EDISON

Regeneus

Clinical trials imminent

Moving to human clinical trials for key products

Pharma & biotech

Regeneus will take a significant step forwards in the current quarter when it launches first-in-man trials for its Progenza off-the-shelf stem cell therapy and its human cancer therapeutic vaccine. The cancer vaccine could make Regeneus a player in the buoyant immuno-oncology space. Licensing deals, particularly for Kvax, CryoShot and Cell Secretions cream are further potential catalysts in 2015. After reviewing our clinical development timelines, our valuation is now A$106m (A$0.51 per share).

Year end	Revenue (A$m)	PBT* (A$m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
06/13	1.8	(5.2)	(5.03)	0.0	N/A	N/A
06/14	2.0	(7.5)	(4.51)	0.0	N/A	N/A
06/15e	1.6	(7.9)	(3.78)	0.0	N/A	N/A
06/16e	2.1	(7.0)	(3.36)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation, exceptional items and share-based payments, but now including R&D tax incentive payments.

Phase I trials in Q215 for Progenza…

Regeneus will take major step forward in developing its key programmes in the current quarter when it initiates a Phase I trial of Progenza, its off-the-shelf stem cell product. The trial will recruit patients with knee osteoarthritis, an indication where the company's patented process of including cell secretions in the injected product should give it an advantage over other stem cell products in development. Recent preclinical studies also pointed to good efficacy for Progenza in this indication. New legislation in Japan offer Progenza a potential speedy path to market.

…and human cancer vaccine a major step forwards

The company's autologous human cancer vaccine will also enter the clinic this quarter. This therapy is potentially applicable to a wide range of cancer types, because it is a personalised vaccine created using the patient's own tumour tissue. The trial is likely to attract interest from pharma companies looking for new products in the buoyant immune-oncology space. The vaccine may be highly complementary to the immune checkpoint inhibitor therapies that are revolutionising treatment of a number of cancers.

Valuation: Adjusted to A$106m, A$0.51 per share

After reviewing our clinical development timelines, we have delayed product launch dates by two to four years. However, the impact of the later launch dates and lower success probabilities for veterinary products has been largely offset by a longer sales horizon, a higher assumed royalty rate for Progenza, and restoring CryoShot in Europe into our valuation model. The changes reduce our overall valuation slightly to A$106m (vs A$110m) or A$0.51/share (vs A$0.53), but this still represents clear upside to the current share price. Further upside potential could also follow the securing of global or regional partners for Regeneus' products, which in the near term could be for Kvax, CryoShot and topical Secretions. Near-term earnings are downgraded on lower HiQCell forecasts.

17 April 2015

Price	**A$0.14**
Market cap	**A$29m**
	US$0.77/A$
Net cash (A$m) at H115	6.7
Shares in issue	208.9m
Free float	77%
Code	RGS
Primary exchange	ASX
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(10.3)	(18.8)	(69.8)
Rel (local)	(12.6)	(27.5)	(72.3)
52-week high/low	A$0.43		A$0.13

Business description

Regeneus is an Australian biotech company developing mesenchymal stem cell (MSC) products for musculoskeletal conditions, and cancer vaccines, for humans and animals. Progenza is a key pipeline product and will enter a Phase I study for osteoarthritis in Q215.

Next events

Progenza: start Phase I	Q215
Human cancer vaccine: start Phase I	Q215
Stem cell secretions: secure partner	2015
CryoShot canine: secure partner	2015

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Edison profile page

Regeneus is a research client of Edison Investment Research Limited

Investment summary

Company description: Stem cells and cancer vaccines

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. The initial stem cell products were autologous (using the patient's own cells), but the primary focus is now on its off-the-shelf, allogeneic (donor) stem cell products. Recent regulatory change in Japan offers a potential fast path to market for Progenza, its off-the-shelf human stem cell product, which will begin human trials in Q215. In 2013 Regeneus acquired cancer vaccine technology, which gives it a foothold in the hot immuno-oncology space – first-in-man trials to be approved in Q215. The shares have been listed on the ASX since the IPO in September 2013, which raised A$10.5m from the sale of 42m shares at A$0.25 per share. Regeneus raised a further A$6m at A$0.26/share in August/September 2014 and held A$6.7m in cash as of 31 December 2014.

Valuation: A$106m or A$0.51 per share

We value Regeneus at A$106m, or A$0.51per share, based on a sum-of-the-parts DCF model, using a standard 12.5% discount rate. This includes H115 (31 December 2014) net cash of A$6.7m. This is not a price target, and represents fair-value for the stock today, based on the potential development multiple programmes, including Progenza (worldwide), HiQCell (Australia, Singapore), CryoShot (worldwide), Kvax (worldwide) and human cancer vaccine (worldwide). Progenza is the key long-term value driver, with peak sales estimated at A$1.75bn, 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. We have assumed timely clinical and commercial progress for multiple programmes across multiple geographies, but any delays/setbacks would have a negative impact on our valuation. Regeneus has submitted patent applications to cover a range of current and future products, but many of these have yet to be granted, which adds an element of risk. In January 2015 Australia's TGA issued a discussion paper regarding the regulation of autologous stem cell therapies. There is a risk that this process could lead to regulatory change that restricts the availability of HiQCell in Australia, although this product only contributes less than 2% of our valuation.

