EDISON

Tissue Regenix

Cardiac division report

Keeping the beat - next-generation heart valves

Healthcare equipment & services

Tissue Regenix's (TRX) investment story is built on dCELL, a versatile regenerative medical technology and its potential applications across the subsectors: cardiac, wound care and orthopaedics. The cardiac division has a proven technology with the broadest clinical experience, with 10 years of clinical follow-up data recently presented. We maintain our sum-of-the-parts valuation at £338m.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
01/15	0.1	(8.2)	(1.2)	0.0	N/A	N/A
01/16	0.8	(10.0)	(1.4)	0.0	N/A	N/A
12/16e	2.4	(11.3)	(1.4)	0.0	N/A	N/A
12/17e	6.4	(11.6)	(1.5)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

First dCELL human heart valve licenced to JV

In January 2016 Tissue Regenix entered into a joint venture (JV) agreement with a German tissue bank. It has received a non-exclusive licence to its human dCELL heart valves and DermaPure. The JV provides ethical access to human tissue (supply is a limiting factor to commercialisation) and will pursue the regulatory submissions in Germany, potentially leading to a first product launch of dCELL heart valves in 2017. Tissue Regenix intends to replicate this business model to commercialise in other EU jurisdictions in the future.

10 years of clinical data follow-up

The dCELL human heart valves (CardioPure HV) in Brazil have reported 10 years of clinical data, with more than 1,500 patients treated. The data has demonstrated superior results over cryopreserved alternatives (with the Brazilian tissue bank having converted to use only the dCELL process). It has demonstrated reduced immunogenic reaction, calcification and promotion of repopulation by the body's own cells, potentially reducing the need for recurring surgeries.

Progression on multiple fronts

Recent announcements demonstrate progress in its other two divisions. This includes commercialisation in wound care (first group purchasing organisation contract in the US) and regulatory progress in orthopaedics (CE mark application for OrthoPure XT brought forward and promising US regulatory discussions).

Valuation: Sum-of-the-parts valuation of £338m

We recently revisited a number of our key valuation assumptions to reflect the clarity on launch timeframes, associated costs and updated revenue guidance. We maintain our DCF valuation at £338m or 44.4p per share. According to our model, the current price gives a free option on wound care, the most commercially advanced division, and does not reflect the full pipeline potential, which could ultimately be an acquisition target as a whole or by division.

15 September 2016

Price	**18.5p**
Market cap	**£141m**
	£/$1.3
Net cash (£m) at 31 January 2016	19.9
Shares in issue	760.1m
Free float	65%
Code	TRX
Primary exchange	AIM
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(1.3)	4.2	7.3
Rel (local)	1.8	(6.8)	(1.3)
52-week high/low	21.63p		13.25p

Business description

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

Next events

CE mark submission/grant/ launch of OrthoPure XT	End 2016/ early 2017
CE mark submission/grant/ launch of OrthoPure XM	2018
HCTP pathway/OrthoPure HM/HT US launch	Late 2017/ early 2018

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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 regenerating 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, following 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, comprising a US wound care subsidiary, orthopaedic and cardiac business divisions. Its UK office, production facility and laboratories are in Leeds, 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 £338m

We recently revisited a number of our key valuation assumptions to reflect the clarity on launch timeframes, associated costs and updated revenue guidance. We maintain our DCF valuation at £338m or 44.4p per share, subject to potential dilution from an estimated £15m funding requirement in 2018 to deliver on our forecast growth trajectory, via a hybrid distribution strategy and including development of OrthoPure XT and XM in the US. This dilution would be reduced, or not required, if the US approval were to be undertaken alongside a partner. We value the wound care business at £251m, the orthopaedics division at £77m and the cardiac division at £39m, based on risk-adjusted cash flows for each division depending on each stage of development; we add reported FY16 net cash of £19.9m. According to our model, the current price gives a free option on wound care, the most commercially advanced division. There are a number of near-term catalysts ahead, including the potential CE mark grant and launch of OrthoPure XT, which would lead us to increase the probability of success for these products.

