EDISON

Regeneus

Initiation of coverage

Multipotent(ial) opportunities

Pharma & biotech

Regeneus is focused on the development and commercialisation of its adipose (fat) derived mesenchymal stem cell technology. This has the potential to deliver multiple product opportunities across animal and human health markets. Following its A$10.5m IPO on the ASX in September 2013, the company is embarking on an expansive plan to leverage its product portfolio. We value Regeneus at A$141m, or A$0.77 per share, with Progenza (allogeneic stem cells for osteoarthritis) the key long-term value driver; a Phase I/II study is planned to start in H115.

Year end	Revenue (A$m)	PBT* (A$m)	EPS* (A$)	DPS (A$)	P/E (x)	Yield (%)
06/12	1.26	(4.94)	(0.03)	0.0	N/A	N/A
06/13	1.81	(7.71)	(0.05)	0.0	N/A	N/A
06/14e	2.64	(9.19)	(0.04)	0.0	N/A	N/A
06/15e	3.91	(10.59)	(0.04)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation, exceptional items and share-based payments. PBT excludes R&D tax rebate.

A solid base for growth

Regeneus has been commercialising autologous (patient-derived) stem cell-based products on the Australian veterinary (AdiCell) and human (HiQCell) markets since 2008 and 2011, respectively. Allogeneic (donor-derived) versions are now available (CryoShot for animals) and in development (Progenza for humans). All these products are used to treat musculoskeletal conditions in animals and humans, including osteoarthritis, tendinopathy and ligament injuries. Regeneus has also licensed rights (for animal use) to an autologous cancer vaccine, Kvax.

Multiple opportunities for expansion

The strategy is to increase the commercial value of these products in existing markets (Australia), while seeking to roll out certain products in the US, EU, Japan and Singapore in animal and human markets. This helps to de-risk the investment proposition away from the binary biotech model, although it adds an element of execution risk in attempting to deliver multiple projects across many markets.

Clinical validation required

Although AdiCell/CryoShot (A$0.8m sales since launch) and HiQCell (A$1.2m) are available in Australia, this is on the basis of being either a trial product, or exempt from standard regulatory approval on the back of clinical safety and efficacy data. The next phase of development will therefore test Progenza, CryoShot and Kvax in randomised, placebo-controlled clinical studies, which could generate the required data to enable greater market penetration and deliver long-term value.

Valuation: A$141m or A$0.77 per share

We value Regeneus at A$141m, or A$0.77 per share, based on a sum-of-the-parts DCF model, including potential development of multiple programmes. Progenza is a key long-term value driver (A$1.5bn peak sales potential) so clinical/regulatory progress would provide upside by de-risking the product (currently 15% probability).

25 March 2014

Price	**A$0.48**
Market cap	**A$89m**
	A$1.1/US$
Net cash (A$m) at 31 December 2013	6.6
Shares in issue	184.4m
Free float	83%
Code	RGS
Primary exchange	ASX
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(6.8)	29.7	N/A
Rel (local)	(5.3)	28.8	N/A
52-week high/low	A$0.60		A$0.24

Business description

Regeneus is an Australian biotechnology company marketing and developing mesenchymal stem cell (MSC) products for musculoskeletal conditions in humans and animals. Three products, HiQCell (human), AdiCell and CryoShot (animals), are available commercially in Australia. Progenza (allogeneic, off-the-shelf) will enter a Phase I/IIa study for osteoarthritis in H115.

Next events

Kvax: start registration efficacy study (US)	Q214
HiQCell: commercial launch in Singapore	H214
CryoShot: Australia RCT results	H214
Progenza: Start Phase I/II study in OA patients	H115

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Edison profile page

Investment summary

Company description: Exploiting adipose stem cell technology

Regeneus is an Australian (Sydney) biotechnology company, founded in 2007 to develop and commercialise the use of adipose (fat) derived cells, including mesenchymal stem cells (MSCs), to treat inflammatory conditions in animals and humans. AdiCell (autologous) was launched in Australia in 2008 to treat canine orthopaedic conditions, but is now effectively being replaced by CryoShot (allogeneic), which has been available on a pre-registration trial basis since 2012. HiQCell (autologous) was introduced in Australia in 2011 for human osteoarthritis. Fiscal FY14 revenues (mainly HiQCell and CryoShot) are estimated at A$2.6m. The shares have been listed on the ASX since the IPO in September 2013, which raised A$10.5m (A$9.6m net) from the sale of 42m shares at A$0.25 per share. Regeneus has 32 FTEs and held A$6.6m in cash as of 31 December 2013.

Valuation: A$141m or A$0.77 per share

We value Regeneus at A$141m, or A$0.77 per share, based on a sum-of-the-parts DCF model, using a standard 12.5% discount rate. This includes H114 (31 December 2013) net cash of A$6.6m. This is not a price target, and represents fair-value for the stock today, based on the potential development multiple programmes, including HiQCell (Australia, Germany, Singapore), Progenza (worldwide), CryoShot (worldwide) and Kvax (worldwide). Progenza is the key long-term value driver, with peak sales estimated at A$1.5bn, so clinical and regulatory progress over the next few years would significantly de-risk the product, which currently has a 15% probability of success.

Sensitivities: Clinical and commercial execution risk

Regeneus is subject to the risks typically associated with biotech company drug development, including the possibility of unfavourable or ambiguous outcomes in clinical trials, success of competitors and commercial decisions by partners or potential partners. Likewise, the company is commercialising certain products itself in Australia and Singapore (and potentially other territories), which adds an element of execution risk given the investment in infrastructure required. We have assumed timely clinical and commercial progress for multiple programmes across multiple geographies, which should be achievable, but any delays/setbacks would have a negative impact on our valuation. Development/commercialisation/distribution partners will need to be secured in multiple territories to enable the roll-out of these products. Regeneus has submitted patent applications to cover a range of current and future products, but these have yet to be granted, which adds an element of risk, particularly in relation to certain autologous products, which can be developed by medical and veterinary specialists.

