Hot Topics in Medicine Webinar Series
August 5, 2026

A Rolling Update on Anti-Obesity Pharmacotherapy

Eduardo Grunvald, MD, FACP

Medical Director, Center for Advanced Weight Management
Bariatric and Metabolic Institute
University of California San Diego
Division of General Internal Medicine
Division of Minimally Invasive Surgery

UC San Diego
Health System

Relevant Disclosures

Research Support	Obesity Treatment Foundation
	Aardvark Therapeutics
	Novo Nordisk
Advisory	B2M Medical (2021 – 2024)
	Elevai, Inc (2024-2025)
Consulting	Eli Lilly (2025-2026)
	Novo Nordisk (2019 - 2026)
	Aardvark Therapeutics (2025)
	Pfizer/Metsera (2025-2026)
	Currax Pharmaceuticals (2021)
	Gelesis, Inc. (2021)

UC San Diego
Health System

Learning Objectives

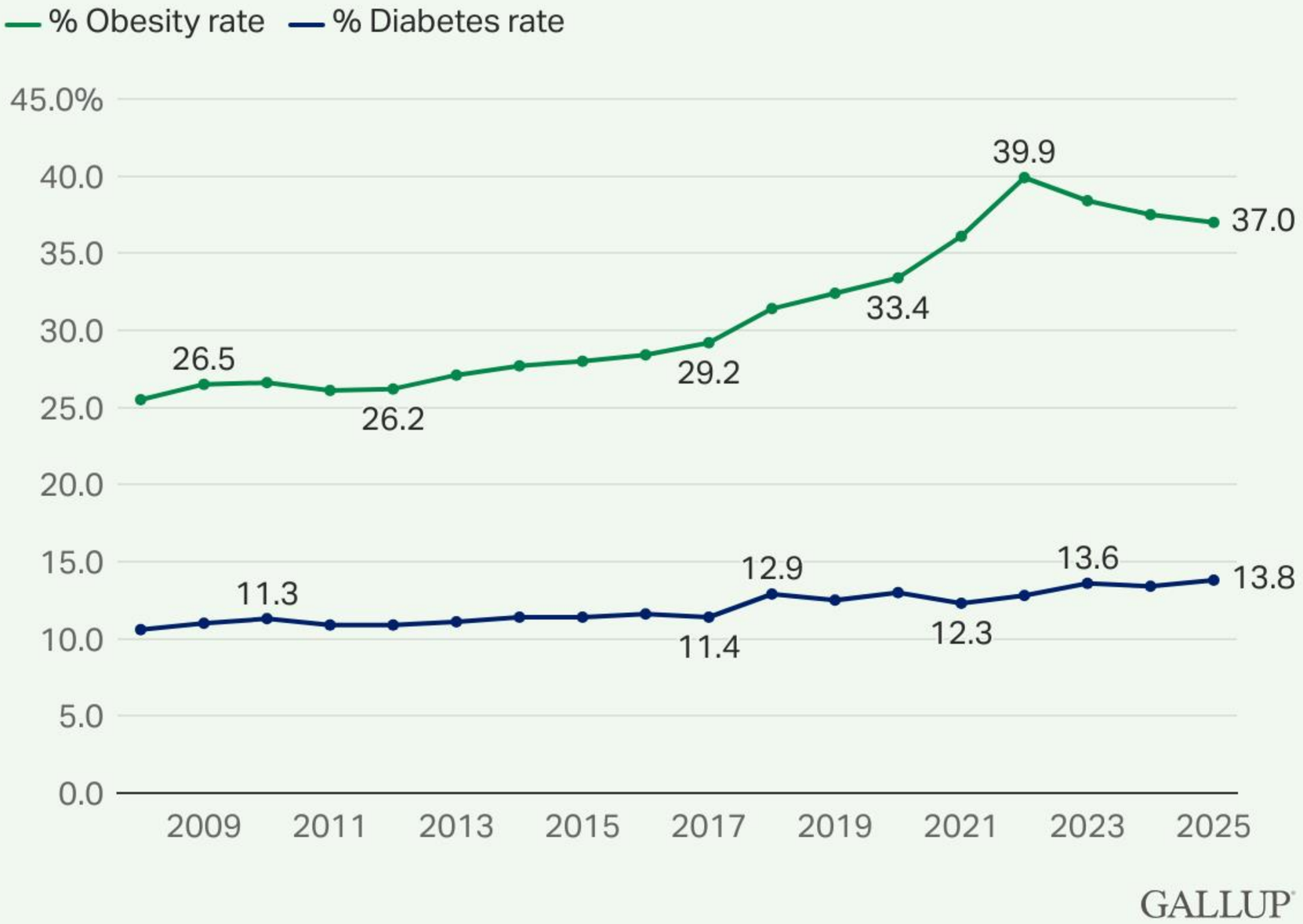
1. Understand current options for anti-obesity pharmacotherapy

2. Be prepared for emerging anti-obesity drugs

3. Feel comfortable choosing the right drug for the right patient

UC San Diego
Health System

Obesity Showing Signs of Decline in U.S.

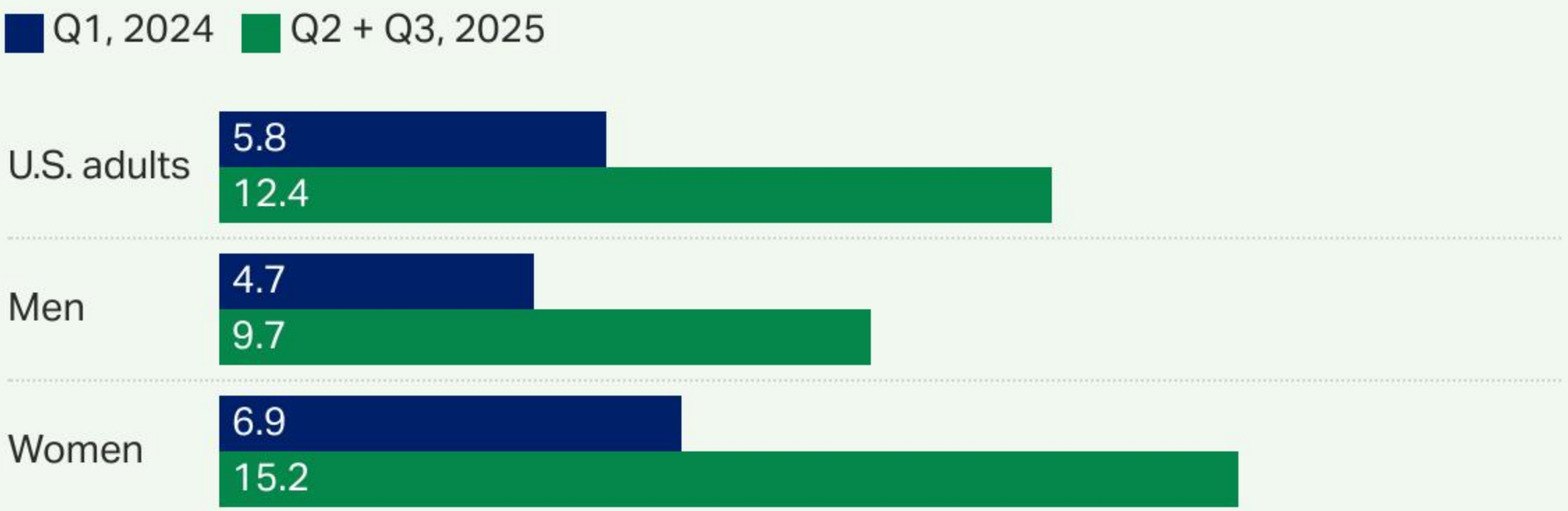


UC San Diego Health System

Use of Weight Loss Injectables More Than Doubles in Under Two Years

Have you ever taken an injection for weight loss such as semaglutide (brand names Ozempic and Wegovy) or liraglutide (brand name Saxenda)?

