EDISON

Regeneus

Cancer vaccine licence

Pipeline expansion

Pharma & biotech

Regeneus has added another project to its portfolio, with licensing of global rights to an autologous human cancer vaccine that is expected to enter the clinic in Q115. Developed at the Kolling Institute, Sydney, the technology was already licensed to Regeneus for veterinary applications (Kvax), which is now in a US marketing trial for osteosarcoma in dogs. Cancer immunotherapy, including multiple approaches to cancer vaccines, is a biotech hotspot and we look forward to progress with Regeneus's new candidate. Our overall valuation is now A$145m, or A$0.79 per share.

Year end	Revenue (A$m)	PBT* (A$m)	EPS* (A$)	DPS (A$)	P/E (x)	Yield (%)
06/12	1.26	(4.95)	(0.03)	0.0	N/A	N/A
06/13	1.81	(7.72)	(0.05)	0.0	N/A	N/A
06/14e	1.97	(9.65)	(0.04)	0.0	N/A	N/A
06/15e	3.47	(10.85)	(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.

Option exercised

Regeneus held an option to license global rights to develop the Kolling Institute's cancer vaccine technology for human uses, having secured veterinary rights (developed as Kvax) in January 2013. The decision to exercise this option, with a Phase I safety study to start in Q115, is a positive development given burgeoning interest in the cancer immunotherapy field, although fresh funds will be required. The trial design and target tumour have yet to be confirmed.

Kvax advances in the US

The recent agreement with a US vet health care services group means Kvax can now enter a marketing trial, aimed at treating osteosarcoma in dogs; positive data are important to support commercialising the product in the US. Hennessy Research will manufacture the vaccine, which involves removing a small amount of tumour or biopsy from the dog to produce a personalised (autologous) therapy.

MSC development on track

While the cancer vaccine technology is an increasingly important part of Regeneus's portfolio, the core business and key valuation driver remains its adipose (fat)-derived mesenchymal stem cell (MSC) technology, being developed across multiple areas and geographies. Progenza, an allogeneic (off-the-shelf) MSC product for osteoarthritis, is expected to enter a Phase I/II study in H115.

Valuation: Adjusted to A$145m, A$0.79 per share

Including the human cancer vaccine adds A$5m to our DCF model, based on indicative peak sales of A$500m, a launch in 2020 and a 10% probability of success. Our overall valuation is now A$145m (A$0.79/share) vs A$141m (A$0.77/share), after also adjusting for FY14e cash of A$3.5m (vs A$6.6m at H114). Even with a A$3.3m estimated R&D tax rebate in September, fresh funds are required by H115 to support current plans to advance multiple programmes.

22 July 2014

Price	**A$0.30**
Market cap	**A$55m**
	A$1.07/US$
Net cash (A$m) at 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	(23.1)	(26.8)	N/A
Rel (local)	(24.8)	(27.9)	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. HiQCell (human) and CryoShot (animal), are available commercially in Australia. Progenza (allogeneic, off-the-shelf) will enter a Phase I/IIa study for osteoarthritis in H115.

Next events

HiQCell: commercial launch in Singapore	H214
Progenza: pre-clinical safety data/Phase I/II study design	H214
CryoShot: Australia clinical trial results	H214
Human cancer vaccine: Start Phase I safety study	Q115

Analysts

Christian Glennie +44 (0)20 3077 5727

Dr Mick Cooper +44 (0)20 3077 5734

healthcare@edisongroup.com

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Human cancer vaccine play

Cancer immunotherapy is a broad and burgeoning field, covering a number of classes of agents – vaccines, DC-based vaccines, adoptive T-cell therapies, immune checkpoint inhibitors – and the inherent potential (proven with some approved products) of this approach to treating cancer is vast. Although the bulk of current excitement surrounds the anti-PD-1 immune checkpoint inhibitors, cancer vaccines are likely to become an important component of attacking cancers, particularly in combination with other agents.

A dendritic cell (DC)-based vaccine, Provenge, gained FDA approval in 2010 for the treatment of prostate cancer, the only approved cancer vaccine to date; FY13 sales of Provenge were $285m, although previous consensus had been >$1bn. Multiple cancer vaccine types – from whole tumour cell, cell and tumour lysate, tumour antigen, dendritic cell, DNA- and bacterial-derived vaccines – are in development, increasingly in advanced stages of clinical studies.

Autologous cancer vaccination involves the removal of a tumour or biopsy from the 'patient' (animal or human) as the source material to produce a personalised vaccine, which stimulates the immune system to see cancer cells as foreign, prompting immune cells, particularly T-cells, to attack the tumour cells.

Rights secured

Through an agreement with Northern Sydney Local Health District (NSLHD), Regeneus now holds exclusive worldwide rights to develop and commercialise an autologous human cancer vaccine. The technology was developed at the Bill Walsh Translational Cancer Research Laboratory, which is part of the Kolling Institute of Medical Research at Royal North Shore Hospital in Sydney. This candidate is a whole tumour cell-derived vaccine, based on tumour lysate (protein) coupled with an adjuvant, streptavidin, to help stimulate a T-cell response.

