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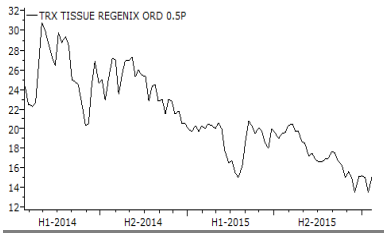
Pharmaceuticals & Biotech



Source: Fidessa

Market data	
EPIC/TKR	TRX
Price (p)	15.3
12m High (p)	23.6
12 Low (p)	14.8
Shares (m)	759.7
Mkt Cap (£m)	115.9
EV (£m)	95.4
Free Float* (%)	65%
Market	AIM

**As defined by AIM Rule 26*

Description

TRX is a UK-based medical devices company in regenerative medicine. Its patented decellularisation ('dCELL') technology removes DNA and other cellular material from animal/human tissue leaving an acellular tissue scaffold, not rejected by the body, which can then be used to repair diseased or worn out body parts. Launched DermaPure in US to treat chronic wounds and, potentially, other applications in sports medicine, heart valve replacement and vascular disease.

Company information	
CEO	Antony Odell
CFO	Ian Jefferson
Executive Chair	John Samuel

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www.tissueregenix.com

Next event	
Ongoing	> Medicare cover
1H 2016	SurgiPure XD 510(k)
1H 2016	DermaPure RCT data
May 2016	FY 2016 results
2H 2016	OrthoPure CE Mark
2H 2016	RCT trial completes

Analysts

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Tissue Regenix

From development – into the commercial world

Tissue Regenix is no longer an R&D play. Its dCELL® technology enables production of 'like-for-like' tissue specific, structure-preserving scaffolds that have been validated in multiple clinical settings. Following the US launch of DermaPure®, we expect a series of further product launches over the next two years in Orthopaedic Sports Medicine and heart valve replacement, substantial markets with significant unmet medical need. The company continues to build long term value despite short term monthly cashburn of ~£0.8m. An NPV of 42p is driven by 3 core product areas; the true value of the platform & product streams has still to be elucidated.

- **Strategy:** To build a regenerative medicine business with a portfolio of products using the dCELL platform, underpinned by compelling clinical and economic outcomes designed to drive higher adoption rates, whilst retaining the strategic and corporate flexibility that the four therapeutic corporate entities provide.
- **Commercial traction building:** Primary focus is on the commercial roll-out of DermaPure in the US although near term catalysts include the 2016 launch of OrthoPure XM/XT for the treatment of meniscal tears and tendon repair in Europe as well as the US launch of OrthoPure human tissue variants.
- **Valuation:** Key milestones driving near-term valuation include the 510(k) approval of SurgiPure XD, evidence of revenue momentum and surgeon adoption of DermaPure as well as the EU launches of OrthoPure XM/XT and CardioPure HV with commercial partners.
- **Risks:** Clinical and regulatory (three outstanding clinical trials in order to achieve approvals), financial (further funding for OrthoPure US trial costs but these could be through partnerships) and commercial (rollout of DermaPure in the US) but mitigated by hybrid sales strategy.
- **Investment summary:** TRX is building long term value with three clear value drivers: wound care in commercialisation, sports medicine in regulatory phase, and cardiac in late clinical, all the time de-risking the business for the investor as well as any potential acquirer. As with many technology rich/platform companies, the inherent value lies in terminal value of such cashflows. The probability adjusted NPV is 42p.

Financial summary and valuation

Year end Jan (£000)	2014	2015	2016E	2017E	2018E	2019E
Sales	6	100	494	2,067	6,073	14,716
Underlying EBIT	-6,483	-8,189	-10,013	-12,443	-13,350	-9,752
Reported EBIT	-6,577	-8,369	-10,203	-12,653	-13,580	-10,002
Underlying PTP	-6,209	-8,021	-9,890	-12,280	-13,279	-9,626
Statutory PTP	-6,303	-8,201	-10,080	-12,490	-13,509	-9,876
Underlying EPS (p)	-0.9	-1.0	-1.2	-1.5	-1.6	-1.1
Statutory EPS (p)	-0.9	-1.2	-1.2	-1.5	-1.6	-1.1
Net (debt)/cash	18,483	10,257	20,450	8,814	15,825	6,215
Shares issued	8	5	18,972	0	20,000	0
P/E (x)	-	-	-	-	-	-
EV/sales (x)	-	-	-	-	-	-

Source: Hardman & Co Life Sciences Research

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Executive summary

Regenerative medicine company...

Tissue Regenix is a UK-based medical technology company, focused on developing a broad range of room temperature off-the-shelf regenerative medical products using biological (human & animal) materials to create replacement tissue types to be commercialised through a hybrid model of direct sales and distributors. The Company was formed in 2006, based on research from the University of Leeds.

...based on patented and proven technology platform ....

The broad diverse product range is based on its patented dCELL technology, which generates acellular tissue scaffolds from human donor (allograft) or animal tissues (xenograft) by removing all cells, cell debris, DNA and RNA. These can be used then to replace damaged body parts/tissues, without the need for anti-rejection drugs.

....that creates like for like tissue specific products unlike competitor products being adapted to multiple disease states and clinical settings

The dCELL technology allows for a 'like-for-like' tissue specific, structure-preserving process unlike competitor technologies which use a single tissue type (eg. placental tissue) that is then adapted to address multiple disease states in multiple clinical settings. Equally, the process does not use high-concentration detergents, solvents, or chemical fixatives that may compromise tissue structure, unlike many early decellularisation techniques. Instead the allografts maintain the relevant and appropriate scaffold structure, with the appropriate strength and viability of the tissue it is replacing to create an environment conducive to recellularisation or cell migration which occurs during the natural healing process.

Company structure

TRX has established a corporate structure that provides flexibility in terms of business development as well as financing needs. Underneath the PLC, Tissue Regenix Limited holds all the IP from which exclusive sub-licenses have been granted to each of the therapeutic companies, namely Wound Care, Cardiac, Orthopaedics and Vascular. This should enable management to balance the financing needs of each business with the differing timescales needed to fully develop their respective product pipelines.

Rich product pipeline

Already validated in multiple and varied clinical settings

The dCELL platform has been validated in multiple and varied clinical settings, which is expected to lead to a series of product launches over the next two years from each of the three business units.

Product Pipeline- launch timetable

			2014	2015	2016	2017	2018	2019	2020	2021	Regulatory clearance
DermaPure HD	Human	Chronic wounds	US	US - Q code reimbursement							HCT/P 361
SurgiPure XD	Porcine	Hernia repair			US						510(k)
SurgiPure HD	Human	Breast reconstruction			US - TBC						HCT/P 361
SurgiPure HD	Human	Tissue augmentation			US						HCT/P 362
OrthoPure HM	Human	Meniscal repair			US						HCT/P 363
OrthoPure HT	Human	ACL repair			US						HCT/P 364
OrthoPure XM	Porcine	Meniscal repair				EU					CE Mark
OrthoPure XT	Porcine	ACL repair				EU					CE Mark
CardioPure HV	Human	Heart valve				EU					CE Mark
OrthoPure XM	Porcine	Meniscal repair							US (TBC)		PMA
OrthoPure XT	Porcine	ACL repair							US (TBC)		PMA

Source: Hardman & Co Life Sciences Research

Hybrid sales model – US woundcare sales force supported by regional distributors

Business model – hybrid distribution

TRX has adopted a hybrid sales model, combining regional distributors with its own proprietary field force in the US. Currently 15-strong, the intention is to build the US sales force to around 30 persons. In Europe the intention is to launch OrthoPure and CardioPure through distributors or partnerships.

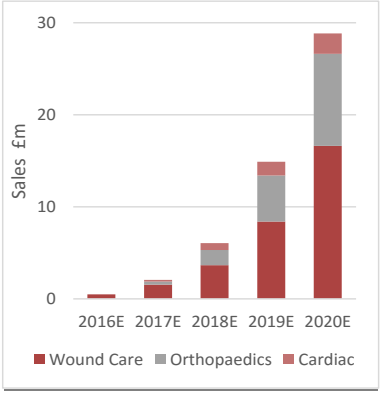
Addressing large markets with unmet clinical need

TRX's family of products, DermaPure, OrthoPure and CardioPure are addressing large market segments that are still have a significant unmet clinical need, in Wound Care, Sports Medicine injuries and heart valve replacement, respectively.

Key milestones

Whilst initial investor focus has been on DermaPure, a number of important milestones are expected in the next 18 months. Whilst positive DermaPure experiences will drive surgeon adoption in both chronic and acute wound settings, critical to the nearer term success of DermaPure is the account approvals and continued reimbursement approvals from both federal and commercial payors. Within Orthopaedics, the approval of SurgiPure XD, whilst not expected to be a significant commercial opportunity, is highly relevant as it will demonstrate to investors and potential partners that it has the quality systems in place for the FDA to approve a porcine derived tissue for hernia repair. European studies for the approval of its porcine meniscus and tendon are expected by end 2016 which should enable CE Mark approval and a European launch in 2017. OrthoPure HM and OrthoPure XT (both human tissue variants of meniscus and tendon) are expected to be cleared and launched in the USA during 2016. Finally, clinical data to support a European launch of CardioPure HV, a human heart valve, in 2017 is expected to be released during 2016.

Sales model



Source: Hardman & Co Life Sciences Research

Key milestones

	2H 15	1H 16	2H 16	1H 17	2H 17
DermaPure HD	Medicare coverage expansion				
		RCT trial completion	RCT trial results		
SurgiPure XD		510(k) approval			
SurgiPure HD		Tech transfer to US			
OrthoPure HM		Tech transfer to US			
OrthoPure HT		Tech transfer to US			
OrthoPure XM			CE Mark		
OrthoPure XT			CE Mark		
CardioPure HV			Paediatric data		EU launch

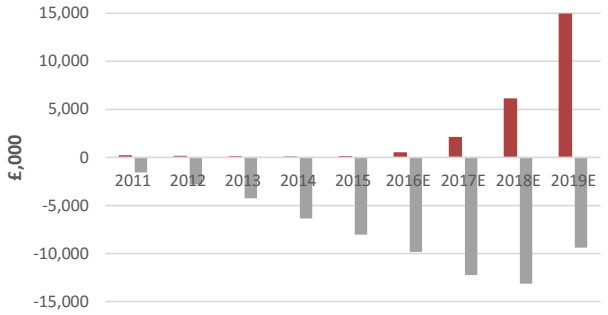
Source: Hardman & Co Life Sciences Research

Investment conclusion

Tissue Regenix is at a very interesting stage in its lifecycle, having launched DermaPure in the US and validated the dCELL technology platform in multiple tissue types which has applicability in multiple clinical settings. Whilst not always immediately relevant as market focus is given to the early commercial traction and adoption of DermaPure, the significance of this should not be underestimated in our opinion. Although seemingly an early stage company, there is limited regulatory risk given that DermaPure is already launched and that the human versions of OrthoPure and CardioPure are approvable through HCT/P 361 pathway in the US and EU Tissue Directive rather than via clinical trials. Only OrthoPure XT/XM requires FDA clearance via a PMA study, and the decision to undertake such studies (the costs of which are included in our model) will only be determined on the outcome of the CE Mark studies expected to readout in 2H 2016.

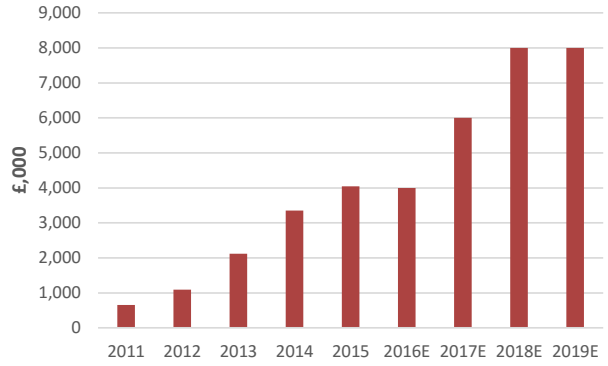
A DCF valuation of £316m or 42p per share is derived from free cashflow forecasts out to 2025 with a terminal growth rate of 2%. Like many early stage commercial companies, the value of the technology platform lies primarily in the terminal value. In this case it accounts for 98% of the NPV as TRX continues to invest in building the dCELL platform. The most significant sensitivity to the potential value of TRX is the share of hard to heal wounds that DermaPure is able to secure in the USA. Our base case is for DermaPure to secure a ca.4% share of the US market in 2025. If one was to assume that TRX can capture 10%, the NPV rises to 119p.