% Yes, I have



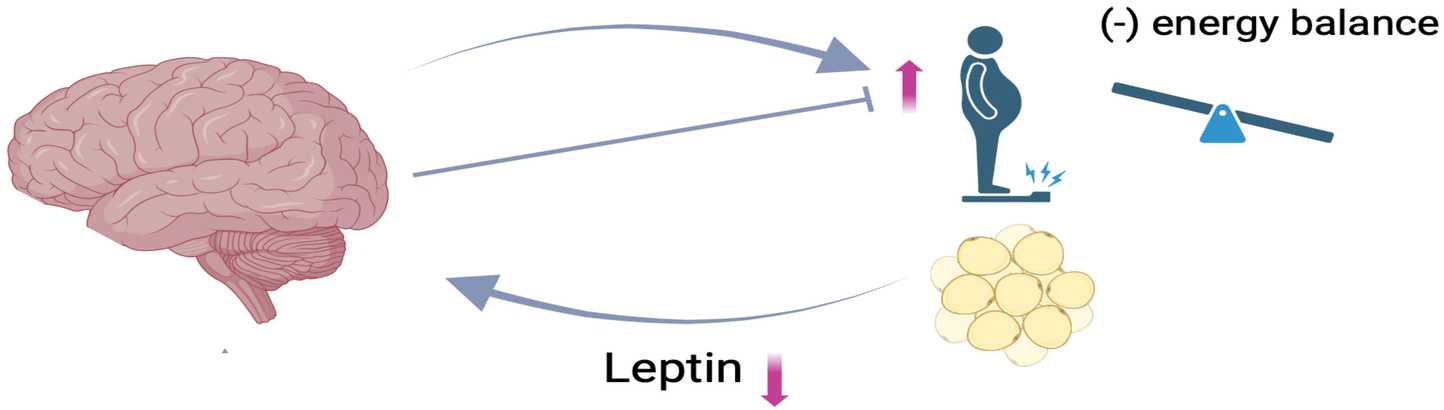
GALLUP

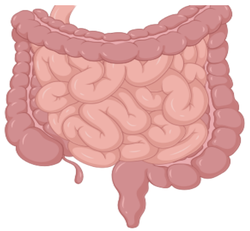
UC San Diego
HEALTH SYSTEM

Pharmacotherapy

UC San Diego Health System

Drug	Mechanism of Action	Approval
Phentermine	▸ Norepinephrine reuptake inhibition ▸ Some dopamine reuptake inhibition	**1959**
Orlistat (Alli™ and Xenical™)	▸ Gastrointestinal lipase inhibitor ▸ Inhibit GI fat absorption	**1999**
Phentermine/Topiramate ER (Qsymia™)	• Norepinephrine reuptake inhibition • GABA receptor modulation • ? increase metabolic rate	**2012**
Bupropion/Naltrexone SR (Contrave™)	▸ Dopamine reuptake inhibition ▸ Opioid receptor antagonism ▸ Enhanced POMC (pro-opiomelanocortin) neuron activation	**2014**
Liraglutide 3 mg (Saxenda™, now generic)	▸ CNS GLP1 (glucagon-like peptide 1) receptor activation ▸ Glycemic control ▸ Delayed gastric motility	**2015**
Semaglutide 2.4* mg SC and 25 mg PO (Wegovy™) ***(7.2 mg approved 3/19/26)**		**2021 (2026^{PO})**
Tirzepatide (Zepbound™)	▸ CNS GLP1 and GIP receptor activation ▸ Glycemic control ▸ Delayed gastric motility	**2023**

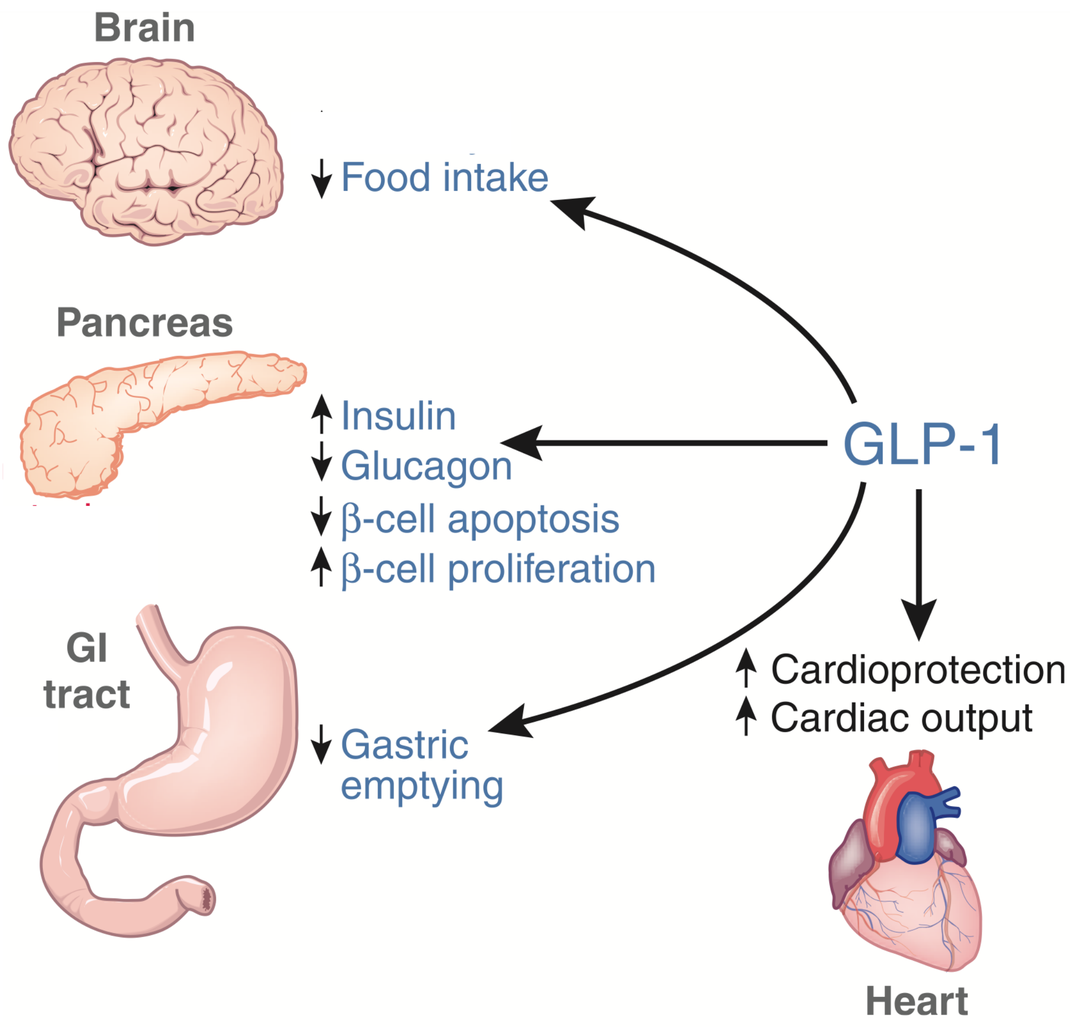




GLP-1
Glucagon-like Peptide-1

UC San Diego
Health System

GLP-1



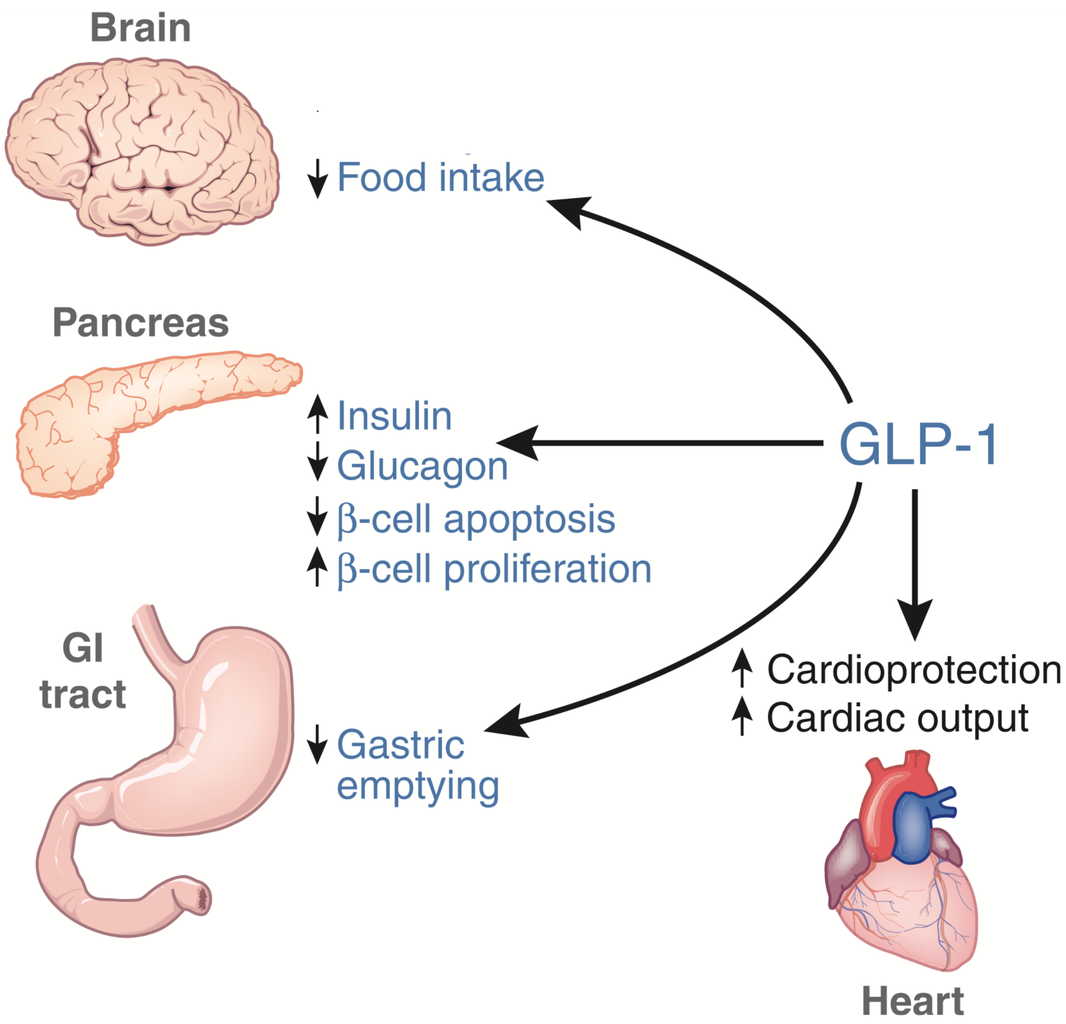
Adapted from Seino Y, et al., *J Diabetes Investig* 2010;1:8-23

