

Kuros Biosciences (KURN.SW)

Initiation Report

LifeSci Investment Abstract

Kuros Biosciences (SIX: KURN.SW) is a commercial-stage company that is developing a portfolio of orthobiologics for spine fusion surgeries and a broad range of orthopedic/dental applications. The Company recently launched their bone graft substitute *MagnetOs* in the US and EU, which could provide a safe and effective alternative to autograft. Kuros is also developing KUR-113, a growth factor-based bone graft substitute containing fibrin/PTH, and plans to launch a Phase II study in spinal fusions in early 2019. Data from an earlier trial in open tibial fractures point to a differentiated product with a favorable safety and efficacy, suggesting that KUR-113 could expand Kuros' overall market opportunity down the road.

Key Points of Discussion

- **Kuros to Initially Focus on the Spine Market.** Kuros is striving to become a leader in the field of bone graft substitutes with two main products: MagnetOs and KUR-113. MagnetOs is a synthetic bone graft substitute intended to serve as a safe, less invasive alternative to autograft, and KUR-113 is a fibrin/parathyroid hormone peptide (PTH) combination intended to promote bone regeneration in spinal fusion procedures and a range of other orthopedic applications. The Company's initial focus is on the spine market, due to the majority of bone void fillers being used in spinal surgeries. The product officially launched in the US in June 2018 and the Company is now focused on growing sales of the product in both the US as well as the EU. Kuros' initial strategy is to sell MagnetOs through a direct sales force targeting KOL spine surgeons (to provide important initial validation) and indirectly through distributors. The orthobiologics market is projected to reach a value of over \$3.4 billion by 2030, with a potential opportunity for Kuros exceeding \$500 million by 2025.
- **Large Market Opportunity for Kuros' Products in the Spine Market.** Spinal deformities affect as much as 32% of the adult population and over 60% of the elderly population. Spinal fusions are surgical procedures that can address chronic back pain caused by degeneration (e.g. arthritis), trauma, or instability to the spine. The spine is a flexible structure composed of alternating bone (vertebrae) interspaced with cartilage (discs). The basic idea is to fuse, or grow, two or more vertebrae together so that they heal into a single, solid bone. This is achieved by removal of the damaged disc, placement of an inter-body cage (an implant to provide internal fixation), and providing some type of bone material (e.g. bone graft or bone graft substitute) to help promote the fusion. Spinal fusion eliminates motion between vertebrae and also prevents the stretching of nerves and surrounding ligaments and muscles, thereby preventing a main contributor to ongoing pain. In 2015, there were roughly 488,000 spinal fusion procedures performed in the US.

Expected Upcoming Milestones

- H2 2018 – Launch of post-marketing study for MagnetOs.
- H1 2019 – Launch Phase II spine fusion study for KUR-113.
- 2020 – Interim data from Phase II spine fusion study for KUR-113.
- 2021 – Phase III trial for KUR-113.

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Market Data

Price	\$8.64
Market Cap (M)	\$71
EV (M)	\$54
Shares Outstanding (M)	8.2
Fully Diluted Shares (M)	8.8
Avg Daily Vol	5,576
52-week Range:	\$7.64 - \$14.77
Cash (M)	\$16.7
Net Cash/Share	\$2.04
Annualized Cash Burn (M)	\$10.8
Years of Cash Left	1.5
Debt (M)	\$0.0

Financials

FY Dec	2016A	2017A	2018A
EPS H1	(2.68)A	(1.11)A	NA
H2	NA	NA	NA
FY	(3.89)A	(2.39)A	NA

- **Potential for Kuros' Fibrin/PTH Product.** Fibrin sealants without biologics have been used commercially for more than 30 years, primarily for the prevention of blood loss during surgical procedures. As a result, biocompatible and biodegradable fibrin sealants have a generally well-documented safety profile. KUR-113 is composed of fibrin and a biologically active fragment of PTH which upon local release promotes bone regeneration by acting directly on pre-osteoblasts and osteoblasts. The material conforms to the space in which it is injected, permitting its use in surgeries involving small or complex injury sites and minimally invasive spinal procedures. There is a large established market for bone graft products containing growth factors and meaningful uptake could be possible if Kuros successfully makes it through clinical trials with a clean safety profile. In this case, Kuros could take market share from autograft (comparable efficacy, avoid co-morbidities of autograft) as well as Medtronic's *InFuse* (comparable efficacy, cleaner safety profile).
- **Phase II Trial for KUR-113 in Interbody Spine Fusion to Start in Early 2019.** Kuros plans to launch a Phase II dose-finding study in spinal fusion patients in early 2019 comparing KUR-113 vs. autograft in lumbar interbody spinal fusions. The product has been previously tested in 200 patients with open tibial fractures and was found to have a favorable safety and efficacy profile, which provides some degree of confidence on the likelihood for a successful readout from the trial. Positive results could set the stage for a pivotal trial launch in 2021, and if the results are positive, a regulatory filing in early 2024.
- **Safety Issues for Medtronic's *InFuse* Product Has Created an Opening in the Market.** Studies have shown that using Medtronic's *InFuse* Bone Graft can result in adverse side effects in the body. In 2011, it was reported that a number of Medtronic- sponsored studies failed to mention the life-threatening side effects of *InFuse*. In early, unpublished clinical studies, *InFuse* was shown to potentially inflame nearby tissues and bones, cause urinary problems, and stimulate cancer growth. Other side effects include: back and leg pain, radiculitis (pain spreading through spinal nerves), implant displacement, retrograde ejaculation, male sterility, infection, osteolysis (degeneration of bone tissue), ectopic bone formation (unwanted bone in the spinal canal), and death. Approximately 15 to 20% of patients who have received *InFuse* surgery report leg and back pain. The product was linked to a 43% higher overall complication rate than traditional bone grafts. Despite the potential for complications, *InFuse* remains one of the largest-selling bone graft substitute products.

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Company Description

Kuros Biosciences is a commercial stage company focused on developing treatments that promote bone regeneration and tissue repair. In 2000, it spun out from Eidgenössische Technische Hochschule Zürich (ETHZ), and together with the University of Zürich developed its TG Hook technology. In January 2016, Cytos Biotechnology (SIX: CYTN) and Kuros Biosurgery Holding AG (“Kuros”) merged to create Kuros Biosciences. In early 2017, Kuros acquired Xpand Biotechnology to improve its orthobiologics portfolio through the addition of the *MagnetOs* product.

Kuros has appealing commercial prospects in key segments of the bone graft substitute market. The Company has already received marketing clearance for *MagnetOs* in Europe and the US with sales beginning in March and June 2018, respectively. Their *Fibrin/PTH* product, KUR-113, is currently being tested in clinical trials with a Phase II trial vs. autograft in spine fusion surgeries starting in early 2019. **Figure 1** shows Kuros Biosciences’ full development pipeline.¹ With *MagnetOs* already approved and beginning to sell, Kuros can begin to scale their commercial infrastructure in preparation for a potential launch down the road for KUR-113, a product whose approval could be transformative for the Company and whose launch could be bolstered by the existing commercial footprint.

Figure 1. Kuros’ Development Pipeline



Surface Science Orthobiologics (CE Mark/510k)				
Product	Therapeutic Area	Preclinical	Regulatory Submission	Market Clearance
MagnetOs Granules (EU)	Orthopedics, Spine, Dental			
MagnetOs Granules (US)	Spinal Fusion (posterolateral)			
MagnetOs Putty (EU)	Orthopedics, Spine, Dental			
MagnetOs Putty (US)	Spinal Fusion (posterolateral)			

Fibrin/PTH Growth Factor-based Orthobiologics (NDA/MAA)					
Product	Therapeutic Area	Preclinical	Phase 1	Phase 2	Phase 3
KUR-113 (EU & US)	Spinal Interbody Fusion*				
KUR-111 (EU & US)	Tibial Plateau Fractures				
KUR-113 (EU & US)	Tibial Shaft Fractures				

Sealant – legacy portfolio

Product	Therapeutic Area	Non-clinical	Pilot	Pivotal	Registration
Neuroseal (EU)	Dural sealant				
Neuroseal (US)	Dural sealant				

Source: Kuros Biosciences

MagnetOs: A Bone Graft Substitute to Direct Bone Formation

MagnetOs is a synthetic bone graft substitute intended to fill bony voids in the skeletal system. It has a unique submicron surface topology to aid in the regeneration of bone tissue and consists of hydroxyapatite and tricalcium phosphate. *MagnetOs* resorbs and is replaced with bone during the healing process, which can facilitate spinal fusion when used with interbody cages or contribute to the healing of fractures.

The product has been approved as a bone void filler for a range of orthopedic and dental indications in the EU and as a bone graft extender for posterolateral spinal fusions in the United States and EU. *MagnetOs* has been shown to have comparable efficacy to autograft, thus having potential as an alternative that can avoid the morbidity associated

¹ <http://www.kuros.ch/pipeline-2/pipeline.html>

with autograft. The product officially launched in the US in June 2018 and the Company is now focused on growing sales of the product in both the US as well as the EU. The Company plans to conduct a post-marketing study

MagnetOs comes in two formulations: granules or putty. The granules are synthetic, osteoconductive bone void fillers consisting of 65%-75% tricalcium phosphate and 25-35% hydroxyapatite. They are packaged for single use only. *MagnetOs* Putty has the same chemical composition and ratios as *MagnetOs* Granules, but is premixed with a rapidly resorbing synthetic polymeric binder (LEOL) composed of poly (lactic acid) and poly (ethylene glycol) to provide cohesion between the granules. *MagnetOs* Putty comes in four sizes in block form.

Mechanism of Action

There are three mechanisms by which bone healing is promoted: osteoconduction, osteoinduction, and osteogenesis. Osteoconduction is the process by which an implanted scaffold passively allows for the ingrowth of host capillaries, perivascular tissue, and mesenchymal stem cells on the surface. Osteoinduction recruits osteoprogenitor cells to differentiate into osteoblasts and osteocytes. The three processes, in addition to their source examples, are summarized in **Figure 2**.

Figure 2. Bone Graft Healing Mechanisms

Approaches	Principles	Typical Examples
Osteoconduction	The process in which the bone graft material acts as a scaffold for new bone formation on the native bone	Autogenous bone graft
Osteoinduction	Recruits mesenchymal stem cells, osteoprogenitor cells, and growth factors to induce bone growth	Bone morphogenetic proteins, bone marrow mesenchymal stem cells
Osteogenesis	Formation of new bone from osteocompetent cells	Osteoblasts, osteocytes, fresh marrow

Source: LifeSci Capital

MagnetOs serves as the bone scaffolding matrix through osteoconduction and uses the body's potential to generate bone by activating local stem cells. The materials present in *MagnetOs* is rapidly resorbed after implantation, allowing for osteoconductive bone growth on the granules. *MagnetOs* has both osteoconductive and osteoinductive effects. Calcium phosphates are the most commonly used synthetic osteoconductive scaffolds because they biodegrade slowly, have superior strength in compression, and provide a porous osteoconductive surface. The micropores in calcium phosphate are able to trigger osteoinduction through their unique surface architectures.² **Figure 3** shows scanning electron microscopy (SEM) images of the surface of standard calcium phosphate granules (left) compared with the surface of *MagnetOs* granules (right). This difference in topography allows for a better induction and resorption profile *in vivo*.