Sales and EBITDA



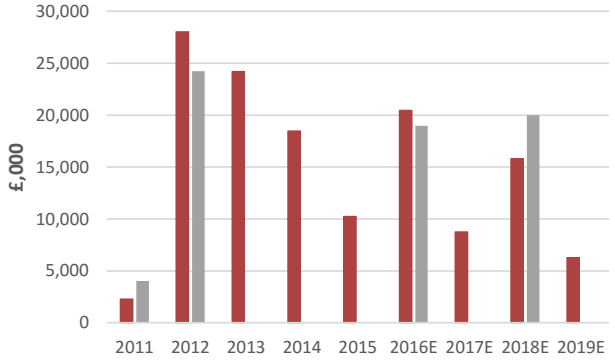
- DermaPure was launched in 2014 in the US into the in-patient hospital segment of the market for acute and chronic wounds
- Broader reimbursement coverage gained access to out-patients settings in 2015 and adoption of hybrid sales model
- SurgiPure XD is expected to gain US 510(k) approval in mid-2016. Approval will be a significant regulatory milestone
- European launch of OrthoPure XM/XT through distributor model in 2017 and OrthoPure HM/HT in the US in 2016
- CardioPure HV European launch expected in 2017 through distributor model

R&D investment



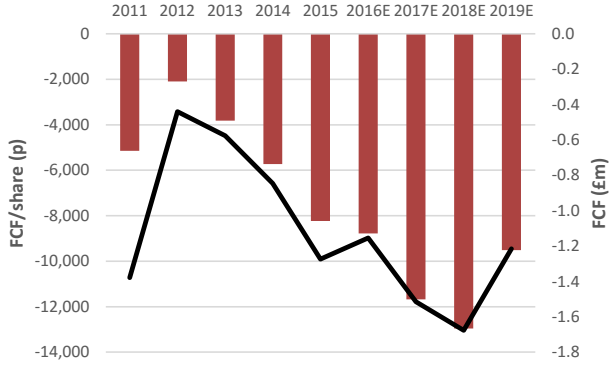
- Cumulative investment in R&D since 2006 has been ca.£19.7m
- R&D investment is forecast to rise following March 2015 £20m Placing to secure CE Mark for OrthoPure XM/XT in Europe
- In the US funds will be used to complete processes to achieve clearance for human versions of OrthoPure HM/HT for meniscus and ligament repair
- We also assume that the costs of a PMA study for the porcine meniscus and ligament products are borne by the Company, commencing in 2018

Net cash and share issues



- Since AIM admission in 2010, £47.2m (£49.5m gross) has been raised to fund the business
- £19m (£20m gross) was raised in January 2015 to commercialise further DermaPure in the US, to launch SurgiPure XD (porcine hernia patch in US), to fund the development, manufacturing set-up, launch, sales & marketing and working capital build of the human meniscus and ligament products (OrthoPure HM and XT) in the US
- We estimate a further £15m will be required should the Company choose to fund the US PMA study of porcine meniscus/ligament products (OrthoPure XM and XT)

Cashflow



- Despite cash burn increasing, through 2018, we consider the investment to be creating long term value in the business
- Investment has already demonstrated the application of dCELL process to multiple clinical settings
- Clinical applications are all in areas of high unmet medical/clinical need; namely chronic and acute/complex wounds, sports medicine and cardiac valves

Source: Company data; Hardman & Co Life Sciences Research

Strategy and technology

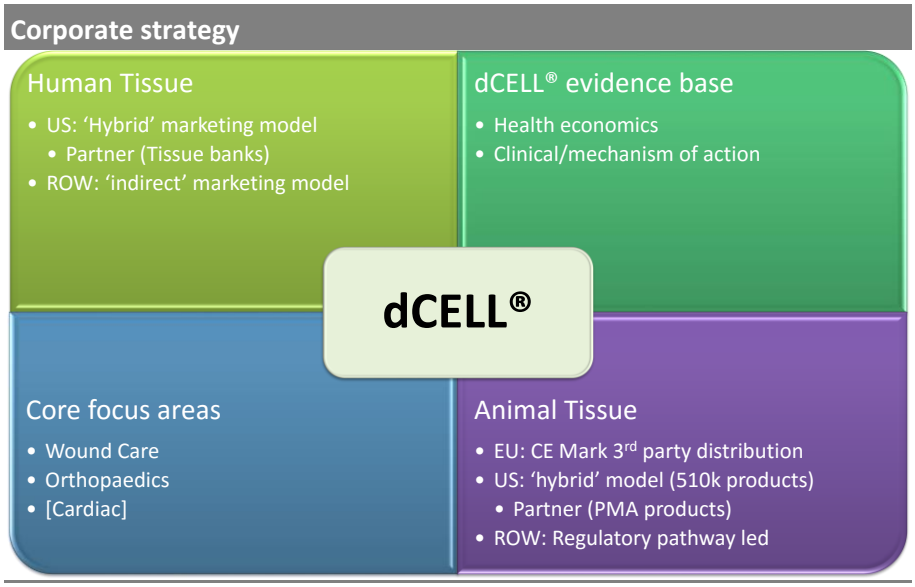
To become a leader in regenerative medicine...

Tissue Regenix's strategic focus can be summarised as:

- Exploiting the emerging market of regenerative medicine; the process of replacing, engineering or regenerating human cells, tissues or organs to restore or establish normal function thus obviating the need for metal or synthetic implants; working to restore structure and function of damaged tissues and organs. It is also working to create solutions for organs that become permanently damaged

...by exploiting proprietary decellularisation platform technology

- Maximising the value of its technology platform and clinically validated medical applications. The corporate flexibility that comes from having established, from the onset, individual therapeutic companies responsible for the development of the platform in different applications should enable management to balance the financing needs of each business with the differing timescales needed to fully develop their respective product pipelines



Source: Tissue Regenix

No longer considered a research play as its commences commercialisation of multiple products in the next 18 months

Tissue Regenix should no longer be considered a research "play". It has moved beyond that phase, having shown that its dCELL platform technology can be commercialised in the USA as well as critically, developing reimbursable products. All too often we see medical device companies that have not addressed the issue of reimbursement until way down the track. Its lead product, DermaPure is being rolled out into the US market. The next significant milestone is expected to be the US 510(k) approval of its porcine surgical mesh in 1H 2016, SurgiPure XD, which will demonstrate that it has the quality systems in place to generate approvable medical devices.

The value of Tissue Regenix lies in the ability of management to develop and commercialise this platform, maximising the breadth of product opportunity that now exists within the group. The Company is entering the commercial phase were greatest value is expected to be created.

- dCELL technology platform is the core to the investment case – the ability to prepare like-for-like tissues, using both human and animal tissues, for implantation in specific clinical applications

- Human tissue – using decellularised tissues from approved human tissue banks, TRX has commenced commercial operations for DermaPure (chronic and acute wound care) in the US through a hybrid marketing model, using a small direct sales force supported by regional/local distribution partners in the US. Longer term, human-based tissue products will be sold globally but through indirect marketing channels

- dCELL evidence base. Although relatively little evidence (clinical or economic) is required to get a medical device approved in the US (510(k)) or Europe (CE Mark), TRX is set on generating the relevant clinical and economic evidence to drive adoption rates in the market place rather than simply seeking the minimum hurdle to get approval. To that extent TRX is conducting a significant number of clinical case studies in chronic wounds as well acute wounds.

- Animal tissue. To maximise the dCELL technology platform and exploit larger volume global clinical applications, TRX is developing a range of animal-based (porcine) medical devices to address these market needs. With a clearly defined regulatory pathway compared with human-based tissues, TRX will similarly apply a hybrid marketing model in the US for 501(k) products although is likely to pursue a partnership model with those products requiring financially more onerous PMA regulatory clearance.

- Core focus areas – whilst dCELL technology has very broad applicability, TRX is initially focusing on three areas, namely Wound Care, Orthopaedics/sports medicine and Cardiac.

dCELL – platform technology

The dCELL process

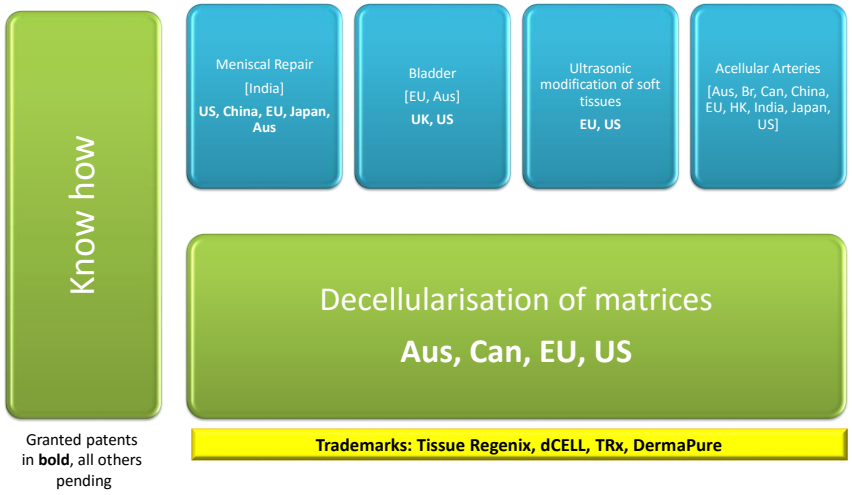
Source: Tissue Regenix

Tissue Regenix's product range is based on its dCELL technology platform – a way of removing cells (decellularisation) to create a biological scaffold which can be stored at room temperature (in the case of the heart valve, in a regular refrigerator) and used without any changes to current surgical techniques to treat patients with the risk of the implant being rejected by the recipients' immune system and thereby allowing for the recellularisation of the scaffold by the patients' own cells.

In the widest sense the core patent (7,354,749) describes a method of decellularising a tissue matrix using low concentration sodium dodecyl sulphate (SDS – anionic surfactant used in many cleaning and hygiene products) and proteinase inhibitors and, by doing so, preserving the tissue's physical structure or histo-architecture. The process itself takes relevant human (cadaver) or animal tissue and removes the cells, cell debris, DNA and RNA within the structure of relevance, for example dermis, meniscal cartilage or heart valves, so that the product can be stored for later use. The dCELL process removes over 99% of cellular debris, DNA and RNA.

This is in marked contrast to other decellularised products and approaches that use higher concentrations of reagents that may destroy the tissue structure whilst also removing less of the DNA and cellular debris. The dCELL process ensures the biomechanical structure and function of the donor tissue is retained as far as possible.

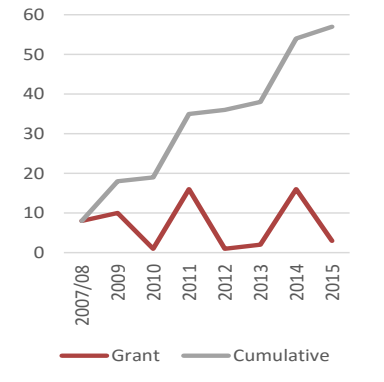
Intellectual property



Granted patents in **bold**, all others pending

Source: Tissue Regenix

Patent portfolio expanding



Source: Tissue Regenix

The tissue, once decellularised, can be stored at room temperature and be used straight from the sterilised pack, unlike cryopreserved tissues which have to defrosted and/or re-hydrated if freeze dried. This has significant commercial as well as user benefits.

This patented technology underpins both the broad development opportunities which are being pursued as well as its commercialisation strategy. The core patent, granted in 2002, expires in 2022, however, the Company has continued to extend its patent estate with almost 60 granted patents. The Company continues to prosecute patents for arteries, bladder etc which are expected to provide further additional growth opportunities in the future, as clinical validation has yet to commence in these areas. In addition to its patent portfolio, there is a substantial amount of "know how" involved particularly with the way in which different tissues are processed, for example, ligaments behave differently to dermis or meniscal cartilage.

As an example of the future opportunities that the dCELL technology offers, TRX had granted in 2014 a patent for producing a natural, acellular matrix scaffold for subsequent bladder replacement in which decellularisation is carried out on a distended bladder, which retains the strength as well as compliance of natural material. It is estimated that over 400m people worldwide suffer from some form of bladder dysfunction that includes, for example cancer, congenital abnormalities, nerve damage or trauma. Currently, surgical reconstruction with vascularised segments of the patient's own tissue derived from their stomach or intestine is undertaken but this is associated with significant clinical complications that arise due to the exposure of the epithelial lining of the intestine to urine. TRX is seeking to provide a natural biomaterial that is immunologically inert and able to support recellularisation.

Platform validation

As an investment thesis, TRX should no longer be viewed as an R&D story, in our opinion. The dCELL platform has been validated in multiple clinical settings, with the current focus of commercialisation across three broad areas, namely in Wound Care, Orthopaedics and/or Sports Medicine and Cardiac.

Unlike most decellularised competitors such as LifeCell (Alloderm, Strattice) in which a single tissue type and process is used to address different clinical settings, Tissue Regenix uses a like-for-like approach of matching similar tissue types to the particular clinical situation. It is able to do so because of its tissue-specific and structure-preserving dCELL process. Other areas, targeted but yet to be clinically validated, include arterial vasculature, bladder, and liver amongst others.

