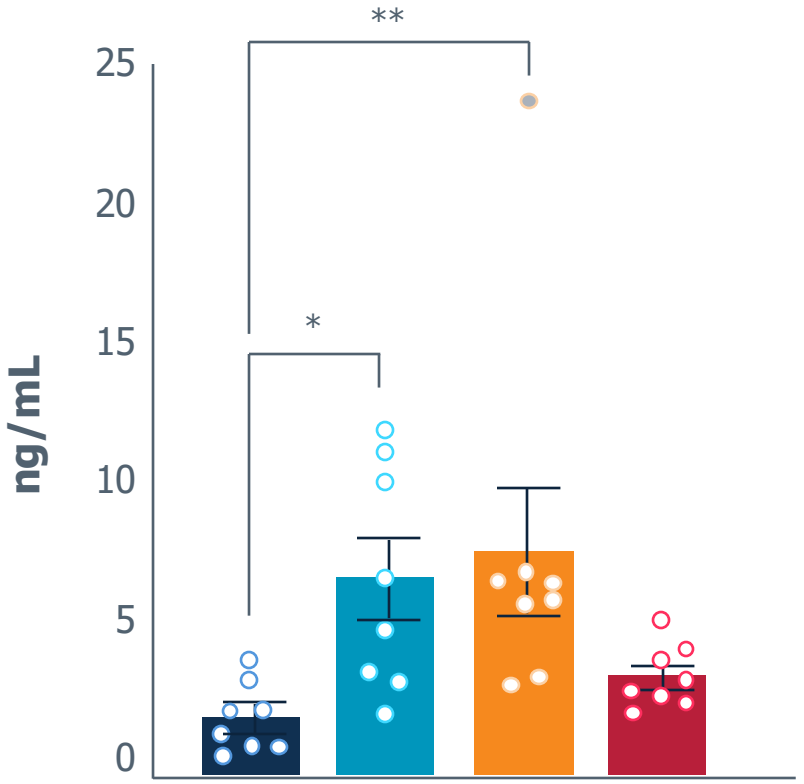
A) Fasting Blood Glucose

(Week 8, 4–6 hour fasted)[1]



B) Fasting Insulin

(Week 8, 4–6 hours fasted)[1]



Vehicle Control

Semaglutide (10 nmol/kg)

AAV-INS-GLP1RA 1st Gen (10e12)

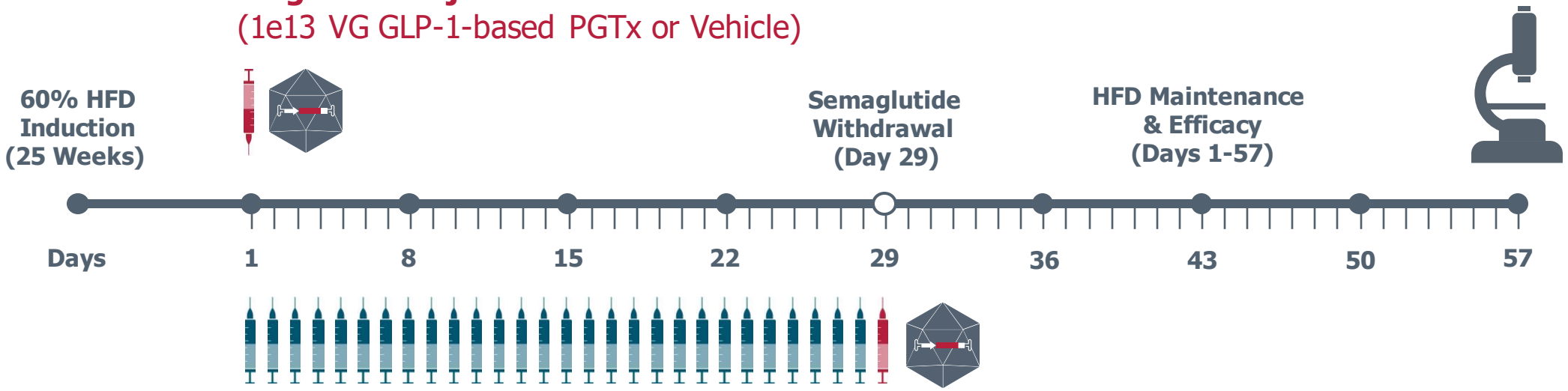
AAV-INS-GLP1RA 2nd Gen (5e12)†

†Regulatory element modification

1. Rajagopalan et al. ADA 2023 oral presentation. Control #2023-A-3216-Diabetes. Mean ± SEM shown; *p<0.05, **p<0.01, ****p<0.0001; n=8 per group. AAV=adeno-associated virus, Gen=generation, GLP1=glucagon-like peptide 1, GLP1RA=GLP1 receptor agonist, INS=insulin promoter, PGTx=pancreatic gene therapy

