

Orthopedics Focus

# Emerging Companies to Watch

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## Advanced Biomaterial Systems (Private)

Chatham, NJ

### Overview

Advanced Biomaterial Systems (ABS) develops biomaterials and delivery systems designed to treat diseases of the musculoskeletal system damaged by disease, infection or trauma. The company's products streamline operative procedures and improve patient safety. ABS markets its products to orthopedic and radiological surgeons.

### Products

The company's delivery technology includes the Plexis Bone Void Filling System for percutaneous procedures and the twistOR PrePack Mixing and Dispensing System for total joint replacement procedures. ABS biomaterials include the Concert family of bone cements.

The twistOR system combined with Concert Bone Cement is the only bone-cement mixing and delivery system on the market with a preloaded mixing chamber and a vacuum monomer injection system. The Plexis Bone Void Filling System consists of a sterile integrated mixing and delivery device. Plexis is designed to mix and deliver a number of biomaterials, including PMMA bone cement. The system eliminates the need for separate syringes, bowls, tubes, or injectors.

Plexis' metered dispensing mechanism, which operates by rotating a mixer handle, permits precise control of both material volume and placement. A counterclockwise turn of the handle stops material flow immediately. A vacuum port permits mixing of materials under vacuum, if needed.

ABS' Concert Cranioplast is a two-part resinous material for repair of cranial defects. The material comes in a sterile single-dose package and requires, on average, 23% less monomer than competitive products. Concert Spine VR Radiopaque Bone Cement is FDA approved for use in vertebroplasty and kyphoplasty procedures, and for use in the fixation of prosthetic devices to living bone.

### Sales

In April 2006, the company initiated the development of a direct field sales force in the interventional spine and orthopedics markets. ABS has identified approximately 20 key geographies to be grown within the next two years; growth will be supported by the addition of product lines and the creation of additional territories.

## Alphatec Spine (ATEC)

Carlsbad, CA

### Overview

Alphatec Spine develops products for the surgical treatment of spine disorders. The company's portfolio includes a variety of spinal implant products and systems addressing the cervical, thoracolumbar, intervertebral, minimally invasive, allograft, and motion preservation markets. Principal product offerings are focused on the U.S. spine fusion market, which is estimated to approach \$5.9 billion in 2007.

The company's range of products includes spinal implants and systems comprised of components such as spine screws, spinal spacers, and plates. As an alternative to metal and synthetic materials, Alphatec distributes allograft spacers to be used in spine fusion.

### Physician partnerships

Alphatec focuses on a "surgeons' culture," emphasizing collaboration with spinal surgeons to conceptualize design and co-develop new products. In-house manufacturing capabilities enable the company to rapidly prototype and manufacture products engineered to meet the needs of surgeons and patients.

One such illustration of this strategy is the April 2007 license agreement with Dr. Roger P. Jackson, for the global rights to use the minimally invasive surgical rod insertion and reduction tools of his design. Alphatec also licensed proprietary methodologies to which Dr. Jackson has proprietary rights.

### Intellectual property

Alphatec has 18 issued U.S. patents, one foreign patent and 24 pending patent applications – 16 U.S., four international and four foreign national.

### Status

The company was founded in 1990 as a contract medical device manufacturer. In March, 2005 Alphatec was acquired by a group of investors led by HealthpointCapital LLC. In addition to its U.S. operations, the company also markets a range of spine and orthopedic products in Japan through its subsidiary Alphatec Pacific.

## **Amedica (Private)**

Salt Lake City, UT

### **Market opportunity**

Currently marketed hip, knee and spine implants have certain performance limitations due to the materials from which they are made. To address this problem, Amedica has developed Micro Composite Ceramic technologies (MC2). MC2 encompasses a range of high-strength ceramics made from doped silicon nitride. The material is suited to applications where high wear resistance and strength are critical, particularly in articulation.

MC2 technology offers physicians and patients an alternative to other synthetic and allograft bone implants used for the restoration of spinal anatomy. Such spinal implants are estimated to comprise an annual U.S. market segment of more than \$600 million.

### **Products**

In February 2006, Amedica received clearance from FDA to market its Arx Ceramic Spinal Spacer System. It is the first load-bearing ceramic spinal implant system cleared for use in humans. The intervertebral spacers are made from silicon nitride. This material does not interfere with imaging modalities -- there is no halo created with MRI or CT imaging. The ceramic material also facilitates device placement and follow-up.

### **Pipeline**

Amedica's pipeline includes the Altia Ceramic Cervical Disc. Joint implants under development include the Infinia Total Hip and Knee implants. Amedica's spinal products complement each other, accommodating a variety of surgical approaches, and are designed as a procedural solution for stabilization of the cervical and lumbar spine. The company will begin commercializing its Ceramic Intervertebral Spacers, a Cervical Plating System and a Pedicle Screw System in 2008, pending additional FDA clearances.

### **Financing**

In March, 2006 the company completed a private placement of its Series C Convertible Preferred Stock, raising \$16.8 million in gross proceeds. Creation Capital LLC served as the sole placement agent for the financing. Amedica has raised over \$31 million since November 2003.

## Anika Therapeutics (ANIK)

Woburn, MA

### Market opportunity

Osteoarthritis is a common cause of physical disability among adults -- the knee is one of the most affected joints. In the U.S., osteoarthritis of the knee affects as many as 50 percent of people between ages 45 and 74. In severe cases, osteoarthritis of the knee can lead to disability and may require surgery to replace the knee joint.

### Lead product

Anika Therapeutics develops, manufactures and commercializes therapeutic devices designed to repair, protect and heal bone, cartilage and soft tissue. Anika's lead product is Orthovisc, used to relieve knee pain due to osteoarthritis. Orthovisc is FDA approved for use in patients who have failed to respond adequately to conservative non-pharmacologic therapy and to simple analgesics.

Anika's products are based on hyaluronic acid (HA), a natural chemical found throughout the body. HA enhances joint function by coating, cushioning and lubricating soft tissues. Orthovisc is injected directly into the knee, where it may help restore the cushioning properties of joint fluid, providing up to six months of relief from knee pain.

Orthovisc is available in the U.S. through DePuy Mitek Inc., a subsidiary of Johnson & Johnson. In 2007, the product received its own Medicare reimbursement code. Orthovisc may be administered by an orthopedic surgeon or rheumatologist.

### Ophthalmic applications

Anika also applies its hyaluronic acid technology in the ophthalmic space. In 2005 these products were responsible for 51% of the company's earnings. Anika's viscoelastic solutions can be used in most ophthalmic intraocular surgeries, including cataract extraction, IOL insertion and removal, corneal surgery, and glaucoma surgery. Cataract extraction and IOL (intraocular lens) implantation is the most common surgical procedure performed in the U.S. and most other industrialized, affluent nations. More than 14.0 million cataracts were removed worldwide during 2003.

### Results

Anika reported product revenue of \$5.1 million for the fourth quarter of 2006, compared with \$4.8 million in the prior same period. For the year ended December 31, 2006, product revenue increased 17% to \$23.95 million, compared with \$20.53 million for 2005.

## Ascension Orthopedics (Private)

Austin, TX

### Market opportunity

Arthritis affects as many as 40 million Americans -- nearly one in every six people. Approximately 21 million people have osteoarthritis, and another 2.1 million have rheumatoid arthritis. By 2020, 60 million people will suffer from the disease. Rheumatoid arthritis is a systemic disease that can affect all of the joints of the body. The disease attacks both the joint surface and soft tissues of the joints. Arthritis of the hand can be particularly debilitating, as these joints are important for gripping and holding things. A patient suffering from arthritis of the finger joints may suffer from pain, swelling, loss of function, and deformity.

### Surgical intervention

Arthritis may be treated with regular exercise, splinting, medications and injections of anti-inflammatory drugs. As the disease progresses, surgical intervention may be required. Ascension Orthopedics offers a variety of products for most types of surgery. A synovectomy is generally done in less severe cases of joint disease in RA patients. This procedure involves the removal of the synovium or tissues lining the joints. This can reduce swelling and pain and slow down the destruction of finger joints. To reduce pain, a surgeon may choose to join the bones in a joint together, known as arthrodesis; the operation may result in a loss of motion but can eliminate the pain.

Osteotomy or cutting the bone can be performed to correct deformities and reduce pain. This is primarily performed in weight bearing joints. Finally, arthroplasty, or total joint replacement, is a removal of the damaged bone, which is then replaced by an artificial joint. Finger joint arthroplasty has been performed for more than 30 years. Traditionally, damaged or diseased finger joints have been replaced with a silicone spacer. This type of replacement can provide for satisfactory results in low demand patients. For high demand patients, Ascension Orthopedics has designed a finger joint replacement for the MCP and PIP joint.

### PyroCarbon

Ascension's implants are made from PyroCarbon, a high strength ceramic-like isotropic coating over a graphite substrate. PyroCarbon's biochemical, biomechanical compatibility promotes appositional bone growth resulting in a stable bone/implant interface. Over two million PyroCarbon mechanical heart valve prostheses have been implanted since 1969, demonstrating the materials biocompatibility and strength and wear resistance.

Lab testing has shown the wear rate for a PyroCarbon on PyroCarbon joint surface is less than one tenth that of metal on polyethylene, the current standard of care. Tissue samples examined during long term follow-up of PyroCarbon MCP implants averaging 11.8 years showed no evidence of degeneration or intracellular wear.

## **Bacterin (Private)**

**Belgrade, MT**

### **Reduced infection**

Bacterin International designs, tests and licenses bioactive coating for medical applications. To date, the firm has invested more than \$80 million in the research and development of its biofilm technology. The company's anti-infective coating for medical devices prevents microbial formation and growth, significantly reducing infection rates associated with device implantation. Bacterin's proprietary bioactive coating can be applied to medical products to release an array of bioactive molecules, including anti-inflammatory compounds, pain-control drugs, antithrombotic agents, and antimicrobials.

### **Revenues**

Bacterin's revenues are derived from three main sources: licensing fees from medical device manufacturers for use of the delivery technology, contract development revenue to tailor the coating process to each client's specific product application, and sales Bacterin's branded medical devices and biologic products.

### **Products**

Bacterin products for transplantation include OsteoSponge, a demineralized bone matrix (DBM) allograft that is malleable and retains osteoinductive and osteoconductive properties. Also available is OsteoWrap, a flexible thin sheath of cortical bone that can be rolled, wrapped, or easily cut with a scalpel. Bacterin is able to apply its bioactive coatings to the tissue prior to implantation. OsteoSponge and OsteoWrap are available in the U.S. and internationally.

The company's Bacterin Via Wound Drain, currently available, is a fully channeled suction drain designed to improve patient safety and comfort. Via's flexible silicone core and low profile minimizes tissue trauma pain on removal. The device uses four channels to reduce the risk of occlusion.

Branded products in the pipeline include Elutia, an antimicrobial wound drain. Elutia is coated with silver sulfadiazine and inhibits the formation of biofilm for up to seven days after insertion.

### **Background**

Bacterin joined TechRanch, an internationally recognized incubator located in Bozeman, MT, in 2002 for its entrepreneurial support. In 2003, Bacterin successfully left TechRanch and opened its own headquarters in Belgrade.

## **BioniCare Medical Technologies (Private)**

**Sparks, MD**

### **Market opportunity**

Approximately one in three Americans suffers from arthritis and other rheumatic conditions – that’s nearly 70 million people – making arthritis one of the most prevalent and costly diseases in the U.S. Currently, over seven million Americans are partially disabled due to arthritis, and as the population ages, so will this figure; by 2020 this number is expected to reach 12 million.

Osteoarthritis, also known as degenerative joint disease, results from physical changes in joints and surrounding tissues. It is commonly a result of aging, obesity or repetitive joint use. Most total hip replacements and 95% of total knee replacements are due to this debilitating condition. Rheumatoid arthritis is a disease characterized by chronic inflammation of the joint lining; onset typically occurs in one’s twenties and thirties.

There is no cure for most types of arthritis – treatments are typically focused on controlling symptoms rather than eliminating the disease. Nearly 10 million arthritis sufferers take anti-inflammatory drugs (NSAIDs) – while widely used and frequently effective, side effects include gastrointestinal bleeding and hypertension. NSAID bleeding, ulcerations, and perforations may cause as many as 16,500 U.S. deaths each year. Knee and hip replacements are also growing in popularity as increased patient activity has led to a rising incidence of arthritis at an early age.

### **Product**

BioniCare offers the first and only non-drug, non-invasive option cleared by FDA for reducing pain and symptoms associated with osteoarthritis of the knee, and for overall improvement of the knee as assessed by physician’s global evaluation. The device operates by delivering low-level pulsed electrical stimulation to the knee (the electrical stimulation is not felt). In clinical studies of patients who used the device for the recommended 6-10 hours a day, significant relief of pain and symptoms were witnessed, as were improvements in function. The device is designed for use during the day or at night, although it is recommended that it be worn at night to maximize patient comfort. The company offers a similar device for relieving hand pain associated with rheumatoid arthritis.

### **Reimbursement**

BioniCare has a dedicated reimbursement team to help patients through the medical claim and appeal process. They will examine insurance benefits and determine if coverage will cover the expense, submit claims to Medicare or other insurance companies, and if needed, file claims appeals. Forthcoming data will offer evidence of the long-term clinical benefits of the BioniCare Knee Device and seek to demonstrate cost benefits.

## **Biorthex (Private)**

Quebec, CANADA

### **Market opportunity**

One of the greatest challenges in the orthopedic field involves the permanent fixation of metal implants to bone. Leading procedures use screws, glue, cement and porous surface treatments. These technologies carry high failure rates, often leading to expensive surgical revisions.

### **Technology**

The use of Biorthex's interbody fusion material, Actipore, enables a less invasive surgical procedure that may shorten hospital stay and accelerate recovery time. Actipore is a porous biomaterial derived from nitinol technology that permits bone cell growth into the biomaterial's pores for a rapid and solid attachment to bone structure without the need for bone grafting or cement.