Financials: IPO funds near-term, more required in H215

Regeneus recorded A$0.78m in revenues for fiscal H114 (half-year ended 31 December 2013), vs A$0.87m for fiscal H113. This was attributed to HiQCell (A$0.32m), CryoShot ($0.11m) and R&D-based licence fees (A$0.35m). Operating expenses increased significantly in fiscal H114 to A$6.8m (vs A$4.2m in H113), partly as a result of IPO costs and IPO-related bonuses (A$0.4m) / non-cash option expenses (~A$1m). We expect operating expenses to be lower in fiscal H214 (January-June 2014). Net cash as of 31 December 2013 was A$6.6m, which the company estimates is sufficient into fiscal H215 (January-June 2015); this assumes that Regeneus will receive an R&D-based tax rebate of A$3m (related to R&D expenses in FY14) in fiscal H115. A tax refund of A$2.3m (for FY13) was received in fiscal H114. The Australian government's R&D tax incentive scheme effectively reimburses 45% of eligible R&D costs and companies can receive one-off, lump-sum cash payments each year, related to R&D expenses in the prior year. For Regeneus, this is recorded as an income tax benefit on the P&L.

Advancing adipose derived MSCs

Regeneus is focused on developing and commercialising its proprietary, adipose (fat) derived stem cell technology platform. So far this has delivered three products to the Australian market (AdiCell and CryoShot for the veterinary market; HiQCell for human health), and the strategy is expand the commercial potential of these products through launches in new territories. Meanwhile, the company is also developing new products – Progenza (allogeneic cells for human health), Secretions (dermatology) and Kvax (autologous canine cancer vaccine) – which hold potential to reach the key global markets and be commercialised alone, or in partnership with regional players. The product portfolio (Exhibit 1) therefore offers a mixture of near- and long-term opportunities, with a number of fast-track routes to market. This helps to de-risk the investment proposition away from the classical binary biotech model, although it adds an element of execution risk in attempting to deliver multiple projects in different segments of global markets.

Exhibit 1: Regeneus product portfolio

	HiQCell	CryoShot	Progenza	Cancer vaccine (Kvax)	Secretions (topical)
Market	Human	Veterinary	Human	Veterinary (& human)	Human
Cell source/type	Autologous, adipose-derived	Allogeneic, adipose-derived	Allogeneic, adipose-derived	Autologous	Xenogeneic, (bovine) adipose-derived
Cell production	Unexpanded cells, point of care	Expanded cells, off the shelf	Expanded cells, off the shelf	Unexpanded cells, point of care	Cell secretions from expanded cells, off the shelf
Mode of admin	Intra-articular	Intra-articular	Intra-articular	sc injection	Topical
Primary indication	Osteoarthritis	Osteoarthritis	Osteoarthritis	Osteosarcoma	Acne
Regulatory status	Exempt biological under medico single patient procedure	Trial product availability (limited). Safety and efficacy studies required for full registration/approval	Biologic requiring multiple safety and efficacy clinical studies for approval	Biologic requiring safety and efficacy clinical studies for approval (some regions exempt)	Varies, depends on therapeutic claim/concentration
Key target markets	Australia, Singapore, Germany	Australia, US, EU, Japan	Australia, US, EU, Japan	Australia, US	Australia
Partner(s)	Cryosite Ltd – cryopreservation technology	Provet – distribution partner		Kolling Institute of Medical Research	

Source: Company documents; Edison Investment Research

HiQCell – adipose, autologous advantages

Adipose (fat) tissue has been shown to be an important source of bioactive factors, such as paracrine (cell-signalling) factors that are involved in a variety of wound healing and regenerative processes, including inflammation. Adipose tissue contains a number of different cell types that can be released from the connective tissue by enzymes (eg collagenase). Centrifugation then separates these cells into multiple layers, including adipocytes and pelleted cells that are referred to as the stromal vascular fraction (SVF). The SVF includes T-regulator cells, macrophages, endothelial cells, smooth muscle cells and high numbers of mesenchymal stem cells (MSC). Importantly, the SVF from adipose tissue contains approximately 500-1,000 times more MSCs per gram than bone marrow.[1] Adipose tissue can be obtained via minimally-invasive liposuction, the SVF (with a high-density of MSCs) is generated within a few hours, and re-injection of a patient's own cells (autologous) avoids potential auto-immune/rejection responses. The CD biomarkers on the cells produced appear to be consistent with current initiatives to standardise and characterise adipose-derived stromal and stem cells[2]. It is the paracrine factors produced by the MSCs that are believed to impart anti-inflammatory and regenerative effects.

1 On average, 100ml of human adipose tissue yields about 1 x 10^6 stem cells. Meliga E, et al (2007). Adipose-derived cells. Cell Transplant. 2007;16 (9): 963-70.

2 Bourin P, et al (2013). Stromal cells from the adipose tissue-derived stromal vascular fraction and culture expanded adipose tissue-derived stromal/stem cells: a joint statement of the International Federation for Adipose Therapeutics and Science (IFATS) and the International Society for Cellular Therapy (ISCT). Cytotherapy. 2013 Jun;15 (6): 641-8.

A summary of the HiQCell procedure is displayed in Exhibit 2. HiQCell is typically used to treat knee and hip joints in patients with osteoarthritis (OA) and tendinopathy, degenerative/overuse disorders affecting cartilage and tendons, respectively. As an autologous human cell therapy (HCT), obtained during a medical procedure conducted by medical practitioners, and processed by trained Regeneus technicians, HiQCell is exempt from standard regulation by Australia's regulatory agency, the Therapeutic Goods Administration (TGA). Clinical studies to determine safety and efficacy are therefore not required.