Financials

Regeneus recorded A$1.14m in revenues for H115 (half-year ended 31 December 2015), vs A$0.78m for FY H114. This was attributed to HiQCell (A$0.53m), CryoShot ($0.06m) and other (A$0.55m), which includes R&D-based licence fees. Cash balance at 31 December 2014was A$6.7m, boosted by a A$6m (net) capital raise in August/September, and the receipt of an A$3.7m R&D tax incentive lump-sum, relating to R&D expenditure in FY14. Under the Australian R&D tax incentive scheme, approximately 45% of eligible R&D costs can be reimbursed. The cash burn rate in Q215 was A$3.1m, which included A$0.5m of redundancy payments. The company is targeting a reduction in the quarterly cash burn rate to A$1.7m by the end of FY15 (we assume this will be achieved in Q415). Our model estimates a YE15e cash balance of approximately A$3m, which means a fresh financing requirement in FY16 remains, and we assign A$5m to long-term debt in FY16, a further A$6m in FY17 and A$4m in FY18, as per our standard policy.

Advancing adipose-derived MSCs and cancer vaccines

Regeneus is developing and commercialising its proprietary, adipose (fat) derived stem cell technology platform and its cancer vaccines. Two products are currently available in the Australian market (CryoShot in field trials for the veterinary market; HiQCell for human health). The company is also developing new products – Progenza (allogeneic stem cells for human health), Secretions (dermatology), a therapeutic human cancer vaccine and Kvax (autologous canine cancer vaccine) – which hold potential to reach the key global markets. The product portfolio (Exhibit 1) therefore offers a mixture of near- and long-term opportunities, with a number of fast-track routes to market.

Exhibit 1: Regeneus product portfolio

	Progenza	HiQCell	CryoShot	Human cancer vaccine	Kvax canine cancer vaccine	Secretions (topical)
Market	Human	Human	Veterinary	Human	Veterinary	Human
Cell source/type	Allogeneic, adipose-derived	Autologous, adipose-derived	Allogeneic, adipose-derived	Autologous	Autologous	Allogeneic, adipose-derived
Cell production	Expanded cells, off the shelf	Unexpanded cells, point of care	Expanded cells, off the shelf	Soluble proteins from patients own tumour	Soluble proteins extracted from patients own tumour	Cell secretions from expanded cells.
Mode of admin	Intra-articular	Intra-articular	Intra-articular	Intradermal injection	sc injection	Topical
Primary indication	Osteoarthritis	Osteoarthritis	Osteoarthritis	Solid tumours	Solid tumours, Osteosarcoma (dogs)	Acne
Regulatory status	Biologic requiring multiple safety and efficacy clinical studies for approval	Exempt biological under medico single patient procedure	Trial product availability (limited). Safety and efficacy studies required for full registration/ approval	Biologic requiring safety and efficacy clinical studies for approval in most markets	US, Aus - exempt biological not requiring approval. Other markets may require safety and efficacy clinical studies for approval	Varies, depends on therapeutic claim. Approval not required for cosmetic claims.
Key target markets	Initial target Japan; then Australia, US, EU	Australia, Singapore, Germany	Australia, US, EU	Australia, US, EU, Japan	Australia, US, EU	Australia, US EU, Japan
Partner(s)		Cryosite – cryopreservation technology	Provet – distribution partner; Lonza – manufacturing partner	Kolling Institute of Medical Research	Kolling Institute of Medical Research. VCA for US clinical trial	

Source: Company documents; Edison Investment Research

Progenza – off-the-shelf stem cells on the fast track to Japan

The most valuable product in the company's portfolio is Progenza, an allogeneic (donor) product containing adipose-derived mesenchymal stem cells (MSC) that have been multiplied in cell culture. Adipose tissue is a rich source of MSCs and is readily obtainable from a liposuction procedure, which should enable Regeneus to manufacture millions of doses of Progenza from a single donor (5-10m cells per dose). The culture-expanded MSCs are frozen and stored in liquid nitrogen.

MSCs have some unique properties, including the ability for cells from unrelated individuals to escape rejection by the recipient's immune system, which means there is no need for donor/host matching. This ability to use MSCs from a single donor to treat many different patients should give Progenza the convenience, scalability and profit margins typical of an off-the-shelf pharmaceutical.

Progenza is initially being developed as a treatment for patients with osteoarthritis of the knee. When Progenza is injected into a damaged joint the MSCs secrete anti-inflammatory cytokines and growth factors, creating an environment in which the damaged tissues can be repaired.