Nitinol is biologically and biomechanically compatible. The isotropic interconnected porous structure and the capillary wicking forces actively draw essential fluids and nutrients into the implant, allowing for strong, rapid growth of newly forming bone cells through an ultra porous scaffold. Nitinol material in its solid form is FDA-approved and has been used clinically worldwide for over a decade.

Actipore has superior compressive strength in comparison to bone, while sharing a similar modulus of elasticity, minimizing the risk of stress shielding. Its elasticity resembles that of cancellous bone. The material is MRI and CT scan compatible.

### **Products**

Biorthex offers two products for lumbar fusion and one for cervical fusion. In development, Actipore ALF is a device for lumbar fusion via an anterior approach. Biorthex is also developing its Actipore technology to be used as a surface coating and in components for hip and knee implants.

### **Partnership**

In July 2006, the company initiated a research collaboration with Nitinol Device & Components, a subsidiary of Johnson & Johnson. Biorthex owns the exclusive worldwide rights to develop, manufacture and commercialize Actipore.

## Cayenne Medical (Private)

Scottsdale, AZ

### Overview

Cayenne Medical is a multi-disciplinary company operating in the soft tissue reconstruction segment of the sports medicine market. Its current focus is anterior cruciate ligament (ACL) reconstruction using minimally invasive techniques. While advancements in arthroscopic surgery have expanded the range of possible treatments for joint injuries, many companies' fixation devices have not addressed surgical complications of fixation strength and postoperative laxity.

### Product

Cayenne's AperFix System enables surgeons to perform ACL reconstruction using the hamstring and other soft tissue grafts. The AperFix System consists of femoral and tibial implants that are made from PEEK, a polyetheretherketone material with well-documented strength, rigidity and the ability to pass x-rays and other forms of radiant energy with little attenuation. The two implants are preloaded onto disposable handles for single-handed, rapid delivery. During the procedure, active tension is applied to eliminate graft laxity.

### Status

Cayenne has received 510(k) market clearance from FDA for the AperFix System; the product is now available for clinical use. Each implant has been designed to utilize aperture fixation and tendon-bone compression, key factors for secure fixation and healing. Preliminary studies demonstrate the system's high pull-out, aperture and tendon bone compression forces.

In February 2007, the company closed a \$12.7 million Series B financing led by Split Rock Partners. The official launch of AperFix followed the American Academy of Orthopaedic Surgeons annual meeting.

## CeraPedics (Private)

Lakewood, CO

### Market opportunity

The bone-substitutes market is among the fastest growing sub-sectors of the orthopedic market, estimated at \$847 million. The use of synthetics accounted for approximately 50% of the market in 2005 and is expected to grow, fueled in part by safer and more innovative and economical technologies.

### Trial

CeraPedics' bone-substitutes program is in later stages of development. It has the first and only bone substitute product to use small peptide technology to mimic the organic phase of autogenous bone (bone grafted from the patient). The company is developing P-15 bone graft substitutes and a P-15 surface modification for coating orthopedic implants. P-15 is a synthetic peptide that mimics the Type-I collagen, which is involved in the binding and migration of cells, leading to the formation of new bone. CeraPedics' products incorporate P-15 that is identical to the naturally occurring cell-binding domain of Type-I collagen. The peptide promotes the attachment of anchorage-dependant cells to biocompatible surfaces.

### Product

CeraPedics believes that its P-15 Putty, completely synthetic in nature, will be competitive with allograft (bone taken from cadavers), autograft and other synthetic products. In June 2006, the company reported results from a P-15 bone substitute trial that showed the product to be a safe and effective alternative to autograft. In 1999, the product received PMA approval for use in the oral cavity, and since that time, 250,000 doses have been used with no safety concerns. Unlike bone growth factor products produced by competitors Stryker and Medtronic, P-15 will only grow in the presence of bone forming cells, thereby avoiding the potential risk of ectopic bone formation (bone formation outside of the intended area). Additionally, as a synthetic, P-15 Putty can be priced significantly less than growth factors, and can fall under existing reimbursement guidelines.

### Future plans

CeraPedics is planning additional clinical trials to assess the safety of P-15 Putty in other orthopedic applications. Additionally, in June 2006, the company signed an agreement with BioD LLC to develop products for the orthopedic market using the P-15 bone substitute and BioD's proprietary stem cell procurement procedure. The companies anticipate that negotiations and planning for the extension of this agreement to be finalized after initial feasibility studies are completed.

## **Cervitech (Private)**

Rockaway, NJ

### **Market opportunity**

Nearly 80% of all Americans will suffer from at least one significant episode of back or neck pain in their lifetime. Back and neck pain is the leading cause of disability for people between 19 and 45 years old; it represents 16% of all workers compensation claims.

Chronic pain that is non-responsive to conservative therapy is often treated by removing the diseased disc and bone and then fusing the vertebrae. Approximately 400,000 spinal fusion procedures are performed each year to decompress the spinal cord or nerve roots and to rigidly fuse two vertebrae together. Traditional spinal fusion use metal plates, rods and screws. It is very successful in resolving the pain but will result in a loss of motion within the fused joint.

### **Product**

Cervitech has developed the Porous Coated Motion (PCM) Artificial Disc to provide relief without losing motion at the treated joint. The PCM replaces a damaged disc, while preserving joint motion.

The implant has an upper and lower metal endplate to which a plastic spacer made from high impact Polyethylene is attached. The endplates are designed to bond with the neighboring vertebrae. The upper half of the implant can slide and rotate forward and backward relative to the lower half, unlike conventional fusion devices that lock the vertebrae in place.

The surgery lasts approximately two hours; most patients leave the hospital the following day. During the procedure, the surgeon accesses the spine from the front of the neck, removes the damaged disc, and after shaping the edges of the vertebrae to ensure a proper fit, the PCM Disc is inserted.

### **Status**

In the U.S., the device is FDA approved for investigational use only. FDA is allowing select doctors to use the disc on a specific number of patients that meet certain eligibility criteria. Internationally, the device is available and undergoing a large multi-center observational trial. To date, over 1,000 PCM discs have been implanted in 20 countries.

## Cytori Therapeutics (CYTX)

San Diego, CA

### Overview

The number-one killer in America is cardiovascular disease. Following a heart attack, a significant area of heart muscle surrounding the infarct is alive but at risk of dying. Cytori Therapeutics is developing adipose stem cell treatments to prevent further cellular death.

Preclinical data suggest that adipose stem cells improve heart function through several cellular mechanisms aimed at reducing the size of the perfusion defect. These include angiogenesis, or new vessel growth, as well as the prevention of further cell death. The company believes its technology also has applications for spine and orthopedic disorders.

### Technology

Cytori's technology entails the collection of adipose-derived stem cells in a minor liposuction-like procedure. Stem cells are separated and concentrated using Cytori's Celution System. An hour later they are available for re-injection. Cells are delivered via a catheter into the coronary artery or directly into the heart muscle.

In addition to stem cells, adipose tissue contains regenerative cells that contribute to healing. Cytori believes these stem and regenerative cells may be useful for treating spine and orthopedic disorders and vascular conditions, and in performing reconstructive surgery. Cytori has sponsored two clinical trials for cardiovascular disease.

### Trials

The company's trials for chronic myocardial ischemia and heart disease began in early 2007. Cytori's Apollo trial will be a patient safety and feasibility study to evaluate adipose stem and regenerative cells as a treatment for heart attacks. The patients' own adipose stem cells will be processed using the company's Celution System and injected into the coronary artery. The patients will be followed for six months before evaluation.

### Other applications

The company plans to apply the adipose-derived stem and regenerative cells to synthetic implants used in aesthetic and reconstructive surgery. This "cell-enhanced tissue transfer" involves the transfer of soft tissue from one part of the body to another. The tissue is augmented with a patient's own stem and regenerative cells. Potential applications include breast reconstruction, breast augmentation, dermal filler, and as a treatment for complications of tumor removal and radiation damage in breast cancer patients. More than one million women worldwide are diagnosed with breast cancer annually, which can often result in significant skin damage and tissue loss.

## Disc Dynamics (Private)

Eden Prairie, MN

### Overview

In the past five years, one-third of Americans over age 18 had a back problem severe enough to seek professional help. Disc Dynamics, Inc. (DDI) has developed the DASCOR Disc Arthroplasty System, for patients suffering from chronic low back pain caused by degenerative disc disease. The system provides a minimally invasive surgical alternative for treating lower back pain.

### Technology

Unlike total disc replacement, where the entire spinal disc is replaced, the DASCOR Disc Arthroplasty System replaces an abnormal disc nucleus with an artificial device that conforms to the disc nucleus space; it is designed to perform like a natural healthy nucleus. The procedure is a minimally invasive alternative to radical surgery that preserves the anatomy of the spine.

### Procedure

In the first step of the procedure, the surgeon accesses the spine by creating a small entry site in the annulus or outer portion of the disc. The abnormal nucleus is then removed through the entry site, and a catheter tube with a specially designed balloon is inserted into the disc space. The balloon is filled with contrast solution that allows it to be seen on an X-ray. These images insure proper positioning and sizing of the final implant. The catheter is then removed. A flowable polymer inserted into the nucleus creates a firm but pliable implant. This process takes just minutes, allowing for shorter operating times.

### Status

The system has been CE marked in Europe and is currently undergoing U.S. clinical trials. The U.S. pilot study is designed to evaluate the initial safety and efficacy of the device in subjects with single-level degenerative disc disease of the lumbar spine from L2 to the sacrum.

Disc Dynamics is a privately owned company incorporated in 2000. The last financing was completed in July 2004.

## Exactech (EXAC)

Gainesville, FL

### Market opportunity

According to the CDC, an estimated 46 million adults in the U.S. have reported having some form of arthritis, rheumatoid arthritis, gout, lupus, or fibromyalgia. By 2030, an estimated 67 million Americans who are 18 or older are projected to have doctor-diagnosed arthritis.

### Overview

Exactech develops orthopedic implant devices, surgical instruments and biologic materials used in the restoration of bones and joints that have deteriorated as a result of injury, or diseases such as arthritis.

Exactech markets its products in the U.S. and Australia, and to countries in Europe, Asia and Latin America. In 2006, the company surpassed \$100 million in annual sales. Each of Exactech's operating segments experienced continued growth for the year.

### Products

Exactech's biologics division's Optecure line of demineralized bone matrix (DBM) products has been expanding rapidly since its introduction in 2004. Opteform is a DBM-based allograft that offers the flexibility of dry material for a wide range of mixing options and applications. The grafts have osteoinductive, osteoconductive and osteogenic factors. Opteform is delivered as a dry, powdered room temperature mix. It is also available frozen in a variety of disc sizes or syringes. Opteform is 510(k) cleared for use as a bone void filler in the spine, pelvis and extremities. Regeneration Technologies, Exactech's distribution partner, has had continued success with this product line.

In 2006, Exactech launched a rotating bearing knee for international distribution. The device improved upon Exactech's unicondylar option and refined a number of its existing instrumentation systems. The company also introduced computer-assisted navigation support for total joint arthroplasty.

### Marketing

In the past year, Exactech has increased market penetration of its Novation hip system and saw market share gains with its Equinox shoulder implants and Cemex bone cement product line. The company began full-scale marketing of the Equinox primary and fracture systems in 2005 and of Cemex Genta, a bone cement containing antibiotics, in 2004.

### Pipeline

Exactech is developing a variety of new products, including the Accelerate Platelet Concentration System. Accelerate, a means of extracting autologous growth factors and fibrinogen from patients' own blood to improve the healing quality of joints and tissue following orthopedic procedures, will be introduced in 2007. Meanwhile, the biologics division is launching extensions of the Optecure brand, including a formulation that contains cortical cancellous bone chips.

## **Fonar (FONR)**

Melville, NY

### **Market opportunity**

Of the approximately 10 million MRI scans performed in the U.S. each year, nearly one-half image the spine. Sixty-five million Americans suffer from back pain, making it the most common reason for seeking medical care. In the U.S., over 800,000 spine surgeries are performed each year, 10-40% of which are unsuccessful. In fact, failed spinal surgery is so common that it is now labeled Failed Back Surgery Syndrome, characterized by intractable pain and various degrees of incapacity.

### **Product**

Fonar has developed an upright MRI system that can image the spine in a weight-bearing state. Conventional MRI image the patient in a fully reclined position. By sitting upright, surgeons are able to better visualize pathologies and accurately assess the full extent of a problem. In multiple studies, it was shown that the diagnosis made by a surgeon changed when they had access to upright imaging. Furthermore, conventional MRI often failed to accurately identify the structural sources of pain.

### **Intellectual property**

In the MRI space, Fonar is pitted against such industry giants as GE, Hitachi, Phillips, and Siemens, all of which have revenues in excess of \$60 billion per year. Fonar's strong IP position includes over 60 patents related to upright MRI. The company recently signed an agreement with GE, which has agreed to stay out of the market until at least Q1 2009. Still, these behemoths hold influence over the radiologists who most often make hospital purchasing decisions. Despite the superiority of its MRI, Fonar faces an uphill battle.

### **Marketing**

In an effort to convince consumers and ultimately spine surgeons that Fonar technology is needed, the company has initiated a direct-to-consumer advertising campaign on prominent television networks. If surgeons decide that spine surgery necessitates an upright pre-operative scan, Fonar can expect to install upwards of 5,000 units in the U.S. alone. Patients prefer to be scanned upright, as it avoids the claustrophobic feelings of traditional MRI. Instead of staring into space, patients are able to watch a 42" plasma TV while the procedure is performed.

### **Manufacturing**

Fonar has a 200,000 square-foot manufacturing facility capable of producing 12-16 units per month. Output could increase rapidly, as over 90% of Fonar's materials are outsourced, which allows for higher product margins. In addition to its upright MRI, the company produces Fonar 360, a scanner allowing 360-degree access to the patient and real-time image guidance.

