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Tissue Regenix

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Healthcare equipment & services

14 October 2015

Tissue Regenix's (TRX) investment story is built on dCELL, a versatile regenerative medical technology, and its potential across the subsectors: wound care, orthopaedics and cardiac implants. We forecast that the US Wound Care subsidiary will be a driver of rapid group sales growth from the FY15 starting point of £0.1m, rising to £74m in FY21 boosted by product launches from all three divisions. Our sum-of-the-parts valuation is £325m.

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	0.4	(9.8)	(1.3)	0.0	N/A	N/A
01/17e	3.2	(11.6)	(1.5)	0.0	N/A	N/A

Note: *PBT and EPS are as reported.

Wound care is the commercial entry point

The US Wound Care division launched DermaPure HD, a dermal substitute used in advanced wound care, in 2014. Clinical studies demonstrate that DermaPure is effective in healing both chronic and acute wounds. DermaPure is well positioned in this competitive market by virtue of its efficacy in hard-to-heal chronic wounds and those of larger surface area. The division is the key revenue driver of our forecast increase from £0.4m in FY16 to £19.3m in FY20 as it expands its distribution reach.

Orthopaedics and cardiac divisions soon to follow

Through its Orthopaedics division, TRX targets the significant medical need in meniscus and anterior cruciate ligament (ACL) repair. Our peak sales estimate is $384m for the division. A 60-patient EU clinical trial of OrthoPure porcine meniscus tissue scaffold is underway, and CE mark submission and launch is planned in late 2016. Human tissue OrthoPure for the US is close behind. Meanwhile, in 2017 TRX plans to launch its dCELL human heart valves in Europe. Collectively, TRX could find profitable niches in these three large and highly competitive markets.

Funded for DermaPure growth

TRX reported £0.3m of US DermaPure sales in H115 and signed distributor stocking contracts worth a minimum of $0.8m over 12 months. TRX has achieved reimbursement coverage for 65% of Medicare beneficiaries since launch, which is set to be a key growth driver. In H115 TRX raised £19m net issuing 105.3m shares to develop and launch human tissue OrthoPure in the US, porcine OrthoPure in CE mark regions, and to expand the US wound care sales force.

Valuation: Sum-of-the-parts valuation of £325m

Our sum-of-the-parts DCF valuation is £325m, or 43p/share, using a 12.5% WACC. We value the wound care franchise at £175m, orthopaedics at £95m and the cardiac division at £35m. 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.

Price	**15.75p**
Market cap	**£120m**
	£/$1.54
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	(8.7)	(17.1)	(30.0)
Rel (local)	(11.2)	(12.3)	(31.7)
52-week high/low		24.75p	14.75p

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	2015
Completion of chronic wound care study	2015
510k of SurgiPure XD	2016
Initiation of OrthoPure XT study/CE mark grant/launch of OrthoPure XM	2015/16
HCTP pathway/OrthoPure HM/HT US launch	2016
dCELL human heart valve launch in Europe	2017

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Edison profile page

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 £325m

Our DCF valuation is £325m or 43p 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 £175m, the orthopaedics division at £95m and £35m 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 growth in H115

TRX reported sales of £0.3m in the six-month period ending July 2015, in line with progress in obtaining US reimbursement coverage for DermaPure. TRX signed two stocking distributor agreements for DermaPure worth a minimum of $0.8m over 12 months. Operating expenses rose to £4.4m in H115 from £3.8m as TRX expanded its US direct sales force. TRX raised £19m net in January, issuing 105.3m shares, to develop and launch human tissue OrthoPure in the US and porcine OrthoPure in CE mark regions and to expand the US direct sales force. Our FY16 group sales estimate is £0.4m, rising to £75m in FY21. The main growth drivers are wound care (estimated FY21 net sales of £33.9m) and orthopaedics (estimated net sales of £33.3m in FY21). We forecast FY18 cardiac sales of £0.1m, reaching £6.4m in FY21. We estimate FY16 group operating costs of £10.4m, rising to £14.3m in FY17 as TRX invests in the development of OrthoPure, SurgiPure and dCELL valves. Consequently, our estimated year-end 2016 net cash is £19.5m, 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 are a limited amount of data published by TRX to demonstrate how well its products perform in humans.

dCELL: A growth platform for tissue regeneration

The investment story is built on the versatility of the dCELL technology, which TRX is using to develop regenerative medical devices across three high-growth markets. TRX is focusing on wound care, sports medicine and cardiac applications. The adoption of biological, as opposed to standard treatments, is driven by the need for earlier intervention and cost savings and for longer-term healing solutions. Our combined sales estimates are £42m of net sales by 2020, which we forecast will take TRX to profitability. There is a range of potential catalysts on the horizon that could lead towards delivering the estimated commercial potential. TRX is operating in highly innovative areas where, if commercial traction is achieved, it could make these products attractive to larger medical devices companies needing to enhance their portfolios. The dCELL process enables the removal of cells from soft tissue so that they can be implanted for a wide range of healthcare applications. The dCELL process removes DNA and cells in a manner that minimises rejection and with a low incidence of side effects compared to established brands. The process minimises the use of detergents and chemicals, allowing the tissue matrix to be repopulated swiftly with the patient's own cells. A significant commercial advantage is that dCELL tissue can be stored and transported cost effectively. Having started with human tissue implants, TRX will launch porcine tissue implants, which will pave the way for much greater commercial scale, easier sourcing and lower-cost processing.