Financials: Wound care sales growth in CY16

We forecast £40.7m in net sales by 2019e, which should take TRX to profitability. We expect a key driver of this to be from the wound care division as detailed in our January note on the wound care division. We estimate that group revenue will increase from £2.4m in 2016e (new financial year end) to £40.7m in 2019e. The main growth drivers for reaching our £40.7m 2019 group sales forecast are wound care (£27.4m), orthopaedics (£9.6m) and cardiac (£3.6m). Based on end-January 2016 net cash of £19.9m, TRX has a cash runway for the immediate pipeline (OrthoPure, SurgiPure and dCELL valves). 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, with the wound care division being the most advanced. TRX operates in competitive markets where sustained investment in development and marketing is required to maintain the profile of the products. Commercial success in the cardiac division depends on the success of the regulatory process, reimbursement and surgeon uptake. 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; the cardiac division is the subject of this report. The dCELL process creates a tissue scaffold that, once implanted, is repopulated with human cells during the healing process. The technology benefits from several features, which the company indicates 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 in a fridge.

Having launched a human tissue-derived wound care product (DermaPure) in 2014 (£0.8m net revenue to date), TRX is developing a versatile range of human and animal tissue-based devices in wound care, as well as sports medicine and cardiac devices. These are discussed in our initiation report of October 2015, our January 2016 report, which focused on the wound care division and our July 2016 report, focused on the orthopaedic division.

The heart of the matter

TRX is providing access to decellularised human pulmonary or aortic donor heart valves, CardioPure HV, which were developed by Pontificia Universidade Catolica do Parana (PUCPR) Brazil and spearheaded by Professor Francisco da Costa, using dCELL technology. The first patient was implanted with a human pulmonary valve c 10 years ago. To date, more than 1,500 patients in total have been implanted with dCELL heart valves – 1,400 human pulmonary valves and approximately 100 with human aortic valves – resulting in a significant body of clinical evidence.

The rationale for dCELL heart valve implants (CardioPure HV) is the high efficacy rate and ability to overcome many of the major shortcomings of standard heart valve replacements. Currently, available heart valve replacements are either mechanical, made from synthetic material or made from animal or human tissue. The major downside for mechanical valves is the need for life-long anti-coagulation medicines. For patients under 60 who undergo valve replacement surgery, it is likely that they will outlive their valve, and the potentially superior longevity prospects of a dCELL valve could be an attractive selling point. Tissue valves tend to need replacing every 10-15 years due to calcification mainly caused by immunogenic reaction, eg 52% of infants need to be reoperated on within five years (see article by Nelson et al, 2014). In addition, in younger patients, body growth might require a larger valve to be inserted. Other essential characteristics of an ideal heart valve replacement therapy include sufficient structural durability, absence of thrombogenicity, resistance to infections, lack of antigenicity, 'off the shelf availability', excellent haemodynamics, an

intrinsic regenerative capacity and potential to grow with the patient. CardioPure HV potentially offers:

- not requiring long-term anti-coagulation medicine;
- not requiring cryopreservation (freezing) offering better results;
- less immunogenic reaction (see article here) and valve calcification,
- Very low peak gradients;
- having the potential to integrate (repopulate) (see article here), reducing the need for reoperation;
- having a reduced risk of rejection and infection due to the potential of dCELL heart valve regeneration; and
- off-the shelf availability, although for human valves limited by donor availability (see below).

TRX is in a position to launch its human dCELL heart valves commercially now that it has built up clinical evidence, has the funding and established the route to market (JV). It plans to do this in 2017 via its recently established joint venture (GBM-V) and aims to subsequently develop and launch a xenogenic version of the graft under the CE mark process. In future, we expect TRX to develop a xenogenic dCELL valve for the US, although we wait confirmation of the details of this strategy.