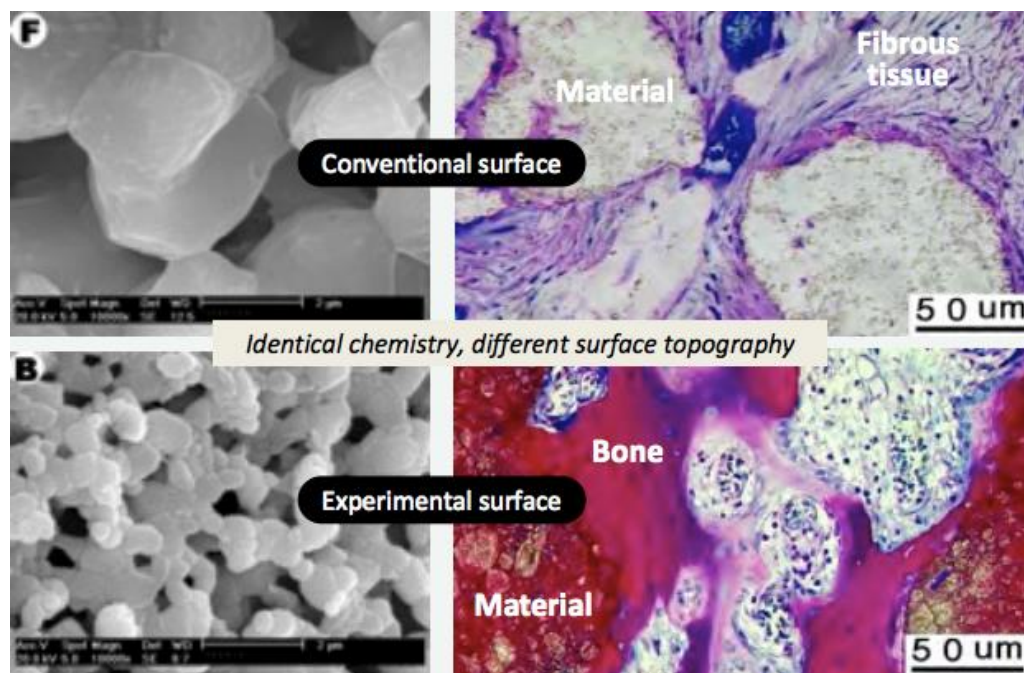
² Zhang, J, et al., 2015. Microporous calcium phosphate ceramics driving osteogenesis through surface architecture. *J Biomed Mater Res A*, 103(3), pp1188-1189.

MagnetOs has a unique surface topography. Preclinical tests have found that stem cells cultured on conventional surfaces form fibroblasts and fibrous tissue, but if the same stem cells are grown in squares, they go on to become bone cells. Surface topography by itself can therefore influence the fate of stem cells. Conventional surfaces look like other commercially available options as shown below in **Figure 3**, but *MagnetOs* is created from materials with the same chemistry but a smaller surface topography in order to enhance osteoinduction. From this surface topography, the *MagnetOs* experimental surface gives rise to bone while conventional surfaces generate fibroblasts after 12 weeks, as shown by preclinical trials. By changing the surfaces of calcium phosphate, the material is endowed with unique biological properties without the addition of growth factors or stem cells.

Tricalcium phosphate, the predominate phase of calcium phosphate in *MagnetOs* has a long history of use in bone graft substitutes owing to its resorption characteristics. Hydroxyapatite, the other component of *MagnetOs*, is the main inorganic mineral of tooth enamel and bone. By weight, hydroxyapatite comprises 50% of bone.³ Hydroxyapatite is used to generate bone scaffolding because of its ideal pore size and morphology. Hydroxyapatite has controlled pore size distribution as well as interconnected porosity, thereby exhibiting stronger bone bonding ability.⁴ The interconnected pores provide a pathway for tissue growth, leading to a strong mechanical and biological fixation of the implant with the original tissue.

This ratio of calcium phosphates to hydroxyapatite makes *MagnetOs* granules capable of rapidly inducing together with an optimized resorption profile. That product has demonstrated equivalent efficacy to the gold standard, autograft from the iliac autograft. *MagnetOs* may have a wide range of applications, appears to have a good safety profile, is easy to apply, and provides controlled bone formation.

Figure 3. Topography of Standard Calcium Phosphate Granules (top) and *MagnetOs* Granules (bottom)

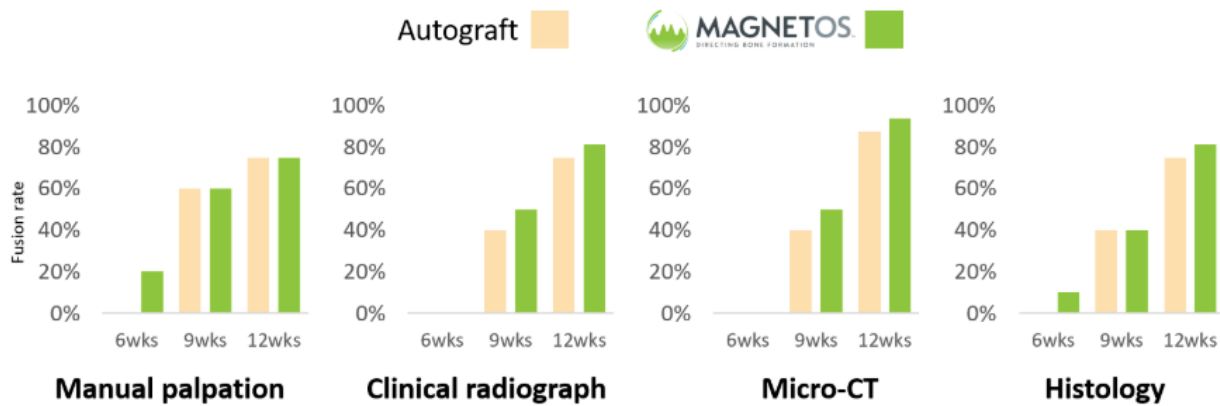


Source: Kuros Biosciences

³ Roberts, TT, et al., 2012. Bone grafts, bone substitutes, and orthobiologics. *Organogenesis*, 8(4), pp114-124.

⁴ Dasgupta, S, 2017. Hydroxyapatite scaffolds for bone tissue engineering. *Bioceram Dev Appl*, 7(2).

Figure 4. Comparison of Autograft “Gold Standard” and *MagnetOs* Efficacy



Uses for *MagnetOs*

MagnetOs has a wide range of uses, serving as a bone void filler for spinal fusions and other types of surgical procedures. A bone void occurs when part of a bone is missing or damaged and needs to be replaced. This may be due to a fracture, disease of the bone through osteonecrosis or cancer, tooth loss, or surgically implanted devices. In the EU, the bone void filler has a broad indication in the areas of orthopedic, spine, and dental use. In the U.S., the bone graft extender is approved for posterolateral spine fusion use only, with the goal of future expansion. Kuros is focused first on the spinal fusion market, which is the largest market for bone graft substitutes. Below we discuss disease background information for both spine fusions as well fractures, another area which Kuros is pursuing for *MagnetOs*.

Spinal Fusions

Spinal fusions are surgical procedures that can address chronic back pain caused by degeneration (e.g. arthritis), trauma, or instability to the spine. The spine is a flexible structure composed of alternating bone (vertebrae) interspaced with cartilage (discs). The basic idea is to fuse, or grow, two or more vertebrae together so that they heal into a single, solid bone. This is achieved by removal of the damaged disc, placement of an inter-body cage (an implant to provide internal fixation), and providing some type of bone material (e.g. bone graft or bone graft substitute) to help promote the fusion. Spinal fusion eliminates motion between vertebrae and also prevents the stretching of nerves and surrounding ligaments and muscles, thereby preventing a main contributor to ongoing pain. Although fusion will take away some spinal flexibility, most spinal fusions involve only a small number of segments of the spine and do not limit motion very much, particularly in the lumbar part of the spine.

Disease Pathogenesis and Causes

Causes of Spinal Deformity. A wide variety of etiologies can necessitate spinal fusion surgeries, including trauma, tumors, infections, inflammatory diseases, connective tissue disorders, degenerative disorders, and post-surgical complications. A modest loss of correct spinal alignment and range of motion are typical of the aging process, due in part to the continuous force placed on load-bearing vertebrae throughout life. However, a range of conditions can accelerate or exaggerate this process. Some of the conditions that can require spinal fusion procedures:

- **Degenerative disc disease (DDD)** – This condition results from a compromising of one or more intervertebral discs, which are the fibrous cartilage between adjacent vertebrae that allows for limited motion and provides cushioning. DDD can cause pain, stenosis, and allow for an increased range of motion, which stresses the surrounding anatomy. DDD also correlates with alterations in spinal curvature, which are due to compensatory mechanisms.
- **Degenerative spondylolisthesis** – In this condition, a vertebral body slips forward relative to the vertebral body below it, leading to sagittal malalignment and potentially spinal stenosis. Spondylolisthesis is most common at the L4-L5 or L3-L4 level.
- **Ankylosing spondylitis** – Ankylosing spondylitis is a form of arthritis that primarily affects the spine and leads to chronic inflammation and pain. In severe cases, the inflammation can trigger new bone growth that results in the fusion of vertebrae in a fixed, forward-leaning posture.
- **Osteoporosis** – Osteoporosis can lead to vertebral compression fractures (VCFs) that disrupt the normal curvature of the spine.
- **Trauma** – Severe trauma can lead to significant spinal injury that interrupts spinal alignment.

Treatment

Treatment plans differ substantially among patients. Physicians typically attempt non-surgical therapies prior to considering fusion surgery. A surgeon may also be reluctant to operate on an individual who is in poor health or has a high body mass index (BMI).

Traditionally, surgical intervention is custom-tailored to the patient's specific deformity and clinical symptoms and requires extensive pre-surgery planning to reduce the risk of complications. The surgical strategy is also dictated by the abilities and preferences of the surgeon. The goals of surgery are to reduce existing pressure on nerves and stabilize the spine through the fusion of 2 or more vertebrae. Pedicle-screw systems, used in combination with osteosynthesis rods, are a mainstay in most spinal fusion procedures to ensure that the spine remains fixed and conducive to vertebral fusion. Interbody devices, commonly referred to as cages, are also frequently used in fusion surgeries to further promote bone growth between adjacent vertebrae. In severe cases, osteotomies can be performed, which entail the removal of bone from the spine to help achieve the proper sagittal correction. Over the long-term, new bone growth fuses instrumented vertebrae together.

In general, single-level fusions of the lumbar spine are the most common fusion procedures performed. However, deformity or degenerative indications typically require instrumentation of multiple segments to ensure spinal stability.⁵ The instrumentation must span the extent of the deformity at a minimum and often extends well beyond its boundaries to ensure that the implants end at stable points in the spinal curvature. This often necessitates that instrumentation extend distally to L3 or L4, assuming these vertebrae are not a part of the deformity. Proximally, instrumentation that ends at the thoracolumbar junction or in the middle of the thoracic curve has high rates of complications, so multilevel fusions typically extend proximally to roughly T3 or T4. Thus, the treatment of degenerative and deformity indications typically involves long multilevel fusions sometimes connecting to the pelvis to ensure stability.

⁵ Good, CR, et al., 2011. Adult spine deformity. *Current Reviews in Musculoskeletal Medicine*, 4(4), pp159-167.

Potential Complications. Surgery to correct adult spinal deformities are prone to a number of clinically-significant complications.^{6,7} A recent meta-analysis of 3299 patients across 19 studies determined an overall complication rate of roughly 41%.⁸ A patient's age and the number of levels requiring fusion are two significant risk factors for complications in patients over the age of 65. Some of these complications include:

- **Malalignment** – As many as 62% of patients remain sagittally malaligned postoperatively.⁹
- **Pseudoarthrosis** – Pseudoarthrosis is the failure of two vertebral levels to fuse and is a common complication in fusion surgeries to correct spinal deformities. Several factors have been shown to significantly heighten the risk of pseudoarthrosis, including: preoperative thoracolumbar kyphosis greater than 20° (p=0.0001), age greater than 55 (p=0.001), instrumentation down to sacral spinal levels (p=0.002), and the instrumentation of 13 or more vertebrae (p=0.037).¹⁰ Pseudoarthrosis can lead to deformity progression, disc space collapse, and instability of the spine.
- **Rod Failure** – Roughly 9% of rods break within 1 year of implantation.¹¹
- **Proximal Junction Kyphosis (PJK)** – PJK is the development of pathological kyphosis above a long-segment spinal instrumentation. PJK can disrupt sagittal alignment and reduce spinal stability.¹² PJK can be observed as early as 2 months postoperatively with roughly 66% of cases identified within 3 months.^{13,14}
- **Flat-Back Syndrome** – This results from an insufficient correction of lumbar lordosis, which leaves the patient leaning forward and unable to stand up straight.
- **Neurological Injury** – This occurs in less than 5% of spinal deformity surgeries. Risk factors for neurological deficits include use of a combined anterior and posterior approach, rigid deformities, and hyperkyphosis.¹⁵
- **Pulmonary Problems** – Complications relating to pulmonary function are a common cause of morbidity following spinal fusion surgery. Postoperative chest radiographs in as many as 64% of patients show abnormalities, such as pleural effusion, partial lung collapse, or infiltrates.¹⁶

⁶ Baron, EM and Albert, TJ, 2006. Medical complications of surgical treatment of adult spinal deformity and how to avoid them. *Spine*, 31, S106-118.