Regeneus did not pay any upfront fee, but will be required to pay royalties (4-7% on gross sales) to NSLHD on commercialisation of the product.

Regeneus already held rights to the programme for veterinary applications. Recently published research[1], in a rat model of glioma and a safety study in 25 dogs, produced encouraging results for the streptavidin (immunostimulant)-based 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).

Progressing to the clinic

Regeneus plans to initiate a first-in-man Phase I safety study in Q115, while funding further research at the Bill Walsh Cancer Research Lab. 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.

The trial design and tumour target have yet to be confirmed, although as a safety study using an experimental treatment, tumours that have limited treatment options and/or an aggressive disease progression are the most likely targets. The primary aim would be to generate safety data, some indication of immune activation and perhaps a tentative insight into efficacy.

1 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 21 February 2014.

Assuming an acceptable safety profile, subsequent studies may look to introduce the vaccine at an earlier stage of disease progression, which is increasingly viewed as a more optimum time for an effective immune response to be stimulated, particularly if used in combination with other agents.

Kvax advances

Regeneus recently entered into an agreement with a US vet health care services group to conduct a marketing trial in the US with Kvax, the company's autologous canine cancer vaccine. This is the same cancer vaccine technology developed by the Kolling Institute.

The trial will be conducted at two US sites and will test two doses of Kvax in treating osteosarcoma in approximately 20 dogs. Progression-free survival and overall survival times will be the primary assessment measures. Hennessy Research will manufacture the vaccine for the US market, including this study and subsequent commercialisation.

The results of the marketing trial are therefore important in supporting full commercialisation in the US. 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.

MSC development continues

Although the cancer vaccine technology is an increasingly important part of Regeneus' portfolio, the core business and key valuation driver remains its adipose (fat) -derived mesenchymal stem cell (MSC) technology. MSCs, for human and veterinary applications, are being developed across multiple areas and geographies.

Progenza, an allogeneic (off-the-shelf) MSC product for osteoarthritis (OA) is expected to enter a Phase I/II study in H115. In April 2014, Regeneus received ethics approval in Australia to collect stem cells from human donors to produce the Progenza product for a clinical study in human volunteers with knee OA. This product could hold significant long-term potential, so progress is important in building up the value of Regeneus's portfolio.

Meanwhile HiQCell, an autologous MSC product available in Australia for musculoskeletal disorders (including OA), has also shown promise as a potential treatment option for chronic neuropathic pain. Results from an open-label study[2] in 10 patients with persistent, severe and intolerable pain in the face and dental region showed significant reductions in pain intensity scores and in using pain medication.

The results from this study highlight the potential versatility of Regeneus's MSCs, beyond the current focus on musculoskeletal conditions.

Valuation

Including the human cancer vaccine adds A$5m to our DCF model, based on indicative peak sales of A$500m, a launch in 2020 and a 10% probability of success. Our overall valuation is now A$145m (A$0.79/share) vs A$141m (A$0.77/share), after also adjusting for FY14e cash of A$3.5m (vs A$6.6m at H114). Our sum-of-the-parts DCF model is summarised in Exhibit 1 and our key assumptions are displayed in Exhibit 2.

2 Vickers ER, Karsten E, Flood J, and Lilischkis R. A preliminary report on stem cell therapy for neuropathic pain in humans. Journal of Pain Research 2014:7 255–263.

Exhibit 1: 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	1.6	4	75%	30% effective royalty rate	1.1	0.01
HiQCell	Human – OA (knee/hip surgeries)	Germany	Registration	2015	16.8	26	65%	30% effective royalty rate	10.6	0.06
Progenza	Human – OA	Australia / Japan / EU / US	Phase IIa (planned)	2018 (Japan); 2020 (Aus); 2021 (EU/US)	328.1	1,526	15%	Royalty (15%)	43.9	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	28.7	45	65%	30% effective royalty rate	18.2	0.10
CryoShot	Animal – OA	US	Registration studies	2017	30.9	54	65%	30% effective royalty rate	19.7	0.11
CryoShot	Animal – OA	Japan	Registration studies	2016	4.0	10	65%	30% effective royalty rate	2.2	0.01
Kvax canine vaccine	Dog cancer	WW	Marketing studies	2016	32.6	37	50%	30% effective royalty rate	15.6	0.08
Human cancer vaccine	Solid tumours	WW	Phase I-ready	2020	78.5	500	10%	13% net royalties	4.9	0.03
Portfolio total					**554.9**				**141.8**	**0.77**
Cash (FY14e)									3.5	0.02
Overall valuation									**145.3**	**0.79**

Source: Edison Investment Research

Exhibit 2: Regeneus valuation model assumptions

Product	Setting	Region	Status	Launch	Key assumptions
HiQCell	Human – OA (knee/hip surgeries)	Australia	Marketed	2011	Knee/hip surgeries used as a proxy for market opportunity; 45,000 knee surgeries (5% HiQCell peak penetration) + 36,000 hip surgeries (5% HiQCell peak penetration); current use mainly knee (66%) vs hip (10%); A$4,800 per procedure (includes cryo preservation fee and repeat doses); 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; 175,000 knee surgeries (2% HiQCell peak penetration in 2021) + 245,000 hip surgeries (1% HiQCell peak penetration); equivalent A$5,000 per procedure (includes cryo preservation fee and 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; six yrs to peak); A$10,000 per procedure (A$7,500 in EU).
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	US	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.
Kvax 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.
Human cancer vaccine	Solid tumours	WW	Phase I-ready	2020	$500m peak sales indicative potential (non-cancer specific); 13% net royalty rate after 4%-7% pay-away to Northern Sydney Local Health District (NSLHD).