Wound care prospects: Extending channels and product lines

TRX Wound Care, the US subsidiary established in 2012, is the most commercially advanced of the three divisions. It launched its first product, DermaPure HD, an acellular human tissue skin substitute for hard-to-heal chronic wounds, including diabetic foot ulcers (DFUs), venous leg ulcers (VLUs) and acute wounds in the US and Europe in June 2014. TRX has reported wound care revenues of just £0.1m to date (in the year to January 2015), although launch has been a two-step process and TRX initially had no reimbursement coverage in place. The company first launched into inpatient wound care facilities that treat only 20% of wounds, where dermal substitutes are not reimbursed so clinics are more cost conscious. Over the past 12 months, the company has obtained Medicare coverage for 65% of patients in US outpatient centres (c 37 million patients), which treat over 80% of wounds. This enables TRX to execute Phase II of its strategy, to reach out to patients treated in outpatient facilities. Current distribution channels serve c 12% or a total of 1.5 million patients in the largest Medicare jurisdictions, so the company is engaged in expanding its direct sales force from the current sales organisation of 15+, recruiting new distributors to reach out to c 11 million additional patients in these large jurisdictions initially. Subsequently, TRX is aiming to obtain 100% Medicare coverage and to move to the next largest territories. It is building a family of dermal substitutes that access the wider high-growth markets and could compete with established wound care and surgical tissue regeneration companies by extending its commercial reach.

Exhibit 1: 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

Wound care and the rise of skin and dermal substitutes

Up to 2.5 million patients worldwide pa suffer from hard-to-heal ulcers of the lower limbs such as DFU and VLU, caused by vascular insufficiency associated with diseases such as diabetes and obesity, with c 1.5m new cases pa in the US.[1] The standard treatment for advanced wounds such as DFU is sharp debridement followed usually by negative pressure wound therapy, which is successful in around 40% of cases. However, around 60% of wounds are more persistent and failure to heal can lead to serious infection and even limb amputation and death. The cost of chronic wound treatment, chiefly associated with nursing resources, hospital admittance and complications such as infection in the US, is c $25bn pa. Harder-to-heal wounds are being treated increasingly using skin and dermal substitute products – particularly in the US, primarily in chronic wound care clinics and increasingly for surgical procedures to heal acute wounds and burns. The largest segment of the US advanced wound care market is biological skin and dermal substitutes (2014 sales were c $525m), which is estimated to grow at 9% CAGR from 2014-19[2] driven by ageing population growth and with increasing emphasis on earlier intervention and cost reduction. The ex-US biological wound care market is much more embryonic – valued at $30m.

Exhibit 2: 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

Acellular dermal matrices (ADM) from human tissue such as DermaPure HD are regarded as minimally processed, classified by the FDA as banked human tissue and recovered, processed, stored and distributed in accordance with the standards of the American Association of Tissue Banks (AATB) and can be commercialised pending HCT/P 361clearance of the tissue bank with no regulatory burden directly on TRX. Porcine dermis xenografts are classed as medical devices subject to regulatory FDA approval via 510k clearance in the US based on substantial equivalence to a predicate device. The wound care subsidiary anticipates the outcome of its 510k submission for SurgiPure XD, a thicker graft, in Q116. In regions outside the US, TRX might in future develop a porcine version of DermaPure, subject to forming new regional partnerships. NHS Blood & Transplant (NHSBT) retains the commercial rights to DermaPure HD in the UK.

DermaPure potential is backed by strong clinical data

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.

Exhibit 3: 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 6 weeks	49.5%
Mean reduction in wound size at 6 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

A UK study of DermaPure HD in 20 DFU/VLU patients was conducted in collaboration with NHSBT on patients with chronic wounds. DermaPure was applied to the wounds, which were dressed with

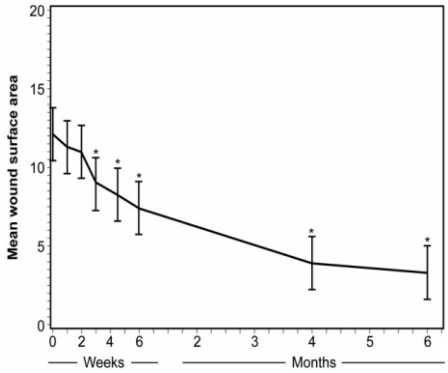
[1] BIOMedGPS/SmartTRAK.

[2] BIOMedGPS.

negative pressure wound therapy (NPWT) for one week. The study demonstrated that DermaPure met the primary outcome measure despite the treatment-resistant nature of the wounds.

Exhibit 4 demonstrates the progress in wound healing with DermaPure vs comparators over time. Although the study was not controlled, separate studies of standard treatment with NPWT show that it heals up to 40% of venous ulcers and that around 25-50% of ulcers persist for more than one year, reinforcing the rationale for DermaPure in the harder-to-heal population. NPWT is a more labour-intensive process and requires a minimum of three bandage changes per week.

Exhibit 4: Plot of mean changes in wound surface area from baseline



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

DermaPure was also shown to promote enhanced 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. Headline observations from weekly follow-up (from one to six weeks) resulted in the observations shown in Exhibit 5.

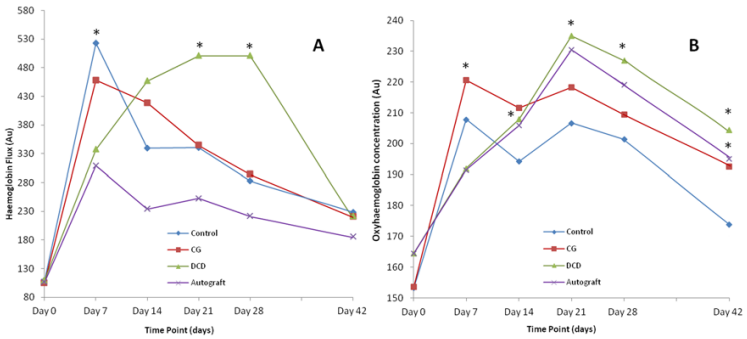
Exhibit 5: Headline observations from DermaPure acute wounds study

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

Furthermore, the measurement of haemoglobin flux and oxyhaemoglobin concentration, processes essential in acute wound healing, illustrated in Exhibit 6, showed that DermaPure outperformed the controls in the study.