⁷ Emami, A, et al., 2002. Outcome and complications of long fusions to the sacrum in adult spine deformity: luque-galveston, combined iliac and sacral screws, and sacral fixation. *Spine*, 27, pp776-786.

⁸ Yadla, S, et al., 2010. Adult scoliosis surgery outcomes: a systematic review. *Neurosurgery Focus*, 28, e3.

⁹ Moal, B, et al., 2014. Radiographic Outcomes of Adult Spinal Deformity Correction: A Critical Analysis of Variability and Failures Across Deformity Patterns. *Spine Deformity*, 2(3), pp219-225.

¹⁰ Kim, YJ, et al., 2006. Pseudoarthrosis in Adult Spinal Deformity Following Multisegmental Instrumentation and Arthrodesis. *Journal of Bone and Joint Surgery*, 88(4), pp721-728.

¹¹ Smith, JS, et al., 2014. Prospective multicenter assessment of risk factors for rod fracture following surgery for adult spinal deformity. *Journal of Neurosurgery: Spine*, 21(6), pp994-103.

¹² Cammarata, M, et al., 2012. Biomechanical Analysis of Proximal Junctional Kyphosis: Preliminary Results. *Research into Spinal Deformities* 8, International Research Society of Spinal Deformities, pp299.

¹³ Lau, D, et al., 2014. Proximal Junctional Kyphosis and Failure after Spinal Deformity Surgery: A Systematic Review of the Literature as a Background to Classification Development. *Spine*, 39(25), pp2093-2102.

¹⁴ Yagi, M, et al., 2012. Incidence, risk factors, and natural course of proximal junctional kyphosis: surgical outcomes review of adult idiopathic scoliosis. Minimum 5 years of follow-up. *Spine*, 37, pp1479-1489.

¹⁵ Bridwell, KH, et al., 1998. Major intraoperative neurologic deficits in pediatric and adult spinal deformity patients. Incidence and etiology at one institution. *Spine*, 23, pp324-331.

¹⁶ Baron, EM, et al., 2006. Medical Complications of Surgical Treatment of Adult Spinal Deformity and How to Avoid Them. *Spine*, 31(19 supp.), pp106-118.

Revision or salvage surgeries are follow-up procedures to correct a failed fusion procedure. A study examining 1,879 patients who underwent multilevel spinal fusion surgeries to treat a spinal deformity revealed a cumulative 4-year revision rate of 18%.¹⁷ Another study examining the long-term revision rate found that 37% of individuals undergoing fusion procedures required a revision surgery 10 years or more after the original procedure.¹⁸ Some of the situations that warrant revision surgery include implant failure, painful pseudoarthrosis, progressive deformity, flat-back syndrome, adjacent segment degeneration, vertebral body fracture, and unacceptable residual deformity. Patients with multiple comorbidities may not be suitable candidates for revision surgery, due to both the physiological strain of the operation and the higher rate of complications associated with revision surgery.

Fractures and Bony Voids

Causes and Pathogenesis. Fractures are typically caused by high-impact trauma that can result from a car accident, fall, or other forceful physical event. A range of conditions can contribute to bone weakness and increase an individual's susceptibility to bone fractures. Some of these conditions are:

- **Osteoporosis.** Osteoporosis is a bone disease characterized by low bone mass and micro-architectural deterioration of bone tissue. This skeletal erosion leads to increasingly fragile bones that are prone to fracture. One type of osteoporotic fracture is a vertebral compression fracture (VCFs), which affects a vertebral body and often requires treatment with bone grafts.
- **Cancer.** Bone is the most common site of cancer metastasis. When cancer spreads to the skeleton, osteoclasts, the cells that promote bone degradation, are stimulated by cytokines and growth factors. This results in enhanced bone resorption, which can compromise the structural integrity and cause substantial pain.¹⁹
- **Stress Fractures.** These fractures are overuse injuries that result from the bone wearing down at a faster rate than the bone creation process.²⁰
- **Bone Cysts.** Bone cysts are simply fluid-filled lesions of the bone that result from blockages in venous flow. This increases pressure and the concentration of inflammatory factors, which can contribute to pathogenic fractures.²¹

Symptoms. In the case of severe fractures, they are easily visible and identifiable. For more minor fractures, the primary symptom is pain. There may be swelling or bruising over the bone, in addition to a visible deformity. Pain generally worsens at the site of the injured area during movement or changes in pressure.

¹⁷ Glassman, SD, et al., 2015. Revision Rate After Adult Deformity Surgery. *Spine Deformity*, 3(2), pp199-203.

¹⁸ Frymoyer, JW, et al., 1978. Failed lumbar disc surgery requiring second operation. A long-term follow-up study. *Spine*, 3(1), pp7-11.

¹⁹ Coleman, RE, 2006. Clinical Features of Metastatic Bone Disease and Risk of Skeletal Morbidity. *Clinical Cancer Research*, 21(12), pp6243s-6249s.

²⁰ Dugan, SA, et al., 2007. Stress Fractures and Rehabilitation. *Physical Medicine and Rehabilitation Clinics of North America*, 18(3), pp401-416.

²¹ Mascarid, E, et al., 2015. Bone cysts: Unicameral and aneurysmal bone cyst. *Orthopaedics & Traumatology: Surgery & Research*, 101(supp. 1), pp119-127.

Diagnosis. Fractures can be diagnosed with visual interpretation of an X-ray, CT, or MRI scan. To detect bone disorders, a bone scintigraphy may be used as well. A bone scintigraphy is a bone scan that uses small amounts of radiotracers that give off radiation in the form of gamma rays in order to generate an image of the skeletal system.

Bone Grafts

Bone grafts are used to aid in the healing of bone fractures or deformities that are difficult to treat or fail to properly heal as well as to promote spinal fusion with the use of interbody cages. Bone grafts can accelerate the repair process, restore shape, and stabilize the fracture. Bone voids need to be filled in order to promote optimal healing. It was originally accomplished through autograft, where tissue was collected from one of the patient's non-essential bones such as the iliac crest.²² Due to issues of cost and pain at the graft site, a variety of grafting alternatives have been developed. Bone grafts aid in the formation of new bone through the following principles:²³

- **Osteogenesis** – Osteogenesis is the formation of new bone tissue by transplanted osteogenic precursor cells.²⁴
- **Osteoinduction** – Osteoinduction is the process of stimulating progenitor cells to differentiate into osteoblasts, which are cells capable of forming new bone at the graft site. Osteoinduction is mediated in part by the release of growth factors such as bone morphogenic proteins (BMP).
- **Osteoconduction** – Osteoconduction involves the formation of a scaffold on which new bone tissue can grow.²⁵

Bone grafting is utilized in most types of reconstructive orthopedic surgeries involving defects of the skeleton to promote bone repair and provide mechanical support. The available types of bone graft and their main properties are presented in **Figure 5** and discussed below. These are intended to provide treatment for bone fractures and mechanical defects.

- **Autograft** – This procedure involves harvesting healthy bone from the patient and implanting the tissue into the injured site. Typically, bone is harvested from a region of the pelvis called the iliac crest. Autograft is capable of osteoinduction, osteoconduction, and osteogenesis, making it a reliable source of bone graft.²⁶ Although there are no biocompatibility issues with autograft, it often leads to persistent donor site pain and other complications. This has reduced its use in favor of newer grafting options.

²² Sarkar, SK and Lee, BT, Hard tissue regeneration using bone substitutes: an update on innovations in materials. *Korean Journal of Internal Medicine*, 30(3), pp279-293.

²³ Khan, S and Cammisa, F, 2005. The Biology of Bone Grafting. *Journal of the American Academy of Orthopaedic Surgeons*, 13(1), pp77-86.

²⁴ Beaman, FD, et al., 2006. Bone Graft Materials and Synthetic Substitutes. *Radiologic Clinics of North America*, 44(3), pp451-461.

²⁵ Boden, S., 2002. Overview of the Biology of Lumbar Spine Fusion and Principles for Selecting a Bone Graft Substitute. *Spine*, 27(16S), ppS26-S31.

²⁶ Cypher, TJ and Grossman, JP, 1996. Biological principles of bone graft healing. *Journal of Foot and Ankle Surgery*, 35, pp413-417.

- **Allograft** – Allograft is considered to be the next best option to autograft and is typically biocompatible. In this procedure, fresh bone is harvested from a cadaver or from a patient undergoing a replacement surgery necessitating bone removal. This procedure eliminates donor site complications resulting from autograft, but introduces the risk of disease transmission.²⁷ Despite procedures to mitigate this risk, diseases can still be transmitted, including human immunodeficiency virus (HIV), hepatitis C virus (HCV), and hepatitis B virus (HBV).²⁸ Demineralized Bone Matrix (DBM) is a type of allograft that modifies the donor bone via an acid extraction process. It leaves beneficial growth factors, proteins, and collagen required for osteoinduction, while removing the cells.
- **Synthetic Bone Graft Substitutes** – An alternative to grafting real bone is the use of synthetic bone graft substitutes. Synthetics eliminate many of the complications associated with autograft and allograft, including issues of donor morbidity, disease transmission, and supply limits.²⁹ The synthetics category can be divided into three groups:
 - **Ceramics** – This category includes grafts made out of a variety of materials, such as hydroxyapatite (HA), tricalcium phosphate (TCP), calcium phosphate, and glass ceramics. Ceramics are biocompatible, osteoconductive, and in some cases osteogenic. However, ceramic grafts have minimal osteoinductive properties.³⁰
 - **Polymers** – The polymers used for bone grafting are either natural or synthetic, both of which are osteoconductive, osteogenic, and biocompatible. Natural polymers are known to undergo bioresorption but are not osteoinductive. Two common natural polymers are collagen and fibrin. Synthetic polymers can be engineered to achieve a variety of properties, including osteoinduction in some cases. Examples of synthetic polymers include poly-glycolic acid (PGA) and poly-lactic acid (PLA). Despite many advantages of polymer-based grafts, most lack mechanical strength and osteoinductive properties.³¹
 - **Composites** – Composite grafts utilize the combination of multiple bone graft options, creating a full spectrum of ways to customize bone grafts. The main goal of this application is to maximize osteogenesis, osteoinduction, and osteoconduction. Key factors used with this approach are bone morphogenic proteins (BMPs), insulin-like growth factors (IGFs), transforming growth factors (TGFs), and stem cells.
- **Cell-based matrices** – Cell-based matrices (CBMs) are allografts seeded with live mesenchymal stem cells (MSCs). MSCs are used in bone grafts because they are able to differentiate into osteoblast cells and contribute to the production of bone. Available CBMs contain MSCs and demineralized bone derived from cadavers, which are harvested within 72 hours of death and cryogenically frozen. There is limited evidence that the MSCs can survive the transplantation process and it is a relatively expensive bone grafting option.³²

²⁷ Faour, O., Dimitriou, R., et al., 2011. The use of bone graft substitutes in large cancellous voids: Any specific needs? *Injury*, 42(2), ppS87-S90.

²⁸ Ng, VY, 2012. Risk of Disease Transmission With Bone Allograft. *Orthopedics*, 35(8), pp679-681.

²⁹ Lind, M and Bunger, C, 2001. Factors stimulating bone formation. *European Spine Journal*, 10(2), ppS102-9.

³⁰ Beaman, FD, et al., 2006. Bone Graft Materials and Synthetic Substitutes. *Radiologic Clinics of North America*, 44(3), pp451-461.

³¹ Garcia-Gareta, E, et al., 2015. Osteoinduction of bone grafting materials for bone repair and regeneration. *Bone*, 58756-3282(15), pp279-283.

³² Skovrlj, B, et al., 2014. Cellular bone matrices: viable stem cell-containing bone graft substitutes. *The Spine Journal*, 14(11), pp2763-72.