## FzioMed (Private)

San Luis Obispo, CA

### Market opportunity

Post-surgical adhesions are fibrous bands of scar tissue that can form inside the body following surgery. Adhesions are typically triggered by surgical trauma such as cutting, manipulation or suturing. Complications from adhesions include chronic back or pelvic pain, intestinal obstruction and infertility. Adhesions make subsequent surgeries more difficult to perform; they can reform even if removed surgically.

### Products

FzioMed develops synthetic, absorbable biomaterials based on a polymer technology called Oxiplex. The company has formulated products for use in a range of medical specialties, including spine surgery, gynecological surgery, general surgery, orthopedics, dermatology and cosmetic surgery.

Oxiplex is applied during surgery and forms a barrier to adhesion formation during the normal healing process. The company's CE-approved adhesion prevention products include Oxiplex/SP for spine surgery and Oxiplex/AP for laparoscopic gynecological surgery, both for sale in 45 countries outside the U.S. Oxiplex is absorbed by the body over time and cleared via normal processes. As such, it does not need to be removed after application.

Pre-clinical and clinical data have demonstrated the safety and biocompatibility of Oxiplex. Oxiplex does not disrupt normal healing when applied to tissues. The viscoelastic properties of the material facilitate its manufacture into a variety of bioabsorbable product types including gels, films, solutions, foams, sponges, and powders. Specific characteristics such as adherence, elasticity, strength, viscosity and absorption allow Oxiplex to be tailored for use in targeted medical applications. Oxiplex can be stored at room temperature; it is provided sterile and ready to use, and requires no mixing before use.

FzioMed is expanding the Oxiplex platform into new surgical applications, including drug delivery, tissue healing and coating, and osteoarthritis.

Also available from FzioMed, Laresse Dermal Filler is a clear, smooth gel formulated for use in the correction of facial soft tissue contours such as wrinkles and folds that result from aging, sun damage and scarring. Other biomaterials such as polyesters, hyaluronan, collagen, and fibrin may be derived from animal or bacterial by-products and may provoke a complicating inflammatory or immune response, or are expensive to manufacture. Others require multi-step mixing before use or cannot be used in minimally invasive surgical applications. Currently, Laresse is only available in the European Union.

## **Globus Medical (Private)**

**Audobon, PA**

### **Market opportunity**

It is estimated that 80-85% of the U.S. population will experience significant back pain at some point in their lifetime. Degenerative disc disease is most often remedied using fusion surgical techniques, where damaged and diseased discs are removed, disc height is restored and adjacent vertebrae are fused together. While often initially effective in providing pain relief, there are several drawbacks, primarily related to the reduction of mobility and flexibility caused by the fusing of formerly independent vertebrae. Non-fusion techniques and devices provide stabilization and restoration of disc height without the resultant loss of flexibility and mobility.

### **Overview**

Globus Medical, a spinal implant manufacturer with more than \$100 million in annualized revenue, has a portfolio of spinal fusion and minimally invasive products, and biomaterials in development. The company specializes in the development of motion sparing technology.

### **Products**

In July 2005, Globus initiated a clinical trial for its Secure-C Cervical Artificial Disc under an Investigational Device Exemption granted by FDA. The Secure-C Cervical Artificial Disc device consists of a central ultra-high molecular weight polyethylene component sandwiched between two titanium plasma-sprayed cobalt-chromium-molybdenum alloy endplates. Globus's semi-constrained design is intended to facilitate a full range of motion in a secure platform. As these concepts are developed and perfected, growth in the spinal implant market is expected to mirror that of artificial hip and knee joint replacements over the past 10-15 years.

Globus has implemented and refined process of rapid product development that relies heavily on multiple, rapid iterations of the design-prototype-test cycle. The company's in-house prototyping, craftsmen and machinists combined with focused product development teams, enable rapid product development from concept through product launch, including FDA approvals and the sourcing of launch-quantity volumes from third-party manufacturers.

In addition to Secure-C, Globus has a number of motion-sparing products in various stages of development. The company's line of fusion products includes the Sustain line of spacers, the Protex pedicle screw, AccuFlex technology, and the Assure cervical plate system.

### **Distribution**

Globus distributes its products through a sales force consisting of exclusive independent distributors and direct representatives. The company manufactures its products through a network of over forty international and domestic third-party manufacturers.

### **Funding**

Globus has raised \$9 million in equity in three separate rounds of financing. Employees and sales professionals of the company's products own over 80% of the equity in the company. In September 2006, Globus closed on a \$10 million Credit Facility with Silicon Valley Bank.

## GraMedica (Private)

Shelby Township, MI

### Market opportunity

By middle age, the average person has walked 75,000 miles. The function of the foot is to transfer the weight of the body to the ground and to propel the body. The function of the ankle bone or talus is to transfer the weight of the tibia and fibula to the heel bone and the rest of the foot.

Hyperpronation, or excessive pronation of the foot, is a hereditary condition caused by underdevelopment of the ankle or heel bones. Hyperpronation is a very common condition. This abnormal motion leads to deformity of the foot. Even though hyperpronation is not a life-threatening deformity, it must be aggressively treated. By the time most people reach middle age they begin to develop problems with their feet, knees, hips, and back.

Hyperpronation of the foot is often ignored or treated inappropriately until symptoms appear and there is damage to the body. As with any other deformity, the sooner treatment is initiated the better the outcome. Oral medications or physical therapy do not address the underlying deformity. Arch supports treat abnormal foot motion; sometimes this is all that is needed to bring relief. Most often, there is temporary relief followed by recurrence of the symptoms.

### Product

GraMedica provides foot and ankle surgeons with products to help eliminate foot and ankle problems. The company's initial product is the HyProCure Sinus Tarsi Implant. This orthotic realigns the bones of the hind foot and in doing so helps restore the alignment of the rest of the body. The minimally invasive procedure is permanent, and completely reversible. The implant fits into this space to prevent the abnormal motion, but maintain the normal motion between these bones. This procedure has been effectively performed on patients from three years old to a patient 91 years of age. HyProCure has been available since September 2004.

## Hanger Orthopedic Group (HGR)

Bethesda, MD

### Structure

Hanger Orthopedic Group, Inc. comprises four wholly owned subsidiary businesses serving different segments of the orthotics and prosthetics industry. Orthotics is the custom design, fabrication and fitting of braces and supports for the treatment of musculoskeletal conditions. These conditions range from short-term, sports-related injuries to long-term, progressive neurological diseases such as multiple sclerosis and amyotrophic lateral sclerosis. Prosthetics is the custom design, fabrication and fitting of artificial limbs. Hanger also offers post-mastectomy care and a specialty footwear program for diabetics.

### Orthotics and prosthetics

Hanger's orthotics and prosthetics delivery business is the largest of the four business units. It comprises 600 patient care centers across the U.S. and employs nearly 25% of the nation's orthotics and prosthetics professionals. Each year the company treats 650,000 patients. Hanger's business includes Southern Prosthetic Supply (SPS), which consists of distribution centers managing the supply chain of orthotic and prosthetic components to Hanger and third-party patient care centers. SPS has the lowest backorder and shipping error rates in the industry. Hanger also operates Linkia, the largest orthotic and prosthetic managed care network in the country. Linkia offers utilization management, electronic billing, eligibility verification, and a single fee schedule.

### Electrical stimulation

Innovative Neurotronics, a wholly owned subsidiary, develops electrical stimulation devices to improve the functionality of an impaired extremity. The company's Myo-Orthotics Technology improves the functionality of impaired limbs for better mobility. It is a potential solution to Dropfoot, a condition caused by weakness or paralysis of the muscles involved in lifting the front part of the foot. This condition is most often caused by an interruption in the signal from the brain to the peroneal nerve. People with multiple sclerosis (MS), spinal cord injuries, traumatic brain injuries, cerebral palsy and stroke may experience the effects of the condition.

Myo-Orthotics Technology merges orthotic technology, which braces a limb, with electrical stimulation, which restores specific muscle function. Myo-Orthotics Technology restores the functionality of an impaired limb by recreating a natural nerve-to-muscle response.

## Harvest Technologies (Private)

Plymouth, MA

### Market opportunity

The body responds to injury by initiating a series of regeneration and remodeling steps. The steps are controlled by bioactive proteins found in platelets, plasma, and white blood cells. Increasing the concentration of these bioactive proteins may act as a catalyst to accelerate the wound healing process.

Adult stem cells derived from bone marrow may be used in tissue regeneration. To date, 20 published studies involving 1,500 patients have validated this approach. Concentrated autologous adult stem cells from bone marrow are extensively used in tissue regeneration in cardiovascular and vascular diseases. A concentrate of these cells contains not only stem cells and precursor cells as a source of regeneration tissue, but also accessory cells that support angiogenesis and vasculogenesis by producing several growth factors and cytokines.

### Status

Autologous adult stem cells derived from bone marrow have been difficult to process outside the human body. Current processing and concentrating techniques require six to 12 hours of preparation. Harvest Technologies uses autologous bone marrow to process large quantities of adult stem cells at the point of care in only 15 minutes. Harvest has received clearance in Europe to concentrate the cellular components from bone marrow through the Bone Marrow Aspirate Concentrate (BMAC) System. The product is marketed under the SmartPReP 2 brand.

A planned multi-center U.S. clinical study using the BMAC System will target patients with Critical Limb Ischemia (CLI) or clogged arteries in the lower legs. Patients with CLI are at risk for amputation. 500,000 people worldwide suffer from CLI. In the U.S., approximately 160,000 amputations are performed each year as a result of this condition. A pilot study in Europe using BMAC resulted in a 60 percent reduction in major amputation.

The concentrate produced by the BMAC System has been shown to generate more mononuclear cells with enhanced viability compared to concentrations obtained by using the most common laboratory methods. BMAC requires one-third less aspirate of bone marrow from the patient.

## I-Flow Corporation (IFLO)

Lake Forest, CA

### Overview

I-Flow Corporation develops ambulatory drug delivery systems for pain management and infusion therapy. The company's line of compact and portable infusion pumps includes catheters and pain kits to administer medications directly to the wound site as well as administering local anesthetics, chemotherapies, antibiotics, diagnostic agents, nutritional supplements and other medications.

### Products

ON-Q C-bloc is a continuous nerve block infusion system designed to slowly infuse local anesthetic near a nerve for regional anesthesia and post-operative pain relief. It relieves pain narcotic-free while allowing patients to have both continuous and on demand pain relief.

In 2004, I-Flow phased out its electronic infusion products, which included the I-Flow IP pump and the VOICELINK Remote Programming System, in favor of its non-electric products line. These pumps use a reusable mechanical infuser and specially designed administration set. The devices are used to deliver medications which require slow and continuous infusion.

A review of data from 44 studies and 2,141 patients, published in December 2006 by the *Journal of American College of Surgeons*, offers quantitative and qualitative evidence demonstrating the superiority of the pain relief therapy provided by ON-Q as compared to narcotics, the current standard of care. Benefits included better pain relief, less need for narcotics, reduction hospital-stay length by an average of one day, and higher patient satisfaction.

ON-Q is now covered by Medicare to treat post-surgical pain under the hospital outpatient payment system. Procedures performed in the hospital can be reimbursed using ON-Q.

### Subsidiary

I-Flow sells and distributes its products throughout the United States, Canada, Europe, Asia, Mexico, Brazil, Australia, New Zealand and the Middle East. InfuSystem, Inc., a wholly owned subsidiary of I-Flow Corporation, is primarily engaged in the rental of infusion pumps on a month-to-month basis for the treatment of cancer.

## Impliant (Private)

ISRAEL

### Market opportunity

Lumbar spinal stenosis is a narrowing of the spinal cord which causes nerve pinching. The most common form is degenerative stenosis, occurring in virtually the entire adult population as a result of aging. The narrowing results in compression of spinal nerves and nerve roots, causing a host of symptoms, including lower back and extremity pain.

### Product

Impliant is developing the TOPS System, a posterior motion preservation system for patients suffering from mild to moderate spinal stenosis. TOPS is designed to alleviate persistent leg and low back pain without sacrificing range motion. Unlike existing treatments that use spinal fusion, the TOPS System recreates near normal motion in all directions – flexion, extension, lateral bending, and axial rotation. Currently, 400,000 patients worldwide undergo fusion surgery each year.

The TOPS System is indicated for use in patients who have had at least six months of failed, conservative treatment prior to surgery and are between 45 and 75 years old. TOPS replaces the bony and soft tissues that are removed or compromised during surgical decompression. Like fusion, the system is anchored to the spine using pedicle screws. Unlike fusion, these screws are able to move continuously.

TOPS has demonstrated a significant improvement in pain and function in VAS, ODI, and ZCQ measurement. In addition, an independent radiological examination of Impliant's pilot study patients showed no screw loosening or breakage, no post-operative increase in spondylolisthesis, no loss in anterior disc height, and the establishment of motion at the operative segment.

### Status

Impliant, a privately held company, raised its first round of venture capital in 2000. In December 2004, the company secured \$18 million in Series C financing from a group of investors including Radius Ventures, the Hospital for Special Surgery and Elron Electronic Industries Ltd. In October, 2006, Impliant enrolled its first patient in a trial for the TOPS System.

## Innovative Spinal Technologies (Private)

Mansfield, MA

### Market opportunity

An estimated 260,000 lumbar fusions will be performed this year to treat common disorders of the spine. Procedures typically involve highly invasive open techniques or minimally invasive techniques that force the surgeon to trade ease-of-use or system strength.

### Product

Innovative Spinal Technologies has developed the Paramount Pedicle Screw System to address the needs of the spine surgeon and patient with a minimally invasive procedure that does not compromise strength. Potential benefits of Paramount include lessened operative time, reduced blood loss, less issue trauma and scarring, less postoperative pain, and a shorter hospital stay.