Exhibit 6: Progress in the rate of haemoglobin flux and oxyhaemoglobin concentration in acute study



Source: Greaves et al, Acute Cutaneous Wounds Treated with Human Decellularised Dermis Show Enhanced Angiogenesis during Healing Note: Control = no intervention, CG = Integra Matrix Wound Dressing, DCD = DermaPure.

A US Phase IV clinical validation study of hard-to-heal chronic wounds was started in August 2014 to support marketing and reimbursement strategy and provide data for line extensions. The primary outcome measure of the ongoing multicentre study is incidence of wound healing.

Exhibit 7: Use of a novel regenerative tissue matrix to heal wounds

RESULTS - OUTCOME MEASURES					
Week	3	5	7	9	11
Average Surface Area Reduction From Baseline	67%	78%	90%	93%	100%
Time to Complete Healing / Closure	Average time to heal was 6.5 weeks.				
Number of Applications	Average number of applications = 1.1				

Source: Tissue Regenix

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. The crossover stage of the study with standard of care (debridement, dressing and offloading) is ongoing, with final results anticipated in Q415.

Dermal substitutes: Significant growth driver in the wound care landscape

The wound care biologic skin substitutes market is a small but fast-growing segment of the wound care treatment landscape. Such products offer efficacious alternatives to standard of care and can generate significant cost savings.

Exhibit 8: Cross-section of leading biological skin replacement grafts

Brand/indications	Product description	Data from IFUs
DermaPure HD/Tissue Regenix/chronic and acute wounds	Acellular human tissue derived dermal substitute. Decellularised via dCELL process. Unit sizes 2x3cm, 3x4cm, 4x6cm.	In six-month UK study, 60% of patients with hard-to-heal chronic wounds were completely healed. The primary outcome measure, a reduction in wound surface area, was met in 100% of participants. HCT/P 361 cleared.
Dermagraft/Organogenesis /DFU	Human fibroblast (neonatal foreskin) derived. Cryopreserved, stored continuously at -75°C ± 10°C. Single unit size 5x7.5cm.	Dermagraft plus SOC resulted in significantly more patients with DFUs >6 weeks' duration achieving complete wound closure by 12 weeks vs conventional therapy (30% vs 18%, p=0.023). FDA -cleared via PMA.
Apligraf/Organogenesis/ DFU/VLU	Bilayered living skin substitute derived from human neonatal foreskin and bovine tissue. Room temperature storage. Single unit size circular disc c 75mm diameter.	Apligraf plus compression therapy vs SOC more effective in achieving complete wound closure by week 24 (57% vs 40%) than SOC. In ulcers >1 year's duration, more than twice as effective in achieving complete wound closure by week 24 (47% vs 19%, p=0.002). FDA-cleared via PMA.
EpiFix/MiMedx/chronic and acute wounds	Dehydrated human amnion/chorion membrane allograft. PURION process separates, cleans and dehydrates the tissue. Unit sizes 1.5cm^2-49cm^2.	In a 25 pt study of EpiFix (n=13) vs SOC (n = 12), after four and six weeks of treatment, the overall healing rate with application of EpiFix was 77% and 92% vs SOC 0% and 8% respectively. HCT/P 361 cleared.
Integra/Bilayer Wound Matrix/chronic and acute wounds	A porous matrix of cross-linked bovine tendon collagen and glycosaminoglycan and a semi-permeable silicone layer. +10°C to +30°C. Nine unit sizes from 5x5cm to 20x25cm.	May be used in conjunction with negative pressure wound therapy. 510k cleared in 2002. 10 patients, with an average 11-year history of diabetes mellitus. The greatest mean wound reduction was c 95% in week 12. Seven of 10 patients achieved complete wound closure by week 12.
Grafix/Osiris/chronic and acute wounds	Cryopreserved placental membrane acellular matrix. Stored frozen at -75°C to -85°C. Range of unit sizes.	62% of patients receiving Grafix had complete wound closure vs only 21% ($p < 0.0001$) receiving conventional treatment. HCT/P 361 cleared.

Source: Edison Investment Research, company websites

Tissue Regenix and the wound care competition

Four companies dominate more than 80% of the US biological wound care market. The market-leading chronic wound care products are Dermagraft and Apligraf, which jointly hold around 34% market share in 2014. EpiFix (MiMedx, Georgia), indicated for chronic and acute wound care indications including burns and trauma, held 17.8% in 2014 (FY14 $118m net sales across wound care). Osiris and Integra hold between them a further 30% of the US market and the remainder is fragmented. DermaPure HD is well positioned in this competitive market by virtue of its efficacy in hard-to-heal chronic wounds and those of larger surface area. A lower number of applications of DermaPure per patient are needed in chronic wound healing, only 1.1 compared to four for EpiFix, making it more convenient, quicker and more cost-effective to use. The average price per closure

with EpiFix is $2,440,[3] while DermaPure is priced at around $1,540 per procedure based on 1.1 applications at an ASP of $1,400. It is available in a range of graft sizes with additional sizes due to be launched, meeting the needs of healthcare providers and minimising wastage compared to Dermagraft and Apligraf (single large-unit sizes). Additionally, it is easier and more 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. In acute wounds, study results indicate DermaPure's equivalence over reference treatment Integra, so TRX will compete on the basis of greater ease of use and absence of immunogenic substances such as silicon and glycosaminoglycan in dCELL-based DermaPure and the relative difficulty of use of Integra, which involves sequential procedures.

