EDISON

Tissue Regenix

Wound care focus report

Strong prospects in wound care

Healthcare equipment & services

Tissue Regenix's (TRX) investment case is built on dCELL, a patented decellularised tissue scaffold, whose regenerative properties are applied in wound care, orthopaedics and cardiac implants. We see wound care as the main driver for TRX's growth and our sum-of-the-parts valuation of £346m. Our forecasts and valuation are unchanged, but updated for a stronger US dollar.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
01/14	0.0	(6.3)	(0.9)	0.0	N/A	N/A
01/15	0.1	(8.2)	(1.2)	0.0	N/A	N/A
01/16e	0.5	(10.5)	(1.4)	0.0	N/A	N/A
01/17e	3.5	(12.5)	(1.6)	0.0	N/A	N/A

Note: *PBT and EPS are as reported.

Wound care market set for sustainable growth

The $8.5bn global advanced wound care market is set to sustain 4-5% CAGR driven by an ageing population and rising incidence of ailments such as diabetes and obesity. We expect innovation adoption to remain brisk, notably in the US, with a low double-digit growth rate expected in the $0.5bn dermal substitute market. With the top three players controlling half the market, industry consolidation looks set to continue, focusing on building scale and securing new technologies.

TRX's technology well positioned in wound care

TRX is a new entrant with a novel dermal substitute, DermaPure HD, launched in 2014. In a competitive market, we believe it is well placed due to the proven efficacy of DermaPure to treat both chronic and acute wounds, but also from a regulatory and health economic perspective. TRX's technology benefits from being clean, easy to handle and effective at promoting healing.

Wound care should be TRX's chief growth driver

We expect US DermaPure to accelerate from £0.3m in H115, helped by distributor stocking contracts worth at least $0.8m over 12 months. In addition, having secured reimbursement coverage to 65% of Medicare beneficiaries since launch, TRX is now able to expand into the bigger outpatient chronic wound care market from its initial acute care focus. The launch of allograft and xenograft dCELL-based products, covering a broad range of indications, should make wound care TRX's key growth driver. We forecast Wound Care divisional revenues to rise from £0.5m in FY16 to £32m in FY21 representing 46% of the group.

Valuation: Sum-of-the-parts valuation of £346m

As a result of US dollar strength , we raise our SOTP DCF valuation from £325m to £346m, or 45.6p/share, using a 12.5% WACC. We value the wound care franchise at £188m, orthopaedics at £101m and the cardiac division at £37m. The current market capitalisation, which is subject to an estimated funding requirement of £15m needed to develop OrthoPure XT and XM in the US, does not reflect the full pipeline potential, which could ultimately be attractive to larger medtech companies.

22 January 2016

Price	**15.25p**
Market cap	**£116m**
	£/$1.44
Net cash (£m) at end July 2015	25
Shares in issue	759.7m
Free float	65%
Code	TRX
Primary exchange	AIM
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	4.3	(9.0)	(21.8)
Rel (local)	9.7	(0.3)	(11.1)
52-week high/low		20.8p	13.2p

Business description

Tissue Regenix is a UK-based company developing and commercialising medical devices for regeneration of soft tissue. It has three divisions including a US-based wound care subsidiary, orthopaedics/sports medicine and a cardiac division.

Next events

Expansion of wound care sales channels	2016
Completion of chronic wound care study	H116
510k of SurgiPure XD	2016
Initiation of OrthoPure XT study/CE mark grant/launch of OrthoPure XM	2016
HCTP pathway/OrthoPure HM/HT US launch	2016

Analysts

Hans Bostrom +44 (0)20 3681 2522

Linda Pomeroy +44 (0)20 3077 5730

healthcare@edisongroup.com

Edison profile page

Tissue Regenix is a research client of Edison Investment Research Limited

Investment summary

Company description: Versatile regenerative technology

Tissue Regenix (TRX) is a spin-out from Leeds University, established in 2006. It develops and commercialises medical devices for the regeneration of human tissues and organs based on a patented decellularisation technology known as dCELL. The business model is based on commercialising dCELL through partners, initially in the human tissue market and subsequently to achieve regulatory clearance, with animal tissue implants allowing greater commercial scale. The dCELL process removes cells and DNA from human and animal tissue for transplantation and repair, minimising the risk of rejection and infection and overcoming the limitations of standard treatments. TRX is developing dCELL-based products for a range of applications and indications across three divisions including a US Wound Care subsidiary, Orthopaedic and Cardiac business divisions. Its UK office is in York, with production and laboratories in Swillington, UK. The US wound care subsidiary is based in San Antonio, Texas. The company employs 60 staff and has raised c £50m since flotation on AIM in 2010, via its reverse takeover of Oxeco.

Valuation: Sum-of-the-parts valuation of £346m

Our DCF valuation is £346m (raised from £325m reflecting dollar appreciation) or 45.6p/share based on a WACC of 12.5%, subject to potential dilution from an estimated £15m funding required to deliver on our estimated growth trajectory. We value the wound care business at £188m, the orthopaedics division at £101m and £37m for the cardiac division, based on risk-adjusted cash flows for each division according to the stage of development; we add end-July 2015 net cash of £25m. According to our model, the current price gives a free option on Wound Care, the most attractive and most commercially advanced division. There are a number of near-term catalysts ahead, including the potential CE mark grant and launch of OrthoPure XM and US launch of OrthoPure HM/HT via the HCTP pathway, which would lead us to increase the probability of success for these products.

Financials: Wound care sales due to accelerate in 2016

TRX reported sales of £0.3m in the six-month period ending July 2015. We expect two stocking distributor agreements for DermaPure to be signed, worth at least $0.8m over 12 months, and broader US reimbursement coverage should propel growth in FY17 and beyond. The main growth drivers for reaching our £79m FY21 group sales forecast are Wound Care (£36.2m), Orthopaedics (£35.6m) and Cardiac (£6.9m). TRX raised £19m net in January 2015, by issuing 105.3m shares, to develop and launch human tissue OrthoPure in the US and porcine OrthoPure in CE mark regions, as well as to expand the US direct sales force. We estimate year-end 2016 net cash at £18.8m, sufficient to fund TRX into early 2018. Our forecasts indicate that TRX would require an additional £15m funding to cover FDA studies for OrthoPure porcine products.

Sensitivities: Next-generation medical devices

All three divisions depend on the availability of reimbursement for the products. While the Wound Care division is well advanced in this respect, TRX is operating in competitive markets where sustained investment in development and marketing is required to maintain the profile of the products. Commercial success in wound care is dependent on TRX continuing to extend its distribution and reimbursement channels. TRX is running a hybrid distribution strategy and might require additional funding if it appoints additional direct wound care sales reps. Human tissue products are dependent on the availability of donated tissue and on forming new collaborations with human tissue banks. Porcine products offer significant potential in terms of ease of supply and lower-cost processing, although there is a limited amount of data published by TRX to demonstrate how well its products perform in humans.

