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Business & Innovation

Super-buff cattle may hold key to treating muscular diseases

Cambridge biotech trying to
mimic breed's genetics

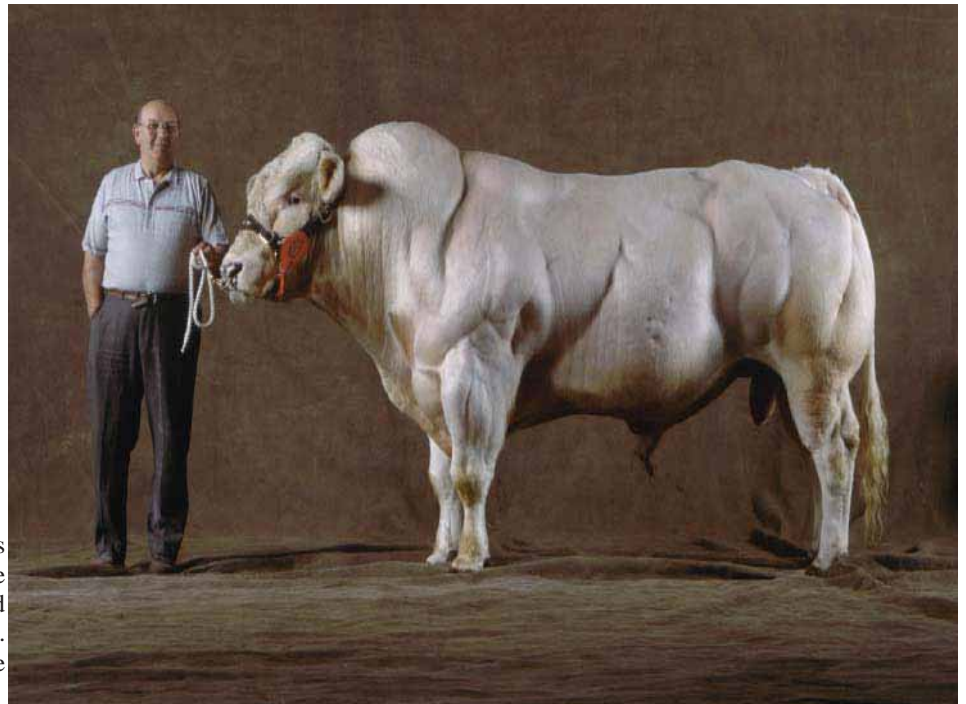
By Stephen Hume

CAMBRIDGE — When John Knopf walks into a meeting and wants to blow people's minds, he just pulls out a picture of a cow clearly not a normal animal. The massive white bull nearly explodes with muscles, a Mr. Olympia with hooves. The breed, a Belgian blue, is a genetic freak.

The picture has been known to derail business conversations. People want to know what made the beast so big. "Everyone talks about it," said the longtime biotechnology executive. "Sometimes they say, 'You've got to get me some of this stuff.'"

There isn't any "stuff" available yet, and Knopf's company, Acceleron Pharma Inc. isn't promising a bigger cow. But by mimicking the curious genetics of the breed, it's hoping to make a drug that shifts human muscles into the same kind of overdrive. If it works, Acceleron's drug could repair the damage done by ALS, muscular dystrophy, and cancer — diseases that can kill people by dramatically weakening them.

"There's a real significant need for these patients," said Knopf. "Clearly patients are dying from lack of musculature." Since its founding in 2003, the privately held Acceleron has won \$56 million in blue-chip venture-capital backing with the bold proposition that it can discover new ways to regulate the body's tissues and systems. Its first potential drug, an injection



to boost bone growth, is already in human testing. The goal is to help repair the bones of people with cancer, and perhaps someday people with osteoporosis as well. Acceleron expects to report results of a first small human test in September, and start a larger clinical trial by the end of the year.

The muscle drug is further away. So far the company has only tested the drug in lab animals, which — like the outsize Belgian blue cattle — tend to experience dramatic gains in muscle mass without exercise.

There's a surprisingly simple explanation for the cow's pneumatic bulk. Its body lacks a protein that works as

an "off" switch for muscle growth. Called myostatin, the substance patrols the bodies of normal cows — and humans — to keep the muscles in check. By designing a drug to absorb and block myostatin, Acceleron is essentially removing the "off" switch for muscle growth.