Figure 5. Properties of Available Bone Graft Solutions

Graft Type	Osteogenesis	Osteoconductivity	Osteoinductivity	Biocompatibility
Autograft	✓	✓	✓	✓
Allograft	Some	✓	✓	Variable
DMB	Requires Bone	✓	✓	✓
Ceramics	Some	✓	Minimal	✓
Natural Polymers	✓	✓	–	✓
Synthetic Polymers	Minimal	✓	Minimal	✓
Supplemental Factors	✓	–	✓	✓

Source: LifeSci Capital

Market Information

Spinal Fusion Epidemiology

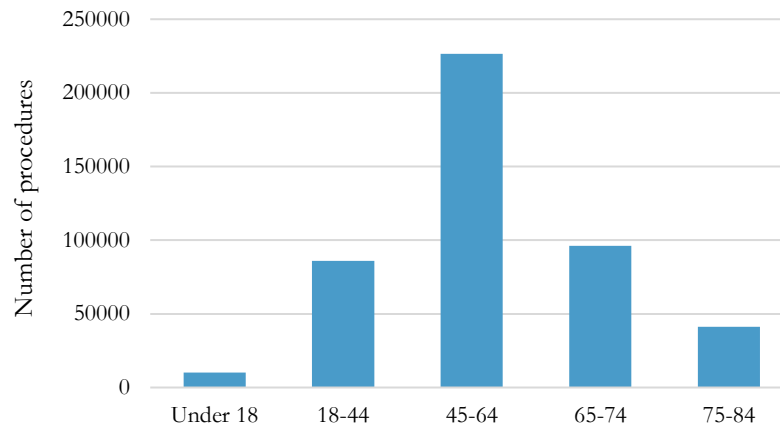
Spinal deformities affect as much as 32% of the adult population and over 60% of the elderly population.^{33,34} In 2015, there were roughly 488,000 spinal fusion procedures performed in the US including roughly 356,000 thoracolumbar spinal fusion surgeries. Use of spinal fusion surgeries has grown at a faster rate than the use of other common inpatient procedures. **Figure 6** highlights data from the Centers for Disease Control and Prevention (CDC) on the age distribution of patients undergoing spinal fusion surgery. The procedure is most commonly performed on individuals aged 45-64. As of 2008, roughly 30% of spinal fusion surgeries were covered by Medicare and 52% were paid for by private insurance.³⁵

³³ Schwab, F, et al., 2005. Adult scoliosis: prevalence, SF- 36, and nutritional parameters in an elderly volunteer population. *Spine*, 30, pp1082-1085.

³⁴ Schwab, FJ, et al., 2008. Predicting outcome and complications in the surgical treatment of adult scoliosis. *Spine*, 33, pp2243.

³⁵ Rajaei, SS, et al., 2012. Spinal Fusion in the United States: Analysis of Trends from 1998 to 2008. *Spine*, 37(1), pp67-76.

Figure 6. Age Distribution of Spinal Fusion Surgeries



Source: Centers for Disease Control and Prevention

Fractures Epidemiology

The estimated number of fractures in men and woman aged 40 years or more in 2000 was 1,406,000 in the US and 3,119,000 in the EU.³⁶ Fragility fractures were estimated to exceed 2 million in 2005, with total costs exceeding \$17 billion.³⁷ Between 1998 and 2008, the annual number of spinal fusion discharges increased by 137% from 174,223 to 413,171. The national bill for spinal fusion increased 7.9-fold.³⁸ In Europe, the incidence rate of spinal fusion increased from 11.5 to 18.5 per 100,000 people per year between 2001 and 2006, and was above 20 per 100,000 people per year in the last 4 years. In the same period, the patients' mean age increased from 48.1 to 55.9 years. These statistics suggest that as the population ages, the number of people requiring surgical interventions for the treatments of fractures. This growing market emphasizes the importance of having better and more efficient bone graft substitutes to fill bone voids. In particular, the broad label in Europe should facilitate greater uptake than in the US, where the labeling is specific to spinal fusion surgeries.

Market Size

Worldwide, bone graft substitutes are used in roughly 900,000 orthopedic procedures each year. Kuros can compete in the two largest segments of the bone graft market: *MagnetOs* may take market share within the synthetics category, while the company's other product, KUR-113, a fibrin/PTH combination described later in this report, could compete with the growth-factor based products. Both products may also simply provide an alternative to autograft for some patients. Sales of *MagnetOs* are likely to grow slowly in the first few years as the company rolls out their selective launch mainly to KOLs in the spine space.

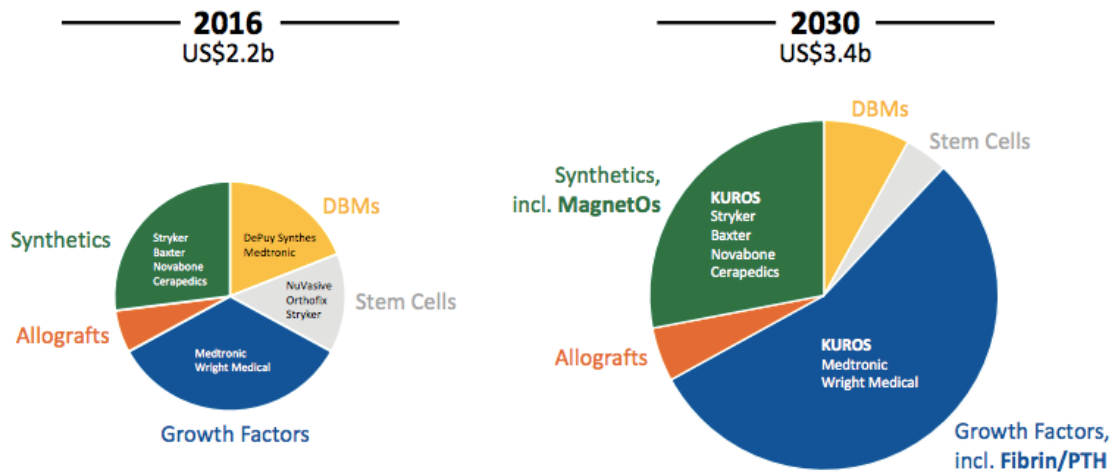
³⁶ International Osteoporosis Foundation

³⁷ Ensrud, KE, 2013. Epidemiology of fracture risk with advancing age. *J Gerontol A Biol Sci Med Sci*, 68(10), pp1236-1242.

³⁸ Rajaei, SS, et al., 2012. Spinal fusion in the United States: analysis of trends from 1998 to 2008. *Spine*, 37(1), pp67-76.

Kuros expects that the orthobiologics market is projected to reach a value of over \$3.4 billion by 2030 (**Figure 7**). The forecasted growth in the spine market could provide a major tailwind for the company as it tries to capitalize on its products' unique properties. It should be noted that this is already a fairly crowded space and so product differentiation (and educating the community of such) will be key to driving sales. However, there remains a medical need for autograft alternatives, so showing comparable results to autograft is likely sufficient to gain meaningful market share. Positive results from Kuros' post-marketing study could provide upside potential.

Figure 7. Rapidly Growing Orthobiologics Market

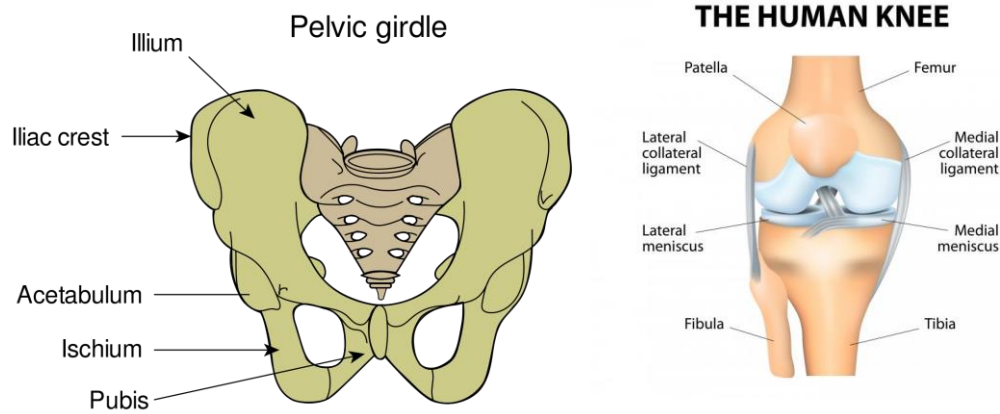


Source: Kuros Biosciences

Preclinical Studies

Preclinical results have demonstrated that *MagnetOs* shows comparable fusion rates to autologous bone graft (ABG), the “gold standard,” in sheep. In this study, a posterolateral spinal fusion surgery was performed. Results were evaluated 6, 12, and 26 weeks after surgery, showing that the BCP material was comparable to the gold standard autograft. Spinal PLF surgery was performed on 24 Merion sheep at L2-3 and L4-5 spinal levels. Autologous bone graft was collected from the distal femur and iliac crest. Following this, decortication, a procedure of removing the membrane of an organ, of the transverse processes (TP) was done. Ideal levels at 10 cc (cubic centimeters) of graft material (ABT, BCP granules, and BCP putty) were implanted in the posterolateral regions of each side, including the inter-transverse process space. The sheep were sacrificed after 6, 12, and 26 weeks.

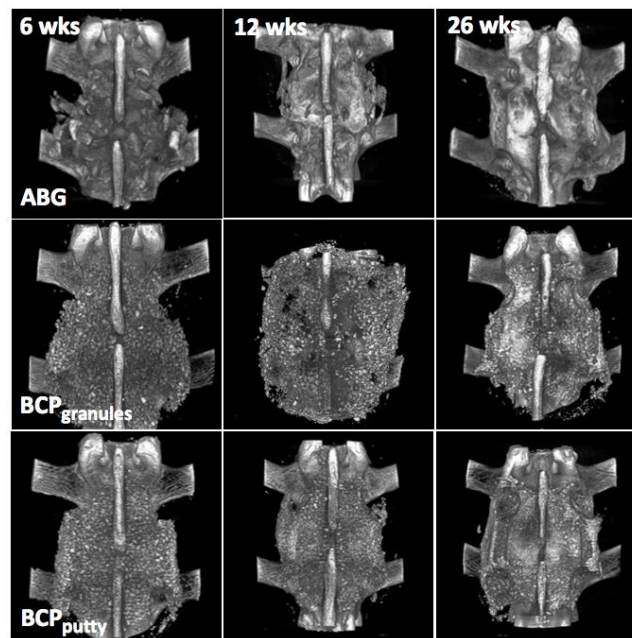
Figure 8. Depictions of the Iliac Crest and Distal Femur



Source: LifeSci Capital

All animals recovered with no adverse events. The various studies show comparable results between *MagnetOs* and the gold standard autograft. Firstly, through micro-CT scanning, it was shown that all graft material remained in the implantation areas, with a progression of solid fusion mass overtime. As shown in **Figure 9**, all grafting materials were well-contained at the implantation sites, with progression of a solid fusion mass over time.

Figure 9. Micro-CT Reconstructions of Levels Treated with ABG (top), BCP granules (middle), and BCP Putty (bottom) from 6 to 26 weeks



Source: LifeSci Capital

Fusion analysis via manual palpation showed a 100% fusion rate for each group from week 12 onwards (**Table 10**).

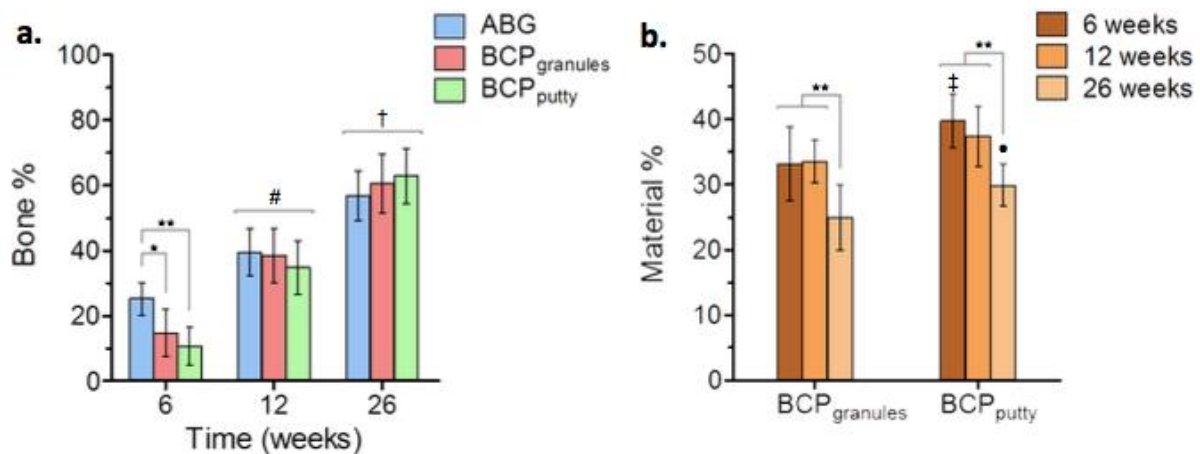
Table 10. Fusion Analysis via Manual Palpation

	6 weeks	12 weeks	26 weeks
ABG	3/5	6/6	5/5
BCP _{granules}	1/5	6/6	5/5
BCP _{putty}	1/5	6/6	5/5
p value*	0.50	0.99	0.99

Source: Kuros Biosciences

There were no significant differences in fusion rates determined between treatments. By histomorphometry, bone progression in the fusion mass displayed equivalent outcomes by treatments from week 12 forward (**Figure 11a**). After 26 weeks, bone proportion in the fusion mass had reached $56.8 \pm 7.6\%$, $60.6 \pm 9\%$ and $62.8 \pm 8.4\%$ for ABG, BCP granules, and BCP putty, respectively. Resorption of BCD was proven by the decrease of material proportion (**Figure 11b**).