Exhibit 1: Portfolio of cardiac applications

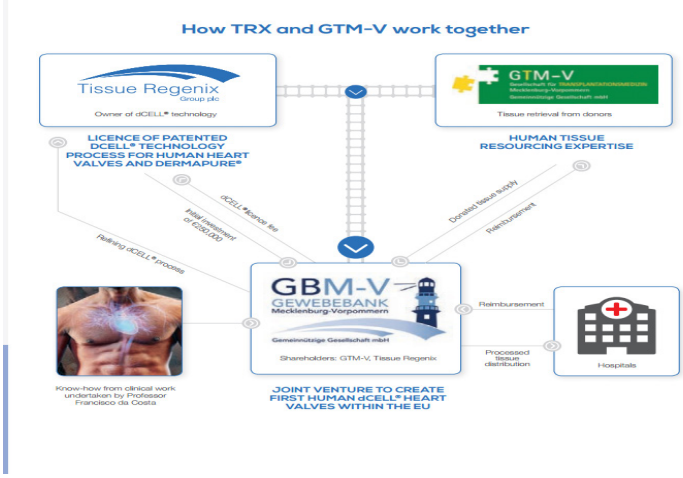
Product	Intended use	Description	Time to market
CardioPure HPV	Replacement of diseased, damaged, malformed or malfunctioning native or prosthetic pulmonary valves	Human pulmonary heart valve	EU launch expected H1 CY17 On the market in Brazil
CardioPure HAV	Replacement of diseased, damaged, malformed or malfunctioning native or prosthetic aortic valves	Human aortic valve	EU launch expected H1 CY17 On the market in Brazil

Source: Tissue Regenix

Commercialisation – joint venture (GBM-V)

In January 2016 Tissue TRX entered into a joint venture agreement with a German tissue donation organisation (GTM-V), based in Rostock, Germany, to form the first German, multi-tissue bank, GBM-V. TRX has granted a non-exclusive licence to the JV for human dCELL heart valves (first licence to be granted) and DermaPure. The joint venture will prepare the regulatory submission to the German authorities, with the first products planned to be launched in 2017, depending on regulatory approval. The partnership brings together the ability to procure donor tissue (a key limiting factor, as discussed below) and experience in managing the German regulatory approvals (GTM-V) and access to the patented dCELL process for heart valves and DermaPure. Tissue Regenix intends to replicate this business model in other jurisdictions in the future.

Exhibit 2: Joint venture overview



Source: Company presentation

Initially, TRX will launch into a select group of European and RoW geographies.

Exhibit 3: Cardiac division commercial estimates

Product	Number of procedures, pricing and peak sales forecast
dCELL human valves - Europe/Asia Pacific	Around 2,200 pulmonary and 1,500 aortic valve donors pa at an ASP $7,000[1] in Europe in line with cryopreserved allografts. Peak net sales $13.7m aortic/$4.9m pulmonary, peak penetration 30% for each type in line with potential if TRX attains a similar market share as CryoLife. Probability of success 100%, as already launched and trialled in over 1,500 patients.
dCELL porcine valves - CE mark regions	100k procedures pa, ASP $7,000. Estimated peak penetration 5%, total net sales of $39m. Probability of success 60%.
dCELL porcine valves - US via IDE	100k procedures pa, ASP $9,000. Estimated peak penetration 6%, total net sales of $76m. Probability of success 30%.

Source: Edison Investment Research

dCELL valves overcome shortcomings of standard valves

Heart valve replacement is indicated for patients with valvular heart disease, an important clinical problem worldwide. For an overview of the heart and valves please see here. The global market for heart valve replacement procedures is 225,000 a year according to TRX. The prevalence of heart valve disease is increasing in the Western world due to growing ageing populations and the consequent increase in degenerative valve disease, and in the developing world due to the inadequate treatment of rheumatic heart disease and increasing access to healthcare. As a result, the number of heart valve interventions is expected to increase to over 800,000 annual procedures worldwide by 2050.[2] The most prevalent valvular heart disease is aortic stenosis (AS).[3] This forms around 75% of all heart valve replacements (the remainder is comprised of mitral and pulmonary valve replacements). The prevalence of aortic valve disease increases with age, ranging from 2% of people over the age of 65, through to 4% percent over 85. Congenital aortic valve disease occurs in 0.3% of births.

The current options available for heart valve replacements include:

- Mechanical valves (prosthetic valves). These are made of immunologically inert material, with an unlimited life span. They are, however, prone to blood clot formation and therefore require life-long anti-coagulation medication.

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

[2] Biological heart valves, European Heart Journal (2015) 36, 325–332 doi:10.1093/eurheartj/ehu483.

[3] EACTS guidelines, European Heart Journal.