Platform validation

					Commercial	
Tissue	**Type**	**Indication**	**Process**	**Clinical**	**US**	**EU**
Wound Care						
Dermis	Human	Chronic wounds	✓	✓	2014	TBD
	Human	Pressure ulcers	✓		TBD	TBD
	Porcine	Hernia	✓		2016	TBD
	Human	Dental	✓	✓	2016	TBD
	Human	Burns	✓	✓	TBD	TBD
	Human	Breast reconstruction	✓	✓	TBD	TBD
Orthopaedic						
Dermis	Human	Tissue augmentation (orthopaedic sheath)	✓	✓	2016	TBD
Meniscus	Porcine	Partial meniscectomy	✓	✓	TBD	2016
	Human	Partial meniscectomy	✓		2016	TBD
Tendon	Porcine	ACL	✓	✓	TBD	2016
	Human	ACL	✓		2016	TBD
	Human/porcine	PCL, MCL, LCL, MPFL	✓		TBD	TBD
	Human/porcine	Foot, ankle, shoulder, elbow	✓		TBD	TBD
Cardiac						
Heart valve	Human	Pulmonary valve	✓	✓	TBD	2017
	Porcine	Pulmonary valve	✓		TBD	TBD
	Human	Aortic	✓	✓	TBD	2017
	Porcine	Aortic	✓		TBD	TBD
Other						
Vessels	Porcine	Various (arteries)	✓		TBD	TBD
Bladder	Porcine	Various	✓		TBD	TBD

ACL – anterior cruciate ligament; MCL – medial collateral ligament; LCL – lateral collateral ligament; MPFL – medial patellofemoral ligament

Source: Tissue Regenix

Product nomenclature

Given the source of tissue types (human or animal) TRX have named their products with suffixes such as HD or XT to describe both source of the material as well as its clinical application. For example, DermaPure HD refers to the brand name, DermaPure, as being from Human tissue as applied to the Dermis in wound repair. OrthoPure XM refers to xenograft (animal) tissue, in this case pig, as applied to meniscal repair; OrthoPure XT – xenograft for tendon repair.

Regulation – route to market

The following table summarises the different regulatory pathways which Tissue Regenix must comply with in its core geographic territories, in order to gain clearance and approval to market its products.

USA

In the USA, the FDA recognises three classes of medical devices: Class I, 2, and 3. TRX is developing both Class 2 and 3 devices which, respectively, are eligible for either a 510(k) premarket submission or a Premarket Approval (PMA) application using an investigational device exemption (IDE - allowing the device to be used in a clinical study to collect safety and effectiveness data to support the PMA application or 510(k) submission). Given that some products are utilising donor human tissue, these products are subject to a different regulatory pathway, namely HCT/P 361.

HCT/P 361

In the USA, human cells or tissue intended for implantation, transplantation, infusion, or transfer into a human recipient is regulated by The Center for Biologics Evaluation and Research (CBER) as a human cell, tissue, and cellular and tissue-based product or HCT/P. Where the product is minimally manipulated, intended for homologous use only, not combined with another article and has no systemic effect (except in certain situations) then the product is further classified under section 361. All TRX's human-derived acellular products are "361 products".

Regulatory pathway

	USA		Europe	
	Pathway	Clearance/ Approval	Pathway	Clearance/ Approval
Wound Care				
DermaPure HD	HCT/P 361	2014	n/a	n/a *
SurgiPure XD (xenograft)	510(k)	2016	CE Mark	TBD **
SurgiPure HD	HCT/P	2016	n/a	n/a
Orthopaedic				
OrthoPure HM	HCT/P 361	2016	n/a	n/a
OrthoPure HT	HCT/P 361	2016	n/a	n/a
OrthoPure XM (xenograft)	PMA	2020+	CE Mark	2017
OrthoPure XT (xenograft)	PMA	2020+	CE Mark	2017
Cardiac				
human	HCT/P 361	TBD	EU Tissue Directive	2017
xenograft (porcine)	PMA	TBD	CE Mark	TBD

** NHS Blood & Transport retain commercial rights in UK*
*** potential to develop porcine version but likelihood in partnership*
Source: Company reports; Hardman & Co Life Sciences Research

FDA draft guidance, issued on 28th October 2015, caused some confusion in the market in that the guidance refers to the homologous use of amniotic allografts, derived from human donor placenta.

Homologous use means that a human cellular or tissue product (HCT/P) is used clinically in a manner where it performs the same basic function or functions in the recipient as in the donor. This is potentially relevant to those products using, for example, amniotic (placental) tissue to treat wounds. Operationally, the definition of homologous use is being questioned because non-homologous use of placental tissue for wound care, by definition, arguably makes those allografts a biological product rather than simply an HCT/P 361 which would require extensive safety and efficacy testing and a different regulatory clearance pathway. At best this can only be helpful to Tissue Regenix, whose products using dCELL are all for homologous use – tissue specific clinical applications.

510(k) Clearance

TRX is developing SurgiPure XD as a hernia mesh using porcine xenograft material and must demonstrate that the device is substantially equivalent to a predicate device (LifeCell's Strattice). The FDA typically has 90 days to clear the device, ask questions, or reject the application which is expected to be made in 1H 2016 after the Company has addressed to the satisfaction of the FDA the questions that it has raised. Having submitted the 510(k) for SurgiPure XD in 3Q 2015 TRX has received first responses and questions which the Company expects to have responded to by early 2016.

Pre-market Approval (PMA)

PMA submissions will be required for its porcine-derived Class III implantable orthopaedic products. This standard is higher than is required for 510(k) submissions and requires formal clinical studies to demonstrate both safety and efficacy to support the claims made for the device.

Europe – CE Mark

Tissue Regenix is developing Class IIb (surgically invasive devices with higher risk) and Class III (highest risk devices, including all implantables) devices. Both require CE Mark certification which verifies (self-certification using a Notified Body) that the device meets all regulatory requirements of the Medical Devices Directive. TRX expects to CE Mark both its porcine-derived meniscus and tendon products, OrthoPure XM and OrthoPure XT, in 2016 and 2017, respectively.

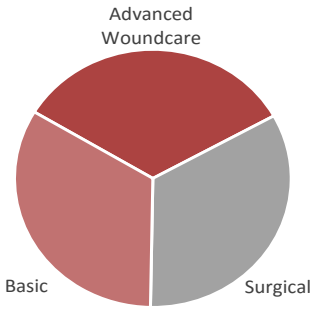
Europe – Human tissue directive

The regulatory pathway for TRX's human heart valve is via the EU Tissue Directive. This sets standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells intended for human application. Clearance for its human-derived heart valve in 2017.

Wound Care

Introduction

Global Woundcare Market – >$20bn



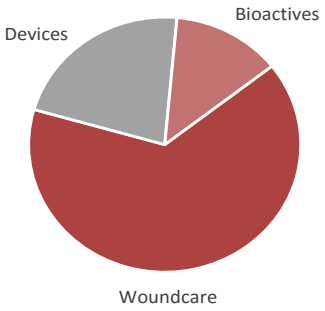
Source: Smith & Nephew

Tissue Regenix Wound Care Inc was established in San Antonio, Texas, USA in November 2012 to exploit and commercialise its range of wound care products, initially DermaPure HD and thereafter, SurgiPure XD. It is currently not part of the business plan to sell DermaPure HD in Europe, partly due to potential supply constraints, but also due to the heterogeneous nature of the markets and poorer reimbursement environment. Whereas the skin substitute market is worth ca.$526m in 2014 in the USA, the European market is worth only ca.$25m.

Production and sourcing for DermaPure HD is outsourced to Community Tissue Services (CTS) in the USA where it takes tissue from human cadavers and applies the dCELL process. Product is finished and stored at CTS distribution and, upon customer request, it is shipped to the desired location for customer use. Porcine derived dermal tissue for SurgiPure XD is processed and packaged at the Company's Leeds facility and will be shipped to TRX Wound Care Inc.

The global market for products to treat wounds is worth more than $20bn, according to Smith & Nephew, and includes Advanced Wound Care products (dressings, devices and bioactives) as well as Basic products (commoditised tapes, bandages etc) and Surgical products (stitches, staples etc).

Global Advanced Woundcare – >$8.1bn



Source: Smith & Nephew

The Advanced Wound care segment of the market is worth ca.$8.1bn globally of which the US accounts for ca.40% or $3.2bn. Market growth of ca.7% is being driven by aging demographic profit as well as the enormous growth in diabetes and obesity in whose populations there is a greater prevalence of chronic wounds.

Drivers of chronic wounds

	Comment
Age	Increasing proportion of elderly. Prevalence of VLU is 1-3% in the elderly[1]
Diabetes	17m with diabetes in 2000 set to rise to 366m in 2030[2]. Prevalence of DFU is 1-6% of patients annually and up to 25% of diabetics over lifetime[3]
Obesity	BMI >30. 34.9% or 78.6m of U.S. adults are obese[4]. 15-20% surgical site infection

Source: Hardman & Co Life Sciences Research

It is estimated that $24-38bn is spent on treating venous leg ulcers and diabetic foot ulcers in the USA,[5,6] prompting the need for more efficacious solutions than the current standard of care (SOC) which is not effective is not effective; either clinically or economically.

[1] Margiolis et al 2002. J. Am. Ac. Derm 46, 381-6
[2] WHO Diabetes/facts/world/figures
[3] NHS Fact Sheet No.37 March 2002
[4] www.cdc.gov/obesity/data/adult
[5] Rice et al 2014. Diabetes Care 37, 651-8
[6] Rice et al 2014. J. Med. Econ (17)5, 347-356

Current standard of care typically includes compression bandaging with or without negative wound pressure therapy. However, it is expensive, labour-intensive and not always successful with ca.30-75% healing rates seen in venous ulcers[7]. To address these hard to heal wounds companies have developed active healing solutions, including growth factors, device combinations including negative pressure wound therapy (NPWT) and extracellular matrices including dermal skin substitutes.

Wound care portfolio

Product	Description
DermaPure HD	Allograft human dermis for treatment of chronic, hard-to-heal wounds (diabetic foot ulcers, venous leg ulcers). Initial launch in 2014
SurgiPure XD	Xenograft (porcine) dermis for surgical hernia repair. Submitted 510(k) in 3Q 2015 with approval expected in 1H 2016
SurgiPure HD	Human tissue version of SurgiPure will be developed for tissue augmentation segment of the market, including tendon repair in foot and ankle procedures. HCT/P 361 clearance expected 2016. Later applications will be developed for breast reconstruction

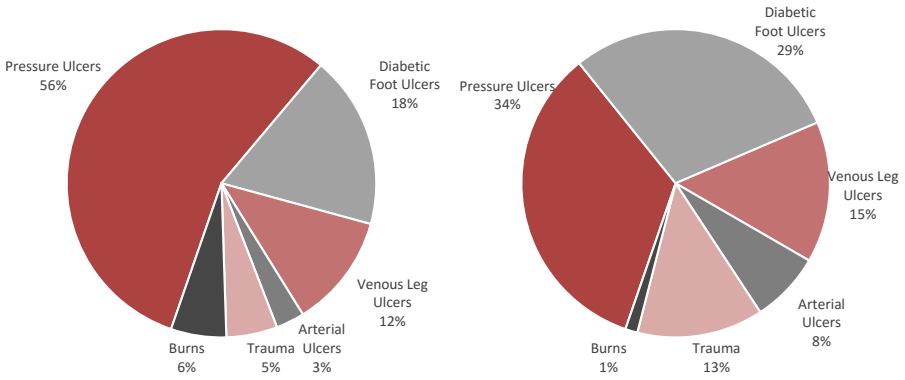
Source: Hardman & Co Life Sciences Research

Addressable market

Initial focus on the US market, estimated to contain ca.3.2m hard to heal wounds

It is estimated that in the US there are ca.8m wounds of which ca.3.2m are described as chronic or hard to heal wounds (defined as persisting for longer than 42 days or of frequent recurrence). These wounds typically represent >80% of the healthcare costs compared with ca.20% for acute wounds.[8]

US Wounds



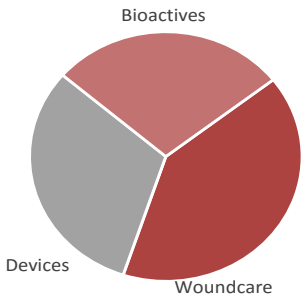
Source: Tissue Regenix, BioMedGPS

Chronic wounds represent an enormous burden both on the patient as well as society/payors and is only expected to worsen given the three key drivers behind chronic wound prevalence.