One of the unique attributes which distinguishes Progenza from other allogeneic stem cell products in development is the company's patented process of combining cell secretions produced by the stem cells in culture (sometimes referred to as conditioned media) together with the MSCs themselves in the final product. Including the secretions in the product confers two advantages. Firstly, it acts as a cryopreservative, helping the cells survive the freezing and thawing process. Secondly, evidence from animal studies indicates that the secretions provide an immediate anti-inflammatory effect when Progenza is injected into a diseased or damaged joint.

New Japanese laws offer a faster route to market

New legislation that took effect in Japan in November 2014 allows for expedited conditional approval of regenerative medicine products on the basis of safety and early evidence efficacy, offering a potential accelerated route to market for Progenza. The new laws mean that Phase II clinical data, which confirms safety and indicates potential efficacy, may be sufficient to gain conditional approval in Japan, compared to the standard route of conducting much larger and costly Phase III studies. Conditional approval for a cell therapy would be valid for up to seven years, and importantly, use of the product could also benefit from national reimbursement. Full approval would be contingent on conducting a confirmatory Phase III style study and submitting the results to the Japanese regulatory body, the PMDA, within seven years of conditional approval.

Regeneus has already engaged local advisers in Japan to assess the regulatory and market requirements to gain approval to conduct a Phase II study of Progenza in Japan. This will likely require a local development and commercialisation (and possibly manufacturing) partner. We note that the outcome of the Phase I safety study in Australia with Progenza will be important in determining the next steps required for development in Japan.

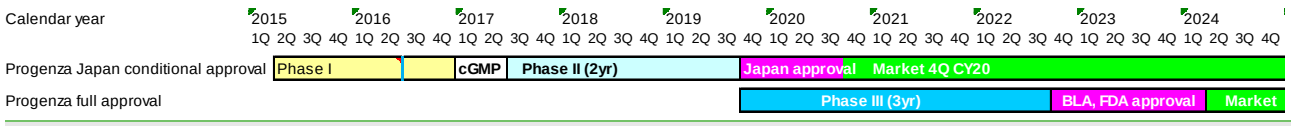
Progenza first in man trial about to begin

Regeneus expects to initiate a first-in-man Phase I trial of Progenza in Q215, and has submitted the trial design for ethics approval. The trial will be a randomised, double-blind, placebo-controlled study to evaluate the safety, tolerability and preliminary efficacy of Progenza in patients with osteoarthritis of the knee. We expect the trial to recruit patients with knee pain and minimal to moderate radiographic changes (eg Kellgren-Lawrence Grade 2 or 3 osteoarthritis). Regeneus has manufactured the cells for this trial in the TGA-licensed, GMP-accredited cell manufacturing facility operated by Cryosite (ASX: CTE) in Sydney, Australia.

The primary objective will be to assess the safety and tolerability of Progenza when injected into the knee of patients, but the trial will also assess the impact of treatment on pain and function, as well as changes to intra-articular cartilage and other knee joint structures as assessed by MRI.

While we expect patients to be followed for 12 months after treatment, initial safety results based on three-months of follow-up could be available in H116. In our time line we assume that this will enable Regeneus to partner in H216, with the partner funding the manufacture of GMP product for a Phase II trial in Japan. We assume that the Phase II trial will commence in H217, with results available in 2019, allowing for conditional approval and a market launch in Japan in 2020 (see Exhibit 2).

Exhibit 2:Edison's assumed Progenza development timeline



Source: Edison Investment Research

We assume that if the Phase II trial shows that Progenza is an effective treatment for osteoarthritis, a Phase III trial programme will be undertaken to pursue full regulatory approval in the US and Europe as well as Japan. Allowing three years for the Phase III trial programme and 18 months for filing and regulatory approval, we assume a market launch in the US and Europe in 2024.

Preclinical studies confirm safety and efficacy of Progenza

In March 2015 Regeneus completed a preclinical study of Progenza in a rabbit model of knee osteoarthritis. The study showed that Progenza was safe and well tolerated, even at doses well over the intended human dose. Injection of Progenza into knees with osteoarthritis halted the

deterioration, in contrast to the vehicle-treated control group, which continued to deteriorate over the seven-week study.

Need for alternatives to treat OA

Osteoarthritis (OA) is an 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 (affecting 11.5% of people >70 years old, and 19.4% in those aged >80 years[1]) 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. A total joint arthroplasty (knee/hip replacement) can be the final treatment option when NSAIDs and corticosteroid therapy 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 delaying the need for joint replacement.

HiQCell

Regeneus currently markets an adipose-derived cell treatment in Australia that is known as HiQCell. HiQCell is a same-day treatment that involves injecting a mixture of regenerative cells into affected joints and/or tendons. The regenerative cells are isolated from a sample of adipose tissue collected from the patient in a mini-liposuction procedure. As an autologous human cell therapy, obtained during a medical procedure conducted by medical practitioners, HiQCell is exempt from standard regulation by Australia's regulatory agency, the Therapeutic Goods Administration (TGA).

