

'If you can preserve muscle strength, you will age healthier'

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Ridgeline CEO says that new drug candidate improves bone health as well as muscle strength.

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Sarcopenia is the degenerative loss of skeletal muscle mass and tissue quality that leads to decreasing muscle strength, function and regenerative ability in older adults. There are no approved treatments to prevent, slow or reverse this condition. However, University of Texas spin-out [Ridgeline Therapeutics](#) aims to change this. The company is working on transformative drugs that rejuvenate muscle stem cells, advancing a daily pill to delay the onset and reduce the severity of sarcopenia in aging adults.



Longevity.Technology: *Ridgeline is developing small molecule inhibitors of an enzyme called nicotinamide N-methyltransferase (NNMT), which is critical in regulating energy metabolism and epigenetic pathways. The company says the approach holds potential for treating multiple chronic diseases but has selected muscle regeneration as its first medical indication for clinical trials. For an update on the company's progress towards the clinic, we caught up with Ridgeline founder and CEO Dr Stan Watowich.*

Watowich says that the company's preclinical work, which has already shown that **inhibiting NNMT improves the regenerative capacity of skeletal muscle** in older mice, is progressing rapidly.

"We've completed the rodent studies, and those hit all their safety endpoints, so we're pleased about that," he tells us. "We saw minimal adverse effects, even at very high doses, so we've moved into testing in a mini-pig model, which mimics the human metabolism of our drug much better than other species. We're aiming to establish the highest dose we can safely deliver, and we haven't seen any adverse effects so far, so we're optimistic that the safety targets are well in hand and have been hit."



Dr Stan Watowich, co-founder and CEO – Ridgeline Therapeutics

Lean vs fatty muscle

Perhaps the most exciting progress is the new data from Ridgeline's work in ordinary older mice.

"As before, we're seeing large improvements in strength in the animals, even after a short treatment period," says Watowich. "But our new data shows that in addition to increased muscle strength, the muscles of the treated animals become very lean and not filled with large amounts of fat deposits."

This is relevant, says Watowich, because older adults tend to have fatter muscles than younger adults, even if they are not overweight or obese. This excess muscle fat reduces our muscles' overall quality and performance as we age.

"Almost everyone wants better muscle health without going crazy at the gym, and that seems to be what our drug does," he adds.

Boosting bone health

Beyond the muscles, Ridgeline has now observed that bone health in the treated mice is also improved. Osteoporosis, or the loss of bone mass and density, is another major issue associated with aging – increasing our vulnerability to chronic joint pain, fractures, and spinal problems.

"When we look at the bones of treated elderly animals, they're getting thicker, they're getting stronger, the mineral density is improving," says Watowich. "Now, we can't say it's directly because of our drug. It could be because the muscle is stronger, and if you put more tension on your bone, the bone responds by growing stronger. Or it may be a combination of the two. However, it may not matter how we achieve improved bone strength – it's just important to achieve it."

Based on these observations, Ridgeline believes that improving muscle health will also benefit aging people in other areas of health.

"I'd go as far as to say that if you can preserve muscle strength, you will age healthier," says Watowich. "If we're able to improve muscle strength in older people, we're going to see other benefits rippling out from that – many other diseases are going to be kept at bay."

"From a cardiovascular perspective, if you can keep your strength up, you can be more active, which in turn benefits your heart, prevents the onset of diabetes, and helps maintain your cognitive abilities."

Breaking the vicious cycle

Watowich says muscle decline is a "vicious cycle" in older people.

"When an elderly person reduces their activity, their muscles begin to atrophy," says Watowich. "And once their muscles have atrophied a little bit, they slow down a little bit more, and now their muscles atrophy a little bit more, and on and on it goes. We're hoping to break that cycle, so we are now doing a series of studies to see if we prevent atrophy of immobilized muscles."

Ridgeline is raising a Series A round to take the company through its first-in-human clinical trials, which it expects will commence in the second quarter of next year. According to Watowich, the company's manufacturing strategy is also well ahead of expectations.

"Manufacturing is going better than expected," he says. "We've produced twice as much compound as planned because we were able to rapidly optimise the reaction and increase the yields. So everything is moving ahead, as far as getting the drug into clinical trials goes."





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