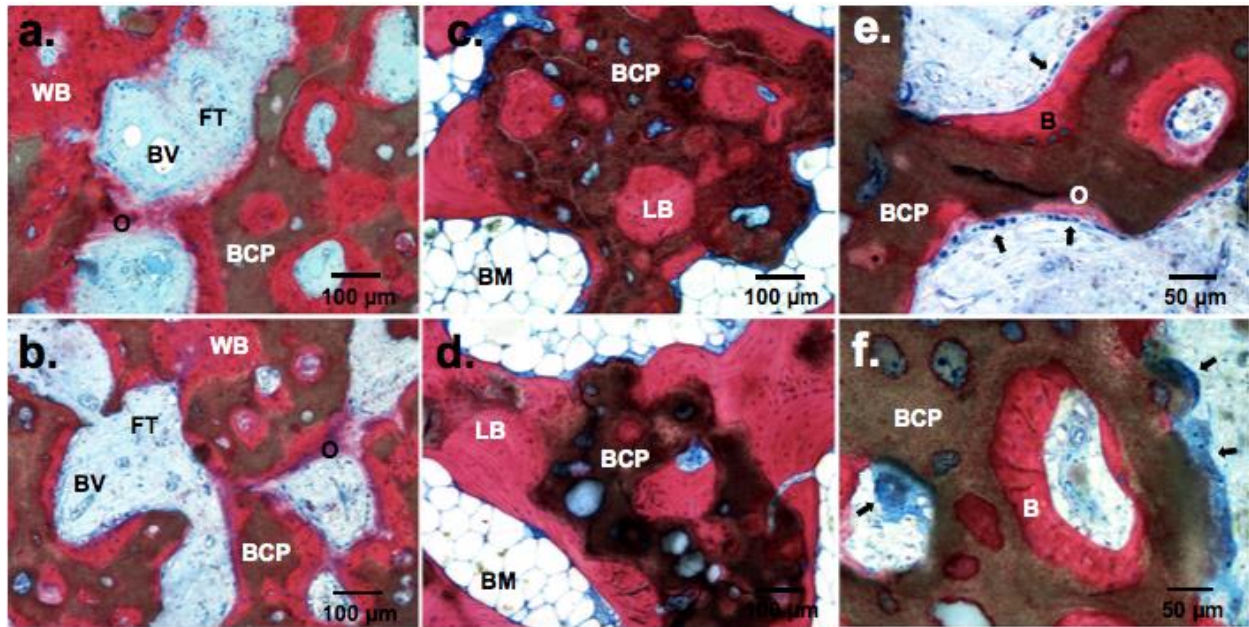
Figure 11. Histomorphometry results of bone tissue (a) and ceramic material (b) in fusion mass



Source: Kuros Biosciences

Histological data showed normal bone morphology and maturation in all groups (**Figure 12**). This shows the progression and maturation of bone tissue from week 6 (a,b) to week 26 (c,d). Osteoblasts deposited bone on the surface of material (e, arrows) and large multinucleated cells were observed resorbing the material (f, arrows).

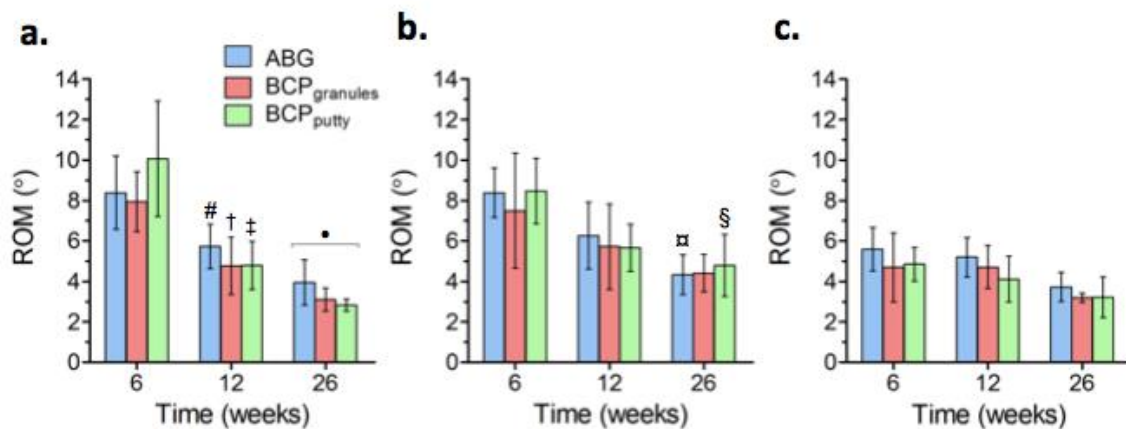
Figure 12. Histology data of progression of bone tissue for BCP granules (a,c) and BCP putty (b,d)



Source: Kuros Biosciences

Biomechanical analysis showed that the range of motion in lateral bending, axial rotation, and flexion-extension were the same at all times (**Figure 13**). The Company observed a statistically significant effect for lateral bending and flexion-extension ($p < 0.05$). The histological results also showed fusion rates of 75%, 92%, and 83% after 12 weeks for ABG, BCP granules, and BCP putty, respectively.

Figure 13. Range of Motion Following Treatment with ABG (a), BPC Granules (b), and BCP Putty (c)



Source: Kuros Biosciences

Clinical Trials Discussion

As of late May 2018, clinical trials have begun for *MagnetOs* granules for maxillary sinus floor elevation with a two-stage implant placement. This dental procedure aims to increase the amount of bone in the posterior maxilla, and is performed when the floor of the sinus is too close to an area where dental implants are to be inserted. The research is being conducted at the University Medical Center (UMC) Utrecht. It will compare *MagnetOs* granules to the gold standard autograft in a controlled open-label, randomized non-inferiority trial with 30 patients. The primary outcome is analysis of the product's effectiveness 4-6 months post-operation. The first patients have been treated.

In June 2018, Kuros announced the start of a new investigator-led randomized controlled trial of *MagnetOs* to study spinal fusion. The primary objective is to demonstrate non-inferiority of *MagnetOs* compared to the current gold standard autograft in instrumented posterolateral spinal fusion. Patients served as their own control with autograft implanted on one side and *MagnetOs* implanted on the other side. The first patients are expected to be enrolled in H2 2018.

Competitive Landscape

Resorption Rate and Injectability are Important Differentiating Factors in the Bone Graft Substitute Market.

Injectable formulations allow bone void filler to contour to the shape of the bone defect. This maximizes the contact between the implant and the endogenous bone tissue to ensure high levels of osteoblast infiltration and rapid bone remodeling. Properly filled voids also fix the bone in place, which promotes bone healing and reduces pain induced from bone instability. Many bone graft substitutes are resorbed at a faster rate than bone remodeling, which results in instability and can complicate treatment. Resorption rates that exceed the rate of bone remodeling can also lead to the formation of fibrous tissue, contributing to the permanence of the bone irregularity. Kuros Biosciences' *MagnetOs* provides mechanical strength until the bone is fully remodeled. In addition, *MagnetOs* has a unique surface topology composed of calcium phosphate that is osteoinductive.

Declining Market Share for Medtronic's *InFuse* May Provide an Opportunity for Alternatives. In 2014, Medtronic (NYSE: MDT) led the bone graft substitute market with a 20% share. This position was largely driven by the company's *InFuse* product, which is a demineralized bone matrix (DMB) containing the bone growth factor recombinant human bone morphogenetic protein-2 (rhBMP-2). Sales of *InFuse*, which account for a substantial portion of sales for the Medtronic's spinal segment, have been declining at an accelerated pace following published reports on a range of serious side effects. These treatment-related side effects include cancer, sterility in men, infections, bone dissolution, and worsening leg or back pain. In light of these recent findings, patients and physicians are likely to gravitate towards safer alternatives. Medtronic is likely to further cede market share to other companies manufacturing bone graft substitutes that have better safety profiles.

Aging Population to Drive Growth in Use of Bone Grafts. Increased utilization of surgical options by the elderly population is likely to expand the market for bone graft products. By 2020, the Centers for Disease Control and Prevention (CDC) estimate that the population of people 65 years or older will reach nearly 55 million in the US, representing 16% growth over the next 5 years. As life expectancy increases and morbidity and disability rates decrease, the elderly are remaining active into later years of their lives and may remain eligible for and more likely to utilize

surgical options than in previous decades.³⁹ This also reflects improvements in surgical procedures and postoperative care that make invasive surgeries more feasible in an aging population. Surgical procedures may include spinal fusion procedures, treatment of osteoporotic fragility fractures, and joint reconstructive surgeries, which have been important drivers of growth for the use of bone graft products.

MagnetOs is substantially equivalent in design and indications to many of the following marketed predicate devices. Each product discussed below has almost the same intended use, product classification, product code, design, structure, site of application, composite materials, and mechanism of action. The limited differences in the products lie in total porosity and the ratio of beta-tricalcium phosphate and hydroxyapatite. Another key distinguisher between *MagnetOs* and competing products is its surface topography, as shown in Figure X. *MagnetOs* maximizes the body's ability to form bone by providing a scaffold with greater surface area and better shape.

Figure 14. Topography of competing bone void fillers



Source: Kuros Biosciences

Vitoss Bone Graft Substitute—Stryker Corporation (NYSE: SYK): Vitoss is the current synthetic bone graft market leader and has been used in over 425,000 implantations worldwide.⁴⁰ It has demonstrated efficacy and safety in multiple prospective and peer-reviewed human clinical studies. Similar to *MagnetOs*, Vitoss is intended to fill bone voids and gaps in the skeletal system, specifically at the pelvis or posterolateral spine. Additional forms of Vitoss were launched in 2012, including Vitoss BBTrauma, which is sole exclusively for trauma surgery due to its greater specific surface area of bioactive glass. Vitoss has an open, interconnected structure that facilitates bone regeneration. It is made up of highly porous calcium phosphate that is up to 90% porous, a property that leads to higher bone fusion rates. Silicon, sodium, and calcium ions of the bioactive glass are released into the surrounding environment to react with body fluids when Vitoss is implanted *in vivo*. This reaction attracts osteoblasts to create a matrix with osteostimulative effects. Vitoss is composed of beta-tricalcium phosphate and resorbs during the natural remodeling process of bone, much like *MagnetOs* does. According to Kuros Biosciences, Vitoss differs from *MagnetOs* in that Vitoss gives rise to fibrous tissue while *MagnetOs* generates a greater amount of new bone tissue in preclinical studies.

Actifuse Bone Graft Substitute—Baxter International Inc (NYSE: BAX): Actifuse is a bio-stimulative scaffold bone graft substitute comprised of silicate substituted calcium phosphate intended to close gaps in the skeletal system that are not intrinsic to the stability of bony structure. Actifuse has shown similar bone fusion rates in comparison to the gold standard care of iliac crest autografts. Actifuse is versatile and resistant to irrigation. It is composed of 0.8% silicon, which has been shown to successfully accelerate bone formation in both preclinical and

³⁹ Cutler, DM, et al., 2013. Evidence for Significant Compression of Morbidity in the Elderly US Population. *National Bureau of Economic Research Working Paper Series*, July 2013, <http://www.nber.org/papers/w19268>.