Exhibit 2: HiQCell procedure overview

Stage	Interaction with:	Location:	Process includes:
Stage 1	Referring practitioner (GP)	Consulting room	Initial consultation/diagnosis; referral to specialist medical practitioner
Stage 2	HiQCell specialist (orthopaedic surgeon / sports physician)	Consulting room	Pre-treatment consultation; HiQCell explained; consent signed; pathology screening
Stage 3	HiQCell specialist	Hospital clinic	Admission; liposuction (100-200ml) to harvest tissue (45 mins); stem cell preparation (enzymes/centrifugation; conducted by trained Regeneus laboratory technician; 45 mins); initial injection of SVF into joint; cryopreservation of excess cells, up to 3 further doses (if elected)
Stage 4	HiQCell specialist	Consulting room	Post-treatment follow-ups at: two weeks, three months, six months and 12 months; input for HiQCell Joint Registry; assessment for follow-up injection of cryopreserved cells (if elected; re-injection conducted in hospital/clinic)

Source: Company documents

HiQCell economics

The entire process, from first consultation to in-clinic treatment and follow-up, typically costs A$9,500 to the patient, which is an out-of-pocket expense (HiQCell is currently not covered by Medicare or any other reimbursement schemes). Cryopreservation is charged at A$2,400 and the follow-up re-injection fee is A$1,200. Regeneus charges the medical practitioner ~A$4,000 per procedure, as well as ~A$1,800 for cryopreservation and ~A$800 per re-injection. Regeneus's 'client' is therefore the medical practitioner, who earns the difference between Regeneus's charges and the patient fees.

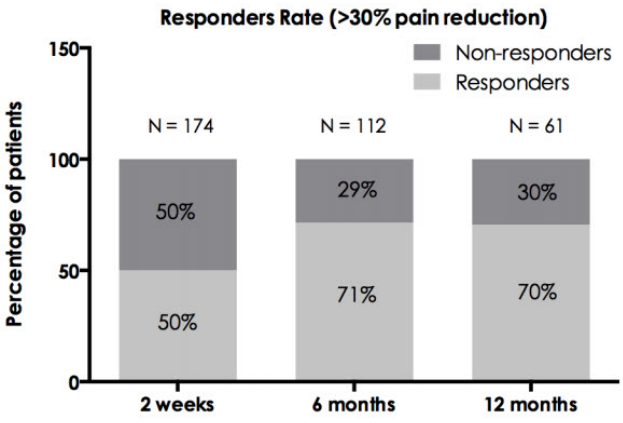
Edison estimates that the effective revenue to Regeneus per HiQCell procedure is ~A$4,800, with 40% of patients electing for cryopreservation and 35% being eligible for re-injection (price range A$3,740 without cryo/reinjection – A$7,190 with cryo/reinjection). Over time, Regeneus hopes to 'pull' more patients into specialist clinics, via direct-to-consumer (DTC) marketing campaigns, and so reduce the initial step of requiring a referral from a general practitioner.

Real-world experience

Although HiQCell does not require standard clinical studies to be available on the market, Regeneus has established 'The HiQCell Joint Registry', which has been tracking the safety and efficacy data from treated patients (if elected) since 2011. Effectively, this is a long-term observational study that collects clinical data and self-reported measurements of pain and functional outcomes, which is intended to continue for five years post-treatment. Overall, Regeneus has reported that, to date, HiQCell has been used in >400 patients, treating >860 joints. And as of 17 September 2013, a total of 238 patients have submitted baseline data for the Registry.

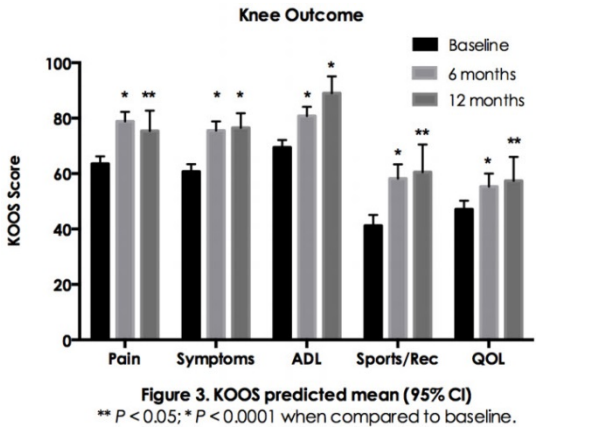
So far, data from the Registry show that HiQCell is safe and well tolerated, and patients experience significant reductions in pain, and improvements in knee functional outcomes and sleep quality (up to 12 months post-treatment). Headline Registry data are displayed in Exhibits 3 and 4. The Knee Osteoarthritis Outcome Score (KOOS) questionnaire (comprised of five subscales: pain, symptoms, activities of daily living, sports & recreational activities and quality of life), ranks knee function from zero (severely limited) to 100 (no limitations). All KOOS sub-scales significantly increased from baseline to six and 12-months post-treatment, indicating an improvement in knee function. These KOOS scores are also comparable to published studies in patients with a total knee replacement.

