



LVL UP RX · CLIENT EDUCATION SERIES

Retatrutide

GLP-1 · GIP · Glucagon Triple Agonist

The Most Advanced Fat Loss Research Compound Available

A complete research guide to Retatrutide — what it is, how three simultaneous receptor pathways redefine fat loss, and what the clinical research actually shows.

FOR RESEARCH PURPOSES ONLY

Everything you need to know about Retatrutide and next-generation fat loss

01	What Is Retatrutide?	Origins, development & what makes it different
02	The Triple Receptor System	GLP-1, GIP & Glucagon — three pathways explained
03	The Science	Mechanism of action at the cellular & metabolic level
04	Key Benefits	Fat loss, metabolic health, cardiovascular & more
05	Retatrutide vs the Class	How it compares to Semaglutide & Tirzepatide
06	Who Is It For?	Ideal candidates, buyer profiles & use cases
07	Protocols & Delivery	Administration, titration & cycling guidance
08	Stacking	Synergistic combinations for comprehensive results
09	What to Expect	Timeline, realistic outcomes & side effect profile
10	Research Notes	Disclaimer, compliance & selected references

“ Every previous generation of weight-loss peptides targeted one or two metabolic receptors. Retatrutide targets three simultaneously — and clinical trials showed average fat loss of 24.2%, a number that wasn't considered achievable without surgery just five years ago.

Table of Contents

What's inside this guide

1

WHAT IS RETATRUTIDE?

Next-Generation Triple Agonist

What Is Retatrutide?

The most advanced metabolic research compound in the GLP-1 class

Retatrutide (LY3437943) is a next-generation triple receptor agonist developed by Eli Lilly and Company. It simultaneously activates three metabolic hormone receptors — GLP-1 (glucagon-like peptide-1), GIP (glucose-dependent insulintropic polypeptide), and Glucagon — making it the first and only compound in its class to target all three pathways at once.

Unlike its predecessors — Semaglutide (GLP-1 only) and Tirzepatide (GLP-1 + GIP) — Retatrutide adds glucagon receptor agonism as a third metabolic lever. This addition is not incremental. Glucagon receptor activation directly drives energy expenditure and fat mobilization through mechanisms entirely absent in prior compounds — fundamentally changing what fat loss pharmacology is capable of.

Retatrutide is currently in Phase 2/3 clinical trials and has not received FDA approval. It is available for research purposes as an investigational compound. Clinical data published in the New England Journal of Medicine (2023) showed average weight loss of 24.2% at 48 weeks — the highest ever recorded in an obesity pharmacology trial.

3x**RECEPTORS**

GLP-1 · GIP · Glucagon

24.2%**AVG FAT LOSS**

at 48 weeks

Eli**LILLY**

original developer

Ph.2/3**TRIALS**

investigational

The Evolution of the GLP-1 Class

Retatrutide did not emerge in isolation — it represents the third generation of a rapidly advancing class of metabolic compounds:

GENERATION	COMPOUND	RECEPTORS	AVG WEIGHT LOSS
1st Gen	Liraglutide / Saxenda	GLP-1 only	~8%
2nd Gen	Semaglutide / Wegovy	GLP-1 only	~14.9%
3rd Gen	Tirzepatide / Mounjaro	GLP-1 + GIP	~20%
Next Gen	Retatrutide	GLP-1 + GIP + Glucagon	~24.2%

Each generation roughly doubled the fat-loss ceiling of the previous. Retatrutide's addition of glucagon receptor activity is the mechanism behind this leap — and it represents an entirely new category of metabolic effect that the prior compounds simply cannot produce.

Retatrutide

Next-Generation Triple Agonist

2

THE TRIPLE RECEPTOR SYSTEM

GLP-1 · GIP · Glucagon Explained

The Triple Receptor System

Three pathways — each essential, each distinct

To understand why Retatrutide works so differently from prior compounds, you need to understand what each of its three receptor targets actually does.