RJVA-001 prototype* vs Semaglutide

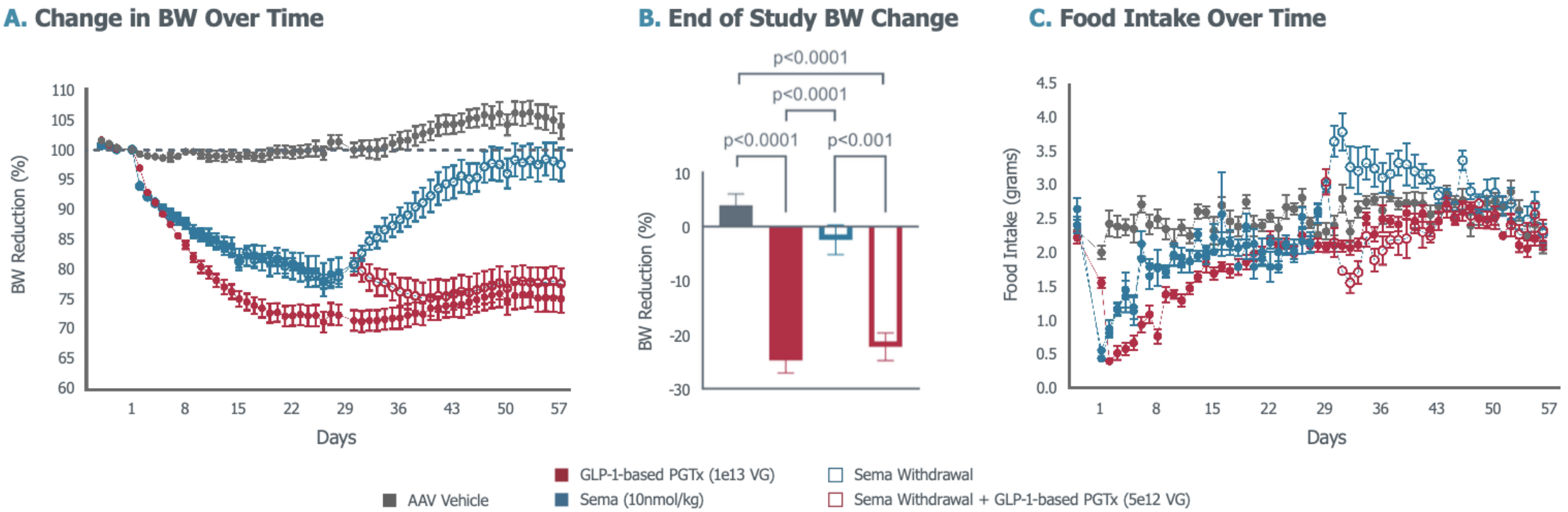
Design of POC efficacy study in DIO mouse (standard obesity model)



Fitzpatrick AL et al. WCIRDC 2023 oral presentation; AAV=adeno-associated virus, BW=body weight, BWL=body weight loss, DIO=diet-induced obesity, GLP1=glucagon-like peptide 1, GLP1RA= GLP1 receptor agonist, HFD=high fat diet, INS=insulin promoter, I.P.=intraperitoneal, PGTx=pancreatic gene therapy, S.C.=subcutaneous