TRX is set to extend its US commercial reach

While TRX reported just £0.1m of DermaPure sales in 2014 (seven months of trading), it has made significant progress in laying the ground to execute its staged commercial strategy since launch in the $865m US wound care market, obtaining Medicare 65% reimbursement coverage over the next 12 months. The company is focusing on building channels in the key regions to cover 1,000+ outpatient centres across the US, starting with CGS and Novitas jurisdictions, the largest Medicare administrative agencies. TRX reports that its current sales force and distributors reach only around 1.5 million patients in these jurisdictions. It is taking an opportunistic approach to penetrating the remaining states under these key jurisdictions over the next 12-24 months by expanding the direct sales force and seeks to appoint additional distributors.

Exhibit 9: Wound care commercial status

Tissue Regenix'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

Exhibit 10: 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 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

In the initial phases, we are conservative with penetration estimates <1% in the US given that TRX is still building distribution channels.

Acute wound and burns treatment is a larger market for DermaPure

TRX is extending the applications of DermaPure into acute wound care management, initially targeting severe burns and abrasions in the US with the human tissue product. In acute wound care the commercial potential for dermal substitutes is greater than in chronic wounds because the average number of grafts used per patient is higher. A minimum of two applications is needed to cover larger wound surface areas and we estimate an average graft cost per procedure of $4,200.

[3] Source: MiMedx.

The use of skin autografts is the gold standard for restoration of epidermal function of the skin in burn patients. The limitations of autograft include risk of additional scarring and wounds and inadequate available skin. Integra bilayer wound matrix is a temporary graft, approved for the treatment of acute burns and for the management of surgical and trauma wounds. TRX initially targets 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.

Line extensions including surgical matrices are a future growth driver

SurgiPure XD is being targeted initially for hernia repair in 2016. Growth drivers of the surgical matrices market (US sales of $360m in Q115) include the need to evaluate new cost-effective biological options to cut down incidences of reintervention and infection using first-generation 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 paves the way for SurgiPure XD including Strattice Tissue Matrix (KCI/Acelity), SurgiMend (TEI Biosciences). We have been initially conservative and estimate that the market share of SurgiPure XD would be less than 0.5% in the initial launch years as there are no published data on the product. 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.[4] In future, TRX will 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. We await confirmation of the timelines before adding in sales estimates for SurgiPure HD.

Sports medicine: A $1.6bn market opportunity

TRX is developing acellular tissue scaffolds derived from human and animal tissue to repair tendon and meniscus injuries, two of the most common sports injuries. The emphasis is increasingly on earlier intervention and cost reduction by preventing longer-term risks such as osteoarthritis. The shortcomings of existing treatment methods include a high degree of invasiveness and very poor long-term outcomes. The family of dCELL OrthoPure grafts is targeted at high-growth global markets where there are few effective alternatives.

Exhibit 11: Orthopaedics/Sports Medicine pipeline

Product	Development route	Launch timeline
OrthoPure XM – porcine meniscus	CE mark	2016
OrthoPure XT – porcine tendon	CE mark	2017
OrthoPure HM – human meniscus	US – human tissue	2016
OrthoPure HT – human tendon	US – human tissue	2016
OrthoPure XT/XM – porcine tendon/meniscus	US – PMA	Estimated 2020

Source: Company reports

The market for orthopaedic soft tissue repair products consists of surgical solutions for damage to the knee (ligaments, cartilage and meniscus) and to the shoulder (rotator cuff). In 2011 this market was valued at c $1.4bn in the US and $240m in Europe and forecast to grow at 7% pa to 2016 (MRG), not accounting for the additional costs of pain relief medication, physiotherapy or hospital stays. Market expansion is being driven by growth in the population aged over 50 years old, rising obesity rates and rising participation in sports, leading to sport-related injuries. Overall, the market is moving in favour of soft tissue biological allografts, in search of alternatives to the gold-standard autografts of bone and soft tissue. By contrast, pricing of orthopaedic metal implants is falling and these are increasingly becoming commodity products. In turn, biologics are becoming increasingly attractive acquisition targets for medical device companies seeing price erosion in metal implants.

[4] Company guidance.

CE mark study of OrthoPure started in Q115, launch on horizon

TRX is initially focusing on the porcine meniscus scaffold, OrthoPure XM for the European market, and a 60-patient clinical trial in the EU is underway. Success criteria include changes in pain and functional scores measured over 24 months and the company expects to apply for a European CE mark with six-month data in H116. It also plans to launch the human meniscus/tendon products OrthoPure HM/HT in the US via the HCTP pathway in late 2016, supported by the European data for submission. Case studies indicate that porcine tissue has the biomechanical and immunogenic properties required of orthopaedic tissue scaffolds. Production and sourcing processes for the human meniscus scaffold OrthoPure HM are being negotiated with the human tissue bank Community Tissue Services (CTS) in the US. Launch of OrthoPure HM in the US is targeted for late-2016. Further out, the launch of OrthoPure XT in Europe for ACL repair is planned in 2017. Subject to funding, TRX plans to initiate US studies for OrthoPure XT/XM for estimated launch in 2020. Human tissue implants can be commercialised following the human tissue HCTP (human cells, tissues, and cellular and tissue-based products) pathway as for skin replacement grafts, although animal tissue implants are subject to full FDA clearance, a much longer and more costly process.

Meniscal surgery is by far the most common orthopaedic operation, with over 600,000 operations in Europe and nearly one million in the US in 2014 (MRG estimates). However, current surgical options are limited, with only 10-20% of meniscal tears being suitable for repair and the remaining 80% requiring removal of part or whole meniscus. Partial/full meniscectomy is less than ideal as it can lead to early knee dysfunction, osteoarthritis (OA) and severe knee pain. Any meniscal repair solution must be able to restore the load-bearing and shock-absorbing functions of the knee, reduce pain and ultimately reduce the long-term need for knee replacement. TRX's OrthoPure XM will target the irreparable meniscus tear segment where there is currently significant unmet medical need (c 600,000 patients pa worldwide). The outcome of a single study by YHEC[5] showed that partial replacement of meniscus using OrthoPure was cost effective compared to a partial meniscectomy and indicated a saving of £590.33, calculating the total procedure costs and a higher-quality adjusted life year (QALY) score of 17.08 vs 16.59. Longer-term outcomes remain to be seen and, potentially, additional cost efficacy studies would be needed, with the cost-saving strategy based on the goals of early intervention.