- Tissue valves (biological, bio-synthetic or bio-prosthetic valves), usually made from animal tissue (porcine or bovine). They do not need blood thinning medication but reoperations and replacement are typically required after 10-15 years due to calcification of the leaves, inflammation and tearing,[4] making them inappropriate for young patients. Young patients will typically require multiple operations as the body grows and a larger valve is necessary.
- Allograft valves, which are:
  - obtained from human donors and are usually cryo-preserved (eg CryoLife's CryoValve), although not in Brazil where Professor da Costa's superior results with dCELL has moved the market away from cryopreservation. These are typically used in paediatric patients. Like biological valves, there is no need for anticoagulant therapy. Additionally, allografts have native-like haemodynamic (blood flow) performance, cause less immunogenic reaction and should last longer. However, the availability of valves is limited by the supply of suitable donors (see below).
  - obtained from patient and human donor: Ross procedure (a pulmonary autograft where a diseased aortic valve is replaced with the person's own pulmonary valve, which is itself then replaced with a pulmonary allograft taken from human donors). Pulmonary autograft replacement of the aortic valve is currently the operation of choice in infants and children, but it is a more complex operation with associated co-morbidities.

The majority of heart valve replacements are achieved with open heart surgery. However, a growing alternative for patients unable to undergo surgery is a Transcatheter aortic-valve replacement (TAVR). TAVR is a technique where the new valve is delivered through a catheter and positioned in place without removing the old, damaged valve. The market leader, Edwards LifeSciences has indicated that the potential TAVR market size is over $5bn and that it expects to expand its patient base to intermediate and lower risk patients.

Competition

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. The remainder of the US market is dominated by Medtronic (26%), St Jude Medical (17%) and Sorin (now LivaNova) (5%). 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 in 2008). Exhibits 4 and 5 outline xenograft and homograft/allograft competitors (not mechanical valves).

Exhibit 4: Competitor overview – Xenograft valves

Company	Edwards Lifesciences	Medtronic	St. Jude	LivaNova
Brand	Perimount, Magna	Hancock II, Mosaic	Trifecta, Biocor	Mitroflow, Soprano
Valve Material	Bovine pericardium	Root Porcine	Bovine Pericardium	Bovine Pericardium
Frame Material	Elgiloy	Delrin	Titanium	Plastic

Source: Company data and Edison Investment Research

Exhibit 5: Competitor overview - homografts/allografts

Company/Product	Indication	Features
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.
CryoLife/SynerGraft - pulmonary valve	Pulmonary valve	Decellularised using SynerGraft process to remove allogeneic donor cells

Source: Edison Investment Research, company websites

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

Growing body of evidence (for CardioPure)

CardioPure HV has been implanted in over 1,500 patients to date, with 10 years of follow-up data recently presented. Exhibit 6 outlines key studies.

Exhibit 6: Clinical studies overview

Clinical study	Overview	Findings
Fresh decellularised pulmonary valve allografts for RVOT* reconstruction during the Ross operation	10-year follow-up of 155 patients receiving a dCELL pulmonary heart valve in a long term study of 374 patients, mean age of 30.8 +/- 13.1 years.	CardioPure HV was shown to be more effective than standard cryo-preserved valves with less immunogenic reaction, no increase of pressure gradients, lower incidence of structural valve deterioration (SVD), minimal or absence of calcification and greater freedom from re-operations.
Decellularised allografts for paediatric patients under 12 years of age with complex congenital heart disease	Ongoing study, 100 patients, multi-institutional.	Preliminary results have shown excellent haemodynamics, no calcification and no reoperations for up to nine years
dCELL aortic allografts	10 year follow up, 103 high risk patients with aortic valve disease, mean age range of 46+-17, age range 0.1 to 81 years.	Pressure gradient stable over time, absent or minimal calcification, preserved aortic wall, evidence of repopulation, endothelisation and minimal intimal hyperplasia

Source: Edison Investment Research, company presentations. Note: *RVOT = right ventricular outflow tract.

Long-term driver: Supply does not meet demand

The number of human tissue valves is independent of growth in the overall human valve market, and depends solely on the number of available donors. The supply of human donor pulmonary and aortic valves is limited to only 3,700 pa in the US, or around 7% of RoW total heart valve replacement procedures.[5]

The processing of donor tissue is controlled by licensed tissue banks. Currently, most human heart valves are processed using cryopreservation technique (stored frozen at -135°C after processing the donated tissue), although data have been presented that demonstrate a better outcome with dCELL (see above). The collection, paperwork, processing and preparation of human tissue are performed by tissue banks. The tissue banks are non-profit organisations with a code of ethics.