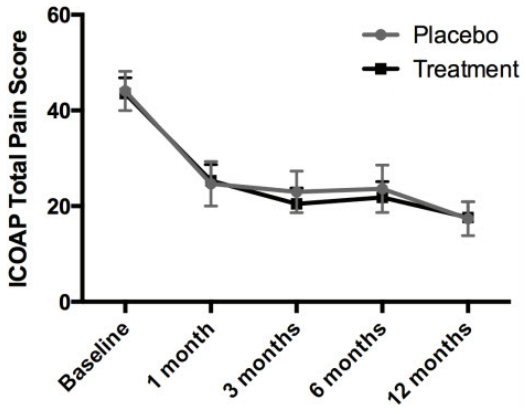
Regeneus has established The HiQCell Joint Registry, which has been tracking the safety and efficacy data from almost 400 treated patients. So far, data from the Registry show that HiQCell is safe and well tolerated, and patients experience significant reductions in pain, and improvements in knee functional outcomes and sleep quality (up to 12 months post-treatment).

However, the OSCARS, randomised, double-blind, placebo-controlled study of HiQCell for the treatment of knee osteoarthritis in 40 patients showed that while patients treated with HiQCell experienced significant reductions in pain when compared to baseline, placebo-treated patients showed a similar level of improvement (Exhibit 3). 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 osteoarthritis (Exhibit 4). An elevated level of CTX-II is proposed as a marker of cartilage degradation.[2]

Over 600 patients have been treated by medical practitioners with HiQCell. In the past tissue harvested by the medical practitioner has been processed by trained Regeneus technicians to extract the HiQCell stem cell preparation for injection into the patient. That business model has not been profitable, so Regeneus is moving to a model where it receives a licence fee of aroundA$1,000 for each HiQCell procedure. Regeneus is currently negotiating to launch HiQCell in Singapore in associating with Singapore General Hospital. We expect the HiQCell business in Singapore to operate on a similar licence fee basis.

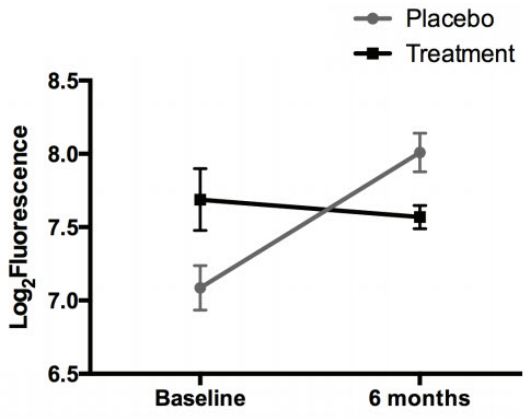
1 Epidemiology of Osteoarthritis (2005).
2 Lotz M, et al (2013). Value of biomarkers in osteoarthritis: current status and perspectives. Ann Rheum Dis. 2013 Nov 1;72 (11): 1756-63.

Exhibit 3:Total pain scores



Source: Regeneus website, OSCARS interim report (Oct. 2013)

Exhibit 4:Circulating serum MIF levels



Source: OSCARS interim report (October 2013)

CryoShot – a veterinary solution

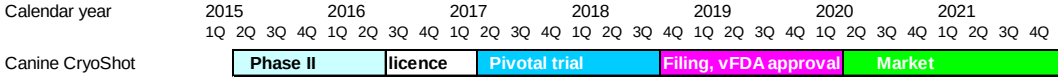
CryoShot is a convenient, allogeneic (off-the-shelf) product containing MSCs derived from the fat tissue of donor animals and expanded in cell culture. CryoShot is currently available in Australia as a pre-registration veterinary product for trialling purposes. Registration will be required for wider uptake in Australia, and prior to launch in the global markets of Europe, US and Japan. Regeneus has engaged the FDA and EMA over the trials required for registration, and has opened an INAD (investigational new animal drug) application with the US FDA's Center for Veterinary Medicine.

Regeneus has designed a randomised, placebo-controlled registration (pivotal) trial of canine CryoShot. The trial, which had been planned to commence in Q415, was designed to use the Canine Brief Pain Inventory questionnaire[3] (CBPI) to assess the impact of CryoShot treatment on pain and inflammation in pet dogs with clinical cases of osteoarthritis. As part of the preparations for the trial the manufacturing process for canine CryoShot was successfully transferred to Lonza in the US, where it had been undergoing final scale-up development prior to GMP manufacture.

However, as part of the company's strategy to reduce cash burn and move to out-licensing wherever possible, the company may now conduct a randomised trial in the US using research-grade CryoShot product manufactured at the company's facilities in Australia. This trial, which could start as early as Q215, would recruit pet dogs with clinical cases of osteoarthritis. The trial would be equivalent to a Phase II study and would generate data that could be used to drive a licensing deal with a marketing partner.

