Sermorelin — Basic Review Questions

1. What is sermorelin, what type of peptide is it, and what is its regulatory status?

Answer: Sermorelin is a synthetic GHRH analog — specifically GHRH(1-29), the first 29 amino acids of the body's natural growth-hormone-releasing hormone, which is the biologically active part. It was the first peptide made to mimic GHRH, and it is given by subcutaneous injection. It is notable in this group for once being FDA-approved (as Geref, for diagnostic use and pediatric growth hormone deficiency), but it was later withdrawn from the market and is now used as a compounded, off-label preparation in adults.

2. How does sermorelin work, and how does it differ from taking growth hormone directly?

Answer: It binds the GHRH receptor on the pituitary and stimulates the body's own growth hormone (GH) release in natural pulses, which then raises IGF-1 — and because the body's normal feedback (somatostatin) stays intact, the effect is self-limiting. Importantly, it does not just release GH; by activating GH gene transcription it actually builds up the pituitary's GH-producing capacity ("pituitary reserve") over time. This is the opposite of injected synthetic GH, which bypasses the body's control, can suppress the gland, and antagonizes insulin. Sermorelin restores the body's own function rather than replacing it.

3. How does sermorelin relate to Mod GRF 1-29 and CJC-1295?

Answer: Sermorelin is the original, foundational GHRH analog, and the others in this group are modified versions of it. It has the shortest half-life (about 10–15 minutes). Mod GRF 1-29 is sermorelin's stabilized successor — the same active sequence with four substitutions that extend the half-life to about 30 minutes — and CJC-1295 is that modified core plus a "DAC" that stretches it to several days. So all three share the same mechanism and active sequence; they differ mainly in how long they last.

4. What notable effects does sermorelin have beyond raising GH?

Answer: Two stand out. First, sermorelin directly activates sleep-regulating neurons in the brain through the GHRH receptor itself — independent of GH release — so it can improve deep (NREM) sleep through a mechanism that does not depend on downstream GH. This makes GHRH analogs like sermorelin preferable to the GHRP-type secretagogues for sleep. Second, clinical work in older adults showed meaningful immune-system activation (increases in various immune cell populations and signaling). Both are alongside its core GH/IGF-1 effects on body composition and recovery.

5. Why is sermorelin often combined with a GHRP such as ipamorelin?

Answer: Because the two activate different receptors on the same pituitary cell, producing a greater-than-additive ("synergistic") GH pulse. Sermorelin works through the GHRH receptor (building and loading GH), while a GHRP such as ipamorelin works through the ghrelin receptor (directly triggering release and lifting the somatostatin brake). Together, more GH is built, more is released, and less is held back. Ipamorelin is

the preferred partner because it is the cleanest GHRP, without the cortisol or prolactin elevation seen with others.

6. What is the state of the evidence, and what should be checked before starting?

Answer: Sermorelin actually has the most independent clinical-trial support of the GHRH analogs: several small studies in aging adults showed restored GH and IGF-1 toward youthful levels, along with improvements in lean mass, muscle strength, and immune markers. The limitation is that these trials are small and short, with no large or long-term RCTs and women underrepresented. A practical prerequisite: thyroid status should be checked first, because hypothyroidism blunts the GH response — an apparent non-responder may just need thyroid correction. As with all GH-axis agents, active cancer is a contraindication, and use beyond the original approved indications is off-label.