⁴⁰ Stryker Orthobiologics Internal Sales Data, April 2012.

clinical studies. Implantation of Actifuse at the bone site results in the releases of ion that leads to a resultant negative charge at the graft site. This process increases the rate of cell attachment proteins that are adsorbed into the graft. The high concentration of proteins further accelerates bone formation as osteoblasts and osteoclasts are stimulated infiltrate into the graft material and remodel the tissue.

chronOS Bone Void Filler—Depuy Synthes Institute of Johnson & Johnson (NYSE: JNJ): chronOS granules and preforms are synthetic, porous, osteoconductive, resorbable calcium phosphate bone substitutes that can replace autologous bone harvesting. chronOS granules consist of a radiopaque material, beta-tricalcium phosphate. This material contains both calcium and phosphorous. chronOS bone void fillers have been used clinically in Europe for over 20 years. It is replaced with bone in 6 to 18 months. The compressive strength of the product is approximately that of human cancellous bone. chronOS can be used in bony voids or caps that are not intrinsic to the stability of the bony structure. The product is biocompatible, resorbable, porous, osteoconductive, and improves regeneration with its macropores and micropores that serve as cell scaffolding.

CERAMENT—Zimmer Biomet (NYSE: ZBH): CERAMENT is an injectable synthetic bone graft substitute combining hydroxyapatite and calcium sulfate with a radiopacity enhancing agent. The composition includes 40% hydroxyapatite and 60% calcium sulfate, in addition to the liquid radiopacity enhancing component containing iohexol. The material is injected into cavities or drill holes through narrow-gauge needles and enhances direct contact between an implant and original bone. The matrix creates an osteoconductive framework that allows for new bone formation.

CuriOs—Progentix Orthobiology B.V.: CuriOs is a synthetic, osteoconductive micro-structured calcium phosphate resorbable bone void filler or autologous bone graft extender used for the repair of bone defects and gaps. It is comprised of a beta-tricalcium phosphate and hydroxyapatite and resembles human spongy bone. Once resorbed, the site is replaced by bone and soft tissue during the natural healing process. This allows for the treatment of surgically created or trauma-induced osseous defects. The product can be used in conjunction with other fixation devices. Progentix Orthobiology received FDA approval for this product in 2009.

OsSatura BCP—IsoTis N.V.: OsSatura BCP is a biphasic calcium phosphate, osteoconductive, bio-stable bone graft substitute with interconnected porosity. It mimics the structure of natural spongy bone, degrades in stages, and is made up of 80% hydroxyapatite and 20% beta-tricalcium phosphate. The slower degrading, porous hydroxyapatite provides long-term support and recruits endogenous bone morphogenetic proteins that convert stem cells into bone-forming cells while the faster degrading beta-tricalcium phosphate re-precipitate.

MBCP Granules—Biomatlante. MBCP is a biphasic calcium phosphate synthetic bone graft substitute with micro- and macro-porous structure that resembles human bone. It consists of 60% hydroxyapatite and 40% beta-tricalcium phosphate. MBCP promotes new bone formation through the release of calcium and phosphate ions while dissolving. It is intended to serve as a bone void filler in gaps that are not intrinsic to stability of the structure and specifically for femoral or tibial osteotomies. The product received both FDA approval and CE marking.

This pilot study was conducted to evaluate MBCP performance in safety and efficacy in bone regeneration after osteonecrosis biopsy of the femur head.⁴¹ This non-randomized, single group assignment, open label trial was conducted among 12 patients who underwent osteonecrosis biopsy of the femur head in order to evaluate the safety and efficacy of MBCP. The primary outcome measures were the occurrence of adverse events in addition to infection

⁴¹ <https://clinicaltrials.gov/ct2/show/NCT00289575>

and inflammation of the drilled area. Secondary outcome measurements included pain and function, in addition to bone reconstruction that was evaluated with a scanner and radiography during a one-year follow-up.

Attrax Putty—NuVasive (Nasdaq: NUVA): Attrax Putty is a synthetic, osteoconductive bone void filler comprised of calcium phosphate granules and hydroxyapatite with an advanced bio-dissolvable polymer carrier. Its unique, biotextured surface provides an instructive environment for mesenchymal stem cells to differentiate into bone-forming osteoblasts. Attrax granules are combined with Alkylene Oxide Copolymer, a polymeric blend, which provides intraoperative flexibility.

The first ongoing (2015 to July 2018) clinical trial is being conducted to demonstrate the non-inferiority of Attrax Putty as a bone graft substitute for autograft in instrumented posterolateral fusion of the thoracolumbar spine.⁴² The randomized, double blind, controlled trial was conducted with 100 participants who underwent spinal fusion. The control group underwent autograft, while the experimental group received 8-10 cc of Attrax Putty. The primary outcome measurements were the posterior spinal fusion rate after one year, assessed via CT-scans. Secondary outcome measures included resorption characteristics during the first year, the volume of bridging bone mass, pain scale, and posterior spinal fusion rate after two years. The second ongoing clinical trial (closing July 2020) compares Attrax Putty to autograft in extreme lateral interbody fusion (XLIF).⁴³ This trial enrolled 70 participants. The primary outcome measurement was the number and percentage of subjects with radiographically apparent fusion in 24 months. The secondary outcome measurements included the rate of complications attributed to the use of Attrax, the change in self-reported pain, and clinical outcome scores from pre-operation through 24 months.

KUR-113: A Fibrin/PTH-Based Orthobiologic for Use in Spinal Fusion Procedures

Kuros is also developing KUR-113, which contains fibrin/parathyroid hormone peptide (PTH), as a readily injectable orthobiologic product that can be used in spinal fusion surgeries and in treating certain types of fractures. KUR-113 is composed of a variant of parathyroid hormone (vPTH) and a fibrin sealant, which provides for slow, controlled release of vPTH over time. PTH is the active ingredient in Eli Lilly's *Forteo* (teriparatide). The fibrin matrix also plays a role in bone healing by providing a physical scaffold for cell ingrowth. There is potential to use the underlying technology to encapsulate a wide range of other biologics, such as transforming growth factor-beta 1 (TGF-b), platelet derived growth factor (PDGF), and bone morphogenetic protein (BMP).

While the Company is presently focused on use of the product for spinal fusion procedures, there are many other applications that could be pursued down the road and the Company has previously conducted trials in tibial fractures, which will likely accelerate the development timeline for this product. The Company previously reported positive results with KUR-113 from an open-label Phase IIb clinical trial in 200 patients with open tibial shaft fractures. The primary endpoint of the study was the proportion of patients healed at 6 months after surgery, comparing KUR-113 in combination with standard of care (SOC) to SOC alone. In the intent-to-treat (ITT) population, the healing rate at 6 months after surgery, as assessed using radiographic and clinical criteria, was 65% for patients treated with SOC alone versus 76%, 80%, and 69% for the 0.133, 0.4, and 1.0 mg/mL of KUR-113 groups respectively. In the per-protocol (PP) population, the healing rates were 63% in the SOC alone group versus 74%, 83%, and 75% for the 0.133, 0.4, and 1.0 mg/mL KUR-113 groups respectively. For both analyses, the 0.4 mg/mL group had significantly

⁴² <https://clinicaltrials.gov/ct2/show/NCT01982045>

⁴³ <https://clinicaltrials.gov/ct2/show/NCT02250248>

better healing than the SOC-only group. The Company plans to launch a Phase II study in spinal fusion patients in 2019. Kuros expects for a Phase III launch in 2021, and a regulatory filing in early 2024. There is a pressing need in the market for safe and effective bone graft products containing growth factors, and this product is well-positioned to fill this need. A commercial launch for KUR-113 down the road would likely benefit from the commercial infrastructure built for *MagnetOs*.

Mechanism of Action

Fibrin is a natural biomaterial and a structural component of blood clots. It acts as a healing matrix, promotes tissue repair, and restores tissue function. Fibrin is formed when soluble precursor fibrinogen molecules naturally polymerize into a solid, degradable matrix. The mechanism of coagulation includes the activation, adhesion, and aggregation of a variety of blood factors followed by the deposition and maturation of fibrin. The process is triggered when tissue factor, a membrane protein abundantly present in cells surrounding blood vessels, binds to factors in the blood that activate the prothrombin protein, which activates thrombin. Finally, thrombin activates factor XIII.⁴⁴ Activated factor XIII (FXIIIa) is a transglutaminase enzyme responsible for stabilizing the clot via covalent cross-linking of fibrin. The absence or decreased hereditary expression of factor VIIIa is evident in cases of hemophilia, a condition in which the ability of blood to clot is significantly reduced.

Fibrin sealants without biologics have been used commercially for more than 30 years, primarily for the prevention of blood loss during surgical procedures. As a result, biocompatible and biodegradable fibrin sealants have a generally well-documented safety profile and are the most effective tissue adhesives currently available. Fibrin sealants are made up of purified, virus-inactivated human fibrinogen, human thrombin, and occasionally other added components, such as virus-inactivated human factor XIII.⁴⁵ These components mimic the final steps of the coagulation cascade described above that ultimately form a fibrin clot.

Kuros Biosciences' unique TG-Hook technology builds on the last step of the blood coagulation cascade. The Company's key proprietary technology allows biologics such as growth factors to covalently link to fibrin-based biomaterials and for the biologics to naturally be released by endogenous enzymes into the tissue. Through this technology, the biologics become integral parts of the biomaterial. The TG-hook mechanism exploits FXIIIa transglutaminase activity that cross-links fibrin molecules to form a blood clot. Because the polymer is made up of all-natural materials, it biodegrades over time and leaves healed tissue. The material solidifies and cross-links *in situ* to match the shape of the area to which it is administered, which allows for injections into smaller, more complex injuries and access sites such as fine fractures and minimally invasive spinal procedures.

KUR-113 is composed of fibrin supplemented with a growth factor (PTH). The biologic has been designed to only be active when it is cleaved through the activation of the endogenous protease plasmin by infiltrating cells. In this way, the material is effective in responding to the local healing environment, becomes locally available, and improves the healing process.

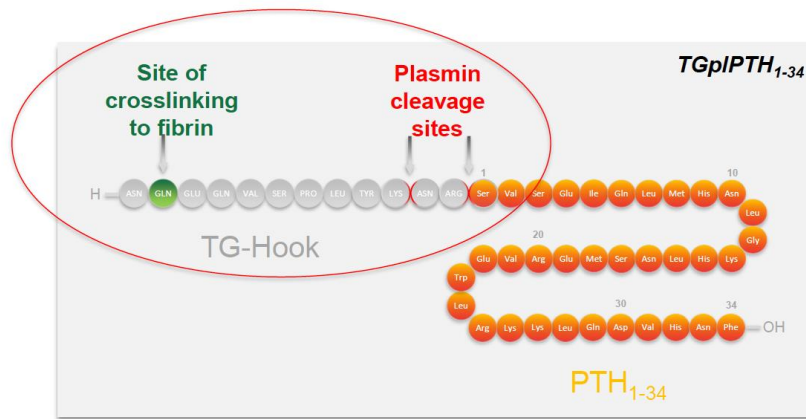
Figure 15 shows the PTH growth factor variant containing a TG-Hook. The TG-hook contains a transglutaminase substrate which allows for FXIIIa mediated crosslinking to fibrin. In addition the TG-hook contains plasmin cleavage sites which allow for enzymatic PTH release, for example by cellular activation of plasmin. KUR113 uses a biologically

⁴⁴ Dahlback, PJ, 2000. Blood coagulation. *The Lancet*, 355(9215), pp1627-1632.

⁴⁵ Jackson, MR, 2001. Fibrin sealants in surgical practice: an overview. *Am J Surg*, 182(2), pp1-7.

active fragment of PTH which upon local release promotes bone regeneration by acting directly on pre-osteoblasts and osteoblasts. Fibrinogen possesses distinct proteolytic cleavage sites for plasmin, which give rise to fibrin fragments.

Figure 15. Amino Acid Sequence of PTH Growth Factor Variant Containing a TG-Hook



Source: Kuros Biosciences

Preclinical Data

In a preclinical study, 32 sheep underwent spinal fusions and were then treated with either an autograft, 0.45 mg/mL of the bone growth factor BMP-2, or 0.4 mg/mL of KUR-113 prior to the operation. The bone area at the site of operation was analyzed at 4 months and 10 months to compare fusion rates via CT scans, and quantify the amount of bone generation that occurred over the course of the healing process. While both treatments resulted in a 100% fusion rate, the bone area was found to be greatest (54%) in animals treated with KUR-113 compared to those treated with a traditional autograft or BMP-2. This result is shown in **Figure 16**. Further, the spine had no significant histopathological changes to the local tissue. This suggested that a technology like KUR-113 with a fibrin/PTH delivery system could be effective in promoting bone healing and regeneration.

