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BEST PRACTICES

AWARDS

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2020 BEST PRACTICES AWARD



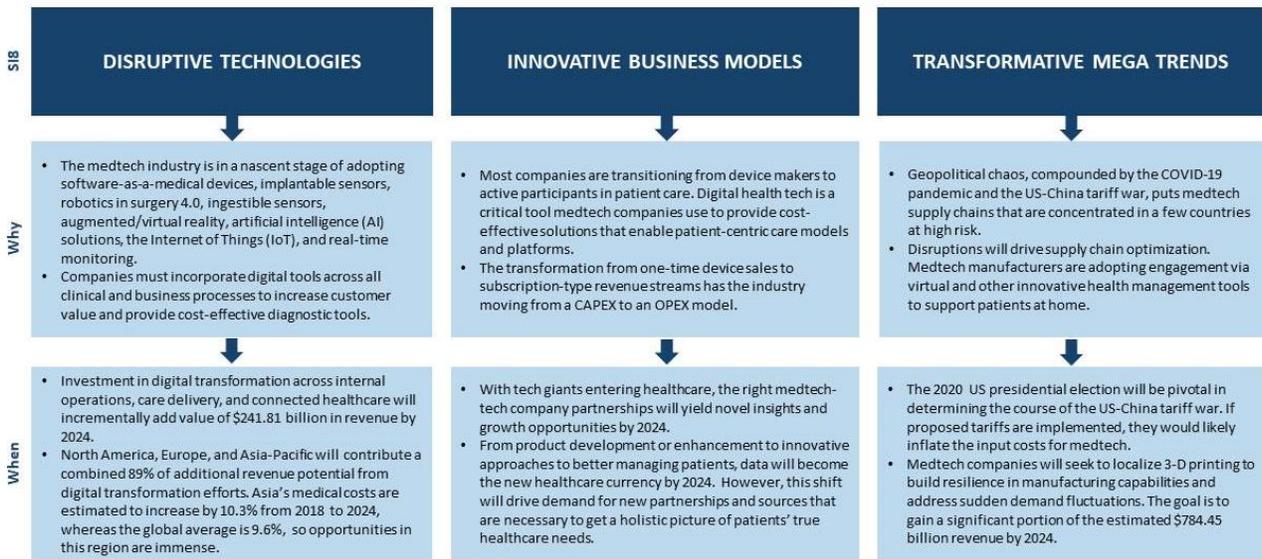
**2020 EUROPEAN
ORTHOPEDIC AND TRAUMA
ENTREPRENEURIAL COMPANY OF THE YEAR AWARD**

Strategic Imperatives

Frost & Sullivan identifies three key strategic imperatives that impact the medtech industry: disruptive technologies, innovative business models, and transformative Mega Trends. Every company that is competing in the medtech space is obligated to address these imperatives proactively; failing to do so will almost certainly lead to stagnation or decline. Successful companies overcome the challenges posed by these imperatives and leverage them to drive innovation and growth. Frost & Sullivan’s recognition of Syntellix is a reflection of how well it is performing against the backdrop of these imperatives.

THE IMPACT OF STRATEGIC IMPERATIVE 8™ ON THE MEDTECH INDUSTRY

The following 3 strategic imperatives will ensure growth in the medtech industry.



Best Practices Criteria for World-Class Performance

Frost & Sullivan applies a rigorous analytical process to evaluate multiple nominees for each award category before determining the final award recipient. The process involves a detailed evaluation of best practices criteria across two dimensions for each nominated company. Syntellix excels in many of the criteria in the orthopedic and trauma implants space.

AWARD CRITERIA	
<i>Entrepreneurial Innovation</i>	<i>Customer Impact</i>
Market Disruption	Price/Performance Value
Competitive Differentiation	Customer Purchase Experience
Market Gaps	Customer Ownership Experience
Leadership Focus	Customer Service Experience
Passionate Persistence	Brand Equity

MAGNEZIX Implant Replaces Conventional Implants with Unique Dissolving and Healing Promoting Capabilities

Following a bone fracture or osteosynthesis, temporary fixation is the standard surgical procedure in which screws, nails, or plates are implanted to temporarily hold the patient’s bone (and/or ligament) in place until it reunites. In a majority of cases, stainless steel or titanium is the implant material of choice. The challenge, however, is the high possibility of these foreign and permanent materials to cause long-term problems like functional disabilities, allergies, irritation of tissue and/or becoming toxic/carcinogenic when allowed to remain in the body. Often, a second surgical procedure is medically indicated or performed preventively to remove the implant, which involves considerable costs, related operative risks and possible complications.