GIP

Glucose-dependent Insulinotropic Polypeptide

UC San Diego
HEALTH SYSTEM

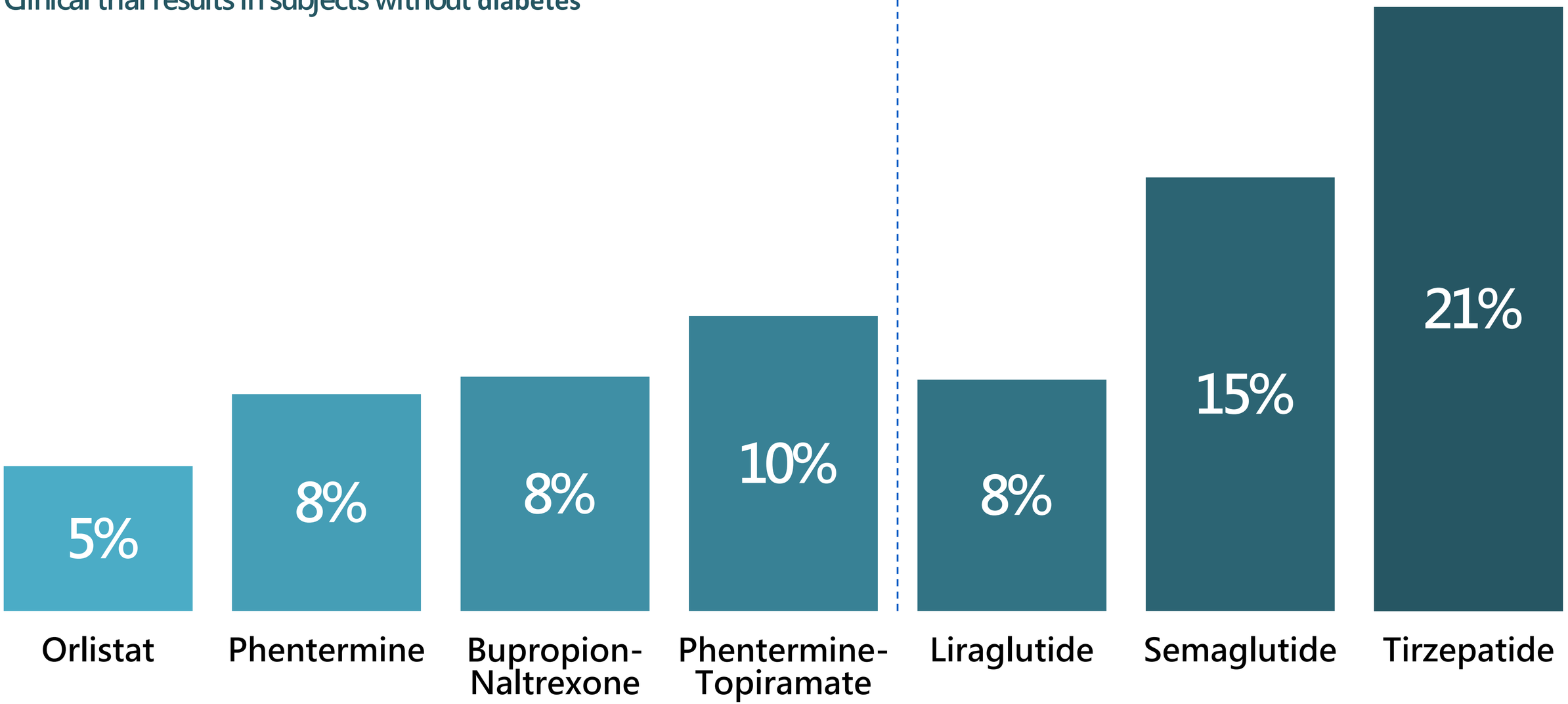
GIP



Adapted from Seino Y, et al., *J Diabetes Investig* 2010;1:8-23

Comparative Weight Loss Effectiveness

Clinical trial results in subjects without diabetes

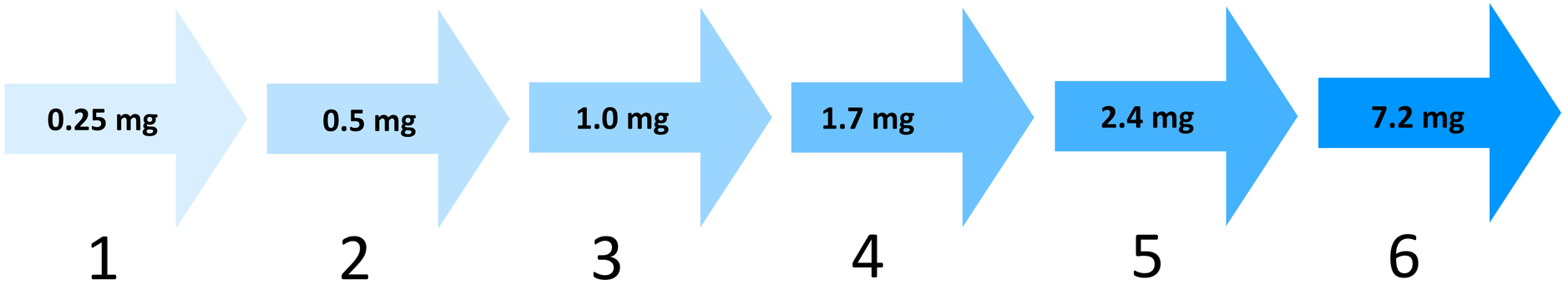


*Data from intention-to-treat analyses

UC San Diego Health System

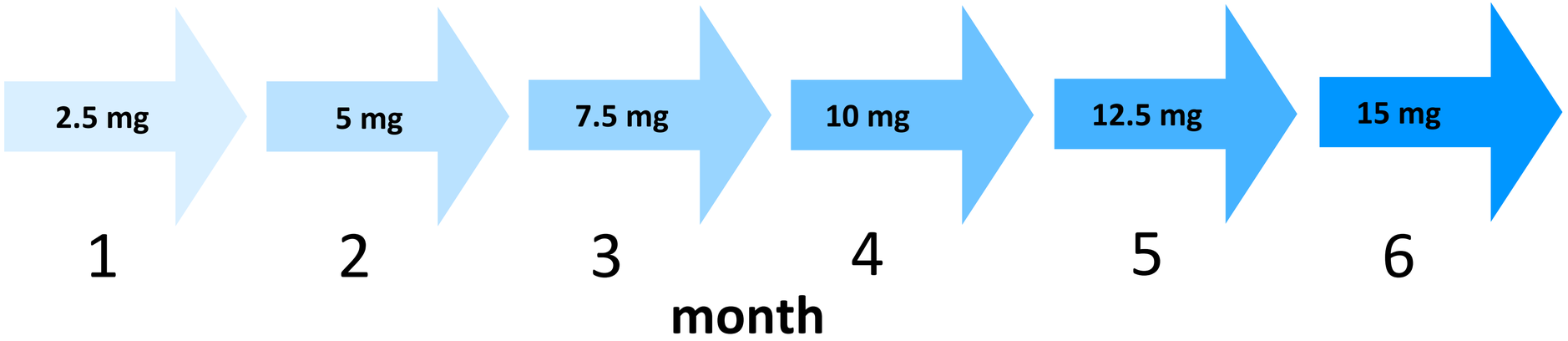
Semaglutide (Ozempic and Wegovy)

Weekly Subcutaneous Self-injection



Tirzepatide (Mounjaro and Zepbound)

Weekly Subcutaneous Self-injection



UC San Diego Health System

Titration pitfalls

- **Go low and slow**
  Weight management is a marathon, not a sprint
- **If 2-3 weeks of medication lapse, consider restarting titration**
  Use clinical judgment
- **Greater than 5% monthly weight loss, consider maintaining dose**
  Lower risk of adverse effects. Expert opinion.
- **Discontinuation**
  They can be discontinued abruptly, but some titrate to minimize "hunger shock"

Oral GLP-1

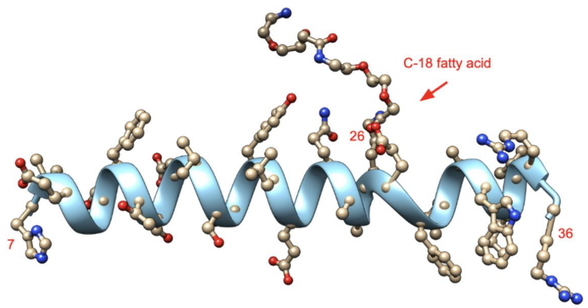
UC San Diego
HEALTH SYSTEM

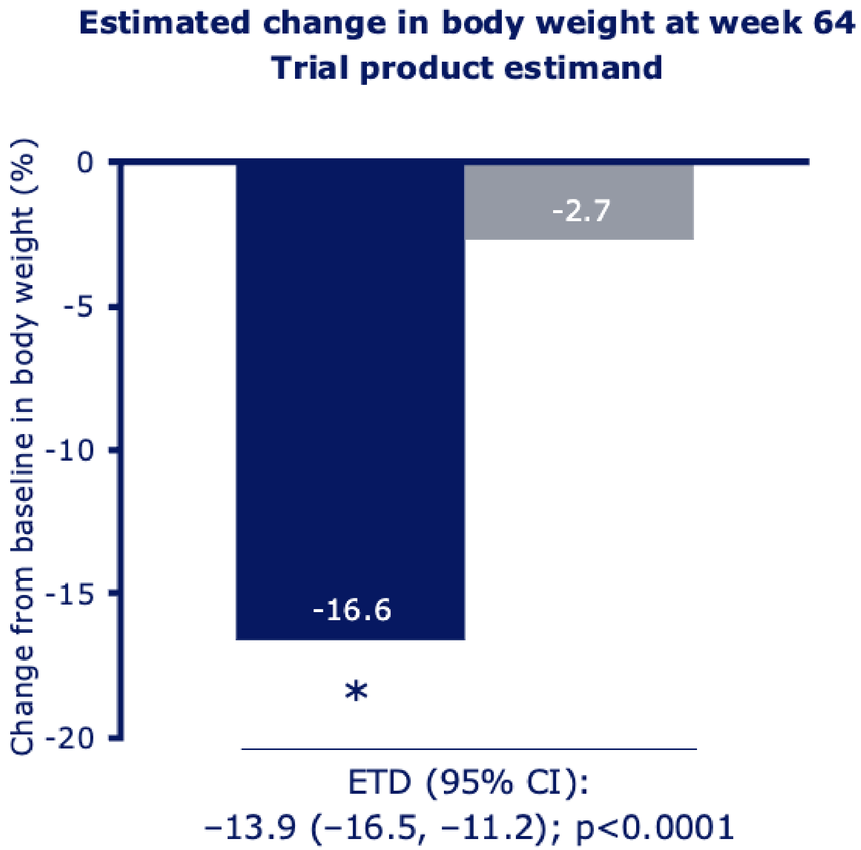
Oral Semaglutide (Oral Wegovy) 25 mg

Peptide

Semaglutide 14 mg (Rybelsus) for DM

Empty Stomach





Garvey WT et al. Presented at the 42nd Annual Meeting of The Obesity Society held at ObesityWeek, November, 2024, San Antonio, TX