Exhibit 3: Responder rate (>30% pain reduction)



Source: The HiQCell Joint Registry

Exhibit 4: KOOS questionnaire analysis (n=193)



Source: The HiQCell Joint Registry

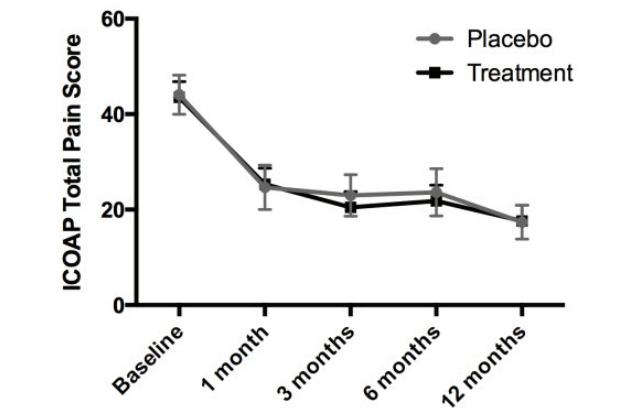
Clinical experience

Perhaps the most comprehensive assessment of HiQCell's treatment benefit was the Phase II (OSCARS), randomised, double-blind, placebo-controlled study of HiQCell for the treatment of knee osteoarthritis in 40 patients. Interim results were released in October 2013.

Patients (with OARSI grade 1 or 2 OA) were randomised (20:20) to receive a single intra-articular (joint) injection of HiQCell or saline (placebo) into the test knee. All patients underwent the liposuction procedure. The primary endpoint was a reduction in pain symptoms, measured by a patient-reported, OA specific pain questionnaire ICOAP (intermittent and continuous osteoarthritis pain index).[3] Secondary endpoints included assessments of long-term safety, biomarkers of disease progression and quality of life.

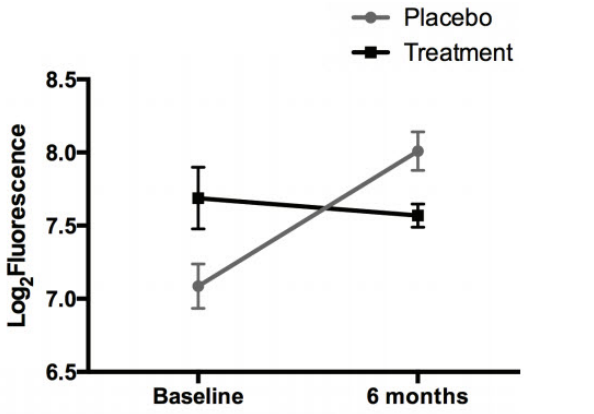
HiQCell was shown to be effective in reducing pain, according to the ICOAP index, although placebo patients experience similar reductions in pain scores (Exhibit 5). However MRI data and analysis of biomarkers of cartilage degradation – collagen fragment (CTX-II) in urine, and migration inhibitory factor (MIF) in serum – indicate that HiQCell has the potential to slow disease progression in OA (Exhibit 6). An elevated level of CTX-II in particular is proposed as a marker of cartilage degradation[4].

Exhibit 5: ICOAP total pain scores



Source: OSCARS interim report (October 2013)

Exhibit 6: Circulating serum MIF levels



Source: OSCARS interim report (October 2013)

3 Hawker G, et al (2011). Measures of Adult Pain. Arthritis Care & Research. Vol. 63, No. S11, November 2011, pp S240 –S252.

4 Lotz M, et al (2013). Value of biomarkers in osteoarthritis: current status and perspectives. Ann Rheum Dis. 2013 Nov 1;72 (11): 1756-63.

Progenza – off-the-shelf option

As a logical follow-on to HiQCell, Regeneus is developing an allogeneic (off-the-shelf) version of its adipose-derived stem cell technology. In contrast to HiQCell being exempt from regulatory approval, an allogeneic version, developed using fat derived from a donor, would be characterised as a biological medicine. The standard clinical trial process to determine safety and efficacy would therefore be required in order to gain regulatory approvals.

Regeneus is now acquiring the fatty tissue as the source of its cell therapy, and will conduct the required pre-clinical and cryopreservation studies in 2014 to gain ethics approval to start a Phase I/II study. Clinical trial lots will be produced in collaboration with Cryosite, a TGA-licensed facility in Sydney. The study is scheduled to start in H115 and render results by mid-2016. Given the prior clinical experience with HiQCell, the plan is to conduct this trial in patients with osteoarthritis of the knee (not healthy human volunteers), which could generate initial proof-of-concept data.

Need for alternatives to treat OA

Osteoarthritis (OA) is an idiopathic, incurable chronic musculoskeletal disease, regarded as a leading cause of functional disability among adults in developed countries. OA onset is most closely associated with ageing (for example, more severe grade 3-4 knee osteoarthritis affects 11.5% of people <70 years old, and 19.4% in those aged >80 years[5]) and the key effects are cartilage degradation and pain. It is classically referred to as a non-inflammatory disease but it is increasingly evident that inflammation plays a major role in OA disease progression. Patients with OA are typically managed with non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics to alleviate OA symptoms and to control the pain in affected joints. Intra-articular injections with hyaluronic acid-based products (e.g. Synvisc (Sanofi) US$500m sales in FY13) are also used extensively. A total joint arthroplasty (knee/hip replacement) is the ultimate treatment option when these therapies no longer provide symptomatic relief.

Alternative mid-stage treatment options are therefore required, and the potential regenerative effects of mesenchymal stem cells (MSCs) could provide such an option. Of particular relevance is the potential for MSCs to reduce disease progression, providing more than just symptomatic pain relief. As such, an off-the-shelf, MSC-based product such as Progenza could offer a significant advance in the treatment of OA, particularly in potentially reducing the time, and/or need, to joint replacement.

CryoShot – a veterinary solution

Regeneus's first marketed product was AdiCell, an autologous cell-based treatment for animals with orthopaedic conditions similar to HiQCell. AdiCell was launched in Australia in 2007 and has been used to treat >400 canine and equine orthopaedic 'patients' with good reported clinical outcomes. This relates to reductions in pain, lameness and stiffness, as reported by dog owner questionnaires.