Exhibit 12: Available treatments for meniscus surgery

Procedure	Market share	Comments
Surgical meniscal repair	43% of repairs in US, 8/% in EU	<20% of tears are amenable to surgical repair requiring sutures, resorbable tacks and more expensive 'hybrid' devices.
Full/partial meniscectomy	56% in US, 92% in EU	Risk of osteoarthritis and need for partial or total knee reconstruction later on.
Allograft (following full meniscectomy)	0.2% (US only)	From human cadavers, high cost, requires size matching, limited supply, risk of infection/rejection.

Source: MRG data, company websites

The approaches being developed for meniscal repair can be categorised as solid, non-resorbable implants that permanently replace part or whole meniscus and porous, resorbable scaffolds that support new tissue regeneration and ingrowth. The wave of new meniscal implants appears safe, but high-quality comparative clinical data, particularly showing superiority to partial meniscectomy, is generally lacking creating a high unmet need for alternative methods.

ACL rupture is an increasingly common sports injury and there were an estimated 230,000 European and 500,000 US knee ligament reconstructions in 2014 (c 90% involving the ACL), with growth forecast at 5% pa (MRG estimates). The key market drivers are related to an ageing but active population, as well as a rise in sporting injuries in the younger age groups. According to MRG, the US/EU market for ACL reconstruction was worth almost $750m in 2014. It is growing at

[5] York Health Economics Consortium.

7% pa, mainly due to the extensive use of costly fixation devices (the biggest players are Smith & Nephew, DePuy Mitek and Arthrex). Eighty percent of ACL injuries are surgically treated and, currently, almost all ACL reconstruction procedures use one of two graft types: autograft (usually from the patient's patella or hamstring tendon) or allograft (tendons from cadavers). Both have significant shortcomings. TRX plans to initiate CE mark studies of OrthoPure XT during 2016.

Exhibit 13: Available treatments for ACL repair

Procedure	Approx %	Description
Autograft	74% (c 90% in Europe)	Patient's own tendons used; no associated risk of disease transmission or graft rejection. The gold standard in terms of strength and bone incorporation is the "bone-tendon-bone" (BTB) graft where the patella tendon plus adjacent bone are removed. Alternatively, soft tissue autografts use hamstring or quadriceps tendons as graft material. Negatives: removal of patient's own donor tissue causes pain/morbidity at the donor site. Requires increased surgical/recovery time (and cost).
Allograft	25% (c 9% in Europe)	More common in the US and in multi-ligament injuries. Donated and sterilised cadaveric human tissue from commercial tissue banks: typical cost is $2,500-3,000 for a ready-to-implant ACL allograft. Negatives: can carry risks of infection/rejection. Sterilisation can weaken tissue. EU tissue banks have limited supplies.
Artificial ligaments	<1% (ex-US only)	Europe only after high rates of failure and complications led to banning of synthetics in the US. First-generation materials were non-biodegradable synthetic fibres (silver, carbon, polyethylene, Gore-Tex or Dacron). Second-generation polymers (eg Type I collagen, silk fibres), often biodegradable, may be superior. Negatives: may not be structurally and mechanically strong enough; risks of foreign body reactions/infections.
Ligament scaffolds	0%	Xenograft and human bioscaffolds in development.

Source: Company websites

OrthoPure is a very promising alternative and the unmet need is high

The immediate prospects are for launch of OrthoPure XM and XT in Europe, anticipated in 2016/17 and for the human tissue OrthoPure HM and HT in the US. The company anticipates keen reactions from surgeons who see great potential in a room temperature, off-the-shelf biological allograft. However, as with any new technology, uptake is likely to be gradual in the early stages of commercialisation and will depend on the outcome of the CE Mark studies. TRX will target early-stage distributors to launch OrthoPure and intends to initially approach five or six European regions more amenable to new technologies. In the US plans are underway to recruit a US-based commercial head and TRX is negotiating a new partnership with CTS as it has done for DermaPure to commercialise OrthoPure HT/HM. Ligament and tendon repair using allografts is already more advanced than meniscus in the US, valued at c $330m,[6] but both have high growth potential. Progress would depend on data and from the experience of porcine implants in CE mark regions.

Exhibit 14: Commercial estimates for OrthoPure

Product	Addressable population	Forecasts	Next news
OrthoPure XM – porcine meniscus	320k failed meniscus procedures pa across Europe and RoW.	ASP of $2,500 peak penetration of 5.5%, net sales of $66m.	CE mark grant and launch in 2016.
OrthoPure XT – porcine tendon	520k ligament repairs pa in Europe and RoW, 96% via autografts.	ASP of $1,800, peak penetration of 6%, net sales of $111m.	CE mark grant and launch in 2017.
OrthoPure HM/HT – human meniscus/human tendon	Number of procedures as per CE mark territories, limited by availability of human tissue, c 20,000 pa per tissue type.	ASP of $2,500. Peak penetration of 20% meniscus/25% tendon, Net sales of $12.4m/$15.5m respectively.	US launch in 2016 via HCTP pathway.
OrthoPure XT/XM – porcine tendon/meniscus	520k ligament repair procedures pa/320k failed meniscus procedures pa in US	ASP of $2,500. Peak penetration of 7%, net sales of $109m/ ASP of $2,500. Peak penetration of 7%, net sales of $70m	Confirmation of timeline and initiation of US study.