UC San Diego Health System

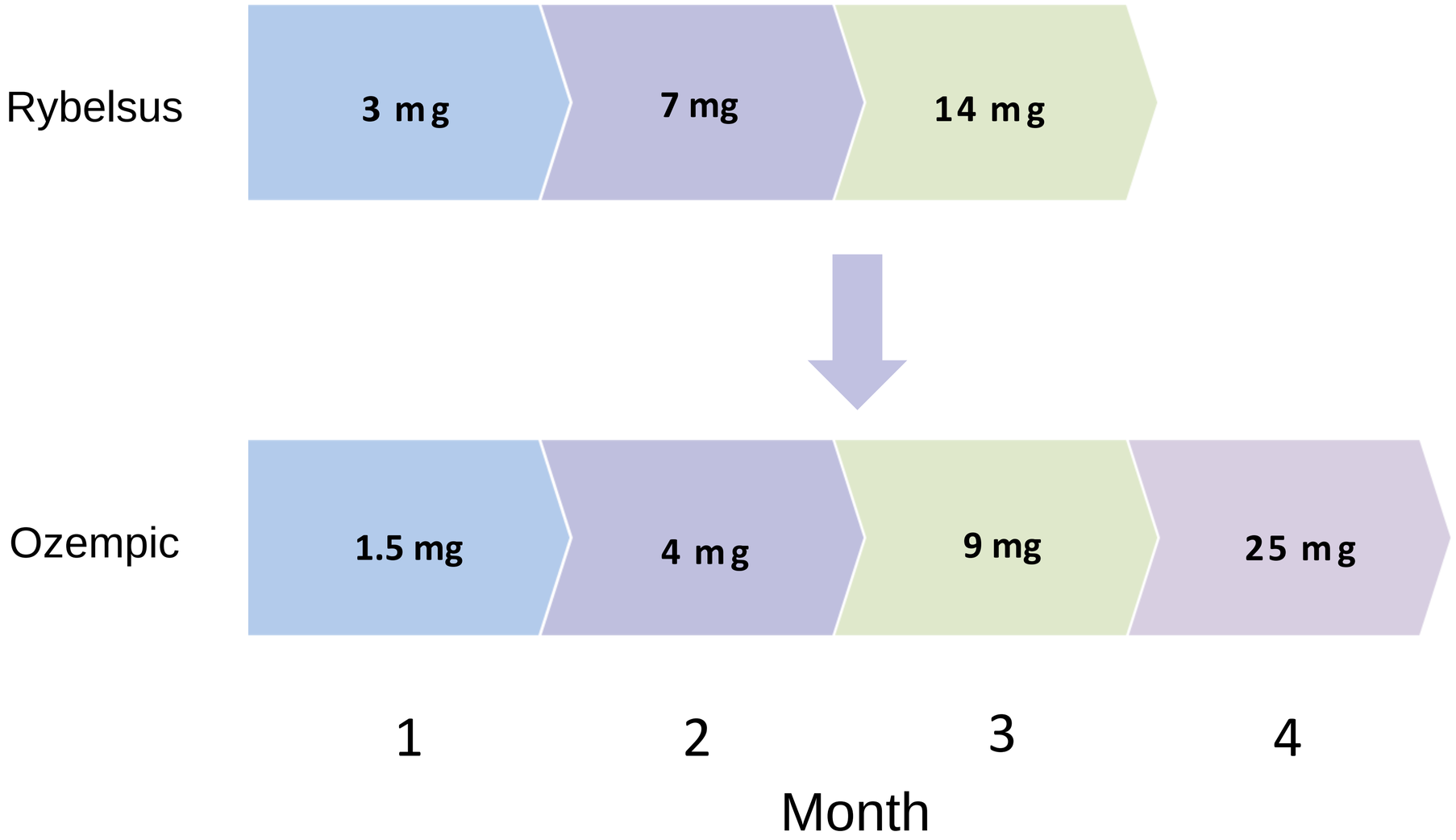
Oral Semaglutide (Wegovy) Titration Schedule

Daily oral tablets

UC San Diego Health System

Oral Semaglutide for Type 2 Diabetes

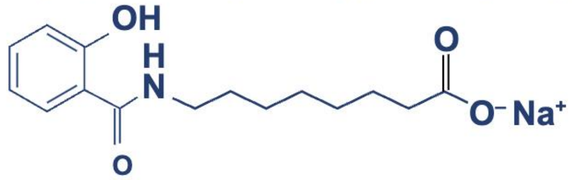
Daily oral tablets

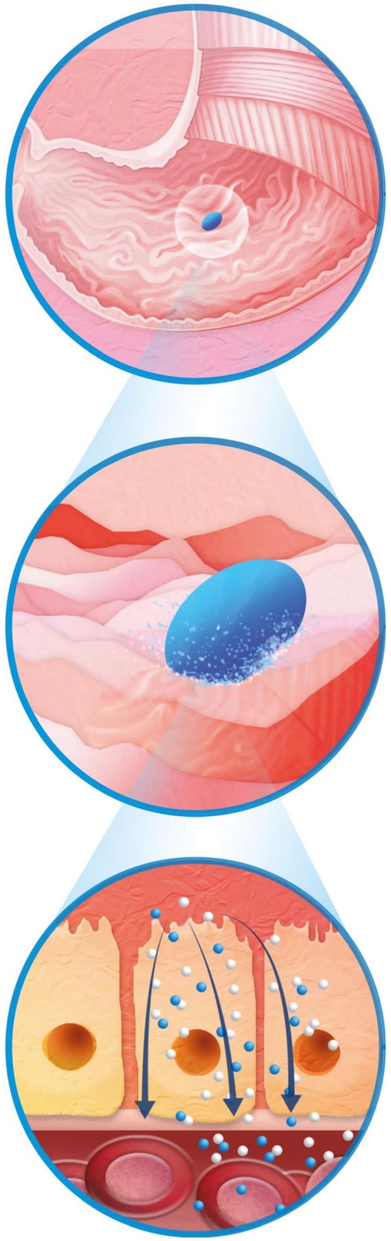


UC San Diego Health System

SNAC

Sodium **N**-[8-(2-Hydroxybenzoyl) **A**mino] **C**aprylate





- Semaglutide absorbed in gastric mucosa
- Degraded in low pH
- SNAC raises pH around the tablet
- SNAC increases transcellular permeability

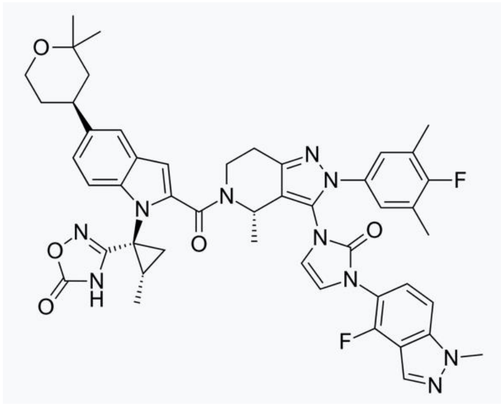
Solis-Herrera C et al. Clin Diabetes 2024;42(1):74-86
Aroda VR et al. Rev Endocr Metab Disord 2022;23(5):979-994

UC San Diego Health System

Orforglipron (Foundayo)