To penetrate the market, TRX needs to demonstrate that the dCELL process will be an improvement on the current technique and that by using the donated tissue, it will be able to further optimise the use of donated tissue to benefit more people who require transplants. Hence the importance of the study outlined above.

Clearly, the availability of human donor hearts poses a problem so if the dCELL process can improve on the properties of porcine tissue valves, it could revolutionise the treatment of patients with heart valve defects. Valves that induce no immunogenic reaction and are less prone to degeneration promote repopulation by the body's own cells and thereby regenerate with the patient's body and eliminate the need for recurring surgeries. Moreover, if the low levels of calcification and low immune system activation levels observed in human dCELL valves extend to dCELL-treated xenogenic valves, then these could eventually become the treatment of choice.

TRX has not yet confirmed its US cardiac strategy, although the most likely option in our 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.

[5] Source AATB.

Sensitivities

For the group as a whole, key sensitivities include execution of the wound care commercial strategy and the rate of clinical progress in wound care and orthopaedics. Commercialisation of wound care products is dependent on raising the visibility of DermaPure among key opinion leaders (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

The company has announced that it will alter its reporting year end from January 2017 to December 2016; the years quoted refer to the new year-end reporting periods. We recently revisited a number of our key valuation assumptions to reflect the clarity on launch timeframes, associated costs and updated revenue guidance. We maintain our DCF valuation at £338m or 44.4p per share using a WACC of 12.5%, subject to potential dilution from an estimated £15m funding requirement (2018) needed to deliver on our estimated growth trajectory, via a hybrid distribution strategy and including development of OrthoPure XT and XM. This would be reduced or not required if the US approval is undertaken alongside a partner, or if OrthoPure XM goes down the 510k route instead of an IDE/PMA route. We recently increased the sales mix costs in both the wound care division (35%, from 30%) and orthopaedic division (45%, from 30%), altered the launch date for OrthoPure XM in the EU to 2018 (2017) and for OrthoPure HM and HT in the US to 2018 (2017). We also rolled the model forward to Q116e (please note the change in year end, so first forecast year is 2016e), updated the $:£ exchange rate ($1.44 to $1.3), adjusted the probability of an IDE in the US to 30% (from 35%) and use reported cash of £19.9m at end FY16 (vs £25m at 31 July 2015). We also split out central costs as the company has started to break figures into respective divisions.

Exhibit 7: Sum-of-the-parts valuation

Sum-of-the-parts valuation	Peak net sales $m	Operating margin	Value of divisions (£m)	Value per share (p)
Wound Care Inc	245.34	25%	251.2	33.1
Orthopaedic	270.18	33%	77.1	10.1
Cardiac	132.94	24%	39.2	5.2
Unallocated costs			-49.9	-6.6
net cash Jan 2016			19.9	2.6
SOTP			**338**	**44.4**

Source: Edison Investment Research

We value the three divisions in discrete units owing to the various growth trajectories and estimated profitability. We value the wound care business at £251m, the orthopaedics division at £77m and the cardiac division at £39m, based on risk-adjusted cash flows for each division according to the stage of development (see Exhibit 8). We assume a higher success probability for human tissue due to lower regulatory risk. 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.

According to our model, orthopaedics and cardiac alone account for the current share price, leaving wound care as an option for free. Exhibit 9 illustrates our forecast divisional and group sales and profitability 2016e to 2021e.

Exhibit 8: Probabilities for developing products

Pathway	Probability	Products
CE mark	60%	Porcine dCELL heart valves/OrthoPure XM/XT
Human tissue products	80%	OrthoPure HM/HT
IDE - US	30%	Porcine dCELL heart valves/OrthoPure XM/XT