Figure 16. Efficacy in Fibrin/PTH in Spinal Bone Healing

	% Fusion (μ CT)	% fusion (Histology)	Bone Area in Cage (net tissue %)
Autograft	100 %	100 %	48% \pm 8%
Infuse (0.45mg/ml BMP2)	100 %	100 %	43% \pm 7%
Fibrin/PTH (0.4mg/ml)	100 %	100 %	54% \pm 7%

Source: Kuros Biosciences

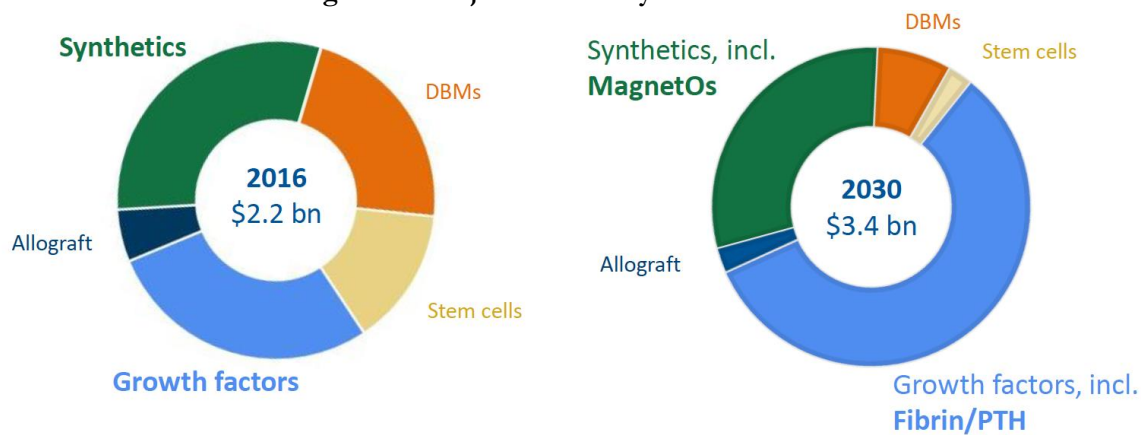
Market Information

Market Size

Growth factors and synthetics currently comprise a growing market. In 2016, there was a total of \$2.2 billion in sales and the sales may grow up to \$3.4 billion by 2030, expanding at a rate of 2.4% per year. Kuros' orthobiologics/PTH platform may be able to garner a significant portion of this growth factor market because of the product candidates' superiority in safety.¹⁰ By 2030, the Company expects that *MagnetOs* and fibrin/PTH technology platforms will be the gold standard in their respective segments. This market projection and distribution is shown in **Figure 17**.

In the indication of bone fractures, the increasingly elderly population in the US and the EU as well means that the prevalence of individuals more susceptible to fractures as a whole may be increasing as well. Given that the US population is approximately 325 million, that the incidence of tibial plateau fractures is 10.3 per 100,000, and that the incidence of tibial shaft fractures is 16.9 per 100,000, KUR-111 and KUR-113 are projected to service approximately 33,300 individuals and 50,000 individuals in the US, respectively. While this is not a significant market size, the lack of competitors working on products that combine fibrin with growth factors suggests that the Company may be able to garner a significant portion of the market if its products meets endpoints in future pivotal Phase III trials. Current competitors in the market produce BMP-2 and BMP-7, two growth factors that have been linked to unwanted ectopic bone growth. If the Company can show that its fibrin/PTH technology is not susceptible to this side effect, then it will demonstrate a stronger safety profile than current options on the market.

Figure 17. Projected Bone Synthetics Market



Source: Decision Resources (Millennium Research Group) and Kuros estimate

Clinical Data Discussion

Phase II Trial in Open Tibial Shaft Fractures

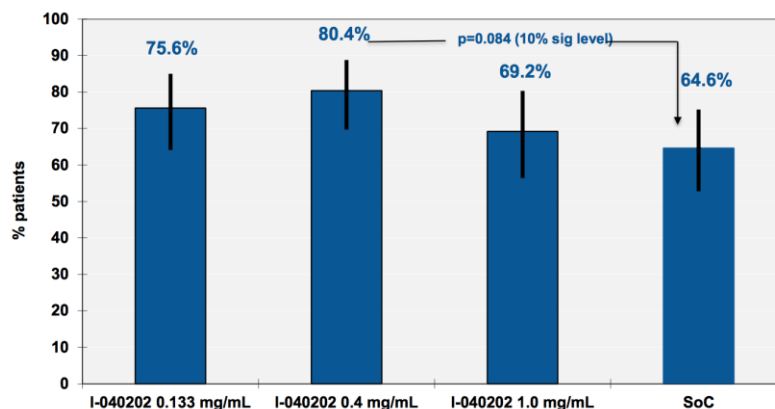
Kuros successfully completed a Phase IIb trial evaluating KUR-113 in 200 patients with open acute tibial shaft fractures. The trial met its primary endpoint of demonstrating a higher healing rate of 80.4% for the 0.4 mg/ml group compared to 64.6% for standard-of-care, at 6 months after surgery as assessed by investigators using radiographic and clinical criteria. KUR-113 also lowered the rate of repeat surgeries. In addition, no safety issues were seen. Moreover,

Kuros has also completed preclinical development in spinal fusion surgery with efficacy similar to current treatment options, and the Company plans to begin Phase II trials for this indication in 2019.

Trial Design. A randomized, controlled, open-label (dose-blinded) Phase II dose finding study was conducted to determine the safety and efficacy of KUR-113 in patients with open tibial shaft fractures.⁴⁶ A total of 200 patients were randomized and treated in 31 centers across Europe. Results from three groups receiving three doses of KUR-113 (0.133, 0.4, or 1.0 mg/ml) in combination with standard of care (SOC) were compared to those who had received SOC alone. The primary endpoint of the study was the proportion of patients healed at 6 months post-operation between the two groups.⁴⁷

Trial Results. Treatment with KUR-113 resulted in healing rates of 69.2-80% across the three doses, compared with a healing rate of 64.6% in the SOC-only cohort. A summary of results is shown in **Figure 18**. There were no safety issues in the trial. The primary endpoint of this trial was the proportion of patients healed six months after surgical treatment by clinical assessment. In the intent-to-treat (ITT) population, the healing rate at six months, analyzed via radiographic and clinical criteria, was 64.6% for patients treated with SOC alone versus 75.6%, 80.4%, and 69.2% for the 0.133, 0.4, and 1.0 mg/mL KUR-113 groups, respectively. In the PP (per protocol) population, the healing rates were 63% in the SOC alone group versus 74%, 83%, and 75% for the 0.133, 0.4, and 1.0 mg/mL KUR-113 groups, respectively. The results suggest that KUR-113 can improve bone healing following a tibial fracture.

Figure 18. Percentage of Fracture Healing by Treatment Type at 6 Months



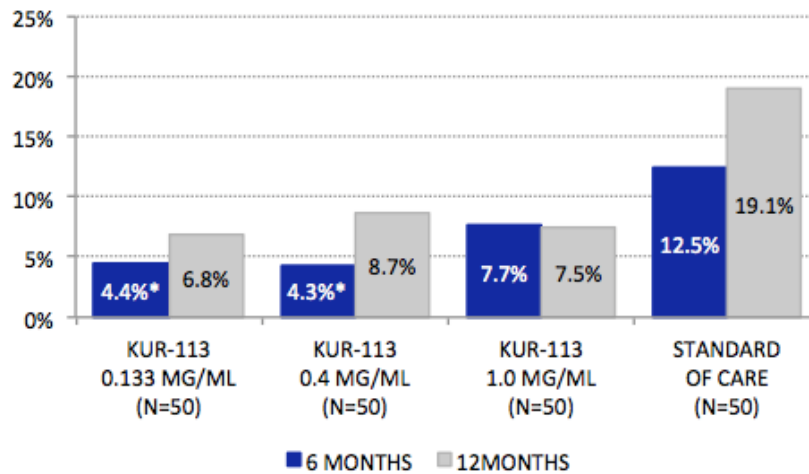
Source: Kuros Biosciences

The Phase IIb trial also reached a secondary endpoint of successfully reducing the re-operating rate, shown below in **Figure 19**. This so-called secondary intervention rate is the proportion of patients with secondary interventions (another surgery) due to persistent non-union (fracture not healing). In the low (0.133 mg/mL) and medium (0.4 mg/mL) dose cohorts of KUR-113, there was a statistically significant decrease in the secondary intervention rate (4.4% and 4.3% vs. 12.5% with standard of care) six months after surgery. While the secondary intervention rate for KUR-113-treated cohorts was numerically superior to standard of care at 12 months after surgery (6.8% and 8.7% vs. 19.1% for SOC),

⁴⁶ http://www.kuros.ch/uploads/news/id9/KUROS_n339087_v1_11_Kuros_02_TSF_PIIb_Results_6m.pdf

⁴⁷ <http://www.kuros.ch/kur-113/>

Figure 19. Percentage of Secondary Intervention by Treatment Type at 12 Months



Source: Kuros Biosciences

Phase II for Spinal Fusion

A full preclinical development program has been completed, including primates, and has been presented to the FDA. On securing sufficient funding and agreement on the final Phase III clinical trial design of KUR-113 in bone healing, the Company plans to start Phase IIb dose-finding trials in spinal fusion followed by a Phase III study. Phase IIb development will start in 2019, followed by a Phase III trial launch in 2021.

Competitive Landscape

Aging Population is Expected to Reshape the Spinal Fusion Market. By 2020, the Centers for Disease Control and Prevention (CDC) estimate that the elderly population 65 years or older will reach nearly 55 million, representing 16% growth over the next 5 years. As life expectancy increases and morbidity and disability rates decrease,⁴⁸ the elderly are remaining active into later years of their lives and may be more likely to utilize surgical options than in previous decades. New spine products and advanced surgical techniques have been developed for elderly patients with osteoporosis which may broaden the pool of eligible patients.

Medtronic's InFuse Provides an Indicator for Potential of Kuros' Product. Medtronic's (NYSE: MDT) InFuse (hBMP-2) is a growth factor that induces mesenchymal stem cell (MSC) and osteoprogenitor cell differentiation into osteoblasts. Recombinant BMP-2 (rhBMP-2) is the only highly osteoinductive bone graft that has been approved by the FDA as a substitute to autografts. rhBMP-2 has been tested in oral-maxillofacial, lumbar spine, and orthopedic trauma indications. The mechanism of action for rhBMP-2/ACS is shown in **Figure 20**.

⁴⁸ Cutler, DM, et al., 2013. Evidence for Significant Compression of Morbidity in the Elderly US Population. *National Bureau of Economic Research Working Paper Series*, July 2013, <http://www.nber.org/papers/w19268>.

Figure 20. Mechanism of Action for rhBMP-2/ACS

1	Implantation	rhBMP-2/ACS is implanted.
2	Chemotaxis	Migration of mesenchymal stem cells and other bone-forming cells to site of implantation.
3	Proliferation	rhBMP-2/ACS provides an environment where stem cells multiply prior to differentiation.
4	Differentiation	rhBMP-2 binds to specific receptors on the stem cell surface signaling them to differentiate into osteoblasts.
5	Bone formation and angiogenesis	Osteoblasts respond to local mechanical forces to produce new mineralized tissue replacing the ACS. New blood vessel formation is observed at the same time.
6	Remodeling	The body continues to remodel bone in response to local environmental and mechanical forces, resulting in normal trabecular bone.