Of the ca.$3.2bn US market for Advanced Wound products, the Biologics or Bioactives segment was worth ca.$865m in 2014 and comprises three broad segments, namely; skin substitutes, collagen active dressings and topical preparations. Of this the skin substitute market is the largest, worth an estimated $526m in 2014, growing at ca.10%[9] in 2014, which itself can be subdivided into:

[7] O'Meara S et al 2012. Cochrane Database Syst Rev 11, CD000265
[8] Silver Book. Chronic Diseases 2004
[9] SMARTRAC Wound Biologics Market – Tissue Regenix Capital Markets Day 2015

US Advanced Wound Market – $3.2bn

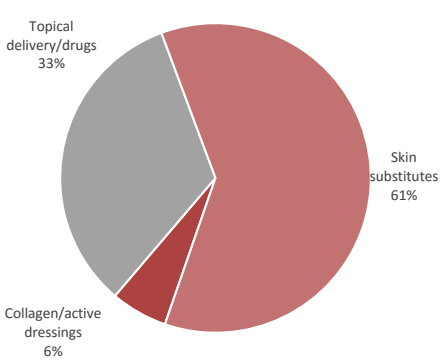


Source: Smith & Nephew

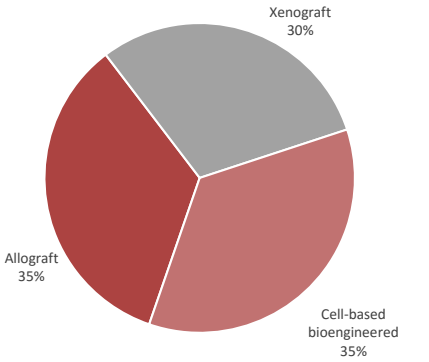
- Allografts; tissues derived from human sources such as TRX's DermaPure HD, Integra LifeSciences' BioFix (human placental membrane) and Mimedx's EpiFix (human placental membrane). Growth in 2014 was estimated to have doubled at the expense of the cell-based bioengineered products
- Xenografts; tissues derived from animal sources, typically bovine or porcine, such as TEI Biosciences' PriMatrix. Growth in 2014 was around 33%
- Cell-based bioengineered products; tissues that are grown in cultured medium, such as Organogenesis' Dermagraft and Apligraf. Sales fell ca.34% as part of the continued downtrend post reimbursement changes in December 2012

Whilst it represents a large and attractive market place, it is a competitive market place with many players (60+) and blighted, in many respects, by the lack of compelling clinical and economic evidence. TRX is seeking to address this discrepancy with a significant amount of case studies and economic modelling that illustrates a lower total cost of care.

US Wound Biologics/Bioactives Market



2014 Wound Biologic Market: $865m



2014 Skin substitute Market: $526m

Source: Tissue Regenix, BioMedGPS

DermaPure

DermaPure is a decellularised human dermis for the treatment of chronic as well as severe acute wounds and burns.

Key features of DermaPure

Features	Benefits
Tissue structure preserved	Collagen I, III, IV and Elastin, Laminin, Fibronectin and intact vascular channel preserved Preserved because of use of ultra-low concentrations of SDS and proteinase inhibitors
Histo-compatible	Removal of up to 99% of DNA-containing nucleated cells and cellular tissue reduced probability of rejection
Off the shelf product	Room temperature storage No thawing, rehydration or rinsing prior to application Lower storage costs Less set up time for physician

Source: Hardman & Co Life Sciences Research

KOL led case studies support DermaPure use

Its early commercialisation is supported by three, albeit small studies, together with an increasing number of Key Opinion Leader-led case studies.

60% of chronic wounds healed with a single application

- Its efficacy is best illustrated in a small 20-patient UK study[10] conducted with National Health Service Blood and Transplant (NHSBT) assessing its application in treatment-resistant lower limb ulcers with a mean ulcer duration of 4.76 years and mean size of 13.11cm^2. 60% of patients, whose wounds were covered with a single application of DermaPure, exhibited complete healing with an average 87% reduction in size after 6 months.

Acute wounds – a statistically significant increase in blood vessel in growth

The study also described histological evidence of incorporation into the host tissue with biomechanical properties similar to normal tissue together with evidence of cell migration and blood vessel regrowth (angiogenesis). This is relevant as scaffold characteristics including elasticity, porosity and bio-compatibility, have been shown in other studies to support beneficial cellular activity during healing.[11, 12]

- In a separate study in 50 healthy volunteers assessing the angiogenic response in acute wounds to autograft, collagen-GAG scaffold or DermaPure, those given DermaPure saw a statistically significant increase in angiogenesis after wounding compared with controls.[13] Angiogenesis or new capillary formation is highly relevant in the wound healing process.

Only 1.1 applications used for complete wound closure

- In a poster presentation at the Symposium on Advanced Wound Care in May 2015, an interim analysis on a range of different wounds (DFU, necrotising fasciitis, trauma (shrapnel)) showed that patients treated with DermaPure exhibited clinical effectiveness with an average healing time of 6½ weeks and complete wound closure as well as positive economic outcomes; using only 1.1 applications.

Randomised controlled trial designed to demonstrate efficacy versus standard of care

In 3Q 2014, Tissue Regenix initiated a Phase IV prospective, multi-centre (six centres), randomised, single blind study in 50 patients with hard to heal chronic, neuropathic diabetic foot ulcers with a cross-over design after 12 weeks for the standard care (debridement and compressed bandaging) arm. The primary endpoint is complete wound closure at 12 weeks. Although recruitment has been slower than anticipated, due mainly to the fact that during the two-week pre-treatment screening period, patients saw a >30% reduction in ulcer size, more than 50% of patients have been enrolled. We expect this trial to complete recruitment in 2016, with trial results potentially due by end 2016. This study, however, represents only part of the overall clinical strategy given the large number of clinical case studies.

Room temperature stable off-the shelf product

DermaPure is stored at ambient temperature and comes hydrated, with only a simple rinse required prior to use. It requires no thawing, no rehydrating or special storage conditions. This is a significant consideration when considering the additional costs seen in thawing or rehydrating competitive products as well as associated storage costs. There is little set up time for the physician.

Commercialisation

Phased roll-out in the US but structure and strategy should build long term value

The roll out of DermaPure into the US market continues to build with a clearly defined, structured and measured approach. We don't expect sales to be explosive in the early years, rather building as the user experience across the broad range of wound types, already seen, expands and as the cohort of clinical data, fortified by the RCT results in 2H 2016, continues to develop:

[10] Greaves NS et al. *Wound Repair Regen*. 2013;21(6): 812-822
[11] Rehfeldt F et al. *Adv Drug Deliv Rev* 2007; 59: 1329–39.
[12] Engler AJ et al. *Cell* 2006; 126: 677–89.
[13] Greaves NS et al. *PLoS One* 2015, 10(1): 1-18

- **Phase I – in-patient hospital use**

  DermaPure HD was launched in the US in June 2014 into the hospital in-patient segment of the market where around 20% of chronic wounds are treated

- **Phase 2 - out-patient use**

  Q code notification received on 4 November 2014 from the Centers for Medicare and Medicaid Services (CMS), which enables out-patient facilities (Wound care clinics, Out-patient Surgical Centers, Ambulatory Surgery Centers and physician offices) to use DermaPure for Medicare and Medicaid beneficiaries and receive reimbursement

- **Medicare coverage expansion during 2015**. DermaPure is now accessible in 31 US states to 63% of the 37m beneficiaries enrolled under the Medicare programme (federal health insurance programme for people 65 years or older)

DermaPure – Medicare coverage

MAC Jurisdiction	States	Date	Covered lives (000s)	Non-covered lives (000s)	% of total
Novitas	AR, CO, DE, LA, MD, MS, NJ, NM, OK, PA, TX, Washington DC	Mar 2015	8,919		24%
Noridian	AL, AZ, CA, HI, MT, NV, ND, OR, SD, UT, WA, WY	Jun 2015	6,460		17%
NGS	MN, NY, NH, VT, ME, MA, RI, CT			7,099	19%
WPS	NE, KS, IA, MO, IL, WI, MI, IN			4,134	11%
Palmetto	NC, SC, VA, WV	Jun 2015	3,397		9%
First Coast	FL, PC, US Virgin Is	Jul 2015	2,559		7%
Cahaba	TN, AL, GA			2,563	7%
CGS	KY OH	Apr 2015	1,921		5%
Total			**23,255**	**13,796**	**100%**
			63%	**37%**	

MAC – Medicare Administrative Contractor
Source: Tissue Regenix

Further coverage is expected over the course of 2016.

- **Building Key Opinion Leader (KOL) network**. The Company had 17 healthcare professional agreements with KOLs in September, rising to 25 by year end and 40 over time. These KOLs publicly describe and endorse their experiences of DermaPure at conferences and peer to peer events. Without their clinical evaluation and some level of endorsement, it is difficult to drive usage into the broader out-patient clinics

- **Hybrid sales model**, with a direct sales force of 15 persons, as well as distributors covering three regions in the USA (West, Central and East regions). The target is initially to focus on those states that have Medicare coverage building the sales force to 25-30 as further coverage is granted

- **Expanded product range to reflect users' needs.** TRX launched DermaPure in three sizes (2x3 cm, 3x4 cm and 4x6cm) ranging in price from $795 to $1,995 but has recently added 1x2cm and 2x2 cm sizes ($525 and $725), firstly to address the high percentage of chronic VLU and DFU that are under $5cm^2$ and secondly, to address those procedures/out-patient clinics which are reimbursed on a per square centimetre basis

Competition

The key competitor products to DermaPure HD are highlighted in the following table. It is worth pointing out, however, that in the past year, due to reimbursement cuts introduced from 1 January 2013 for cell based bioengineered products (from $2,200

to $1,400) such as Dermagraft and Apligraf, this segment of the market fell ca.34% to $186m due to the fact that without patient co-pays, out-patient clinics could not make a profit, given that most patients required more than one application.

Competitive position – dermal skin substitute

Company	Brand	Product type	Comment
Organogenesis	Dermagraft	Cell based bioengineered	Cryopreserved human fibroblast
Organogenesis	Apligraf	Cell based bioengineered	Off the shelf bilayer of human fibroblast and bovine tissue
MiMedx Group	EpiFix	Allograft	Off the shelf amnion/chorion placental membrane
Integra	BioFix	Allograft	Off the shelf amnion placental tissue
Osiris Therapeutics	Grafix	Allograft	Cryopreserved human placental membrane
DermaSciences	Amnioexcel	Allograft	Off the shelf amnion placental tissue
Soluble Solutions	TheraSkin	Allograft	Cryopreserved epidermis/dermis
Smith & Nephew	Oasis	Xenograft	Porcine small intestinal submucosa
ACell	Maristem	Xenograft	Porcine urinary bladder matrix
TEI Biosciences*	PriMatrix	Xenograft	Foetal bovine dermis

**acquired by Integra LifeSciences in August 2015*

Source: Company reports; Hardman & Co Life Sciences Research

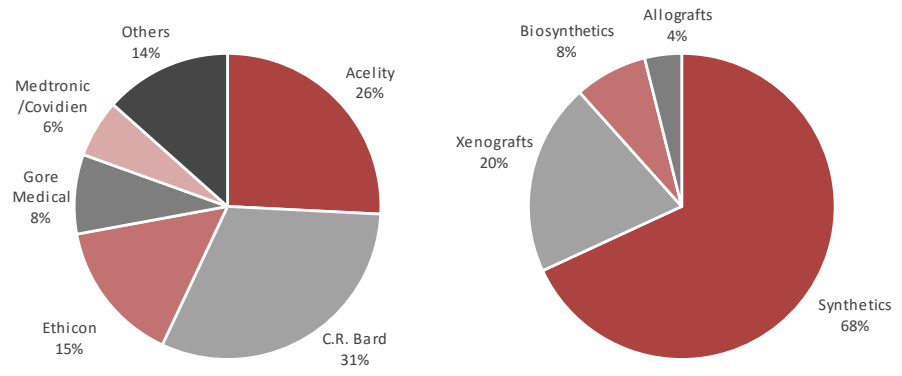
SurgiPure XD

First porcine-based tissue for hernia repair currently at the FDA with launched anticipated in mid-2016

SurgiPure XD is a decellularised porcine dermis, around 1-2mm in thickness, (compared with 0.2-0.3m for DermaPure) to be used to surgically repair hernias.

Having submitted a 510(k) to the FDA in 3Q 2015 and received first responses from the FDA, the company expects to gain approval in the US in 1H 2016 with a launch in 2H 2016. Approximately, 600,000 inguinal or groin hernia repair operations are performed annually in the USA[14]; a market worth an estimated $1.1bn out of the larger $1.4 surgical matrices market, which also includes breast reconstruction. The market is largely controlled by 5 players with more than 10 other companies comprising 14% of the market. From a product perspective, the market is dominated by synthetic matrices (68%) with higher growth rates seen in biosynthetic matrices which have come at the expense of xenografts (20% of the market or $57m) and allografts which declined 6% and 22%, respectively in 1Q 2015.

US surgical matrices market



Surgical Matrices market: $361m (1Q 2015) **US Hernia market: $282m (1Q 2015)**

Source: Tissue Regenix, BioMedGPS

[14] Society of American Gastrointestinal and Endoscopic Surgeons

FDA approval is a significant regulatory milestone demonstrating quality management systems in place

From an investors' perspective, however, the approval of SurgiPure XD should be viewed as a major technical and regulatory milestone. Not only does it demonstrate that TRX is able to take a porcine tissue through the FDA but that it is also compliant with all medical device quality management systems. Suffice it to say, this is potential incremental value for SurgiPure XD, with little or no development risk attached.

A 5% share of the xenograft segment would imply potential sales of ca.$10-15m, or ca.20-25% of the xenograft segment. Given limited clinical usage to date we expect sales to build steadily with rising surgeon awareness and increasing adoption rates.