GLP-1

Appetite
Controller

- Appetite suppression
- Slows gastric emptying
- Insulin regulation

GIP

Metabolic
Amplifier

- Amplifies insulin
- Fat metabolism
- Synergy with GLP-1

Glucagon

Fat
Mobilizer

- Energy expenditure
- Lipolysis activation
- Metabolic rate up

GLP-1 — The Appetite Controller

GLP-1 (Glucagon-Like Peptide-1) is secreted by intestinal L-cells in response to food. It slows gastric emptying (food leaves the stomach more slowly, prolonging fullness), signals the brain to reduce hunger, and stimulates glucose-dependent insulin secretion. GLP-1 receptor agonism is the foundation of all compounds in this class — from Liraglutide to Retatrutide. In Retatrutide, GLP-1 handles appetite suppression and the core blood sugar regulatory effects.

GIP — The Metabolic Amplifier

GIP (Glucose-Dependent Insulinotropic Polypeptide) is secreted by intestinal K-cells. It amplifies the insulin response to meals and plays a key role in fat metabolism and energy storage regulation. When combined with GLP-1, GIP creates a synergistic metabolic effect that is significantly greater than GLP-1 alone — this is why Tirzepatide, which adds GIP to GLP-1, substantially outperformed Semaglutide in trials. In Retatrutide, GIP provides this same metabolic amplification.

Glucagon — The Fat Mobilizer

Glucagon is the third and most consequential addition. Secreted by pancreatic alpha cells, glucagon is classically known as a counter-regulatory hormone to insulin — it raises blood sugar during fasting by stimulating liver glucose production. But at the glucagon receptor level, it also directly stimulates lipolysis (the breakdown of stored fat), increases energy expenditure (raises metabolic rate), and enhances fatty acid oxidation in the liver. This is the mechanism that prior compounds entirely lack — and it is why Retatrutide's fat-loss results exceed everything that came before it. Neither Semaglutide nor Tirzepatide activates glucagon receptors.

THE KEY INSIGHT: GLP-1 and GIP primarily reduce what goes in (appetite, caloric intake, fat storage). Glucagon directly increases what goes out (energy expenditure, fat mobilization, metabolic rate). Retatrutide is the first compound to attack fat loss from both sides of the energy equation simultaneously.

The Triple Receptor System

GLP-1 · GIP · Glucagon Explained

3

THE SCIENCE

Mechanism of Action at the Cellular Level

The Science Behind Retatrutide

How triple agonism works at the molecular level

Central Nervous System Effects

All three receptors targeted by Retatrutide are expressed in the hypothalamus — the brain's primary hunger and energy regulation center. GLP-1 receptor activation reduces the activity of hunger-promoting neurons. GIP receptor activation in the brain suppresses reward-driven eating. Glucagon receptor activation signals energy sufficiency. The combined CNS effect produces a level of appetite suppression significantly deeper than GLP-1 alone — many clinical trial subjects reported food becoming almost disinteresting.

Adipose Tissue & Lipolysis

Glucagon receptor activation in fat tissue directly stimulates hormone-sensitive lipase — the enzyme that breaks down stored triglycerides into free fatty acids for energy. This makes Retatrutide uniquely capable of directly mobilizing fat stores, not just reducing the rate at which new fat is deposited. In clinical trials, reductions in visceral (deep abdominal) fat were particularly pronounced — a metabolically significant finding given visceral fat's role in cardiovascular and metabolic disease risk.

Hepatic Metabolism

The liver is a primary site of glucagon action. Retatrutide's glucagon receptor component enhances hepatic fatty acid oxidation — increasing the rate at which the liver burns fat for energy rather than storing it. This also reduces liver fat content (hepatic steatosis), making Retatrutide of significant interest in metabolic-associated fatty liver disease research.