Syntellix, a disruptive biomedical engineering, material and life science company headquartered in Germany with a second HQ in Singapore, has achieved a groundbreaking innovation with the internationally marketed MAGNEZIX implant portfolio, made of the name-giving magnesium-based alloy

“The MAGNEZIX implant’s unique capability of converting metal to bone makes it an ideal implant of the future.”

- **Dr Bejoy Daniel,**
Senior Industry Analyst

with metallic properties of high stability and resilience. The MAGNEZIX material distinguishes from other competing metallic materials due to its bioabsorbability, as the implant will degrade in the body and be replaced by endogenous bony tissue, which nullifies the need for a second surgical procedure to remove a foreign body. Magnesium, which contributes to over 90% of the MAGNEZIX alloy, demonstrates

osteoconductive properties; it initiates an alkaline pH shift, which is indicated by scientific studies to trigger human osteoblast cells that synthesize new bone.¹ The idea was to design a stable metal implant that supports the bone healing process and degrades once healing is ensured. The MAGNEZIX implant

¹ Galow AM, Rebl A, Koczan D, Bonk SM, Baumann W, Gimsa J. “Increased osteoblast viability at alkaline pH in vitro provides a new perspective on bone regeneration.” *Biochem Biophys Rep.* 2017;10:17-25. Published 2017 Feb 27. doi:10.1016/j.bbrep.2017.02.001

offers many advantages that ultimately can help save countless lives by several reasons, for example eliminating the need for multiple implant-related removal surgeries. Moreover, the potential time and financial savings gained from fewer surgeries and hospital admissions as well as post-operative treatments are significant.

Frost & Sullivan is impressed that Syntellix has combined metallic stability with proven bioabsorbability, to create an unprecedented implant. The MAGNEZIX implant's unique capability of replacing metal by bone makes it an ideal implant of the future. This is in particular the case for sports medicine, when quick and safe recovery is required and as well in pediatric orthopedics, where removal of implants in the growing skeleton is considered mandatory and anesthesia is tied to higher risk.

Bioabsorbable Implant Helps Mitigate a Patient's Risk of HAI

Healthcare-associated infections (HAIs) have become a significant global public threat, and with the COVID-19 pandemic, public awareness about disease transmission has spiked. Apart from the

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considerable costs to hospitals, patients and healthcare providers, HAIs reduce the quality of a patient's life resulting from functional disability. Several studies indicate that HAIs are largely linked to an overall increase in length of hospitalization. HAIs are a major contributor to morbidity and mortality in healthcare facilities. According to the WHO, hundreds of millions of patients worldwide are affected by HAIs each year. Recent data shows that 15% of total hospital expenditure and activities in OECD countries are a direct result of treatment-related adverse events and infections. In Germany alone, a country well-known for high health care standard, an estimated

400,000 to 600,000 HAI cases are reported each year, of which an approximate 10,000 to 20,000 lead to patient's death. With the need for second surgeries to remove titanium and stainless steel implants, the chance of infection increases. Syntellix's MAGNEZIX implant helps to reduce the spread of HAIs by avoiding unnecessary removal of material and the corresponding risk of infection during a second operation or in-patient stay, making a significant contribution to patient safety - especially important during the COVID-19 pandemic. Widespread use of MAGNEZIX implants could help to reduce the infection-related cost burden, whereby all participants in the health care system could profit sustainably.

Innovative, Advantageous Product Geometry and Material Design to Address the Shortcomings of Traditional Metallic and Polymer Implants

Often considered as resorbable alternative to titanium or steel implants, polymer implants (based on PGA or PLA) are used, yet they have limitations like, among others, less robust mechanical properties. When absorbable implant materials based on polymers are used in patients, questions arise about tolerability and biocompatibility. A major advantage of MAGNEZIX over other existing resorbable polymer materials is the higher strength and excellent biocompatibility with a predictable degradation course, making it the right choice for a wide range of medical applications which require safe temporary

fixation, without leaving any foreign material in the patient. MAGNEZIX implants are used for medical indications such as intra and extra articular fractures, bony avulsion of ligaments and tendons, and even

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in cases of osteochondral fractures and flakes. The underlying material technology offers enormous potential benefits for better patient care by transferring its application to other medical fields such as neurosurgery, oral and maxillofacial surgery or dental implantology. Aside from combining the advantages of polymers (absorbability) and metal (strength) to achieve the ideal stability and degradation, magnesium-based MAGNEZIX implants take one step further, as they are essentially replaced by dense bony structure during the healing process, leaving no hollow space in the bone where the implant was initially placed. MAGNEZIX has an elasticity which is similar to the human bone and thus leads to a

relief of the bone that prevents the negative stress shielding effect as well as osteopenia. In general, pain perception for patients is highly reduced. Studies carried out by foot surgeon specialist Dr. Klauser, who attracts a large number of patients all over Germany, demonstrate the clinical superiority of MAGNEZIX when compared to titanium implants.² The study shows better performance of Syntellix products with a very high rate of patient satisfaction and minimal negative effects in comparison to 100 titanium implant cases.