Innovator of versatile regenerative technology

TRX develops and commercialises medical devices for the regeneration of human tissues and organs based on a patented decellularisation technology, dCELL. This process removes cells and DNA from human and animal tissue for transplantation and repair, minimising the risk of rejection and infection. The company's business model is based on commercialising dCELL through partners, initially in the human tissue market and subsequently to achieve regulatory clearance, with animal tissue implants allowing greater commercial scale.

dCELL: A growth platform for tissue regeneration

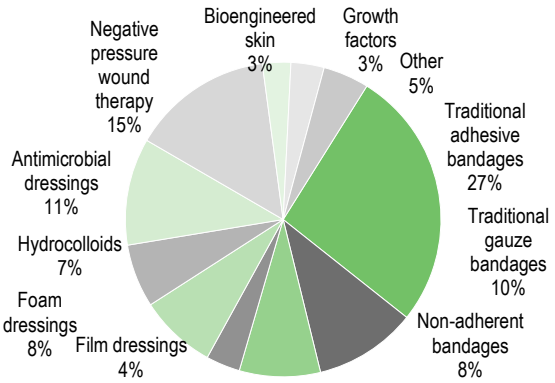
TRX's investment story is built on the versatility of its patented dCELL technology, used to develop regenerative medical devices across three areas with high growth potential: wound care, sports medicine and cardiac applications. Wound care is the most advanced of the three target areas and the subject of this report. The dCELL process creates a tissue scaffold which, once implanted, is repopulated with human cells during the healing process. The technology benefits from several features, which we believe differentiate it from existing treatment alternatives:

- it allows for the removal of DNA and cells from soft tissue in a manner that minimises rejection and is associated with a low incidence of side effects;
- it minimises the use of detergents and chemicals, allowing the tissue matrix to be repopulated swiftly with the patient's own cells; and
- dCELL tissue can be stored and transported cost-effectively at room temperature.

Having launched a human tissue-derived wound care product (DermaPure HD) in 2014, TRX is developing a versatile range of human and animal tissue-based devices in wound care, as well as sports medicine and cardiac devices, discussed in our initiation report published in October 2015.

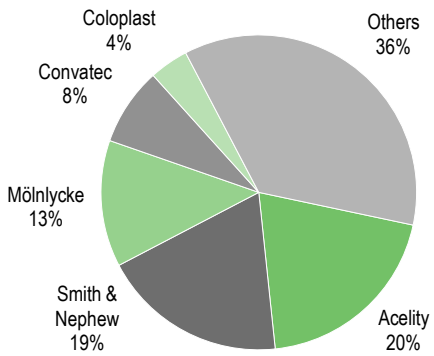
Wound care market

Exhibit 1: Global wound care market segmentation



Source: BioMedGPS, Smith & Nephew

Exhibit 2: Competitive landscape in $8.5bn advanced wound care market



Source: Smith & Nephew

We consider that the global wound care market offers attractive growth prospects, with 4-5% forecast sales CAGR in 2015-18. Its key drivers are an ageing population (2.5% CAGR 2015-50e of people over 60 based on WHO data), aggravating chronic diseases such as diabetes and obesity, as well as growing prevalence of surgical site infections caused by resistant bacterial strains. Overall price inflation is minimal. This masks the fact that basic products, such as gauze and bandages, experience price erosion while novel ones, such as dermal substitutes, growth factors, debridement agents, still have pricing power.

Three companies – Acelity (US), Smith & Nephew (UK) and Mölnlycke (Sweden) – control just over half the global market. Numerous small, mostly local competitors and new technology companies such as TRX represent the rest. As the amalgamation of three mid-sized companies (KCI, LifeCell and Systagenix), Acelity has been the key driver of recent industry consolidation. Over the years, the market has proved receptive to new entrants whose products offer compelling health economic benefits and improve clinical outcomes. Examples include KCI (negative pressure wound therapy), MiMedx (amnion-based skin substitutes) and Mölnlycke (silicone wound dressings).

Large wound dressing brands typically generate annual sales of up to $50m with some advanced products clocking up revenues in excess of $200m, such as Smith & Nephew's enzymatic debridement agent, Santyl. Large suppliers often source new growth products externally through acquisitions and licensing agreements, but also work actively with product line extensions of their existing products. In view of this market structure, we believe TRX has two main strategic options longer term: either to develop into a fully-fledged wound care supplier, most likely through acquisitions, or to sell itself to a bigger competitor.

Medical burden of wounds drives new technology investments

Skin wounds have a variety of causes, including thermal burns, venous stasis, ischaemia, pressure, trauma, surgery or underlying skin disorders (eg epidermolysis bullosa). While acute wounds represent the vast majority of wounds, the value of products used in each treatment used is low. Chronic wounds, such as diabetic foot ulcers, vascular ulcers and pressure ulcers, put the patient at risk of infection, amputation and possibly death and their management demands vast human and financial resources.

Exhibit 3: US and worldwide wound prevalence

Types of wound	US prevalence (m)	Worldwide prevalence (m)	Healing time (days)	Estimated CAGR (2007-16e)
Surgical wounds	67	110.3	14	3.6%
Traumatic wounds	N/A	1.6	28	1.7%
Lacerations	N/A	20.4	14	1.2%
Burn wounds (outpatient)	1.3	3.4	21	1.0%
Burn wounds (medically treated)	N/A	6.5	21	1.3%
Burn wounds (hospitalised)	N/A	0.2	50	1.1%
Pressure ulcers	2.5	8.5	N/A	6.9%
Venous ulcers	2.5	12.5	N/A	6.7%
Diabetic ulcers	1.5	13.5	70-150	9.3%
Amputations	0.086	0.2	N/A	1.2%
Carcinomas	N/A	0.6	14	3.0%
Melanoma	N/A	0.1	14	3.2%
Complicated skin cancer	N/A	0.1	28	3.1%

Source: MedMarket Diligence

The sharp rise in diabetes and obesity, plus an ageing population, mean that chronic wounds should become a growing health and cost of care problem and thus a priority for medical advances: in the US eight million individuals (1% of the adult population and 3.6% of the over-65s) are estimated to suffer from chronic wounds.[1] Diabetic foot ulcers (DFU) and venous leg ulcers (VLU) are particularly difficult and expensive to heal. Pressure ulcers are also prevalent, developing in 8-15% of all hospital patients, and cause a fourfold increase in mortality.[2]

The cost of chronic wound care in the US is estimated at $25-50bn annually, mainly consisting of nursing time and hospital admittance costs. In Europe, wound care costs represent as much as 3-4% of healthcare budgets. The direct cost of materials such as dressings is estimated to be 15-20%

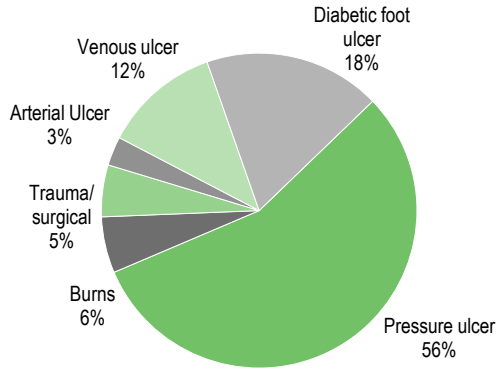
[1] Sen et al. Human Skin Wounds: A Major and Snowballing Threat to Public Health and the Economy. Wound Repair Regen. 2009;17(6):763–771.

