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# Cerapedics: A PMA First Opens New Opportunities in Cervical Spine Osteobiologics

*The $2.85 billion osteobiologics market is one of the fastest growing, albeit controversial, sectors of spine surgery. Cerapedics has the potential to begin a new era by gaining the first FDA PMA for a bone graft enhancer for cervical spine fusion in a field lacking convincing clinical data.*

by
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Bone regeneration consists of complex processes, such as inflammation and formation of fibrous tissue and bony callus. Although scientists' understanding of these processes is improving, the science still remains tantalizingly elusive, and available products, while widely used, lack satisfactory clinical data confirming their efficacy.

In part, the osteobiologics world is still grappling with a backlash from the implosion of *InFuse*, **Medtronic PLC**'s one-time bestselling bone morphogenetic protein 2, (BMP-2), a bone graft enhancer that came under intense scrutiny beginning in 2008 with a series of FDA warnings about side effects and overuse in off-label indications. (*See "In Spine, it's the Old vs. the New and Everyone vs. Cost,"* The MedTech Strategist, *November 25, 2014*.) More broadly, spine surgery providers are frustrated by a plethora of marketed, expensive products, none of which, with the exception of *InFuse*, is supported by rigorous, reproducible clinical data. In many cases, there is a complete lack of any clinical data. This information gap has been characteristic of the field for some time, but it is an increasing handicap in the wake of *InFuse* and as value and cost become bigger parts of reimbursement and clinical decision-making.

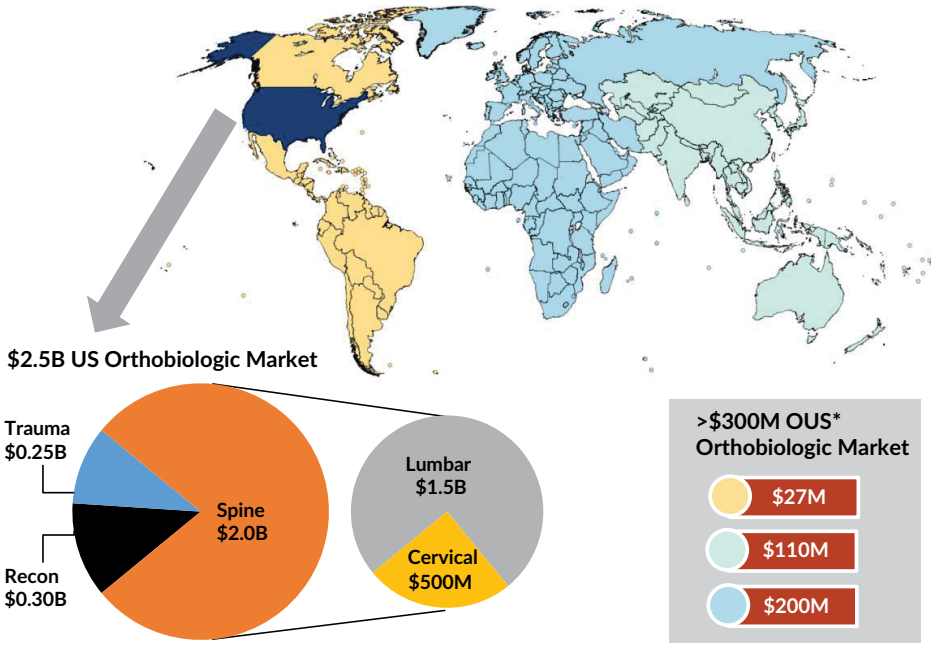
At the October 2015 North American Spine Society (NASS) annual meeting, a member of the audience in a biologics and evidence symposium, who also sits on his hospital's purchasing committee, summed up the prevailing sentiment: "They're [companies] talking to people like me who are not PhDs and don't understand the topics as well. But how can a company possibly get a living cellular product out so quickly with not one human study?"