Non-peptide small molecule GLP-1 agonist

No food restriction

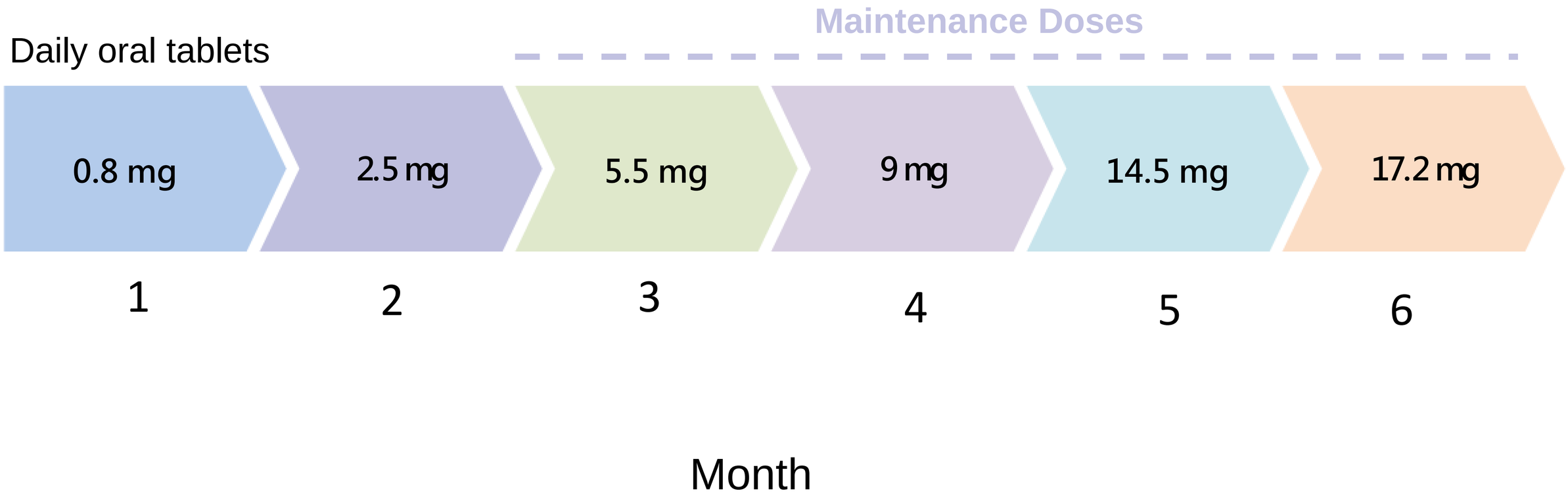


Efficacy Estimand Results				
	Orforglipron 6 mg	**Orforglipron 12 mg**	**Orforglipron 36 mg**	**Placebo**
Primary Endpoint				
Mean percent change in body weight from avg. baseline of 103.2 kg (227.5 lbs) and 37.0 BMI[i]	-7.8% (-8.0 kg; -17.6 lbs)	-9.3% (-9.4 kg; -20.7 lbs)	-12.4% (-12.4 kg; -27.3 lbs)	-0.9% (-1.0 kg; -2.2 lbs)
Key Secondary Endpoints				
Percentage of participants achieving body weight reductions of ≥10%[i]	35.9 %	45.1 %	59.6 %	8.6 %
Percentage of participants achieving body weight reductions of ≥15%[i]	16.5 %	24.0 %	39.6 %	3.6 %

Eli Lilly Press Release August 7 2025

UC San Diego Health System

Orforglipron (Foundayo) Titration Schedule



UC San Diego Health System

Orforglipron (Foundayo) Drug Interactions and Clinical

CYP3A4 Inhibitors

Orforglipron is metabolized by CYP3A4. Limit to 9 mg daily with with strong inhibitors (eg, clarithromycin). Avoid with inhibitors that also affect OATP1B* (eg, ritonavir, cyclosporine).

CYP3A4 Inducers

Avoid strong inducers (carbamazepine). For moderate moderate inducers (efavirenz), monitor clinical effectiveness and escalate orflorglipron dose as needed.

Simvastatin

Limit dose to 20 mg once daily when used with orforglipron due to increased exposure of simvastatin acid.

Oral Medications & Contraceptives

Delayed gastric emptying may reduce absorption. Use non- or barrier methods for 30 days after initiation and each dose escalation.

Pregnancy

Patients should be counseled consistent and reliable use of contraception.

Hepatic Impairment

Do not use orforglipron in patients with severe hepatic impairment (Childs-Pugh C).

Renal Impairment

Orforglipron is metabolized in the liver. No dose adjustments are necessary with renal impairment. Monitor renal function if volume depleted.

OATP1B: Organic Anion Transporting Polypeptide 1B

GLP-1 Conversions

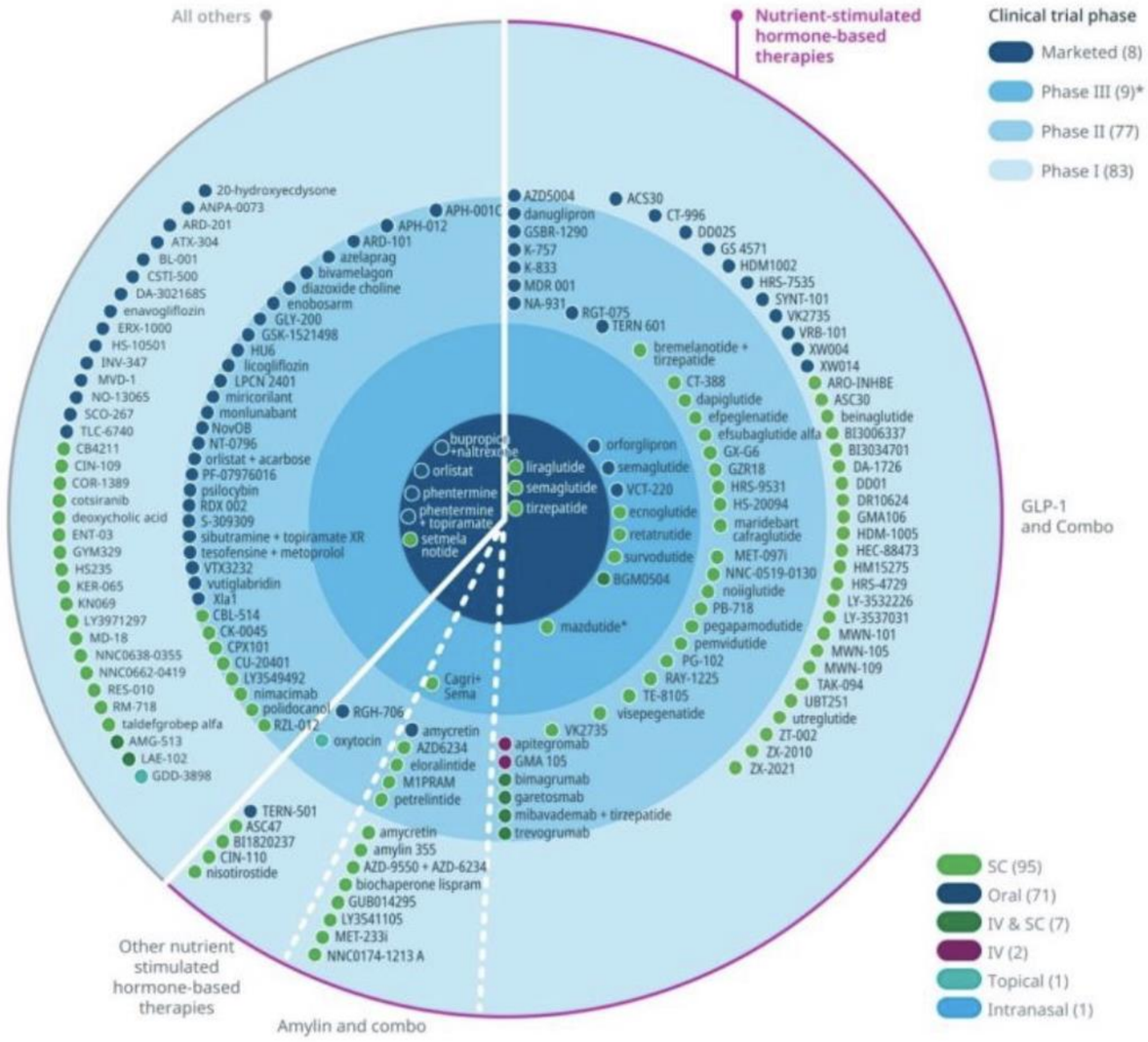
This is not based on definitive bioequivalence and should be used as a clinical guide. Ultimately clinical judgment prescribing practices.

Agent	Route and Interval	Comparative Doses (mg)					
Semaglutide	SC Weekly	0.25	0.5	1.0	1.7	2.4	7.2
Semaglutide	PO Daily	4	9			25	
Tirzepatide	SC Weekly		2.5		5	7.5	
Orforglipron	PO Daily	0.8	0.8	0.8	0.8	0.8	0.8