[2] Professor Marco Romanelli, University of Pisa, Smith & Nephew Capital Markets Day November 2015.

of total care costs, according to Smith & Nephew. The cost of treatment per patient varies enormously depending on ulcer duration and severity, but figures range from $10,500 to $33,900 for VLU treatment and from $1,890 to $27,700 per DFU episode.[3] [4]

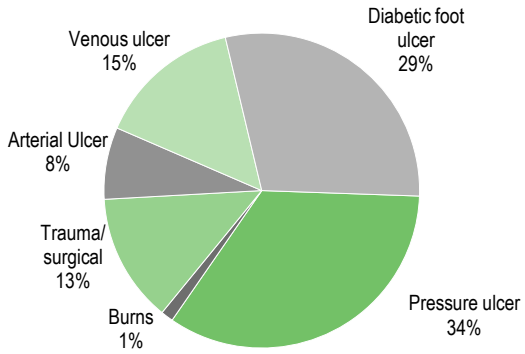
We envision a sharper focus on health economics to drive demand for products with demonstrable clinical benefits. In this spirit, the US Affordable Care Act incentivises care givers to achieve better care at lower overall cost for any given treatment episode.

Exhibit 4: US prevalence of all wounds (8 million pa)



Source: BioMedGPS

Exhibit 5: US prevalence of hard-to-heal wounds* (3.2 million pa)



Source: BioMedGPS. Note: *<50% surface area reduction in four weeks.

Complexity of wound care is a challenging hurdle

Wound care is not the focus of any single physician speciality, but is handled by a range of medical professionals such as vascular surgeons, gynecologists and dermatologists. Consequently, finding consensus about treatment protocols is challenging, which is exacerbated by great variations in reimbursements and budgets of treating facilities. Moreover, patient populations are affected by a high degree of co-morbidities and adverse socioeconomic factors, which often undermines compliance with prescribed treatments. In clinical trial settings, these challenging preconditions are compounded by patients showing much improved results compared to real life, thanks to the controlled conditions, which distorts the outcomes, not least in the control arm. Indeed, several novel treatments have shown good results in Phase II only to fail in Phase III. Recent examples including aclerastide for DFU (Derma Sciences) and HP802-247 for VLU (Smith & Nephew). Accordingly, even well-designed randomised controlled trials with standardised outcome measures struggle to produce approvable regulated wound products.

Treatment guidelines

Typical wound healing protocols include risk factor modification, offloading, debridement and a protective dressing. Risk factor modification includes elimination or minimisation of causes for wounds, such as ischaemia. The US Wound Healing Society has issued treatment guidelines (see Exhibit 6) using debridement (removal of necrotic tissue), antibiotic treatment, moist dressings, complete pressure off-loading (DFU) and compression bandages (VLU) as first-line treatment. Second-line treatments include hyperbaric oxygen (HBOT) and negative pressure therapy (NPWT), widely used in the US but less so in Europe. Dermal substitutes, so-called Cellular and Tissue products (CTP), are widely adopted in the US with the aim of improving healing rates and reducing secondary complications, such as infections and amputations. According to US Wound Registry

[3] Ma et al 2013 Annual Meeting of the American Venous Forum 2013.

[4] Stockl et al, Diabetes Care September 2004 vol. 27 no. 9 2129-2134.

analysis (2005-10), 51% of wounds healed with standard care, while hard-to-heal chronic wounds required advanced therapies such as HBOT, NPWT or dermal substitutes.

Exhibit 6: First-line standard of care for diabetic foot and venous leg ulcers/advanced moist wound dressings

Diabetic foot ulcers – standard of care	Comments	Typical Outcomes data
Debridement (surgical/sharp, mechanical, enzymatic/collagenase, hydrogel, sterile maggots) Infection elimination (antibiotics) Wound dressing (gauze/moist dressing) Off-loading of pressure	• Limited clinical trial data - trials small and under powered • "More good quality Randomised Control Trials (RCTs) are needed to determine the clinical effect of debridement on healing" (source: Cochrane Wounds Group report 2010).	24% ulcers healed at 12 weeks 31% ulcers healed at 20 weeks (source: Margolis et al. 1999).
Venous leg ulcers – standard of care	**Comments**	**Typical Outcomes data**
Compression (bandages, stockings, mechanical) Debridement Wound dressings (for open ulcers) Antibiotics	• Compression is better than no compression, multi layer, elastic bandages appear superior to short-stretch minimal stretch bandages • "The evidence base to support (debridement) in VLU is very limited" (Cochrane Wounds Group report 2015).	13% ulcers > 5 cm², >6m duration heal at 26wks 95% ulcers < 5 cm², <6m duration heal at 26wks (source: Margolis et al. Am J Med. 2000 Jul;109(1):15-9).
Moist wound dressings (advanced)	**Types**	**Examples (Company)**
Designed to manage exudate and maintain moist environment. They may have anti-microbial effect.	Hydrocolloid Hydrogels Foams Films Alginates Silver-impregnated Enzymatic debridement (collagenase)	Granuflex (ConvaTec), Comfeel (Coloplast) Aquaform (Maersk Medical), Intrasite gel (S&N) Allevyn, Cavi-Care (S&N), Biatain (Coloplast), Tegaderm (3M), OpSite (S&N) Calcium alginate (S&N), Kaltostat (ConvaTec), Acticoat (S&N), Urgosorb (Urgo) Santyl (S&N)

Source: US Wound Healing Society, Edison Investment Research, company data

Exhibit 7: Second-line therapies for diabetic foot and venous leg ulcers

Adjunct therapies	How delivered	Comments
Hyperbaric oxygen (HBOT) – DFU only For non-healing infected deep ulcers reaching tendons or bone, unresponsive to at least one month of standard care.	Delivered in hyperbaric facility (>500 in US), usually in 60- to 120-minute sessions. Expensive and time-consuming	• Some evidence of healing benefit at 6wks in DFU, limited evidence of longer-term benefit. • No evidence for benefit in VLUs, arterial or pressure ulcers (Cochrane Wounds Group).
Negative pressure wound therapy (NPWT) Porous dressing applied to wound, connected to drainage tube. Negative pressure is thought to promote wound healing by increasing blood flow and oxygenation, reducing oedema by removing wound fluid, and removing exudate and bacteria.	• **Traditional Stationary Devices** include V.A.C (KCI/ Acelity), Renasys EZ, Renasys EZ PLUS (Smith & Nephew), Invia (Medela); • **Portable:** RENASYS GO (S&N), V.A.C.Via (KCI), • **Disposable (single dressing used for seven days):** PICO single use (S&N) - not covered by all insurers • **Non-powered:** SNaP (Spiracur) - not covered by Medicare insurers	• Some encouraging data in DFU on reducing time to heal and wound area, e.g. 43% healed with NPWT vs 29% with advanced moist wound therapy at 16 wks. (source: Blume et al, 2008). • Limited evidence of benefit in VLU (source: Cochrane Wounds Group report 2015, analysis of 13 trials).

Source: Edison Investment Research, company data and Cochrane Wounds Group

Wound care procedures are by and large performed in an outpatient setting in Europe with a well-developed system of specialised wound nurses, not least in the UK. In the US, the lion's share of procedures are performed in wound care centres – the commercial operators Healogics and Restorix are the two biggest – but surgery centres and physician offices also perform a large number of procedures.

Dermal substitutes: A growth market targeted by TRX

CTPs are either biomaterial (synthetic) or cellular matrices (minimally or extensively manipulated human or animal tissue). When applied to a wound they act like an autologous skin graft and provide the functions of normal skin. The field is crowded, with more than 70 products available, the most important of which are illustrated in Exhibit 8. While Medicare covers most products, private health insurance providers like UnitedHealth and Aetna currently regard only a handful as "medically necessary" for the treatment of VLU and DFU. However, TRX expects a growing adoption of DermaPure as a result of Medicare coding, coverage and utilisation. Private health insurers also administer Medicare managed plans that typically follow the reimbursement rules stipulated by Medicare.