Source: Edison Investment Research, company data

We estimate that OrthoPure XT/XM would be launched in the US in 2020 via investigational device exemption (IDE) studies, which typically take >24 months subject to funding (at an estimated total cost of <$20m). We include the cost of the studies in our forecasts. Our estimated penetration rates in human tissue are higher than for porcine products in CE mark regions because the US is a more developed sports medicine market than RoW and CTS is one of the largest US tissue banks. Our estimated market shares in porcine tissue are based on the approximate share of smaller peers in the sports medicine space. The ASPs used are company guidance.

[6] Company estimate.

Heart valves ready for launch

TRX is commercialising decellularised human donor heart valves, which were developed by Pontificia Universidade Catolica do Parana (PUCPR) Brazil using dCELL technology; PUCPR has implanted over 1,000 patients with dCELL valves resulting in a significant body of clinical evidence. The rationale for dCELL heart valve implants is the high efficacy rate and ability to overcome many of the major shortcomings of standard heart valve replacements. Heart valve replacement is indicated for patients with valvular heart disease. The most prevalent form is aortic stenosis (AS)[7] and this forms around 75% of all heart valve replacements, c 300k procedures worldwide pa. It is a disease primarily of older adults (2-7% of the population >65 years). Congenital aortic valve disease occurs in 0.3% of births. TRX is planning commercial launch of human dCELL heart valves during 2017 and aims to subsequently develop and launch a xenogenic version of the graft under the CE mark process. In future, TRX plans to develop a porcine dCELL valve for the US.

Competitor landscape, dCELL valves overcome shortcomings of standard valves

The worldwide tissue heart valve market is dominated by Edwards Lifesciences. It holds a c 48% share in the US and 54% in Europe with its bioprosthetic Perimount bovine tissue valve. Such valves perform well for up to 15 years, making them particularly suitable for older patients. Longer-term data suggest that such bioprosthetic valves require replacement every 10 to 15 years due to calcification, inflammation and tearing.[8] The remainder of the US market is dominated by Medtronic (26%), St Jude Medical (17%) and Sorin (5%). The limitations of mechanical heart valves include the requirement for use of lifelong coagulation medicine. The newer generation of implantable 'tissue engineered' grafts accounts for c 4% of the US heart valve market. CryoLife is a leader in human tissue valves (35k sold since launch).

Exhibit 15: Features of cardiac valve homografts/allografts

Company/product	Indication	Features	Market size
Tissue Regenix/dCELL valve	Aortic/pulmonary – paediatric and adult use. Replacement of diseased, damaged or malformed/malfunctioning native or prosthetic valves.	No viable cells. Extracellular matrix is retained. Clinically proven reduction in immunogenic response as primary cause of valve degeneration.	Implanted in over 1,400 patients through PUCPR chiefly in children <12 years. Expansion into Europe and Asia Pacific. Regulatory pathway human tissue via approved tissue bank/porcine tissue valves cleared via CE mark or PMA.
CryoLife/CryoValve – aortic valve	Replacement of diseased, damaged, malformed or malfunctioning native or prosthetic aortic valves.	Retains viable cells, recommended by the current STS Clinical Practice Guidelines for extensive active endocarditis.	Limited by the number of heart valve donors pa. Approved via humanitarian use designation (HUD) in 2009.
CryoLife/SynerGraft – pulmonary valve	Pulmonary valve.	Decellularised using SynerGraft process to remove allogeneic donor cells.	FDA cleared in 2008 via 510k decision pending on reclassification.

Source: Edison Investment Research, company websites

Clinical experience with dCELL valves eases the route to commercialisation

In total, dCELL valves have been implanted in more than 1,400 patients. TRX's partner PUCPR has conducted comparative studies of dCELL valves using parameters in compliance with clinical practice guidelines.[9] The first short and midterm aortic valve results on 41 patients implanted with dCELL human aortic valves from 2005-10 were published by Professor Affonso da Costa in 2010. Key findings of the aortic study included low and stable cardiac gradients over the study period indicating freedom from dysfunction. Scans showed the absence of calcification, a particular problem in this young patient cohort.

[7] EACTS guidelines, European Heart Journal.

[8] Naso F et al: First quantification of alpha-Gal epitope in current glutaraldehyde-fixed heart valve bioprostheses, Xenotransplantation 2013.

[9] European Society of Cardiology, European Heart Journal 2015.

Exhibit 16: Right ventricular outflow (RVOT) gradients

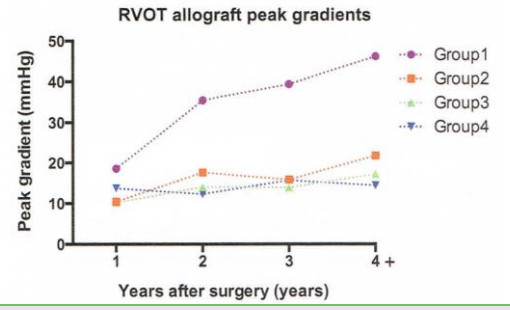
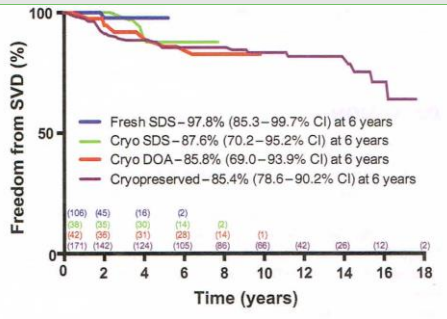


Exhibit 17: Freedom from structural valve dysfunction



Source: FDA da Costa et al. European Journal of Cardio-Thoracic Surgery. Key: Group 1 cryopreserved grafts, Group 2 Cryopreserved grafts, decellularised with deoxicholic acid, Group 3 Cryopreserved valves decellularised with SDS, Group 4 fresh dCELL valves.

