# 3 generations of weight-loss drugs

Peptide Lab · Episode 09 · Free guide

It started with lizard spit. One switch, then two, then three. What each one adds, and what the evidence says.



For learning only, not medical advice. Talk to a doctor first.

# Where it started

**2005:** scientists copied a hormone found in Gila monster saliva. It became exenatide, the first drug of its kind, approved for diabetes.

It copies a gut signal called GLP-1.

Every drug in this guide belongs to the same family.

# How the switches work

Think of each signal as a switch on your cells.

- **GLP-1:** slows how fast food leaves your stomach, and tells your brain you're full.
- **GIP:** a gut hormone that helps control blood sugar.
- **Glucagon:** tells the liver to use stored energy.

Each new generation switches on one more.

# Generation 1 - Semaglutide

**One switch: GLP-1.**

- Approved for type 2 diabetes (2017) and for weight (2021).
- In its big trial, people lost about 15% of their weight on average, versus about 2% on placebo.

● **Proven in humans**

# Generation 2 · Tirzepatide

**Two switches: GLP-1 + GIP.**

- Approved for type 2 diabetes (2022) and for weight (2023).
- In the first head-to-head trial (2025), people lost about 20% on it, versus about 14% on semaglutide.

● **Proven in humans**

# Generation 3 · Retatrutide

**Three switches: GLP-1 + GIP + glucagon.**

- Lilly reports even bigger weight loss in its big trials.
- Company results so far. Full papers still coming.
- Not approved anywhere yet. Lilly plans to apply to the US FDA.

◐ **Reported**

# Side by side

| Generation | Drug | Switches | Status | Stamp |
|---|---|---|---|---|
| 0 | Exenatide | 1 | Approved for diabetes (2005) | ● Proven |
| 1 | Semaglutide | 1 | Approved for diabetes and weight | ● Proven |
| 2 | Tirzepatide | 2 | Approved for diabetes and weight | ● Proven |
| 3 | Retatrutide | 3 | In trials, not approved | ◐ Reported |

# A faster car isn't a safer car

- More switches doesn't prove a drug is safer.
- Stomach side effects like nausea, vomiting and diarrhea are common with all three.
- In one big Retatrutide trial, more people stopped because of side effects than on placebo.

**Ask about side effects as carefully as you ask about results.**

# My own test

I'm testing generation three myself, with a doctor.

- My waist
- An InBody scan
- Blood tests

No doses here, ever. I'll share what I measure, not what you should take.

# Before you talk to your doctor

Which generation is it, and is it approved where I live?

_____

What does the best trial say, and who ran it?

_____

What side effects should I watch for?

_____

How will we measure the result?

_____

# Save this. Ask your doctor.

1. What problem are we treating?
2. What research backs this tool?
3. How will we measure the result?

I'm Ly. I'm not a doctor. I'm experimenting and sharing my results. Don't copy me.

No doses, no sources, nothing for sale. For learning only, not medical advice. Talk to a doctor first.

**Next episode: the trade-offs of GLP-1 drugs. Follow Ly for Peptide Lab.**