The use of biologics in wound care outside the US is limited, due to constrained healthcare budgets, a more conservative use of tissue-derived products and greater hurdles in the production of processed human tissue. Competition over tissue processed by tissue banks is tight, particularly

in orthopaedic applications, as is the regulation of trade of human tissue in Europe. Moreover, religious and other sociological considerations have an impact on the use of porcine devices, which are an order of magnitude cheaper to manufacture than human tissue-based products. However, xenografts are rarely used in dermal applications, as they are seen as less efficacious.

Exhibit 8: Bioengineered skin for DFU and VLU

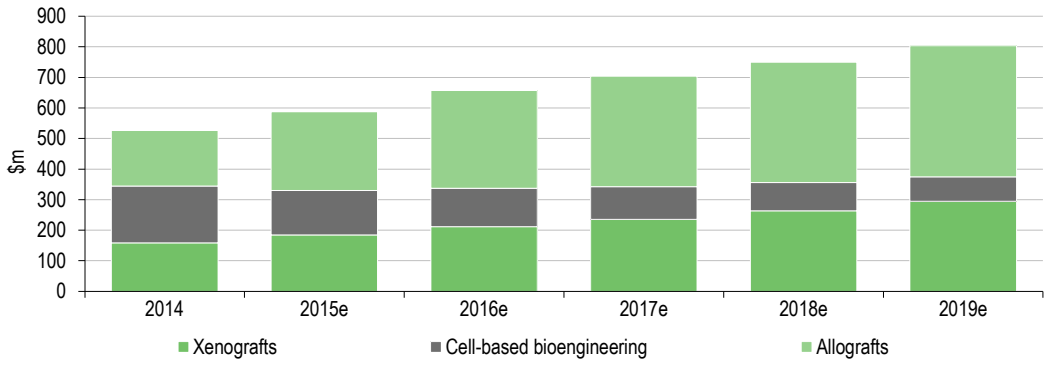
Product	Description	Available sizes (cm^2)	Product cost (per unit)	CMS reimbursement
Apligraf (Organogenesis)	Bilayered living skin substitute from neonatal foreskin	44 (disc)	c $1,000-1,600	High
Dermagraft (Organogenesis)	Human neonatal foreskin fibroblasts cultured on a polyglactin scaffold	37	c $1,000-1,600	High
DermaPure (Tissue Regenix)	Human dermis from cadavers, decellularised	2, 4, 6, 12, 24	c $1,400	High
EpiFix (MiMedx Group Inc)	Dehydrated human amniotic (placental) membrane allograft	1.5-49	Starting from $320	High
Grafix Core, Grafix Prime (Osiris Therapeutics, Inc)	Cryopreserved amniotic (placental) membrane allograft	2, 3, 6, 12, 25	Not known	High
Graftjacket regenerative tissue matrix (KCI)	Decellularised human skin tissue matrix	16, 24	Not known	High
PriMatrix Dermal Repair Scaffold (TEI Biosciences)	Acellular collagen dermal tissue matrix from fetal bovine skin	9 – 250	Not known	High
Oasis Wound Matrix (Smith & Nephew)	Porcine submucosa derived matrix	10.5, 21, 35, 70, 140	From $126	Low
TheraSkin (Soluble Solutions)	Cryopreserved human skin allograft from cadavers	13, 39	Not known	Low

Source: Edison Investment Research, UnitedHealthcare, CMS, company data.

The dermal substitute market is highly competitive

Four companies control nearly three-quarters of the $865m[5] US biological wound care market, comprised of dermal substitutes, topical delivery/drugs and collagen/active dressings. The European market is valued at $25m and the market in the rest of the world a mere $7m.

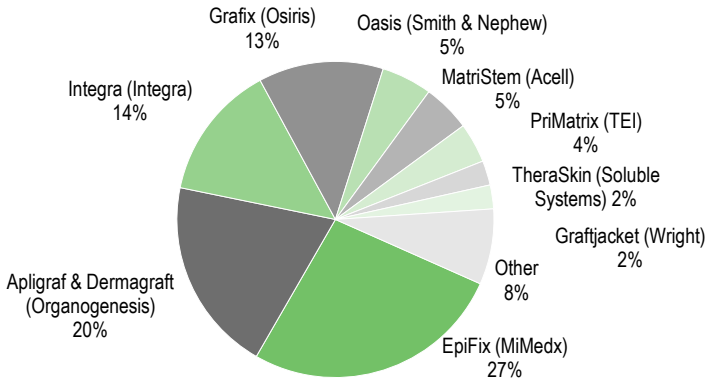
Exhibit 9: US skin substitutes market (9% CAGR)



Source: BioMedGPS

[5] BioMedGPS.

Exhibit 10: US dermal substitute market shares Q215



Source: SmartTRAK (MiMedx)

The biggest category is dermal substitutes (2014: $526m), in which amnion-based EpiFix (MiMedx) has overtaken the manipulated skin grafts Dermagraft and Apligraf (Organogenesis) as the leading product following changes to Medicare reimbursement rates in 2014. Of the 6.5m chronic wounds there were 665,800 applications of CTPs in 2013, accounting for 222,000 wounds, assuming three applications per wound. The vast majority were used in the treatment of DFU and VLU.

Reimbursement of skin substitutes in transition in the US

In October 2014, the Centers for Medicare & Medicaid Services (CMS) introduced a new reimbursement system for wound care in the outpatient setting with the purpose of reducing wastage and cost. Previously, facilities would claim two separate payments through the Outpatient Prospective Payment System (OPPS) for the cost of a wound care procedure (eg debridement) and the cost of the skin substitute product, based on their historic average sales price (ASP) plus 6%. Under the new system, skin substitutes are reimbursed at a fixed price for the entire procedure by bundling the product payment with the procedure payment and adjusted for wage index. Products are assigned to high/low-cost groups (Exhibit 11) as a function of the size of the graft.

Exhibit 11: Medicare payments for skin substitutes for DFU/VLU (OPPS rates for 2016)

Reimbursed procedure based on wound size/body area (CPT code)	High-cost group payment		Low-cost group payment	
	Hospital OP	ASC	Hospital OP	ASC
Wound <100cm^2 on leg or all wound sizes on foot (CPT 15271, CPT 15275, CPT 15277)	$1,411	$789	$428	$239
Wound >100cm^2 on leg (CPT 15273)	$2,137	$1,195	$1,411	$789

Source: Edison Investment Research. Note: Debridement is considered a component code of CPT 15271-7 and not separately reimbursed. OP = outpatient, ASC = Ambulatory Surgery Center.

We expect the availability of smaller sizes of skin substitutes to be critical under the new system. According to MiMedx, the median size of ulcers is 1.35 cm^2 for DFU and 2.32 cm^2 for VLU, with 67% of DFU and 77% of VLU being under 5cm^2, prompting TRX and others to manufacture increasingly smaller patches (Exhibit 8). Pricing details for many products are sketchy, but range from $126/unit for Oasis, a xenograft in the low-cost group, to a starting point of $595 for DermaPure and more than $1,000/unit for Apligraf/Dermagraft and in the high-cost group. Even compared to the relatively inexpensive EpiFix (starting from $320 per patch), DermaPure HD comes out more favourably in terms of cost per wound closure. Based on an average price point of $1,400, we estimate treatment costs using DermaPure at $1,540 based on 1.1 applications, compared to an average treatment cost using market-leading EpiFix at $2,440[6] owing to multiple applications.