Insulin Sensitivity & Glucose Metabolism

GLP-1 and GIP together produce a robust, glucose-dependent insulin response — meaning insulin secretion is amplified when blood glucose is elevated but not when it's normal, reducing hypoglycemia risk compared to traditional diabetes medications. Combined with the metabolic improvements from glucagon receptor activity and weight loss itself, Retatrutide produces significant improvements in insulin sensitivity and HbA1c (blood sugar control).

Cardiovascular Effects

GLP-1 receptor agonists as a class have demonstrated cardiovascular protective effects in multiple large trials. By combining this with the metabolic improvements driven by GIP and glucagon receptor activation — including reduced visceral fat, improved lipid profiles, and better blood sugar regulation — Retatrutide is expected to carry significant cardiovascular benefit. Dedicated cardiovascular outcomes trials are ongoing.

Retatrutide

The Science — Mechanism of Action

3x

RETATRUTIDE Triple Agonist · Next-Generation Fat Loss

GLP-1 · GIP · Glucagon — Three Pathways. One Compound.

Key Benefits of Retatrutide

Clinical and research-supported areas of effect

Fat Loss & Body Composition

The headline finding — and the most significant in obesity pharmacology history:

- ◆ Average 24.2% body weight reduction at 48 weeks in Phase 2 clinical trials (New England Journal of Medicine, 2023)
- ◆ Significant reductions in visceral (abdominal) fat — the most metabolically dangerous fat depot
- ◆ Preserved lean muscle mass during fat loss — unlike many caloric restriction approaches
- ◆ Continued weight loss trajectory observed through the full 48-week trial period
- ◆ Some trial subjects achieved 30%+ body weight reduction

Metabolic Health

- ◆ Significant improvements in HbA1c (blood sugar control) in subjects with type 2 diabetes
- ◆ Reduced fasting blood glucose and post-meal glucose spikes
- ◆ Improved insulin sensitivity independent of weight loss effects alone
- ◆ Reduced triglycerides and improved lipid panel in clinical subjects
- ◆ Reduction in liver fat content — relevant to NAFLD/MASLD research

Appetite & Behavioral Effects

- ◆ Profound appetite suppression — multiple trial subjects described food cravings as dramatically reduced or absent
- ◆ Reduced reward-driven eating and food preoccupation
- ◆ Improved satiety — smaller portions produce complete fullness
- ◆ Reduced emotional eating and hunger-related anxiety

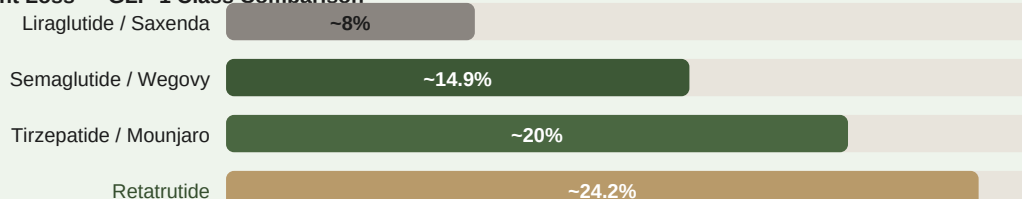
Cardiovascular & Systemic

- ◆ Reduced blood pressure documented in trial subjects
- ◆ Improved cardiovascular risk markers including lipids and inflammatory markers
- ◆ Reduced waist circumference — a direct cardiovascular risk marker
- ◆ Potential hepatoprotective effects through reduced liver fat

Clinical Weight Loss Comparison

Average Weight Loss — GLP-1 Class Comparison

Clinical trial data



Retatrutide

Key Benefits — What the Research Shows

5

RETATRUTIDE VS THE CLASS

How It Compares

Retatrutide vs the Class

Why triple agonism changes what's possible

	SEMAGLUTIDE	TIRZEPATIDE	RETATRUTIDE
Receptors	GLP-1	GLP-1 + GIP	GLP-1 + GIP + Glucagon
Avg Weight Loss	~14.9%	~20%	~24.2%
Appetite Suppress.	Strong	Very Strong	Exceptional
Fat Mobilization	Indirect only	Indirect only	Direct (glucagon)
Energy Expenditure	Minimal	Moderate	Significant increase
Visceral Fat	Moderate reduction	Strong reduction	Very strong reduction
Liver Fat	Some improvement	Strong improvement	Strong improvement
FDA Approval	Yes (Wegovy)	Yes (Zepbound)	Investigational
Muscle Preservation	Moderate	Good	Good