If the Phase II trial begins in Q215, results could become available in H116. If the trial is successful we would expect Regeneus to out-license canine CryoShot to a partner who would be responsible for finalising manufacture of CryoShot to cGMP standards (possibly with Lonza) prior to conducting a pivotal efficacy trial. We assume the pivotal trial will start in H117, allowing a filing for US/EU marketing approval in H218 and market launch in 2020 (Exhibit 5).

Exhibit 5: Edison's assumed CryoShot development timeline



Source: Edison Investment Research

3 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.

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. The vaccine is potentially applicable to a wide range of solid tumour types.

Regeneus has an exclusive worldwide licence from the Kolling Institute for commercialisation of the cancer vaccine technology for veterinary and human applications.

Recently published research,[4] in a rat model of glioma and a safety study in 25 dogs, reported encouraging results in animals treated with the autologous vaccine, which combines soluble tumour proteins with the immunostimulant streptavidin. 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).

Canine cancer vaccine marketing trial underway

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.

In September 2014 the company initiated a marketing study in conjunction with Dr Phil Bergman of VCA, the largest veterinary services group in the US, to generate real-world clinical study results in osteosarcoma. The trial results will be used to support uptake of the vaccine by veterinarians. Regeneus has appointed Hennessy Research to manufacture Kvax in the US market. Regeneus is planning to sponsor other cancer-specific studies in Australia to generate additional data.

Kvax became commercially available in Australia in September 2014, but we do not expect significant uptake until randomised trial data are available. Regeneus is exploring regulatory requirements for market access to the UK and other European countries, as well as Japan.

First-in-man trial of human cancer vaccine to start this quarter

Regeneus is on track to initiate a human clinical trial of the cancer vaccine in patients with solid tumours in Q215. Leading oncologists Professor Stephen Clarke and Associate Professor Nick Pavlakis from the University of Sydney's Northern Clinical School at the Kolling Institute will be the investigators on the trial, which is likely to recruit patients with limited treatment options and/or aggressive disease progression. While the primary endpoint of the single arm, open label trial will be safety, it will also collect preliminary data on immune activation and other efficacy data. Regeneus has obtained ethics approval to collect tumour samples from patients and is already collecting and banking tumour samples in preparation for the commencement of the trial.

Assuming that the safety profile is acceptable, subsequent studies may introduce the vaccine at an earlier stage of disease progression, which is viewed as a more optimum time for an effective immune response to be stimulated. This could include use as adjuvant therapy to prevent recurrence after surgical removal of the tumour, perhaps as part of a combination therapy. The vaccine is an exempt biological under Australian regulations, so it could be made available commercially without additional regulatory approval. We assume it will generate modest revenue in Australia and similar markets from 2020 onwards once preliminary efficacy data is available. We assume full regulatory approval in major markets in 2024.

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

Cancer immunotherapy is a burgeoning field, covering a number of classes of agents that can enable the host immune system to recognise, attack and destroy cancer cells. While the bulk of the current excitement surrounds the anti-PD-1 immune checkpoint inhibitors, these treatments will not work on their own if the patient fails to mount an adequate immune response to the tumour. Taking the brake off immune response with PD-1 blockade, while simultaneously pressing the accelerator with active immunotherapies such as Regeneus' cancer vaccine, is increasingly regarded as offering potential for dramatically increasing the proportion of patients who respond to treatment. This means that Regeneus' cancer vaccine is likely to attract significant interest from pharma companies if it is shown to stimulate an effective immune response against tumour cells in human clinical trials.

Topical secretions cream ready for commercialisation

Regeneus has developed a cream that contains adipose-derived cell secretions for topical treatment of a variety of inflammatory skin conditions including acne. While growing in culture, cells release biologically active substances such as cytokines and growth factors that help reduce inflammation and promote healing of damaged tissue. The company has completed a preclinical toxicology study that showed that the product is safe and well tolerated. Company research shows that secretions applied to the skin have an anti-inflammatory effect, accelerate wound healing and reduce scarring.

Regeneus is seeking a commercialisation partner for an acne product with cosmetic claims that would not require regulatory approval. At this stage we do not include the secretions product in our valuation model, although we acknowledge that it is a near term commercialisation opportunity.