SurgiPure HD

Potential to have human version of thicker dermis for use in breast reconstruction

SurgiPure HD is a decellularised human dermis, thicker than DermaPure HD, that is being developed as a surgical patch for use in soft tissue augmentation procedures in which matrices are used to reinforce Achilles tendon or rotator cuff injuries. This is a market currently worth ca.$70m and used in around 38,000 procedures. At a later date, SurgiPure HD will be targeted at the US breast reconstruction market, via a HCT/P 361 clearance route. This market is worth ca.$300m and grew at ca.16% in 1Q 2015 according to BiomedGPS, driven by high risk patients opting for mastectomy and implant-based reconstructions. Allografts are the product of choice and account for 83% of the market. Acelity dominate this market with AlloDerm (used also in hernia repair) with a share of around 75%. It is not yet clear when SurgiPure HD will be launched but a 5% share of the market would generate revenues of ca.$15-20m.

DermaPure sales model

Sales model assumes only modest penetration of chronic wound segment – building a positive clinical experience will drive revenues longer term

We forecast DermaPure sales of ca.£0.5m in FY2016, rising to £11.6m in 2020 based on an increase in direct sales reps and the build-up of distributor channels. Positive clinical case study evaluations, coupled with value analysis approvals, should ensure greater market share which is estimated to reach 0.8% of all hard to heal wounds or 5.6% of the forecast use of allograft by 2020.

DermaPure – US sales model

Year end Jan (£000)	2016E	2017E	2018E	2019E	2020E
Direct sales					
Units per month	75	225	506	886	1,329
Volume	900	2,700	6,075	10,631	15,947
% growth		200%	125%	75%	50%
Price per unit	850	800	750	750	750
Direct sales	**765**	**2,160**	**4,556**	**7,973**	**11,960**
Sales reps	15	25	30	30	30
Sales per rep (000)	51	86	152	266	399
Distributor sales					
Volume	0	500	1,500	4,500	13,500
% growth			200%	200%	200%
Price per unit (distributor margin)	510	480	450	450	450
Distributor sales	**0**	**240**	**675**	**2,025**	**6,075**
Total US sales ($)	**765**	**2,400**	**5,231**	**9,998**	**18,035**
US (£)	**494**	**1,548**	**3,375**	**6,451**	**11,636**
US volume (total)	900	3,200	7,575	15,131	29,447
Allografts (m)	0.36	0.40	0.44	0.48	0.52
% allograft	0.3%	0.8%	1.7%	3.2%	5.6%
Hard to heal wounds (m)	3.33	3.39	3.44	3.50	3.56
% hard to heal	0.0%	0.1%	0.2%	0.4%	0.8%

Source: Hardman & Co Life Sciences Research

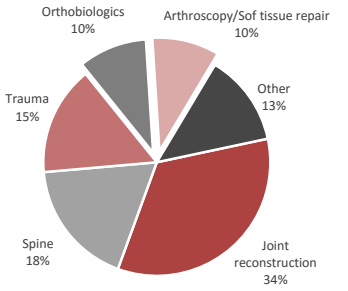
Orthopaedics – Sports Medicine

Introduction

Technology applied to sports medicine market where high unmet need for repair of orthopaedic soft tissues – meniscus and ligament

The global orthopaedics market is estimated to be worth $45.5bn, growing at around 3-5% pa. TRX is developing a range of products with applications in two segments accounting for 20% of the market; namely the ca.$5bn Sports Medicine (Arthroscopy and soft tissue repair) and the $4.4bn Orthobiologics markets. Orthobiologics are products that improve the healing of broken bones, muscles, tendons, and ligaments; typically produced from substances that are naturally found in your body.

Orthopaedic market - $45.5bn



TRX's products are targeted at the soft tissue repair segment. These tissues have relatively poor healing capabilities compared to most other tissue types and for which the use of scaffolds is considered a way of promoting more functionally appropriate healing. Demographics continue to drive this segment of the market with a desire to extend active life styles without the early intervention of more invasive (and costly) joint (mainly knee) replacement.

Drivers of sports medicine injury

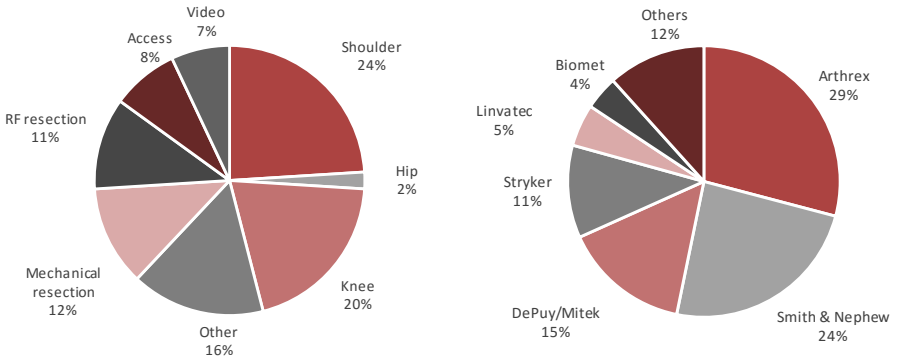
Drivers	Restraints
Aging demography; desire to remain active	Rising cost of surgical procedures
Rising obesity impacting on weight bearing joints and tissues	Limited claim on surgeries by insurers/patient co-pays
Lack of substitution for orthopaedic soft tissue repair surgery	Lack of awareness among people regarding orthopaedic soft tissue repair
Rising sports-related injuries	

Source: Hardman & Co Life Sciences Research

Entering a large ($2.1bn) and fast growing market (7-14%)

The sports medicine market can be broken down into joint repair products (shoulder, knee and hip), worth ca.$2.1bn, growing at 7-14%, and arthroscopic enabling technologies, worth $2.5bn growing at 3-6%. This comprises mainly hardware (instruments, access and visualisation products) which is of no relevance to TRX. The leading four companies account for ca.80% of the market.

Global sports medicine market



2013 Sports Medicine Market: $4.6bn

Source: Smith & Nephew

Initial focus on the US market with human tissue and EU markets with xenograft

The joint repair market comprises products currently used to repair cartilage, ligament and tendon within the respective joints. For example, a meniscus tear is a rupturing of one or more of the fibrocartilage strips in the knee called menisci, which can occur during innocuous activities such as walking or squatting but, more commonly, by a twisting movement at the knee when the knee is bent, during physical exertion. The meniscus can be damaged in the elderly following prolonged wear and tear; categorised as a degenerative tear.

A market leading portfolio of tissue repair products

Tissue Regenix's pipeline includes both human and porcine tissue types which have different regulatory clearance pathways. Like DermaPure, the human tissues will be cleared under the HCT/P 361 pathway. However, the xenograft products are reviewed as Class III medical devices, given that they are implanted in the patient, and require modest clinical studies for European approval (CE Mark) but more extensive safety and efficacy studies in the USA (PMA).

The aim is to provide room temperature "off the shelf" products that require minimal preparatory work for the surgical team prior to implantation that ultimately are not constrained by donor tissue supply and quality, and can be translated to the clinic as Class III devices.

Sports Medicine portfolio

Product	Description
OrthoPure HM	Human meniscus, targeted for US launch in 1H 2017 via HCT/P 361 clearance
OrthoPure HT	Human tendon, targeted for US launch in late 2016 via HCT/P 361 clearance
OrthoPure XM (xenograft)	Porcine meniscus, targeted for EU launch in 2017 following CE Mark approval. Clinical study commenced in March 2015 (enrolment completed in 1/2016. US launch not expected until 2020+ following outcome of PMA study which commences post-outcome of EU study
OrthoPure XT (xenograft)	Porcine tendon, targeted for EU launch in 2017 following CE Mark approval. Clinical study commenced December 2015. US launch not expected until 2020+ following outcome of PMA study which is expected to start following the outcome of EU study
SurgiPure HD	Human dermis (thicker than DermaPure) for tendon augmentation procedures. Patch material for tendon reinforcement (eg. Rotator cuff, Achilles tendon) to be launched in the US in 2016 via HCT/P 361 clearance

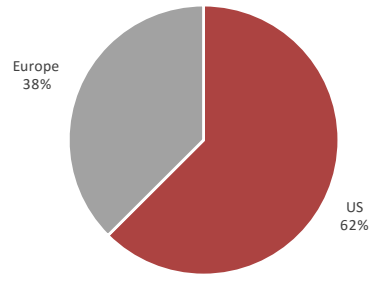
Source: Hardman & Co Life Sciences Research

Addressable market

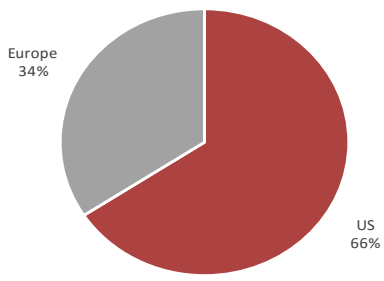
Tissue Regenix is focused initially on two key market segments, namely meniscal repair and ligament reconstruction.

Addressing large markets with unmet medical need

Meniscal repair and Ligament repair



2014 – Meniscal repairs – 1.6m



2014 ACL repairs – 750,000

Source: various sources

The meniscal surgery market is the most common orthopaedic procedure undertaken with an estimated 1.6m operations in the US and Europe whereas ligament repair procedures, predominantly that of the knee (anterior and posterior cruciate ligaments – ACL/PCL), amount to some 0.75m, of which 0.25m are in Europe. In the US, about 20% of the knee ligament procedures use human allograft; a market restricted by donor supply.

The meniscus is a crescent-shaped cartilage inside either side of the knee which acts as a shock absorber between the long bones of the leg. It can be damaged by injury or overuse, causing pain, swelling and locking of the knee.

- Meniscus - current treatments include:
  - stapling or suturing of the damaged/torn meniscus
  - partial removal (meniscectomy) of the torn meniscus
  - implantation of meniscal allografts but there is limited supply of donor cadaver tissue
  - implantation of biodegradable implants by 'keyhole' knee surgery. The implant works as a scaffold to support re-growth and repair of the damaged meniscus. However, NICE point out that there is insufficient statistical evidence to claim it is superior to partial meniscectomy[15].
- ACL/PCL – current treatments are autografts (using patient's own tendon), allografts (using donor cadaver tissue) or synthetic ligaments, which are no longer approved in the US given high failure rates.

The cost of an allograft ACL in the US is ca.$2,000, implying a potential addressable market of around $1.5bn. With regards meniscal repair, and assuming a similar selling price the total addressable market is around $3.75bn.

Similar to the wound care market, it is a competitive space with over 300 companies seeking to develop products within the sports medicine/orthobiologics space.

OrthoPure XM

Decellularised porcine meniscus

OrthoPure XM is a decellularised porcine meniscus being developed as a regenerative scaffold in the meniscal tear market.

Partial meniscectomy is the current standard of care, when suturing and/or stapling are inappropriate. This segment represents ca.80% of the addressable market.

TRX commenced a clinical study in March 2015 assessing the safety and efficacy of OrthoPure XM in patients with chronic pain, following a previously failed meniscal repair or partial meniscectomy.

The intention is to generate clinical based outcomes that will support approval and reimbursement

The primary objective of the study is to generate sufficient data to gain CE Mark approval in Europe which is expected in 4Q 2016. Although TRX intends to recruit 60 patients into the trial, CE Mark submission will occur when 20 patients have completed 6-months follow-up. The Company announced completion of enrolment on 18th January 2016. MRI assessment will also be undertaken to assess the integration of the dCELL meniscus with that of the recipient's remaining meniscus.

[15] NICE interventional procedure guidance [IPG430] July 2012

Underpinned by the clinical results in Europe, the exploitation of US markets will take longer

OrthoPure XM – clinical trial	
	Comment
Patients	60 patients, 9 sites in UK, Poland and Spain
Primary objective	Safety and performance in improving pain
Secondary objective	Improvement in knee function
Outcomes	Measured at 3, 6, 12 and 24 months: VAS, IKDC, KOOS and LYSHOLM at 0, 3, 12, and 24 mths MRI follow-up at 3, 12 and 24 mths
Inclusion criteria	Irreparable medial or lateral meniscus rear or loss with intact rim 18 to 55 years Stable knee joint ICRS (International Cartilage Repair Society) Grade I or II No more than 3 surgeries on involved meniscus
Major exclusion criteria	Total meniscal loss Significant malalignment of knee Advanced osteoarthritis Concomitant surgery required

VAS - Visual Analogue Scale, IKDC – International Knee Documentation Committee Score; KOOS - Knee injury and Osteoarthritis Outcome Score; LYSHOLM - Lysholm knee score
Source: Tissue Regenix

Decellularised porcine tendon for ligament repair, initially in the knee

OrthoPure XT

OrthoPure XT is a decellularised porcine tendon being developed as a regenerative scaffold for the treatment and repair of ACL/PCLs, replacing the need for autografts which are associated with significant co-morbidity arising from removing a patients' own tendon, and allografts (human cadaver) for which there is an inadequate supply.