The Paramount Pedicle Screw System employs a simplified rod delivery system and an integrated screw and rod assembly that enables a single-step screw and rod insertion. The delivery system uses a non-cannulated screw design with a K-wire guided tip for accurate screw placement and enhanced strength. The Paramount System received FDA pre-market clearance in December 2005. The device is now available nationwide through a direct network of sales consultants.

Innovative also offers the Paramount VBR System, an inserter for the PEEK implant, a polyether-etherketone fusion cage. VBR increases the accuracy of implant placement by allowing the surgeon to better manipulate the cage in-situ. The device incorporates a lever actuated release. Innovative plans to develop a line of MIS surgical products along with fusion and motion preserving implants. The company currently markets the Paramount NAV, a surgical navigation aid that lessens fluoroscopic exposure, through a joint venture with GE Healthcare.

### Funding

In August 2005, Innovative closed a \$39 million Series B financing. The funding, one of the largest amounts of capital ever raised by a fledgling spinal implant company, was led by OrbiMed Advisors, MPM Capital, and JPMorgan Partners. The funds were used in R&D and to augment Innovative's work force. The company seeks to monetize the intellectual property of spine surgeons developed through the course of their day-to-day activities.

## **Invibio (Private)**

**West Conshohocken, PA**

### **Market opportunity**

Historically, metallic fixation devices have been used for soft tissue repair. However, there are inherent problems with stiff metals. Metallic implants contribute to stress shielding and bone weakening at the fracture site. Additionally, metallic implants may be removed due to irritation to surrounding soft tissue. Biomaterials are extremely strong, biocompatible and, because they are radiolucent, allow surgeons to monitor the bone growth and healing without the obstruction of the implant on the X-ray image.

### **Overview**

Invibio provides medical device manufacturers with implantable-grade PEEK-OPTIMA, an alternative to stainless steel and titanium, and ENDOLIGN polymers and medical-grade PEEK-CLASSIX polymer for the development of long- and short-term implantable medical devices.

### **Materials**

PEEK-OPTIMA has no adverse effects on the surrounding tissue or healing process. The biocompatible and stable polymer is available in a range of forms and can be processed via injection molding, extrusion or compression molding. PEEK-OPTIMA granules are available in three different viscosities and are appropriate for use in injection molding, extrusion, and compression molding. Stock shapes are available for machining. Applications include the following: Spinal cages, suture anchors, surgical screws, femoral implants, dental healing caps, heart valves and intracardiac pumps.

ENDOLIGN composite is a non-metallic biomaterial available for medical implants that combines the high strength found in metals with the biocompatibility and imaging compatibility of polymers. ENDOLIGN comprises continuous carbon fibers in a PEEK-OPTIMA polymer matrix, offering significantly enhanced mechanical properties. In high-load trauma applications, such as bone fracture plates, screws and intramedullary nails, ENDOLIGN's strength allows it to function as a replacement for metals, including cobalt-chromium alloys, titanium alloys and stainless steel.

Invibio's PEEK-CLASSIX polymer is a biocompatible implantable polymer used in the development of medical device applications requiring blood or tissue contact of less than 30 days. It can be repeatedly sterilized using conventional sterilization methods including steam, gamma radiation and ethylene oxide processes without the degradation of its mechanical properties. Applications include the following: catheters, tubing, drug delivery devices, blood management, laparoscopes, and other surgical instruments.

## IsoTis OrthoBiologics (ISTSF)

Irvine, CA

### Market opportunity

Bone graft substitutes, processed allograft products, and genetically engineered bone growth factors have significant future potential within orthopedics. Demographics will be the biggest driver of value and volume in the bone graft substitutes market. As the global population continues to age, and the average level of physical activity grows, the number of orthopedic procedures, which require the use of bone grafts and substitutes, will continue to increase. Further, minimally invasive procedures will encourage a greater percentage of the population to seek treatment.

Bone grafts, which are supplemental bone materials used to replace existing natural bone that has been damaged by trauma or disease, have been used in orthopedic surgical procedures for many years. The most common method of assisting the body's regenerative ability has been the use of autograft, in which bone is harvested from the same patient, and implanted at or near the repair site. The implanted bone acts as a scaffold for new bone growth. While autograft promotes rapid healing and carries no risk of disease transmission, there are disadvantages to this painful procedure: An infection may develop at the bone harvest site, there is risk of injuring surrounding structures during harvest, and the supply of autograft bone is limited.

### Products

IsoTis OrthoBiologics has developed synthetic bone grafting materials that incorporate demineralized bone matrix (DBM) in order to provide the benefits of autograft with few of the drawbacks. The company's technology promotes bone growth and rapid healing. The OrthoBlast II, DynaGraft II, and Accell product lines are well recognized and accepted in the orthopedic community. In addition, the company markets its synthetic bone graft substitute, OsSaturaT, and a family of other small medical devices.

### Sales

IsoTis OrthoBiologics has substantial critical mass in the rapidly growing field of orthobiologics. Its primary goals are to grow sales and improve margins. The company achieved 2004 product revenues of \$25 million, up from \$5 million in 2003. In North America, IsoTis has created an independent distribution network. A sales team headquartered in Lausanne, Switzerland fuels the company's rapidly expanding international presence; IsoTis hopes to establish a stronghold in this highly fragmented, underdeveloped marketplace.

The company intends to substantially increase sales to its existing customer base by offering a combined "natural" and "synthetic" product mix. Combining natural and synthetic technology platforms will enable IsoTis OrthoBiologics to obtain regulatory approval for a number of new, superior bone graft substitute products going forward, and launch these products through the existing distribution channels.

### Management

IsoTis has been led by CEO Pieter Wolters since 1997. Wolters raised over EUR 100 million in equity, initially from a range of blue chip venture capital funds, and in October 2000, through IsoTis' IPO. The company trades on the Toronto Stock Exchange under the symbol ISO.

## **K2M (Private)**

Leesburg, VA

### **Market opportunity**

Fusions are primarily performed to provide stability to the spine, by making two separate bones grow together, which eliminates motion between them. As movement is a natural function of the spine, surgeons will try to prevent this movement if the motion between the two segments of the spine is the source of pain. Spine hardware is designed to stabilize the spine until a bony fusion can form. Hardware is only used when a fusion between two or more segments of the spine is the surgical procedure's goal. The U.S. spinal stabilization market is estimated at \$850 million annually.

### **Overview**

K2M uses direct surgeon input to guide product development. The company's board of scientific advisors is made up of 16 leading surgeons, who collaborate on product design and implementation, and meet quarterly to discuss and critique new ideas. K2M's range of spine products includes fusion devices for less invasive surgery.

### **Products**

The MESA Spinal System came to the company's advisory board as a partially developed concept. The board saw the value of the device and quickly moved forward with development. MESA is a pedicle screw technology that transmits no torque to the spine during implant locking. MESA has the lowest profile of any pedicle screw on the market. The system utilizes specially designed instruments that give the surgeon greater control and allow for more versatile placement. At the time of its September 2006 launch, the device had been utilized successfully in 200-plus surgeries.

In April 2007, the company announced the Serengetti Minimally Invasive Retractor System. Serengetti offers improved visualization and access in posterior spine procedures that require screw and rod placement. Serengetti's screw-based design enables percutaneous delivery -- by establishing a fixed position, the placement eliminates retractor re-positioning typically associated with competitive systems, potentially reducing surgical procedure time. The retractor better preserves muscle and neurovasculature, which may lead to reduced post-operative pain and shorter recovery time for the patient.

Also in K2M's portfolio is Pyrenees, a low-profile thoracolumbar plate system designed to secure and stabilize the anterior column of the spine in fractures, tumors, and degenerative conditions. The plate provides compression and fixation across a bone graft while incorporating locking technology whereby each screw head forms an autogenic lock to the plate upon insertion.

## Kensey Nash Corporation (KNSY)

Exton, PA

### Overview

Kensey Nash Corporation designs, develops and manufactures products commercially available in the endovascular and biomaterials markets. Its principal product lines are used in cardiology and orthopedics (principally sports medicine and spine surgery).

### Products

Kensey's resorbable medical implants include the Angio-Seal Vascular Closure Device, used to close arteries. The device seals femoral artery punctures following catheterization procedures, allowing for shortened hospital stays. Angio-Seal creates a mechanical seal by sandwiching the arteriotomy between a bio-absorbable anchor and collagen sponge, which dissolve within 60 to 90 days. Available since 1996, it was the first resorbable biomaterial component on the market.

Angio-Seal has been marketed and sold by St. Jude Medical since 1999. Kensey receives 6% of all end user sales. The device has a current worldwide market penetration of 45-50%; the vascular puncture market is worth an estimated \$1 billion in annual sales. Royalties from Angio-Seal (\$19.6 million in fiscal 2006) are a substantial part of the company's revenues.

Also in the cardiovascular market, Kensey has launched the TriActiv System, a device which provides embolic protection during the treatment of diseased saphenous vein grafts. TriActiv is available for sale in the U.S. and European Union. A newly introduced sales and marketing team is encouraging growth in the endovascular market overseas. The costs associated with investment led to a downturn in financial results for fiscal year ended 2006.

### Partnerships

The Kensey Nash Biomaterials Division partners with companies in the orthopedics, soft tissue, and spine markets. In 2006, this division was responsible for 39% of the company's total revenues. Kensey manufactures the Vistoss Scaffold Foam, on behalf of OrthoVita. The foam is used in bone graft procedures to aid in the healing response.

Kensey markets over 100 other products that are used in cardiology, sports medicine, orthopaedics, dentistry, and drug delivery.

## **KFx Medical Corporation (Private)**

**Carlsbad, CA**

### **Market opportunity**

Rotator cuff repairs are among the most common orthopedic procedures performed, with over 700,000 annual cases worldwide, of which approximately 400,000 are done in the U.S. Only 25% of all rotator cuff repairs are performed arthroscopically, as many surgeons lack the knot-tying and suture-passing skills required to perform this procedure.

Single-point fixation has a re-tear rate greater than 50%. The high re-tear rates have prompted surgeons to search for more robust suture-anchor configurations, including double-row fixation. Existing research supports the benefits of two-point fixation for rotator-cuff repair. The technique better replicates the natural anatomic footprint of the rotator cuff's connection to bone. In retrospective clinical analysis, double-row fixation showed better outcomes when compared to single-point fixation techniques.

Clinical applications involving double-row fixation that use current anchoring technology for arthroscopic rotator cuff repair brings increased operating room time and a steep learning curve due to more anchors, complex suture management and knot tying. Minimally invasive techniques typically result in less pain and are faster but require surgeons to have advanced arthroscopic skills.

### **Product**

KFx Medical has developed the SutureCross Knotless Anatomic Fixation System, a suture-anchoring system that enables surgeons to perform double-row fixation techniques without knot tying or suture passing. The system simplifies surgical techniques, making arthroscopic procedures accessible to a wider range of surgeons. SutureCross shortens procedure time and in doing so reduces costs. The device received FDA 510K approval in August 2006.

The system consists of two implantable components -- knotless suture lock bone screws, and nail suture anchors with two pre-attached sutures. Each of the implantable components has a corresponding disposable delivery device. Clinical research has demonstrated the system's effectiveness in reducing gap formation (elongation at the repair site associated with the formation of adhesions and poor functional outcomes) by as much as 50% compared to other double row repairs.

## **Kyphon (KYPH)**

Sunnyvale, CA

### **Market opportunity**

The thick portion of bone at the front of each vertebra is referred to as the vertebral body. A vertebral compression fracture (VCF) occurs when the vertebral body fractures and collapses. Most VCFs are caused by osteoporosis, from which one in three women and one in eight men over the age of 50 suffer. Compression fractures may also occur as a result of certain types of cancer or tumors.

Multiple VCFs can cause the spine to shorten and angle forward, resulting in kyphosis -- a stooped or "hunchbacked" posture. Over time, this alteration in posture can have a compression-like effect on internal organs, causing medical complications unrelated to your spine.

### **Products**

Kyphon has developed a device designed to restore and preserve spinal function and diagnose low back pain using a minimally invasive procedure. VCFs have traditionally been treated with bed rest, medication and bracing, all of which help to decrease a patient's pain but do not address the spinal deformity. Surgery can address the deformity but is typically reserved for cases of major neurologic deficiency and mechanical instability.

Kyphon's Balloon Kyphoplasty is a minimally invasive option that addresses both the deformity and the pain by stabilizing the fracture and helping to correct the vertebral body deformity. During the operation, balloons are used to gently raise the collapsed vertebra in an attempt to return them to the correct position. The benefits of treatment include a reduction in back pain and improved mobility.

Balloon Kyphoplasty is associated with a low complication. By achieving fracture stabilization and correction of spinal deformity, patients experience significant reduction in pain and improvement in mobility, reducing the number of days in bed and increasing overall quality of life. Kyphoplasty products are available for sale in the U.S. and in Europe. The company trades on the Nasdaq stock exchange under the symbol KYPH.

## Langer (GAIT)

Deer Park, NY

### Orthotics market

An orthotic is a device designed to align the foot and ankle into the most anatomically efficient position. The plastic body of the orthotic helps to re-align the foot by redirecting and reducing certain motion that takes place during the gait cycle. New alignment often helps alleviate problems in other parts of the body.

### Overview

Langer, Inc. designs, manufactures and distributes a broad range of products targeting the orthopedic, orthotic and prosthetic markets. Langer offers more than 500 orthopedic products, including custom foot and ankle orthotic devices, pre-fabricated foot products, rehabilitation products, and gel-based orthopedic and prosthetics products. Weakness in the company's U.S. and Canadian therapeutics footwear programs have led to a decrease in sales in recent years.

### Subsidiary

Langer's subsidiary Bi-op also sells orthotics, primarily in Canada. The company markets rehabilitation devices, custom-built footwear, orthopedic corsets, and other prostheses. The 2005 sales decline at Langer was partially offset by growth at Bi-op, where sales increased 17%.