Valuation

We value Regeneus at A$106m, or A$0.51 per share (previously A$110m, A$0.53/share),with the impact of later launch dates for key products largely offset by a longer sales horizon (2035 vs 2030), higher Progenza royalty rate (20% vs 15% previously) and restoring potential sales for CryoShot in Europe into the model. Our sum-of-the-parts DCF valuation model is summarised in Exhibit 6, with key assumptions displayed in Exhibit 7. We note the following key adjustments, following our review of clinical development timelines, success probabilities and royalty rates:

- Progenza – market launch in Japan in 2020 (previously 2018) and EU/US in 2024 (previously 2021). We assume Regeneus will seek development/commercialisation partners which would conduct a Phase II trial in Japan at the completion of the upcoming Phase I trial. We allow for a full Phase III program prior to launch outside Japan in 2024. We move to a lower price assumption (A$5,000 vs prior A$10,000 based revised company expectations) offset by higher uptake – no change to total sales. Royalty rate increased to 20% (was 15%) with all of the value of the product assumed to be paid as royalties – actual deal metrics are likely to include a lower royalty rate, with part of the deal value paid out as upfront and milestone payments rather than all as royalties.
- CryoShot in the US – probability of success lowered to 30% (previously 65%) as the upcoming randomised trial will not be a registration trial but will gather data for a potential licensing deal. Market launch now assumed to be 2020 (previously 2017). Positive results from randomised trials would give a valuation uplift.
- CryoShot in Europe – restored into the valuation model given our assumption that Regeneus will out-license CryoShot to a global marketing partner who would be expected to seek marketing approval in Europe as well as in the US.
- CryoShot in Australia – product registration and full commercialisation now assumed to be 2020 (previously 2017) in line with US launch. CryoShot remains unregistered and in-market

use is restricted to a trial basis with veterinary practitioners until full registration is achieved. Peak sales forecast now A$4m vs A$6m previously. We note that Regeneus is focused on generating clinical trial data on CryoShot and is seeking development/commercialisation partners in Australia and globally.

- For Kvax we lower our probability of success to 40% (previously 60%) until we see evidence of efficacy in randomised trials in dogs. Commercial launch now 2018 (previously 2016) to allow time for mature randomised trial data to be available to support marketing efforts. Peak sales increased to A$43m (previously A$37m) on additional data on the incidence of dog cancers.
- Human cancer vaccine – We increase our probability of success to 15% (previously 10%) with the company expecting the Phase I trial to commence in Q215 Market launch now 2024 (previously 2020) to allow for Phase II and III trial programmes. We allow for modest preapproval revenue from the autologous cancer vaccine from 2020 onwards.
- HiQCell – changed revenue forecasts to a licence fee model (plus a labour charge if Regeneus undertakes the stem cell preparation process); peak licence fee revenue forecast in Australia now A$0.6m (820 patients, 100% gross profit margin) in 2020, vs A$4m peak gross sales under our previous full-service sales model. Peak licence fee revenue forecast in Singapore now A$0.5Mm (550 patients) in 2024, (vs prior A$3m gross sales).
- Cash flow forecasts now extend to 2035 (previously 2030) to allow for 12-year market exclusivity for biologicals in the US and 2024 market launch for Progenza. We do not include a terminal value in our valuation model.

Exhibit 6: Regeneus valuation model and key assumptions

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	2.2	0.6	65%-100%	Licence fee, processing fee	1.7	0.01
HiQCell	Human - OA	Singapore	Marketed	2015	1.3	0.5	90%	Licence fee	1.2	0.01
Progenza	Human - OA	Australia/ Japan/EU/US	Phase I (planned)	2020 (Japan); 2024 (EU/US/Aus)	428.9	1,754	15%	Royalty (20%)	59.3	0.28
Human cancer vaccine	Solid tumours	WW	Phase I (planned)	2024	58.8	500	15%	13% net royalties	7.6	0.04
CryoShot	Animal - OA	Australia	Pre-registration field trials	2012	10.5	4	30%-100%	Operating profit (40%-60%)	1.9	0.01
CryoShot	Animal - OA	EU	Registration studies	2020	23.6	45	30%	30% effective royalty rate	6.6	0.03
CryoShot	Animal - OA	US	Registration studies	2020	29.8	54	30%	30% effective royalty rate	7.5	0.04
Kvax canine vaccine	Dog cancer	WW	Marketed (Aus) Marketing studies (US)	2016 (Aus); 2018	34.9	43	40%	30% effective royalty rate	13.6	0.07
Portfolio total					591.1				99.5	0.48
Net cash (H115e - as of 31 Dec 2014)									6.7	0.03
Overall valuation									106.2	0.51

Source: Edison Investment Research

Our valuation model applies a standard 12.5% discount rate and includes H115 (31 December 2014) net cash of A$6.7m. We assume that product sales peak six years after market launch, plateau at that level for five years, and then decline at 10% per year. For simplicity, we do not include upfront and milestone payments from any future licensing deals, and instead assume that the full value of the product will be paid as a royalty. 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.