Management has indicated that it commenced recruitment into a prospective single arm multi-centre study in late 2015 with 40 patients who have a partial or complete ACL tear/rupture. Enrolment is expected to be faster than for the meniscus study. Its European submission (CE Mark) is expected in late 2016 with subsequent launch in 2017.

OrthoPure XT clinical trial	
	Comment
Patients	40 patients, 9 sites in UK, Poland and Spain
Primary objective	Safety and performance (side to side knee movement)
Secondary objective	Improvement in knee function
Outcomes	Measured at 3, 6, 12 and 24 months: VAS, IKDC, KOOS and LYSHOLM at 0, 3, 12, and 24 mths MRI follow-up at 3, 12 and 24 mths Arthrometer readings at 0, 3, 6, 12 and 24 mths
Inclusion criteria	Partial or complete ACL tear 18 to 60 years Normal ACL on contralateral knee ICS classification Grade I or II
Exclusion criteria	No previous ACL surgery on target knee No surgical intervention on target knee in prior 3 mths Current ACL injury on contralateral knee Meniscal repairs on target knee requiring >33% meniscectomy

Source: Tissue Regenix

US strategy

TRX is currently in discussions with the FDA to determine exactly what type of studies are required, including European clinical trial data, to secure approval in the US market for both OrthoPure XM and XT. The technical dossier (biomechanical, preclinical, scientific, virology and biocompatibility data) is being collated and we expect clinical trials to commence in late 2016 at the earliest. We would anticipate that such a study would need to enrol at least 200 patients with a minimum follow-up of 1 year which would imply filing in 2019 and PMA at the earliest in 2020. The study could be funded by TRX alone or in collaboration with a partner. That decision will become clearer once CE Mark studies have completed.

But initial experience to be gained by launching human tissue variants

In the meantime, TRX is refining the development process for human versions of OrthoPure with technology transfer to a suitable human tissue bank ongoing. In addition, TRX is developing SurgiPure HD which will be applicable in treating soft tissue augmentation procedures, in which matrices are used to reinforce Achilles tendon or rotator cuff injuries. This is a market currently worth ca.$70m and used in around 38,000 procedures. Both OrthoPure HM/HT and SurgiPure HD are expected to be launched in late 2016.

Commercialisation

Commercialised via distribution model in Europe...

Tissue Regenix does not intend to have a direct sales capability in Europe. Rather it will use a third party distribution model supported by TRX marketing and sales personnel. The Company is in active discussions with distributors who have orthobiologics experience and who are capable of selling both OrthoPure XM and XT. Similar to DermaPure's focused launch in the US, TRX intends to target key European markets (UK, Spain, Poland, Italy and Germany) where access and reimbursement is more favourable whilst also building its KOL network, funding further clinical trial series and registries, all of which will be used to build awareness and support reimbursement studies, which will provide incremental data to support a future US launch.

.....active dialogue with potential distributors

Forecast European sales of ca.£8m in 2020

Consequently, we don't envisage a rapid sales ramp, but rather a steady one to demonstrate clinical utility, positive economic outcomes but, in doing so, we believe that build in incremental value for the likely second stage, that of partnering with a large sports medicine company. Our model assumes 12,000 procedures per annum by 2020 representing ca.1.4% of the addressable market, and sales of ca.£8m in 2020.

OrthoPure – European sales model

Year end Jan (£000)	2016E	2017E	2018E	2019E	2020E
Volume	0	500	2,000	6,000	12,000
% growth	0%	0%	300%	200%	100%
Europe sales (€)	0	450	1,800	5,400	10,800
Europe (£)	**0**	**333**	**1,333**	**4,000**	**8,000**
Meniscectomy/ACL procedures	0.85	0.85	0.85	0.85	0.85
% meniscectomy/ACL market	0.0%	0.1%	0.2%	0.7%	1.4%

Source: Hardman & Co Life Sciences Research

Cardiac

Introduction

Development of human aortic or pulmonary valves with PUCPR

10-year follow-up data to support use of CardioPure

Tissue Regenix has developed a process to produce a decellularised human donor heart valve, CardioPure HV, which has now been implanted into over 1,400 patients. This has been a long term project, given the need to assess safety and efficacy of implanted valves, but the Company now has up to 10-year follow-up data in over 200 patients. This has led to significant external interest from potential licensing partners, given the low calcification rates and need, therefore, for re-intervention, which the Company has indicated are entering an advanced stage.

Aortic valve replacement (AVR) is the result of aortic valve disease, which occurs when the aortic valve no longer functions correctly and can be either inherited or develop over time. AVR techniques include biological replacement, mechanical replacement, and the Ross procedure (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 a human cadaver). Pulmonary autograft replacement of the aortic valve is the operation of choice in infants and children, but it is a more complex operation with associated co-morbidities.

The market for cardiac valves can be summarised:

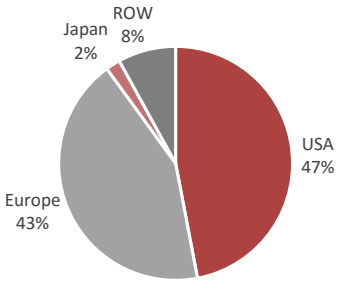
- Mechanical valves (prosthetic valves), made of immunologically inert material, with an unlimited life span. The downside is that they are prone to blood clot formation, therefore requiring life-time anti-coagulant therapy.
- Tissue valves (biological, bio-synthetic or bio-prosthetic valves), usually made from animal tissue (porcine or bovine). These do not need blood thinning medication but reoperations and replacement are typically required after 10-15 years. Around 80% of aortic valves are replaced with a tissue valve according to Cleveland.org.
- Allograft valves, obtained from human donors, are typically cryo-preserved (eg. CryoLife's CryoValve). These are typically used in children or young women who still might want to have children. Like biological valves there is no need for anti-coagulant therapy. Additionally, allografts have native-like haemodynamic (blood flow) performance, cause less immunogenic reaction and should last longer. However, the availability of suitable donor valves is limited by the supply of suitable donors; ca.5,000 pa globally.

Addressable market

The global market for heart valve replacement procedures is around 225,000[16] of which ca.70,000 are in the USA[17] with a similar number in Europe and the balance in the rest of the world. The market is dominated by Edwards Lifesciences who forecast the market to be worth ca.$1.5bn in 2014 and growing rapidly given the deployment of transcatheter heart valves (TAVR); the new valve is delivered through a catheter which repairs the valve without removing the old, damaged valve. The replacement valve is wedged into the aortic valve's place but is a procedure typically reserved for patients for whom an open heart procedure is too risky and where there is no other

[16] http://www.medsolution.com/surgery_cardiothoracic-heartvalv.asp
[17] www.womensheart.org/content/HeartSurgery/heart_valve_replacment.asp

Global heart valve market (2014) - $1.5bn

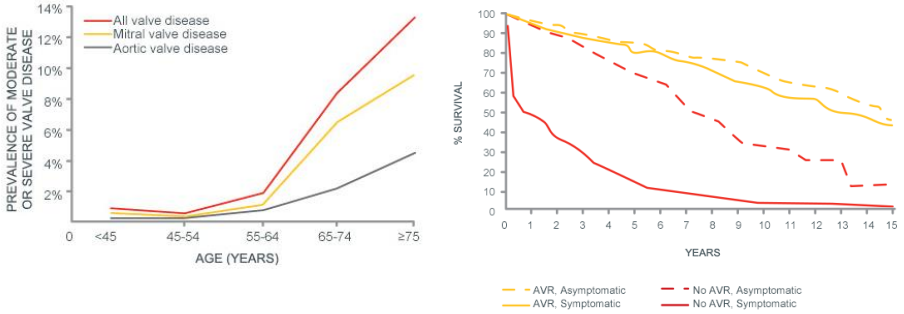


Source: Edwards Lifesciences

option. The fact that these patients are normally in their 80s, are less active and have other co-morbidities make them a better candidate for this type of treatment. Edwards, however, anticipates a late 2016 US approval to treat intermediate risk patients as well as plans to start a trial in patients with a lower risk indication. Surgical replacement of heart valves within the younger population will likely remain the technique of choice.

The prevalence of aortic valve disease increases with age, ranging from 2% of people over the age of 65, 3% over 75, and 4% percent over 85. More than one in eight people over the age of 75 have moderate or severe valve disease[18].

Cardiac – prevalence of valvular disease and patient survival[19]



Source: Hardman & Co Life Sciences Research

Aortic valve replacement (AVR) is the standard of care for aortic stenosis (AS) as there are no medications to reverse or slow the progression of AS. Mortality in AS patients is high without AVR - 3% to 4% soon after symptoms appear and 7% among patients on a waiting list for AVR. In contrast, mortality in a fit patient is 1% to 2% after AVR. Median survival with AVR is around 14-15 years, whereas without AVR it is less than 7 years or 1 year if symptomatic. AVR is consequently deemed an appropriate and effective surgery for elderly. In contrast to the regular adult patient population, the majority of valve replacements in congenital defect heart valves is on the right side with a growth tendency in the western world (STS database).

Valve replacement surgery typically costs around $165,000 ($80,000-$200,000 range), according to an American Heart Association report[20]. A typical tissue valve costs $5-7,000 depending on the territory in which it is sold.

CardioPure HV

CardioPure HV is a decellularised human pulmonary or aortic heart valve, developed by Pontifica Universiadade Catolica do Parana (PUCPR) in Brazil, using the dCELL technology. It has been implanted in over 1,400 patients with good long term outcomes having been presented at the major cardiac conferences in the past year. Key data include:

- 10-year follow up of 155 patients receiving a dCELL pulmonary heart valve in a long term study of 414 patients. The implants were in younger patients with mean age of 30.8 +/- 13.1 years). CardioPure HV was shown to be demonstrably more effective than standard cryo-preserved valves with less immunogenic reaction, no increase of pressure gradients over time, lower incidence of

[18] Nkomo VT et al. Lancet 2006; 368:1005-11.
[19] Brown ML et al. J Thorac Cardiovasc Surg 2008; 135(2): 308-15
[20] http://circ.ahajournals.org/content/123/4/e18.full.pdf

structural valve deterioration (SVD), minimal or absence of calcification and greater freedom from re-operations.[21]

- 10 -year follow-up of 103 high risk patients with aortic valve disease (mean age range of 46± 17; age range 0.1 to 81 years) who have received aortic valves. Only 3 patients required a re-operation. A partial repopulation of these grafts was also observed.
- A retrospective analysis of over 100 patients below the age of 12 years is expected to be presented in 2016. Management has indicated encouraging initial findings in this group which would enable CardioPure to be effectively positioned in younger AVR patients who generally opt for mechanical valves because they are very durable, despite the need for lifetime blood thinning agents, and want to avoid/prolong the need for future re-operations.

Commercialisation

TRX is expected to launch CardioPure HV in 2017, initially in Europe with Asia Pacific being cited by management as the next likely region, given the level of interest that has been expressed by potential partners. TRX will not commercialise CardioPure HV in the USA, given the recent changes to the regulatory pathway for human heart valves which are no longer approved via the HCT/P 361 route, but instead are now classified as a medical device that requires a PMA study. It is possible in the longer term that TRX will entertain the idea of developing a porcine heart valve.

We forecast a 2017 European launch with only modest penetration, given the lack of suitable donor valves, ramping to ca.1% penetration of the European aortic valve replacement segment of the market, which implies sales of ca.£1.6m in 2020.

CardioPure – European sales model

Year end Jan (£000)	2016E	2017E	2018E	2019E	2020E
Volume	0	50	200	350	438
% growth	0%	0%	300%	75%	25%
Price per unit	0	5,000	5,000	5,000	5,000
Europe sales	0	250	1,000	1,750	2,188
Europe (£)	0	185	741	1,296	1,620
AVR in Europe	0	56,000	56,560	57,126	57,697
% AVR	0.0%	0.1%	0.4%	0.6%	0.8%

Source: Hardman & Co Life Sciences Research

Competition

The key competitor products to CardioPure HV are highlighted in the following table.

Competitive position – surgical aortic and pulmonary valves

Company	Brand	Product type
Edwards Lifesciences	Perimount, Magna	Bovine
Medtronic	Freestyle, 3f	Porcine, equine
St Jude Medical	Trifecta	Bovine
Sorin	Mitroflow	Bovine
CryoLife	CryoValve	Human

Source: Company reports; Hardman & Co Life Sciences Research

[21] Kneib C, et al. Tissue Antigens 2012;80: 165–74.

Financials & Investment case

Profit & Loss

Sales of £0.5m expected in FY 2016 and rising to ca.£29m in 2020....

... but conservative wound care penetration forecasts...

...limited OrthoPure sales....