Looking at incidence and problem rates of implant removal surgeries, in a Dutch survey 96% of 250 respondents observed peri-operative problems and furthermore, 87% observed post-operative problems.³ Various medical literature sources report significant overall complication rates of conventional implants at about 40%, refracture rates at 27%, nerve lesion rates at 40%, post-surgery infection at 20%, and pain after removal in 7 to 20% of cases.⁴ After marketing tens of thousands MAGNEZIX implants not a single serious incident has been attributed to the product, proving a clean sheet in the area of product integrity and safety. A rapidly growing number of more than 35 international publications on various clinical applications demonstrate the fascinating performance of Syntellix’s MAGNEZIX implants in terms of safety, efficacy, reliability, patient advantages, patient satisfaction, and product superiority. MAGNEZIX does not only serve the process of temporary fixation and stabilization, but of real osteosynthesis and sustainable healing.⁵

Syntellix already offers 6 main product families with 184 derivatives based on its unique MAGNEZIX material comprised of screws and pins with advantageous geometries and design features that enable

² Klauser H. Internal fixation of three-dimensional distal metatarsal I osteotomies in the treatment of hallux valgus deformities using biodegradable magnesium screws in comparison to titanium screws. *Foot Ankle Surg.* 2019 Jun; 25 (3): 398-405. doi: 10.1016/j.fas.2018.02.005. Epub 2018 Feb 16. PMID: 30321972.

³ Vos D, Hanson B, Verhofstad M. Implant removal of osteosynthesis: the Dutch practice. Results of a survey. *J Trauma Manag Outcomes.* 2012;6(1):6. Published 2012 Aug 3. doi:10.1186/1752-2897-6-6

⁴ Bostman, Ole MD; Pihlajamaki, Harri MD Routine Implant Removal after Fracture Surgery: A Potentially Reducible Consumer of Hospital Resources in Trauma Units, *The Journal of Trauma: Injury, Infection, and Critical Care*: November 1996 - Volume 41 - Issue 5 – pgs. 846-849.

⁵ May, H., Alper Kati, Y., Gumussuyu, G. et al. Bioabsorbable magnesium screw versus conventional titanium screw fixation for medial malleolar fractures. *J Orthop Traumatol* 21, 9 (2020). <https://doi.org/10.1186/s10195-020-00547-7>

the surgeon to conduct a smooth, easy, and fast surgical procedure. The CS compression screws are usually applied for fixation of small bone fragments, apical, osteochondral, and cancellous fragments such as fore foot / ankle, knee, and hand / wrist. Pins are usually applied for fixation of small bone or apical fragments. Syntellix's CBS cortical screws are standardly used in surgical fracture treatment for shoulder, foot/ankle, knee, elbow, and hand/wrist. In larger-sized MAGNEZIX CS^c implants, the top layer is converted into a dense, porous, and strongly adherent magnesium-based oxide film. This surface finish acts as a protective layer and is fully bio-absorbable, too. It causes a significant delay in the degradation process and therefore helps to maintain the desired higher integrity of the implant for a longer period where necessary and thus to facilitate an extended range of indications in larger bones and joints. Syntellix also offers MAGNEZIX StarFuse, an innovative product geometry for the forefoot, mainly for correction of stiff toe joint, hammer toes and claw toes and IFS^c for applications in sports medicine like cruciate ligament fixation. Moreover, Syntellix's competence and strategic ambitions go far beyond, with potential applications in cardiovascular, plastic surgery, drug delivery systems, neurological disorders, and beyond healthcare applications as well.

Magnesium as the Essential Element for Bone Repair

One decisive difference between Syntellix's magnesium-based technology and titanium solutions is that titanium is a substance that the body does not require. It might develop into titanium dioxide, a potentially harmful toxin, genotoxin and carcinogenic. A few-nanometres-thick layer of amorphous TiO₂

“The unique combination of features like metallic stability, full bio-absorbability and osteoconductivity, paired with outstanding tolerability and anti-infectious properties, completed by a low level of radiological artifacts and easy application, makes MAGNEZIX an ideal material for use in medical applications and beyond.”