Moreover, unless Medicare beneficiaries have taken out secondary insurance coverage they are liable for a 20% co-payment, making patients sensitive to the number of treatment episodes before

[6] MiMedx.

the wound heals. This pitches patients against physicians, who have historically benefited from products requiring multiple procedures. However, the new bundled reimbursement incentivises physicians to minimise overall treatment cost, which we expect to be supportive for the use of DermaPure HD, intended for single application.

Regulatory scrutiny is intensifying

The use of tissue for human use is subject to regulations depending on its source: xenograft (animal derived tissue, eg porcine, bovine, ovine), human allograft (cadaver or live donor) or cell-based bioengineered tissue, illustrated in Exhibit 12. Acellular dermal matrices from human tissue, such as DermaPure HD, are regarded as minimally processed and classified by the FDA as donated human tissue. It can therefore be commercialised pending clearance of the participating tissue bank with no regulatory burden directly on the manufacturer, unlike many of its competitors.

Historically, regulatory oversight for many tissue-based products has been relatively relaxed. However, in late October 2015 the FDA issued draft guidance on homologous use of human cells, tissues, and cellular and tissue-based products, particularly relating to the fast-growing use of amniotic tissue-based products. We expect the intensified regulatory scrutiny to prompt major players to invest more in controlled trials to support efficacy claims for their products and convince healthcare insurers to cover their use. Based on the FDA's proposed changes, we do not expect any impact on DermaPure. Conversely, usage may slow some amnion-based products in the event that 510k clearance becomes mandatory for their use. Earlier in 2015, the FDA also issued a draft on what tissue is considered minimally manipulated. DermaPure is considered minimally manipulated and approved as a homologous use product (dermis for dermis replacement) and should remain unaffected.

Exhibit 12: Regulation of tissue and cell-based medical products in the US and Europe

	Human tissue (allograft)		Animal tissue (xenograft)
	Donated tissue	**Engineered products (matrices)**	**Engineered products (matrices)**
US	• Minimally manipulated banked human tissue (for homologous use) - no approval necessary • or Humanitarian Device Exemption	• PMA (dressings that interact with body, Class III higher-risk device, longer-term skin substitutes) - need to demonstrate safety and clinical efficacy	• FDA 510 (k) (scaffold dressings, Class II lower-risk devices) - must demonstrate safety • Pre-market approval
EU	• Minimally manipulated, homologous use tissue - Human Tissues and Cells Directive 2004 applies • Heterologous use grafts would be classified as ATMP medicinal products (requiring EMA approval)	Human (viable or non-viable/acellular), substantially manipulated 'tissue engineered products' as defined by the Advanced Therapy Medicinal Products regulation (2007) - require centralised EMA approval	• Class III medical devices, must apply for CE mark - requires clinical testing • The EU Medical Device Directive only applies to animal-origin acellular (non-viable) matrix products, not human or viable tissue engineered products

Source: Edison Investment Research, European Commission and FDA

In Europe, TRX is reviewing its distribution options and may look to establish agreements with local tissue banks, from which it may secure a licence fee. The use of medical products originating from an EU tissue bank (unless minimally manipulated like DermaPure) is governed by the Advanced Therapy Medicinal Products regulation. Unlike products under the Medical Device Directive, such as xenografts, this regulatory pathway necessitates clinical trials. Once approval is granted, it covers the entire European Union. Human tissue derived products fall under a variety of national legislation. For example, in Germany human tissue-derived products like DermaPure are regulated by the federal institute for vaccines and biomedicines, the Paul-Ehrlich Institute, and in the UK by the Human Tissue Authority.

Commercial strategy

TRX's commercial strategy focuses on building a portfolio of dermal substitutes (xenografts and allografts) addressing a range of indications and price points, while extending its commercial reach by adopting a hybrid strategy of sales reps and independent distributors.

Exhibit 13: Wound care commercial status

TRX's current position	Market potential
Patients with access to Medicare coverage for DermaPure	24m patients or 65% of 37m covered lives.
Stage I – inpatient wound care	3.6m trauma wounds and burns/1.3m chronic wounds pa. Total 6.5m chronic wounds pa/18m trauma wounds pa.
Stage II – outpatient wound care	14m trauma wounds and burns/5.2m chronic wounds pa.
TRX sales reps	15, covering five states in east and central regions under CGS.
TRX distributorships	Two signed in April and July 2015, covering three of 12 states under Novitas jurisdiction, the largest of the eight US Medicare agencies with 12m beneficiaries. Min commitment $750m sales to July 2016.

Sources: Company information, Human Skin Wounds, Sen et al/NIH Research Portfolio

DermaPure HD was launched in the US and Europe in June 2014. In the first phase, TRX addressed inpatient settings, representing 20% of wounds, such as acute care hospitals and Veterans Affairs (VA) hospitals. Reflecting the need to educate new users in the early phase, TRX generated a mere £0.1m in DermaPure HD revenues in 2014.

The second phase of the DermaPure launch is now underway, targeting outpatient facilities that deal with about 80% of chronic wounds and where Medicare is the main payer. Having been awarded the requisite Q code in late 2014, eight out of 11 Medicare reimbursement agencies have now approved the reimbursement of DermaPure, making it accessible to two-thirds of Medicare beneficiaries (1.5 million addressable patients). By targeting the outstanding north-eastern, Georgia and the Michigan/Illinois Medicare agents, TRX is aiming to secure full coverage in the future.

TRX adopts a hybrid strategy of employed sales reps (15) and independent distributors, allowing it to build channels in 1,000+ outpatient centres across the 30 states where it currently enjoys Medicare coverage. It has also deployed sales resources in non-Medicare covered states targeting physicians in the hospital setting. TRX's reps primarily target larger hospital institutions, groups of hospitals (GPOs/integrated networks) and wound care chains.

We consider DermaPure HD to be well positioned by virtue of the indications of good efficacy in hard-to-heal chronic wounds and the fact that it is economic to store and use. For example, Dermagraft must be stored at -75°C ± 10°C, while DermaPure is stored and transported at room temperature. The absence of immunogenic substances such as silicon and glycosaminoglycan in the dCELL extraction process makes DermaPure a 'cleaner' alternative to many other skin substitutes. As the product launch is still at an early stage, we forecast <1% market share in the US in FY21 with $6m in sales. To contextualise our $31m peak sales estimate for Derma Pure in more than 10 years' time, we note that MiMedx reached over $100m in sales with its amnion-based product only a few years after launch.

Exhibit 13: DermaPure key benefits

Requirements of dermal substitutes	DermaPure features
Clinically effective	Proven efficacy in chronic and acute wound healing, equivalent or superior to standard treatments.
Mimics natural skin	The natural features, function and biomechanical properties of the dermis are preserved, no chemicals or detergents are used that prevent repopulation of the dermis with the patient's own cells.
Presents low risk of infection and immunogenicity	Studies show dCELL process lowers risk of infection and rejection seen in products retaining viable cells.
Easy to store	Stored and transported at room temperature, a significant cost benefit over leading cryopreserved products.
Easy to use	Off-the-shelf product.

Source: Company data, Edison Investment Research

DermaPure potential is backed by strong clinical data

As discussed in our initiation report, there is a growing body of peer-reviewed clinical evidence for DermaPure HD, illustrating the efficacy of the allograft in both chronic and acute wound care settings. A UK study of DermaPure HD in 20 DFU/VLU patients demonstrated that DermaPure met the primary outcome measure despite the treatment-resistant nature of the wounds.