In a tricky environment, **Cerapedics Inc.** believes its heavily data-driven approach to developing a suite of osteobiologics is a winning competitive advantage. It is taking what CEO Glen Kashuba calls a "disruptive" approach to marketing its first FDA-approved product, *i-FACTOR*, a bone graft enhancer for

Figure 1

**2015 Worldwide Orthobiologic Market**

**Regional Breakdown of $2.85B Worldwide Market**




*OUS = Outside US

Sources: Cerapedics, U.S. Market for Orthopedic Biomaterials, iData Research, June 2013; Orthopedic Network News, Vol 24, No. 4, October 2013

cervical spinal fusion that is based on a proprietary small peptide technology platform consisting of P-15 bound to an anorganic bone mineral (ABM). It is not the only company pursuing this strategy. (*See "Bioventus: A New Kind of Orthobiologics Joint Venture,"* The MedTech Strategist, *April 27, 2015*.) But *i-FACTOR*, which FDA greenlighted on November 3, is only the second osteobiologic in spine to be approved under the PMA regulatory route (*InFuse* was the first). Moreover, it is the first osteobiologic to gain FDA approval for use in anterior cervical discectomy and fusion (ACDF) procedures.

Despite the shortcomings, the field of osteobiologics, particularly those devoted to spine, is one of the most dynamic subsegments of the orthopedics industry, growing at 11% per year, excluding *InFuse*, says Jeffery Marx, PhD, Cerapedics' president and COO. Including *InFuse*, that figure drops to approximately 4%, which is still healthy compared to most spine subsectors. The total US market for spine osteobiologics was roughly $2 billion in 2013, 75% for lumbar indications and 25% cervical, he notes *(see Figure 1)*. Even as the field grows, the need for better bone graft substitutes remains acute, procedures such as ACDF, which is commonly recognized as having a high success rate, plagued by variable metrics and misunderstood fusion rates. A key problem is the diversity of definitions of a solid fusion, Marx noted in a talk last spring at the Canaccord Genuity Musculoskeletal meeting. Citing a literature review that appeared in the *Asian Spine Journal* (2008; 2[2]:127-143), he said that in 604 papers reviewed from 1966 to 2004, only a small percentage of studies employed a stringent definition of a solid fusion.

With minimal regulatory requirements for getting to market in the US and elsewhere, all other products that make up the osteobiologics market, excluding *InFuse* and autograft, have been approved either as Class II devices or minimally manipulated tissue (MMT). The latter group, which includes stem-cell grafts, does not need FDA approval and is widely used in lumbar and cervical fusion procedures, says Kashuba. MMTs currently comprise a $200 million market, but, given the lack of data, commercial payors consider them experimental and, almost universally, do not cover them, with the exception of allograft and autograft (*see Figure 2*).

## A Nuanced Tack for De-Risking Reimbursement

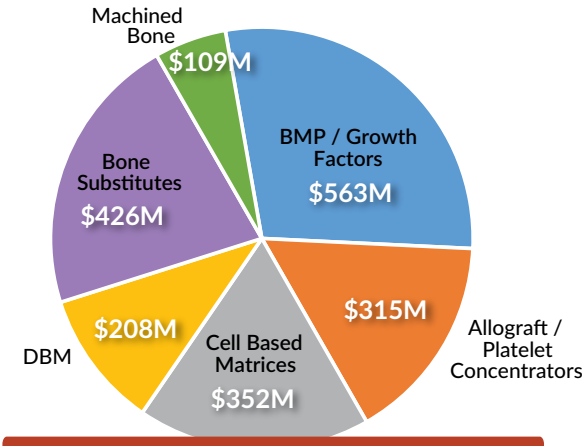
This conundrum led Cerapedics to take a more nuanced approach to reimbursement. Increasingly, payors subtract the expense of excluded items from final DRG payments, or deny the DRG payment outside of their coverage policies. This means that hospitals that use bone grafts other than autograft in cervical fusions may not get the full payment, or any payment, for DRG 473, which was $13,300 in 2015. "There is a growing trend across medical devices in which private payors look at itemized lists of specific products used by a hospital and go right down the line and identify products that they do not cover and subtract that out of the price of the DRG, and in some cases they deny the entire DRG if one component is not covered, even if the rest are," says Kashuba.

Because Cerapedics' product is on-label for cervical fusion and backed by extensive Level 1 data, the more restrictive reimbursement represents an "opportunity out of the gate," he says. "Our data separates us from the pack." Near-term, the company can attract hospitals and surgeons because it anticipates that *i-FACTOR* bone graft will be immediately eligible for transitional or "implied" coverage. This essentially provides reimbursement by default based on the product's compliance with certain criteria payors look for in their coverage policies (these criteria, while specific to each insurer, are public and include clinical data, on-label FDA approval, and volume).