The experience with AdiCell led to the development of HiQCell for human use, but also a more convenient, allogeneic (off-the-shelf) product derived from the fat tissue of donor animals. CryoShot offers many advantages, in being a less invasive procedure for animals, reducing time and money invested for the veterinarian and a more guaranteed concentration and quality of regenerative cells. A summary of the manufacturing and delivery process for CryoShot is displayed in Exhibits 7 and 8.

CryoShot is currently available in Australia as a pre-registration veterinary product for trialling purposes, which restricts use to 100 vials (2ml) per trial. For wider uptake in Australia, and prior to launch in the global markets of Europe, US and Japan, registration will be required, based on the evidence of clinical studies to demonstrate safety and efficacy of CryoShot. To this end, Regeneus is conducting a placebo-controlled study of CryoShot in Australia in up to 180 dogs with osteoarthritis, which uses the Canine Brief Pain Inventory (CBPI) to assess pain and inflammation.

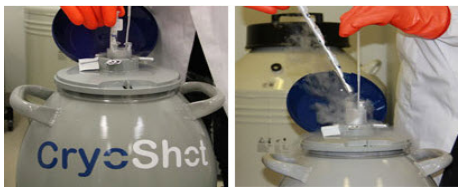
5 Epidemiology of Osteoarthritis (2005).

Exhibit 7: CryoShot manufacturing/admin process

Step	Process
1	Adipose tissue is collected from donor animals
2	Processed to isolate the regenerative cells
3	Cultured to increase the regenerative cells
4	Frozen in liquid nitrogen
5	Shipped to the vet
6	Thawed and injected

Source: Company documents

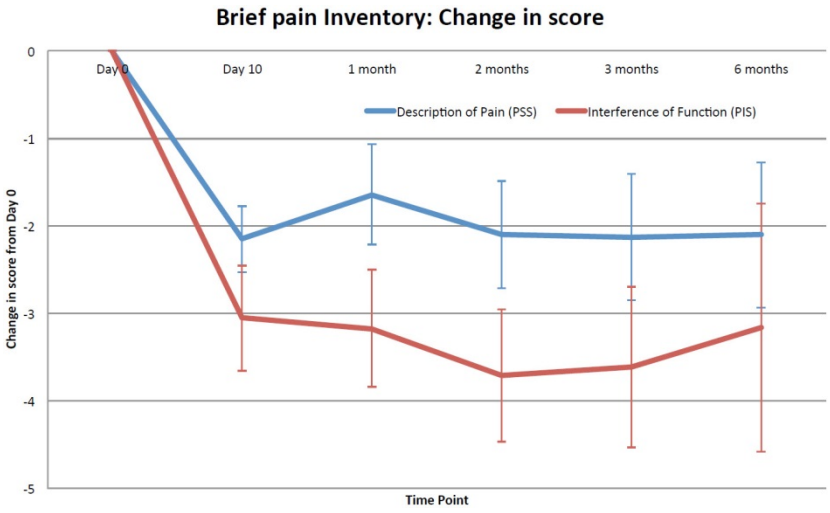
Exhibit 8: CryoShot 2ml vials stored in liquid nitrogen



Source: Company website

Regeneus has also been running an open label with CryoShot in 29 dogs and initial data (Exhibit 9) seems encouraging, specifically in terms of reductions in the pain severity score (PSS) and pain interference score (PIS) at multiple intervals (day 10 and months one to six) compared to baseline (day 0). A recent study to evaluate carprofen (vs placebo) as a treatment for the control of pain and inflammation in dogs with osteoarthritis determined that treatment success can be defined as a reduction of ≥1 in PSS and ≥2 in PIS.[6] The data so far (albeit in modest numbers of dogs) suggest that CryoShot is meeting this treatment success threshold. Final results are expected in H214.

Exhibit 9: Interim pain score data from CryoShot clinical study (Australia)



Source: Company documents. Notes: Description of Pain = PSS; Interference of Function = PIS; Number of dogs at each time interval: Day 0 (29 dogs), Day 10 (24), 1 month (19), 2/3 months (15), 6 months (7).

Regeneus has engaged the FDA and EMA over the registration trials required for approval. This study, expected to be conducted in the US, will contain a placebo arm and will use the CBPI scale of pain and inflammation. Lonza will manufacture the CryoShot product to be used in the registration trial in the US.

Kvax – a versatile cancer vaccine

In January 2013, Regeneus entered into a collaboration with the Kolling Institute of Medical Research for the development of an autologous cancer vaccine. This involves the removal of a tumour or biopsy from the 'patient' (dog/human) as source material to produce a personalised vaccine, which stimulates the immune system to see cancer cells as foreign, prompting T-cells to attack the tumour cells. Cancer vaccine as a technology has been studied extensively in clinical trials and multiple companies are currently developing variations on the same overall principle. Regeneus has an exclusive worldwide licence from the Kolling Institute for commercialisation of the cancer vaccine technology for veterinary applications, and an option over use in humans.

6 Brown DC, Bell M, Rhodes L (2013). Power of treatment success definitions when the Canine Brief Pain Inventory is used to evaluate carprofen treatment for the control of pain and inflammation in dogs with osteoarthritis. Am J Vet Res. 2013 Dec;74 (12): 1467-73.

Recently published research[7], in a rat model of glioma and a safety study in 25 dogs, produced encouraging results with the streptavidin (immunostimulant)-based autologous vaccine. Rats receiving two vaccinations demonstrated a significant ($p<0.05$) survival advantage compared with controls (streptavidin only), and also led to remission rates of 30-60% in the aggressive 9L glioma model. Use of Kvax in dogs, which presented to veterinary clinics in Sydney with a range of cancer types (melanoma to bone cancer), showed no adverse reactions and 63% (7/11) of diseased dogs survived longer than would otherwise be expected (based on tumour grade, histology, and/or oncology report).