RJVA-001 prototype* vs Semaglutide

Weight loss and food intake in DIO mouse model



Fitzpatrick AL et al. WCIRDC 2023 oral presentation

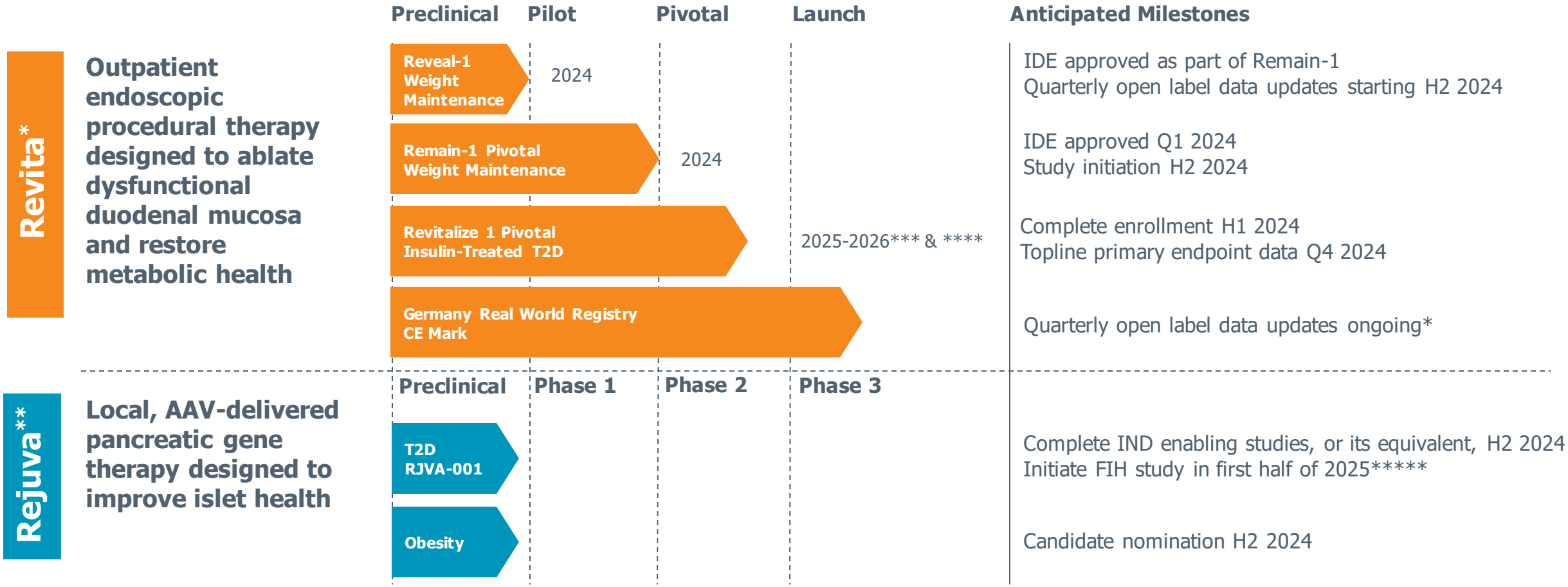
RJVA-001 summary

Nutrient-responsive GLP-1 via intrapancreatic gene therapy

- Utilizes Fractyl's proprietary intrapancreatic delivery system – invented to enable local delivery of pancreatic gene therapy vectors
- Designed for improved potency and tolerability compared to other approaches
- Efficacy in db/db and DIO mouse models of T2D and obesity superior to chronic semaglutide
- Regulatory alignment on IND-enabling studies for T2D FIH study
- RJVA-001 candidate nominated in H1 2024
- Clinical trial initiation in T2D expected in 2025

Well-funded with recent IPO proceeds of $110M

Financed to support operations through multiple near-term milestones



*Revita has been granted Breakthrough Device designation for the hydrothermal ablation of the duodenal mucosa to improve glycemic control and eliminate insulin needs in T2D patients inadequately controlled on long-acting insulin; and CE mark obtained from EU and UK in 2016 for Revita for the improvement of glycemic control in patients with inadequately controlled T2D despite oral and/or injectable glucose lowering medications and/or long-acting insulin; **Product candidates under our Rejuva gene therapy platform will undergo Phase 1, Phase 2 and Phase 3 clinical trials; ***The Revitalize-1 study is a pivotal study in patients with inadequately controlled T2D despite being on up to three ADAs and daily insulin; ****If PMA approved; *****Subject to IND approval

IND = Investigational New Drug Application with FDA or comparable regulatory body; IDE = Investigational Device Exemption with FDA or comparable regulatory body; FIH = first-in-human; PMA = Premarket Approval

Pioneering metabolic therapeutics company

Differentiated assets, near term catalysts, capital efficient operating model

Targeting Unmet Needs in Major Metabolic Markets	Obesity and Type 2 Diabetes (T2D)
Revita® Duodenal Mucosal Resurfacing	Proprietary device and delivery system platform enables privileged access to gut and pancreas for durable glucose control and weight maintenance
Rejuva® Pancreatic Gene Therapy Platform	Novel locally administered, AAV-based pancreatic gene therapy with potential for remission of obesity and T2D
Multiple Anticipated Near-Term Catalysts	Revita Pivotal Studies in T2D and weight maintenance, Revita commercial pilot in Germany, Rejuva FIH in T2D
Strong Balance Sheet	IPO in Q1 2024 with capital to fund key Revita and Rejuva catalysts

Thank you!

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