Progenza remains the key long-term value driver, with peak sales estimated at A$1.75bn, 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 7: Regeneus valuation assumptions

Product	Setting	Region	Status	Key assumptions
HiQCell	Human - OA (knee/hip surgeries)	Australia	Marketed	Average A$900 licence fee per patient(includes cryo preservation and repeat doses); peak of 820 patients treated in 2020; sliding scale of probability (100% near-term to 65% post-2020)
HiQCell	Human - OA (knee/hip surgeries)	Singapore	Marketed	1,000 PRP procedures/year (used as a proxy for market opportunity); 50% due to OA; 25% HiQCell peak penetration in 2025 (550 procedures). Licence fee A$900 per patient.
Progenza	Human - OA	Australia/ Japan/EU/US	Phase I (planned)	Prevalence ~10% of >55yrs in all regions; 10% suitable candidates for treatment; 10% Progenza peak market share (2029 in US/EU); A$5,000 per procedure (A$3,750 in EU).
Human cancer vaccine	Solid tumours	WW	Phase I (planned)	$500m peak sales indicative potential (non-cancer specific); 13% net royalty rate after 4%-7% pay-away to Northern Sydney Local Health District (NSLHD).
CryoShot	Animal - OA	Australia	Pre-registration field trials	~4,500 small animal vet practitioners; 5% peak penetration in 2023, 75x per year, at A$250 per dose; sliding scale or probability (100% near-term to 30% post-2020)
CryoShot	Animal - OA	EU	Registration studies	~90,000 small animal vet practitioners; peak penetration in 2025, with 3% use CryoShot, 50x per year, at A$250 per dose; 30% probability with studies/partners to complete
CryoShot	Animal - OA	US	Registration studies	~50,000 small animal vet practitioners; peak penetration in 2025, with 5% use CryoShot, 75x per year, at A$250 per dose; 30% probability with studies/partners to complete
Kvax canine vaccine	Dog cancer	WW	Marketed (Aus) Marketing studies (US)	~540/100,000 annual incidence of dog cancers; ~860,000 cancers US/EU/Japan/Aus; assume 10% get drug/vaccine treatment; 25% peak Kvax penetration of treated dogs by 2023 (=21,600 Kvax treatments); A$2,000 per treatment course; 40% probability with studies/partners to complete

Source: Edison Investment Research

Sensitivities

With regard to Progenza, CryoShot, Kvax and the human cancer vaccine, the key long-term valuation drivers, we have assumed timely clinical and commercial progress in multiple regions, which should be achievable, but any delays/setbacks would have a negative impact on our valuation. A commercialisation deal for the secretions technology represents potential upside, as we do not currently include secretions products in our valuation model. The decision to scale back on the self-commercialisation of HiQCell in Australia and reduce overall expenditure helps to reduce the execution risk previously highlighted.

In January 2015 Australia's TGA issued a discussion paper regarding the regulation of autologous stem cell therapies. There is a risk that this process could lead to regulatory change that restricts the availability of HiQCell. However, with HiQCell only contributing A$0.01/share to our valuation this would not be a significant threat to the company's business model.

Financials

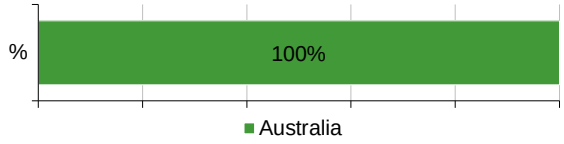
Regeneus ended fiscal H115 (31 December 2014) with A$6.7m in cash and equivalents, boosted by a A$6m (net) capital raise in August/September, and the receipt of the A$3.7m lump-sum tax rebate that was included in the FY14 income statement, relating to R&D expenditure in FY14. Under the Australian government's R&D tax incentive scheme, approximately 45% of eligible R&D costs can be reimbursed.

The cash burn rate in Q215 was A$3.1m, which included A$0.5m of redundancy payments. The company is targeting a reduction in the quarterly cash burn rate to A$1.7m by the end of FY15 (we assume this will be achieved in Q415). Our model estimates a YE15e cash balance of approximately A$3m, which means a fresh financing requirement in FY16 remains, and we assign A$5m to long-term debt in FY16, A$6m in FY17 and A$4m in FY18, as per our standard policy.