### Skin care

Langer offers a line of skincare products, including scar management therapeutics and gel-based therapeutic gloves and socks, primarily through its Silipos brand, acquired in September 2004. These products are designed to improve skin appearance and transmit moisture agents, vitamins and nutrients to the skin. The proprietary gel used in bandages, wraps, and pads incorporates a medical grade mineral oil that gradually diffuses onto the skin to reduce friction and pressure, improve skin elasticity, and minimize scarring.

Adding to the skin care line, in January 2007, Langer completed the acquisition of Twincraft, a manufacturer of specialty bar soap focused on the health and beauty market. The purchase price was \$26.9 million, the majority being paid in cash.

## LDR Spine (Private)

Austin, TX

### Market opportunity

Worldwide, over sixty percent of spine procedures are performed by neurosurgeons and orthopedic surgeons in the U.S. Almost 80 percent of the dollar volume generated worldwide finds its way here, due to favorable pricing, reimbursement and demographics.

### Overview

LDR Medical, based in France with U.S. headquarters in Austin, TX, develops medical devices used to treat spinal disorders. The company founded LDR Spine USA in late 2004 to expand its U.S. presence.

### Products

To date, five LDR products have received 510(k) clearance from FDA. The company plans to initiate two investigational device exemption studies to gain PMA clearance for Mobidisc and Mobi-C. These discs incorporate a mobile bearing design that provides six independent degrees of freedom to give patients a natural range of mobility. The device is accompanied by simple instrumentation designed to assist the surgeon. A lumbar study is scheduled to commence in the second half of 2007.

LDR's flagship product for spine fusion surgery is Easyspine, a system that uses one-third the inventory of conventional pedicle screw and rod designs. The multi-axial screw and rod connection require less torque, offer greater fixation strength, and come with pre-loaded set screws, reducing intraoperative time.

Complementing Easyspine is ROI, a lumbar device that is modular and compatible with LDR's custom-fitted bone substitute, BF+. Also included in the fusion portfolio is MC+, a cervical device with easy-to-use instrumentation.

### Status

Despite the short time these products have been available, they now command over 25 percent market share in the French spine market. MC+ and ROI are approved in the U.S. as partial lumbar vertebral body replacements.

LDR has a presence in 26 countries worldwide through a direct sales organization in France, the U.S., China and Brazil, and through distributors elsewhere.

## LifeCell (LIFC)

Branchburg, NJ

### Overview

LifeCell's cryopreservation technique allows biological tissues and cells to be preserved without damaging structural or biochemical integrity. AlloDerm, LifeCell's first clinical product, was brought to market in 1994. To date, the technology has been used in more than 900,000 grafts and implants.

### Product

AlloDerm is an acellular dermal matrix derived from donated human skin tissue supplied by tissue banks. AlloDerm is prepared using a multi-step process that removes both the epidermis and the cells that can lead to tissue rejection and graft failure, without damaging the matrix. AlloDerm is FDA approved and meets the standards of the American Association of Tissue Banks.

AlloDerm was originally developed as a graft for burn patients. The tissue preservation technology makes each donor tissue graft more effective by preserving the biochemical and structural components of the tissue. The graft's versatility has led to its use in a number of reconstructive applications including reconstructive and general surgery which are marketed through a direct sales team. These include the skin grafts, abdominal wall and breast reconstruction.

AlloDerm offers strength comparable to synthetics with a more pliable tissue matrix. The graft supports rapid revascularization and remodeling into native tissue, minimizing the risk of infection and rejection and helps prevent adhesion of the visceral contents to the graft, which can reduce the possibility of additional complications, such as bowel blockage or herniation. Clinical trials have demonstrated that the technology leads to substantially fewer complications than synthetics, including seroma, dehiscence and recurrence. AlloDerm may reduce the length of hospital stay and associated medical costs.

### Partnerships

In addition to its in-house sales efforts, LifeCell has partnered with several outside partners. These include Boston Scientific for Repliform, its urogynecologic product; Wright Medical Group for GraftJacket, used in orthopedic surgical procedures; and Stryker for AlloCraft DBM, a demineralized bone matrix used in grafting procedures.

### Status

In June 2007, the company received 510(k) clearance for its Strattice tissue matrix, a soft tissue repair product. Like AlloDerm, Strattice is intended for use in soft tissue repair procedures including breast reconstruction and hernia repair.

## **Mako Surgical Corporation (Private)**

**Fort Lauderdale, FL**

### **Product**

Mako Surgical Corporation's Haptic Guidance System allows orthopedic surgeons to pre-operatively plan the alignment and placement of knee resurfacing components and to intra-operatively make complex, anatomic, tissue-sparing and bone-conserving cuts precisely and accurately.

The first application of the company's technology is the surgical execution of a unicondylar knee arthroplasty to treat patients suffering from early stage degenerative joint disease of the knee. Unicondylar implants are by design a less invasive alternative to total knee arthroplasty. The surgery requires very precise resection of bone and alignment of the implant components. The Haptic Guidance System provides the surgeon with the ability to pre-operatively optimize the size and alignment of the implant and, with the support of virtual visualization and surgeon interactive robotics, execute the arthroplasty through a small incision. The software supports intra-operative measurement tools that enable the surgeon to "tune" the knee with respect to joint kinematics.

The Mako Haptic Guidance System provides the potential for improved patient outcomes, minimal hospitalization and shorter rehabilitation. It gives surgeons an early intervention option to treat patients with unicompartmental osteoarthritis of the knee, allowing patients to retain their pre-operative lifestyle. The system may eliminate inconsistency of resection and potential for mal-alignment often attributed to jig bases and knee system instruments.

The first clinical use of the Haptic Guidance System took place in June 2006. The procedure was executed through a 2.5 inch incision. Early results are promising: 18 additional patients have received implants, and all are being followed and radiographically evaluated with CT scans to verify the system's pre-operative planning precision with the post-operative implant position.

### **Status**

Mako Surgical Corp. has raised more than \$25 million in venture capital financing to date. The company has more than 230 patents and patent applications in the areas of robotics, haptics, robotic surgery, image guided surgery and implants; it has more than 100 products in its pipeline.

## Millenium Biologix (MBC)

Ontario, CANADA

### Market opportunity

Orthopedic surgeons commonly use autograft tissue because of performance limitations and concerns associated with bone replacement materials, which often use source products derived from animals or human cadavers. Currently, 60 to 70 percent of all major orthopedic procedures involve autograft tissue. The need for additional surgery to obtain the autograft from a second surgical site increases both cost and patient risk; many patients suffer long-term problems such as chronic pain at the harvest site.

### Technology

Millenium Biologix's Skelite technology is a synthetic material that promotes rapid healing. Using the body's natural recovery process, the implant is slowly replaced by the orderly growth of new bone, a process known as remodeling. Skelite is the foundation of several product lines aimed at clinical applications in orthopedics. The synthetic bone graft and autologous tissue engineering scaffold line was launched for commercial sale in June 2003.

### Products

Pending FDA review, Millenium's Bone and Cartilage Stimulating Peptides (BCSPs) are an alternative to existing growth factors. The hybrid implants are manufactured in a synthetic process that precludes potential disease transmission. BCSP small molecular weight peptides are synthesized from sequence data in a standard process that avoids the expensive recombinant technologies required to produce Bone Morphogenetic Proteins.

A second opportunity lies in the emerging field of tissue engineering, where Millenium is investigating automated tissue engineering systems. The company's Autologous Clinical Tissue Engineering System (ACTES) automatically verifies that the process of cell multiplication and tissue growth is proceeding correctly using a built-in quality assurance system of sensors and genomic arrays. If successful, this will allow patients' own tissues to be produced safely, reliably and efficiently within regional healthcare systems.

### Partnerships

Global commercialization of Millenium's products is achieved through targeted corporate alliances that provide marketing, sales and distribution. In addition, Millenium has an evolving network of corporate and university R&D alliances in North America and Europe to support its in-house product development programs. Millenium trades on the Toronto Stock Exchange under the symbol MBC.

## Minrad (BUF)

Orchard Park, NY

### Market opportunity

Minimally invasive surgeries for pain and spine have grown rapidly due to the benefits of reduced operating time and costs, reduced trauma and faster recovery for the patient. Minrad seeks to capitalize on the rise of these less invasive procedures. The company's medical device products incorporate patented real-time image-guidance technologies that enable medical professionals to improve the accuracy of interventional procedures, and provide a significant reduction in radiation exposure for both patients and medical professionals.

### Products

SabreSource is a real-time image-guidance system which Minrad believes offers a significant enhancement to the precision of surgical procedures. SabreSource uses x-ray and laser technology that enables medical professionals to visualize both the surface point of entry and true angle of approach required to reach an internal treatment area or biopsy site.

Minrad's technology represents a significant technical advancement to image guided systems -- the ability to visualize both the surface point of entry and the true angle required to precisely target an internal area in real time. The system provides physicians improved control and visualization versus non-real-time systems. SabreSource has the ability to handle multiple targets while limiting the need to reposition the fluoroscope. The accuracy of the system allows the x-ray to be turned off during the procedure, which can result in a significant reduction in radiation.

The SabreSource equipment is designed to retrofit any number of existing mobile C-arm fluoroscopes manufactured by other companies. There is an approachable market of approximately 125,000 C-arm systems; the system sells for \$20,000.

Utilizing this technology, the company has developed a line of handheld companion instruments for the SabreSource system (bone and core tissue biopsy, spinal and aspirating needles, procedure syringes, and a catheter introducer), which illuminate when they are aligned to the proper angle of approach to sub-surface treatment or biopsy site. The Light Sabre has an accuracy claim of +/- 3mm at a depth of 100mm.

### International reach

To date, Minrad has signed eight international distribution agreements. Its contracts with Taiwan and China will total \$2.1 million by 2008. Agreements with Mexico, Venezuela, Hong Kong, Brazil, Turkey and Greece require minimum purchases of \$5.7 million by 2009 to maintain exclusivity.

### Inhalation anesthetics

Despite growth opportunities in image guidance, Minrad's revenues rely predominantly on inhalation anesthetics, including enflurane, isoflurane and sevoflurane. Sevoflurane is the largest inhalation anesthesia agent in the world (\$1 billion market), and Minrad anticipates U.S. approval in 2007; Minrad currently distributes sevoflurane in six countries.

Minrad has disclosed anesthesia & analgesia contracts that need to generate over \$54 million in annual revenues in 2007, \$103 million in 2008 and \$125 million in 2009 in order to maintain exclusivity.

Minrad is leveraging its inhalation anesthetics and medical device expertise to develop a conscious sedation drug delivery system, which would provide pain relief for patients without loss of consciousness. Inhalation anesthetics offer numerous benefits to competitive products such as nitrous oxide and sedatives/hypnotics. The company plans to file for 510(k) approval for the drug delivery device in 2007. Once approved, Minrad will file an IND for the anesthetic agent it chooses to use and will then begin Phase III trials. The company estimates a market potential of over \$1 billion.

## Nanogen (NGEN)

San Diego, CA

### Market opportunity

As the biomedical industry works to gain a better understanding of the molecular basis of disease, the need for specific methods to detect genetic variation are becoming increasingly central to research.

### Products

Nanogen's core technologies, including the NanoChip platform, are well suited to molecular genetics. The company's product line includes instruments, electronic microarrays, reagents, ELISAs and rapid tests sold directly to end-users through licenses, and through a network of distributors in North America, Europe and Asia.

Nanogen's electronic microarray platforms provide an alternative to traditional real-time PCR (polymerase chain reaction, a method of duplicating small amounts of DNA to assess its make-up). Using electronic arrays, Nanogen is able to screen samples for multiple genetic markers simultaneously. This is particularly useful when dealing with complex genetic disorders involving multiple genes or multiple alleles.

Central to Nanogen's product line is its rapid quantitative test, including NT-proBNP, a diagnostic used to detect heart failure (and to detect the severity of the failure). NT-proBNP has been cleared by FDA and is pending approval in the EU. Nanogen is also collaborating with Jurilab (based in Finland) to investigate genetic markers associated with Acute Myocardial Infarction, hypertension and type-2 diabetes.

Nanogen's NanoChip microarray technology is an open platform that allows customers to run common assays as well as customize their own assays. Nanogen's real-time PCR probes, primers, and reagents work with most commercially available thermocyclers and PCR master mixes. This flexibility allows for easy expansion across markets.

### Status

In December 2006, the company was awarded a \$4.5 million contract from the U.S. Centers for Disease Control to develop a point-of-care diagnostic for Avian flu. The contract came at a time of strong growth for the company. Total revenues for the fourth quarter of 2006 nearly tripled to \$8.7 million, from \$3.1 million for the same period in 2005.

## NeuroMetrix (NURO)

Waltham, MA

### Market opportunity

Neuropathies are diseases of the peripheral nerves and parts of the spine that are often associated with lower back pain, diabetes, or carpal tunnel syndrome. Accurately diagnosing these disorders is an indispensable component of formulating a fast and effective course of treatment.

Historically, this required sending a patient off-site, usually to a neurologist for a formal nerve conduction study. There are over two million such studies performed in the U.S. each year.

### Product

With the introduction of the NeuroMetrix NC-stat System, physicians are now able to diagnose neuropathies at the point of care, leading to faster diagnosis and earlier, more effective therapy. The NC-stat System consists of the NC-stat Monitor, disposable biosensors (eight nerve specific biosensors exist), and a docking station, which enables the physician to transmit data to a central location, where data is analyzed and returned. The system is designed to allow allied health or nursing staff to conduct the procedure; test results are available in 15-25 minutes.

### Financial potential

NeuroMetrix believes in-office testing could expand the market for nerve conduction studies to as many as 9.5 million procedures annually, creating a \$1 billion market opportunity. Available since May 1999, the NC-stat System is currently being used in 3,600 physicians' offices by 10,000 physicians; more than 500,000 patients have been tested to date. As use of the NC-stat System has increased, so has reimbursement from third-party and governmental agencies, which has and will continue to be key to adoption of the system.