An update on 99 patients at up to 10 years of follow up, showed 94% freedom from reoperation and confirmed these findings, and was presented in May at the Heart Valve Society inaugural scientific meeting in Monaco. The data form the subject of peer-reviewed journals that should assist in obtaining future reimbursement coverage.

A long-term study by the same centre in 414 patients who received pulmonary homografts during a Ross procedure was conducted in 1995-2013. The dCELL treated valves (group 4) showed virtually no increase in gradients over time, in contrast to the standard cryopreserved grafts (group1). An increase in gradients can be considered as a first indicator for longer-term valve failure. Consequently freedom from structural valve deterioration was also significantly lower (97.8% vs 85.4%) in the dCELL group compared to cryopreserved grafts. The study demonstrated excellent long-term survival in line with the general population and a low incidence of reoperation. The mean patient age was 30.8±13.1 years. Heart valve allograft degeneration mechanisms are multifactorial, however immunogenic reaction is considered to be a predominant factor. In this respect it was demonstrated that dCELL was effective in reducing or even ruling out human humoral immune response against viable material present in donor cells.

A differentiated tissue heart valve offers commercial potential

The dCELL human heart valve is a promising treatment for heart valve disease sufferers, initially ex-US. However, the supply of human donor pulmonary and aortic valves is limited to only 3,700 pa in the regions, or around 7% of RoW total heart valve replacement procedures.[10] Initially, TRX will launch into a select group of European and RoW geographies.

Exhibit 18: Market assumptions dCELL heart valves

Product	Number of procedures, pricing and peak sales forecast	Next news
dCELL human valves – Europe/Asia Pacific	c 2,200 pulmonary and 1,500 aortic valve donors pa at an ASP $7,000[11] in Europe in line with cryopreserved allografts. Peak net sales $13.7m aortic/ $4.9m pulmonary, peak penetration 30% for each valve type in line with potential if TRX attains a similar market share as CryoLife.	Data update and paediatric data in 2016. Authority approval and launch in 2017. Human tissue implants, no regulatory studies required.
dCELL porcine valves – CE mark regions	100k procedures pa, ASP $7,000. Estimated peak penetration 5%, total net sales of $39m.	Confirmation of strategy. Potential CE mark and launch in 2020.
dCELL porcine valves – US via IDE	100k procedures pa ASP $9,000. Estimated peak penetration 6%, total net sales of $76m.	Confirmation of US strategy. Estimated launch 2021, IDE cost c $20m.

Source: Edison Investment Research

The dCELL valves could be most suited to emerging regions with a high incidence of heart valve disease in paediatric populations, given the success of bovine pericardial valves in treating older populations. TRX is negotiating new tissue bank partnerships and seeks to appoint distributors initially. TRX has not yet confirmed its US cardiac strategy, although the most likely option in our

[10] Source AATB

[11] http://content.onlinejacc.org/article.aspx?articleid=1389318.

view is an approach with the porcine version subject to completing the longer development process via an investigational device exemption (IDE), as there would be limited commercial potential with a human tissue valve. Potential would depend on uptake in CE mark regions. The ASP in the US is likely to be at least 30% higher than in CE mark regions in line with peer group pricing. We include the $20m cost of obtaining the IDE in our forecasts.

Sensitivities

Key sensitivities include execution of the wound care commercial strategy and the rate of clinical progress in wound care and orthopaedics. Commercialisation of the wound care products is dependent on raising the visibility of DermaPure among KOLs, which are typically conservative in adopting new technologies. While existing study data demonstrate excellent results, larger studies could be needed to differentiate the products from the range of skin substitutes available. The orthopaedics division is at an earlier stage of development and although its products potentially meet a significant innovation gap, there are limited published clinical data to substantiate them. US development of porcine orthopaedic products would require additional potentially dilutive funding. The cardiac division has a proven technology with the broadest clinical experience, although the process of market access and commercialisation is costly compared to the market size for human heart valves. Each division is subject to additional funding to support ongoing studies and/or to grow sales forces that could prove dilutive to current shareholders.

Valuation

Our sum-of-the-parts DCF valuation of TRX is £325m or 43p per share, not including the potential dilution if TRX raises an additional £15m needed to conduct PMA studies for OrthoPure XT/XM. We use a WACC of 12.5% and value net operating cash flows to 2029, risk-adjusted according to development stage, using a terminal value of 2%. We value the three divisions as discrete units owing to the varying growth trajectories and estimated profitability. The Wound Care and Orthopaedics divisions represent the largest proportion of our valuation.

Exhibit 19: Sum-of-the-parts valuation

	Peak net sales ($m)	Operating margin	£m	p
Wound Care Inc	281.9	25%	175.4	23.1
Orthopaedic	383.8	33%	95.0	12.5
Cardiac	133.0	24%	35.0	4.6
Unallocated costs			(4.0)	(0.6)
Net cash July 2015			24.9	3.3
SOTP			**325.0**	**42.8**

Source: Edison Investment Research

We adjust all developing products, using standard medtech probabilities of success, as shown in Exhibit 20, and assume a higher success probability for human tissue due to lower regulatory risk.

Exhibit 20: 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 21 illustrates our forecast divisional and group sales and profitability from 2016-21. We estimate that TRX will become profitable in 2020, on this basis trending towards a 20% group operating margin in 2021.