Exhibit 14: Headline results of the UK study of DermaPure HD in chronic wounds

Outcome measure	Result
Reduction in wound surface area	Primary outcome measure, satisfied in 100% of participants
Mean reduction in wound size at six weeks	49.5%
Mean reduction in wound size at six months	87%
Mean ulcer duration and surface area	4.76 years/13.11cm^2
Proportion of patients completely healed	60%

Source: Bayat, A et al, Single stage application of a novel decellularised dermis

Furthermore, DermaPure HD has been shown to enhance angiogenesis vs controls in a 50-patient study in acute wounds. Angiogenesis, or new capillary formation, is crucial to prompt wound healing and scar prevention. The study compared wound healing with DermaPure to healing with collagen-GAG scaffold (Integra Matrix Wound Dressing), autograft and no intervention, with the main observations summarised in Exhibit 16.

Exhibit 15: Headline observations from DermaPure acute wounds study

Measure	Outcome in DermaPure samples
Wound healing efficacy	Normal healing, at four weeks wound site resembled natural tissue.
Biomechanical and structural characteristics	Equivalent or superior in DermaPure samples vs controls.
Markers of angiogenesis	Promotes significant late upregulation of PROK2 and MT6-MMP genes p<0.05 related to angiogenesis vs controls.

Source: Greaves et al, Acute Cutaneous Wounds Treated with Human Decellularised Dermis Show Enhanced Angiogenesis during Healing

A US multi-centre clinical validation case series of hard-to-heal chronic wounds was initiated in August 2014 to support the company's marketing and reimbursement strategy and to provide data for line extensions. The primary outcome measure of the study is incidence of wound healing. Secondary measurements include the quality and rate of wound healing. Interim results from the 10-patient study presented at the Symposium on Advanced Wound Care (SAWC), Arizona in May 2015 represented a significant step towards raising the profile of DermaPure HD among key opinion leaders. Because of rigorous inclusion/exclusion criteria, enrolment has been slower than expected such that results, previously expected in Q415, are likely to become available in H116.

Acute wound and burns treatment is a larger market for DermaPure

TRX is also promoting the application of DermaPure HD in acute wound care management, initially targeting lower extremity amputations, surgical wounds and burns. These are considered complex wounds treated in the acute setting. The commercial potential for dermal substitutes in burns alone (10 million cases per year globally) should be at least as significant as chronic wounds (35 million cases per year globally) because the average number of grafts used per patient would be higher. A minimum of two applications is needed to cover larger wound surface areas and we estimate the average graft cost per procedure at c $4,000. The use of skin autografts is the gold standard for the restoration of epidermal function of the skin in burn patients. The limitations of autografts include risk of additional scarring and inadequate available skin. TRX initially intends to target treatment of severe burns and abrasions, a population of around one million patients pa in the US, expanding into other indications such as trauma wounds, subject to clinical data.

Exhibit 16: Tissue Regenix wound care pipeline

Product description	Indications	Description	Status/estimated launch date
DermaPure HD	Diabetic foot ulcer (DFU)/ Venous leg ulcer (VLU)/acute wound care	Allograft - donated human tissue	Launched in the US/Europe in 2014. US clinical validation trial underway.
SurgiPure XD	General surgery, hernia repair	Xenograft – porcine tissue	510k submitted, launch estimate 2016.
SurgiPure HD	Hernia/orthopaedic use/breast reconstruction	Allograft – donated human tissue	Launch date to be confirmed.

Source: Company data, Edison Investment Research

Line extensions including surgical matrices are a future growth driver

Having started with human tissue implants, TRX is developing porcine tissue implants, which could pave the way for greater commercial scale, easier sourcing and lower-cost processing.

SurgiPure XD, a xenograft based on the dCELL technology, is being developed initially for hernia repair with a US launch prepared for 2016, subject to FDA approval. TRX submitted a 510(k) application in Q415, making an approval in the course of 2016 possible.

Growth drivers of the surgical matrices market (US sales of $360m in Q115) include the need to cut down complications (reintervention and infection) associated with the use of currently available mesh products. The US surgical matrices market is led by Bard/Davol, LifeCell/Acelity (AlloDerm, a decellularised human tissue product) and J&J/Ethicon. A range of animal tissue surgical patches is already on the market, which paves the way for SurgiPure XD, including Strattice Tissue Matrix (KCI/Acelity) and SurgiMend (TEI Biosciences). As there are no published data on the product, we conservatively estimate that the market share of SurgiPure XD would be less than 0.5% in the initial launch years. There are c 1m hernia repairs pa and around 25% of patients suffer complications from hernia mesh. Currently, the reimbursement per procedure for surgical soft tissue patches is c $7,500.[7] In future, TRX plans to target a range of new soft tissue replacement/augmentation indications for a human tissue version of SurgiPure HD, including breast reconstruction and soft tissue tendon repair, with a sales price per patch of c $2,000, well above the chronic wound care setting. However, SurgiPure HD does not currently have a reimbursement code. We await confirmation of the timelines before adding in sales estimates for SurgiPure HD.

Exhibit 19: Commercial estimates for wound care products

Product	Addressable population	Forecasts	Potential next catalysts
DermaPure HD chronic wounds	1.5m venous and diabetic foot ulcers procedures pa in US: 60% hard-to-heal	Launched in 2014, peak net sales estimate $65m, penetration 4.5% of hard-to-heal wounds. ASP $1,400, average 1.1 applications per procedure.	Additional reimbursement coverage, potential expansion of distribution channels.
DermaPure HD acute wounds	Approximately 1m severe burns and abrasions pa in US	Launched in 2014, peak net sales estimate of $137m at 4.5% penetration. ASP $1,400, average two applications per procedure.	Additional reimbursement coverage, potential expansion of distribution channels.
SurgiPure XD – initially in hernia repair	c 1.5m hernia repair procedures pa in the US, of which c 25% suffer complications with SOC	ASP $7,500 (our estimate) per procedure. Peak net sales estimate of $80m.	Study data, 510k clearance and launch in 2016. Reimbursement strategy.

Source: Edison Investment Research, procedural stats: Journal of Investigative Dermatology/Millennium Research Group estimates

Financials

We forecast £45m in net sales by 2020e, which should take TRX to profitability. We see a sequence of potential catalysts over the next couple of years that could lead towards delivering the estimated commercial potential. Our revenue estimates are calculated net of a 30% distributor margin for simplicity across all three divisions, assuming that TRX continues to operate a hybrid distribution strategy. We forecast wound care revenue of £0.5m in FY16, rising to £1.6m in FY17, driven by the commercial focus on outpatient wound care clinics and continuing expansion of distribution channels. We forecast wound care operating expenses of £4.9m in FY16 including SG&A of £2.8m and R&D of £2.4m, rising to £6.6m in FY17 (SG&A of £3.7m and R&D £3.3m) to cover ongoing DermaPure and SurgiPure studies and expansion of the direct sales force to enable the full roll-out to wound care clinics. Wound care operating expenses are forecast to increase to £8.6m in FY18, in line with the launch of successive products. We estimate that the subsidiary will become profitable in 2020, realising £0.8m of operating profit.

