monoconal antibodies being trialed with GLP1s to repserve muscle

The leading monoclonal-antibody strategies paired with GLP-1–based weight-loss drugs target the **myostatin/activin–ActRII axis.** The goal is not merely to preserve DXA lean mass—which includes non-muscle tissue—but to shift drug-induced weight loss toward fat while retaining skeletal muscle and, ideally, function.

Most important programs

Antibody	Target / mechanism	GLP-1 partner studied	Trial status and key finding
Bimagrumab	Blocks activin type-II receptors (ActRIIA/IIB), reducing signaling from myostatin and activins	Semaglutide	Phase 2 BELIEVE trial. At 72 weeks, high-dose bimagrumab + semaglutide produced about 22.1% mean weight loss; 92.8% of lost mass was fat, with lean mass largely preserved. [1] [2]
Apitegromab	Selectively neutralizes latent myostatin, limiting conversion to active myostatin	Tirzepatide	Phase 2 EMBRAZE (NCT06445075): 102 adults, 24 weeks. Apitegromab reduced lean-mass loss by 1.9 kg versus tirzepatide alone, corresponding to 54.9% relative lean-mass retention, while total weight loss was similar. [3] [4]
Trevogrumab (REGN1033)	Anti-myostatin / anti-GDF-8 antibody	Semaglutide	Phase 2 COURAGE (NCT06299098). Regeneron reported that adding trevogrumab prevented roughly half of the semaglutide-associated lean-mass loss at 26 weeks. [5] [6]
Garetosmab	Anti-activin A antibody	Semaglutide, with or without trevogrumab	Also studied in COURAGE as a dual-pathway approach. The logic is that activin-A neutralization may complement direct myostatin inhibition; however, the clearest reported effect so far is from trevogrumab-containing arms. [5]

Mechanistic distinction

- **Apitegromab and trevogrumab** are more myostatin-focused. Apitegromab is notable for binding latent myostatin, aiming for target selectivity rather than broadly blocking ActRII ligands. [3]
- **Bimagrumab** is broader and acts at the shared receptor level. Blocking ActRIIA/IIB can inhibit signaling from myostatin plus other activin-family ligands, which may explain its unusually strong fat-loss/recomposition signal—but can also imply a wider biological footprint. [2] [7]

- **Garetosmab** neutralizes activin A, potentially addressing an additional negative regulator of muscle mass when used alongside anti-myostatin therapy. [5]

What the data do—and do not—show

The strongest published proof-of-concept so far is:

1. **Bimagrumab + semaglutide:** major total weight loss with a highly favorable fat-to-lean loss ratio over 72 weeks. [1]
2. **Apitegromab + tirzepatide:** a controlled 24-week result showing materially less lean-mass loss, without blunting total weight loss. In the reported data, the lean fraction of weight lost shifted from approximately 30% with tirzepatide alone to 15% with the combination. [8]
3. **Trevogrumab + semaglutide:** promising phase-2 preservation of lean mass, but the detailed peer-reviewed dataset is less mature than the published BELIEVE and EMBRAZE results. [5]

The key caveat is that **lean mass is not equivalent to contractile skeletal muscle**. DXA lean mass includes body water, organs, connective tissue, and glycogen-associated water. For a muscle-preservation claim to be clinically convincing, programs still need to demonstrate durable effects on muscle volume/quality and function—e.g., strength, stair-climb, chair-rise, gait, power, falls/frailty endpoints—especially in older adults, sarcopenia-risk populations, and during prolonged maintenance.

Practical status

None of these antibody-plus-GLP-1 combinations is currently an established standard obesity treatment. They remain investigational, and their risk–benefit profile needs longer-term evaluation. Reported adverse effects with bimagrumab included muscle spasms, diarrhea, and acne; GLP-1 adverse effects remained typical gastrointestinal effects. Apitegromab's phase-2 safety profile was broadly similar to placebo alongside tirzepatide, but that was a small, short proof-of-concept trial rather than definitive long-term safety evidence. [2] [3]

The short answer: **bimagrumab, apitegromab, and trevogrumab are the primary mAbs to watch**, with garetosmab as a potential activin-A add-on. Of them, bimagrumab has the most dramatic semaglutide body-composition data, while apitegromab provides the cleanest recent myostatin-selective tirzepatide proof-of-concept.

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