Exhibit 21: Estimated divisional revenue and profitability

£m	2016	2017	2018	2019	2020	2021
Wound Care - revenue	0.44	1.55	4.71	10.75	19.32	33.87
growth		351%	303%	228%	180%	175%
Wound Care - operating profit	(4.52)	(5.31)	(4.29)	(2.15)	0.77	5.76
Orthopaedics - revenue	0.00	1.68	6.37	12.76	19.94	33.31
growth		N/A	379%	200%	156%	167%
Orthopaedics - operating profit	(3.90)	(4.61)	(5.73)	(1.77)	2.73	8.81
Cardiac - revenue	0.00	0.00	0.12	1.17	3.06	6.42
growth		N/A	N/A	1,000%	262%	210%
Cardiac - operating profit	(1.62)	(1.87)	(2.43)	(3.75)	(2.27)	(1.10)
Group revenue	0.44	3.23	11.20	24.69	42.32	73.60
Growth		731%	346%	220%	171%	174%
Group operating profit	(10.04)	(11.79)	(12.45)	(7.67)	1.23	13.47
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 (£74m).There is a range of potential value drivers for TRX: in 2015 we anticipate that it will report data from the ongoing chronic wound care study. In 2016, events that would lead us to increase the probability of success for the individual products include 510k clearance of SurgiPure XD, OrthoPure XM CE mark grant and launch and US launch of OrthoPure HM/HT. Launch of the dCELL human heart valve is planned during 2017.

Financials

TRX reported £0.3m of H115 revenue vs zero in H114, progressing in line with expanded reimbursement coverage for DermaPure in the US. Opex rose to £4.4m vs £3.8m in H114 as the company invested in its US commercial infrastructure. End-July 2015 net cash stood at £24.9m following a £19m net equity raise in January. 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 £0.4m 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 £2.7m and R&D of £2.2m, rising to £6.6m in FY17 (SG&A of £3.5m and R&D £3.2m) 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 £8.1m 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. In FY17, TRX targets launch of OrthoPure products in CE mark regions; we estimate £1.7m of net revenue in launch year, rising to £12.8m in FY19. Our forecast expenses are £4.0m in FY16 rising to £6m in FY17 and to £10.7m in FY18 to cover clinical studies for OrthoPure in the US and Europe. The cardiac division is set to launch dCELL heart valves in FY18, with sales of £0.1m in launch year rising to £1.2m in FY19. Our estimated cardiac opex in launch year is £2.6m rising to £4.6m in FY19, adding £13m over the period to 2021 to cover the estimated cost of the IDE for porcine valves. Group gross margin will trend from 78% in FY16 fluctuating towards 80% in the longer term as more porcine tissue products are launched across all three divisions, owing to the lower cost of production of these products. We estimate that group revenue will increase from £0.4m in FY16 to £74m in FY21, reaching profitability on a margin of 3% in 2020, when we estimate 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 and to launch wound care products 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.

Exhibit 22: Financial summary

£000s	2014	2015	2016e	2017e	2018e
Years ending 31 January	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Net revenue	6	100	442	3,235	11,196
Cost of Sales	0	0	(97)	(745)	(2,501)
Gross Profit	6	100	345	2,490	8,696
Operating expenses	(6,459)	(8,318)	(10,384)	(14,280)	(21,144)
EBITDA	(6,453)	(8,218)	(9,900)	(11,512)	(12,248)
Operating Profit (normalised)	(6,577)	(8,369)	(10,040)	(11,790)	(12,448)
Exceptionals	0	0	0	0	0
Other	0	4	4	0	0
Operating Profit	(6,577)	(8,365)	(10,036)	(11,790)	(12,448)
Exceptionals	0	0	0	0	0
Net Interest	274	168	209	146	62
Profit Before Tax (norm)	(6,303)	(8,201)	(9,830)	(11,644)	(12,386)
Profit Before Tax (as reported)	(6,303)	(8,197)	(9,826)	(11,644)	(12,386)
Tax	710	620	685	582	619
Other	0	0	0	0	0
Profit After Tax (norm)	(5,593)	(7,581)	(9,145)	(11,062)	(11,766)
Profit After Tax (as reported)	(5,590)	(7,581)	(9,141)	(11,062)	(11,766)
Average Number of Shares Outstanding (m)	636	636	698	760	760
EPS - normalised (p)	(0.88)	(1.19)	(1.31)	(1.46)	(1.55)
EPS - reported	(0.88)	(1.19)	(1.31)	(1.46)	(1.55)
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	927	908	1,268
Intangible Assets	0	0	0	0	0
Tangible Assets	472	435	927	908	1,268
Investments	0	0	0	0	0
Current Assets	19,610	12,238	21,389	10,449	14,044
Stocks	0	34	101	368	1,028
Debtors	1,127	1,947	1,801	1,772	4,601
Cash & equivalents	18,483	10,257	19,486	8,309	8,415
Income taxes	0	0	0	0	0
Other current assets	0	0	0	0	0
Current Liabilities	(1,104)	(1,095)	(621)	(1,225)	(2,398)
Creditors	(1,104)	(1,095)	(621)	(1,225)	(2,398)
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	21,695	10,132	(2,086)
CASH FLOW					
Operating Cash Flow	(6,121)	(8,285)	(10,372)	(11,065)	(14,396)
Net Interest	274	168	209	146	62
Tax	474	0	1,095	0	0
Capex	(358)	(114)	(675)	(259)	(560)
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)	9,229	(11,177)	(14,894)
Opening net debt/(cash)	(24,206)	(18,483)	(10,257)	(19,486)	(8,309)
HP finance leases initiated	0	0	0	0	0
Other	0	0	(0)	0	0
Closing net debt/(cash)	(18,483)	(10,257)	(19,486)	(8,309)	6,585

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	27.8
Woodford Investment Management	15.5
Techtran Group	13.6
Baillie Gifford & Co	4.9
University of Leeds	4.5
Jupiter Asset Management	4.5
NFU Mutual	4.2

Companies named in this report

Bard/Davol, CyroLife, DePuy Mitek, Edwards Life Sciences, Integra, J&J/Ethicon, LifeCell/Acelity, MiMedx, Osiris, Smith & Nephew, St Jude, TEI Biosciences.

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