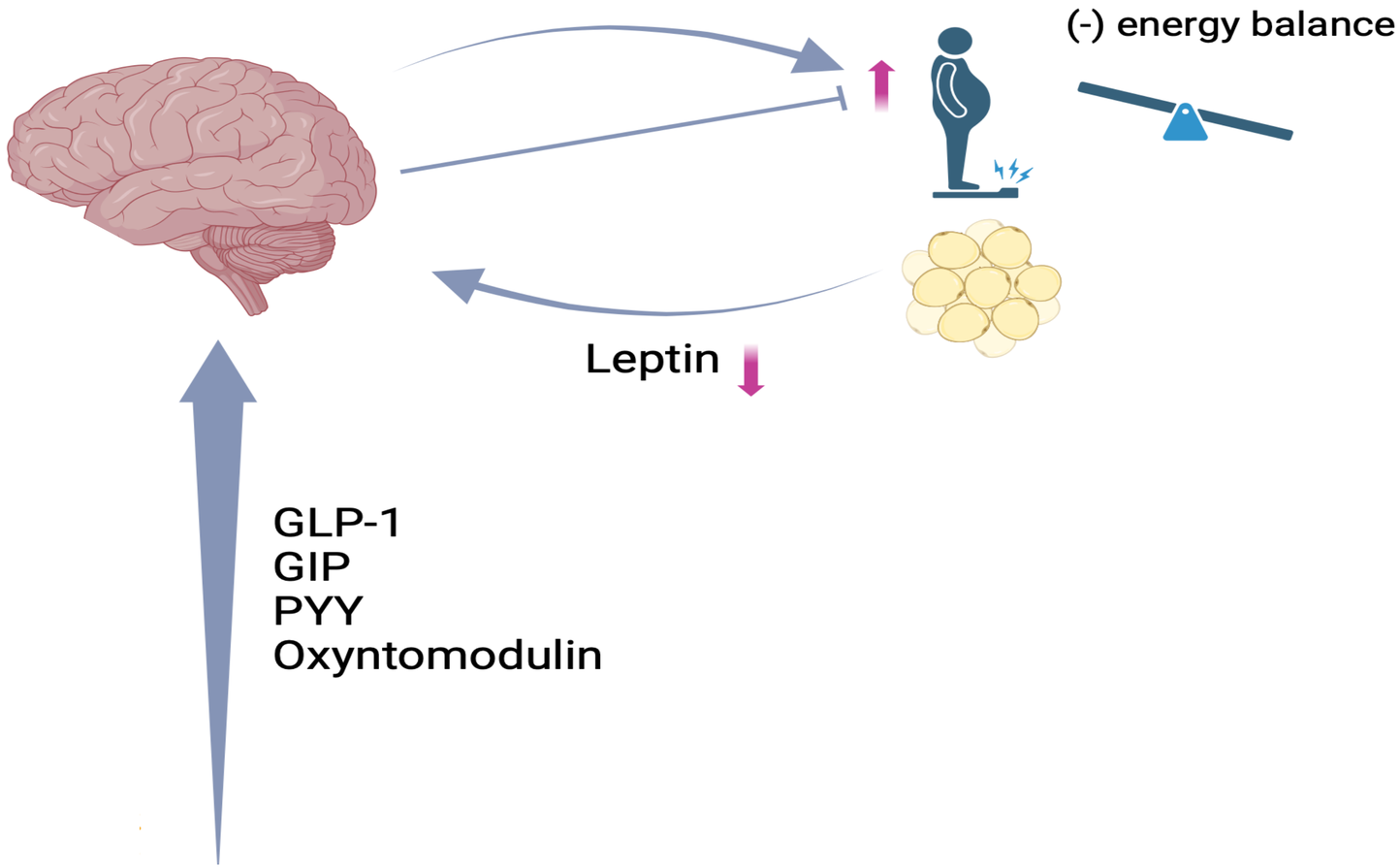
Whitley et al. Clin Diabetes. 2023;41(3):467-473
Wegovy Prescribing Information Revised 30/2026
Novo Nordisk Announcement 2/4/26

UC San Diego Health System

Obesity pipeline by phase, target and route of administration

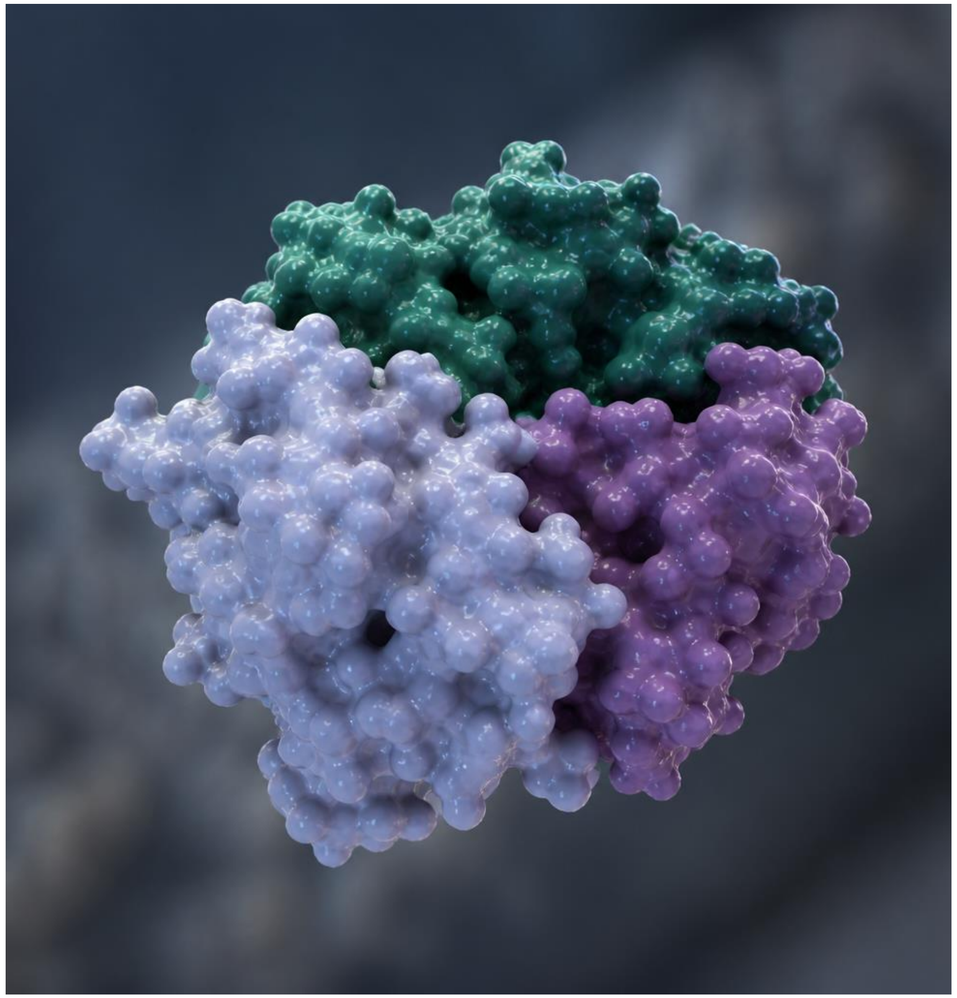


Source: IQVIA Institute Global Trends in R&D 2025 Report



Retatrutide: "Triple G" agonist

Overview of Mechanism, Efficacy, and Safety



- **Mechanism of Action**

  Triple hormone receptor agonist (GLP-1, GIP, and Glucagon) driving metabolic synergy through satiety, insulin sensitivity, and thermogenesis.

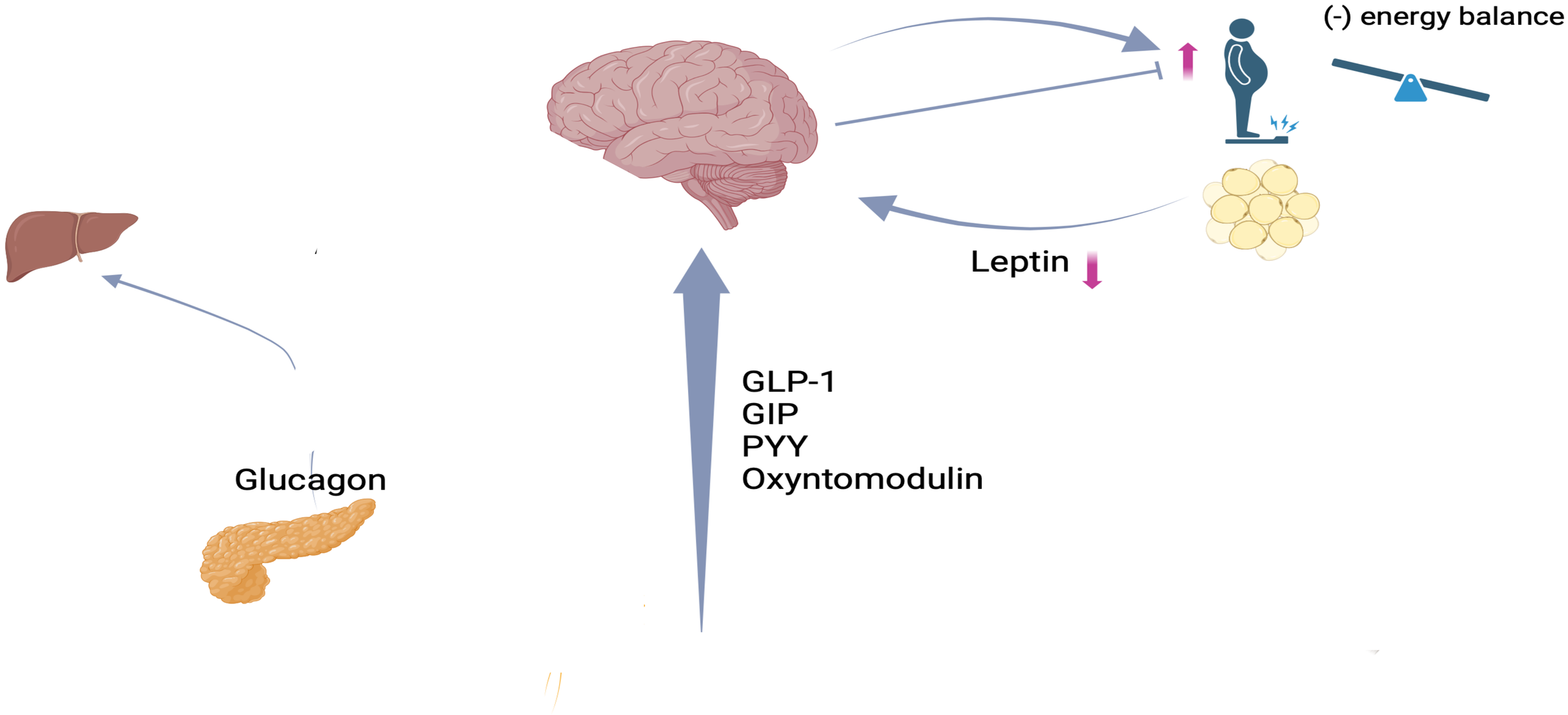
- **Weight Loss Effectiveness**

  Demonstrates potent, dose-dependent efficacy with up to 24-30% mean
  weight reduction observed at 48-104 weeks in clinical studies.