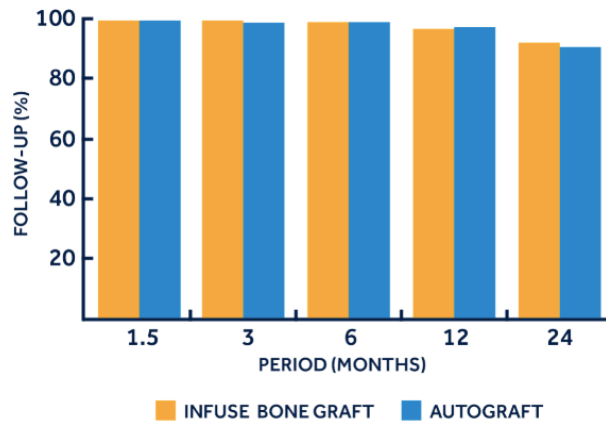
Source: LifeSci Capital

InFuse was first approved for spinal fusion surgery in 2002 and in 2004 for tibia fractures, both potential indications intended for KUR-113. *InFuse* has positive osteoconductive (animal-derived collagen), osteoinductive, and osteogenic properties thanks to its potent and targeted bone growth factor rhBMP-2 (recombinant human bone morphogenetic protein-2). This product reached sales of \$900 million in 2011, providing a good indicator for the potential uptake of Kuros' orthobiologic product, which also contains a potent bone growth factor that promotes bone repair. PTH is produced by the parathyroid glands and acts upon mesenchymal stem cells (MSC's). rhPTH (recombinant human parathyroid hormone) such as Eli Lilly's Forteo (teriparatide) has shown to increase bone mineral density in lumbar spines and femoral necks, and reduces the overall fracture risk, when used in a pulsatile fashion. KUR-113 demonstrated cell mediated bone generation in two successful Phase IIb trials.

However, the product ran into trouble surrounding Medtronic's marketing efforts and side effects that emerged with the product. Despite its safety issues, *InFuse* remains the largest-selling bone graft substitute in the market, as there is currently no other alternative. If Kuros can demonstrate that their product is both safe and effective, it may have a strong competitive advantage and be able to capture a large share of this market segment. The success of the *InFuse* product, even in spite of the safety issues seen, speaks to the demand in the market for a bone graft product that contains growth factors and the willingness among payers and physicians to incorporate this type of product into treatment.

Clinical studies have compared patients who received *InFuse* Bone Graft versus autograft for lumbar fusion procedures. The results show that *InFuse* Bone Graft heals patients with comparable success to that of autograft. Furthermore, it saves patients from pain and complications present in the bone harvesting necessary for autograft. The study included 279 patients, 136 of whom were treated with autograft via the iliac crest, and 143 of whom received the *InFuse* Bone Graft treatment. The >90% patient response rate at 24 months validates the potential of this product to be used in place of autograft.

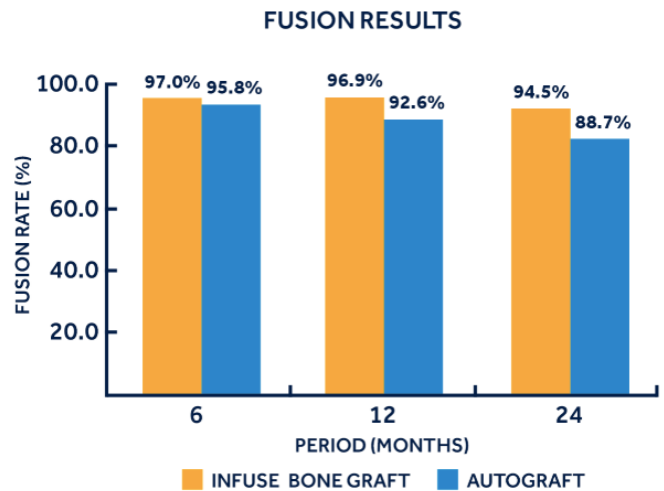
Figure 21. Patient Response Over a 24-Month Period.



Source: Medtronic

Fusion was analyzed via radiograph and CT scans with sagittal and coronal reconstruction. The results show that at 24 months, the fusion rate for patients receiving the *InFuse* Bone Graft was 94.5%, while the fusion rate for patients receiving an autograft was 88.7%. This result is shown in **Figure 22**.

Figure 22. Results of fusion via *InFuse* Bone Graft and Autograft



Source: Medtronic

Safety Issues Have Plagued Medtronic's *InFuse* Bone Graft. Studies have shown that using Medtronic's *InFuse* Bone Graft can result in adverse side effects in the body. In 2011, Dr. Eugene J. Carragee and colleagues reported that a number of Medtronic-sponsored studies failed to mention the life-threatening side effects of *InFuse*. Furthermore, it found that Medtronic-sponsored researchers were receiving \$1 to \$23 million per year in royalties and consulting fees from 1996 to 2010. In early, unpublished clinical studies, *InFuse* was shown to potentially inflame nearby tissues and bones, cause urinary problems, and stimulate cancer growth. Other side effects include: back and leg pain, radiculitis (pain spreading through spinal nerves), implant displacement, retrograde ejaculation (occurs when semen enters the bladder), male sterility, infection, osteolysis (degeneration of bone tissue), ectopic bone formation

(unwanted bone in the spinal canal), and death. Approximately 15 to 20% of patients who have received *InFuse* surgery report leg and back pain. The product was linked to a 43% higher overall complication rate than traditional bone grafts. Medtronic was accused of paying off doctors to deliberately hide the complications. Despite these reports, *InFuse* remains one of the largest-selling bone graft substitute products.⁴⁹

Other Notable Competitors

OP-1 Implant – Stryker (NYSE: SYK): OP-1, also known as BMP-7, is a pure osteoinductive growth factor specific to bone growth and formation. It recruits stem cells from surrounding tissue and initiates a bone formation cascade. OP-1 Implant is made up of bovine bone collagen and recombinant human OP-1, another growth factor.

Osteocel Plus – NuVasive (NYSE: NUVA): Osteocel Plus is an allograft cellular bone matrix containing mesenchymal stem cells (MSCs) and osteoprogenitor cells combined with demineralized bone matrix (DBM) and cancellous bone. The surgical process begins with the collection of selected donor tissue, and results in a cellular allograft to retain its native bone-forming cells. Cell-rich cancellous bone is also processed to selectively rid it of immunogenic components from the hematopoietic stem cells (e.g. blood cells and lymphocytes), while retaining viable MSCs and osteoprogenitor cells. Osteocel processing also incorporates antimicrobial and antimycotic treatments to eliminate potential contaminants, while sustaining the cells. Efficacy is comparable to autograft, but is only in limited indications (e.g. the lower spine, tibial repair, dental).

Trinity ELITE – Orthofix (NYSE: OFIX): Trinity ELITE is a third-generation, putty-like allograft with viable cells that provides an alternative to autograft. It provides an environment in which osteogenic cells differentiate into osteoblasts, and secrete cytokines that recruit other bone-forming cells. Osteoinductive signals from the growth factors in demineralized bone component promote bone growth by stimulating the bone-forming activity of the endogenous cells, in addition to recruiting the patient's own cells to the site of repair. The cancellous bone matrix acts as a three-dimensional scaffold that is remodeled and then serves to facilitate the growth of new bone and support vascularization.⁵⁰

Neuroseal: A Dural Sealant Product

Kuros Biosciences' Neuroseal (KUR-023) is a dural sealant legacy product, which was developed as an adjunct to suturing after cranial or spinal surgery in order to prevent cerebrospinal fluid (CSF) leaks. Post-operative CSF leaks result in significantly increased costs due extended hospital stays and treatment costs. Neuroseal is a sprayable, synthetic, biodegradable gel that immediately adheres to and provides a watertight seal over the dura mater membrane. Neuroseal is based on two synthetic polymers that cross-link *in situ* at the site of administration to seal the tissue without any heat generation or significant biocompatibility concerns. The product received CE marking for cranial use in 2017, allowing for its commercialization in Europe. However, further development of Neuroseal was halted in order to focus on *MagnetOs* and the fibrin/PTH technology platform.

⁴⁹ <https://www.drugwatch.com/infuse/>

⁵⁰ <http://web.orthofix.com/Products/Products/Trinity%20ELITE/Trinity-ELITE-Technical-Monograph.pdf>

Management Team

Dr. Joost de Bruijn

Chief Executive Officer

Joost de Bruijn founded Xpand Biotechnology BV in 2005 and remained Chief Executive Officer of Xpand after the acquisition by Kuros in early 2017. Dr. de Bruijn also holds the positions of Professor of Biomaterials at Queen Mary University of London, UK (since 2004) and Professor of Regenerative Medicine and Entrepreneurship at Twente University, the Netherlands (since 2011). In 2007, he founded Progentix Orthobiology that signed an exclusive development agreement with NuVasive in 2009 for a novel family of calcium phosphate synthetic bone substitutes. Prior to founding Xpand he was Research Director Bone at IsoTis for seven years, during which he specialized in bone tissue engineering technologies that were brought to clinical application. Dr. de Bruijn has more than 20 years experience in academia and the life science industry. He has published 165 papers in peer-reviewed journals, and is the inventor of 24 patent families. Dr. de Bruijn is scientific editor and reviewer for numerous international biomaterials, tissue engineering and regenerative medicine journals. He received his PhD from Leiden University in 1993.

Michael Grau

Chief Financial Officer

Michael Grau is Chief Financial Officer (CFO) of Kuros since February 2018. Mr. Grau has a track record of 25 years' experience in corporate finance, controlling, accounting and general management in diverse industries and, since 2001, with a focus on medtech, biotech and pharma. Before he joined Kuros, he served as CFO of Proteros Biostructures, a biotech company focusing on enabling lead discovery, Correvio, a Geneva-based hospital specialty pharma company, and Endosense, another Geneva-based private medtech company. Mr. Grau was responsible for multiple capital market transactions, financing rounds and several merger and acquisition agreements for public and private companies. He started his career working for KPMG Pat Marwick. Mr. Grau holds a BA in European Finance and Accounting from Bremen University, Germany, and Leeds University, U.K., and an executive MBA from Henley Business School at the University of Reading, U.K. Mr. Grau is citizen of Germany.

Dr. Alistair Irvine

Chief Business Officer

Alistair Irvine joined Kuros as director of business development in 2006 after a career as a technical and commercial consultant to the biotechnology industry. Prior to his work, he was deputy director of R&D operations manager at Innovata plc, where he managed research programs in the fields of gene expression, cell culture, polymer science and oncology. In addition, he was involved in business development. Prior, Dr. Irvine was head of biology at ML Laboratories plc, as well as sub-divisional head research and group leader immunotherapy at Cobra Therapeutics Ltd. He also was senior scientist with Therexsys Ltd. Dr. Irvine has been working in the biotechnology/medtech industry for over 20 years. Dr. Irvine holds a PhD in molecular biology from the University of Sheffield, UK, and a BSc in biochemistry from the University of Edinburgh, UK. He is British citizen.

Dr. Philippe Saudan

Chief Development Officer

Dr. Philippe Saudan was appointed Chief Development Officer (CDO) in August 2016. He has spent more than 17 years in the pharmaceutical industry and held different management roles in R&D. Dr. Saudan has considerable experience in R&D and international project management of multidisciplinary programs. In his last position, he served as Chief Scientific Officer of Cytos Biotechnology, where he worked at the interface between pre-clinical research, manufacturing and development of several clinical projects. Since February 2016, Dr. Saudan was working as Head of Integration of Kuros Biosciences. In this position, he was closely involved in the different development programs in tissue repair and regeneration. Dr. Saudan holds a PhD in biology from the University of Lausanne, Switzerland. Dr. Saudan is a Swiss and British citizen.

Frank-Jan van der Velden

Head of Business Affairs and Finance of Kuros Biosciences B.V.

Frank-Jan van der Velden was a co-founder of Xpand Biotechnology BV and acted as executive board member since then. He co-founded several other Dutch companies in the field of regenerative medicine, i.e. CellCoTec, Progentix Orthobiology and Materiomics. Before he co-founded Xpand, Mr. van der Velden was partner at management consultants Krüger & Partners for 10 years. Prior to that, he acted as director of Quote Media Holding. Currently, Mr. van der Velden is a board member of RiverDiagnostics International, member of the executive board of Materiomics and chairman of the supervisory board of TIIN Techfund III BV, a venture capital fund for technology start-ups. Mr van der Velden is a graduate of Erasmus University Rotterdam School of Management.

Risk to Investment

We consider an investment in Kuros Biosciences to be a high-risk investment. Although Kuros has received approval for *MagnetOs* in Europe and the US, it is unclear if the Company will be able to grow sales of these products. In addition, there is no guarantee that Kuros' clinical-stage product candidates will be able to achieve regulatory approval in their targeted markets. Kuros has not reached profitability or positive cash flow and may need to seek additional financing in the future. The targeted markets are competitive and susceptible to pricing pressures, and unknown competitors may emerge.

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