Acceleron's bone drug works in a similar way. Drugs already exist that promote the growth of new bone, but they have shortcomings: some can be delivered only directly to a particular bone, and another can't be used in the cancer patients who could benefit from it. Acceleron's approach is to remove the body's "off" switch for bone growth by blocking a substance that

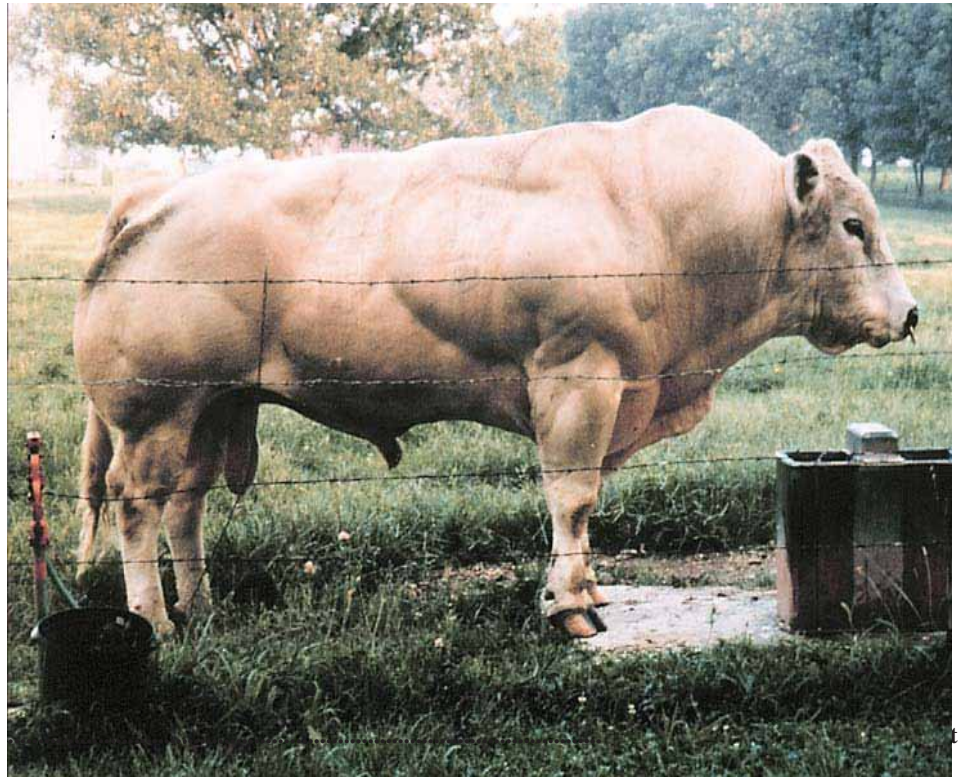
impedes new bone formation. In some cancer patients, bones can become almost porous, breaking easily, and causing health risks that last even after the cancer has gone into remission.

Acceleron's executives believe it is the only company looking into this approach to fixing damaged bones. But in the muscle arena, Acceleron is facing significant competition. Two giants of biotechnology are also developing myostatin inhibitors: the West Coast powerhouse Amgen Inc. and Wyeth.

Wyeth makes an antibody that specifically binds to myostatin and takes it out of commission. The company started testing the drug on muscular dystrophy patients in 2005 and initially expected results by late last year, but they have not yet been disclosed. A Wyeth spokesman this week said the data are still being analyzed. Amgen's drug is also in clinical trials, but the company has revealed little information about it.

Acceleron, meanwhile, is brewing its experimental drug in its Cambridge-port headquarters, a red liquid sloshing back and forth in a first-floor bioreactor. This year the company plans to ask the FDA for permission to test the drug in humans, with tests possibly beginning in 2008.

Although the initial use of the drug is for patients with muscle-wasting diseases, the implications haven't been lost on a very nonmedical audience: bodybuilders. A number of bodybuilding websites are tracking the progress of myostatin research, and some companies have introduced unregulated supplements with names like MyoZap and Myostim, which claim to boost



muscle growth by blocking myostatin. Any legitimate treatment, however, is years away. When and if it appears, Acceleron knows there will be a waiting black market.

"We'll be aware of it, and just do the best we can as a company to monitor this," said Knopf.

Meanwhile, Acceleron is at a turning point. The 75-person company is without a chief executive — Knopf, the president, is acting as an interim chief — and considering whether to go public. In the future it would like to apply

its technology to other body systems and tissues, including fat and blood vessels. Knopf, one of its cofounders, is well aware of the almost science-fiction appeal of his company's research.

"If you'd said to me 10 years ago, what are the chances there's going to be a therapy that increases muscle mass while people sit on the couch, I'd have said zero," said Knopf. "But these things are coming."

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