... and no account of OrthoPure (porcine variant) in the US

Sales

TRX reported 1H 2016 sales of £0.252m, following the launch of DermaPure in the USA in June 2014. It wasn't really until TRX achieved reimbursement clearance (Q code) in November 2011 that it was able to begin to market the product to out-patient clinics which began to accelerate as coverage was approved in the various MAC Jurisdictions. Sales are expected to be ca.£0.5m in FY 2016, rising to £2.0m in FY 2017, driven largely by DermaPure as greater awareness and increased KOL sponsorship drives adoption from out-patient clinics. We currently forecast ca.£0.5m of revenues for OrthoPure in FY 2017. Revenue forecasts take account of the hybrid nature of sales capture, with a 40% distributor margin assumed for DermaPure in the USA, OrthoPure XM/XT and CardioPure HV in Europe.

We forecast Group revenues of ca.£29m in 2020, comprising sales of £19m for DermaPure, £8m for OrthoPure XM/XT in Europe and £2m for CardioPure HD in Europe. OrthoPure revenues could be potentially higher pending the outcome of CE Mark studies, expected in 2H 2016.

Gross margins of 74-78%

Gross profit

Cost of goods are expected to be ca.23-24% of the sales in FY2016, falling to 22-23% in FY2017/18 before rising to around 25-26% in 2020. Although the cost of goods on porcine-based products (OrthoPure XM/XT and SurgiPure XD) is expected to be less that on human tissues, gross margins actually fall slightly to over the forecast period as a consequence of distributor based revenues, in which we assume a 40% distributor margin

Operating expenses rising to ca.10.2m in FY16 (+23%), reflecting commercial build-up in

Operating expenses

Operating expenses have risen from ca.£3m in FY 2012 to £8.3m in FY 2015 as a consequence of rising development costs, PLC overheads and the build-up of a commercial organisation in the USA from late 2012. These expenses are expected to rise to £10.2m in FY 2016 of which ca.£4m can be attributed to Development costs; the balance of ca.£6.2m (+46%) driven by the creation of a 13-person sales force in the USA. Within these costs are the commissions, payable to its direct sales force in the US, which are estimated to be about 40% of gross revenues.

EBITDA positive in 2020...

...assuming a 1.2% share of hard-to heal wounds in 2020...

... which would be as much as £10m if achieved a 3% share

Profitability

We forecast Tissue Regenix to become profitable in 2020 with an EBITDA contribution of ca.£0.5m. Our forecasts are highly sensitive to the penetration rates for OrthoPure and DermaPure. A positive Phase IV post-launch randomised controlled study for DermaPure versus standard of care, expected to report in 2H 2016, would most likely increase adoption rates and market penetration. Equally, we have yet to see the outcomes for two CE Mark studies recently started for OrthoPure XM/XT, which could have a significant impact on OrthoPure revenues in 2020. Revenues and EBITDA, given the good gross margins (higher for porcine-derived tissues), are highly susceptible to market share assumptions. For instance, the model only assumes a 1.2% share of hard to heal wounds for DermaPure in 2020, rising to 4.3% in 2025. Should TRX be able to achieve a 3% share of the hard-to-heal wounds in 2020 (implying ca.100k units per annum), EBITDA would rise to around £10m.

R&D tax credits

Under the UK patent box TRX receives R&D tax credits which will help to offset corporation tax payable on US and European profits as they arise. Tax payable by the company is not expected to be paid until 2021 at the earliest.

Profit & Loss account

Year end Jan (£000)	2013	2014	2015	2016E	2017E	2018E	2019E	2020E
Sales	**49**	**6**	**100**	**494**	**2,067**	**6,073**	**14,716**	**28,259**
COGS	0	0	0	-116	-468	-1,381	-3,781	-7,540
Gross Profit	**49**	**6**	**100**	**377**	**1,599**	**4,691**	**10,935**	**20,719**
SG&A	-2,257	-3,133	-4,240	-6,200	-7,853	-9,831	-12,467	-15,477
R&D	-2,122	-3,356	-4,049	-4,000	-6,000	-8,000	-8,000	-5,000
Underlying EBITDA	**-4,256**	**-6,359**	**-8,038**	**-9,823**	**-12,253**	**-13,140**	**-9,532**	**243**
Depreciation & Amortisation	-74	-124	-151	-190	-190	-209	-220	-231
Licensing/Royalties	0	0	0	0	0	0	0	0
Other income	0	0	0	0	0	0	0	0
Underlying EBIT	**-4,330**	**-6,483**	**-8,189**	**-10,013**	**-12,443**	**-13,350**	**-9,752**	**12**
Share based costs	-82	-94	-180	-190	-210	-230	-250	-270
Exceptional items	0	0	0	0	0	0	0	0
Statutory Operating profit	-4,412	-6,577	-8,369	-10,203	-12,653	-13,580	-10,002	-258
Net financial income	440	274	168	123	164	71	127	50
Pre-tax profit	**-3,890**	**-6,209**	**-8,021**	**-9,890**	**-12,280**	**-13,279**	**-9,626**	**61**
Exceptional items	0	0	0	0	0	0	0	0
Reported pre-tax	-3,972	-6,303	-8,201	-10,080	-12,490	-13,509	-9,876	-209
Reported taxation	474	710	620	810	800	1,200	1,600	1,600
Underlying net income	**-3,416**	**-5,499**	**-6,679**	**-9,080**	**-11,480**	**-12,079**	**-8,026**	**1,661**
Statutory net income	-3,498	-5,593	-7,581	-9,270	-11,690	-12,309	-8,276	1,391
Period-end shares (m)	653	653	654	760	760	759.7	759.7	759.7
Weighted average shares (m)	635	636	637	749	760	759.7	759.7	759.7
Fully diluted shares (m)	653	653	654	765	777	776.6	776.6	776.6
Underlying Basic EPS (p)	**-0.54**	**-0.87**	**-1.05**	**-1.21**	**-1.51**	**-1.59**	**-1.06**	**0.22**
U/l Fully-diluted EPS (p)	**-0.52**	**-0.84**	**-1.02**	**-1.19**	**-1.48**	**-1.56**	**-1.03**	**0.21**
Statutory Basic EPS (p)	-0.55	-0.88	-1.19	-1.24	-1.54	-1.62	-1.09	0.18
Stat. Fully-diluted EPS (p)	-0.54	-0.86	-1.16	-1.21	-1.51	-1.59	-1.07	0.18
DPS (p)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Growth								
Sales	n/a	-88%	1567%	394%	319%	194%	142%	92%
Operating ratios								
Cost of goods	0.0%	0.0%	0.0%	23.5%	22.6%	22.7%	25.7%	26.7%
Gross margin	n/a	n/a	n/a	76.5%	77.4%	77.3%	74.3%	73.3%
SG&A	n/a	n/a	n/a	1256%	380%	162%	85%	55%
R&D	n/a	n/a	n/a	810%	290%	132%	54%	18%
EBITDA	n/a	n/a	n/a	n/a	-593%	-216%	-65%	1%
Operating profit	n/a	n/a	n/a	n/a	-602%	-220%	-66%	0%
Reported tax rate	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

Source: Company reports; Hardman & Co Life Sciences Research

Balance sheet

- TRX ended FY2015 with net cash of £10.3m. Having raised a net £19m in January 2015 we forecast TRX to have net cash of £20.45m at 31st January 2016
- Our forecasts assume that TRX continues to invest behind its pipeline of products which include a PMA study for both OrthoPure XM and XT in the US which will cost around $20m (£13m)
- To remain cash positive, these costs are likely to be borne either by a further equity funding (estimated £20m) or the possibility of a collaboration with potential future partner
- It is certainly not clear yet which route will be pursued. Much will depend on the outcome of the two CE Mark studies currently being undertaken for OrthoPure XM and XT in Europe, the results from which are expected in 2H 2016.

Balance sheet

@31st Jan (£000)	2013	2014	2015	2016E	2017E	2018E	2019E	2020E
Shareholders funds	24,466	18,978	11,578	21,280	9,590	17,281	9,005	10,397
Cumulated goodwill	0	0	0	0	0	0	0	0
Total equity	24,466	18,978	11,578	21,280	9,590	17,281	9,005	10,397
Share capital	3,264	3,267	3,271	3,798	3,798	3,798	3,798	3,798
Reserves	21,202	15,711	8,307	17,482	5,792	13,483	5,207	6,599
Capitalised R&D	3,355	5,632	8,109	10,087	13,434	17,833	21,314	21,307
Long-term loans	0	0	0	0	0	0	0	0
Bank overdrafts	0	0	0	0	0	0	0	0
less: Cash & securities	24,206	18,483	10,257	20,450	8,814	15,825	6,215	5,490
Invested capital	**3,615**	**6,127**	**9,430**	**10,917**	**14,209**	**19,289**	**24,105**	**26,214**
Fixed assets	238	472	435	388	366	379	438	555
Intangible assets	0	0	0	0	0	0	0	0
Capitalised R&D	3,355	5,632	8,109	10,087	13,434	17,833	21,314	21,307
Stocks	0	0	34	65	210	613	1,424	2,944
Trade debtors	2	0	40	41	175	558	1,424	2,944
Other debtors	705	1,127	1,907	1,907	1,907	1,907	1,907	1,907
Trade creditors	-205	-368	-312	-65	-158	-446	-997	-1,766
Tax liability	-54	-55	-73	0	0	0	0	0
Other creditors	-426	-681	-710	1,883	1,925	2,019	2,334	3,084
Debtors less creditors	22	23	852	377	199	463	929	1,409
Invested capital	**3,615**	**6,127**	**9,430**	**10,917**	**14,209**	**19,289**	**24,105**	**26,214**
Key metrics	**2013**	**2014**	**2015**	**2016E**	**2017E**	**2018E**	**2019E**	**2020E**
Net cash/(debt)	24,206	18,483	10,257	20,450	8,814	15,825	6,215	5,490
Net debt/equity (%)	98.9%	97.4%	88.6%	96.1%	91.9%	91.6%	69.0%	52.8%
After-tax ROIC	-94.5%	-89.8%	-70.8%	-83.2%	-80.8%	-62.6%	-33.3%	6.3%
Interest cover (x)	-	-	-	-	-	-	-	-
Dividend cover (x)	-	-	-	-	-	-	-	-
Cap-ex/depreciation (x)	2.1	2.9	0.8	0.8	0.9	1.1	1.3	1.5
Cap-ex/sales (%)	316.3%	5966.7%	114.0%	28.9%	8.6%	3.7%	1.9%	1.2%
Net asset value/share (p)	3.9	3.0	1.8	2.8	1.3	2.3	1.2	1.4
Stock days	-	-	-	80	60	55	50	50
Debtor days	-	-	-	50	50	50	50	50
Creditor days	-	-	-	80	45	40	35	30

Source: Company reports; Hardman & Co Life Sciences Research

Cashflow

- TRX has had an increasing free cash outflow over the past three years as it has ramped up both marketing and development capabilities across a broad pipeline of product families
- The incremental increase (ca.£9-10m estimate) in R&D investment in 2017 and 2018 to fund potential US studies for OrthoPure XM/XT in the USA drops straight through the cashflow statement
- Free cash outflows therefore are expected to continue to rise, peaking in FY2018 at ca.£13m after which DermaPure becomes sufficiently well established to begin to offset underlying burn
- Our forecasts do not assume any revenues from OrthoPure XM/XT in the USA. In the event that TRX markets OrthoPure XM/XT on its own in the US, there would likely to an increase in investment and working capital towards the end of the decade. In contrast, a decision to out-license or partner the product could result in an up-front milestone receipt.
- The outcome of these CE Mark studies should determine the route for exploiting the US market and whether or not the ca.$20m investment in clinical trials is justified.

Cashflow

Year end Jan (£000)	2013	2014	2015	2016E	2017E	2018E	2019E	2020E
Operating profit/(loss)	-4,412	-6,577	-8,369	-10,203	-12,653	-13,580	-10,002	-258
Depreciation	74	124	151	190	200	209	220	231
Amortisation	0	0	0	0	0	0	0	0
Stocks	0	0	-34	-31	-145	-403	-811	-1,520
Working capital	-86	238	-213	-248	-42	-94	-316	-750
Share based payment	82	94	180	190	210	230	250	270
Company op cashflow	**-4,342**	**-6,121**	**-8,285**	**-10,101**	**-12,431**	**-13,637**	**-10,659**	**-2,027**
Net interest	440	274	168	123	164	71	127	50
Tax	239	474	0	1,342	810	800	1,200	1,600
Operational cashflow	-3,663	-5,373	-8,117	-8,636	-11,458	-12,766	-9,332	-378
Capital Expenditure	-155	-358	-114	-143	-178	-223	-278	-348
Sale of fixed assets	0	0	0	0	0	0	0	0
Free cashflow	**-3,818**	**-5,731**	**-8,231**	**-8,779**	**-11,636**	**-12,989**	**-9,610**	**-725**
Dividends	0	0	0	0	0	0	0	0
Other investments	0	0	0	0	0	0	0	0
Cashflow after investments	**-3,818**	**-5,731**	**-8,231**	**-8,779**	**-11,636**	**-12,989**	**-9,610**	**-725**
Share repurchases	0	0	0	0	0	0	0	0
Share issues	3	8	5	18,972	0	20,000	0	0
Change in net debt	**-3,815**	**-5,723**	**-8,226**	**10,193**	**-11,636**	**7,011**	**-9,610**	**-725**
Opening net cash	28,021	24,206	18,483	10,257	20,450	8,814	15,825	6,215
Closing net cash	**24,206**	**18,483**	**10,257**	**20,450**	**8,814**	**15,825**	**6,215**	**5,490**
Hardman cashflow/share (p)	-0.6	-0.8	-1.3	-1.2	-1.5	-1.7	-1.2	0.0

Source: Company reports; Hardman & Co Life Sciences Research

Valuation

Discounted cashflow

The best approach, in our opinion, to valuing medical device companies is to prepare detailed discounted cashflow analyses of key products. Unlike pharmaceutical products whose cashflows typically decline rapidly after patent expiry and in which there is little terminal value, medical devices, particularly in wound care, have everlasting brand value, if managed correctly, and consequently have a terminal value which, for an early stage company, typically represents the lion share of the NPV.