We estimate that group revenue will increase from £0.5m in FY16 to £79m in FY21, reaching profitability on a margin of 3% in 2020, when we estimate that tax would be payable on a blended basis of 15%, offsetting US corporation tax of 20% against UK patent box R&D tax credit, trending towards 20%. Based on end-July 2015 net cash of £24.9m, TRX has a cash runway for the immediate pipeline (OrthoPure, SurgiPure and dCELL valves) and to launch wound care products

[7] Company guidance.

in the US via a hybrid strategy. Our forecasts indicate that the company has a funding requirement of £15m in 2018 to cover FDA studies of OrthoPure XT/XM.

Valuation: Sum-of-the-parts valuation of £346m

Our DCF valuation is £346m or 45.6p per share using a WACC of 12.5%, subject to potential dilution from an estimated £15m funding requirement needed to deliver on our estimated growth trajectory via a hybrid distribution strategy. We value the wound care business at £188m, the orthopaedics division at £101m and the cardiac division at £37m, based on risk-adjusted cash flows for each division according to the stage of development; we add end-July 2015 net cash of £25m. According to our model, Orthopaedics and Cardiac alone account for the current share price, leaving Wound Care as an option for free. There are a number of near-term catalysts ahead, including the potential CE mark grant and launch of OrthoPure XM and US launch of OrthoPure HM/HT via the HCTP pathway, which would lead us to increase the probability of success for these products.

Exhibit 20: Sum-of-the-parts valuation

	Peak net sales ($m)	Operating margin	£m	p
Wound Care Inc	281.9	25%	187.5	24.7
Orthopaedic	383.8	33%	101.5	13.4
Cardiac	133.0	24%	37.0	4.9
Unallocated costs			(4.7)	(0.6)
Net cash July 2015			24.9	3.3
SOTP			**346.3**	**45.6**

Source: Edison Investment Research

Exhibit 20 illustrates our forecast divisional and group sales and profitability 2016-21. We estimate that TRX will become profitable in 2020, on this basis trending towards an 18% group EBIT margin in 2021. We adjust all developing products, using standard medtech probabilities of success, as shown in Exhibit 21. We assume a higher success probability for human tissue due to lower regulatory risk.

Exhibit 21: Probabilities for developing products

Pathway	Probability	Products
510k - US	60%	SurgiPure XD
CE mark	60%	Porcine dCELL heart valves/OrthoPure XM/XT
Human tissue products	80%	OrthoPure HM/HT
IDE – US	35%	Porcine dCELL heart valves/OrthoPure XT/XM

Source: Edison Investment Research

Exhibit 22: Divisional forecasts

£m	2016e	2017e	2018e	2019e	2020e	2021e
Wound Care - revenue	0.47	1.66	5.04	11.50	20.66	36.22
growth		351%	303%	228%	180%	175%
Wound Care - operating profit	(4.83)	(5.68)	(4.59)	(2.30)	0.83	6.16
Orthopaedics - revenue	0.00	1.80	6.81	13.65	21.32	35.62
growth		N/A	379%	200%	156%	167%
Orthopaedics - operating profit	(4.17)	(4.93)	(6.13)	(1.89)	2.92	9.42
Cardiac - revenue	0.00	0.00	0.13	1.25	3.27	6.86
growth		N/A	N/A	1,000%	262%	210%
Cardiac - operating profit	(1.74)	(2.00)	(2.60)	(4.01)	(2.42)	(1.17)
Group revenue	0.47	3.46	11.97	26.40	45.26	78.71
Growth		731%	346%	220%	171%	174%
Group operating profit	(10.74)	(12.61)	(13.31)	(8.20)	1.32	14.41
Group operating margin	N/A	N/A	N/A	N/A	3%	18%

Source: Edison Investment Research

In a takeover scenario, subject to TRX gaining commercial traction, the valuation of the company could be 5x sales based on the price paid by Integra (wound care) in August to TEI Biosciences for

its range of dermal substitutes, which would imply a valuation of $565m for the group based on a multiple of FY21 sales of $113m (£79m).

There is a range of potential value drivers for TRX: in 2016, events that would lead us to increase the probability of success for the individual products include data from the ongoing chronic wound care study in H116, 510k clearance of SurgiPure XD, OrthoPure XM CE mark grant and launch/US launch of OrthoPure HM/HT. Launch of the dCELL human heart valve is planned during 2017.

Exhibit 23: Financial summary

£'000s	2014	2015	2016e	2017e	2018e
Years ending 31 January	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	6	100	473	3,459	11,974
Cost of Sales	0	0	(104)	(797)	(2,674)
Gross Profit	6	100	369	2,662	9,299
Operating expenses	(6,459)	(8,318)	(11,106)	(15,271)	(22,612)
EBITDA	(6,453)	(8,218)	(10,597)	(12,325)	(13,106)
Operating Profit (normalised)	(6,577)	(8,369)	(10,737)	(12,609)	(13,313)
Exceptionals	0	0	0	0	0
Other	0	4	4	0	0
Operating Profit	(6,577)	(8,365)	(10,733)	(12,609)	(13,313)
Exceptionals	0	0	0	0	0
Net Interest	274	168	209	141	50
Profit Before Tax (norm)	(6,303)	(8,201)	(10,527)	(12,468)	(13,262)
Profit Before Tax (as reported)	(6,303)	(8,197)	(10,523)	(12,468)	(13,262)
Tax	710	620	685	623	663
Other	0	0	0	0	0
Profit After Tax (norm)	(5,593)	(7,581)	(9,842)	(11,845)	(12,599)
Profit After Tax (as reported)	(5,590)	(7,581)	(9,838)	(11,845)	(12,599)
Average Number of Shares Outstanding (m)	636	636	698	760	760
EPS - normalised (p)	(0.88)	(1.19)	(1.41)	(1.56)	(1.66)
Dividend per share (p)	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	100.0	78.0	77.0	77.7
EBITDA Margin (%)	N/A	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A	N/A
BALANCE SHEET					
Fixed Assets	472	435	946	939	1,331
Intangible Assets	0	0	0	0	0
Tangible Assets	472	435	946	939	1,331
Investments	0	0	0	0	0
Current Assets	19,610	12,238	20,673	8,988	11,767
Stocks	0	34	108	393	1,099
Debtors	1,127	1,947	1,801	1,896	4,921
Cash & equivalents	18,483	10,257	18,764	6,699	5,747
Income taxes	0	0	0	0	0
Other current assets	0	0	0	0	0
Current Liabilities	(1,104)	(1,095)	(621)	(1,310)	(2,565)
Creditors	(1,104)	(1,095)	(621)	(1,310)	(2,565)
Short term borrowings	0	0	0	0	0
Contingent consideration	0	0	0	0	0
Long Term Liabilities	0	0	0	0	(15,000)
Long term borrowings	0	0	0	0	(15,000)
Contingent consideration	0	0	0	0	0
Net Assets	18,978	11,578	20,998	8,616	(4,467)
CASH FLOW					
Operating Cash Flow	(6,121)	(8,285)	(11,076)	(11,929)	(15,403)
Net Interest	274	168	209	141	50
Tax	474	0	1,095	0	0
Capex	(358)	(114)	(694)	(277)	(599)
Acquisitions/disposals	0	0	0	0	0
Financing*	8	5	18,972	0	0
Dividends	0	0	0	0	0
Capitalised R&D	0	0	0	0	0
Net Cash Flow	(5,723)	(8,226)	8,507	(12,065)	(15,952)
Opening net debt/(cash)	(24,206)	(18,483)	(10,257)	(18,764)	(6,699)
HP finance leases initiated	0	0	0	0	0
Other	0	0	0	0	0
Closing net debt/(cash)	(18,483)	(10,257)	(18,764)	(6,699)	9,253

Source: Company accounts, Edison Investment Research. Note: *Funding requirement for illustrative purposes shown as increase in debt.