### Sales force

In order to execute on its expansion plans, NeuroMetrix has expanded its direct sales force. It is also expanding its network of independent sales agents – which now total over 1,000 – in order to further penetrate the market of primary and specialty care physicians. Using this approach, NeuroMetrix hopes to target a domestic market of 250,000 physicians.

### Investigation

NeuroMetrix is currently under investigation for marketing of the NC-stat System. Questions have also been raised about the potential for misuse of the device by unqualified personnel. NeuroMetrix is said to be cooperating with the investigation, and management contends that there is no evidence of inappropriate use of the system by physicians. However, these issues have prompted some insurance carriers to alter their categorization of the procedure, which has the potential to disrupt reimbursement. Sales for the quarter ending March 31, 2007 were \$11.8 million, consistent with the same quarter in 2006.

## NuVasive (NUVA)

San Diego, CA

### Market opportunity

Back pain is the leading cause of healthcare expenditures in the U.S. Every year over \$50 billion is spent on diagnosis, treatment and rehabilitation. Spine fusion, a \$2 billion market, is a surgery performed in hospitals to “fuse” or join together part of the spine. A surgeon will perform this operation only after other treatments have failed. Conditions requiring spinal fusion include: spinal injuries, disc problems, abnormal curvature of the spine (like scoliosis) and a weak or unstable spine caused by infections or tumors. More than 325,000 such procedures were performed in 2003. Recovery time from traditional spinal fusion surgery may take upwards of six months.

### Product

NuVasive’s principal product is the minimally disruptive Maximum Access Surgery (MAS) platform. MAS is comprised of three components: Neurovision, a proprietary software-driven nerve avoidance system; MaXcess, a split-blade design retraction system; and specialized implants, like SpheRx and CoRoent which collectively minimize soft tissue disruption during spine surgery while allowing maximum visualization and surgical reproducibility.

The MAS platform is rapidly gaining traction as it offers significant advantages to both patients and surgeons, including reduced hospitalization time and faster recovery. NuVasive has a state-of-the art cadaver operating theater and training facilities focused on educating leading surgeons on the advantages of NuVasive products.

### Performance

Direct sales in 2005 accounted for 30% of total sales, compared with 4% in 2004. In 2005, the MAS system generated nearly 77% of the company’s third-quarter revenue. Traditional fusion products, including saline-package bone allografts and fixation products, contributed the remaining 23% of quarterly revenues.

For the fiscal year ended December 31, 2005, revenues increased 61% to \$61.8 million. Net loss totaled \$30.3 million reflecting an increase in cost of goods sold, higher research and development expenses, an increase in sales & marketing expenses and inclusion of \$12.9 million in-process research & development costs.

For the full year 2006, the company reported revenue of \$98.1 million, a 56.7% increase over the \$62.6 million for the full year 2005.

### Status

In the third quarter of 2006, the NuVasive completed an accelerated buyout agreement with Pearsalls Limited related to the NeoDisc investigational device and related embroidery technology. The company incurred total costs of \$20.1 million in 2006 for this buyout, resulting in a total acquisition cost of \$33.1 million. By completing this buyout, NuVasive eliminated certain royalty obligations as well as \$12 million in potential milestone payments.

### Management

Since 1999, Alexis Lukianov has led NuVasive as CEO. Lukianov has seen the company through venture capital financing, commercialization, and its IPO. He has over 20 years senior management experience in the orthopedic industry.

## ONI Medical Systems (Private)

Wilmington, MA

### Market opportunity

Imaging extremities represents approximately 25% of all magnetic resonance imaging (MRI) done today. Most hospital and imaging centers have lengthy patient backlogs and yet cannot justify the expense of an additional whole-body MRI.

### Product

ONI Medical has developed a family of dedicated-purpose MRI systems to address this market. MSK Extreme, the company's latest offering, is intended to scan the hand, wrist, elbow, foot, ankle and knee.

MSK Extreme offers 1.0 Tesla high-field imaging performance, the same level of performance offered by whole-body MRI systems and five times more powerful than competing low-field extremity systems. The system provides fast scan times, robust pulse sequences for contrast-enhanced studies, late echo imaging and expanded volume fat suppressed visualization. Consistent positioning results in optimal first-time images that often provide better resolution and information than those produced by high-field, whole-body MRI systems using surface coils.

A Windows-based interface and menu-driven screens enable users to quickly learn how to operate MSK Extreme. The system is compatible with industry standard DICOM 3.0 networking capabilities that allow transmission of images for teleradiology diagnosis and consultation. Existing radiological technologists can be quickly trained for maximum staff utilization.

Requiring only 200 square feet of floor space, the unit can be easily placed in hospitals, diagnostic imaging centers and orthopedics/sports medicine practices. Hospitals and imaging centers can decompress their whole-body MRI schedule by transferring the extremity caseload to the MSK Extreme – examination time averages only 30 minutes, maximizing patient throughput. These factors translate into better returns for users. The MSK Extreme needs less than two patients per day in order to provide a return on investment compared with six to eight patients for a whole-body MRI.

## Orthocon (Private)

Colts Neck, NJ

### Market opportunity

Orthopedic and spine surgery are among the fastest growing markets in the medical industry. The orthobiologics segment has an estimated U.S. market potential of over \$2 billion.

### Products

Orthocon has licensed its first four products to outside companies and is now developing new products outside the licensed technology. The company's largest opportunity is the management of post-operative pain following orthopedic and spinal surgical procedures. The products address patient comfort and hospital costs by allowing for earlier discharge.

Orthocon is also developing the Syntinate platform technology, comprised of natural and synthetic orthobiologic compounds with precise absorption and release attributes. The implantable, biodegradable products are intended for intraoperative drug delivery in orthopedic and other surgical and dental procedures.

### Intellectual property

Orthocon's intellectual property includes several patent applications with extensive claims. The company has received a favorable opinion in the preliminary examination of the PCT application. Orthocon's pipeline of products is designed within the claims of pending patent applications.

### Status

The company believes its medical device products are approvable via a 510(k) regulatory path, whereas the drug combination products may require a PMA. A 510(k) has been filed for Syntinate. The company also believes its post-operative pain management product should be approved through a PMA. In February 2006, Orthocon closed a \$10 million Series A financing led by BB Biotech Ventures and Canaan Partners.

## Orthometrix (OMRX)

White Plains, NY

### Overview

An aging population is seen as the principal growth driver of Orthometrix, a diversified company that develops and markets a variety of devices related to the musculoskeletal system. The company's procedures and devices are designed to help increase mobility and treat pain associated with osteoarthritis, plantar fasciitis (foot pain) and other conditions that reduce mobility.

### Products

The company's healthcare division sells and services peripheral Quantitative Computed Tomography (pQCT) bone and muscle measurement systems. In the U.S. and Canada, Orthometrix offers three models of pQCT systems for in vivo and in vitro research. Over the past decade, pQCT has replaced Dual Energy Bone Absorptiometry as the technology of choice for research laboratories specializing in bone disorders such as osteoporosis. The size of this special research niche market is only a few million dollars per year, but most sales are recurrent. Orthometrix also offers two models of pQCT systems for clinical assessment and monitoring of bones. All systems have received 510(k) market clearance from FDA and are principally marketed to pediatrics and orthopedics specialties.

The company's sports and fitness division develops motorized exercise systems for rehabilitation, physical therapy and sports medicine, based on Orthometrix's vibration technology. The devices are marketed in the U.S. and Canada under the name of VibraFlex Rx for the rehabilitation of muscle, tendons and ligaments, and to improve muscle strength and coordination. VibraFlex Rx may also reduce incontinence due to nerve and muscle deterioration caused by aging, pregnancy, childbirth, pelvic surgery or a reduction of estrogen due to menopause.

### Status

Orthometrix has acquired the perpetual exclusive license, in the U.S. and Canada, to Orbasone. The Orbasone platform is derived from the technology used in lithotripsy for the non-invasive treatment of kidney stones (Extracorporeal Shock Wave Therapy or ESWT). The device is used to reduce pain in soft tissues in the foot, ankle, shoulder, knee and elbow areas. Orbasone is well accepted in Europe and Asia, and is now available for sale in Canada following receipt of approval from Health Canada for the treatment of pain associated with plantar fasciitis. Orthometrix is in the process of attaining pre-market approval (PMA) from FDA in the U.S. Two companies have already received PMA market approval for plantar fasciitis. Orthometrix plans to price its Orbasone competitively, below \$200,000.

## Orthovita (VITA)

Malvern, PA

### Market opportunity

Orthovita estimates that each year 700,000 bone grafting procedures are performed worldwide on the spine, extremities and pelvis. Harvesting autografts involves an additional procedure that extends surgical time, adds cost, increases blood loss and patient risk. Allografts, if not procured and treated properly, can lead to infections. Orthovita's technology avoids these two potential complications by regenerating bone and soft tissue synthetically.

### Product

Orthovita's VITOSS Bone Graft Substitute is a bone void filler used to help guide the regeneration of the patient's own bone. It is composed of materials that encourage the flow of blood and nutrients; it integrates well into existing bone and promotes new in-growth and maturation.

VITOSS has been found effective in a variety of applications, including spinal grafting, and the treatment of bone defects due to trauma, degenerative disease and tumors. In 2001 it was approved for use in the U.S. and the EU; since then, over 100,000 units have been sold. A VITOSS Foam product has been co-developed with the Kensey Nash Corporation. It is pliable and can be designed to meet a surgeon's needs for a given procedure.

CORTOSS, a high-strength, bone-bonding, self-setting composite has been engineered to mimic the characteristics of human cortical bone, is the only product in Europe approved for use in vertebral augmentation on the basis of prospective clinical data. Data from controlled, multi-center, clinical trials found that the percutaneous injection of CORTOSS into the affected vertebral body of patients with painful compression fractures resulted in almost immediate pain relief, significantly improved functioning, and reduced disability in a high percentage of patients. The product is pending pre-market regulatory review by FDA.

### Partnership

In December 2006, Orthovita entered into a royalty sale agreement with Angiotech Pharmaceuticals (Angiotech previously made a \$25 million direct investment in Orthovita and owns 12% of the company), whereby Orthovita will purchase the profit-sharing royalty rights for Vitagel Surgical Hemostat. Vitagel is composed of microfibrillar collagen and thrombin in combination with the patient's own plasma. The combination creates a hemostat by forming a collagen/fibrin scaffold with platelets. The product has been found effective in controlling bleeding during orthopedic, cardiac, hepatic and general surgical procedures.

A porous, fine-particle structure encourages flow of blood and nutrients through the entire VITOSS scaffold matrix which is replaced by structured bone similar to adjacent trabecular bone.

## Osiris Therapeutics (Private)

Baltimore, MD

### Overview

Osiris Therapeutics is a stem cell therapeutic company developing and marketing products to treat medical conditions in the inflammatory, orthopedic and cardiovascular space. Stem cells have historically been quite difficult to grow in culture. Osiris' manufacturing methods allow for rapid, controlled growth and the ability to produce large quantities of stem cells from a single donation. Once produced, the cells can be stored in a frozen state, ready to use as they are needed.

In both animal and human clinical studies, scientists and academic researchers have found that Osiris stem cells are generally not rejected by the host's immune system. This feature eliminates the need to tailor stem cells based on donor matching and may mean that patients can forgo the harmful side effects of immune suppression.

### Products

In the orthopedic space, the company currently markets and sells Osteocel, used to regenerate bone. Osteocel is a bone matrix product containing stem cells. Like an autograft, it is biologically active and provides the three beneficial properties of osteoconduction, osteoinduction, and osteogenesis. Unlike autograft, Osteocel does not require a secondary procedure or tissue harvesting. Stem cells contained in Osteocel are capable of differentiating into various cell types and can respond to their environment to differentiate into appropriate tissues as needed. All tissues are tested to ensure that the cells are viable and osteogenic.

Currently being evaluated in a Phase II clinical trial is Chondrogen, used to regenerate meniscus in the knee. The meniscus is a crescent shaped cushion that provides stability in the knee joint. Injury and tears to the meniscus are common, arising from trauma or age. In the weeks following knee surgery, Chondrogen may be used to regenerate meniscal tissue, thereby preventing complications including arthritis.

### Status

Osiris has established a significant patent position in adult stem cell technology. The company has an exclusive license to 47 U.S. patents. In addition to its orthopedic activities, the company is developing uses for stem cells to improve heart function following myocardial infarction and to prevent progression to congestive heart failure. Osiris Therapeutics has entered into a strategic alliance with Boston Scientific Corporation for this product area.

## Osteotech (OSTE)

Eatontown, NJ

### Market opportunity

Bone and tissue transplants are often necessary to correct deformities and repair or reconstruct defects caused by congenital malformations, trauma, infections, cancer and other diseases. For certain procedures, autograft bone can be acquired from another part of the patient's body with an additional operation. For the large number of procedures where this is undesirable or simply not feasible, allograft bone tissue from donated cadavers can be used.

### Overview

Allograft bone tissue is acquired primarily through a network of organ procurement organizations and tissue banks. Osteotech, having established relationships with a number of the largest tissue banks, processes human bone and bone connective tissue for transplantation, with a particular focus on spinal, trauma, and total joint revision procedures.

Since its formation in 1986, the company has become the world's largest processor of aseptic allograft bone tissue, yielding over 2.3 million grafts for its clients. Osteotech processes bone tissue in a microbially controlled environment using a variety of "clean room" techniques. The company utilizes technology that yields a wide array of freeze-dried and frozen tissue products; once stored, freeze-dried tissues may be stored for up to three years, and frozen tissue may be stored up to five years.