- **Safety & Tolerability**

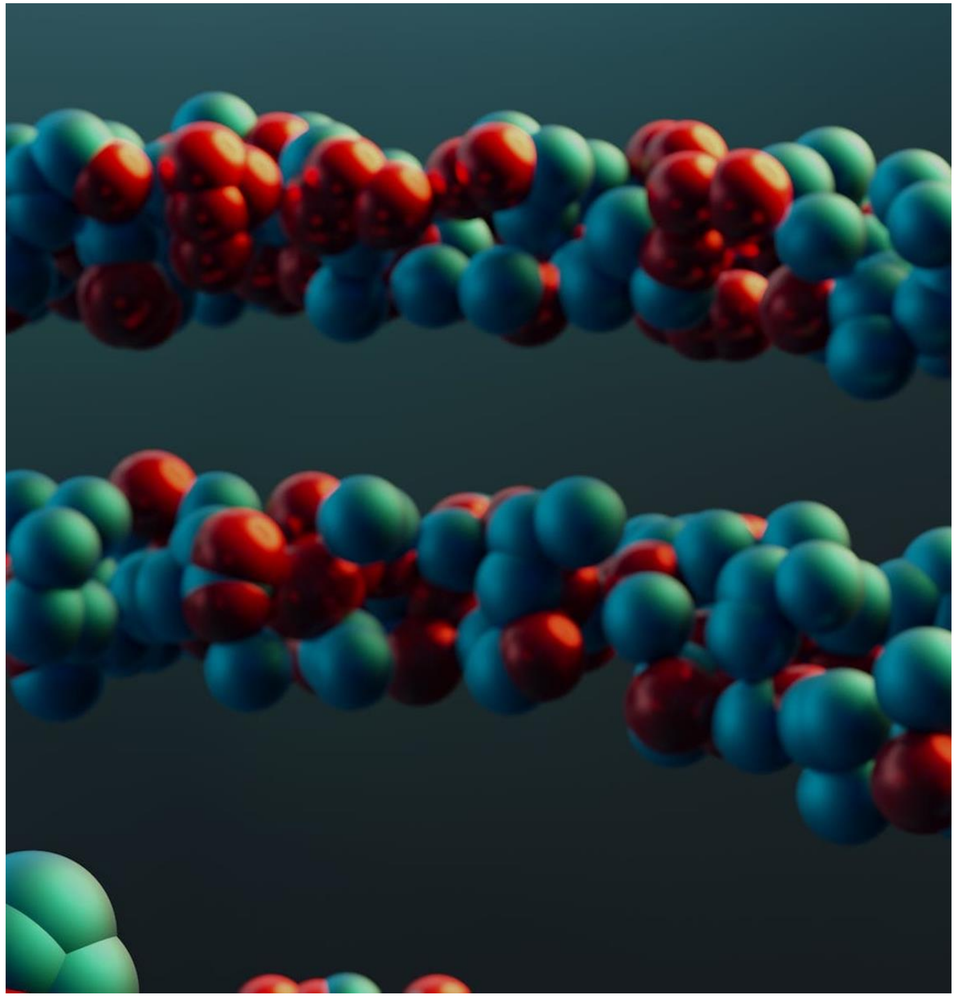
  Primary discontinuation driven by gastrointestinal events; 13% subjects with
  dysesthesias.

Jastreboff AM et al. N Engl J Med. 2023;389(6):514-526
Presentation ADA June 6, 2026



CagriSema: Mechanism and Clinical Profile

A synergistic approach combining GLP-1 and amylin receptor agonism



- **Mechanism of Action**

  Combines Semaglutide (GLP-1) and Cagrilintide (amylin analogue) to increase satiety and reduce energy consumption. Amylin likely targets brain
  areas complementary to GLP-1.

- **Weight Loss Effectiveness**

  Exhibits superior weight reduction compared to semaglutide monotherapy,
  showing a mean weight loss of up to 23%.

- **Clinical Observations**

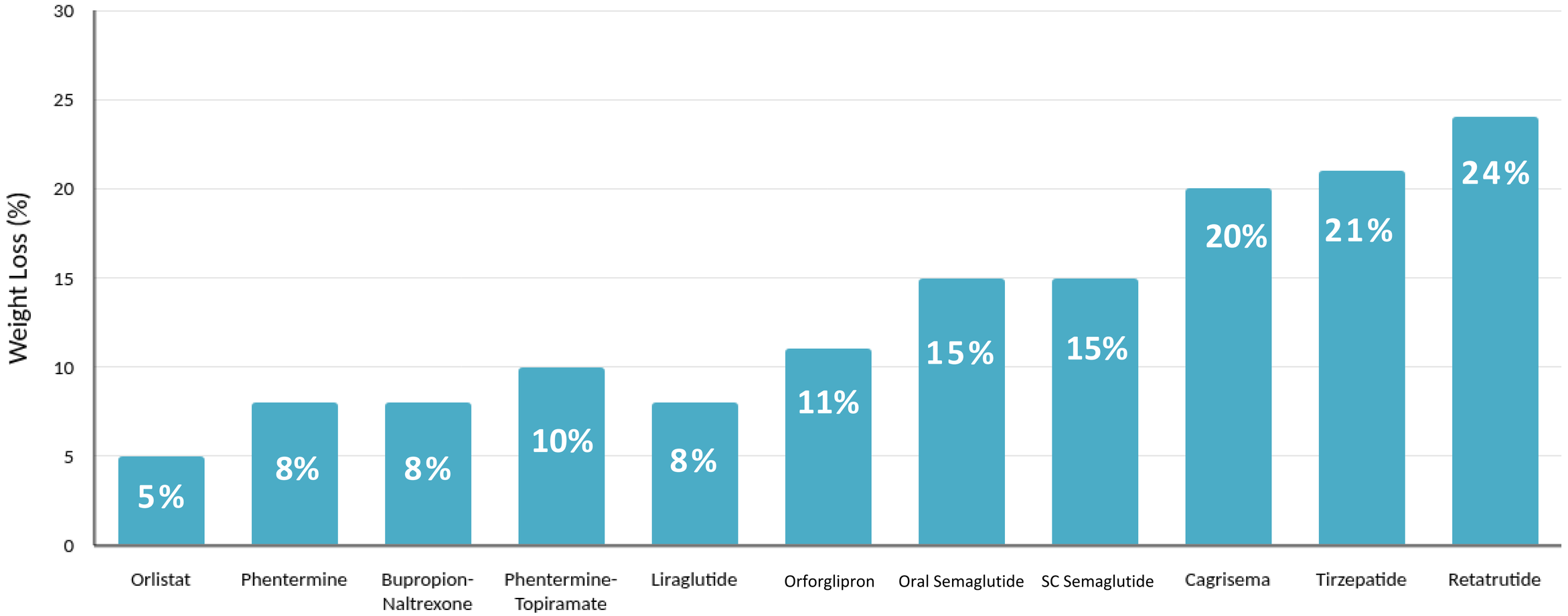
  Adverse effects are GI-related and mild to moderate in severity.