The Glucagon Difference

The single most important differentiator between Retatrutide and every prior compound is glucagon receptor agonism. Here is what this adds that the other compounds simply cannot do:

Direct Fat Mobilization

Glucagon directly activates hormone-sensitive lipase in adipose tissue — the enzyme that breaks stored fat into free fatty acids. Semaglutide and Tirzepatide reduce fat accumulation by reducing intake. Retatrutide additionally breaks down existing stores. This is a fundamentally different mechanism.

Increased Metabolic Rate

Glucagon receptor activation raises basal energy expenditure — the number of calories burned at rest. Weight loss compounds that only reduce intake often trigger metabolic adaptation (the body slowing metabolism in response to caloric restriction). Retatrutide's glucagon component actively counteracts this adaptation.

Enhanced Hepatic Fat Oxidation

Glucagon directly stimulates the liver to oxidize (burn) fatty acids rather than store them — addressing the root cause of fatty liver disease while simultaneously contributing to overall fat reduction.

Retatrutide vs the Class

How It Compares to Prior Compounds

6

WHO IS IT FOR?

Ideal Candidates & Use Cases

Who Is Retatrutide For?

Ideal research candidates and use cases

Significant Weight Loss Goal (20%+ Body Weight)

Individuals for whom prior interventions — diet, exercise, even older GLP-1 compounds — have not produced sufficient results. Retatrutide's clinical data puts 20–30%+ body weight reduction within realistic reach for many research subjects, a range previously achievable only through bariatric surgery.

Those Who Have Plateaued on Semaglutide or Tirzepatide

Individuals who have already used Wegovy or Mounjaro but hit a fat loss plateau or found the results insufficient. Retatrutide's triple-receptor mechanism addresses pathways that prior compounds don't touch — often producing results where others stalled.

Metabolic Syndrome & Insulin Resistance

Those dealing with the cluster of conditions — elevated blood sugar, high triglycerides, excess abdominal fat, high blood pressure — that define metabolic syndrome. Retatrutide addresses every component of this cluster through its three-receptor mechanism.

Body Recomposition Athletes (Cutting Phase)

Competitive athletes and fitness consumers in aggressive cutting phases who want maximal fat loss while preserving lean muscle. Retatrutide's clinical data shows lean mass preservation alongside fat loss — a combination that most caloric restriction approaches fail to achieve.

Type 2 Diabetes Research

Retatrutide's powerful blood sugar regulation effects — through both GLP-1/GIP insulin sensitization and the metabolic improvements from weight loss — make it of significant interest in type 2 diabetes research contexts.

Cardiovascular Risk Reduction Research

Individuals with elevated cardiovascular risk factors who want a research protocol that addresses multiple risk drivers simultaneously: visceral fat, blood pressure, lipids, blood sugar, and inflammatory markers.

Who Is It For?

Ideal Candidates & Use Cases

LVL UP[®]

7

PROTOCOLS & DELIVERY

Administration & Titration Guidance

Protocols & Delivery

How Retatrutide is administered in research contexts

Retatrutide is administered via subcutaneous (SubQ) injection — the same delivery method used in clinical trials. Like all GLP-1 class compounds, slow titration is essential for tolerability. Starting at a low dose and increasing gradually allows the GI system to adapt and significantly reduces the risk and severity of nausea.

The Importance of Titration

Retatrutide's most commonly reported side effects (nausea, vomiting, reduced appetite) are dose-dependent and largely preventable with proper titration. In clinical trials, a slow ramp-up schedule was used to maximize tolerability — this approach is essential and should not be rushed regardless of the desire for faster results.