Contact details	Revenue by geography
The Biocentre Innovation Way Heslington York, YO10 5NY United Kingdom +44 (0)1904 567609 www.tissueregenix.com	N/A

Management team

CEO: Antony Odell	CFO: Ian Jefferson
Antony Odell joined Tissue Regenix as CEO in October 2008. Previous roles include co-director of Xeno Medical, a medical technology consultancy, and CEO for a UK NHS cardiovascular device spin-out, Tayside Flow Technologies. He worked for J&J Medical for almost 10 years in European business development roles for Drug Delivery & Vascular Access and as general manager for Fresenius. Mr Odell holds a degree in physiology and biochemistry from the University of Southampton.	Ian Jefferson has served as CFO at Tissue Regenix since June 2011. He joined AIM-listed COE Group in 2007, took on the role of CEO in 2008, restructured the group and then successfully executed its sale. He has a comprehensive financial and operations background and extensive experience of organisational transformation and M&A. A qualified chartered accountant, Mr Jefferson holds a BSc in Physics with Electronics from Manchester University and an MSc in Applied Radiation Physics from Birmingham University.
Chairman: John Samuel	
John Samuel joined Tissue Regenix as executive chairman in March 2008. A qualified chartered accountant with Price Waterhouse, he has held a number of senior finance positions in industry, including as FD of Whessoe and Ellis & Everard. He was formerly the CEO of the Molnlycke Health Care Group. Until January 2010 he was a partner with Apax Partners.	

Principal shareholders	(%)
Invesco	24.0
Woodford Investment Management	15.0
IP Venture Fund	14.6
Techtran Group	13.6
Baillie Gifford & Co	6.2
University of Leeds	4.5
Jupiter Asset Management	4.5

Companies named in this report

Acelity (LifeCell/KCI), Bard/Davol, Coloplast, Convatec, Edwards Life Sciences, Integra, J&J (Mitek/Ethicon), MiMedx, Mölnlycke Healthcare, Osiris, Smith & Nephew, St Jude, TEI Biosciences.

Edison, the investment intelligence firm, is the future of investor interaction with corporates. Our team of over 100 analysts and investment professionals work with leading companies, fund managers and investment banks worldwide to support their capital markets activity. We provide services to more than 400 retained corporate and investor clients from our offices in London, New York, Frankfurt, Sydney and Wellington. Edison is authorised and regulated by the Financial Conduct Authority (www.fsa.gov.uk/register/firmBasicDetails.do?sid=181584). Edison Investment Research (NZ) Limited (Edison NZ) is the New Zealand subsidiary of Edison. Edison NZ is registered on the New Zealand Financial Service Providers Register (FSP number 247505) and is registered to provide wholesale and/or generic financial adviser services only. Edison Investment Research Inc (Edison US) is the US subsidiary of Edison and is regulated by the Securities and Exchange Commission. Edison Investment Research Limited (Edison Aus) [46085869] is the Australian subsidiary of Edison and is not regulated by the Australian Securities and Investment Commission. Edison Germany is a branch entity of Edison Investment Research Limited [4794244]. www.edisongroup.com

DISCLAIMER
Copyright 2016 Edison Investment Research Limited. All rights reserved. This report has been commissioned by Tissue Regenix and prepared and issued by Edison for publication globally. All information used in the publication of this report has been compiled from publicly available sources that are believed to be reliable, however we do not guarantee the accuracy or completeness of this report. Opinions contained in this report represent those of the research department of Edison at the time of publication. The securities described in the Investment Research may not be eligible for sale in all jurisdictions or to certain categories of investors. This research is issued in Australia by Edison Aus and any access to it, is intended only for "wholesale clients" within the meaning of the Australian Corporations Act. The Investment Research is distributed in the United States by Edison US to major US institutional investors only. Edison US is registered as an investment adviser with the Securities and Exchange Commission. Edison US relies upon the "publishers' exclusion" from the definition of investment adviser under Section 202(a)(11) of the Investment Advisers Act of 1940 and corresponding state securities laws. As such, Edison does not offer or provide personalised advice. We publish information about companies in which we believe our readers may be interested and this information reflects our sincere opinions. The information that we provide or that is derived from our website is not intended to be, and should not be construed in any manner whatsoever as, personalised advice. Also, our website and the information provided by us should not be construed by any subscriber or prospective subscriber as Edison's solicitation to effect, or attempt to effect, any transaction in a security. The research in this document is intended for New Zealand resident professional financial advisers or brokers (for use in their roles as financial advisers or brokers) and habitual investors who are "wholesale clients" for the purpose of the Financial Advisers Act 2008 (FAA) (as described in sections 5(c) (1)(a), (b) and (c) of the FAA). This is not a solicitation or inducement to buy, sell, subscribe, or underwrite any securities mentioned or in the topic of this document. This document is provided for information purposes only and should not be construed as an offer or solicitation for investment in any securities mentioned or in the topic of this document. A marketing communication under FCA Rules, this document has not been prepared in accordance with the legal requirements designed to promote the independence of investment research and is not subject to any prohibition on dealing ahead of the dissemination of investment research. Edison has a restrictive policy relating to personal dealing. Edison Group does not conduct any investment business and, accordingly, does not itself hold any positions in the securities mentioned in this report. However, the respective directors, officers, employees and contractors of Edison may have a position in any or related securities mentioned in this report. Edison or its affiliates may perform services or solicit business from any of the companies mentioned in this report. The value of securities mentioned in this report can fall as well as rise and are subject to large and sudden swings. In addition it may be difficult or not possible to buy, sell or obtain accurate information about the value of securities mentioned in this report. Past performance is not necessarily a guide to future performance. Forward-looking information or statements in this report contain information that is based on assumptions, forecasts of future results, estimates of amounts not yet determinable, and therefore involve known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of their subject matter to be materially different from current expectations. For the purpose of the FAA, the content of this report is of a general nature, is intended as a source of general information only and is not intended to constitute a recommendation or opinion in relation to acquiring or disposing (including refraining from acquiring or disposing) of securities. The distribution of this document is not a "personalised service" and, to the extent that it contains any financial advice, is intended only as a "class service" provided by Edison within the meaning of the FAA (ie without taking into account the particular financial situation or goals of any person). As such, it should not be relied upon in making an investment decision. To the maximum extent permitted by law, Edison, its affiliates and contractors, and their respective directors, officers and employees will not be liable for any loss or damage arising as a result of reliance being placed on any of the information contained in this report and do not guarantee the returns on investments in the products discussed in this publication. FTSE International Limited ("FTSE") © FTSE 2016. "FTSE®" is a trade mark of the London Stock Exchange Group companies and is used by FTSE International Limited under license. All rights in the FTSE indices and/or FTSE ratings vest in FTSE and/or its licensors. Neither FTSE nor its licensors accept any liability for any errors or omissions in the FTSE indices and/or FTSE ratings or underlying data. No further distribution of FTSE Data is permitted without FTSE's express written consent.

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
245 Park Avenue, 39th Floor
10167, New York
US

Sydney +61 (0)2 9258 1161
Level 25, Aurora Place
88 Phillip St, Sydney
NSW 2000, Australia

Wellington +64 (0)48 948 555
Level 15, 171 Featherston St
Wellington 6011
New Zealand