Such status will de-risk the reimbursement uncertainty for hospitals so that they can benefit from the full DRG if they use *i-FACTOR* bone graft for ACDFs. This assumption is further fortified by the expectation that sales will be low during the initial launch, thereby avoiding the radar of insurers, which tend to scrutinize high-volume, big-ticket items.

Figure 2

**2015 US Spine Orthobiologic Market**
**($2.0B)**




Sources: Cerapedics, U.S. Market for Orthopedic Biomaterials, iData Research, June 2013; Orthopedic Network News, Vol 24, No. 4, October 2013

Longer term, the company will be educating payors, surgeons, and hospitals to achieve more formal coverage status among private payors, a process it expects will take a number of months for major insurance companies, as opposed to years, which has been the case for less-studied products. As it prepares for commercial launch, the company has also started discussions with hospitals and distributors around the device's value proposition. The product's pricing isn't public, but Kashuba says it will be lower than that of BMP-2 and will not subject the hospital to reimbursement risk.

The P-15 technology behind *i-FACTOR* bone graft was discovered and isolated in the early 2000s by Rajendra Bhatnagar, a professor of biochemistry and bioengineering at UCSF. A synthetic combination of P-15 and ABM, *i-FACTOR* augments the natural cell attachment process, initiating a signaling cascade that leads to new bone formation. While the original patents on P-15 technology have expired, Cerapedics has IP covering some of its final product formulations.

Initially, the synthetic P-15 was studied in oral applications, and has been implanted in approximately 500,000 dental patients, a "huge benefit in FDA's comfort with the safety profile," says Marx. The IDE clinical trial for *i-FACTOR* bone graft was a randomized, multicenter, prospective study comparing *i-FACTOR* bone graft to autograft for single-level instrumented ACDF procedures inside of a structural allograft ring. Given that it is the first bone graft trial for cervical fusion, the design was based on lumbar spine protocols and negotiations with FDA, he adds.

The 12-month results showed *i-FACTOR* bone graft-treated patients achieved statistically significant, non-inferiority to the control group in each of the four primary endpoints: fusion rate, neck disability index (NDI) scores, neurological outcomes, and safety.

***In the pivotal, 12-month study, results showed 69% of patients who received* i-FACTOR *bone graft met all four primary endpoints combined, compared to 57% of those who were treated with autograft, achieving the statistical cut off for superiority.***

In addition, 69% of patients who received *i-FACTOR* bone graft succeeded in meeting all four primary endpoints combined, compared to 57% of those who were treated with autograft, a result that achieves the statistical cut off for superiority. These findings, including the superiority claim, are in the labeling and can be used to promote the product, Marx notes.

Results from the 12-month study are pending publication, while data from a two-year follow-up will be submitted for journal publication shortly. The company has plans to track subjects for six years, and, since the enrollment took time, it already has compiled some six-year data.

## Prioritizing Osteobiologics in the OR

The company's sales strategy also is a departure from traditional osteobiologics and follows a template set years ago by Orthovita, where Marx previously worked as VP of corporate development and a member of the senior leadership team. A hybrid network of distributors and a direct sales force is being assembled, based on reps' ability to promote clinical data and differentiate the science in this space.

While reps in this field typically do not have much clinical training, Cerapedics hopes to attract some of the former sales network that had been at Orthovita until its sale to **Stryker Corp.** in 2011. These sales people were "brought up the learning curve" to sell based on clinical data, and many of them no longer at Stryker could "find us more appealing," says Marx. This also contrasts with the traditional strategy for osteobiologics, which Kashuba says is typically considered an afterthought by hardware-focused sales teams. Cerapedics, however, is prioritizing its biologic even as it offers surgeons a line of ACDF hardware equipment—including ancillary implants, interbody devices, allograft bone, and instruments—which it developed as a private label. It will be flexible on the hardware pricing, since that is not its primary business, he says. "It is the exact opposite of what the big guys are doing in this space."

Founded in 2006, the company has raised capital from investors, including OrbiMed, MedImmune Ventures, a corporate venture fund of **AstraZeneca PLC**, CVF LLC, a unit of **Henry Crown & Co.**, and NGN Capital. It has been selling *i-FACTOR* bone graft in Europe, where it received the CE mark in 2008 for use in lumbar spinal fusion. Earlier this year, it received the CE mark for a next-generation *i-FACTOR* bone graft that incorporates silk threads. To date, the graft has been used in more than 12,000 surgeries, mostly lumbar.