In November 2013, Regeneus received confirmation from the Center for Veterinary Biologics at the US Department of Agriculture that it can commercialise this product in the US. This is expected to be achieved through a marketing study, to be conducted by a US partner, to generate real-world clinical study level results, which could support greater uptake of the vaccine in the long run. In addition, being an autologous vaccine, Kvax should not be limited to one tumour type, although initial research will focus on osteosarcoma, haemangiosarcoma and melanoma. An example of a marketed product is the canine oral melanoma vaccine (allogeneic) called Oncept, developed by Merial. Oncept was granted conditional approval in 2007 and subsequently awarded a full licence in 2010, after completion of clinical studies in dogs. Annual Oncept sales are estimated at US$4m.

Seeking broad IP coverage

Regeneus has filed nine families of patent applications, which if granted should substantially cover HiQCell, CryoShot and a range of future products. These patents will be fully owned by Regeneus. For the cancer vaccine, the company has exclusively licensed all related technology IP from the Northern Sydney Local Health District.

In relation to autologous products and procedures like HiQCell and AdiCell, it is known that some medical and veterinary specialists have developed and applied their own products along similar lines to the Regeneus versions. However, the impact of this appears to be minimal in the context of the overall market opportunity for these products. For allogeneic products, the relevant IP should afford more standard protection for a biological agent, which will also qualify for 12 years' market exclusivity in the US and 11 years in Europe.

A busy period

We detail the key near-term milestones for each of Regeneus's programmes in Exhibit 10.

Exhibit 10: Key milestone calendar

Product	Event	Date
HiQCell	Commercial roll-out in Singapore	H214
	Regulatory advice/pathway in Germany	H214
	Analysis of Registry (Aus) and MRI data	H214
Progenza	Fat procurement	Q214
	Pre-clinical safety study data	Q314
	Ethics approval for Phase I/II study (study design details)	Q414
	Start Phase I/II study	Q115
	Phase I/II efficacy data	Q216
	Define Japanese regulatory pathway and strategy	H214
CryoShot	Start registration efficacy study (US)	H115
	Registration efficacy results	H116
	Australia RCT results	H214
Kvax	Start efficacy trial in dogs (US marketing study)	Q214
	Efficacy trial results (US)	Q215
	Option to gain exclusive rights for human applications	H214

Source: Company documents

7 Weir C et al (2014). Streptavidin: A novel immunostimulant for the selection and delivery of autologous and syngeneic tumor vaccines. Cancer Immunology Research. Published OnlineFirst February 21, 2014.

Regeneus is attempting to advance multiple programmes across many regions over the next two years. The combination of the product offering and relatively limited regulatory requirements to register these products in these markets suggests this should be achievable.

Valuation

We value Regeneus at A$141m, or A$0.77 per share, based on a sum-of-the-parts DCF model, which is summarised in Exhibit 11. Our key assumptions are displayed in Exhibit 12.

Exhibit 11: Regeneus valuation model

Product	Setting	Region	Status	Launch	NPV (A$m)	Peak sales (A$m)	Probability of success	Economic interest	rNPV (A$m)	rNPV per share (A$)
HiQCell	Human – OA (knee/hip surgeries)	Australia	Marketed	2011	24.2	17	75%-100%	Operating profit (40%-60%)	18.4	0.10
HiQCell	Human – OA (knee/hip surgeries)	Singapore	Registration	2014	1.3	4	75%	30% effective royalty rate	0.8	0.00
HiQCell	Human – OA (knee/hip surgeries)	Germany	Registration	2015	16.4	26	65%	30% effective royalty rate	10.2	0.06
Progenza	Human – OA	Australia/ Japan/EU/ US	Phase IIa (planned)	2018 (Japan); 2020 (Aus); 2021 (EU/US)	327.9	1,526	15%	Royalty (15%)	43.8	0.24
CryoShot	Animal – OA	Australia	Pre-registration	2012	9.6	6	75%-100%	Operating profit (40%-60%)	7.2	0.04
CryoShot	Animal – OA	EU	Registration studies	2017	28.3	45	65%	30% effective royalty rate	17.9	0.10
CryoShot	Animal – OA	USA	Registration studies	2017	30.5	54	65%	30% effective royalty rate	19.3	0.10
CryoShot	Animal – OA	Japan	Registration studies	2016	3.7	10	65%	30% effective royalty rate	1.9	0.01
Canine vaccine	Dog cancer	WW	Marketing studies	2016	32.2	37	50%	30% effective royalty rate	15.2	0.08
Portfolio total					**474.0**				**134.6**	**0.73**
Cash (31 December 2013)									6.6	0.04
Overall valuation									**141.2**	**0.77**