Source: Edison Investment Research

Exhibit 9: Estimated divisional revenue and profitability

£m	2016	2017	2018	2019	2020	2021
Wound care - revenue	2.44	5.18	11.83	27.43	40.07	52.84
Growth	393%	212%	228%	232%	146%	132%
Wound care - operating profit	-1.66	-2.95	-0.71	3.57	10.02	19.02
Orthopaedics - revenue	0.00	1.12	4.07	9.60	15.59	29.32
Growth	N/A	N/A	363%	236%	162%	188%
Orthopaedics - operating profit	-4.23	-2.51	-1.38	-0.38	3.12	8.50
Cardiac - revenue	0.00	0.14	1.39	3.63	7.60	12.15
growth	N/A	N/A	1,000%	262%	210%	160%
Cardiac - operating profit	-2.22	-2.88	-4.44	-2.69	-1.30	2.07

Source: Edison Investment Research

TRX could be an acquisition target either on a divisional basis or for its platform technology as a whole. In a takeover scenario, subject to demonstrating clinical and economic value alongside a clear sales trajectory, the valuation of the cardiac division could be between 2x and 7x sales based on the price paid by Cardinal Health for Cordis Vascular and St Jude Medical's acquisition of Thoratec Corp in 2015 (both in the cardiovascular space, with the higher multiple relating to a technically advanced portfolio). This implies a potential valuation of between $32m and $111m for the cardiac division alone, based on the same 2x and 7x multiple of FY21e cardiac sales of $16m (or £12m), one year post estimated US launch. Equally, in a takeover scenario for the group, subject to gaining commercial traction, it could achieve 5x sales based on the price paid by Integra (wound care) in August 2015 to TEI Biosciences for its range of dermal substitutes. Again, this would imply a valuation of $615m for the group based on a 5x multiple of FY21e sales of $123m (or £94m).

Financials

The company has announced that it will alter its reporting year end from January 2017 to December 2016. As a result, our model shows a 2016 actual and the first year of forecast figures as 2016e. We forecast £40.7m in net sales by 2019, which should take TRX to profitability. We see a sequence of potential catalysts over the next couple of years that could lead to delivering the estimated commercial potential. Our revenue estimates are calculated net of a 35% distributor margin for the wound care and cardiac divisions, assuming TRX continues to operate a hybrid distribution strategy. They are calculated net of a 45% distributor margin for the orthopaedic division, assuming TRX follows a pure distributor sales model. We forecast wound care revenue of £2.4m in 2016, rising to £5.2m in 2017, driven by the commercial focus on outpatient wound care clinics and continuing expansion of distribution channels. In 2017, TRX targets launch of OrthoPure XT in CE mark regions; we estimate £1.1m of net revenue in launch year, rising to £4.1m in 2018, which includes a contribution from the launch of OrthoPure XM. We forecast orthopaedic operating expenses of £4.2m in 2016, including SG&A of £0.8m and R&D of £3.5m, reducing to £2.5m in 2017, as one of the clinical trials completes (SG&A of £1.6m and R&D £1.8m). The cardiac division is forecast to launch dCELL heart valves in 2017, with sales of £0.1m in launch year rising to £1.4m

in 2018. Our estimated cardiac opex in launch year (2017) is £3m rising to £4m in 2018, due to increased R&D costs to cover the estimated cost of the IDE for porcine valves.

We estimate that group revenue will increase from £2.4m in 2016 to £40.7m in 2019, reaching profitability on a margin of 2%, when we estimate that tax would be payable on a blended basis of 15%, offsetting US corporation tax of 20% against a UK patent box R&D tax credit, trending towards 20% by 2025. Based on end-January 2016 net cash of £19.9m, TRX has a cash runway for the immediate pipeline (OrthoPure, SurgiPure and dCELL valves). We do, however, estimate a £15m funding requirement in 2018 to deliver on our estimated growth trajectory, which includes commercialising via a hybrid distribution strategy and development of OrthoPure XT and XM in the US. This amount would be reduced or not required if the US approval and launch are undertaken alongside a partner, or if OrthoPure XM goes down the 510k route instead of an IDE/PMA route.