Exhibit 8: Financial summary

A$'000s	2013	2014	2015e	2016e	2017e	2018e
Year end 30 June	AASB	AASB	AASB	AASB	AASB	AASB
PROFIT & LOSS						
Revenue	1,812	2,003	1,604	2,122	2,725	4,581
Cost of Sales	(581)	(621)	(257)	(337)	(440)	(604)
Gross Profit	1,232	1,381	1,346	1,785	2,285	3,977
R&D expenses	(4,134)	(5,758)	(6,046)	(6,651)	(6,784)	(6,106)
SG&A expenses	(4,549)	(6,756)	(5,769)	(5,000)	(5,357)	(5,782)
EBITDA	(7,256)	(10,800)	(10,051)	(9,491)	(9,527)	(7,590)
Operating Profit (before GW and except.)	(7,437)	(11,118)	(10,460)	(9,853)	(9,844)	(7,894)
Intangible Amortisation	(15)	(16)	(9)	(13)	(13)	(18)
Exceptionals	0	0	0	0	0	0
Other (includes R&D tax credit)	2,535	3,767	2,721	2,993	3,053	2,748
Operating Profit	(4,917)	(7,367)	(7,748)	(6,873)	(6,804)	(5,164)
Net Interest	(278)	(157)	(123)	(175)	(175)	(175)
Profit Before Tax (norm)	(5,180)	(7,507)	(7,862)	(7,034)	(6,966)	(5,321)
Profit Before Tax (FRS 3)	(5,195)	(7,523)	(7,871)	(7,047)	(6,978)	(5,339)
Tax benefit	0	0	0	0	0	0
Profit After Tax (norm)	(5,180)	(7,507)	(7,862)	(7,034)	(6,966)	(5,321)
Profit After Tax (FRS 3)	(5,195)	(7,523)	(7,871)	(7,047)	(6,978)	(5,339)
Average Number of Shares Outstanding (m)	102.9	166.5	208.0	209.4	210.4	211.4
EPS - normalised (c)	(5.03)	(4.51)	(3.78)	(3.36)	(3.31)	(2.52)
EPS - FRS 3 (c)	(5.03)	(4.51)	(3.46)	(3.08)	(3.04)	(2.31)
Dividend per share (A$)	0.0	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET						
Fixed Assets	653	3,170	3,036	2,907	2,883	3,050
Intangible Assets	45	30	51	72	93	105
Tangible Assets	609	1,362	1,206	1,057	1,012	1,167
Investments	0	1,778	1,778	1,778	1,778	1,778
Current Assets	3,370	7,089	6,073	4,942	4,814	4,177
Stocks	231	206	120	157	205	281
Debtors	27	134	134	134	134	134
Cash	534	2,635	2,714	1,275	1,039	630
Other	2,579	4,114	3,104	3,376	3,436	3,131
Current Liabilities	(6,892)	(1,698)	(1,698)	(1,698)	(1,698)	(1,698)
Creditors	(1,842)	(921)	(921)	(921)	(921)	(921)
Short term borrowings	(4,900)	0	0	0	0	0
Other	(150)	(777)	(777)	(777)	(777)	(777)
Long Term Liabilities	0	(253)	(253)	(5,253)	(11,253)	(15,253)
Long term borrowings	0	0	0	(5,000)	(11,000)	(15,000)
Other long term liabilities	0	(253)	(253)	(253)	(253)	(253)
Net Assets	(2,869)	8,308	7,158	898	(5,254)	(9,724)
CASH FLOW						
Operating Cash Flow	(4,618)	(6,239)	(5,621)	(6,194)	(5,929)	(3,920)
Net Interest	0	0	0	0	0	0
Tax	0	0	0	0	0	0
Capex	(277)	(1,176)	(271)	(245)	(306)	(489)
Acquisitions/disposals	0	0	0	0	0	0
Financing	0	10,209	5,971	0	0	0
Dividends	0	0	0	0	0	0
Other	0	4,900	0	0	0	0
Net Cash Flow	(4,895)	7,694	79	(6,440)	(6,236)	(4,409)
Opening net debt/(cash)	(528)	4,366	(2,635)	(2,714)	3,725	9,961
HP finance leases initiated	0	0	0	0	0	0
Other	0	(693)	0	0	0	(0)
Closing net debt/(cash)	4,366	(2,635)	(2,714)	3,725	9,961	14,370

Source: Regeneus accounts, Edison Investment Research

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

CAGR metrics		Profitability metrics		Balance sheet metrics		Sensitivities evaluation	
EPS 11-15e	N/A	ROCE 14e	N/A	Gearing 14e	N/A	Litigation/regulatory	●
EPS 13-15e	N/A	Avg ROCE 11-15e	N/A	Interest cover 14e	N/A	Pensions	○
EBITDA 11-15e	N/A	ROE 14e	N/A	CA/CL 14e	N/A	Currency	◖
EBITDA 13-15e	N/A	Gross margin 14e	N/A	Stock days 14e	N/A	Stock overhang	○
Sales 11-15e	N/A	Operating margin 14e	N/A	Debtor days 14e	N/A	Interest rates	◖
Sales 13-15e	N/A	Gr mgn / Op mgn	N/A	Creditor days 14e	N/A	Oil/commodity prices	○

Management team

CEO: John Martin

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 a former executive and corporate partner of Allen Allen & Hemsley.

Chairman: Dr Roger Aston

Dr Roger Aston is one of the most experienced and commercially astute people in drug commercialisation in Australia. He brings more than 20 years' experience in the pharmaceutical and healthcare industries in senior roles in the United Kingdom, Asia- Pacific and Australia. Dr Aston is also a director or chairman on a number of boards carrying out late-stage drug development.

CSO: Professor Graham Vesey

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.

Principal shareholders	(%)
Professor Graham Vesey (co-founder, founding CEO, now CSO)	7.60%
Limberg Asset Management	5.13%
Thomas Mechtersheimer	4.66%
Professor Marc Wilkins	4.41%
Associate Professor Ben Herbert (co-founder)	4.31%
Hestian	3.56%
John Martin (CEO)	3.39%
Parros	2.61%

Companies named in this report

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