Source: Edison Investment Research

Exhibit 12: Regeneus valuation model assumptions

Product	Setting	Region	Status	Launch	Key assumptions
HiQCell	Human – OA	Australia	Marketed	2011	Knee/hip surgeries used as a proxy for market opportunity; 45k knee surgeries (5% HiQCell peak penetration) + 36k hip surgeries (5% HiQCell); Current use mainly knee (66%) vs hip (10%); A$4,800 effective cost per procedure (includes cryo preservation fee/repeat dose estimates); peak sales in 2025; sliding scale of probability (100% near-term to 75% post-2020)
HiQCell	Human – OA	Singapore	Registration	2014	1,000 PRP procedures/year used as a proxy for market opportunity; 50% due to OA; 25% HiQCell peak penetration
HiQCell	Human – OA	Germany	Registration	2015	Knee/hip surgeries used as a proxy for market opportunity; 175k knee surgeries (2% HiQCell peak penetration in 2021) + 245k hip surgeries (1% HiQCell); equivalent A$5,000/procedure (includes cryo preservation fee/repeat doses); peak sales in 2021, then replaced by Progenza.
Progenza	Human – OA	WW	Phase IIa (planned)	2018 – 2021	Prevalence ~10% of >55yrs in all regions; 10% severe (grade 3+) OA requiring treatment; 5% Progenza peak market share (2025; 6 years to peak); A$10,000 per procedure (A$7,500 in EU); assume out-license after Phase IIb data (estimate A$8m R&D investment required).
CryoShot	Animal – OA	Australia	Pre-registration	2012	~4,500 small animal vet practitioners; peak penetration in 2021, with 5% use CryoShot, 75x per year, at A$250 per dose; sliding scale or probability (100% near-term to 75% post-2020)
CryoShot	Animal – OA	EU	Registration studies	2017	~90,000 small animal vet practitioners; peak penetration in 2025, with 3% use CryoShot, 50x per year, at A$250 per dose; 65% probability with studies/partners to complete
CryoShot	Animal – OA	USA	Registration studies	2017	~50,000 small animal vet practitioners; peak penetration in 2025, with 5% use CryoShot, 75x per year, at A$250 per dose; 65% probability with studies/partners to complete
CryoShot	Animal – OA	Japan	Registration studies	2016	~14,000 small animal vet practitioners; peak penetration in 2025, with 3% use CryoShot, 75x per year, at A$250 per dose; 65% probability with studies/partners to complete
Canine vaccine	Dog cancer	WW	Marketing studies	2016	~175/100,000 annual incidence of dog cancers; ~280,000 cancers US/EU/Japan/Aus; assume 33% get drug/vaccine treatment; 25% peak Kvax penetration of treated dogs by 2021 (=18,500 doses of Kvax); A$2,000/treatment course; 50% probability with studies/partners to complete

Source: Edison Investment Research

Our valuation model applies a standard 12.5% discount rate and includes H114 (31 December 2013) net cash of A$6.6m. We note that there is a risk-adjustment applied to each programme, appropriate to the status of development, and our valuation is not a price target but a fair-value for the stock today. Risk adjustments would unwind as programmes advance through clinical studies, gain regulatory approvals, secure commercial partners, etc.

Specifically, Progenza is the key long-term value driver, with peak sales estimated at A$1.5bn, so clinical and regulatory progress over the next few years would significantly de-risk the product, which currently has a 15% probability of success. Exhibit 13 illustrates the impact on the overall valuation on changing Progenza's probability of success (eg positive Phase I/II data would increase to 20-25%), and varying Regeneus's economic interest in the product, which will depend on multiple factors, including clinical validation data available at the time licensing deals are struck. Note that dilution from any future share issues is not taken into account.

Exhibit 13: Progenza sensitivity analysis (rNPV per share)

	Effective royalty rate			
Probability of success	**10%**	**15%**	**20%**	**25%**
10%	0.61	0.67	0.74	0.80
15%	0.67	0.77	0.86	0.95
20%	0.74	0.86	0.98	1.10
25%	0.80	0.95	1.10	1.25
30%	0.86	1.04	1.22	1.40

Source: Edison Investment Research

Sensitivities

Regeneus is subject to the risks typically associated with biotech company drug development, including the possibility of unfavourable or ambiguous outcomes in clinical trials, success of competitors and commercial decisions by partners or potential partners. Likewise, the company is commercialising certain products itself in Australia and Singapore (and potentially other territories), which adds an element of execution risk given the investment in infrastructure required. We have assumed timely clinical and commercial progress for multiple programmes across multiple regions, which should be achievable, but any delays/setbacks would have a negative impact on our valuation. Development/commercialisation/distribution partners will need to be secured in multiple territories to enable the roll-out of these products. Regeneus has submitted patent applications to cover a range of current and future products, but these have yet to be granted, which adds an element of risk, particularly in relation to certain autologous products, which can be developed by medical and veterinary specialists.

Financials

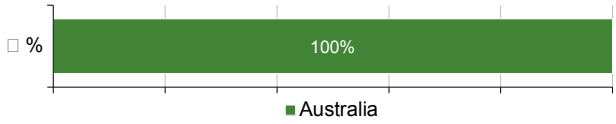
Regeneus recorded A$0.78m in revenues for fiscal H114 (half-year ended 31 December 2013), vs A$0.87m for fiscal H113. This was attributed to HiQCell (A$0.32m), CryoShot ($0.11m) and R&D-based license fees (A$0.35m). Operating expenses increased significantly in fiscal H114 to A$6.8m (vs A$4.2m in H113), partly as a result of IPO costs and IPO-related bonuses (A$0.4m) / non-cash option expenses (~A$1m). Operating expenses are expected to be lower in fiscal H214. Net cash as of 31 December 2013 was A$6.6m, which the company estimates is sufficient into fiscal H215; this assumes that Regeneus will receive an R&D-based tax rebate of A$3m (related to R&D expenses in FY14) in fiscal H115. A tax refund of A$2.3m (for FY13) was received in fiscal H114. The Australian government's R&D tax incentive scheme effectively reimburses 45% of eligible R&D costs and companies can receive one-off, lump-sum cash payments each year, related to R&D expenses in the prior year. For Regeneus, this is recorded as an income tax benefit on the P&L.

To cover the funding requirement by fiscal H215, we have attributed A$10m to long-term debt, as per standard Edison policy. Our financial model is summarised in Exhibit 14.