Source: Edison Investment Research

Sensitivities

The stock-specific sensitivities relate to Regeneus's current plan to commercialise certain products 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 several 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. This 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$0.49m in revenues for fiscal Q314 (January-March 2014), or A$1.3m for the first nine months of 2014. Regeneus noted that revenues (mainly from HiQCell and CryoShot procedures in Australia) during Q314 were slower than expected over the Christmas holiday period. We have therefore reduced our total revenue forecast for FY14 to A$1.97m, vs A$2.64m previously.

We estimate that Regeneus ended FY14 (30 June 2014) with A$3.5m in cash, compared to A$6.6m as of H114 (31 December 2013). Under the Australian government's R&D tax incentive scheme, which effectively reimburses 45% of eligible R&D costs, Regeneus expects to receive A$3.3m in a lump-sum tax rebate in September. Nevertheless, based on projected sales and operating expenses, our financial model indicates a financing requirement in fiscal H115, and we have nominally attributed A$10m to long-term debt, as per our standard policy.

Regeneus plans to advance an extensive product portfolio across multiple geographies and as such, some prioritisation of projects may be a natural outcome as the company assesses its financing options.

Exhibit 3: Financial summary

A$000s	2012	2013	2014e	2015e	2016e
Year-end 30 June	AASB	AASB	AASB	AASB	AASB
PROFIT & LOSS					
Revenue	**1,262**	**1,812**	**1,968**	**3,473**	**8,937**
Cost of Sales	(246)	(581)	(668)	(1,106)	(1,731)
Gross Profit	**1,016**	**1,232**	**1,300**	**2,367**	**7,206**
R&D expenses	(3,212)	(4,134)	(5,375)	(6,719)	(7,726)
SG&A expenses	(2,828)	(4,549)	(5,503)	(6,530)	(7,576)
EBITDA	**(4,910)**	**(7,256)**	**(9,385)**	**(10,658)**	**(7,782)**
Operating Profit (before GW and except.)	(5,017)	(7,437)	(9,568)	(10,869)	(8,080)
Intangible Amortisation	(6)	(15)	(10)	(12)	(16)
Exceptionals	0	0	0	0	0
Other	11	208	86	0	0
Operating Profit	**(5,012)**	**(7,244)**	**(9,492)**	**(10,881)**	**(8,096)**
Net Interest	72	(278)	(81)	18	44
Profit Before Tax (norm)	**(4,945)**	**(7,715)**	**(9,649)**	**(10,851)**	**(8,036)**
Profit Before Tax (FRS 3)	(4,940)	(7,522)	(9,573)	(10,864)	(8,052)
Tax benefit	1,679	2,327	3,300	3,023	3,477
Profit After Tax (norm)	**(3,266)**	**(5,388)**	**(6,349)**	**(7,828)**	**(4,559)**
Profit After Tax (FRS 3)	(3,261)	(5,195)	(6,273)	(7,840)	(4,576)
Average Number of Shares Outstanding (m)	102.9	102.9	149.4	184.5	185.5
EPS - normalised (A$)	**(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**	**1,940**	**2,249**	**2,867**
Intangible Assets	45	45	44	65	87
Tangible Assets	527	609	705	993	1,589
Investments	0	0	1,191	1,191	1,191
Current Assets	**2,724**	**3,370**	**8,262**	**10,528**	**5,771**
Stocks	143	231	311	515	806
Debtors	107	27	112	112	112
Cash	528	534	3,500	5,839	338
Other	1,946	2,579	4,339	4,062	4,515
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)**	**9,063**	**1,639**	**(2,500)**
CASH FLOW					
Operating Cash Flow	**(2,940)**	**(4,618)**	**(6,804)**	**(7,106)**	**(4,569)**
Net Interest	0	0	0	0	0
Tax	0	0	0	0	0
Capex	(421)	(277)	(307)	(555)	(932)
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)	7,867	(7,661)	(5,502)
Opening net debt/(cash)	**(1,590)**	**(528)**	**4,366**	**(3,500)**	**4,161**
HP finance leases initiated	0	0	0	0	0
Other	0	0	0	0	0
Closing net debt/(cash)	**(528)**	**4,366**	**(3,500)**	**4,161**	**9,662**

Source: Regeneus accounts, Edison Investment Research

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
245 Park Avenue, 39th Floor
10167, New York
US

Sydney +61 (0)2 9258 1161
Level 25, Aurora Place
88 Phillip St, Sydney
NSW 2000, Australia

Wellington +64 (0)48 948 555
Level 15, 171 Featherston St
Wellington 6011
New Zealand