- Always begin at the lowest available dose — start low, go slow
- Do not increase dose until the current dose is well-tolerated for at least 2–4 weeks
- Nausea that resolves within a few days at a given dose is normal — nausea that persists or is severe warrants staying at the current dose longer before increasing
- Eating smaller, lower-fat meals during the first weeks helps reduce GI side effects
- Staying well-hydrated is important — reduced food intake can reduce fluid consumption

PHASE	DURATION	KEY NOTES
Loading / Start	Weeks 1–4	Begin lowest available dose; assess GI tolerance; eat small meals
Titration	Weeks 4–16	Increase dose every 4 weeks if well-tolerated; don't rush escalation
Maintenance	Weeks 16+	Target dose reached; consistent weekly SubQ injection; track results
Assessment	Week 12–16	Evaluate body composition changes; adjust protocol if needed

Administration Notes

- SubQ injection using insulin syringe — abdomen, thigh, or upper arm
- Once-weekly injection schedule — same day each week preferred
- Reconstitute from lyophilized powder with bacteriostatic water; swirl gently, do not shake
- Refrigerate after reconstitution; use within 28–30 days; never freeze
- Rotating injection sites reduces localized irritation
- Consistent timing preferred — though exact time of day is flexible

Always consult a qualified healthcare provider before beginning a Retatrutide protocol. Those with personal or family history of medullary thyroid carcinoma, pancreatitis, or Multiple Endocrine Neoplasia syndrome type 2 should discuss contraindications thoroughly with their provider before use.

Stacking Retatrutide

Intelligent combinations for amplified outcomes

Retatrutide is a powerful standalone compound — but it pairs strategically with several other research compounds that address the aspects of body transformation it doesn't directly target.

— The Metabolic Energy Stack

Retatrutide + NAD+

Weight loss creates a caloric deficit — and caloric deficits reduce cellular energy production. NAD+ directly supports mitochondrial ATP production, counteracting the fatigue and metabolic slowdown that often accompanies aggressive fat loss protocols. This combination keeps energy levels high while Retatrutide drives fat reduction — one of the most complementary pairings in the catalog.

BEST FOR: Weight loss · Caloric deficit support · Energy maintenance · Metabolic health

— The Muscle Preservation Stack

Retatrutide + MOT-C

One concern with aggressive fat loss is lean muscle preservation. MOT-C (MOTS-c) activates AMPK pathways, improves insulin sensitivity, and has been studied as an 'exercise mimetic' — preserving and even building muscle during periods of caloric restriction. Combined with Retatrutide's fat-mobilization effect, this stack targets the ideal body recomposition outcome: maximum fat out, muscle preserved.

BEST FOR: Body recomposition · Muscle preservation · Metabolic optimization · Athletes

— The Gut Adaptation Stack

Retatrutide + BPC-157

The early weeks of Retatrutide can be challenging on the GI system. BPC-157, with its well-documented gut lining repair and anti-inflammatory effects, may support the GI adaptation period — particularly for individuals who experience more pronounced nausea or digestive discomfort during titration.

BEST FOR: GI tolerance support · Gut lining health · Early protocol adaptation

— The Complete Transformation Stack

Retatrutide + NAD+ + MOT-C

The most comprehensive body transformation protocol in the LVL UP RX catalog. Retatrutide drives unprecedented fat loss through triple receptor activation. NAD+ maintains cellular energy and mitochondrial function during the deficit. MOT-C preserves lean muscle and optimizes metabolic rate. Together, these three compounds address every major variable in body recomposition simultaneously.