Exhibit 14: Financial summary

A$'000s	2012	2013	2014e	2015e	2016e
Year end 30 June	AASB	AASB	AASB	AASB	AASB
PROFIT & LOSS					
Revenue	**1,262**	**1,812**	**2,641**	**3,910**	**9,211**
Cost of Sales	(246)	(581)	(837)	(1,173)	(1,737)
Gross Profit	1,016	1,232	1,804	2,738	7,474
R&D expenses	(3,212)	(4,134)	(5,375)	(6,719)	(8,062)
SG&A expenses	(2,828)	(4,549)	(5,503)	(6,637)	(7,704)
EBITDA	**(4,910)**	**(7,256)**	**(8,929)**	**(10,366)**	**(7,939)**
Operating Profit (before GW and except.)	(5,017)	(7,437)	(9,112)	(10,606)	(8,276)
Intangible Amortisation	(6)	(15)	(10)	(12)	(16)
Exceptionals	0	0	0	0	0
Other	11	208	86	0	0
Operating Profit	**(5,012)**	**(7,244)**	**(9,036)**	**(10,618)**	**(8,292)**
Net Interest	72	(278)	(81)	19	46
Profit Before Tax (norm)	**(4,945)**	**(7,715)**	**(9,192)**	**(10,586)**	**(8,230)**
Profit Before Tax (FRS 3)	(4,940)	(7,522)	(9,117)	(10,599)	(8,246)
Tax benefit	1,679	2,327	3,000	3,023	3,628
Profit After Tax (norm)	**(3,266)**	**(5,388)**	**(6,192)**	**(7,563)**	**(4,602)**
Profit After Tax (FRS 3)	(3,261)	(5,195)	(6,117)	(7,575)	(4,618)
Average Number of Shares Outstanding (m)	102.9	102.9	148.7	184.5	185.5
EPS - normalised (A$)	**(0.03)**	**(0.05)**	**(0.04)**	**(0.04)**	**(0.02)**
EPS - FRS 3 (A$)	(0.03)	(0.05)	(0.04)	(0.04)	(0.02)
Dividend per share (A$)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	**572**	**653**	**2,033**	**2,378**	**2,986**
Intangible Assets	45	45	44	65	89
Tangible Assets	527	609	798	1,122	1,706
Investments	0	0	1,191	1,191	1,191
Current Assets	**2,724**	**3,370**	**8,324**	**10,820**	**6,030**
Stocks	143	231	390	546	809
Debtors	107	27	112	112	112
Cash	528	534	3,784	6,101	443
Other	1,946	2,579	4,039	4,062	4,667
Current Liabilities	**(1,348)**	**(6,892)**	**(1,138)**	**(1,138)**	**(1,138)**
Creditors	(1,294)	(1,842)	(997)	(997)	(997)
Short term borrowings	0	(4,900)	0	0	0
Other	(53)	(150)	(141)	(141)	(141)
Long Term Liabilities	**0**	**0**	**0**	**(10,000)**	**(10,000)**
Long term borrowings	0	0	0	(10,000)	(10,000)
Other long term liabilities	0	0	0	0	0
Net Assets	**1,949**	**(2,869)**	**9,219**	**2,060**	**(2,121)**
CASH FLOW					
Operating Cash Flow	**(2,940)**	**(4,618)**	**(6,426)**	**(7,064)**	**(4,696)**
Net Interest	0	0	0	0	0
Tax	0	0	0	0	0
Capex	(421)	(277)	(400)	(620)	(961)
Acquisitions/disposals	0	0	0	0	0
Financing	2,300	0	10,077	0	0
Dividends	0	0	0	0	0
Other*	0	0	4,900	0	0
Net Cash Flow	(1,062)	(4,895)	8,151	(7,684)	(5,657)
Opening net debt/(cash)	**(1,590)**	**(528)**	**4,366**	**(3,784)**	**3,899**
Other	0	0	0	0	0
Closing net debt/(cash)	**(528)**	**4,366**	**(3,784)**	**3,899**	**9,557**

Source: Edison Investment Research, company accounts. Note: *A$4.9m convertible notes as of fiscal year-end FY13 fully converted to ordinary shares on IPO listing in September 2013. Non-cash adjustment.

Contact details	Revenue by geography
25 Bridge Street Pymble NSW 2073 Sydney Australia +61 (0)2 9499 8010 www.regeneus.com.au	

CAGR metrics		Profitability metrics		Balance sheet metrics		Sensitivities evaluation	
EPS 09-13	N/A	ROCE 12e	N/A	Gearing 12e	N/A	Litigation/regulatory	●
EPS 11-13	N/A	Avg ROCE 09-13	N/A	Interest cover 12e	N/A	Pensions	○
EBITDA 09-13	N/A	ROE 12e	N/A	CA/CL 12e	N/A	Currency	◖
EBITDA 11-13	N/A	Gross margin 12e	N/A	Stock days 12e	N/A	Stock overhang	○
Sales 09-13	N/A	Operating margin 12e	N/A	Debtor days 12e	N/A	Interest rates	◖
Sales 09-13	N/A	Gr mgn / Op mgn YY	N/A	Creditor days 12e	N/A	Oil/commodity prices	○

Management team

CEO: Graham Vesey	Chairman: John Martin
Professor Graham Vesey is a co-founder and CEO of Regeneus. Prior to co-founding Regeneus, Prof Vesey was a co-founder and executive director of BTF, a biotechnology company acquired by bioMerieux in 2007. He is an adjunct professor at Macquarie University and a senior research fellow at the University of NSW.	Mr Martin was appointed chairman in 2010, having served on the board since early 2009. Previously he held CEO and director roles at ASX-listed and private companies. Mr Martin was co-founder and director of biotech spin outs from Macquarie University, BTF and Proteome Systems. He is currently a principal of The Channel Group, chairman of Ai-Media and director of Eagle Eye Solutions.

Principal shareholders	(%)
Graham Vesey (co-founder, CEO)	8.40
Limberg Asset Management	5.81
Ben Herbert (co-founder, non-exec director)	4.89
John Martin (chairman)	3.31

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Cytori Therapeutics (CYTX); TiGenix (TIG)

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