### Products

The company offers both Demineralized Bone Matrix (DBM) and Base Allograft Bone Tissue. These two operating segments are distinct. The company's proprietary demineralization process creates a product which, when applied to cortical bone, yields allograft bone tissue with osteoinductive (the process by which bone is induced to grow) and osteoconductive (the matrix provided by allograft bone tissue into which the host bone can grow) properties. Revenues from the DBM segment are primarily related to the processing and marketing of Grafton DBM. The DBM segment also draws revenues from the processing of two private label DBM's – DePuy and Smith & Nephew.

In the Base Allograft Tissue Segment the company processes allograft bone tissue into mineralized weight-bearing forms. The variety of forms includes femoral cross sections, fibula wedges and cortical struts. Domestically, allograft tissue forms are marketed and distributed by Osteotech clients. Clients typically pay a per donor fee for the processing of donor tissue. Internationally, tissue forms are marketed and distributed through distributors. The majority of revenues in this segment are generated from Graftech Bio-implants marketed and distributed to hospitals and surgeons.

## Pegasus Biologics (Private)

Irvine, CA

### Overview

Pegasus Biologics uses biotechnologies to manufacture and sterilize bioimplants for soft tissue reinforcement. Pegasus products have applications in large markets fueled by favorable demographics such as an active aging population. Currently, there are approximately 500,000 anterior cruciate ligament (ACL) reconstruction procedures performed worldwide on an annual basis. In the neurosurgical space, there are approximately 100,000 craniotomy procedures where Pegasus technology might be applied.

### Products

The company's UltiSter Sterilization can be used on both animal and human tissue. Existing methods use chemicals or radiation, which may cause tissue damage. Tissue sterilized using this process is available "off-the-shelf" and procedure-ready after a simple rinsing step, eliminating the current use of freezers and the time required for thawing.

UltiSter technology may be particularly suitable for sterilization of allograft tissue and may address current concerns of regulatory agencies overseeing the sterilization of allografts. Ninety-three percent of infections reported to the CDC involve musculoskeletal tissues.

The company's UltiFix Tissue Stabilizing Technology is a non-glutaraldehyde method of stabilizing bioimplants. UltiFix stabilizing agents are water-soluble and biodegradable. They leave a biocompatible and water-soluble residue, unlike current glutaraldehyde agents which may leach toxic residues due to unstable crosslinking bonds.

Pegasus' crosslinking process preserves the natural properties of the tissue and stabilizes it so as to resist degradation. This process can also be adapted to vary the rate of resorption. It is thought that many existing biological patches and grafts resorb before sufficient host tissue remodeling has occurred.

Products include the company's OrthADAPT Bioimplant, a tissue scaffold used in the repair and reinforcement of tendons and ligaments, including ACL reconstruction. Clinical results demonstrate that this bioimplant does not produce any clinically significant inflammatory responses and provides a reliable scaffold during the healing process for rapid, controlled remodeling at the implant site. Pegasus also manufactures the Unite Biomatrix, a sterilized collagen wound dressing. The enzyme resistant collagen scaffold allows for better suture retention.

## Precimed (Private)

Exton, PA

### Overview

Precimed develops instruments for the orthopedic implant market. Headquartered in Switzerland, the company has subsidiaries in the U.K, Japan, Asia and the U.S. Precimed currently employs 445 employees. Its leading products -- instrumentation for hip and knee replacement, trauma and spine -- are sold to more than 260 orthopedic OEM customers.

Growing market segments include minimally invasive surgery, resurfacing, computer-aided surgery, RFID tracking, trays and cases, and disposable instruments. Precimed has more than 75 patents/patents pending. All facilities and processes are ISO-certified. Precimed has 100,000 square feet of manufacturing capacity.

### Product

The company's Build-A-Driver allows customers to specify precise screwdriver needs using a point-and-click Web site. The service offers flexibility in screwdriver design; once options and dimensions are specified, Precimed offers an illustrated and a schematic representation of the driver, and allows one to submit it to Precimed for immediate design and pricing review.

### Partnerships

Precimed's ability to include RFID allows surgeons to keep better track of instruments. Precimed has partnered with MBBS, a supplier of through-metal RFID devices, creating an RFID system that is auto-clavable, and can read and write through metal and survive tray sterilization processes.

Strengthening its Asian presence, the company recently partnered with Fujiflex of Osaka, Japan. The partnership gives both companies access to each other's technology, products and services, which will allow Precimed to increase its presence in the Japanese market by offering its customers better service, improved logistics, and engineering support. Both companies will remain independent.

### Financing

In September 2005, Precimed closed a \$27 million round of financing in an equity transaction to fund the company's growth. The transaction was led by BVgroup Private Equity.

## ReAble (Private)

Austin, TX

### Overview

ReAble (formerly Encore Medical Corporation) develops a range of orthopedic devices, including surgical implants, sports medicine equipment and products for orthopedic rehabilitation, pain management and physical therapy. ReAble's products are used by orthopedic surgeons and physicians, as well as physical and occupational therapists, to treat patients with musculoskeletal conditions resulting from degenerative diseases, deformities, and acute injuries.

### Products - Implants

The company's Surgical Implant Division offers a line of orthopedic implants for knees, hips, shoulders and the spine. ReAble's focus is on alternative bearing systems. VariGrip is a spine fixation product, designed to "hook" onto the lamina of the vertebrae for a secure grip without the use of pedicle screws. It also allows for additional bone at the lateral graft sites and leaves other structures intact, maximizing vertebral strength. When compared to existing systems patients typically experience less post-operative pain due to reduced muscle retraction. Current research and development activities include the Keramos ceramic-on-ceramic acetabular hip implant, Reverse Shoulder Prosthesis and electrotherapy and laser products.

### Products - Rehab

The Orthopedic Rehabilitation Division is split into two brands. Empi is a manufacturer and provider of non-invasive medical products for physical rehabilitation. Products include electrotherapy devices and accessories to treat pain, and restore and maintain muscle function; iontophoresis drug delivery systems; therapy tables; traction devices; and continuous passive motion devices for post-surgical rehabilitation of total joint patients.

Clinical rehabilitation services are provided by Chattanooga Group, a division of ReAble, in business for over 50 years. Chattanooga has four primary divisions, including: patient care, electrotherapy, physical therapy tables and traction and chiropractic.

### Acquisitions

In the past several years, ReAble has completed several significant acquisitions that have expanded its number of distribution partners and customer base in the U.S. and abroad. In March 2007 the company acquired Cefar AB, a European provider of electrotherapy and rehabilitation devices.

### Status

In November 2006 ReAble, through a merger with a newly formed company controlled by Blackstone Capital Partners, went private. And in May 2007, the company announced plans to acquire a public drug-delivery company based in Salt Lake City, IOMED. The \$22 million all-cash deal, expected to close in July 2007 subject to the approval of IOMED shareholders, would increase ReAble's presence in the pain management market, IOMED's primary focus.

## RenGen Biologics (RGBI)

Franklin Lakes, NJ

### Market opportunity

Damage to the meniscus, presented as a tear, can occur by sudden twisting of the knee or by blunt forces exerted onto the meniscus. Injury to meniscus cartilage can result in pain and swelling, or may cause the knee to give way or lock. Approximately 85% of all meniscus procedures involve a partial removal of damaged meniscus tissue.

Worldwide, there are an estimated 900,000 partial meniscectomy procedures performed annually. No new tissue fills the defect left by a partial meniscectomy. Without the protection and support provided by the meniscus, the knee joint can become unstable and the articular cartilage covering the femur and the tibia may begin to deteriorate or degenerate. Over time, the degenerative process can lead to knee pain and osteoarthritis.

### Products

ReGen Biologics develops tissue repair products for U.S. and global markets. The company's collagen scaffold technology includes applications in orthopedics, general surgery, spine, cardiovascular and drug delivery. ReGen's initial focus is on the knee. The company's first approved product is the CMI, a resorbable type I collagen scaffold sutured to the remaining meniscus following a partial meniscectomy. The device is designed to reinforce the remaining tissue and provide a scaffold for the growth of new tissue to replace what was removed in the partial meniscectomy procedure.

### Status

ReGen has received a CE Mark for its CMI meniscus implant product. ReGen AG, the company's European subsidiary, is marketing the product in Italy, Spain, Germany, Switzerland, Austria and Belgium.

In December 2005, ReGen submitted a 510(k) pre-market notification to FDA for clearance of its collagen scaffold product in the U.S. The collagen scaffold is for use as a surgical mesh for soft tissue reinforcement, with one of the designs developed for repair of meniscus defects. In August 2006, FDA indicated that the device was not substantially equivalent to existing Class II devices already in receipt of FDA clearance. ReGen appealed and was permitted, in November 2006, to submit a modified 510(k) for clearance of its collagen scaffold for use in the meniscus.

### Financing

In March, 2007 the company closed a \$3 million private equity placement. The stock trades on the bulletin board under the symbol RGBI.

## Regeneration Technologies (RTIX)

Alachua, FL

### Market opportunity

Tissue surgically transplanted from one person to another is called allograft. Using allograft tissue rather than autograft tissue eliminates the need for a second surgery, allowing the patient to avoid extra pain and chance of infection. Allograft is biocompatible and is reincorporated into the patient's body over time.

### Technology

Regeneration Technologies (RTI) processes human and animal musculoskeletal tissues in producing allograft and xenograft implants. Surgeons use these implants to repair a wide variety of bone and other tissue defects, including spinal vertebrae repair, musculoskeletal reconstruction, fracture repair, joint repair and reconstruction for sports medicine injuries.

Allograft tissue is surgically recovered by staff from a tissue recovery agency using aseptic technique in a hospital operating room or equivalent environment, which reduces the chance for bacterial contamination. Tissues are then processed into transplantable allografts in a clean room environment, minimizing the risk of airborne and other contaminants. Tissues are cleaned, sectioned and formed into precision-shaped implants, demineralized bone matrix for allograft paste products or conventional allografts.

RTI performs a final sterilization step for musculoskeletal bone and soft tissue using its patented BioCleanse Tissue Sterilization Process. BioCleanse eliminates bacteria, fungi, spores and viruses while maintaining the structural integrity and biomechanical properties of the tissue. A quality inspection is completed before distribution, and all allografts are serialized and tracked electronically.

RTI's Sterling line of xenograft implants is derived from bovine bone that comes from a certified closed and organic herd of cattle raised for pharmaceutical use. RTI is the only company in the industry using this sterilization process, which has been reviewed by FDA.

### Distribution

In May 2007, the company entered an exclusive 10-year distribution agreement with Zimmer Holdings for RTI's allograft paste implant. The bone paste implant will be delivered in flowable and moldable formulations, and is composed of inductive and carrier elements that are derived from human bone. The paste is provided pre-hydrated and at room temperature, and is delivered using a single stage delivery system.

## Scott Sabolich Prosthetics & Research (Private)

Oklahoma City, OK

### Market opportunity

Each year in the U.S. approximately 150,000 people experience the loss of a limb. Many are due to trauma, but the majority result from complications of diabetes, vascular disease, or cancer. In some cases, infants are born missing a limb.

### Company overview

Scott Sabolich Prosthetics & Research develops ultra-light upper and lower extremity prosthetics which incorporate a patented socket design. All prosthetics are manufactured at an in-house fabrication facility; the 21,000 square-foot prosthetic center houses a 9,000 square-foot clinical lab. The company markets its services directly to patients.

### Product

The most critical component in all prosthetic designs is the socket; if the socket does not fit accurately and feel comfortable, the patient will not be as active as they'd like. The Sabolich Socket incorporates anatomically designed channels and grooves for various muscle, bone, tendon, vascular and nerve areas. Because of its flexibility, a better fit is possible, allowing for increased lateral stability. Better alignment of the thigh bone prevents shifting within the socket. The system is tailored to each patient to optimize performance and comfort.

### Pipeline

Scott Sabolich Prosthetics & Research has engaged Martin Bionics as a contracted R&D team. Products in developments include a Sensory Feedback System – an effort to restore communication from the prosthesis to the amputee. Sensors incorporated in the prosthesis respond proportionately to the environment and send signals to a microprocessor, which interprets the signals and in turn sends them to stimulators located on the skin of the patient's residual limb. The patient interprets the sensations generated by the prosthesis, called cerebral projections, as if they were generated by their anatomical limb.

The Sensory Feedback System enables the amputee to sense that the prosthesis is an extension of their own body, provides psychological benefits, and may significantly reduce phantom pain. Initial trials with the system demonstrate the mind's ability to sense touch at a distance from the body.

The company's computer-controlled prosthetic joint designs employ a microprocessor to provide appropriate biomechanical functioning, optimal resistance, and joint angle independent of gait speed and/or terrain. Computer-controlled systems may be used on the majority of lower-extremity amputees. Computer-controlled designs are able to provide adaptations to the gait pattern as well as sensory feedback much like the human brain controls anatomical limbs. It is anticipated that this technology will become commercially available within the next two to three years.

## Small Bone Innovations (Private)

New York, NY

### Market opportunity

The baby boomer generation and the aging global population are accelerating the growth of the orthopedic market. The percentage of the global population over the age of 60 will more than double between years 2000 and years 2050. People are working longer and remaining active for their whole lives, demanding the restoration of function and motion, not just the elimination of pain. Companies are growing to meet the demand. Twenty years ago, there were five publicly traded companies in orthopedics; today there are close to 80.

The treatment of small bones and joints encompasses a wide range of medical professionals, including orthopedic surgeons, hand and foot specialists, sports medicine specialists and podiatrists. According to the 2006 AAOS Orthopedic Physician Census, 33% of all U.S. orthopedic fellowships specialized in the small bone and joint anatomies in 1990. By 2000, that figure rose to nearly 45%.

Although the small bone and joint market is a significant part of the overall orthopedic industry, it has not attracted as much attention as areas like total joints, spine and sports medicine. To date, many large orthopedic companies have focused on large bone and joint surgery. This emphasis has left the upper and lower extremities market unconsolidated.