Garvey WT et al. N Engl J Med. 2025;393(7):635-647

UC San Diego
HEALTH SYSTEM

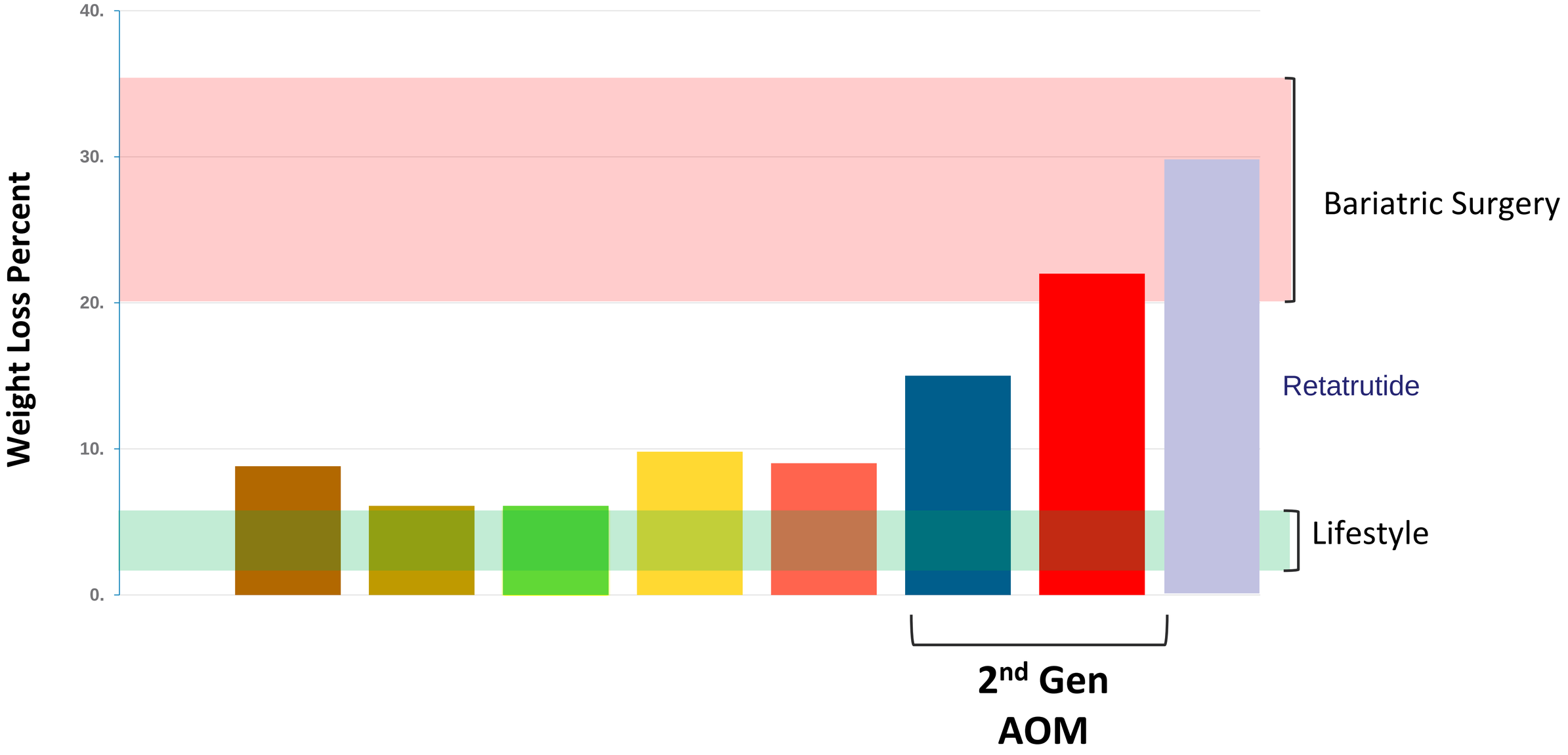
Comparative Weight Loss Effectiveness

Clinical trial results in subjects without diabetes

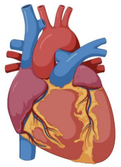


*Data from intention-to-treat analyses

Effectiveness of Anti-Obesity Medications vs. Lifestyle and Bariatric Surgery for Treating Obesity

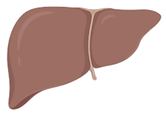


Beyond Weight Loss



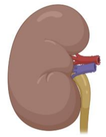
✓ **SELECT Trial**
✓ **STEP-HFpEF**
✓ **SUMMIT**

- ✓ 20% reduction MACE
- ✓ Reduced symptoms and QOL in HFpEF



✓ **Exenatide**
✓ **Liraglutide**
✓ **Semaglutide**
✓ **Tirzepatide**

- ✓ Reduction of steatosis
- ✓ Reduced MASH

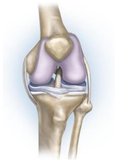


✓ **FLOW Study**

- ✓ Slow progression of CKD
- ✓ MACE
- ✓ All cause mortality

✓ **SURMOUNT OSA**

- ✓ Significant reduction of AHI



✓ **Osteoarthritis**

- ✓ Significant reduction of symptoms
- ✓ Improved function

✓ **Neuroprotection**

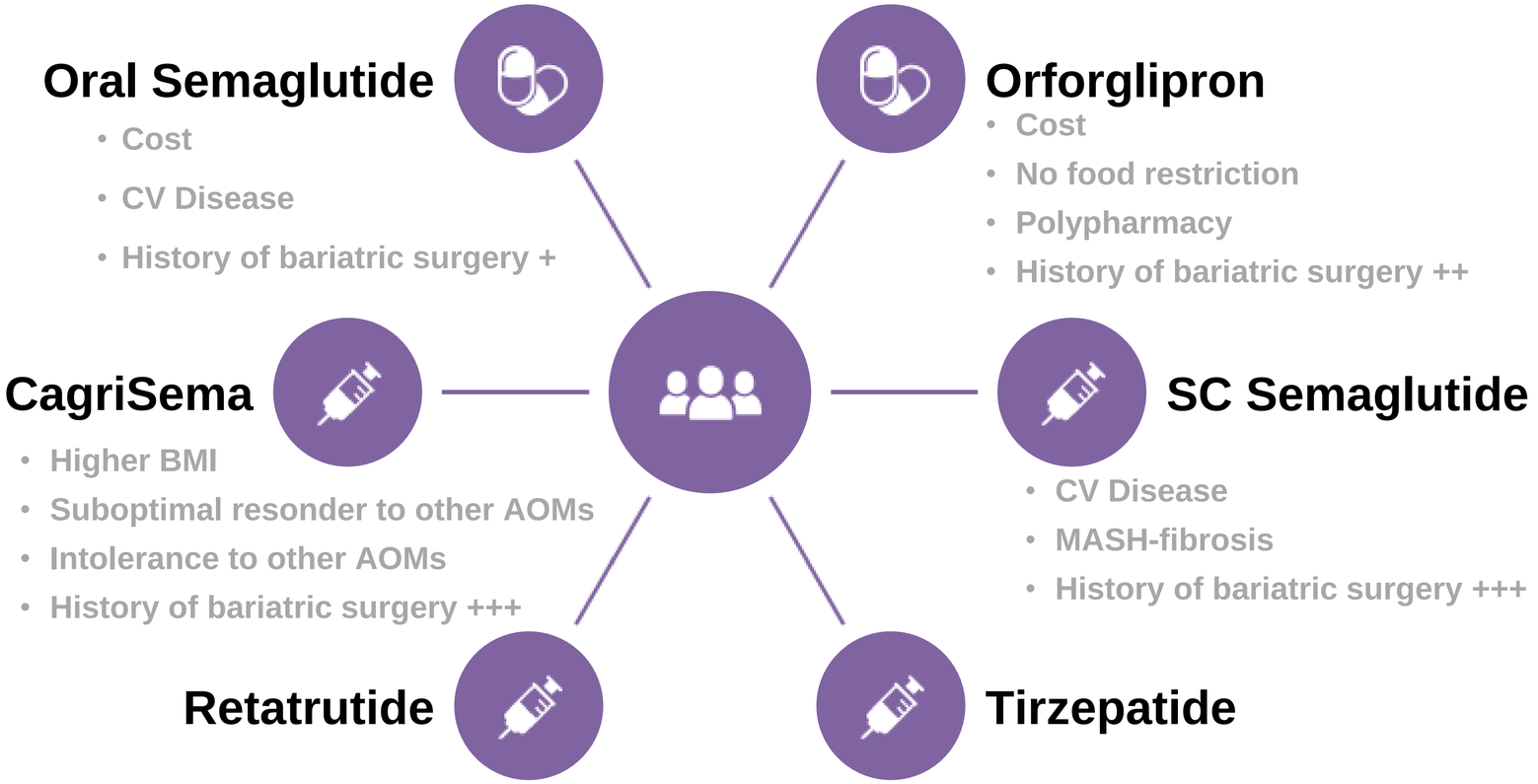
- ✓ Possible benefit for dementia
- ✓ Parkinson’s Disease

✓ **Addiction**

- ✓ Human studies used exenatide
- ✓ Ongoing studies

UC San Diego
Health System

Personalized Care



Oral Semaglutide

- Cost
- CV Disease
- History of bariatric surgery +

Orforglipron

- Cost
- No food restriction
- Polypharmacy
- History of bariatric surgery ++

CagriSema

- Higher BMI
- Suboptimal resonder to other AOMs
- Intolerance to other AOMs
- History of bariatric surgery +++

SC Semaglutide

- CV Disease
- MASH-fibrosis
- History of bariatric surgery +++

Retatrutide

- BMI >50
- OSA
- Severe liver steatosis
- Suboptimal responder to other AOMs
- History of bariatric surgery ++

Tirzepatide

- Moderate-severe OSA
- Higher BMI
- GI Pathology
- History of bariatric surgery +++

UC San Diego Health System

Medicare GLP-1 Bridge

What healthcare professionals need to know to prescribe successfully

Jul 1, 2026 – Dec 31, 2027
$50 / month patient copay

1 Who Qualifies

Patient must be 18+, using the drug to reduce/maintain weight loss (not another indication), and meet ONE tier below:

BMI ≥ 35

No comorbidity required

BMI ≥ 30

+ HFpEF, uncontrolled hypertension*, or CKD stage 3a+
* ≥140/90 on ≥2 meds

BMI ≥ 27

+ pre-diabetes, prior MI/stroke, or symptomatic PAD

Criteria are assessed at GLP-1 THERAPY INITIATION, not the PA date — prior starts still qualify.

Not eligible here: Type 2 diabetes, moderate–severe OSA, or MASH — these route to the patient's regular Part D plan instead.

2 Covered Drugs & Cost

Orforglipron (Foundayo®)

Semaglutide (Wegovy®)

injection & tablets

Tirzepatide (Zepbound®)

KwikPen® only — vials/single-dose pens excluded

$50

flat monthly copay for eligible patients; pen needles are not covered

Plan check: patient must be in a standalone Prescription Drug Plan (PDP) or Medicare Advantage Prescription Drug (MA-PD) plan. Most Special Needs Plan (SNP), Employer Group Waiver Plans (EGWP) and Limited Income Newly Eligible Transition (LI NET) enrollees also qualify.

3 How to Prescribe

1 Write the prescription

Send to pharmacy as usual — “Send to Bridge for weight management”.

2 Submit prior authorization

It will be denied and returned for PA (e-PA or fax) within 24–72 hrs. No response? Download the form yourself.

3 Attest to clinical criteria

Confirm BMI tier + weight-loss intent on the PA form. Decision returns within 72 hours by fax/portal.

4 Resubmit if denied

No formal appeals process — correct and resubmit the PA form if info was missing or incorrect.

Prescriber help line: 855-273-0102 (M–F, 8am–7pm ET)

Source: CMS Medicare GLP-1 Bridge — Information for Providers (cms.gov). Verify current details before prescribing; program details may be updated.

UC San Diego Health System

Thank you

UC San Diego
HEALTH SYSTEM