Exhibit 10: Financial summary

£'000s	2014	2015	2016*	2016e**	2017e	2018e
Years ending 31 December	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS						
Revenue	6	100	816	2,444	6,444	17,279
Cost of Sales	0	0	(154)	(440)	(1,206)	(3,416)
Gross Profit	6	100	662	2,004	5,238	13,864
Operating expenses	(6,459)	(8,318)	(10,904)	(13,345)	(16,815)	(23,627)
EBITDA	(6,453)	(8,218)	(9,997)	(11,131)	(11,427)	(9,756)
Operating Profit (normalised)	(6,577)	(8,369)	(10,242)	(11,401)	(11,673)	(9,971)
Exceptionals	0	0	0	0	0	0
Other	0	4	0	0	0	0
Operating Profit	(6,577)	(8,365)	(10,242)	(11,401)	(11,673)	(9,971)
Exceptionals	0	0	0	0	0	0
Net Interest	274	168	213	149	67	1
Profit Before Tax (norm)	(6,303)	(8,201)	(10,029)	(11,252)	(11,606)	(9,970)
Profit Before Tax (as reported)	(6,303)	(8,197)	(10,029)	(11,252)	(11,606)	(9,970)
Tax	710	620	527	563	580	498
Other	0	0	0	0	0	0
Profit After Tax (norm)	(5,593)	(7,581)	(9,502)	(10,689)	(11,026)	(9,471)
Profit After Tax (as reported)	(5,590)	(7,581)	(9,502)	(10,689)	(11,026)	(9,471)
Average Number of Shares Outstanding (m)	636	636	698	760	760	760
EPS - normalised (p)	(0.88)	(1.19)	(1.36)	(1.41)	(1.45)	(1.25)
Dividend per share (p)	0.0	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	100.0	81.1	82.0	81.3	80.2
EBITDA Margin (%)	N/A	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	N/A
BALANCE SHEET						
Fixed Assets	472	435	901	1,120	1,195	1,326
Intangible Assets	0	0	0	0	0	0
Tangible Assets	472	435	901	1,120	1,195	1,326
Investments	0	0	0	0	0	0
Current Assets	19,610	12,238	22,296	11,902	3,441	11,578
Stocks	0	34	64	241	661	1,404
Debtors	1,127	1,947	2,325	2,679	2,648	5,918
Cash & equivalents	18,483	10,257	19,907	8,982	133	4,257
Income taxes	0	0	0	0	0	0
Other current assets	0	0	0	0	0	0
Current Liabilities	(1,104)	(1,095)	(1,958)	(2,411)	(4,955)	(7,486)
Creditors	(1,104)	(1,095)	(1,958)	(2,411)	(4,955)	(7,486)
Short term borrowings	0	0	0	0	0	0
Contingent consideration	0	0	0	0	0	0
Long Term Liabilities	0	0	0	0	0	(15,000)
Long term borrowings	0	0	0	0	0	(15,000)
Contingent consideration	0	0	0	0	0	0
Net Assets	18,978	11,578	21,239	10,611	(318)	(9,583)
CASH FLOW						
Operating Cash Flow	(6,121)	(8,285)	(9,625)	(11,148)	(9,175)	(11,030)
Net Interest	274	168	213	149	67	1
Tax	474	0	745	563	580	498
Capex	(358)	(114)	(711)	(489)	(322)	(346)
Acquisitions/disposals	0	0	0	0	0	0
Financing	8	5	19,019	0	0	0
Dividends	0	0	0	0	0	0
Capitalised R&D	0	0	9	0	0	0
Net Cash Flow	(5,723)	(8,226)	9,650	(10,925)	(8,850)	(10,876)
Opening net debt/(cash)	(24,206)	(18,483)	(10,257)	(19,907)	(8,982)	(133)
HP finance leases initiated	0	0	0	0	0	0
Other	0	0	0	0	0	0
Closing net debt/(cash)	(18,483)	(10,257)	(19,907)	(8,982)	(133)	10,743

Source: Source: Edison Investment Research, company accounts. Note: *Reported year end 31 January. **First year with year-end 31 December.

Contact details	Revenue by geography
Tissue Regenix Unit 1&2, Astley Way Astley Lane Industrial Estate Swillington Leeds LS26 8XT +44 (0)330 430 3052 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 and 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	18.2
Techtran Group	13.6
Baillie Gifford & Co	7.0
University of Leeds	4.5
Jupiter Asset Management	4.6
NFU Mutual	3.7

Companies named in this report

Edwards Lifesciences, Medtronic, BSC, St Jude Medical, Jena, Direct Flow Medical, CryoLife, Sorin, Cardinal Health, Cordis Vascular, Thoratec Corp, Integra, TEI Biosciences

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