### Background

Viscogliosi Bros., a venture capital firm focused exclusively on the musculoskeletal sector of the healthcare industry, created Small Bone Innovations (SBI) by acquiring established companies in the orthopedic field. The goal was to create a single source of products and technology for surgeons specializing in small bones and joints or limbs. SBI debuted at the AAOS Convention & Exposition in February 2005.

### Products

SBI's acquisitions and technology licenses include the following: Avanta Orthopaedics' hand, wrist, and elbow arthroplasty and trauma products; Envision's implant manufacturing; Actipore's porous metal technology; Artelon's biologically active and biodegradable technologies; Xtremi-T's resorbable trauma technology; and Fixano, S.A.'s line of small bone and joint implants.

The SBI product range is specific to upper and lower extremity small bone applications. Surgical implants covering the shoulder to the hand, and the tibia shaft to the forefoot, may be found in SBI's portfolio. Offerings include arthroplasty products, trauma products, biomaterials, soft tissue and sports medicine products, and small bone orthopedic equipment.

### Status

SBI continues to expand its product pipeline, with more than 40 devices and instruments to further augment its acquired offerings. Viscogliosi provides the capital to fund and sustain growth.

In 2006, SBI received five new FDA 510(k) clearances and completed eight M&A licensing and distribution deals; 19 new products were introduced. The direct sales staff continues to grow, driving seven straight record sales months in 2006. Currently, SBI has 21 direct sales representatives in the U.S. and four direct reps in France.

A key component of the company's strategy is a medical education and training program open to all surgeons. To date, nearly 1,800 surgeons have participated in courses and workshops. Such relationships have helped increase revenues by nearly 30% from 2005 to 2006. There are over 22,000 small bone and joint surgeons working in the U.S.

In April, 2007, SBI secured a \$20 million debt facility financed by the Drawbridge Special Opportunities Fund.

## TiGenix (Private)

Belgium

### Market opportunity

Worldwide, two million articular cartilage defects of the knee are diagnosed each year. Treating symptomatic cartilage defects has become standard policy in the orthopedic practice, yet, to date, no surgical treatment has offered a functional and durable repair. Damage to the cartilage of the knee can cause pain, swelling and mobility problems. If not treated effectively, it is one of the leading causes of osteoarthritis later in life. Treating cartilage problems aggressively is a growing trend as the aging population places increasing importance on life-long mobility and quality of life.

### Product

TiGenix is developing local treatments for damaged and osteoarthritic joints. The company's aim is to stop and reverse cartilage degeneration and prevent the progression to osteoarthritis. ChondroCelect is used in combination with autologous chondrocyte implantation (ACI), a surgical procedure that treats cartilage defects with a patient's own cells. By focusing on the regeneration of stable hyaline-like cartilage, ChondroCelect repairs cartilage defects and postpones the progression towards osteoarthritis.

In an initial surgery, a biopsy is harvested in an arthroscopic procedure. The tissue is then processed and cultured using TiGenix's technology. After approximately five weeks at the company's Cell Expansion Facility, a second surgery is conducted where the damaged cartilage is removed and ChondroCelect is implanted. These cells form the building blocks of new healthy cartilage and integrate with surrounding tissue.

### Status

ChondroCelect has successfully completed FDA Phase III clinical trials. TiGenix aims to commercially launch ChondroCelect in Europe in 2008.

The company's pipeline includes treatments for articular cartilage defects, surgical procedures for such articular cartilage defects, a product to repair cartilage defects in patients with early osteoarthritis, and a technology to repair traumatic lesions in meniscus.

## TissueLink Medical (Private)

Dover, NH

### Market opportunity

Surgeons have been using electrical current to cut and coagulate human tissue for over a century. Traditional devices concentrate energy at the point of contact resulting in temperatures as high as 350°C. At this temperature, fluid in the cells can rapidly vaporize, creating smoke and forming hydrocarbons. Smoke can be a conduit of carcinogens or viral transmission to the surgeon and the operating room staff. Dry tissue can stick to the electrode and result in re-bleeding when pulled off.

### Products/Technology

TissueLink Medical's devices incorporate a proprietary technology that uses fluid to deliver radio-frequency energy directly to tissue. The fluid controls the temperature at the interface, allowing tissue to seal without burning, charring or perforation. The technology received FDA clearance in March 2003.

TissueLink uses a conductive fluid, usually saline, infused at the point of contact to keep the tissue temperatures around 100°C. Any excess energy is boiled off. The result is a lower temperature when compared to dry electro-surgery. Tissue sealing, which stops bleeding, is accomplished by shrinking the naturally occurring collagen found in tissue vasculature.

TissueLink devices prevent bleeding by hemostatically sealing soft tissue and bone. Benefits include a reduction in bleeding by 50%, a 75% reduction in the number of transfusions, and less pain and swelling, potentially leading to greater range of motion and faster recovery. The company's HemoSealing technology enables rapid hemostasis of cut bone, soft tissue, and blood vessels so spine surgeons can minimize intra-and post-operative blood loss.

TissueLink devices are used in surgical oncology, spine surgical and other orthopedic applications.

## Tornier (Private)

Strafford, TX

### Market opportunity

Arthroplasty seeks to restore the function of a damaged joint and relieve pain in individuals suffering from arthritis and traumatic injury. As a surgical procedure, it is usually performed when prior medical treatment has failed. 713,000 arthroplasty surgeries are performed annually in the U.S., according to the American Academy of Orthopaedic Surgeons. Of these, 362,000 are knee surgeries and 295,000 are hip surgeries. The remainder are ankle, shoulder, wrist, and hand surgeries.

There are two types of arthroplastic surgery: joint resection and interpositional reconstruction. In joint resection, a portion of the bone from the stiffened joint is removed, increasing the space between the bone and the socket to increase range of motion. Interpositional reconstruction reshapes the joint and incorporates a prosthetic disk between the bones forming the joint. The prosthesis can be made of plastic, metal or ceramic material, or formed from such body tissue as skin, muscle, or fascia.+

### Overview

Tornier provides orthopedic reconstructive products for surgeons focused on joint replacement arthroplasty. The company's prostheses are designed to closely mimic the mechanics of the human anatomy. Through specialization, Tornier seeks to streamline procedures and improve patient outcomes while focusing on a specialized suite of products.

### Products

Tornier's product line, distributed worldwide, focuses in on elbow, ankle and knee restoration. The HLS Knee System meets the requirements of primary, revision, reconstruction, and unicompartmental arthroplasty. The Shoulder Series has been implanted in 50,000 patients since its introduction.

### Partnerships

In March 2007, Tornier completed the acquisition of DVO Extremity Solutions. In 2005 and 2006, DVO launched a series of distal radius fracture repair systems, establishing the company in a growing segment of the extremity orthopedics market.

Also in March, Tornier entered into a partnership with Bioretec Ltd, a Finnish biomaterials company. The partnership established Nexa Orthopedics, a wholly owned subsidiary of Tornier, as the exclusive U.S. distributor for a line of proprietary, bioresorbable surgical devices to be manufactured by Bioretec.

## TranS1 (Private)

Wilmington, NC

### Market opportunity

Lower back disorders affect 15-20% of the U.S. population and result in approximately 6.5 million doctors' visits each year. These visits are often caused by degenerative disc disease, a painful condition characterized by chronic lower back pain. The specific etiology of degenerative disc disease is unknown. It is believed to be caused by a number of factors, including mechanical, chemical, and age-related changes, autoimmune response, and hereditary factors.

The outcome of this degenerative process is that the disc no longer transmits force normally, and requires that the load distribution function be transferred to other structures such as the facets, ligaments, or annulus, which expands the degenerative process. For patients, this means chronic back pain, radiating pain (if a nerve is affected), muscle weakness and decreased range of motion.

### Technology

TranS1, a privately held medical device company, has developed a minimally invasive solution to treat lower back pain. TranS1's percutaneous access and fusion system enables lumbar fusion to be performed with complete preservation of the annulus and all paraspinal soft tissue structures. AxiaLIF (Axial Lumbar Interbody Fusion) offers a reproducible pre-sacral access route to the L5-S1 vertebral bodies and can be performed through an outpatient surgical procedure, allowing for a rapid return to normal activities.

The AxiaLIF System includes proprietary devices used to access the spine, remove the diseased disc material, re-establish normal disc height, and stabilize the spine to enable lumbar fusion. This procedure is performed via an incision of less than one inch in length, mitigating potential soft tissue trauma. As of January 30, 2007 more than 1,000 patients had used AxiaLIF.

TranS1's minimally invasive approach allows patients to be discharged from the hospital the day after surgery, and return to work in 15 days on average. This is a dramatic reduction in hospital stay, which can otherwise run three to four nights, followed by a one-to-two month recovery period before returning to work.

### Status

In September 2006, TranS1 signed an exclusive agreement with ApaTech for distribution of its AxiaLIF system in the U.K. and Ireland. TranS1 is also developing two mobility platforms – a disc replacement and a prosthetic disc nucleus; both are delivered using the percutaneous, trans-sacral approach.

## Tutogen Medical (TTG)

Alachua, FL

### Overview

Tutogen Medical develops bio-implants and medical devices for tissue and bone repair. The company's main products are allografts (donated human tissues) preserved with the Tutoplast process of tissue preservation and viral inactivation. Tutogen has recently expanded into the xenograft market (tissues from animals). Tutogen offers both traditional grafts and specialty grafts (precision grafts, ready for implantation). Tutoplast is a proprietary tissue processing system designed to significantly reduce the amount of cells, bone marrow and lipid components from processed allograft bone and connective tissue while preserving the extra-cellular matrix (collagen and mineral components). Tutoplast inactivates and removes bacteria and viruses producing a cleaner and safer allograft tissue.

### Security

Tutogen recovers tissue from sites throughout the U.S. and Europe. All suppliers are subject to stringent donor screening procedures. This includes a medical history and social history review, a detailed interview with next of kin, an extensive donor physiological testing and serological testing performed by a third party CLIA certified lab. Tutogen's Florida processing facility is accredited by the American Association of Tissue Banks. The Neunkirchen, Germany facility is ISO9001 and EN4600 certified according to rules established by FDA.

### Partnerships

In November 2006, the company entered a strategic tissue sourcing relationship with Regeneration Technologies. Under the terms of the agreement, Tutogen has first right of refusal to all dermis, fascia and pericardium recovered by Regeneration's donor services. Regeneration has first right of refusal to all soft tissue used in sports medicine surgeries recovered by Tutogen's recover partners.

Tutogen markets its products in 45 countries through a network of independent distributors. These include Zimmer Spine, Zimmer Dental, IOP Inc., and Mentor. In 2006, Tutogen's dental business experienced double digit growth driven by Zimmer Dental's strong distribution network. Tutogen's international business grew 24% driven by stronger European sales.

## US Spine (Private)

Boca Raton, FL

### Overview

US Spine is a privately held, middle-stage medical device company focused on the development and commercialization of spinal implant systems. US Spine's development efforts focus on motion and tissue preservation through the use of advanced biomaterials.

### Products

Biomaterials include the Element Bone Graft Substitute and Origin Structural Allograft. Element is composed of a blend of Hydroxyapatite and Tricalcium phosphate. This composition creates optimal conditions for bone formation. B-TCP/HA has a history of clinical use and is a safe alternative to allograft or autograft and is completely resorbable. Origin Allografts are used in Cervical Interbody Fusion. The grafts are provided in a pre-fitted state.

The Preference Pedicle Screw System is used in posterior internal fixation. The Closure Top interlocks with the Pedicle Screw to eliminate the possibility of head-splay during final tightening. The device's Helical Flange is resistant to cross-threading that can occur with conventional set screws. The Preference Spine System implant components are fabricated from medical grade titanium or titanium alloy. In January 2007, US Spine announced the completion of the first surgeries using the system.

US Spine's Facet Fixation System is an alternative to pedicle screws used in interbody fusion. The gun-like device compresses and fires a trans-facet bolt across the facet joint to immobilize a spinal motion segment. The single-use disposable gun sets the implant trajectory and delivers the implant by squeezing the trigger on the hand piece. The Facet bolt is manufactured using titanium and features a partially-threaded facet screw with a cutting tip, a variable-angle washer and a locking nut. The system is delivered in a sterile package with the implants pre-loaded in the barrel of the gun.

Other devices in US Spine's portfolio include the Spartacus Disc Replacement Device and the Phantom Vertebral Body Replacement.

### Status

US Spine received FDA 510(k) clearance for the device in June 2006. The company is positioning the Facet Fixation System as an alternative to pedicle screw fixation for one and two level spine fusions, an estimated \$600 million dollar segment in the spinal implant market.

## Vertebron (Private)

Stratford, CT

### Overview

Vertebron's portfolio of spinal implant systems includes both motion preservation and fusion technologies. The company focuses on intra-operative flexibility and simplified surgical techniques. Advanced sterilization and packaging technologies have been incorporated to extend implant durability and minimize surface wear and debris generation.

Vertebron implants include artificial discs, cervical plates, pedicle screws and interbody fusion systems which integrate spinal, orthopedic and total joint technologies. Allograft bone remains Vertebron's structural material of choice given its biologic and integration properties; Allosource supplies all such tissues.

### Products

The company's core fusion products, the PSS Pedicle Screw System and the SSP Cervical Plating System, accounted for the majority of revenue growth in 2006. This growth was driven by a strong fourth quarter, spearheaded by the expansion of Vertebron's distribution network.

SSP uses a self-aligning floating tapered ring to ensure secure locking regardless of screw angulation. The device's low profile minimizes the potential for esophageal erosion and patient discomfort. Vertebron's Pedicle Screw System's low profile reduces underside bulkiness, allowing for optimal bone graft placement.

### Funding

Proceeds from the fusion and fixation technologies will support the development and clinical trials of the company's modular motion preservation devices (artificial discs) for both the cervical and lumbar spine, in addition to radiolucent interbody fusion devices.

Internal funding has been secured through spine and total joint surgeons, private investors, and corporate strategic alliances. The first quarter of 2007 was Vertebron's most profitable to date.