Key assumptions

- TRX markets DermaPure and OrthoPure in the US via hybrid distribution model and CardioPure in Europe via distributors
- Forecast free cashflow to 2025
- The weighted average cost of capital is 10.1%
- Terminal growth rate of 2%
- Limited regulatory risk given that DermaPure is already launched and that the human versions of OrthoPure and CardioPure are approvable through HCT/P 361 pathway in the US and EU Tissue Directive rather than clinical trials. Only SurgiPure XD requires FDA clearance via 510(k) which is expected in 1H 2016
- Does not include potential cashflows from OrthoPure XM/XT which could launch in 2020, despite the fact that we include the costs of clinical trials for these indications (ca.$15-20m)

Our DCF model uses the following core inputs, from which the weighted average cost of capital is calculated at 10.1%. Given that most early stage life science companies raise capital from the markets to fund their projects, their WACC is actually the cost of equity and, at this point in time, 10.1% seems to be a sensible figure.

Core inputs	
WACC	**10.1%**
% of debt	0%
% of Equity	100%
Equity Beta	1.00
Average Interest Rate	0.5%
CAPM	10.1%
Risk-free Rate	1.9%
Market return	7.0%
Market Risk	5.1%
Terminal Growth	**2%**

Source: Hardman & Co Life Sciences Research

Net present value – 42p per share

The NPV of the discounted cashflows for the forecast period, and assuming a 2% terminal growth rate, equates to £316m or 42p per share on a fully diluted basis. Like many early stage commercial companies, the value of the technology platform lies primarily in the terminal value. In this case it accounts for 98% of the NPV. TRX continues to invest in building the dCELL platform.

We have not risk adjusted the NPV, given that DermaPure is already being marketed in the US. Although OrthoPure XM/XT and CardioPure HV have yet to be cleared via CE Mark in Europe we consider the risks of not achieving this to be low. Given that we have not included any revenues for OrthoPure XM/XT in the US, where there is the greatest risk of trial failure, we do not need to risk-adjust any associated cash flows (although the full costs of conducting those PMA studies are included), which by doing so actually depresses the NPV calculation.

DCF analysis			
Discounted Cash Flow for Forecast Period (£m)		7	2%
Terminal Value (£m)		288	98%
Total Enterprise Value (£m)		**295**	**100%**
Net cash/(debt) in year 1 (£m)		20	
Implied market value (£m)		**316**	
Fully diluted shares (m)		760	
Implied value per share (p)		**42**	
Risk adjustment/probability	80%	100%	
Risk-adjusted NPV (p)	**33**	**42**	

Source: Hardman & Co Life Sciences Research

Sensitivity analysis

We provide a sensitivity analysis, comparing the effect of WACC against different terminal growth rates.

WACC sensitivity analysis

Terminal growth rate	WACC 8%	9%	10%	11%	12%	15%
0%	43	38	34	31	29	23
1%	48	43	37	34	31	25
2%	56	48	42	38	34	26
3%	66	55	47	42	37	28
4%	81	66	54	48	42	31
5%	107	81	64	55	47	34

Source: Hardman & Co Life Sciences Research

However, the most significant sensitivity to the potential value of TRX is the share of hard to heal wounds that DermaPure is able to secure in the USA. Our base case is for DermaPure to secure a ca.4% share of the US market in 2025, which represents ca.190k units, two thirds of which we estimate to be through its network of distributors. This equates to annual sales of $105m. If one was to assume that TRX can capture 10%, the NPV rises to 119p with sales of $225m.

Company matters

Registration

Incorporated in the UK with company registration number 05969271

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Board of Directors

The Board consists of three executive directors, including the Chairman, and three non-executive directors. Their representation on the various committees is shown in the following table.

Board of Directors

Position	Name	Remuneration	Audit
Chairman	John Samuel		
Chief Executive Officer	Antony Odell		
Chief Financial Officer	Ian Jefferson		
Non-executive director	Allan Miller	M	C
Non-executive director	Randeep Grewal	M	M
Non-executive director	Steven Couldwell	C	M

M = member; C = chair
Source: Company reports

John Samuel – Executive Chairman

John joined Tissue Regenix as Executive Chairman in March 2008. John qualified as a Chartered Accountant with Price Waterhouse and has held a number of senior finance positions in industry, including as Financial Director of Whessoe plc and Ellis & Everard plc. He was formerly the CEO of the Molnlycke Health Care Group, a global provider of single use surgical and wound care products to the healthcare sector. Until January 2010 he was a Partner with Apax Partners LLP.

Antony Odell – Chief Executive Officer

Antony joined Tissue Regenix in January 2008 and was subsequently appointed Managing Director of Tissue Regenix in October 2008. He has extensive commercial experience in the medical technology sector. As well as working as Co-Director of Xeno Medical, a medical technology consultancy, he was CEO for a UK NHS cardiovascular device spin-out, Tayside Flow Technologies Ltd. Antony has a strong corporate sector background having worked for J&J Medical for almost 10 years in European business development roles for Drug Delivery & Vascular Access and as General Manager (UK) for Fresenius (Critical Care & Diagnostics).

Ian Jefferson – Chief Financial Officer

Ian joined Tissue Regenix as Chief Financial Officer in June 2011. Ian was formerly Chief Executive Officer of AIM listed, COE Group plc. Having initially joined COE as CFO in 2007 he became CEO in 2008, restructured the Group and then successfully planned and executed its sale.

Prior to COE, Ian held a number of senior finance positions within LSE-quoted companies, most recently as Group Financial Controller of 600 Group Pl He has a comprehensive financial and operations background and extensive experience of organisational transformation and M&A. A qualified chartered accountant, Ian holds a BSc in Physics with Electronics from Manchester University and an MSc in Applied Radiation Physics from Birmingham University.

Alan Miller – Non-Executive Director

Allan is a founding partner of SCM Private, the wealth management company. He was formerly the Chief Investment Officer and founding shareholder of New Star Asset Management from early 2001 until early 2007. Prior to that, he was a Director at Jupiter Asset Management in charge of their specialist high performance division between 1994 and 2000. He is also a qualified accountant.

Randeep Grewal – Non-Executive Director

Randeep has 15 years' experience working in the institutional investment arena and, until December 2012, was a Senior Portfolio Manager and member of the European equities team at F&C Asset Management. Randeep has also held investment analyst and portfolio management roles at ICAP Equities and Tudor Capital, where he spent 10 years covering and investing in healthcare companies. Randeep has considerable entrepreneurial expertise, having been involved in a number of start-up companies, both personally and as an investor, and qualified in Medicine from the University of Cambridge.

Steven Couldwell – Non-Executive Director

Steven is currently Vice President and Head of Global Biosurgery at Sanofi, which has revenues of approximately $750m. He has a proven international track record in driving revenues and profit growth in both the medical device and CRO industries. Steven was formerly Vice President and General Manager of Covance Laboratories Europe and worked for Smith & Nephew for almost 20 years in a number of roles including President Orthopaedics (Europe) and Senior VP Sales and Marketing for Smith & Nephew's Advanced Wound Management business.

Jonathan Glenn – Non-Executive Director

Jonathan joined the Board on 19th January 2016. He has been Chief Executive Officer at Consort Medical plc since December 2007, having originally joined the company in September 2006 as Chief Financial Officer. Prior to this, he held a number of senior financial roles across the medical industry including Akubio Ltd (2005- 2006) and the Celltech Group plc (1998-2005). He has a broad range of commercial experience across the medical devices industry, particularly with regard to clinical trial management and the US market place. During his time with Celltech he was pivotal in the acquisitions of Chiroscience, Medeva and OGS.

Executive management team

Tissue Regenix has a number of senior executives that support the Board executives, who provide considerable industry expertise, covering manufacturing and quality control, marketing, R&D and business development.

Executive management team	
Name	**Position**
Dr Helen Berry	Research & Technical Manager
Greg Bila	President, Tissue Regenix USA
Peter Hamer	Commercial Director – Orthopaedics
Tony Hewitt	UK Operations Director
Professor Eileen Ingham	Consultant
Mike Izon	Head of QA/RAA
Andrea Rausch	Commercial Director - Cardiac

Source: Company reports

Company history

The origins of Tissue Regenix can be traced to the laboratories of the University of Leeds, where the dCELL technology was developed by Professor Eileen Ingham and Professor John Fisher. The Company was incorporated in the UK in 2006 to develop and commercialise this technology, gaining its first European approval (CE Mark) for its dCELL Vascular Patch in 2010. Since then, Tissue Regenix has developed partnerships with medical research partners including the Pontifical Catholic University of Parana (PUCPR) and Cardioprotese Ltda, both based in Brazil, to develop decellularised heart valves and with the NHSBT to develop human tissue applications. In 2012 the Company opened a US office in the San Antonio, Texas as a precursor to commencing commercial operations which began in 2014 with the launch of dCELL dermis matrix for the treatment of chronic wounds.

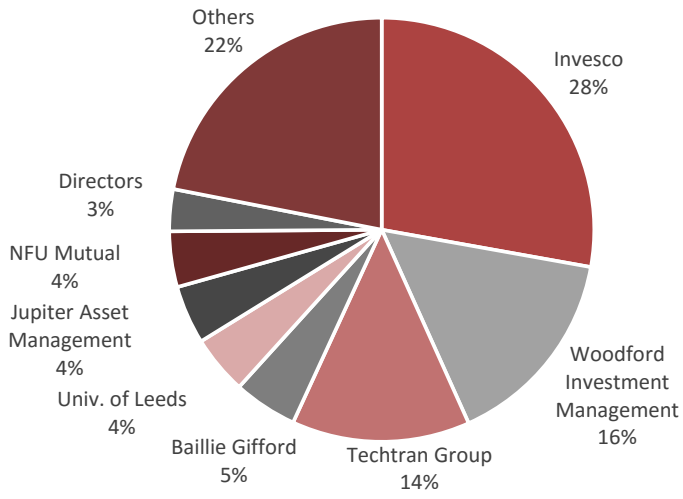
Capital increases

Since its Listing on AIM in 2010, Tissue Regenix has raised £45m gross funds. Year end January 2016 cash balances are estimated to be ca.£21m. Dependent on future development & marketing strategies, further capital may be required.

Share capital

The company has 759,653,093 shares in issue.

Major shareholders



Source: Company reports

Risks

Background

Investments in small early stage companies carry a significant risk and investors must be aware of this fact. In our opinion, the following risks are particularly relevant. Each of them could have an impact on time to reach market, cash flow breakeven and profitability.

Dilution risk

The company has sufficient cash to fund the ongoing development programme for OrthoPure XM/XT in Europe and to expand the commercial structure in the USA for DermaPure. Thereafter, it will most probably need additional capital to fund the additional regulatory studies for OrthoPure XM/XT in the US which we estimate would require an additional £15m.

Commercialisation

Management currently intends to sell the products in the US through a hybrid sales model, using distributors as well its own direct sales force. In Europe it intends to use distributors. For a small company, managing a distributor network presents many challenges.

Manufacturing and suppliers

The current strategy of management is to have out-source the production of human tissue types to appropriate tissue banks in the US. This inherently carry risks of failure over which the Company has a lower degree of control. Problems at contractors' facilities may also lead to delay. The Company has mitigated against this by using large and reputable manufacturers within the human tissue bank market.

Patent robustness

As with all IP-rich companies, there is risk that the intellectual property is insufficiently covered by the global patents, allowing a competitor to gain market access. Any litigation could involve significant costs and uncertainties.

Regulatory

It is important for companies to liaise with regulators on a regular basis throughout the development programme. Any inadequacies could lead to regulatory action such as cessation of product development and loss of manufacturing or product licences. Equally there is a risk for those products which require a clinical study to ensure regulatory clearance that they will fail to meet the predetermined endpoints.

Share liquidity

As with many small cap companies listed on AIM, there can be difficulty in buying and selling shares in volume. Market makers only guarantee prices in a very small number of shares.

Competition

The Company operates in a market dominated by larger competitors, many of which have greater financial resources to fund development programmes, marketing activities, substantive training solutions to potential wound care nurses etc.

Notes

Notes

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