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is commonly formed on the surface of orthopaedic and dental implants made of titanium metal or its alloys.⁶ The number of scientific studies researching on toxicity, allergy, corrosion and yellow nail syndrome in relation to titanium, titanium alloys or titanium implants in the human body seems to be increasing exponentially.⁷ Due to the state of scientific knowledge, the International Agency for Research on Cancer (IARC) of the World Health Organisation (WHO) has declared titanium dioxide as "possibly carcinogenic" in humans and the French government has already banned sales of food containing titanium dioxide. In contrast, magnesium is a mineral the body desperately requires. The

recommended daily dietary intake is approximately 375 to 500 mg. Magnesium is considered a natural element and indispensable for many important functions in the body (including bone formation, as well as muscle and nerve functions). Research from Sichuan University states that hydrogen being released from magnesium implants during the degradation process has the potential to prevent bony cancer from metastasis formation and recurrence.⁸ Similarly, facts on the anti-tumor mechanisms have been drawn by a research group at the National University of Science and Technology, Moscow.

⁶ Skocaj M, Filipic M, Petkovic J, Novak S. Titanium dioxide in our everyday life; is it safe?. *Radiol Oncol.* 2011;45(4):227-247. doi:10.2478/v10019-011-0037-0

⁷ Kim, K.T., Eo, M.Y., Nguyen, T.T.H. et al. General review of titanium toxicity. *Int J Implant Dent* 5, 10 (2019). <https://doi.org/10.1186/s40729-019-0162-x>

⁸ Nan M, Yangmei C, Bangcheng Y. Magnesium metal--a potential biomaterial with antibone cancer properties. *J Biomed Mater Res A.* 2014 Aug; 102 (8): 2644-51. doi: 10.1002/jbm.a.34933. Epub 2013 Sep 10. PMID: 24019294.

Conclusion

With MAGNEZIX implants Syntellix provides a solution to a long existing industry challenge. It is the first magnesium-based, metallically stable bioresorbable orthopedic implant which is CE marked. Health care authorities around the world have approved MAGNEZIX implants and additionally, the FDA has recently granted MAGNEZIX CS 3.2 designation as a “Breakthrough Device”; fewer than 1% of such designations are granted to devices in the orthopaedic field, making the classification highly noteworthy and distinctive. The implants function similar to conventional steel or titanium devices yet without the need for subsequent removal, because the implant is naturally replaced by bone. MAGNEZIX significantly reduces patient risks associated with titanium implants such as allergy, toxic reaction, possible cancer formation, HAI, or even COVID-19 transmission due to removal surgery and hospitalization. This innovation ensures a procedure with less risk and fewer complications; it also saves on surgery time and healthcare costs without any major changes to the standard surgical procedures.

The MAGNEZIX implant offers reliable temporary fixation and stabilization with a unique combination of additional features like metallic stability, full bio-absorbability and osteoconductivity, paired with outstanding tolerability and anti-infectious properties and easy application, makes MAGNEZIX an ideal material for use in medical applications and beyond. Frost & Sullivan agrees with the arising expectation that shortly the era of conventional implants made of steel, titanium or polymers will end and MAGNEZIX implants are becoming the gold standard for the treatment of an increasing number of indications.

With its strong overall performance, Syntellix has earned Frost & Sullivan’s 2020 Entrepreneurial Company of the Year Award.

What You Need to Know about the Entrepreneurial Company of the Year Recognition

Frost & Sullivan's Entrepreneurial Company of the Year Award recognizes the best up-and-coming, potentially disruptive market participant.

Best Practices Award Analysis

For the Entrepreneurial Company of the Year Award, Frost & Sullivan analysts independently evaluated the criteria listed below.

Entrepreneurial Innovation

Market Disruption: Innovative new solutions have a genuine potential to disrupt the market, render current solutions obsolete, and shake up competition

Competitive Differentiation: Strong competitive market differentiators created through a deep understanding of current and emerging competition

Market Gaps: Solution satisfies the needs and opportunities that exist between customers' desired outcomes and their current market solutions

Leadership Focus: Company focuses on building a leadership position in core markets and on creating stiff barriers to entry for new competitors

Passionate Persistence: Tenacity enables the pursuit and achievement of seemingly insurmountable industry obstacles

Customer Impact

Price/Performance Value: Products or services provide the best value for the price compared to similar market offerings

Customer Purchase Experience: Quality of the purchase experience assures customers that they are buying the optimal solution for addressing their unique needs and constraints

Customer Ownership Experience: Customers proudly own the company's product or service and have a positive experience throughout the life of the product or service

Customer Service Experience: Customer service is accessible, fast, stress-free, and high quality

Brand Equity: Customers perceive the brand positively and exhibit high brand loyalty

