

Next Generation Weight Loss Drugs Aim to Save Muscle

Bhanvi Satija And Ludwig Burger

February 19, 2025

399



(Reuters) - About a dozen drugmakers are developing new weight-loss treatments aimed at preserving muscle, and industry analysts, clinical trial experts and doctors say they may also need to demonstrate additional health benefits beyond the numbers on a scale to get approved.

The drugs are being tested to complement or replace the wildly popular Wegovy from Novo Nordisk and Eli Lilly's Zepbound, which in trials helped patients lose 15% to 20% of their weight, but also caused a decline in muscle that some doctors find concerning. In trials of Wegovy, up to 40% of weight loss was from a decrease in lean or fat-free mass, rather than excess fat.

These experimental medicines are still a few years from possible approval.

SCROLL FOR MORE CONTENT

SCROLL FOR MORE CONTENT

Advertisement

The dozen new drugs, including those furthest along in development from Eli Lilly, Regeneron, Scholar Rock and Veru, target proteins tied to muscle preservation or growth. Wegovy and Zepbound target the GLP-1 protein to help control appetite.

Veru was first with results in January from a 168-person trial, showing its enobosarm helped older patients lose 71% less muscle when taken with Wegovy. Data on Lilly's muscle mass-preserving drug, bimagrumab, is due this year.

Westport, Connecticut-based New England Consulting Group estimates the drugs could collectively bring in \$1 billion to \$5 billion a year by the end of the decade. Analysts have projected obesity drugs sales reaching \$150 billion a year by the early 2030s.

SCROLL FOR MORE CONTENT

Advertisement

Some doctors say drugs that improve muscle mass could benefit older or infirm people at greater risk of falls and fractures. A higher portion of muscle can also help patients keep weight off for longer, experts say.

"If the narrative shifts from amount of weight lost over to how long someone can actually keep that weight loss off, that might be a powerful story," said Riley McCarthy, senior project manager at NECG.

How the Food and Drug Administration will approach measuring the benefits of these drugs for the purpose of approving them is uncertain.

FDA draft guidelines published in January say loss of lean mass is not harmful, but still suggest measuring trial participants' muscle-to-fat ratio at least twice. It advised companies testing muscle preservation to consult with the agency early about their chosen methods.

SCROLL FOR MORE CONTENT

SCROLL FOR MORE CONTENT

Analysts and clinical trial experts expressed doubts on whether FDA would approve a drug solely on muscle-mass effect.

"There's a real uphill battle to get something like that approved because the FDA does not approve drugs on the basis of muscle building or muscle preservation in this (obesity) setting," said BMO Capital Markets analyst Evan Seigerman.

Future treatments will need to show benefits such as fewer side effects and improved heart health, he added.

SCROLL FOR MORE CONTENT

Veru's drug helped patients retain their strength to climb a flight of stairs, a benefit the FDA has acknowledged for other types of medicines, and which analysts suggested may get drugs like these over the finish line.

"Longer term, we believe that the FDA would require functional outcome benefits," Leerink analyst David Risinger said.

TARGETING MUSCLE GROWTH

SCROLL FOR MORE CONTENT

Veru, whose drug targets androgen receptor cells to promote muscle growth, will use stair climb ability as a late-stage trial goal.

Lilly, which acquired bimagrumab with its \$1.9 billion purchase of biotech Versanis, is testing the drug alone, and in combination with Zepbound, and will complete a study with Novo's Wegovy begun prior to the 2023 acquisition.

"I think to really show a benefit for combining the two drugs we're probably going to need to see the incremental weight loss, or we're going to need to see real functional benefits to lean mass preservation," Lilly's Chief Scientific Officer Dan Skovronsky said earlier this month.

SCROLL FOR MORE CONTENT

About half of these new drugs target the myostatin protein associated with muscle growth, while others target activin, a protein with multiple biological functions. The drugs were first developed to treat neuromuscular disorders, such as spinal muscular atrophy and Duchenne muscular dystrophy, but none have been approved so far.

The myostatin drugs are believed to help muscles grow and reduce fat because they consume stored energy even when inactive.

Professor Se-Jin Lee, who discovered the myostatin pathway and has advised BioHaven, said these drugs might work best if given with a GLP-1. He said he hoped the combination would allow a reduction in GLP-1 dose, leading to fewer gastrointestinal side effects.

SCROLL FOR MORE CONTENT

BioHaven's drug helped increase lean mass and bone density compared to a placebo in a recent trial, but failed to improve motor function in spinal muscular atrophy patients. The company is planning a mid-stage trial of the drug for obesity.

Analysts and investors are closely watching Lilly's bimagrumab and Regeneron's trevogrumab now in mid-stage studies. Regeneron's drug is also being tested alone and in combination with Wegovy.

Scholar Rock is aiming for a change in lean body mass in the trial of its drug, apitegromab.

SCROLL FOR MORE CONTENT

The treatments "must be able to show not just that there is a structural change in the size of muscles or lean mass, but that there's a performance improvement that comes with that," said Graham McMahon, endocrinologist at the Chicago-based Feinberg School of Medicine. "That's what clinicians like me will be looking for."

(Reporting by Bhanvi Satija in Bengaluru and Ludwig Burger in Frankfurt; Editing by Manas Mishra, Caroline Humer and Bill Berkrot)