BEST FOR: Maximum fat loss · Full body recomposition · Premium transformation protocol

Stacking Retatrutide

Synergistic Combinations

9

WHAT TO EXPECT

Timeline, Results & Realistic Outcomes

What to Expect

A realistic, research-grounded timeline for Retatrutide

Retatrutide's results build progressively over months. The appetite-suppressing effects are typically felt within the first week. Meaningful body composition changes emerge at 4–8 weeks. The most dramatic results in clinical trials accumulated between weeks 12–48. Patience and adherence to titration are essential.

TIMEFRAME	EXPECTED EFFECTS	CLINICAL TRIAL DATA
Days 1–7	Appetite suppression begins; food interest notably reduced	Immediate receptor engagement; nausea most common in first week
Week 2–4	Significant appetite reduction; early weight loss begins	~2–4% body weight loss typically observed
Week 4–8	Consistent fat loss; energy levels stabilizing	~5–10% body weight loss; waist circumference reducing
Week 8–16	Visible body composition changes; metabolic markers improving	~12–18% body weight loss; HbA1c and lipids improving
Week 16–48	Continued fat loss progression; peak results accumulating	~20–24%+ body weight loss; visceral fat dramatically reduced
Beyond 48wk	Maintenance or continued loss depending on protocol	Long-term data pending; weight regain risk if discontinued

IMPORTANT NOTE ON DISCONTINUATION: As with all GLP-1 class compounds, weight regain is common after stopping Retatrutide if lifestyle changes have not been established. Research subjects who discontinued after trials showed partial weight regain over subsequent months. This underscores the importance of using the protocol window to build sustainable behavioral change.

Side Effect Profile

Retatrutide shares the side effect profile of the GLP-1 class, which is well-characterized from years of clinical use with Semaglutide and Tirzepatide:

- Nausea: most common, especially during titration; typically resolves within days at each dose level; manageable with slow titration and smaller meals
- Vomiting: less common; if persistent, stay at current dose longer before increasing
- Reduced appetite: expected and desired effect; ensure adequate nutrition and hydration
- Fatigue: can occur early, particularly during rapid fat mobilization; NAD+ stack helps
- Injection site reactions: mild redness or swelling; resolves quickly
- Constipation or diarrhea: GI motility changes common; typically transient
- Headache: occasionally reported during titration; usually resolves

Rare but important: GLP-1 class compounds carry a theoretical risk of thyroid C-cell tumors (observed in rodents — not confirmed in humans), pancreatitis, and acute kidney injury from dehydration. Anyone with a history of pancreatitis, MEN2 syndrome, or medullary thyroid carcinoma should not use this compound without explicit medical supervision.

Research Notes & Disclaimer

Please read carefully.

All products offered by LVL UP RX are sold strictly as research compounds for investigational use only. They are not intended for human consumption and are not approved by the FDA or any equivalent regulatory authority for therapeutic, preventive, or diagnostic use in humans. Retatrutide is an investigational compound currently in Phase 2/3 clinical trials — it has not received FDA approval as of the date of this guide.

The Research Landscape

Retatrutide has the most clinically robust early-phase data of any compound in the next-generation GLP-1 class. The Phase 2 trial published in the New England Journal of Medicine (2023) was a randomized, double-blind, placebo-controlled study — the gold standard of clinical evidence. Phase 3 trials are ongoing. This guide presents findings accurately and without exaggeration.

What We Will Never Claim

- That Retatrutide treats, cures, or prevents any disease or medical condition
- That Retatrutide is FDA approved or safe for human use as medicine
- That results mirror clinical trial averages — individual responses vary significantly
- That Retatrutide is appropriate for everyone — contraindications exist
- That this compound replaces medical treatment or professional healthcare guidance

Selected Research References

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Retatrutide represents the furthest advance in metabolic pharmacology research to date. At LVL UP RX, we provide access to the most current research compounds alongside the education required to understand them. Knowledge is always the first step.

LVL UP RX · PEPTIDES · SCIENCE-BACKED. RESULTS-DRIVEN.

For research use only. Not for human consumption. Consult a qualified healthcare professional.



Research Notes

Important Information & Compliance

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