

Locate Bio Ltd

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Locate Bio: next-generation orthobiologics

Regenerative medicine company Locate Bio is aiming to transform the musculoskeletal market with its range of therapeutic orthobiologic products.

Lower back pain is the single leading cause of disability in 160 countries, according to the World Health Organization. It is often caused by degenerative disc disease, a progressive and irreversible condition that leads to a loss of disc height that can compress the spinal nerves and cause excruciating, intractable pain with devastating social consequences. Unfortunately, efforts to manage the condition—such as using strong painkillers including addictive opioids and performing spinal fusion surgery—are often inadequate. New and effective orthobiologic products are urgently required to address this significant unmet need.

Poised to radically alter the outlook for both surgeons and patients, Locate Bio is an innovative regenerative medicine company focused on developing next-generation orthobiologics for the musculoskeletal market. This exciting frontier in regenerative medicine involves the use of tissue-forming templates and drugs to accelerate the healing process of injuries or reverse the impact of progressive or chronic conditions.

Unique capability

In developing its best-in-class range of products addressing the repair and regeneration of bone, Locate Bio brings together two core competencies.

One is programmed drug release. Locate Bio was spun-out of the University of Nottingham's school of pharmacy. Utilizing this strong pharma perspective enables the company to take well-known molecules with a long history of clinical use (both therapeutic proteins and small molecules) and optimize their delivery for musculoskeletal conditions. "Bone is a slow-healing tissue, and the controlled and extended-release of molecules should be optimized to better match the biological need," explained Kevin Shakesheff, Locate Bio's Chief Scientific Officer.

The other is producing instructive tissue scaffolds. Using its deep-domain expertise in material science, Locate Bio creates these products, designed to guide the body's natural healing response.

Combining these key capabilities, Locate Bio is developing a diversified orthobiologic company with a range of best-in-class, late-stage, smart-graft products, each with significant disruptive potential.

The company's lead product, LDGraft, is a bone-graft substitute for treating lower back pain caused by degenerative disc disease. LDGraft consists of not only a three-dimensional resorbable scaffold that provides a template for stem-cell attachment (osteoconduction), but also a powerful growth factor, recombinant human bone morphogenetic protein-2 (rhBMP-2), which signals those cells to differentiate into bone (osteinduction). A step

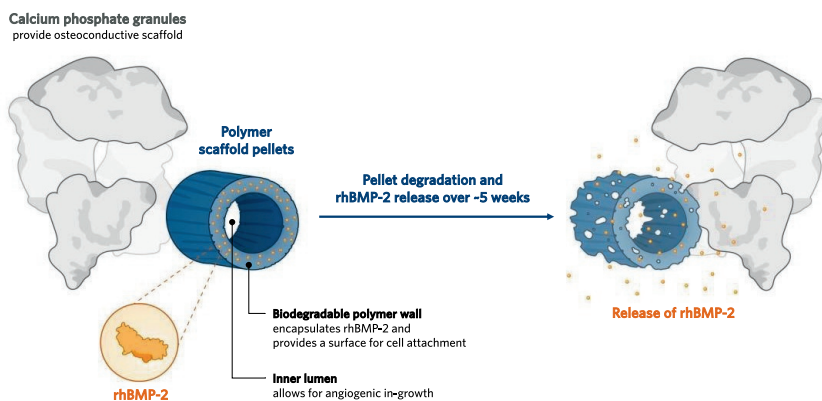


Fig. 1 | Programmed drug release. LDGraft is composed of cylindrical pellets, which comprise a biodegradable polymer that encapsulates recombinant human bone morphogenetic protein-2 (rhBMP-2) within its walls. The polymer degrades, steadily releasing the low-dose rhBMP-2, and the pellets provide a structural surface for cell attachment.

change in performance comes from the controlled and extended release of rhBMP-2. LDGraft contains many cylindrical pellets, the walls of which comprise a biodegradable polymer that encapsulates rhBMP-2. As the polymer degrades, the low-dose rhBMP-2 held within is steadily released, typically over 4–6 weeks. Meanwhile, the pellets provide a structural surface for cell attachment, with the inner lumen allowing for angiogenic in-growth (Fig. 1).

The entrapment of rhBMP-2 within the polymer is the key difference between Locate Bio's delivery and the surface-attachment approach of other products. "With surface attachment, the receptor-binding domain of the protein can still be presenting and therefore bioactive. This leads to a drug burst," explained Shakesheff. "LDGraft differs in that it shields the whole protein so that it is biologically unavailable until released from the polymer—a process that we have optimized over a therapeutically appropriate period of time, overcoming drug burst and potentially, side effects."

CEO John von Benecke pointed out that some alternative products have very good fusion rates but come with side-effect risks, high prices, and poor handling, while others have great handling and good pricing but are not as good at growing bone. "Our design intent from the outset has been to benchmark ourselves against the very best aspect of each of the competition," he said.

Indeed, in nonclinical tests, LDGraft matches the highest fusion rates achieved by products like the Medtronic Inc. Infuse bone graft, but at a substantially lower total dose of rhBMP-2. Moreover, it takes less than 2 minutes to prepare LDGraft compared to around 20 minutes for the current

market leader, and the handling qualities of LDGraft match those of the best alternatives on the market, enabling surgeons to use it to enhance new bone integration or to pack it within an interbody spacer. Clinical trials of LDGraft are scheduled to begin in 2023.

Building a world-leading orthobiologics business

Other exciting and notable orthobiologics in the company's regenerative medicine pipeline include: CertOss, which is a new class of ceramic bone graft with submicron surface features; and CognitOss, which is a controlled and extended-release antibiotic product for orthopedic infections.

Locate Bio is interested in collaborating with those who have an interest in white-label co-development or licensing of LDGraft or its other products.

"We are pioneering an orthobiologics business with a diversified suite of best-in-class technologies that address the performance limitations of existing products," said von Benecke. "Our next-generation products advance the process of tissue repair and will enable orthopedic surgeons to improve the lives of millions of people suffering from debilitating musculoskeletal conditions."

CONTACT

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